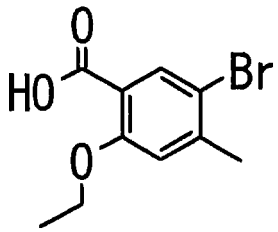
After dissolving 2-hydroxy-4-methylbenzoic acid (24.54 g, 161.29 mmol) in methanol (300 ml), the solution was cooled to -20°C. A solution of bromine (26.03 g) in methanol (50 ml) was added dropwise over 1 hour. The reaction mixture was stirred at room temperature for 1 hour and then concentrated. The residue was heated to dissolution in methanol (100 ml) and water (40 ml) was added. The precipitated crystals were filtered off and washed with 50% methanol-water. The precipitated crystals in the filtrate were also filtered off and washed with 50% methanol-water. The crystals were combined and dried to yield the title compound (24.8 g) as white crystals.

^{1}H-NMR(CDCl3)δ(ppm)

2.37(3H,s), 6.85(1H,s), 7.98(1H,s).

(Step 2) 5-Bromo-2-ethoxy-4-methylbenzoic acid



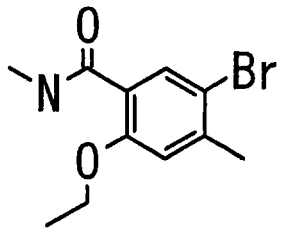
After dissolving 5-bromo-2-hydroxy-4-methylbenzoic acid (9.35 g) in dimethylformamide, potassium carbonate (14 g) and ethyl iodide (8 ml) were added in that order and the mixture was stirred at 50°C for 3 hours. It was then diluted with ethyl acetate, washed with water and brine, dried over

anhydrous magnesium sulfate, filtered and concentrated to yield ethyl 5-bromo-2-ethoxy-4-methylbenzoate. The product was dissolved in ethanol (100 ml), 5 N sodium hydroxide (20 ml) was added and the mixture was heated to reflux for 30 minutes. After adding 5 N hydrochloric acid (25 ml) for neutralization, extraction was performed with ethyl acetate. The extract was dried over anhydrous magnesium sulfate, filtered and concentrated to yield the title compound (10.4 g) as a white solid.

^{1}H-NMR(CDCl3)δ(ppm)

56(3H,t,J=6.8Hz), 2.45(3H,s), 4.31(2H,q,J=6.8Hz), 6.91(1H,s), 8.31(1H,s).

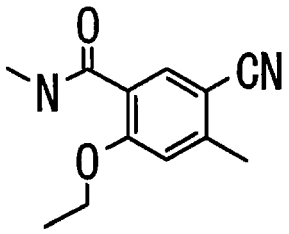
(Step 3) N1,4-Dimethyl-5-bromo-2-ethoxybenzamide



After dissolving 5-bromo-2-ethoxy-4-methylbenzoic acid in tetrahydrofuran (80 ml), triethylamine (3.5 ml) and ethyl chloroformate (2.4 ml) were added while cooling on ice, the mixture was stirred for 1 hour, and then a 40% methylamine aqueous solution (3.5 ml) was added. The reaction mixture was stirred for 1 hour, ethyl acetate was added and the mixture was washed with brine, after which the organic layer was

dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure. The crystals of the residue were washed with hexane and filtered to yield the title compound (5.08 g) as white crystals.

(Step 4) N1,4-Dimethyl-5-cyano-2-ethoxybenzamide



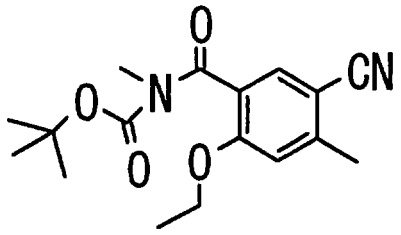
After dissolving N1,4-dimethyl-5-bromo-2-ethoxybenzamide (200 g) in propionitrile (1.5 l), sodium cyanide (72 g), copper iodide (14 g) and tetrakis(triphenylphosphine)palladium (42 g) were added under a nitrogen atmosphere and the mixture was heated to reflux for 5 hours. Ethyl acetate and water were added and the reaction mixture was filtered through celite. The precipitated crystals in the filtrate were filtered off (15.4 g). This filtrate was then separated and washed with brine. The organic layer was dried over anhydrous magnesium sulfate and was concentrated after filtering off the insoluble portion. The obtained crystals were filtered off and washed with ethyl acetate (77.64 g). The crystals were combined to yield the title compound (93.04 g) as a white solid.

^{1}H-NMR(CDCl3)δ(ppm)

1.56(3H,t,J=7.2Hz), 2.57(3H,s), 4.28(2H,q,J=7.2Hz),

6.86(1H,s), 7.93(1H,br), 8.04(1H,s).

(Step 5) *tert*-Butyl N-(5-cyano-2-ethoxy-4-methylbenzoyl)-N-methylcarbamate



After suspending N1,4-dimethyl-5-cyano-2-ethoxybenzamide (92 g) in acetonitrile (1 l), *tert*-butyl dicarbonate (110 g) and dimethylaminopyridine (2.6 g) were added and the mixture was stirred at room temperature overnight. The reaction mixture was heated to 90°C and stirred for 3 hours. *tert*-Butyl dicarbonate (110 g) was further added and the mixture was stirred at 50°C overnight. After cooling to room temperature, the precipitated crystals were filtered off (24.3 g). The filtrate was concentrated and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (81.1 g) as a white solid.

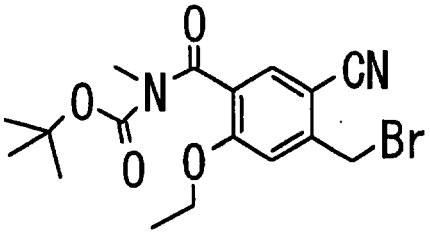
^{1}H-NMR(CDCl3)δ(ppm)

23(9H,s), 1.39(3H,t,J=7.2Hz), 2.55(3H,s), 3.29(3H,s),

4.04(2H,q,J=7.2Hz), 6.72(1H,s), 7.58(1H,s).

(Step 6) *tert*-Butyl N-[4-(bromomethyl)-5-cyano-2-

ethoxybenzoyl]-N-methylcarbamate

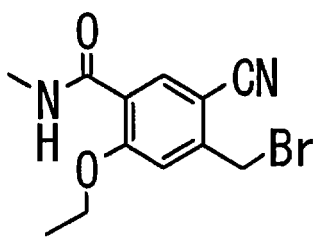


After dissolving *tert*-butyl N-(5-cyano-2-ethoxy-4-methylbenzoyl)-N-methylcarbamate (79.6 g) in carbon tetrachloride, azobisisobutyronitrile (4.1 g) was added and the mixture was heated to reflux. N-bromosuccinimide (50.3 g) was gradually added to the reaction mixture in small portions at a time. After heating to reflux for 2 hours, the mixture was filtered. The filtrate was concentrated and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (29.81 g) as a white solid.

^{1}H-NMR(CDCl3)δ(ppm)

22(9H,s), 1.41(3H,t,J=7.2Hz), 1.56(9H,s), 3.30(3H,s), 4.09(2H,q,J=7.2Hz), 4.60(2H,s), 6.96(1H,s), 7.60(1H,s).

(Step 7) N1-Methyl-4-(bromomethyl)-5-cyano-2-ethoxybenzamide



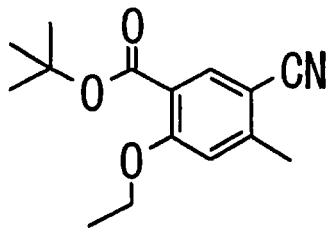
After dissolving *tert*-butyl N-[4-(bromomethyl)-5-cyano-2-ethoxybenzoyl]-N-methylcarbamate (39.9 g) in dichloromethane (300 ml), trifluoroacetic acid (50 ml) was added and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (19.77 g) as a white solid.

^{1}H-NMR(CDCl3)δ(ppm)

1.54(3H,t,J=7.2Hz), 3.02(3H,d,J=4.8Hz),

4.26(2H,q,J=7.2Hz), 4.59(2H,s), 7.19(1H,s), 8.53(1H,s).

(Step 8) *tert*-Butyl 5-cyano-2-ethoxy-4-methylbenzoate



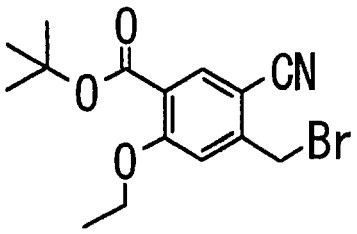
After dissolving 5-bromo-2-ethoxy-4-methylbenzoic acid (10.4 g) in toluene (100 ml) and ethyl acetate (20 ml), dimethylformamide di-*tert*-butylacetal (75 ml) was added and the mixture was heated to reflux for 8 hours. Ethyl acetate was then added, the mixture was washed with 1 N hydrochloric acid and brine in that order, dried over anhydrous magnesium sulfate, filtered and concentrated, and the residue was purified by silica gel column chromatography (solvent:

n-hexane-ethyl acetate) to yield a *tert*-butyl ester (12.27 g) as a colorless oil. This was dissolved in propionitrile, and then sodium cyanide (3.82 g), copper iodide (740 mg) and tetrakis(triphenylphosphine)palladium (2.25 g) were added under a nitrogen atmosphere and the mixture was heated to reflux for 8 hours. Ethyl acetate and water were added, the reaction mixture was filtered through celite and the filtrate was washed with brine. The organic layer was dried over anhydrous magnesium sulfate and was concentrated after filtering off the insoluble portion, and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (9.57 g) as a white solid.

^{1}H-NMR(CDCl3)(ppm)

1.47(3H,t,J=6.8Hz), 1.57(9H,s), 2.53(3H,s), 4.12(2H,q,J=6.8Hz), 6.79(1H,s), 7.95(1H,s)

(Step 9) <u>*tert*-Butyl 4-(bromomethyl)-5-cyano-2-ethoxybenzoate</u>



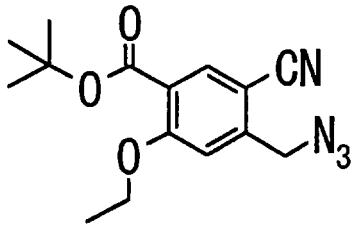
After dissolving *tert*-butyl 5-cyano-2-ethoxy-4-methylbenzoate (8.91 g) in carbon tetrachloride, N-

bromosuccinimide (6.6 g) and benzoyl peroxide (400 mg) were added and the mixture was heated to reflux for 3 hours. The reaction mixture was filtered and concentrated. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield a mixture of the title compound and *tert*-butyl 5-cyano-2-ethoxy-4-methylbenzoate (starting material) (8.80 g) as a white solid.

^{1}H-NMR(CDCl3)δ(ppm)

1.50(3H,t,J=7.2Hz), 1.58(9H,s), 4.18(2H,q,J=7.2Hz), 4.58(2H,s), 7.05(1H,s), 7.98(1H,s).

(Step 10) <u>*tert*-Butyl 4-(azidomethyl)-5-cyano-2-ethoxybenzoate</u>

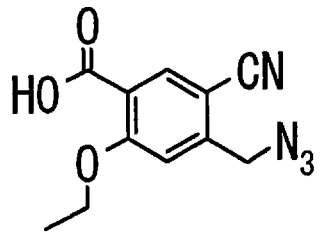


After dissolving *tert*-butyl 4-(bromomethyl)-5-cyano-2-ethoxybenzoate (2.20 g, 70% purity) in dimethylformamide (25 ml), sodium azide (2.1 g) was added and the mixture was stirred at 50°C for 30 minutes. It was then diluted with ethyl acetate, washed with water, dried over anhydrous magnesium sulfate, filtered and concentrated to yield the title compound (1.913 g).

^{1}H-NMR(CDCl3)δ(ppm)

1.49(3H,t,J=6.8Hz), 1.56(9H,s), 4.18(2H,q,J=6.8Hz), 4.62(2H,s), 7.04(1H,s), 8.01(1H,s).

(Step 11) 4-(Azidomethyl)-5-cyano-2-ethoxybenzoic acid

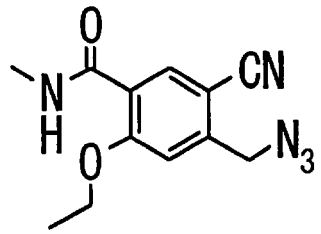


After dissolving *tert*-butyl 4-(azidomethyl)-5-cyano-2-ethoxybenzoate (1.923 g) in dichloromethane (12 ml), trifluoroacetic acid (3 ml) was added while cooling on ice. The mixture was stirred at room temperature for 20 minutes and concentrated. The title compound was obtained as light red crystals.

^{1}H-NMR(CDCl3)δ(ppm)

64(3H,t,J=6.8Hz), 4.47(2H,q,J=6.8Hz), 4.74(2H,s), 7.23(1H,s), 8.46(1H,s).

(Step 12) N1-Methyl-4-(azidomethyl)-5-cyano-2-ethoxybenzamide



After dissolving 4-(azidomethyl)-5-cyano-2-ethoxybenzoic acid in dimethylformamide (20 ml), a 2M tetrahydrofuran solution of methylamine (4.2 ml),

diethyl phosphonocyanidate (1.28 ml) and triethylamine (1.27 ml) were added while cooling on ice. The mixture was stirred at room temperature overnight, diluted with ethyl acetate and washed with water and brine. The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to yield the title compound (931 mg).

After next dissolving N1-methyl-4-(bromomethyl)-5-cyano-2-ethoxybenzamide in dimethylformamide (100 ml), sodium azide (6 g) was added and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with ethyl acetate and washed with water and brine, and then the organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to yield the title compound (15.5 g).

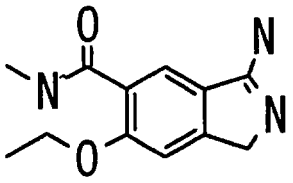
^{1}H-NMR(CDCl3)δ(ppm)

58(3H,t,J=6.8Hz), 3.02(3H,d,J=4.8Hz),

4.32(2H,q,J=7.2Hz), 4.67(2H,s), 7.10(1H,s),

7.74(1H,br), 8.55(1H,s).

(Step 13) N5-Methyl-3-amino-6-ethoxy-1H-5-isoindolecarboxamide



After dissolving N1-methyl-4-(azidomethyl)-5-cyano-2-ethoxybenzamide (931 mg) in tetrahydrofuran

(10 ml), 28% aqueous ammonia (2 ml) and triethylphosphine (0.4 ml) were added in that order. The mixture was stirred at 50°C for 15 minutes. The precipitated crystals were filtered off, washed with tetrahydrofuran, water and ethyl acetate in that order and dried to yield the title compound (365 mg).

^{1}H-NMR(DMSO-d6)δ(ppm)

38(3H,t,J=6.8Hz), 2.79(3H,d,J=4.8Hz),

4.18(2H,q,J=6.8Hz), 4.41(2H,s), 7.27(1H,s),

8.07(1H,br), 8.12(1H,s).

(Example 1: Final step)

Method A

After dissolving *tert*-butyl 4,5-dicyano-2-ethoxybenzoate (440 mg) in dichloromethane (3 ml) and trifluoroacetic acid (3 ml), the solution was stirred at room temperature for 6 hours. The reaction mixture was concentrated to yield a carboxylic acid (350 mg) as a white solid. This was dissolved in dimethylformamide (3 ml), and then triethylamine (0.1 ml), diethyl phosphonocyanidate (0.11 ml) and a 2 N tetrahydrofuran solution of methylamine were added in that order and the mixture was stirred at room temperature overnight. Ethyl acetate was added and the reaction mixture was washed with water. The organic layer was dried over anhydrous magnesium sulfate. After filtering off the insoluble portion,

the filtrate was concentrated and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield an amide (64 mg, 38% yield). This was dissolved in ethanol (3 ml), platinum oxide (20 mg) was added and the mixture was stirred at room temperature overnight. After filtering off the insoluble portion, the filtrate was concentrated and the residue was purified by silica gel column chromatography (solvent: ethyl acetate-methanol-aqueous ammonia) to yield a mixture of amidine regioisomers (17 mg). This was dissolved in ethanol (3 ml), and then 3,5-di-*tert*-butyl 4-hydroxyphenacylbromide (30 mg) was added and the mixture was heated to reflux for 30 minutes. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography (solvent: dichloromethane-methanol) to yield the target compound (12 mg, 7% yield).

Method B

After dissolving N5-methyl-3-amino-6-ethoxy-1H-5-isoindolecarboxamide (389 mg) and 3,5-di-*tert*-butyl 4-hydroxyphenacylbromide in ethanol, the mixture was heated to reflux for 30 minutes. The reaction mixture was concentrated and the residue was purified by silica gel column chromatography (solvent: ethyl acetate-methanol) to yield the target compound (614 mg,

65.7% yield).

^{1}H-NMR(DMSO-d_6)δ(ppm)

1.39(3H,t,J=6.8Hz), 1.42(18H,s), 2.83(3H,d,J=4.8Hz),

4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.48(2H,s), 7.54(1H,s),

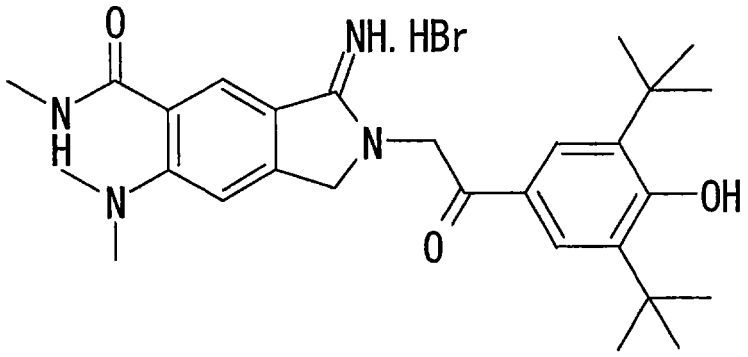
7.77(2H,s), 8.20(1H,q,J=4.8Hz), 8.55(1H,s),

9.13(1H,br), 9.82(1H,br).

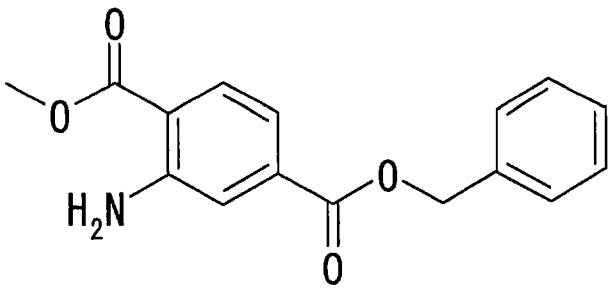
MS:m/e(ESI)480.3(MH+)

<Example 2>

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



(Step 1) 4-Benzyl 1-methyl 2-aminoterephthalate



After dissolving 1-methyl 2-aminoterephthalate (8.00 g, 41.1 mmol) in dimethylformamide (80 ml),

anhydrous potassium carbonate (6.25 g, 45.1 mmol) and benzyl bromide (4.12 ml, 43.1 mmol) were added and the mixture was stirred at room temperature for 15.5 hours. An excess of triethylamine was added, and after stirring for an additional 10 minutes at room temperature, ice water was added and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water and brine and then dried over anhydrous magnesium sulfate. Filtration was performed with silica gel-alumina and the solvent was distilled off under reduced pressure. IPE was added to the obtained oil for crystallization, and the crystals were filtered off. The filtrate was concentrated and then the same procedure was repeated twice to yield the title compound (8.21 g) as a light yellow powder. (70% yield)

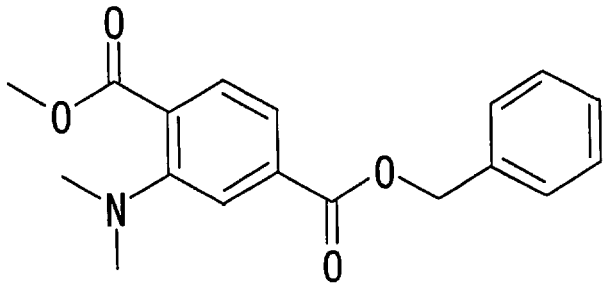
^{1}H-NMR(CDCl3)δ(ppm)

3.89(3H,s), 5.34(2H,s), 5.81(2H,s),

7.28(1H,dd,J=1.6,8.4Hz), 7.32-7.46(6H,m),

7.90(1H,d,J=8.4Hz).

(Step 2) 4-Benzyl 1-methyl 2-(dimethylamino)terephthalate

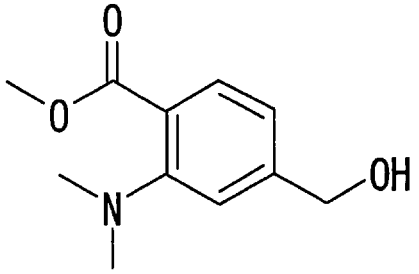


After dissolving 4-benzyl 1-methyl 2-aminoterephthalate (500 mg, 1.75 mmol) in formic acid (2 ml), 37% formalin (0.44 ml, 5.26 mmol) was added and the mixture was heated to reflux for 15 minutes. Ice water was added and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water, saturated aqueous sodium hydrogencarbonate and brine, and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (137 mg) as a yellow oil. (25% yield)

^{1}H-NMR(CDCl3)δ(ppm)

95(6H,s), 3.94(3H,s), 5.38(2H,s), 7.32-7.48(5H,m), 7.57(1H,d,J=8.0Hz), 7.70(1H,d,J=8.0Hz), 7.75(1H,s).

(Step 3) Methyl 2-(dimethylamino)-4-(hydroxymethyl)benzoate



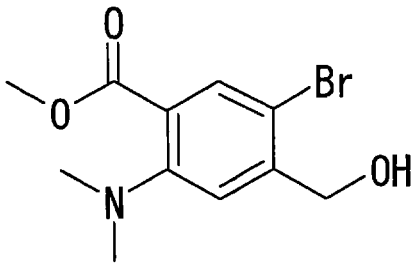
After dissolving 4-benzyl 1-methyl 2-(dimethylamino)terephthalate (1.66 g, 5.3 mmol) in tetrahydrofuran (30 ml), 20% palladium hydroxide-carbon (0.20 g) was added prior to catalytic reduction for 15 minutes at room temperature and normal pressure. The catalyst was separated off, and the solvent was distilled off under reduced pressure to yield a light yellow amorphous substance. This was dissolved in tetrahydrofuran (15 ml), triethylamine (0.81 ml, 5.8 mmol) was added and ethyl chloroformate (0.55 ml, 5.8 mmol) was added dropwise while stirring on ice. After stirring for 30 minutes, the precipitate was filtered off and the filtrate was cooled to -40°C and stirred. A solution of sodium borohydride (0.44 g, 11.6 mmol) in 5 ml of water was added dropwise, and the temperature of the mixture was gradually increased to -20°C over a period of 30 minutes. Acetone was added to the reaction mixture, the insoluble portion was filtered off and the solvent was distilled off under reduced pressure. Water was added to the residue and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water and brine

and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate). The title compound (1.02 g) was obtained as a light yellow oil. (92% yield)

^{1}H-NMR(CDCl3)δ(ppm)

2.93(6H,s), 3.91(3H,s), 4.70(2H,s), 6.89(1H,m), 7.11(1H,m), 7.70(1H,d,J=8.0Hz).

(Step 4) Methyl 5-bromo-2-(dimethylamino)-4-(hydroxymethyl)benzoate



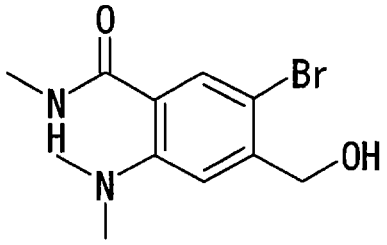
After dissolving methyl 2-(dimethylamino)-4-(hydroxymethyl)benzoate (1.023 g, 4.9 mmol) in a methylene chloride (15 ml) and methanol (6 ml) mixed solvent, calcium carbonate (2 g) was added, the mixture was stirred, and then benzyltrimethylammonium tribromide (2.100 g, 5.4 mmol) was gradually added and the mixture was stirred at room temperature for 50 minutes. The reaction mixture was filtered and the solvent was distilled off under reduced pressure. Water was added to the residue, extraction was performed with ethyl acetate and the ethyl acetate

layer was washed with water and brine. The aqueous layer was then extracted with a methylene chloride and methanol mixed solvent, combined with the ethyl acetate layer, and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.179 g) as a white solid. (84% yield)

^{1}H-NMR(CDCl3)δ(ppm)

92(6H,s), 3.91(3H,s), 4.71(2H,s), 7.22(1H,m), 7.86(1H,s).

(Step 5) N1-Methyl-5-bromo-2-(dimethylamino)-4-(hydroxymethyl)benzamide



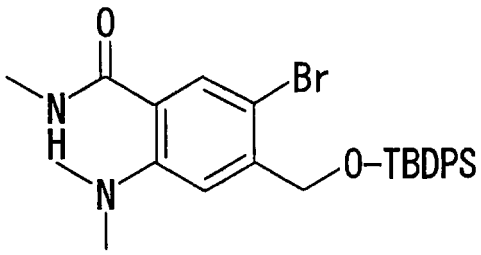
After dissolving the methyl 5-bromo-2-(dimethylamino)-4-(hydroxymethyl)benzoate (1.179 g, 4.1 mmol) in a tetrahydrofuran (10 ml)-methanol (10 ml) mixed solvent, a 1 N sodium hydroxide aqueous solution (9.8 ml, 9.8 mmol) was added and the mixture was heated to reflux for 4 hours. Next, 5 N hydrochloric acid (9.8 ml, 9.8 mmol) was added and the reaction mixture was concentrated under reduced

pressure. Acetonitrile was added to the residue and the mixture was concentrated under reduced pressure, and then the same procedure was repeated twice. Acetonitrile (20 ml), a 2.0 M dimethylamine-tetrahydrofuran solution (4.1 ml, 8.2 mmol), 1-hydroxybenztriazole (1.11 g, 8.2 mmol) and dicyclohexylcarbodiimide (1.69 g, 8.2 mmol) were added to the residue in that order and the mixture was stirred at room temperature for 20 hours. The insoluble portion was filtered off, the reaction mixture was concentrated under reduced pressure, ethyl acetate was added and the mixture was filtered through alumina. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.222 g) as a white solid. (100% yield)

^{1}H-NMR(CDCl3)δ(ppm)

2.76(6H,s), 3.02(3H,d,J=4.4Hz), 4.71(2H,s), 7.41(1H,s), 8.29(1H,s).

(Step 6) N1-Methyl-5-bromo-4-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-2-(dimethylamino)benzamide

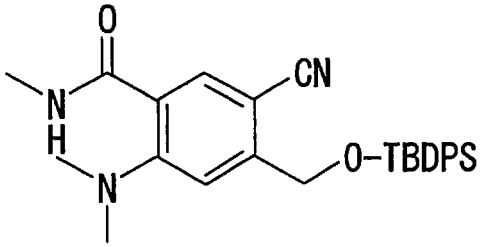


After dissolving N1-methyl-5-bromo-2-(dimethylamino)-4-(hydroxymethyl)benzamide (1.64 g, 5.71 mmol) in dimethylformamide (20 ml), imidazole (0.47 g, 6.9 mmol) and *tert*-butylchlorodiphenylsilane (1.78 ml, 6.9 mmol) were added while cooling on ice and the mixture was stirred at room temperature for 19 hours. The reaction mixture was poured into ice water and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water and brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (2.60 g) as a colorless oil. (87% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.14(9H,s), 2.82(6H,s), 3.02(3H,s), 4.79(2H,s), 7.35-7.48(7H,m), 7.64-7.75(5H,m), 8.37(1H,s).

(Step 7) N1-Methyl-4-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-5-cyano-2-(dimethylamino)benzamide



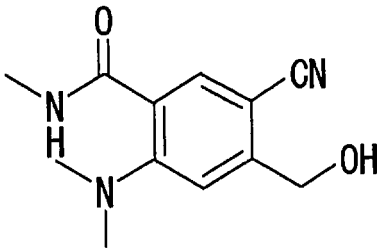
After dissolving N1-methyl-5-bromo-4-({[1-(*tert*-

butyl)-1,1-diphenylsilyl]oxy}methyl)-2-(dimethylamino)benzamide (2.60 g, 5.0 mmol) in dimethylformamide (10 ml), copper (I) cyanide (0.58 g, 6.5 mmol) was added and the mixture was stirred at 180°C for 5 hours. A 5% sodium cyanide aqueous solution (20 ml) was added to the reaction mixture and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water and brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.91 g) as a faint yellow oil. (81% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.14(9H,s), 2.87(6H,s), 3.02(3H,s), 4.95(2H,s), 7.34-7.51(7H,m), 7.60-7.74(4H,m), 7.88(1H,m), 8.11(1H,s).

(Step 8) N1-Methyl-5-cyano-2-(dimethylamino)-4-(hydroxymethyl)benzamide



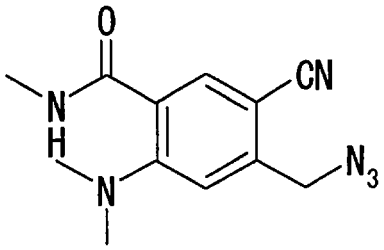
After dissolving N1-methyl-4-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-5-cyano-2-(dimethylamino)benzamide (1.91 g, 4.1 mmol) in

tetrahydrofuran (10 ml), acetic acid (0.64 ml, 11.2 mmol) and 1.0 M tetra-n-butylammonium fluoride (5.4 ml, 5.4 mmol) were added and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure, saturated aqueous sodium hydrogencarbonate was added and extraction was performed with ethyl acetate. The ethyl acetate layer was washed with water and brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then n-hexane was added and the mixture was filtered. The title compound (0.84 g) was obtained as a faint yellow solid. (89% yield)

^{1}H-NMR(CDCl3)δ(ppm)

2.87(6H,s), 3.02(3H,d,J=5.2Hz), 4.89(2H,s), 7.28(1H,s), 7.66(1H,m), 8.09(1H,s)

(Step 9) N1-Methyl-4-(azidomethyl)-5-cyano-2-(dimethylamino)benzamide



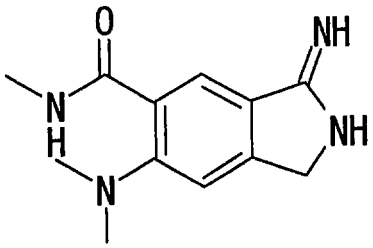
After dissolving N1-methyl-5-cyano-2-(dimethylamino)-4-(hydroxymethyl)benzamide (849 mg, 3.6 mmol) in tetrahydrofuran (20 ml), 1,8-diazabicyclo[5.4.0]undec-7-ene (0.77 ml, 5.1 mmol) and

diphenylphosphoryl azide (1.1 ml, 5.1 mmol) were added and the mixture was stirred at room temperature for 15 hours. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (755 mg) as a faint yellow powder. (80% yield)

^{1}H-NMR(CDCl3)δ(ppm)

2.94(6H,s), 3.03(3H,s), 4.61(2H,s), 7.18(1H,s), 7.53(1H,m), 8.12(1H,s).

(Step 10) N5-Methyl-6-(dimethylamino)-3-imino-5-isoindolinecarboxamide



After dissolving N1-methyl-4-(azidomethyl)-5-cyano-2-(dimethylamino)benzamide (755 mg, 2.9 mmol) in methanol (50 ml), 10% palladium-carbon (50% wet) (0.2 g) was added prior to catalytic reduction for 30 minutes at room temperature and normal pressure. The catalyst was separated off, the solvent was distilled off under reduced pressure and ethyl acetate was added to the residue for crystallization. This was filtered off to yield the title compound (283 mg) as a faint yellow powder. (42% yield)

^{1}H-NMR(DMSO-d_6)δ(ppm)

2.77(6H,s), 2.80(3H,d,J=4.8Hz), 4.42(2H,s), 7.20(1H,s), 7.94(1H,s), 8.58(1H,m).

(Example 2: Final step)

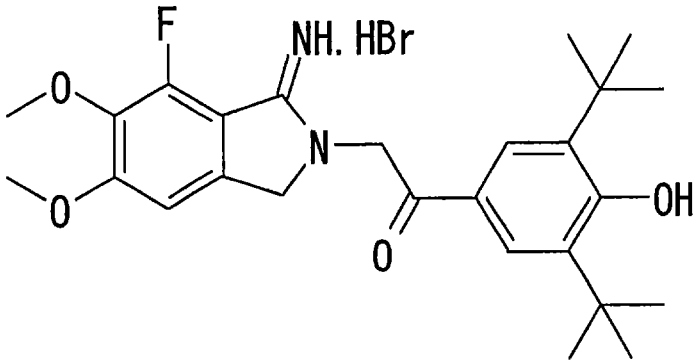
After dissolving N5-methyl-6-(dimethylamino)-3-imino-5-isoindolinecarboxamide (150 mg) and 3,5-di-*tert*-butyl 4-hydroxyphenacylbromide (212 mg) in dimethylformamide (6 ml), the mixture was stirred at room temperature for 14 hours. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the target compound (114 mg) as light yellow crystals. (31% yield)

^{1}H-NMR(DMSO-d_6)δ(ppm)

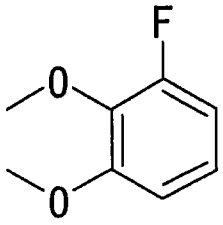
1.44(18H,s), 2.80(3H,d,J=4.4Hz), 2.94(6H,s), 4.75(2H,s), 5.46(2H,s), 7.17(1H,s), 7.79(2H,s), 8.05(1H,s), 8.10(1H,s), 8.37(1H,m), 8.94(1H,s), 9.54(1H,s).

<Example 3>

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-Fluoro-2,3-dimethoxybenzene

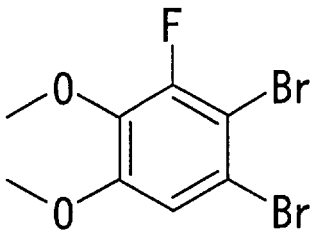


After dissolving the starting material (30 g, 0.234 mol) in dimethylformamide (400 ml), methyl iodide (32 ml, 0.515 mol) and potassium carbonate (80.7 g, 0.515 mol) were added while stirring on ice, and the stirring was continued at room temperature for 18 hours. Water (500 ml) was added and extraction was performed with diethyl ether (400 ml x 2), and then after washing the combined organic layers with brine (400 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound as a light yellow liquid (34 g, 93%).

^{1}H-NMR(CDCl3)δ(ppm)

3.86(3H,s), 3.92(3H,s), 6.65-6.98(3H,m).

(Step 2) 1,2-Dibromo-3-fluoro-4,5-dimethoxybenzene

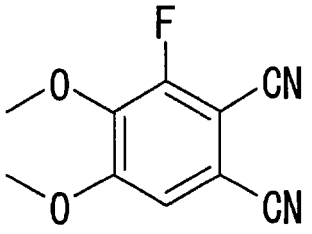


After dissolving 4-fluoro-5,6-dimethoxy-1H-3-isoindoleamine (34 g, 0.218 mol) in acetic acid (100 ml), sodium acetate (35.8 g, 0.437 mol) was added and a solution of bromine (22.6 ml, 0.458 mol) in acetic acid (100 ml) solution was added dropwise over 45 minutes while stirring on ice. After the dropwise addition, the mixture was stirred at 75°C for 10 hours. It was then cooled to room temperature, the solvent was distilled off under reduced pressure, the obtained crude product was dissolved in diethyl ether (400 ml), washed with a saturated aqueous sodium hydrosulfite (200 ml), saturated aqueous sodium hydrogencarbonate (200 ml) and brine (200 ml) in that order and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure to yield a crude product as light yellow crystals (65.4 g, 95.6%). These were used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

3.85(3H,s), 3.90(3H,s), 6.99(1H,s).

(Step 3) 3-Fluoro-4,5-dimethoxyphthalonitrile

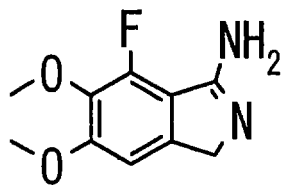


After dissolving the 1,2-dibromo-3-fluoro-4,5-dimethoxybenzene (40 g, 0.127 mol) in dimethylformamide (300 ml), CuCN (34.1 g, 0.381 mol) was added at room temperature while stirring and the mixture was stirred at 150°C for 4 hours. After cooling on ice, a solution of sodium cyanide (44 g) in water (600 ml) was added and the mixture was stirred at room temperature for 10 minutes, after which extraction was performed with ethyl acetate (500 ml x 3) and then after washing the combined organic layers with brine (500 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (white crystals 12.0 g, 46%).

^{1}H-NMR(CDCl3)δ(ppm)

3.99(3H,s), 4.06(3H,s), 7.05(1H,s).

(Step 4) 4-Fluoro-5,6-dimethoxy-1H-3-isoindoleamine



After dissolving 3-fluoro-4,5-dimethoxyphthalonitrile (450 mg, 2.18 mmol) in ethanol (50 ml), platinum oxide (0.1 g) was added. Catalytic hydrogenating reduction was carried out for 3 days at normal temperature and pressure. The catalyst was removed by celite filtration, washing was performed with methanol, and the filtrate was concentrated under reduced pressure. The obtained crude product was purified by silica gel column chromatography (solvent: ethyl acetate:methanol:27% aqueous ammonia = 3:1:0.1) to yield the title compound as a brown solid (200 mg, 43%).

^{1}H-NMR (DMSO-d_6) δ (ppm)

3.76(3H,s), 3.83(3H,s), 4.38(2H,s), 7.08(1H,s).

(Example 3: Final step)

After dissolving 4-fluoro-5,6-dimethoxy-1H-3-isoindoleamine (50 mg) and 3,5-di-*tert*-butyl 4-hydroxyphenacylbromide (93 mg) in dimethylformamide (7 ml), the mixture was stirred at room temperature for 15 hours. The solvent was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: methylene chloride-methanol) to yield the target compound (76 mg) as light yellow crystals.

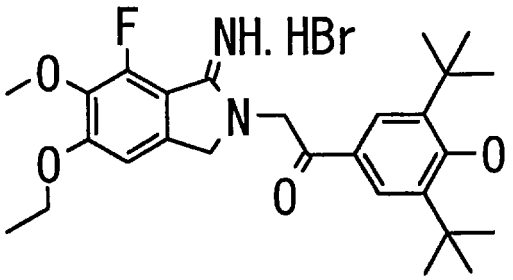
^{1}H-NMR (DMSO-d_6) δ (ppm)

1.41(18H,s), 3.86(3H,s), 3.95(3H,s), 4.79(2H,s),

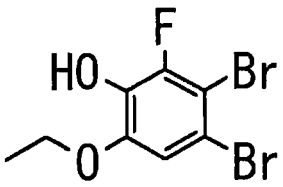
5.47(2H,s), 7.36(1H,s), 7.75(2H,s).

<Example 4>

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 3,4-Dibromo-6-ethoxy-2-fluorophenol



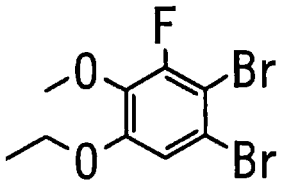
After dissolving 1,2-dibromo-3-fluoro-4,5-diethoxybenzene (5 g, 14.5 ml) in dichloromethane (70 ml), aluminum chloride (3.9 g, 29.3 mmol) was added while stirring on ice. The mixture was stirred at room temperature for 2 hours 30 minutes, 1 N hydrochloric acid (70 ml) was added and extraction was performed with ethyl acetate (70 ml x 2) and then after washing the combined organic layers with brine (50 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to

obtain the title compound (4.31 g, 94%).

^{1}H-NMR(CDCl3)δ(ppm)

1.45(3H,t,J=7.0Hz), 4.10(2H,q,J=7.0Hz), 5.49(1H,s), 6.95(1H,s).

(Step 2) 1,2-Dibromo-5-ethoxy-3-fluoro-4-methoxybenzene

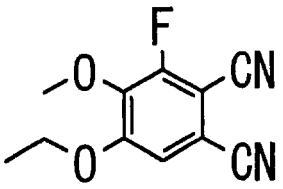


After dissolving 3,4-dibromo-6-ethoxy-2-fluorophenol (3.8 g, 12 mmol) in dimethylformamide (30 ml), methyl iodide (1.5 ml, 24 mmol) and potassium carbonate (3.3 g, 24 mmol) were added and the mixture was stirred at room temperature for 18 hours. Water (80 ml) was added, extraction was performed with diethyl ether (60 ml x 2), and then after washing the combined organic layers with brine (80 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.83 g, 46.7%).

^{1}H-NMR(CDCl3)δ(ppm)

1.45(3H,t,J=7.0Hz), 3.90(3H,s), 4.05(2H,q,J=7.0Hz), 6.99(1H,s).

(Step 3) 5-Ethoxy-3-fluoro-4-methoxyphthalonitrile

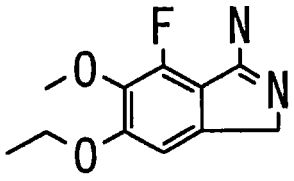


Synthesis was performed in the same manner as Step 3 of Example 3 to yield the title compound.

^{1}H-NMR(CDCl3)δ(ppm)

1.51(3H,t,J=6.7Hz), 4.05(3H,s), 4.16(2H,q,J=6.7Hz), 7.05(1H,s).

(Step 4) 6-Ethoxy-4-fluoro-5-methoxy-1H-3-isoindoleamine



Synthesis was performed in the same manner as Step 4 of Example 3 to yield the title compound.

^{1}H-NMR(CDCl3)δ(ppm)

1.34(3H,t,J=6.7Hz), 3.76(3H,s), 4.08(2H,q,J=6.7Hz), 4.37(2H,s), 7.04(1H,s).

(Example 4: Final step)

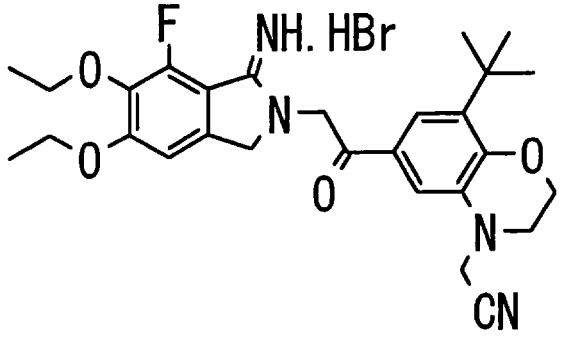
Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

^{1}H-NMR(DMSO-d6)δ(ppm)

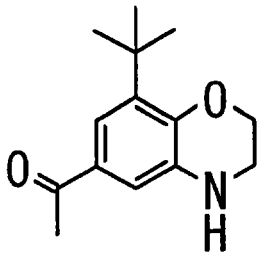
1.34-146(21H,m), 3.87(3H,s), 4.22(2H,q,J=7.0Hz), 4.77(2H,s), 5.47(2H,s), 7.34(1H,s), 7.75(2H,s), 9.03(1H,brs).

<Example 5>

{8-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)acetyl]-2,3-dihydrobenzo[1,4]oxazin-4-yl}acetonitrile hydrobromide



(Step 1) 1-[8-(*tert*-Butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone



Potassium carbonate (4.65 g, 33.7 mmol) and 1,2-dibromoethane (31.7 g, 166.6 mmol) were added to a solution of 1-[3-(*tert*-butyl)-4-hydroxy-5-nitrophenyl]-1-ethanone (8.0 g, 33.7 mmol) in dimethylformamide (200 ml) and the mixture was stirred at room temperature for 12 hours. Ethyl acetate was added, the reaction mixture was washed with water and brine in that order and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue

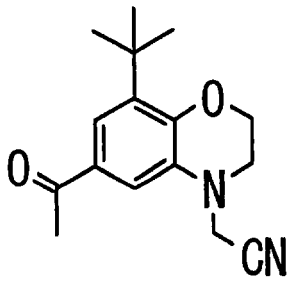
was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield 1-[4-(2-bromoethoxy)-3-(*tert*-butyl)-5-nitrophenyl]-1-ethanone (8.1 g).

After adding 10% palladium-carbon (200 mg) to a solution of this compound (8.1 g, 23.5 mmol) in toluene (300 ml), the mixture was stirred at room temperature for 24 hours under a hydrogen stream. The reaction mixture was filtered through celite, and the filtrate was concentrated under reduced pressure to yield the title compound (5.1 g) as a yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.38(9H,s), 2.52(3H,s), 3.46(2H,t,J=6.8Hz), 4.31(2H,t,J=6.8Hz), 7.12(1H,d,J=2.0Hz), 7.34(1H,d,J=2.0Hz).

(Step 2) [6-Acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-4-yl]methyl cyanide



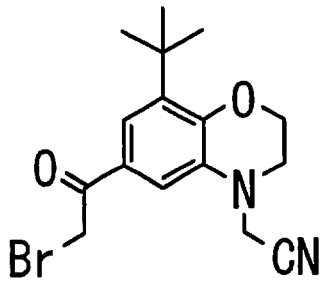
Potassium carbonate (3.6 g, 26 mmol) and bromoacetonitrile (15.4 g, 128.6 mmol) were added to a solution of 1-[8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone (6.0 g, 25.5 mmol) in

dimethylformamide (100 ml) and the mixture was stirred at 90°C for 6 hours. Ethyl acetate was added, the reaction mixture was washed with water and brine in that order and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (6.9 g) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 2.56(3H,s), 3.42(2H,t,J=6.8Hz), 4.24(2H,s), 4.41(2H,d,J=7.8Hz), 7.29(1H,d,J=2.0Hz), 7.48(1H,d,J=2.0Hz).

(Step 3) [6-(2-Bromoacetyl)-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-4-yl]methyl cyanide



Triethylamine (0.76 ml, 5.5 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (0.73 g, 5.5 mmol) were added to a solution of [6-acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-4-yl]methyl cyanide (0.5 g, 1.8 mmol) in tetrahydrofuran (50 ml) while cooling on ice and the mixture was stirred at

the same temperature for 30 minutes, after which N-bromosuccinimide (0.49 g, 2.7 mmol) was added and stirring was continued for 30 minutes. Ethyl acetate was added, the reaction mixture was washed with brine and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (310 mg) as a light yellow solid.

1H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 3.42(2H,t,J=6.8Hz), 4.24(2H,s), 4.40(2H,s), 4.43(2H,t,J=6.8Hz), 7.32(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz).

(Example 5: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

1H-NMR(DMSO-d6)δ(ppm)

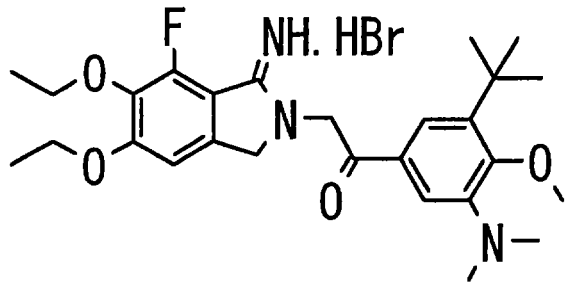
1.29(3H,t,J=7Hz), 1.33-1.42(12H,m), 3.30-3.40(2H,m), 4.11(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.40(2H,m), 4.66(2H,s), 4.80(2H,s), 5.45(2H,s), 7.33(1H,s), 7.40-7.42(2H,m), 9.03(1H,br.s), 9.34(1H,br.s).

MS:m/e(ESI)509.3(MH+)

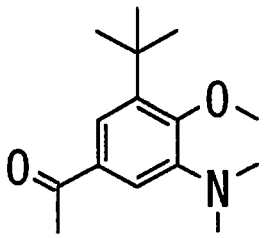
<Example 6>

1-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-

(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-[3-(*tert*-Butyl)-5-(dimethylamino)-4-methoxyphenyl]-1-ethanone



Potassium carbonate (8.5 g, 62 mmol) and methyl iodide (8.8 g, 62 mmol) were added to a solution of 1-[3-amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone (6 g, 21 mmol) in dimethylformamide (50 ml) and the mixture was stirred at room temperature for 13 hours. Ethyl acetate was added, the reaction mixture was washed with water and brine in that order and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.9 g) as a

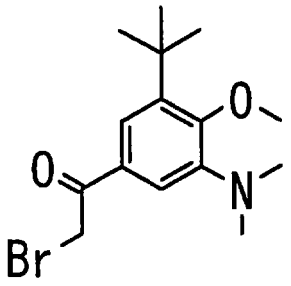
light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 2.58(3H,s), 2.83(6H,s), 3.88(3H,s),

7.47(1H,s), 7.59(1H,s).

(Step 2) 2-Bromo-1-[3-(*tert*-butyl)-5-(dimethylamino)-4-methoxyphenyl]-1-ethanone



Triethylamine (3.2 ml, 22.9 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (3.02 g, 11.4 mmol) were added to a solution of 1-[3-(*tert*-butyl)-5-(dimethylamino)-4-methoxyphenyl]-1-ethanone (1.9 g, 7.63 mmol) in tetrahydrofuran (50 ml) while cooling on ice and the mixture was stirred at the same temperature for 30 minutes, after which N-bromosuccinimide (2.7 g, 15.2 mmol) was added and stirring was continued for 30 minutes. Ethyl acetate was added, the reaction mixture was washed with brine and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound

(2.2 g) as a white solid.

1H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 2.80(6H,s), 3.89(3H,s), 4.42(2H,s),

7.49(1H,s), 7.60(1H,s).

(Example 6: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

1H-NMR(DMSO-d6)δ(ppm)

29(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(3H,t,J=7.2Hz),

2.74(6H,s), 3.82(3H,s), 4.14(2H,q,J=7.2Hz),

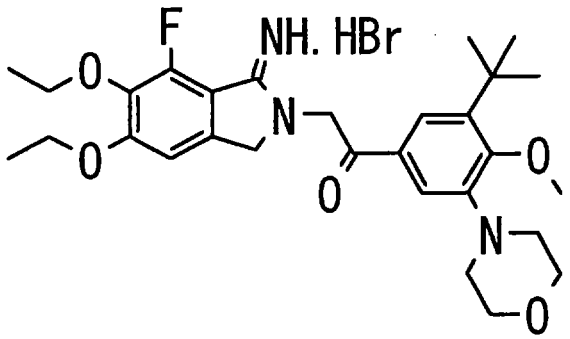
4.21(2H,q,J=7.2Hz), 4.77(2H,s), 5.46(2H,s), 7.32(1H,s),

7.45(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz).

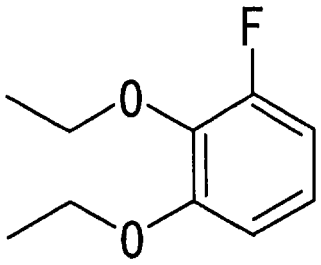
MS:m/e(ESI)486.2(MH+)

<Example 7>

1-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1,2-Diethoxy-3-fluorobenzene

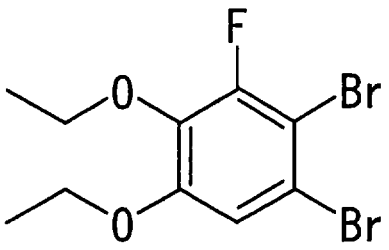


After dissolving 3-fluorocatechol (1200 g) in dimethylformamide (2500 ml) while cooling on ice, potassium carbonate (540 g) was added, after which ethyl iodide was gradually added. The reaction mixture was stirred at room temperature overnight, an ether-hexane solution was added, the mixture was washed with water and brine and the organic layer was dried over anhydrous magnesium sulfate. The solvent of the organic layer was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (269 g) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.35(3H,t,J=7.0Hz), 1.43(3H,t,J=7.0Hz), 4.07(2H,q,J=7.0Hz), 4.12(2H,q,J=7.0Hz), 6.65-6.95(3H,m).

(Step 2) 1,2-Dibromo-4,5-diethoxy-3-fluorobenzene

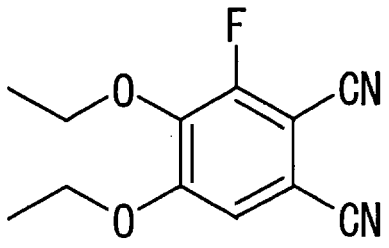


After dissolving the 1,2-diethoxy-3-fluorobenzene (269 g) in acetic acid (2000 ml), sodium acetate (294.5 g) was added. A solution of bromine (178 ml) in 150 ml of acetic acid was gradually added thereto dropwise while cooling on ice. After stirring overnight at room temperature, the mixture was stirred at 70°C for 14 hours. The reaction mixture was poured into ice water, potassium carbonate was added to adjust the pH to 7, and extraction was performed with ether. The organic layer was dried over anhydrous magnesium sulfate to yield the title compound (480 g) as a brown oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.35(3H,t,J=7.0Hz), 1.43(3H,t,J=7.0Hz),
4.04(2H,q,J=7.0Hz), 4.11(2H,q,J=7.0Hz), 6.98(1H,s).

(Step 3) 4,5-Diethoxy-3-fluorophthalonitrile



After dissolving the 1,2-dibromo-4,5-diethoxy-3-

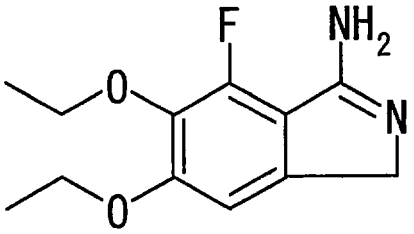
fluorobenzene (480 g) in dimethylformamide (1400 ml), copper cyanide (345 g) was added and the mixture was stirred at 150°C for 3 hours. Saturated aqueous ammonia was added to the reaction mixture, and then the mixture was stirred overnight and extraction was performed with toluene. The organic layer was dried over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (513 g) as white crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.38(3H,t,J=7.0Hz), 1.50(3H,t,J=7.0Hz),

4.16(2H,q,J=7.0Hz), 4.27(2H,q,J=7.0Hz), 7.04(1H,s).

(Step 4) 5,6-Diethoxy-4-fluoro-1H-3-isoindoleamine



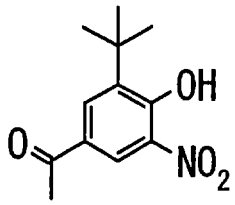
After dissolving 4,5-diethoxy-3-fluorophthalonitrile (103 g) in ethyl acetate-ethanol-methanol (600 ml-600 ml-300 ml), platinum oxide (8 g) was added and the mixture was stirred at room temperature for 4 days under a hydrogen stream. The reaction mixture was filtered through celite, the organic layer was distilled off under reduced pressure

and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (21 g) as yellow crystals.

^{1}H-NMR(DMSO-d_6)δ(ppm)

1.23(3H,t,J=7.0Hz), 1.33(3H,t,J=7.0Hz), 4.01(2H,q,J=7.0Hz), 4.08(2H,q,J=7.0Hz), 4.37(2H,s), 6.0(2H,brs), 7.05(1H,s).

(Step 5) 1-[3-(*tert*-Butyl)-4-hydroxyphenyl]-1-ethanone



Acetyl chloride (287 g) was added to a mixture of aluminum chloride (488 g) and methylene chloride (1.8 l) at -60°C while stirring. 2-*tert*-Butylphenol (500 g) was added at -70°C to -50°C over a period of 1.5 hours, and the temperature was then raised to 0°C. The reaction mixture was poured into ice and extraction was performed with ethyl acetate. The organic layer was washed with brine, the solvent was distilled off under reduced pressure, methanol(1 l) and potassium carbonate (300 g) were added to the residue and the mixture was stirred at room temperature for 2 hours. After adding water to the reaction mixture and neutralizing it with concentrated hydrochloric acid, extraction was performed with ethyl

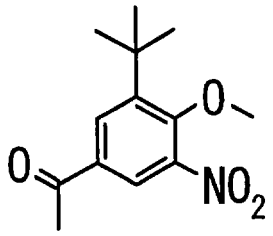
acetate and the organic layer was washed with brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Hexane was added to the residue and the resulting crystals were filtered off to yield the title compound (352 g) as white crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.41(3H,s), 2.55(3H,s), 6.73(1H,d,J=8Hz),

7.72(1H,dd,J=2,8Hz), 7.95(1H,d,J=2Hz).

(Step 6) 1-[3-(*tert*-Butyl)-4-hydroxy-5-nitrophenyl]-1-ethanone



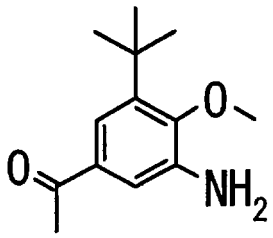
1-[3-(*tert*-Butyl)-4-hydroxyphenyl]-1-ethanone (739 g) was added to a mixture of 69% nitric acid 8354 g), water (1 l) and methylene chloride (2 l) at 10°C to 15°C while stirring. After then adding diethyl ether (3 l) and acetic anhydride (28 ml), 5 N hydrochloric acid was further added at 10°C to 15°C. The temperature of the reaction mixture was raised to room temperature over a period of 1.5 hours, and the mixture was then poured into ice water. The mixture was extracted with diethyl ether, and the organic layer was washed with brine and then dried over

anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to yield the title compound (894 g) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.44(3H,s), 2.60(3H,s), 8.23(1H,d,J=2Hz), 8.61(1H,d,J=2Hz), 11.92(1H,s).

(Step 7) 1-[3-Amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone



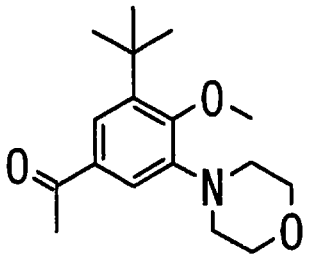
Iron powder (365 g) was added to a mixture of 1-[3-(*tert*-butyl)-4-methoxy-5-nitrophenyl]-1-ethanone (850 g), ammonium chloride (723 g), ethanol (4 l) and water (1 l) at 70°C to 80°C over a period of 1 hour. The reaction mixture was cooled to room temperature and then poured into a mixture of ice water and ethyl acetate and filtered through celite. The organic layer of the mother liquor was washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the resulting crystals were filtered off to yield the title compound (362 g) as white crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.40(3H,s), 2.54(3H,s), 3.76(2H,br.s), 3.83(3H,s),

7.26(1H,d,J=2Hz), 7.39(1H,d,J=2Hz).

(Step 8) 1-[3-(*tert*-Butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone



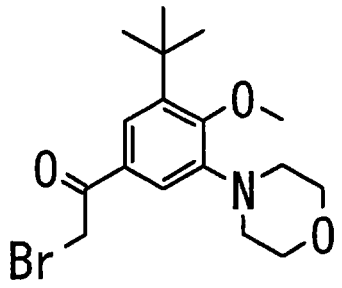
After dissolving 1-[3-amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone (180 g) in dimethylformamide (800 ml), dibromoether (125 ml), potassium carbonate (225 g) and sodium iodide (12.2 g) were added and the mixture was stirred at 80°C for 48 hours. The reaction mixture was cooled to room temperature, 3 l of ether was added and the mixture was washed 3 times with water. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (76 g) as yellow crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 2.56(3H,s), 3.08(4H,t,J=4.4Hz), 3.89(4H,t,J=4.4Hz), 3.98(3H,s), 48(1H,d,J=2.0Hz), 7.65(1H,d,J=2.0Hz).

(Step 9) 2-Bromo-1-[3-(*tert*-butyl)-4-methoxy-5-

morpholinophenyl]-1-ethanone



After dissolving the 1-[3-(*tert*-butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone (76 g) in tetrahydrofuran (600 ml), triethylamine (110 ml) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (75 ml) was added dropwise while cooling on ice. The reaction mixture was stirred for 30 minutes while cooling on ice and then N-bromosuccinimide (70 g) was gradually added. After stirring the reaction mixture for 30 minutes, 2 l of ether was added and the mixture was washed twice with water. The organic layer was dried over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (33.7 g) as light yellow crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 3.08(4H,t,J=4.8Hz), 3.89(4H,t,J=4.8Hz), 3.99(3H,s), 4.40(2H,s), 7.51(1H,s), 7.68(1H,s).

(Example 7: Final step)

After dissolving 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (20 g) and 2-bromo-1-[3-(*tert*-butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone (34.2 g) in dimethylformamide (300 ml), the mixture was stirred at room temperature for 48 hours. The solvent was distilled off under reduced pressure, and ethyl acetate (500 ml) was added to the residue for crystallization. The obtained crystals were filtered and washed with ethyl acetate to yield the target compound (40 g) as white crystals.

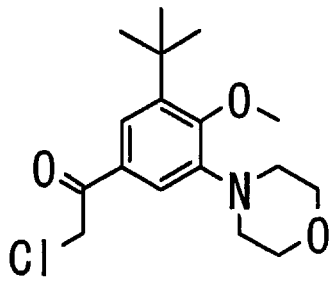
^{1}H-NMR(DMSO-d_6)δ(ppm)

1.29(3H,t,J=6.8Hz), 1.36(9H,s), 1.39(3H,t,J=6.8Hz), 2.95~3.12(4H,m), 3.75~3.84(4H,m), 3.94(3H,s), 4.12(2H,q), 4.20(2H,q,J=6.8Hz), 4.78(2H,s), 5.46(2H,s), 7.33(1H,s), 7.49(1H,s), 7.59(1H,s).

MS:m/e(ESI)528.2(MH+)

<Example 7, Alternative method>

(Step 1) 2-Chloro-1-[3-(*tert*-butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone



After dissolving 1-[3-(*tert*-butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone (9.5 g) in

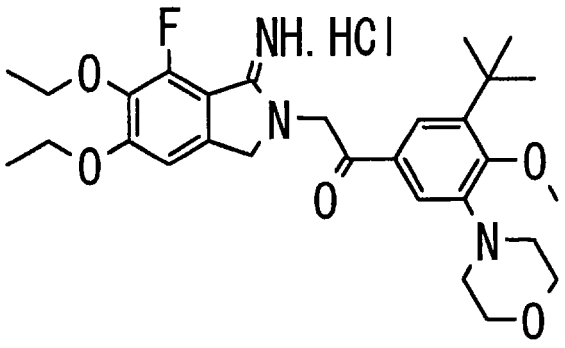
tetrahydrofuran (60 ml), triethylamine (13 ml) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (9.8 ml) were added dropwise while cooling on ice. The reaction mixture was stirred for 30 minutes while cooling on ice and then N-chlorosuccinimide (5.3 g) was gradually added. After continuing to stir the reaction mixture for 30 minutes, ether (2 l) was added thereto and the resulting mixture was washed twice with water. The organic layer was dried over anhydrous magnesium sulfate and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (4.87 g) as light yellow crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 3.06~3.14(4H,m), 3.86~3.94(4H,m), 3.99(3H,s), 4.66(2H,s), 7.26(1H,s), 7.49(1H,s), 7.64(1H,s).

(Example 7, Alternative method: Final step)

1-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride



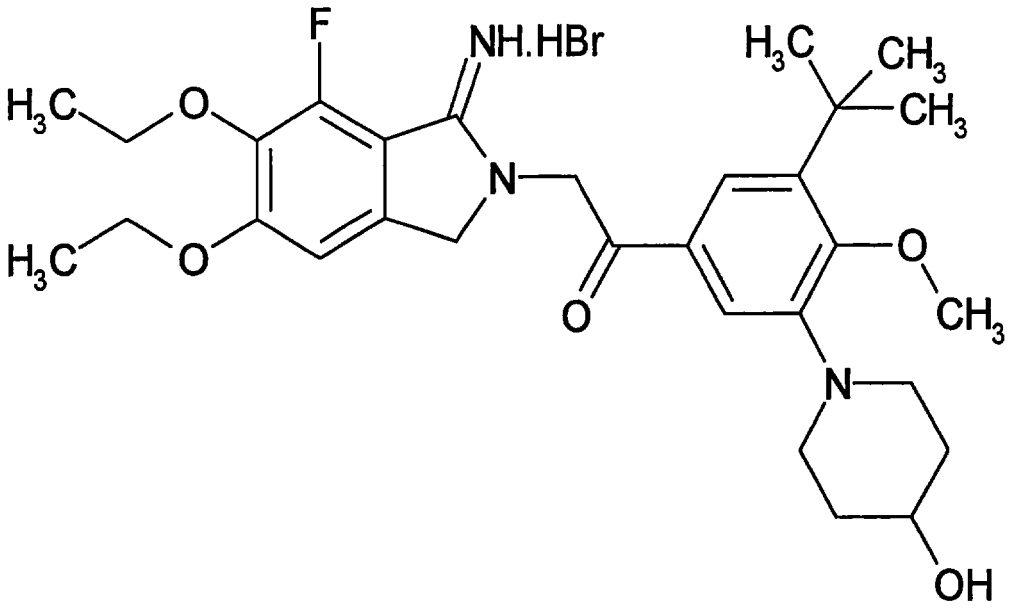
After dissolving 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (3.2 g) and 2-bromo-1-[3-(*tert*-butyl)-4-methoxy-5-morpholinophenyl]-1-ethanone (4.8 g) in dimethylformamide (15 ml), the mixture was stirred at room temperature for 48 hours. The solvent was distilled off under reduced pressure, and 50 ml of ethyl acetate was added to the residue for crystallization. The obtained crystals were filtered and then washed with ethyl acetate to yield the target compound (2.56 g) as white crystals.

^{1}H-NMR(DMSO-d_6)δ(ppm)

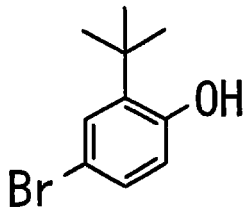
1.29(3H,t,J=6.8Hz), 1.36(9H,s), 1.39(3H,t,J=6.8Hz), 2.95~3.04(4H,m), 3.77~3.85(4H,m), 3.94(3H,s), 4.11(2H,q), 4.20(2H,q,J=6.8Hz), 4.77(2H,s), 5.46(2H,s), 7.32(1H,s), 7.49(1H,s), 7.59(1H,s).

<Example 8>

1-[3-*tert*-Butyl-5-(4-hydroxy-piperidin-1-yl)-4-methoxyphenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 4-Bromo-2-(*tert*-butyl)phenol



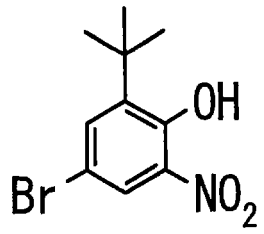
N-bromosuccinimide (580 g) was gradually added to a solution of 2-(*tert*-butyl)phenol (489 g) in acetonitrile (4000 ml) while cooling on ice. After stirring for 4 hours at below 20°C, ether (3000 ml) was added and the reaction mixture was washed twice with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure to yield a crude product of the title compound (746 g) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.20(9H,s), 6.55(1H,d,J=8.4Hz),

7.15(1H,dd,J=8.4Hz,2.0Hz), 7.34(1H,d,J=2.0Hz)

(Step 2) 4-Bromo-2-(*tert*-butyl)-6-nitrophenol



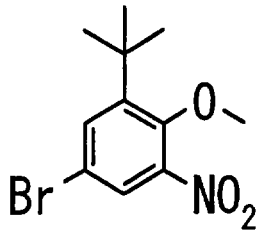
Concentrated nitric acid (112 ml) was gradually added dropwise to a solution of 4-bromo-2-(*tert*-butyl)phenol (485 g) in hexane (3000 ml) while cooling on ice. After stirring for 2 hours at below 20°C, ether (2000 ml) was added and the reaction mixture was washed with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure. Hexane was added to the residue and the precipitated crystals were filtered to yield the title compound (418 g) as yellow crystals.

^{1}H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 7.64(1H,d,J=2.4Hz), 8.14(1H,d,J=2.4Hz),

11.47(1H,s).

(Step 3) 4-Bromo-2-(*tert*-butyl)-6-nitrophenyl methyl ether



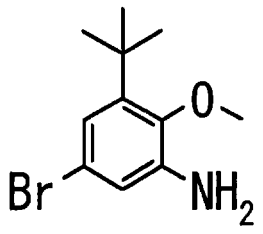
Potassium carbonate (453 g) and methyl iodide (164 ml) were added to a solution of 4-bromo-2-(*tert*-butyl)-6-nitrophenol (600 g) in dimethylformamide (6000 ml) and the mixture was stirred at 50°C for 4 hours. Ether (6000 ml) was added and the reaction mixture was washed 3 times with water. The organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure to yield a crude product of the title compound (569 g) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 3.80(3H,s), 7.61(1H,d,J=2.4Hz),

7.76(1H,d,J=2.4Hz).

(Step 4) 5-Bromo-3-(*tert*-butyl)-2-methoxyaniline



Ammonium chloride (38 g) was added to a solution of 4-bromo-2-(*tert*-butyl)-6-nitrophenyl methyl ether (20.6 g) in methanol-water (140 ml-140 ml) and iron

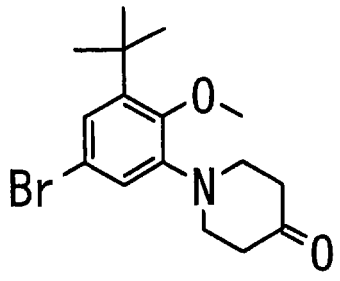
(20 g) was gradually added while heating to reflux. The mixture was heated to reflux for 2 hours and then the reaction mixture was filtered through celite. The filtrate was concentrated under reduced pressure, ethyl acetate was added to the residue and the mixture was washed 3 times with brine. The organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure to yield a crude product of the title compound (16.65 g) as a brown oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 3.68(2H,bs), 3.76(3H,s),

6.78(1H,d,J=2.0Hz), 6.81(1H,d,J=2.0Hz).

(Step 5) 1-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]-4-piperidinone



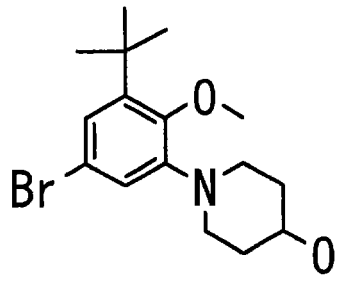
After adding a 37% formaldehyde aqueous solution (7.6 ml, 94 mmol) and anhydrous magnesium sulfate (43 g) in that order to a solution of 5-bromo-3-(*tert*-butyl)-2-methoxyaniline (22 g, 85 mmol) in methylene chloride (170 ml) at room temperature, the mixture was stirred at the same temperature for 4 hours. The

reaction mixture was filtered through celite, and then washing was performed with methylene chloride (100 ml). The obtained filtrate was cooled to -70°C and 2-(trimethylsilyloxy)-1,3-butadiene (16.2 ml, 92.3 mmol) was added. A 1.0 M Et2AlCl-Hex. solution (94 ml, 94 mmol) was also slowly added dropwise, and the mixture was stirred for 12 hours while gradually raising the temperature to room temperature. After completion of the reaction, dilution was carried out with Et_2O while cooling on ice, water (16 ml) was slowly added dropwise, and the mixture was stirred for an additional 2 hours at room temperature. After distilling off the solvent under reduced pressure, tetrahydrofuran (170 ml) was added, the pH was adjusted to 1 with a 1 N hydrochloric acid aqueous solution while cooling on ice, and the mixture was stirred for 1 hour. It was then diluted with water, and $NaHCO_3$ powder was added to render the solution basic, extraction was performed with ethyl acetate and the extract was washed with brine. After drying over anhydrous Na_2CO_3, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (9.0 g) as a brown oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 2.54-2.70(4H,m), 3.25-3.42(4H,m), 3.97(3H,s), 6.99(1H,d,J=2.4Hz), 7.14(1H,d,J=2.4Hz).

(Step 6) 1-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]-4-piperidinol



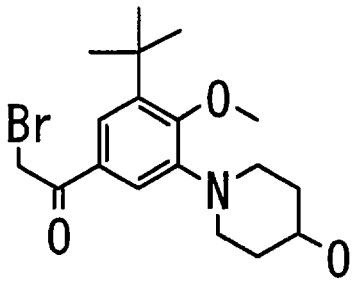
$NaBH_4$ (0.23 g, 6.1 mmol) was added to a mixed solution of 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]-4-piperidinone (2.0 g, 5.9 mmol) in methanol (12 ml)-methylene chloride (12 ml) while cooling on ice. After completion of the reaction, the mixture was diluted with water and extraction was performed with ethyl acetate. The extract was washed with brine and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.3 g).

^{1}H-NMR(CDCl3)δ(ppm)

1.34(9H,s),1.66-1.82(2H,m),1.96-2.13(2H,m),2.62-2.79(2H,m),3.25-3.43(2H,m),3.74-3.87(1H,m),3.89(3H,s), 6.97(1H,s),7.07(1H,s).

(Step 7) 2-Bromo-1-[3-(*tert*-butyl)-5-(4-

hydroxypiperidino)-4-methoxyphenyl]-1-ethanone



A solution of the 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]-4-piperidinol (1.3 g, 3.8 mmol), tributyl(1-ethoxyvinyl)tin (1.5 g, 4.2 mmol), tetrakis(triphenylphosphine)palladium (440 mg, 0.38 mmol) and CsF (1.27 g, 8.4 mmol) in 1,4-dioxane (8 ml) was stirred at 100°C for 2.5 hours under a nitrogen stream. After completion of the reaction, the mixture was cooled to room temperature and diluted with Et_2O, and the insoluble portion was filtered through celite. The solvent was distilled off under reduced pressure, the obtained crude product was dissolved in tetrahydrofuran (8 ml)-water (0.8 ml), N-bromosuccinimide (0.75 g, 4.2 mmol) was added while cooling on ice and the mixture was stirred at the same temperature for 15 minutes. This was diluted with a saturated $NaHCO_3$ aqueous solution and ethyl acetate, and then the organic layer was separated and washed with brine. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel

column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (748 mg, 51%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 1.68-1.85(2H,m), 1.98-2.12(2H,m), 2.68-2.84(2H,m), 3.29-3.47(2H,m), 3.77-3.90(1H,m), 3.99(3H,s), 4.40(2H,s), 7.54(1H,d,J=2.0Hz), 7.66(1H,d,J=2.0Hz).

(Example 8: Final step)

A solution of 5,6-diethoxy-4-fluoro-1H-3-isoindoleamine (38 mg, 0.16 mmol) and 2-bromo-1-[3-(*tert*-butyl)-5-(4-hydroxypiperidino)-4-methoxyphenyl]-1-ethanone (68 mg, 0.18 mmol) in dimethylformamide (2 ml) was stirred at room temperature for 62 hours. After completion of the reaction, the solvent was distilled off and the residue was purified by NAM silica gel column chromatography (solvent: methylene chloride-methanol) to yield the target compound (57 mg) as a brown amorphous solid.

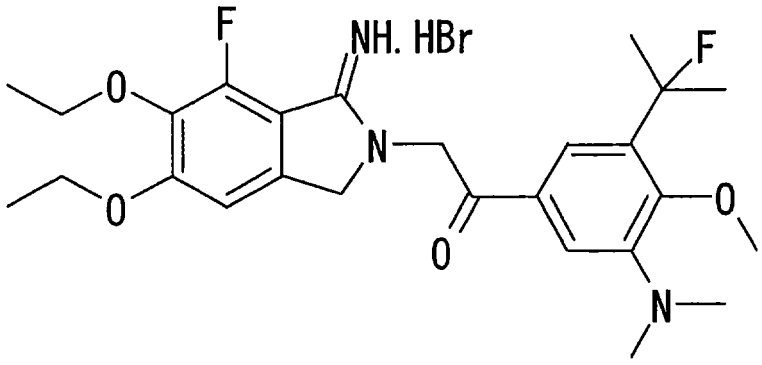
^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=6.8Hz), 1.36(9H,s), 1.40(3H,t,J=6.8Hz), 1.54-1.68(2H,m), 1.84-1.96(2H,m), 2.65-2.78(2H,m), 3.17-3.42(2H,m), 3.58-3.67(1H,m), 3.94(3H,s), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.73(1H,d,J=3.2Hz), 4.78(2H,s), 5.47(2H,s), 7.34(1H,s), 7.51(1H,s), 7.56(1H,s), 8.95-9.11(1H,m), 9.18-

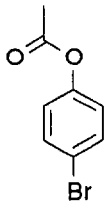
9.36(1H,brs).

<Example 9>

2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-1-[3-dimethylamino-5-(1-fluoro-1-methyl-ethyl)-4-methoxy-phenyl]-ethanone hydrobromide



(Step 1) 4-Bromophenyl acetate



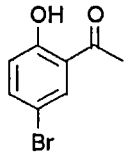
Anhydrous aluminum chloride (21 g) was suspended in methylene chloride (300 mL), and then acetyl chloride (12.3 g) was added while stirring and cooling on ice. The mixture was stirred for 10 minutes while cooling on ice and 4-bromophenol (24.5 g) was added. The reaction mixture was stirred at room temperature for 1 hour, and then ice water was added and extraction was performed with ethyl acetate. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling

off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (23.9 g) as an oil.

^{1}H-NMR ($CDCl_3$)

δ: 2.28(3H, s), 6.98(2H, d, J=10Hz), 7.49(2H, d, J=10Hz).

(Step 2) 1-(5-Bromo-2-hydroxyphenyl)-1-ethanone

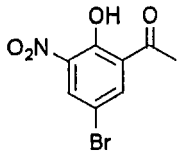


A mixture of 4-bromophenyl acetate (23.9 g) and anhydrous aluminum chloride (30 g) was stirred at 120-140°C for 20 minutes. The reaction mixture was cooled to 60-80°C, ice water was added and extraction was performed with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (21 g) as an oil.

^{1}H-NMR ($CDCl_3$)

δ: 2.61(3H, s), 6.89(1H, d, J=8Hz), 7.55(1H, dd, J=8, 2Hz), 7.83(1H, d, J=2Hz), 12.32(1H, s).

(Step 3) 1-(5-Bromo-2-hydroxy-3-nitrophenyl)-1-ethanone

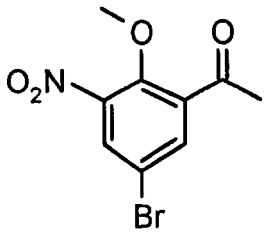


A mixture of 12 mL of concentrated nitric acid and 12 mL of concentrated sulfuric acid was added to a solution of the 1-(5-bromo-2-hydroxy-3-nitrophenyl)-1-ethanone in 80 mL of concentrated sulfuric acid while stirring at -5 to 0°C over a period of 1 hour. Ice water was added to the mixture and extraction was performed with ethyl acetate. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (17.4 g) as yellow crystals.

^{1}H-NMR ($CDCl_3$)

δ: 2.75(3H, s), 8.13(1H, d, J=2Hz), 8.32(1H, d, J=2Hz), 12.90(1H, s).

(Step 4) 1-(5-Bromo-2-methoxy-3-nitrophenyl)-1-ethanone



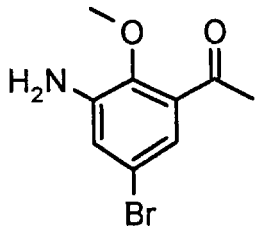
A mixture of the 1-(5-bromo-2-hydroxy-3-

nitrophenyl)-1-ethanone (17.4 g), dimethylsulfuric acid (12.7 g), potassium carbonate (13.8 g) and acetone (200 mL) was heated to reflux for 15 hours, and then water was added to the mixture and extraction was performed with ethyl acetate. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (16.2 g) as a yellow oil.

^{1}H-NMR ($CDCl_3$)

δ: 2.65(3H, s), 3.95(3H, s), 7.91(1H, d, J=2Hz), 8.05(1H, d, J=2Hz).

(Step 5) 1-(3-Amino-5-bromo-2-methoxyphenyl)-1-ethanone



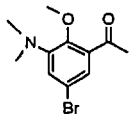
Iron (15 g) was added to a mixture of the 1-(5-bromo-2-methoxy-3-nitrophenyl)-1-ethanone (16.2 g), concentrated hydrochloric acid (20 mL) and methanol (60 mL) at room temperature. After stirring the mixture at 60°C for 1 hour, it was neutralized with saturated aqueous sodium hydrogencarbonate and

extraction was performed with ethyl acetate. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (12.8 g) as a yellow oil.

^{1}H-NMR ($CDCl_3$)

δ: 2.60(3H, s), 3.78(3H, s), 4.00(2H, br.s), 6.99(1H, d, J=2Hz), 7.07(1H, d, J=2Hz).

(Step 6) 1-[5-Bromo-3-(dimethylamino)-2-methoxyphenyl]-1-ethanone

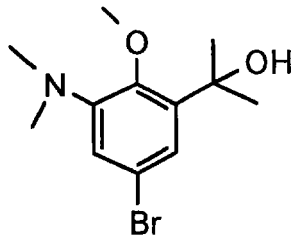


A mixture of 1-(3-amino-5-bromo-2-methoxyphenyl)-1-ethanone (12.8 g), iodomethane (60 mL), potassium carbonate (14.4 g) and N,N-dimethylformamide (200 mL) was stirred at 60 to 70°C for 2 hours. Water was added to the mixture, extraction was performed with ethyl acetate, and the organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (9.6 g) as a yellow oil.

^{1}H-NMR ($CDCl_3$)

δ: 2.60(3H, s), 2.82(6H, s), 3.80(3H, s), 7.08(1H, d, J=2Hz), 7.25(1H, d, J=2Hz).

(Step 7) 2-[5-Bromo-3-(dimethylamino)-2-methoxyphenyl]-2-propanol

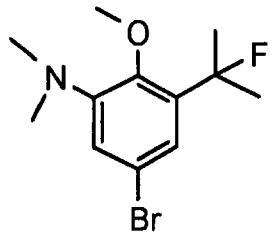


A solution of methylmagnesium bromide in ether was added to a solution of 1-[5-bromo-3-(dimethylamino)-2-methoxyphenyl]-1-ethanone (4 g) in diethyl ether while stirring at -70°C. After stirring at the same temperature for 30 minutes, saturated aqueous ammonium chloride was added, extraction was performed with ethyl acetate, and the organic layer was washed with brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to yield the title compound (3.4 g) as an oil.

^{1}H-NMR ($CDCl_3$)

δ: 1.56(3H, s), 1.58(3H, s), 2.76(6H, s), 3.91(3H, s), 6.95(1H, d, J=2Hz), 7.04(1H, d, J=2Hz).

(Step 8) *N*-[5-Bromo-3-(1-fluoro-1-methylethyl)-2-methoxyphenyl]-*N*,*N*-dimethylamine

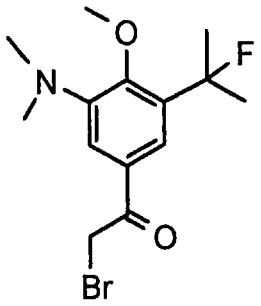


Diethylaminosulfur trifluoride (620 mg) was added to a solution of 2-[5-bromo-3-(dimethylamino)-2-methoxyphenyl]-2-propanol (1 g) in methylene chloride while stirring on ice. After stirring for an additional 30 minutes while cooling on ice, water was added, extraction was performed with ethyl acetate, and the organic layer was washed with brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (680 mg) as an oil.

^{1}H-NMR ($CDCl_3$)

δ: 1.68(3H, s), 1.74(3H, s), 2.76(6H, s), 3.78(3H, s), 6.96(1H, d, J=2Hz), 7.24(1H, d, J=2Hz).

(Step 9) 2-Bromo-1-[3-(dimethylamino)-5-(1-fluoro-1-methylethyl)-4-methoxyphenyl]-1-ethanone



Synthesis was performed in the same manner as Step 7 of Example 8 to yield the title compound as a light yellow solid.

^{1}H-NMR ($CDCl_3$)

δ: 1.70(3H, s), 1.79(3H, s), 2.81(6H, s), 3.79(3H, s), 4.48(2H, s), 7.56(1H, d, J=2Hz), 7.74(1H, d, J=2Hz).

(Example 9: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

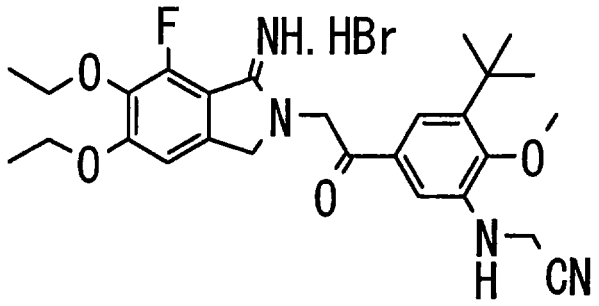
1H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7Hz), 1.40(3H,t,J=7Hz), 1.68(3H,s), 1.74(3H,s), 2.77(6H,s), 3.83(3H,s), 4.11(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.80(2H,s), 5.50(2H,s), 7.34(1H,brs), 7.50(1H,brs), 7,65(1H,br.s).

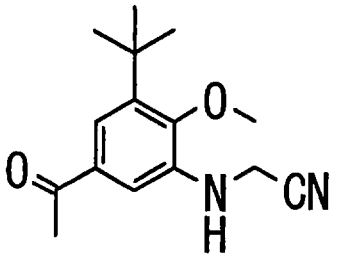
MS:m/e(ESI)490.4(MH+)

<Example 10>

{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenylamino}-acetonitrile hydrobromide



(Step 1) [5-Acetyl-3-(*tert*-butyl)-2-methoxyanilino]methyl cyanide

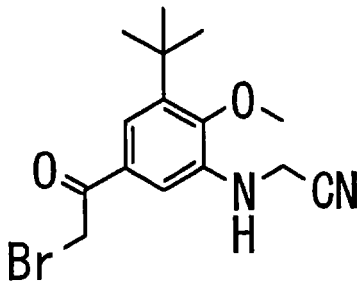


Bromoacetonitrile (6 ml) and potassium carbonate (1.4 g) were added to a solution of 1-[3-amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone (2.0 g, 9.0 mmol) in dimethylformamide (50 ml) and the mixture was stirred at 70°C for 3 hours. The reaction mixture was cooled to room temperature, ethyl acetate was added, washed was performed with water and brine in that order, the organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (3.2 g) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 2.59(3H,s), 3.77(3H,s), 4.20(2H,d,J=4.0Hz), 4.37-4.48(1H,m), 7.25(1H,d,J=2.0Hz), 7.52(1H,d,J=2.0Hz).

(Step 2) [5-(2-Bromoacetyl)-3-(*tert*-butyl)-2-methoxyanilino]methyl cyanide



Triethylamine (3.7 g, 36.9 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (6.5 g, 24.6 mmol) were added to a solution of [5-acetyl-3-(*tert*-butyl)-2-methoxyanilino]methyl cyanide (3.2 g, 12.3 mmol) in tetrahydrofuran and the mixture was stirred for 30 minutes while cooling on ice, after which N-bromosuccinimide (2.6 g, 14.8 mmol) was added and the mixture was stirred for 2 hours while cooling on ice. Ethyl acetate was added, the reaction mixture was washed with water and brine in that order, the organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (2.9 g) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.41(9H,s), 3.79(3H,s), 4.19(2H,d,J=4.0Hz), 4.43(2H,s), 4.37-4.48(1H,m), 7.27(1H,d,J=2.0Hz), 7.58(1H,d,J=2.0Hz).

(Example 10: Final step)

After dissolving [5-(2-bromoacetyl)-3-(*tert*-butyl)-2-methoxyanilino]methyl cyanide (500 mg, 1.4 mmol) and 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (340 mg, 1.4 mmol) in dimethylformamide (20 ml) and stirring the solution at room temperature for 14 hours, the organic layer was concentrated under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol). The obtained crude product was recrystallized from ethyl acetate to yield the target compound (320 mg) as light yellow crystals.

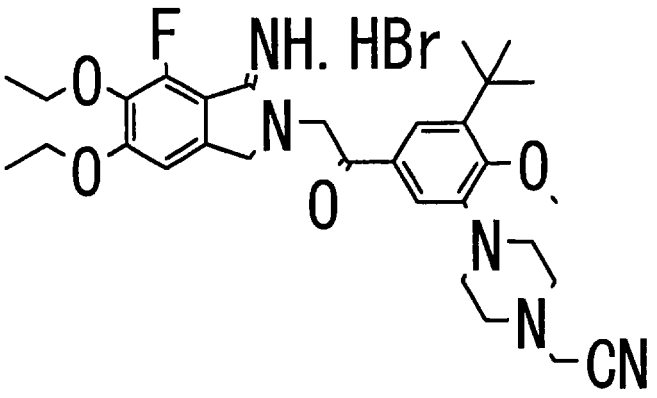
^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7Hz), 1.35-1.42(12H,m), 3.72(3H,s), 4.11(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.36(2H,m), 4.81(2H,s), 5.49(2H,s), 6.15(1H,m), 7.32(1H,br.s), 7.34(1H,br.s), 7.39(1H,br.s).

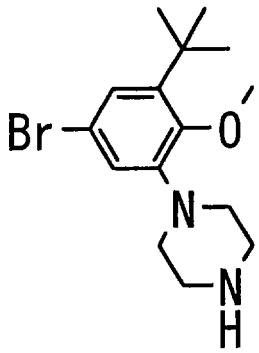
MS:m/e(ESI)497.2(MH+)

<Example 11>

(4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}piperazin-1-yl)-acetonitrile hydrobromide



(Step 1) 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine



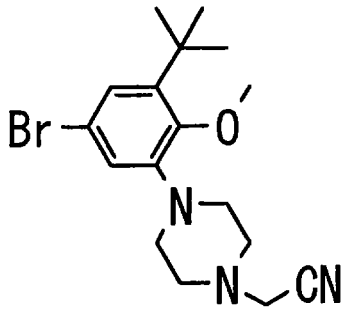
5-Bromo-3-(*tert*-butyl)-2-methoxyaniline (311 g) and bis(2-chloroethyl)amine hydrogenchloride (251 g) were suspended in 4 L of 1,2-dichlorobenzene, and the mixture was vigorously stirred for 22 hours at an external temperature of 200°C. The mixture was cooled to room temperature, and then potassium carbonate (620 g) and water were added and extraction was performed with methylene chloride (6L). After drying over magnesium sulfate, the solvent was distilled off under reduced pressure to yield a black oil (460 g). Purification was performed by NH-silica gel column

chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (161 g) as blackish purple solid (41%).

^{1}H-NMR(CDCl3)δ(ppm)

1.34(9H,s), 1.74(1H,brs), 2.99-3.09(8H,m), 3.90(3H,s), 6.95(1H,d,J=2.4Hz), 7.08(1H,d,J=2.4Hz).

(Step 2) 2-{4-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetonitrile



1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine (550 mg), potassium carbonate (302 mg), dimethylformamide (7 ml) and bromoacetonitrile (0.12 ml) were combined and the mixture was stirred at room temperature for 4 hours. The reaction mixture was diluted with ethyl acetate, the insoluble portion was filtered off, and the concentrated residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (480 mg) as colorless crystals (78%).

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 2.89(4H,brs), 3.18(4H,brs), 3.69(2H,s), 3.88(3H,s), 6.95(1H,d,J=2.4Hz), 7.12(1H,d,J=2.4Hz).

(Example 11: Final step)

After dissolving 2-{4-[5-(2-bromoacetyl)-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetonitrile (361 mg) and 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (201 mg) in dimethylformamide (13 ml), the solution was stirred at room temperature overnight. The dimethylformamide was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield a light brown oil, which was then crystallized from acetonitrile-ether to yield colorless crystals (372 mg)(68%).

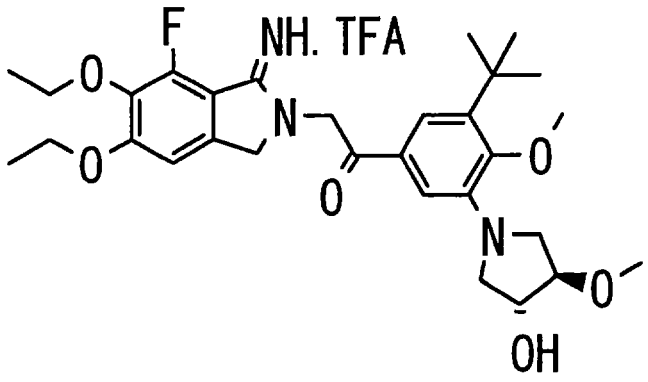
^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz), 2.71(4H,brs), 3.06(4H,brs), 3.83(2H,s), 3.94(3H,s), 4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.48(2H,s), 7.34(1H,s), 7.50(1H,d,J=2.0Hz), 7.59(1H,d,J=2.0Hz), 9.05(1Hbrs), 9.27(1H,brs).

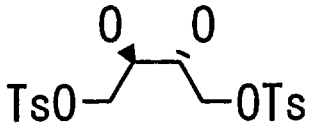
MS:m/e(ESI)566.3(MH+)

<Example 12>

1-[3-*tert*-Butyl-5-((3R,4R)-3-hydroxy-4-methoxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone trifluoroacetate



(Step 1) (2R,3R)-2,3-Dihydroxy-4-{[(4-methylphenyl)sulfonyl]oxy}butyl 4-methyl-1-benzenesulfonate



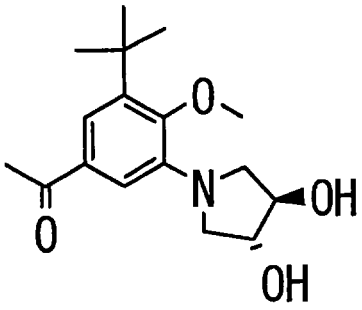
A solution of (4*R*,5*S*)-2,2-dimethyl-5-[(4-methylphenyl)sulfonyl]oxy-1,3-dioxolan-4-yl 4-methyl-1-benzenesulfonate (5.07 g, 10.8 mmol) in a tetrahydrofuran (50 ml)-10% perchloric acid water (50 ml) mixed solvent was stirred at 50°C for 7 hours. The tetrahydrofuran was distilled off under reduced pressure, extraction was performed with ethyl acetate and the extract was washed with brine. After drying with anhydrous magnesium sulfate, the solvent was distilled off to yield a crude product which was then purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (5.14 g). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

2.45(6H,s), 3.87-3.93(2H,m), 4.06(4H,d,J=6.0Hz),

7.36(4H,d,J=8.0Hz), 7.78(4H,d,J=8.0Hz).

(Step 2) 1-{3-(*tert*-Butyl)-5-[(3R,4R)-3,4-dihydroxytetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone



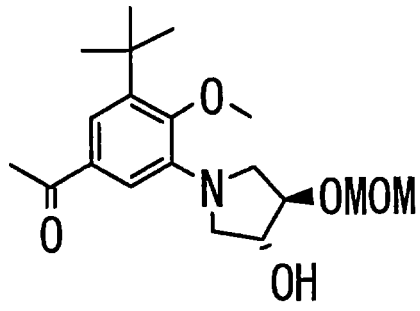
A suspension of 1-[3-amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone (2.0 g, 9.0 mmol), (2R,3R)-2,3-dihydroxy-4-{[(4-methylphenyl)sulfonyl]oxy}butyl 4-methyl-1-benzenesulfonate (5.14 g), NaI (0.27 g, 1.8 mmol) and $NaHCO_3$ (1.9 g) in EtOH (40 ml) was heated to reflux for 48 hours under a nitrogen stream. After distilling off the EtOH under reduced pressure and diluting with water, extraction was performed with ethyl acetate. The extract was washed with brine and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography to yield the title compound (1.32 g, 48%) as a yellow viscous oil from the 1:2 - 1:3

hexane:ethyl acetate elution fractions containing 0.5% methanol.

^{1}H-NMR(CDCl3)δ(ppm)

1.41(9H,s), 2.56(3H,s), 3.04-3.22(2H,m), 3.59-3.78(5H,m), 4.23-4.37(2H,m), 7.35(1H,d,J=2.0Hz), 7.51(1H,d,J=2.0Hz).

(Step 3) 1-{3-(*tert*-Butyl)-5-[(3R,4R)-3-hydroxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone



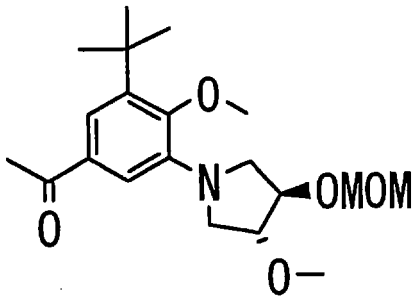
Diisopropylethylamine (2.3 ml, 13 mmol) was added to a solution of the 1-{3-(*tert*-butyl)-5-[(3R,4R)-3,4-dihydroxytetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone (1.32 g, 4.29 mmol) in methylene chloride (10 ml) while cooling on ice, and then MOMCl (0.49 ml, 6.5 mmol) was added dropwise and the mixture was stirred at the same temperature for 10 minutes and then at room temperature for 2.5 hours. After completion of the reaction, it was diluted with water and extraction was performed with ethyl acetate. After washing with brine and drying over anhydrous magnesium sulfate, the

solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (496 mg, 33%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 2.56(3H,s), 3.24-3.36(2H,m), 3.46(3H,s), 3.49-3.62(2H,m), 3.70(3H,s), 3.99-4.08(1H,m), 4.26-4.36(1H,m), 4.68-4.80(2H,m), 7.34(1H,d,J=2.0Hz), 7.52(1H,d,J=2.0Hz).

(Step 4) 1-{3-(*tert*-Butyl)-4-methoxy-5-[(3R,4R)-3-methoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]phenyl}-1-ethanone



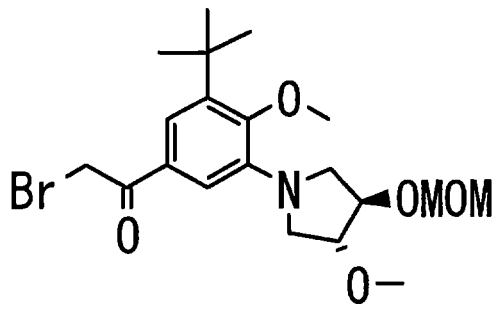
Tetra-*n*-butylammonium bromide (227 mg, 0.704 mmol) and methyl iodide (0.18 ml, 2.9 mmol) were added to a mixed solvent of 1-{3-(*tert*-butyl)-5-[(3R,4R)-3-hydroxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone (496 mg, 1.41 mmol) in a toluene (3 ml)-50% aqueous NaOH (3 ml) mixed solvent in that order at room temperature and the mixture was

stirred for 64 hours. It was then diluted with water, extraction was performed with ethyl acetate and the extract was washed with brine. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (397 mg, 77%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 2.56(3H,s), 3.17-3.26(2H,m), 3.40(3H,s), 3.42(3H,s), 3.48-3.60(2H,m), 3.71(3H,s), 3.90-3.98(1H,m), 4.22-4.28(1H,m), 4.67-4.77(2H,m), 7.34(1H,d,J=2.0Hz), 7.52(1H,d,J=2.0Hz).

(Step 5) 2-Bromo-1-{3-(*tert*-butyl)-4-methoxy-5-[(3R,4R)-3-methoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]phenyl}-1-ethanone



Triethylamine (0.46 ml, 3.3 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (0.37 ml, 1.6 mmol) were added dropwise in that order to a solution of 1-{3-(*tert*-butyl)-4-methoxy-5-[(3R,4R)-3-methoxy-4-

(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]phenyl}-1-ethanone (397 mg, 1.09 mmol) in tetrahydrofuran (4 ml) while cooling on ice, and the mixture was stirred at the same temperature for 20 minutes. N-Bromosuccinimide (290 mg, 1.63 mmol) was then added and stirring was continued at the same temperature for 15 minutes. After completion of the reaction, the mixture was diluted with saturated aqueous sodium hydrogencarbonate and ethyl acetate and the organic layer was separated. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (434 mg, 90%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.41(9H,s), 3.16-3.27(2H,m), 3.41(3H,s), 3.43(3H,s), 3.48-3.60(2H,m), 3.72(3H,s), 3.90-3.97(1H,m), 4.22-4.30(1H,m), 4.42(2H,s), 4.69-4.78(2H,m), 7.37(1H,d,J=2.0Hz), 7.54(1H,d,J=2.0Hz).

(Example 12: Final step)

A solution of 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (211 mg, 0.887 mmol) and 2-bromo-1-{3-(*tert*-butyl)-4-methoxy-5-[(3R,4R)-3-methoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]phenyl}-1-

ethanone (434 mg, 0.977 mmol) in dimethylformamide (4 ml) was stirred at room temperature for 17 hours. After completion of the reaction, the solvent was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield the MOM-protected title compound (543 mg). This was then dissolved in trifluoroacetic acid (3 ml)-H_2O (3 drops) and the mixture was stirred at room temperature for 4.5 hours. The solvent was distilled off under reduced pressure and the resultant product was filtered through a small amount of NAM silica gel. After distilling off the methylene chloride-methanol (20:1 - 10:1) elution fractions under reduced pressure, the residue was triturated in diethyl ether. The obtained crystals were dried to yield the target compound (340 mg, 57%) as a brown amorphous solid.

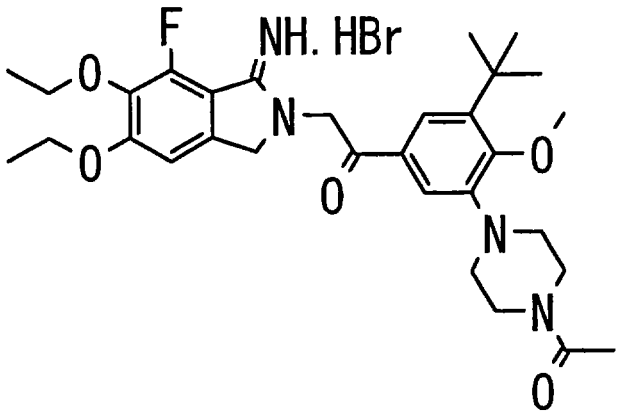
^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(3H,t,J=7.2Hz), 2.91-2.99(1H,m), 3.03-3.12(1H,m), 3.30(3H,s), 3.40-3.58(2H,m), 3.63(3H,s), 3.71-3.79(1H,m), 4.10(2H,q,J=7.2Hz), 4.10-4.30(3H,m), 4.78(2H,s), 5.25(1H,brs), 5.38-5.60(2H,m), 7.30(1H,s), 7.33(1H,s), 7.41(1H,s), 8.99-9.12(1H,m), 9.20-9.40(1H,m).

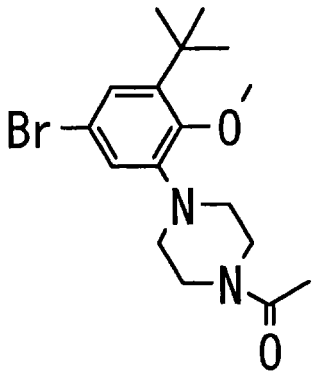
MS:m/e(ESI)558.3(MH+)

<Example 13>

1-[3-(4-Acetyl-piperazin-1-yl)-5-*tert*-butyl-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)ethanone hydrobromide



(Step 1) 1-{4-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-1-ethanone



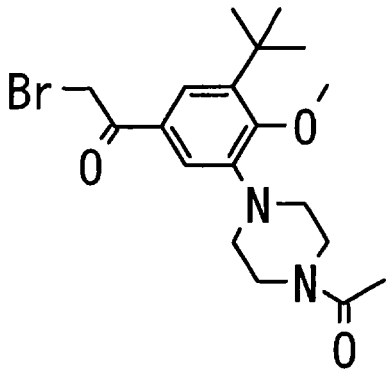
Acetyl chloride (0.10 ml) was mixed with a solution of 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine (370 mg) and triethylamine (0.32 m) in methylene chloride (8 ml), and the mixture was stirred at room temperature for 3 hours. The reaction mixture was diluted with ethyl acetate and, after filtering off the insoluble portion, was

concentrated. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (338 mg) as colorless crystals (81%).

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 2.14(3H,s), 2.96-3.06(4H,m), 3.62(2H,t,J=5.0Hz), 3.78(2H,brs), 3.91(3H,s), 6.93(1H,d,J=2.4Hz), 7.13(1H,d,J=2.4Hz).

(Step 2) 1-[3-(4-Acetylpiperazino)-5-(*tert*-butyl)-4-methoxyphenyl]-2-bromo-1-ethanone



After adding the 1-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-1-ethanone (338 mg), tetrakis(triphenylphosphine)palladium (159 mg), tributyl(1-ethoxyvinyl)stannane (324 mg) and cesium fluoride (306 mg) to degassed dioxane (9 ml), the mixture was stirred at 95°C for 3 hours under a nitrogen stream. The mixture was then cooled to room temperature, diluted with ethyl acetate and filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in

tetrahydrofuran (7 ml) and H_2O (0.7 ml) and cooled to 0°C, and then N-bromosuccinimide (179 mg) was added. After 5 minutes, Na_2SO_3(aq) was added, extraction was performed with ethyl acetate, and the extract washed with brine and then concentrated under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (313 mg) as a light brown oil. (NMR revealed the presence of by-products that could not be easily separated). This was used directly for the following reaction.

(Example 13: Final step)

After dissolving 1-[3-(4-acetylpiperazino)-5-(*tert*-butyl)-4-methoxyphenyl]-2-bromo-1-ethanone containing impurities (209 mg (a portion of the 313 mg from the previous reaction)) and 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (73 mg) in dimethylformamide (5 ml), the mixture was stirred at room temperature overnight. The dimethylformamide was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield a light brown solid which was recrystallized from acetonitrile-ether to yield colorless crystals (83 mg) (21% from 1-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-1-ethanone).

^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz),

2.04(3H,s), 2.93(2H,brs), 2.99(2H,brs), 3.65(4H,brs),

3.96(3H,s), 4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz),

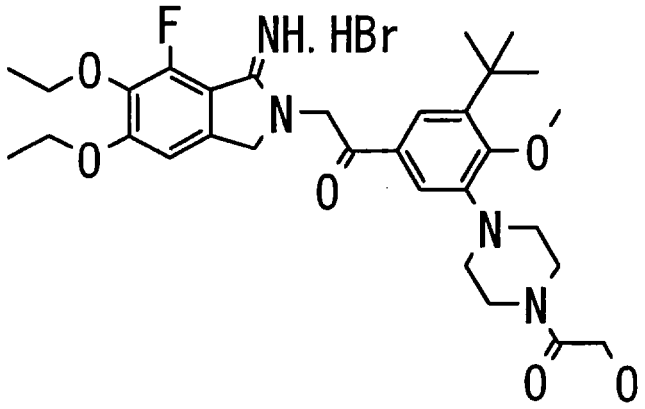
4.79(2H,s), 5.47(2H,s), 7.34(1H,s), 7.49(1H,sz),

7.61(1H,s), 9.05(1Hbrs), 9.27(1H,brs).

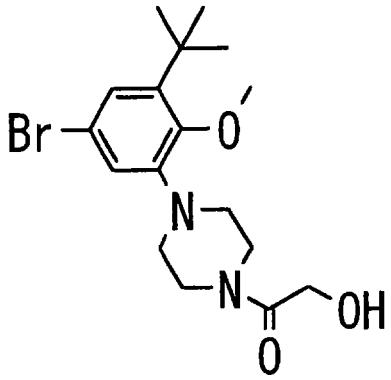
MS:m/e(ESI)569.4(MH+)

<Example 14>

1-{3-*tert*-Butyl-5-[4-(2-hydroxy-acetyl)piperazin-1-yl]-4-methoxy-phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-{4-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-2-hydroxy-1-ethanone



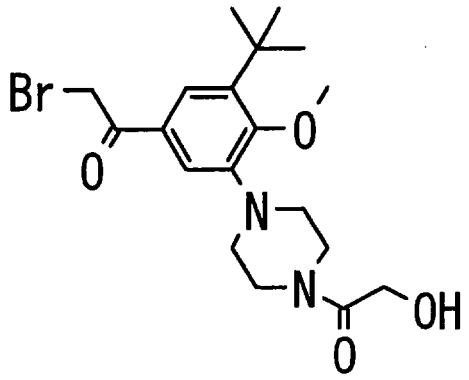
Acetoxyacetyl chloride (0.14 ml) was added to a solution of 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine (360 mg) and triethylamine (0.31 ml) in CH_2Cl_2 (5 ml) while cooling on ice and the mixture was brought to room temperature and stirred for 1 hour. After quenching the reaction with brine, extraction was performed with ethyl acetate to yield a crude product of 2-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-2-oxoethyl acetate as a red oil. This crude product was dissolved in methanol (2.5 ml) and potassium carbonate (167 mg) was added. After 15 minutes, brine was added, extraction was performed with ethyl acetate, the extract was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (285 mg) as light orange crystals (67%).

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 3.05(4H,t,J=4.4Hz), 3.44(2H,t,J=5.2Hz), 3.84(2H,brs), 3.90(3H,s), 4.21(2H,s),

6.93(1H,d,J=2.4Hz), 7.14(1H,d,J=2.4Hz).

(Step 2) 2-Bromo-1-[3-(*tert*-butyl)-5-(4-glycoloylpiperazino)-4-methoxyphenyl]-1-ethanone



After adding the 1-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-2-hydroxy-1-ethanone (285 mg), tetrakis(triphenylphosphine)palladium (128 mg), tributyl(1-ethoxyvinyl)stannane (267 mg) and cesium fluoride (247 mg) to degassed dioxane (8 ml), the mixture was stirred at 90°C for 3.5 hours under a N_2 atmosphere. The mixture was then cooled to room temperature, diluted with ethyl acetate and filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in THF (6 ml) and H_2O (0.6 ml) and cooled to 0°C, and then N-bromosuccinimide (151 mg) was added. After 5 minutes, Na_2SO_3 (aq) was added, extraction was performed with ethyl acetate, and the extract was washed with brine and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl

acetate) to yield the title compound (186 mg) as colorless crystals (59%).

^{1}H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 3.10(4H,brs), 3.48(2H,t,J=4.8Hz), 3.88(2H,brs), 4.00(3H,s), 4.23(2H,s), 4.39(2H,s), 7.50(1H,d,J=2.2Hz), 7.72(1H,d,J=2.2Hz).

(Example 14: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

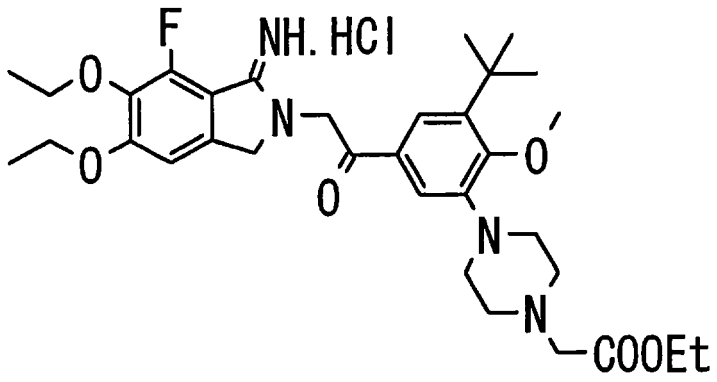
^{1}H-NMR(DMSO-D6)δ(ppm)

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz), 2.98(4H,brs), 3.57(2H,brs), 3.70(2H,brs), 3.96(3H,s), 4.11(2H,q,J=7.0Hz), 4.12(2H,s), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.47(2H,s), 7.34(1H,s), 7.49(1H,d,J=2.0Hz), 7.61(1H,d,J=2.0Hz), 9.05(1H,brs), 9.27(1H,brs).

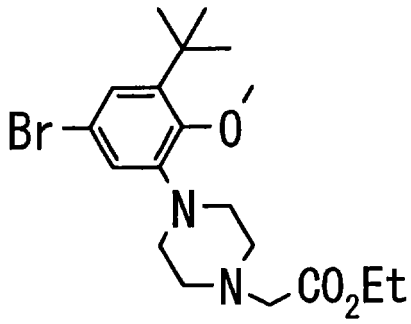
MS:m/e(ESI)585.3(MH+)

<Example 15>

Ethyl (4-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}piperazin-1-yl)-acetate dihydrochloride

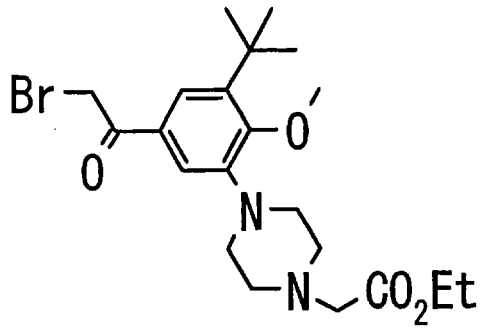


(Step 1) Ethyl 2-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetate



1-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine (750 mg), potassium carbonate (411 mg) and ethyl bromoacetate (0.27 ml) were stirred in dimethylformamide (4 ml) at room temperature for one day. The reaction mixture was diluted with ethyl acetate, the insoluble portion was filtered off and then the concentrated residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (715 mg) as a light red oil (75%).

(Step 2) Ethyl 2-{4-[5-(2-bromoacetyl)-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetate



After adding the ethyl 2-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetate (715 mg), tetrakis(triphenylphosphine)palladium (300 mg), tributyl(1-ethoxyvinyl)stannane (625 mg) and cesium fluoride (578 mg) to degassed dioxane (12 ml) under a nitrogen stream, the mixture was stirred at 90°C for 3.5 hours. The mixture was then cooled to room temperature, diluted with ethyl acetate and filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in tetrahydrofuran (8 ml) and H_2O (0.8 ml) and cooled to 0°C, and then N-bromosuccinimide (339 mg) was added. After 5 minutes, Na_2SO_3(aq) was added, extraction was performed with ethyl acetate, and the extract was washed with brine and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (512 mg) as a light brown oil (65%).

^{1}H-NMR(CDCl3)δ(ppm)

1.30(3H,t,J=7.2Hz), 1.39(9H,s), 2.82(4H,brs), 3.16(4H,brs), 3.32(2H,s), 3.97(3H,s), 4.22(2H,q,J=7.2Hz), 4.40(2H,s), 7.53(1H,d,J=2.4Hz), 7.68(1H,d,J=2.4Hz).

(Example 15: Final step)

(Method 1)

After dissolving ethyl 2-{4-[5-(2-bromoacetyl)-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}acetate (480 mg) and 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (251 mg) in dimethylformamide (10 ml), the mixture was stirred at room temperature overnight. Dimethylformamide was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield a light brown solid (530 mg), which was triturated with ethyl acetate-ether-*n*-hexane to obtain a colorless solid (513 mg). After dissolving this in a small amount of ethanol, 4 N hydrochloric acid-ethyl acetate (6 ml) was added and the solvent was distilled off after 5 minutes. The residue was crystallized from ethanol-ether to yield the target compound (511 mg) as almost colorless crystals (71%).

(Method 2)

Ethanol (2.5 ml) and 4 N hydrochloric acid-dioxane (2.5 ml) were added to *tert*-butyl 2-(4-{3-(*tert*-butyl)-5-[2-(5,6-diethoxy-7-fluoro-1-imino-2,3-

dihydro-1H-2-isoindolyl)acetyl]-2-methoxyphenyl}piperazino)acetate hydrobromide (49 mg) and the mixture was stirred at room temperature for 3 days. After concentrating the reaction mixture under reduced pressure, ethanol was added and the mixture was reconcentrated. The residue was triturated with ether and filtered, and then dried to yield the target compound as a colorless solid (40 mg, 86%).

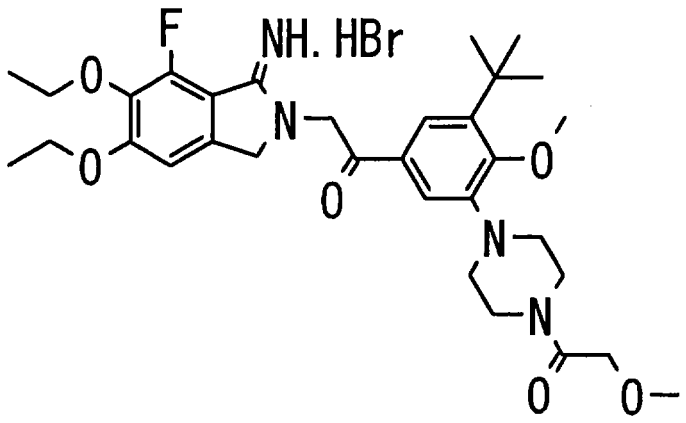
^{1}H-NMR(DMSO-d6)δ(ppm)

1.25(3H,t,J=7.0Hz), 1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz), 3.02-3.70(10H,m), 3.93(3H,s), 4.11(2H,q,J=7.0Hz), 4.18-4.25(4H,m), 4.28(1H,brs), 4.80(2H,s), 5.54(2H,s), 7.34(1H,s), 7.50(1H,s), 7.64(1H,s), 9.08(1H,brs), 9.37(1H,brs).

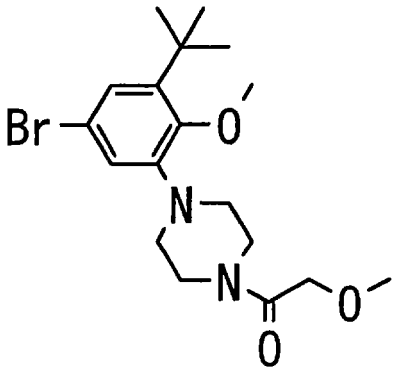
MS:m/e(ESI)613.4(MH+)

<Example 16>

1-{3-*tert*-Butyl-4-methoxy-5-[4-(2-methoxyacetyl)piperazin-1-yl]phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-{4-[5-Bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-2-methoxy-1-ethanone



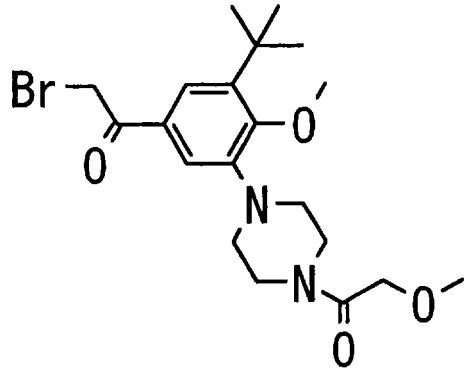
Methoxyacetyl chloride (0.28 ml) was added to a solution of 1-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazine (850 mg) and triethylamine (0.73 ml) in methylene chloride (12 ml) while cooling on ice, the mixture was brought to room temperature and stirred for 1 hour. The reaction mixture was diluted with ethyl acetate, the insoluble portion was filtered off, and the concentrated residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound

(730 mg) as light red crystals (70%).

^{1}H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 3.03(4H,brs), 3.45(3H,s), 3.67(2H,brs), 3.79(2H,brs), 3.91(3H,s), 4.15(2H,s), 6.93(1H,d,J=2.4Hz), 7.13(1H,d,J=2.4Hz).

(Step 2) 2-Bromo-1-{3-(*tert*-butyl)-4-methoxy-5-[4-(2-methoxyacetyl)piperazino]phenyl}-1-ethanone



After adding the 1-{4-[5-bromo-3-(*tert*-butyl)-2-methoxyphenyl]piperazino}-2-methoxy-1-ethanone (730 mg), tetrakis(triphenylphosphine)palladium (317 mg), tributyl(1-ethoxyvinyl)stannane (660 mg) and cesium fluoride (611 mg) to degassed dioxane (16 ml), the mixture was stirred at 90°C for 4 hours under a nitrogen stream. The mixture was then cooled to room temperature, diluted with ethyl acetate and filtered through celite, and the filtrate was concentrated under reduced pressure. The residue was dissolved in tetrahydrofuran (12 ml) and H_2O (1 ml) and cooled to 0°C, and then N-bromosuccinimide (390 mg) was added. After 5 minutes, Na_2SO_3(aq) was added, extraction was

performed with ethyl acetate, the extract was washed with brine and the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (597 mg) as a light green oil. (NMR revealed the presence of by-products that could not be easily separated). This was used directly for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 3.08(4H,brs), 3.45(3H,s), 3.70(2H,brs), 3.82(2H,brs), 4.00(3H,s), 4.16(2H,s), 4.40(2H,s), 7.50(1H,d,J=2.0Hz), 7.71(1H,d,J=2.0Hz).

(Example 16: Final step)

After dissolving 2-bromo-1-{3-(*tert*-butyl)-4-methoxy-5-[4-(2-methoxyacetyl)piperazino]phenyl}-1-ethanone (597 mg (containing impurities)) and 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (224 mg) in dimethylformamide (12 ml), the mixture was stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield the title compound as a light brown solid. This was recrystallized from acetonitrile-ethyl acetate-ether to yield the target compound as light brown crystals (430 mg) (35% from 1-{4-[5-bromo-3-(*tert*-butyl)-2-

methoxyphenyl]piperazino}-2-methoxy-1-ethanone).

^{1}H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz),

2.98(4H,brs), 3.29(3H,s), 3.61(2H,brs), 3.67(2H,brs),

3.96(3H,s), 4.11(2H,q,J=7.0Hz), 4.12(2H,s),

4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.47(2H,s), 7.34(1H,s),

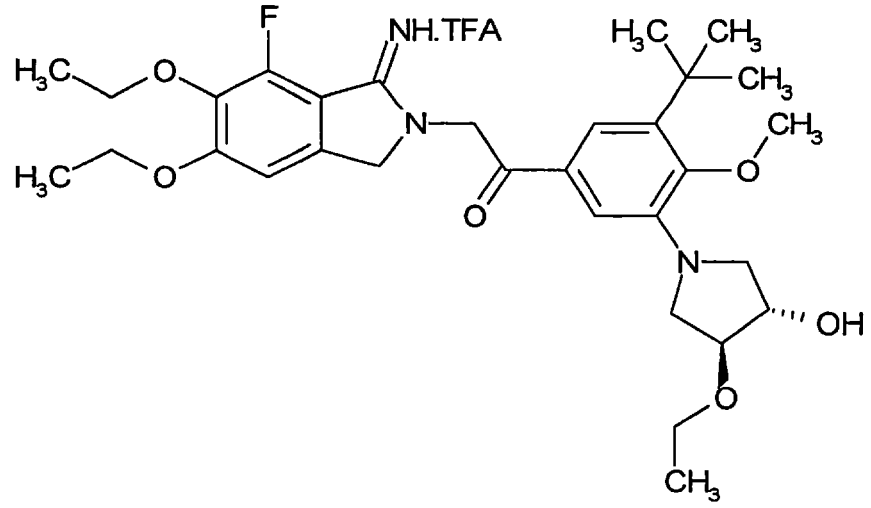
7.50(1H,d,J=2.0Hz), 7.61(1H,d,J=2.0Hz), 9.03(1H,brs),

9.28(1H,brs).

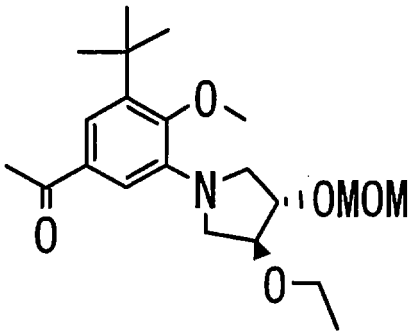
MS:m/e(ESI)599.4(MH+)

<Example 17>

1-[3-*tert*-Butyl-5-((3S,4S)-3-ethoxy-4-hydroxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)ethanone trifluoroacetate



(Step 1) 1-{3-(*tert*-Butyl)-5-[(3S,4S)-3-ethoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone



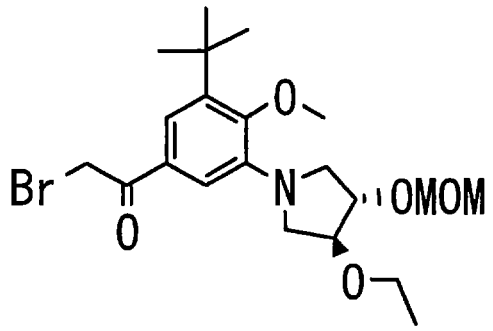
Tetra-*n*-butylammonium bromide (380 mg, 1.18 mmol) and ethyl iodide (0.4 ml, 5.0 mmol) were added to a solution of 1-{3-(*tert*-butyl)-5-[(3S,4S)-3-hydroxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone (830 mg, 2.36 mmol) in a toluene (5 ml)-50% aqueous NaOH (5 ml) mixed solvent at room temperature in that order and the mixture was stirred for 19 hours. After further adding ethyl iodide (0.2 ml) and stirring for 9 hours, more ethyl iodide (0.2 ml) was added and stirring was continued for 60 hours. The mixture was diluted with water, extraction was performed with ethyl acetate and the extract was washed with brine. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (650 mg, 73%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.22(3H,t,J=7.2Hz), 1.41(9H,s), 2.56(3H,s), 3.15-

3.28(2H,m), 3.40(3H,s),3.48-3.65(4H,m), 3.72(3H,s), 3.99-4.08(1H,m), 4.21-4.31(1H,m), 4.68-4.80(2H,m), 7.34(1H,d,J=2.0Hz), 7.52(1H,d,J=2.0Hz).

(Step 2) 2-Bromo-1-{3-(*tert*-butyl)-5-[(3S,4S)-3-ethoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone



Triethylamine (0.52 ml, 3.7 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (0.51 ml, 2.2 mmol) were added dropwise in that order to a solution of 1-{3-(*tert*-butyl)-5-[(3S,4S)-3-ethoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone (650 mg, 1.71 mmol) in tetrahydrofuran (7 ml) while cooling on ice, and the mixture was stirred at the same temperature for 25 minutes. N-bromosuccinimide (427 mg, 2.40 mmol) was then added and stirring was continued at the same temperature for 25 minutes. After completion of the reaction, the reaction mixture was diluted with saturated aqueous sodium hydrogencarbonate and ethyl acetate and the organic layer was separated. The

organic layer was washed with brine and then dried over anhydrous magnesium sulfate. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (795 mg, 100%) as a light yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

1.22(3H,t,J=7.2Hz), 1.41(9H,s), 3.12-3.30(2H,m), 3.40(3H,s), 3.48-3.65(4H,m), 3.73(3H,s), 3.99-4.08(1H,m), 4.18-4.32(1H,m), 4.42(2H,s), 4.63-4.81(2H,m), 7.37(1H,d,J=2.0Hz), 7.54(1H,d,J=2.0Hz).

(Example 17: Final step)

A solution of 5,6-diethoxy-4-fluoro-1*H*-3-isoindoleamine (95 mg, 0.40 mmol) and 2-bromo-1-{3-(*tert*-butyl)-5-[(3S,4S)-3-ethoxy-4-(methoxymethoxy)tetrahydro-1H-1-pyrrolyl]-4-methoxyphenyl}-1-ethanone (200 mg, 0.436 mmol) in dimethylformamide (3 ml) was stirred at room temperature for 68 hours. After completion of the reaction, the solvent was distilled off and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate-methanol) to yield the MOM-protected title compound (235 mg). The product was then dissolved in trifluoroacetic acid (1 ml)-H_2O (1 drop), and the mixture was stirred at room temperature for 1.5 hours. The solvent was distilled off under reduced pressure, the obtained product was

dissolved in ethyl acetate (2 ml) and the resultant solution was slowly added dropwise to stirred Et_2O (20 ml). The obtained crystals were filtered off and dried to yield the target compound (80 mg, 29%) as a brown amorphous solid.

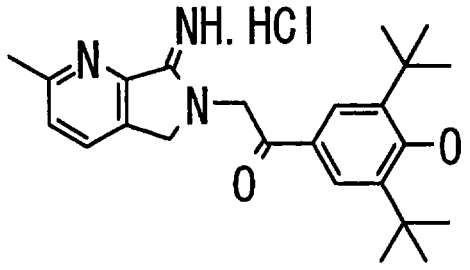
^{1}H-NMR(DMSO-d6)δ(ppm)

1.10(3H,t,J=6.8Hz), 1.29(3H,t,J=6.8Hz), 1.37(9H,s), 1.39(3H,t,J=6.8Hz), 2.90-3.12(2H,m), 3.28-3.58(4H,m), 3.63(3H,s), 3.80-3.89(1H,m), 4.11(2H,q,J=6.8Hz), 4.12-4.31(3H,m), 4.79(2H,s), 5.38-5.57(2H,m), 7.30(1H,s), 7.34(1H,s), 7.41(1H,s), 8.98-9.10(1H,m), 9.20-9.35(1H,m).

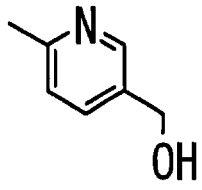
MS:m/e(ESI)572.4(MH+)

<Example 18>

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride



(Step 1) (6-Methyl-3-pyridyl)methanol

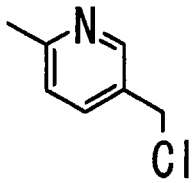


A solution of methyl 6-methylnicotinate (50 g, 0.33 mol) in anhydrous tetrahydrofuran (100 ml) was slowly added dropwise to a suspension of LAH (12.6 g, 0.33 mol) in anhydrous tetrahydrofuran (500 ml) over a period of 30 minutes while cooling on ice, and the mixture was stirred at the same temperature for 1 hour and 20 minutes. After confirming completion of the reaction by thin layer chromatography, H_2O (25 ml) was slowly added dropwise over a period of 30 minutes while cooling on ice, and the stirring was continued at room temperature for 30 minutes. Magnesium sulfate was added for drying, and the precipitate was filtered through celite and washed three times with ethyl acetate. The solvent was distilled off under reduced pressure to yield the title compound (33.6 g, 82%) as a yellow oil.

^{1}H-NMR(CDCl3)δ(ppm)

2.55(3H.s), 4.69(2H.brs), 7.16(1H.d.J=8.4Hz), 7.61(1H.dd.J=8.4and2.4Hz), 8.46(1H.d.J=2.4Hz).

(Step 2) 5-(Chloromethyl)-2-methylpyridine



Triethylamine (96 ml, 0.69 mol) was added to a solution of (6-methyl-3-pyridyl)methanol (28.4 g, 0.23 mol) in methylene chloride (230 ml) while cooling on

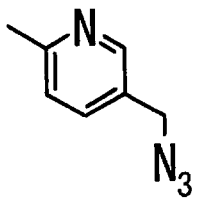
ice. Mesyl chloride (26.8 ml, 0.35 mol) was then slowly added dropwise over a period of 20 minutes at the same temperature and the mixture was stirred for 10 hours while gradually raising the temperature to room temperature. After confirming completion of the reaction by thin layer chromatography, the mixture was diluted with ethyl acetate and poured into saturated aqueous $NaHCO_3$. After separating the aqueous layer, extraction was performed with ethyl acetate, and the collected organic layer was washed with saturated aqueous NaCl and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to yield the title compound (12.2 g). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

2.56(3H.s), 4.56(2H.s), 7.16(1H.d.J=8.0Hz),

7.62(1H.dd.J=8.0and2.4Hz), 8.49(1H.d.J=2.4Hz).

(Step 3) (6-Methyl-3-pyridyl)methyl azide



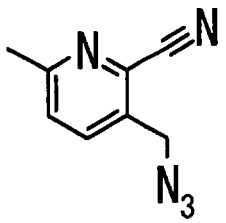
NaN_3 (11.2 g, 172 mmol) was added to a solution of the 5-(chloromethyl)-2-methylpyridine (12.2 g, 86.2 mmol) in dimethylformamide (120 ml) while cooling on

ice and the mixture was stirred at the same temperature for 1 hour and then at room temperature for 2 hours. The reaction mixture was poured into semi-saturated aqueous sodium hydrogencarbonate, extraction was performed with ethyl acetate and the extract was washed with water and saturated aqueous NaCl. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (8.9 g, 26%, two steps) as a colorless oil.

^{1}H-NMR(CDCl3)δ(ppm)

2.57(3H.s), 4.34(2H.s), 7.19(1H.d.J=8.0Hz), 7.55(1H.dd.J=8.0and2.4Hz), 8.45(1H.d.J=2.4Hz).

(Step 4) 3-(Azidomethyl)-6-methyl-2-pyridinecarbonitrile



After adding 30% aqueous hydrogen peroxide (7.5 ml, 6.6 mmol) dropwise to a solution of (6-methyl-3-pyridyl)methyl azide (8.9 g, 6.0 mmol) and maleic anhydride (6.5 g, 6.6 mmol) in methylene chloride (90 ml) over a period of 5 minutes while cooling on ice,

the mixture was stirred at room temperature for 16 hours. Maleic anhydride (3.25 g) and 30% aqueous hydrogen peroxide (3.75 ml) were added in a similar manner while cooling on ice, and the mixture was stirred at room temperature for 4 hours. Saturated aqueous sodium hydrogencarbonate (100 ml) was added to the reaction mixture, $NaHCO_3$ was further added to be basic, and extraction was performed with methylene chloride. The extract was washed with a brine and dried over anhydrous magnesium sulfate, and the solvent was distilled off to yield crude 5-(azidomethyl)-2-methyl-1-pyridiniumolate (7.45 g). This was used without further purification for the following reaction.

Trimethylsilyl cyanide (6.4 ml, 48 mmol) and dimethylcarbamyl chloride (4.2 ml, 46 mmol) were added in that order to a solution of the 5-(azidomethyl)-2-methyl-1-pyridiniumolate (7.08 g, 43.2 mmol) in methylene chloride (80 ml) at room temperature and the mixture was stirred at the same temperature for 23 hours. After confirming completion of the reaction by thin layer chromatography, saturated aqueous sodium hydrogencarbonate (80 ml) was added and the mixture was stirred for 10 minutes. The reaction mixture was diluted with ethyl acetate, the aqueous layer was separated and extraction was performed with ethyl

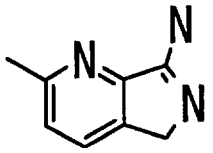
acetate. The collected organic layer was washed with water and brine and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (5.79 g, 56%, two steps) as a colorless oil.

^{1}H-NMR(CDCl3)δ(ppm)

2.62(3H.s), 4.63(2H.s), 7.41(1H.d.J=8.0Hz),

7.76(1H.d.J=8.0Hz).

(Step 5) 2-Methyl-5H-pyrrolo[3,4-b]pyridine-7-amine



Triphenylphosphine (11 g, 42 mmol) was added to a mixed solution of 3-(azidomethyl)-6-methyl-2-pyridinecarbonitrile (5.79 g, 33.4 mmol) in a tetrahydrofuran (120 ml)-H_2O (6 ml) mixed solvent while cooling on ice and the mixture was stirred at room temperature for 22 hours. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography. The solvent was distilled off from the ethyl acetate-methanol-29% aqueous ammonia (40:10:1) elution fraction, and washing was performed with ether-*n*-hexane to yield the title compound (1.65 g, 34%) as a

brown solid. The solvent was also distilled off from the washed mother liquor to yield the title compound (0.49 g). The NMR data for both compounds matched exactly.

^{1}H-NMR(DMSO-d6)δ(ppm)

2.55(3H.s), 4.39(2H.s), 6.27(brs), 7.23(1H.d.J=8.0Hz), 7.84(1H.d.J=8.0Hz).

(Example 18: Final step)

After slowly adding 60% sodium hydride (0.45 g, 11 mmol) to a solution of 2-methyl-5H-pyrrolo[3,4-b]pyridine-7-amine (1.5 g, 10 mmol) in tetrahydrofuran (30 ml) while cooling on ice, the mixture was stirred for 30 minutes. 2-Bromo-1-[3,5-di(*tert*-butyl)-4-hydroxyphenyl]-1-ethanone (4.0 g, 12 mmol) was then added and stirring was continued at room temperature for 2 hours. The solvent was distilled off and then the residue was dissolved in methanol (20 ml) and 4 N hydrochloric acid-ethyl acetate (20 ml) was added dropwise while cooling on ice. After stirring at the same temperature for 30 minutes, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography. The solvent was distilled off from the methylene chloride-methanol (5:1)-3% acetic acid elution fraction under reduced pressure to yield a crude product. The product was dissolved in EtOH and then treated with 4

N hydrochloric acid-ethyl acetate (20 ml). After distilling off the solvent under reduced pressure, the residue was recrystallized from ethanol-ethyl acetate, and the obtained crystals were washed with ethyl acetate and ether in that order and dried to yield the target compound (2.45 g, 56%) as a colorless amorphous solid.

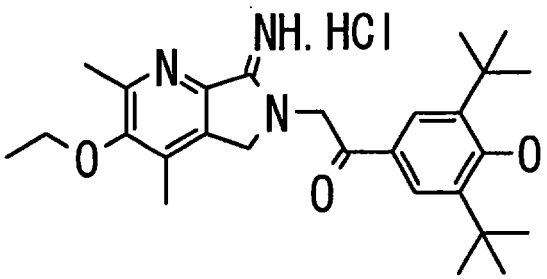
^{1}H-NMR(DMSO-d6)δ(ppm)

1.41(18H.s), 2.67(3H.s), 4.84(2H.s), 5.63(2H.s), 7.70(1H.d.J=8.0Hz), 7.78(2H.s), 8.08(1H.brs), 8.16(1H.d.J=8.0Hz), 9.63(1H.brs), 9.94(1H.brs).

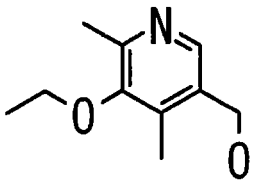
MS:m/e(ESI)394.1(MH+)

<Example 19>

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride



(Step 1) (5-Ethoxy-4,6-dimethyl-3-pyridyl)methanol



A suspension of 4-deoxypyridoxine hydrochloride

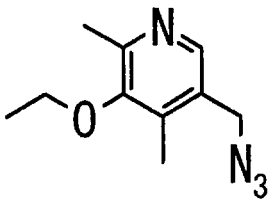
(0.99 g, 5.2 mmol) in dimethylformamide (10 ml) was added dropwise to a suspension of 60% NaH (0.42 g, 10.5 mmol) in dimethylformamide (10 ml) while cooling on ice, and the mixture was stirred at room temperature for 1 day. Ethyl iodide (0.44 ml, 5.5 mmol) was then added dropwise at room temperature and stirring was continued for 17 hours. After confirming completion of the reaction by thin layer chromatography, the mixture was poured into semi-saturated aqueous sodium hydrogencarbonate and extraction was performed with ethyl acetate-tetrahydrofuran (1:1). The extract was washed with brine and dried over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: methylene chloride-methanol) to yield the title compound (0.415 g, 44%).

^{1}H-NMR(CDCl3)δ(ppm)

1.46(3H.t.J=7.2Hz), 2.35(3H.s), 2.63(3H.s),

3.89(2H.q.J=7.2Hz), 4.75(2H.s), 8.36(1H.s).

(Step 2) (5-Ethoxy-4,6-dimethyl-3-pyridyl)methyl azide



Diphenylphosphoryl azide (0.59 ml, 2.7 mmol) and

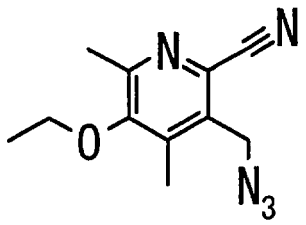
1,8-diazabicyclo[5.4.0]undec-7-ene (0.41 ml, 2.7 mmol) were added dropwise in that order to a solution of (5-ethoxy-4,6-dimethyl-3-pyridyl)methanol (0.415 g, 2.29 mmol) in toluene (5 ml) at room temperature, and the mixture was stirred for 16 hours. After confirming completion of the reaction by thin layer chromatography, the mixture was poured into water and extraction was performed with ethyl acetate. The extract was washed with saturated aqueous NaCl and dried over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (447 mg, 95%) as a colorless oil.

^{1}H-NMR(CDCl3)δ(ppm)

45(3H.t.J=7.2Hz), 2.31(3H.s), 2.54(3H.s),

3.87(3H.q.J=7.2Hz), 8.14(1H.s).

(Step 3) 3-(Azidomethyl)-5-ethoxy-4,6-dimethyl-2-pyridinecarbonitrile



After adding 75% m-chloroperbenzoic acid (600 mg, 2.60 mmol) to a solution of (5-ethoxy-4,6-dimethyl-3-

pyridyl)methyl (447 mg, 2.17 mmol) in methylene chloride (5 ml) while cooling on ice, the mixture was stirred for 5 hours while gradually raising the temperature to room temperature. After confirming completion of the reaction by thin layer chromatography, the mixture was poured into saturated aqueous sodium hydrogencarbonate and saturated with sodium chloride, after which extraction was performed with ethyl acetate-tetrahydrofuran (1:1). The extract was washed with brine and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure to yield crude N-oxide (637 mg). This compound was used without further purification for the following reaction.

Trimethylsilyl cyanide (0.30 ml, 2.2 mmol) and dimethylcarbamyl chloride (0.21 ml, 2.3 mmol) were added in that order to a solution of the N-oxide (333 mg, 1.5 mmol) in acetonitrile (6 ml) at room temperature and the mixture was stirred at the same temperature for 115 hours. After confirming completion of the reaction by thin layer chromatography, saturated aqueous sodium hydrogencarbonate was added and the mixture was stirred for 10 minutes. The reaction mixture was diluted with ethyl acetate, the aqueous layer was separated and extraction was performed with ethyl

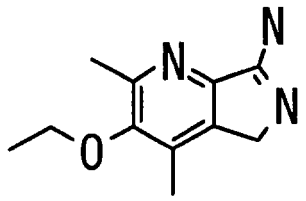
acetate. The collected organic layer was washed with water and brine and then dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (64 mg, 18%).

^{1}H-NMR(CDCl3)δ(ppm)

47(3H.t.J=7.2Hz), 2.36(3H.s), 2.54(3H.s),

3.92(2H.q.J=7.2Hz), 4.59(2H.s).

(Step 4) 3-Ethoxy-2,4-dimethyl-5H-pyrrolo[3,4-b]pyridine-7-amine



Triphenylphosphine (170 mg, 0.648 mmol) was added to a solution of the 3-(azidomethyl)-5-ethoxy-4,6-dimethyl-2-pyridinecarbonitrile (113 mg, 0.489 mmol) in a tetrahydrofuran (3 ml)-H_2O (0.15 ml) mixed solvent while cooling on ice, and the mixture was stirred at room temperature for 2.5 hours. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: ethyl acetate-methanol-29% NH_3(aq)) to yield the title compound (69 mg, 69%) as a

yellow solid.

^{1}H-NMR(DMSO-d6)δ(ppm)

35(3H.t.J=7.2Hz), 2.26(3H.s), 2.46(3H.s),

3.85(2H.q.J=7.2Hz), 4.33(2H.s).

(Example 19: Final step)

After adding 60% sodium hydride (15 mg, 0.38 mmol) to a solution of the 3-ethoxy-2,4-dimethyl-5H-pyrrolo[3,4-b]pyridine-7-amine (69 mg, 0.34 mmol) in tetrahydrofuran (3 ml) while cooling on ice, the mixture was stirred at the same temperature for 10 minutes. 2-Bromo-1-[3,5-di(*tert*-butyl)-4-hydroxyphenyl]-1-ethanone (135 mg, 0.41 mmol) was then added while stirring on ice and stirred at room temperature for 2 hours. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent = methylene chloride:methanol (30:1)-3% acetic acid). The product was dissolved in EtOH and treated with 4 N hydrochloric acid-ethyl acetate (1 ml), and the solvent was distilled off under reduced pressure. The residue was crystallized from ethanol to yield the target compound (52 mg, 32%).

^{1}H-NMR(DMSO-d6)δ(ppm)

1.40(3H.t.J=7.2Hz), 1.42(18H.s), 2.32(3H.s),

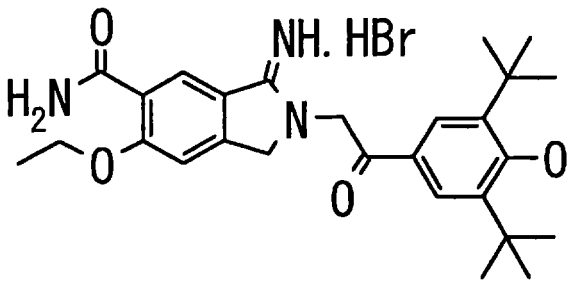
2.58(3H.s), 3.99(2H.t.J=7.2Hz), 4.81(2H.s), 5.52(2H.s),

7.76(2H.s), 8.07(1H.s), 9.37(1H.brs), 9.84(1H.brs).

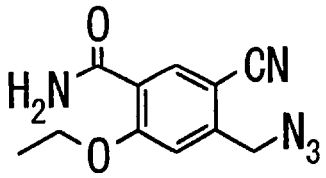
MS:m/e(ESI)452.2(MH+)

<Example 20>

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide



(Step 1) 4-(Azidomethyl)-2-ethoxy-5-(1-ethynyl)benzamide



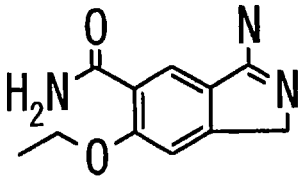
After dissolving 4-(azidomethyl)-5-cyano-2-ethoxybenzoic acid (0.7 g, 2.85 mmol) in tetrahydrofuran (15 ml), triethylamine (0.48 ml, 3.42 mmol) and ethyl chloroformate (0.3 ml, 3.14 mmol) were added while cooling on ice. The mixture was stirred for 10 minutes while cooling on ice, and then 27% aqueous ammonia (10 ml) was added and the mixture was stirred at room temperature for 10 minutes. Water (30 ml) was added to the reaction mixture, extraction was performed with ethyl acetate (20 ml x 3), and then after washing the combined organic layers with brine

(30 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The obtained crude product (0.68 g) was used directly for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.56(3H,t,J=7.3Hz), 4.34(2H,q,J=7.3Hz), 4.68(2H,s), 7.14(1H,s), 8.55(1H,s).

(Step 2) 3-Amino-6-ethoxy-1H-5-isoindolecarboxamide



After dissolving crude 4-(azidomethyl)-2-ethoxy-5-(1-ethynyl)benzamide (0.68 g, 2.8 mmol) in tetrahydrofuran (20 ml)-water (1 ml), triphenylphosphine (1.12 g, 4.3 mmol) was added while stirring at room temperature. The mixture was stirred at room temperature for 23 hours, the solvent was distilled off under reduced pressure and the residue was purified by NAM silica gel column chromatography (solvent: ethyl acetate:methanol:27% aqueous ammonia) to yield the title compound (faint brown crystals, 460 mg, 74.9%).

(Example 20: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

^{1}H-NMR(DMSO-d6)δ(ppm)

1.40(18H,s), 1.41(3H,t,J=7.5Hz), 4.84(2H,s),

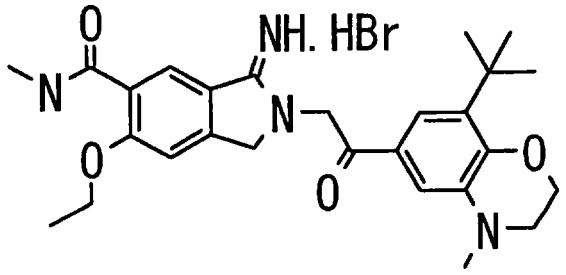
5.48(2H,s), 7.54(1H,s), 7.69(1H,brs), 7.77(2H,s),

8.07(1H,s), 8.63(1H,s), 9.15(1H,brs), 9.82(1H,brs).

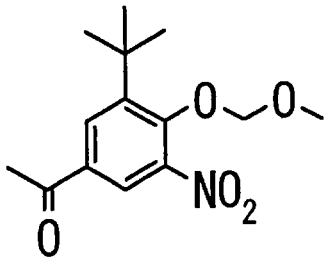
MS:m/e(ESI)466.1(MH+)

<Example 21>

2-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



(Step 1) 1-[3-(*tert*-Butyl)-4-(methoxymethoxy)-5-nitrophenyl]-1-ethanone



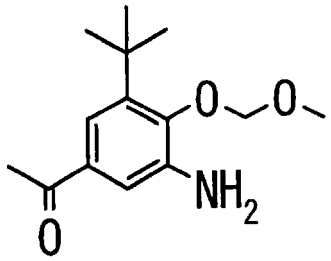
Diisopropylethylamine (65 ml, 373 mmol) was added to a solution of 1-[3-(*tert*-butyl)-4-hydroxy-5-nitrophenyl]-1-ethanone (58.6 g, 247 mmol) in tetrahydrofuran (350 ml) under a nitrogen atmosphere

while cooling on ice, and then chloromethyl methyl ether (24.5 ml, 322 mmol) was added dropwise. After stirring at the same temperature for 30 minutes, ice water (250 ml) was added and extraction was performed twice with ethyl acetate. The organic layer was washed with 1 N hydrochloric acid water, water, saturated aqueous sodium hydrogencarbonate and brine in that order. The organic layer was dried over anhydrous magnesium sulfate and then the solvent was distilled off under reduced pressure to yield the title compound (69.4 g, 99.9% yield) as a light brown oil. This was used without purification for the following reaction.

1H-NMR(CDCl3)δ(ppm)

1.42(9H,s), 2.59(3H,s), 8.08(1H,d,J=2.0Hz), 8.45(1H,d,J=2.0Hz), 11.25(1H,s).

(Step 2) 1-[3-Amino-5-(*tert*-butyl)-4-(methoxymethoxy)phenyl]-1-ethanone



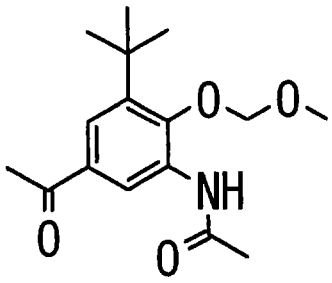
After adding 10% palladium-carbon (50% wet) (14 g) to a solution of the 1-[3-(*tert*-butyl)-4-(methoxymethoxy)-5-nitrophenyl]-1-ethanone (69.4 g,

247 mmol) in toluene (280 ml) at room temperature, the mixture was hydrogenated for 7 hours under normal pressure. The 10% palladium-carbon was removed by celite filtration and the solvent was distilled off under reduced pressure. The residue was recrystallized from hexane to yield the title compound (54.0 g, 87.1% yield) as light green granular crystals.

1H-NMR(CDCl3)δ(ppm)

1.35(9H,s), 2.46(3H,s), 3.57(3H,s), 5.01(2H,s), 5.13(2H,s), 7.14(Ih,d,J=2.0Hz), 7.27(1H,d,J=2.0Hz).

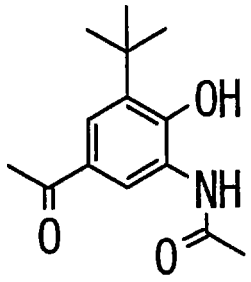
(Step 3) N1-[5-Acetyl-3-(*tert*-butyl)-2-(methoxymethoxy)phenyl]acetamide



Triethylamine (60 ml, 430 mmol) was added to a solution of the 1-[3-amino-5-(*tert*-butyl)-4-(methoxymethoxy)phenyl]-1-ethanone (53.9 g, 215 mmol) in tetrahydrofuran (270 ml) while cooling on ice under a nitrogen atmosphere and then acetyl chloride (23 ml, 323 mmol) was added dropwise. After stirring at the same temperature for 10 minutes, the mixture was stirred at room temperature for 30 minutes. The solvent was distilled off under reduced pressure,

water was added to the residue and then extraction was performed with ethyl acetate. The organic layer was washed with 1 N hydrochloric acid water, water, saturated aqueous sodium hydrogencarbonate and brine in that order. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was recrystallized from ethyl acetate-hexane to yield the title compound (56.2 g, 89.3% yield) as light brown needle-like crystals.

(Step 4) N1-[5-Acetyl-3-(*tert*-butyl)-2-hydroxyphenyl]acetamide



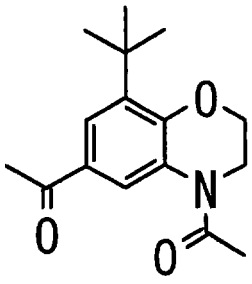
Chlorotrimethylsilane (36.5 ml, 288 mmol) was added dropwise to a solution of the N1-[5-acetyl-3-(*tert*-butyl)-2-(methoxymethoxy)phenyl]acetamide (56.2 g, 192 mmol) and sodium iodide (43.1 g, 288 mmol) in tetrahydrofuran (300 ml) under a nitrogen atmosphere while cooling on ice, and then the mixture was stirred at the same temperature for 10 minutes and at room temperature for 1 hour. The reaction mixture was poured into a saturated aqueous sodium hydrogencarbonate (400 ml)-ice (300 ml) mixed solvent

while stirring. Following extraction twice with ethyl acetate, the organic layer was washed with saturated aqueous sodium hydrogencarbonate and brine in that order. After drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was recrystallized from ethyl acetate-n-hexane to yield the title compound (first crystallization = 30.5 g, second crystallization = 3.55 g, 71.3% yield) as white needle-like crystals.

1H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 2.13(3H,s), 2.49(3H,s), 7.66(1H,d,J=2.0Hz), 7.68(1H,d,J=2.0Hz), 10.04(1H,s), 10.24(1H,s).

(Step 5) 1-[4-Acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone



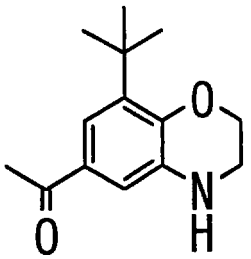
Potassium carbonate (113 g, 818 mmol) and 1,2-dibromoethane (64.1 g, 341 mmol) were added to a solution of the N1-[5-acetyl-3-(*tert*-butyl)-2-hydroxyphenyl]acetamide (34.0 g, 137 mmol) in dimethylformamide (280 ml) under a nitrogen atmosphere, and then the mixture was stirred at 70°C for 17 hours. The solvent was distilled off under reduced pressure,

ethyl acetate was added to the residue and the mixture was washed with water (3 times) and brine in that order. After drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound (36.9 g, 98.1% yield) as light red crystals. These were used without purification for the following reaction.

1H-NMR(CDCl3)δ(ppm)

1.36(9H,s), 2.26(3H,s), 2.50(3H,s), 3.88(2H,t,J=4.8Hz), 4.42(2H,t,J=4.8Hz), 7.63(1H,s), 8.05(1H,s).

(Step 6) 1-[8-(*tert*-Butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone



After adding 6 N aqueous sodium hydroxide (180 ml, 900 mmol) to a solution of the 1-[4-acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone (36.8 g, 134 mmol) in methanol (360 ml) under a nitrogen atmosphere, the mixture was stirred at 70°C for 40 minutes. The methanol was distilled off under reduced pressure, and the precipitated crystals were filtered out and dried under reduced pressure to yield the title compound (30.6 g, 98.1% yield) as bright

golden yellow crystals.

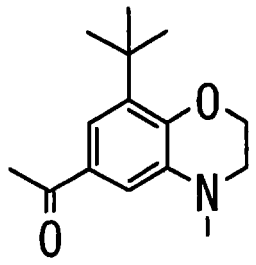
1H-NMR(CDCl3)δ(ppm)

1.33(9H,s), 2.43(3H,s), 3.32(2H,t,J=4.4Hz),

4.19(2H,t,J=4.4Hz), 5.94(1H,s), 7.08(1H,d,J=2.0Hz),

7.10(1H,d,J=2.0Hz).

(Step 7) 1-[8-(*tert*-Butyl)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone



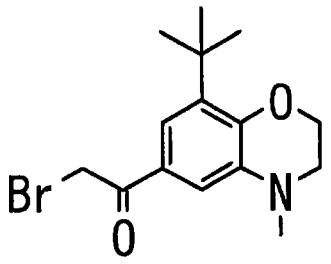
Potassium carbonate (2.43 g, 17.6 mmol) and methyl iodide (1.3 ml, 20.9 mmol) were added to a solution of the 1-[8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone (3.73 g, 16.0 mmol) in dimethylformamide (35 ml) under a nitrogen atmosphere, and the mixture was stirred at room temperature for 1 day. The solvent was distilled off under reduced pressure, ethyl acetate was added to the residue and the mixture was washed with water (twice) and brine in that order. After drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was subjected to silica gel chromatography (Wakogel-C200, 60 g) and then fractionated with 2% ethyl acetate-toluene to yield

the title compound (2.61 g, 66.0% yield) as bright golden yellow crystals.

1H-NMR(CDCl3)δ(ppm)

1.33(9H,s), 2.49(3H,s), 2.89(3H,s), 3.29(2H,t,J=4.4Hz), 4.31(2H,t,J=4.4Hz), 7.13(1H,d,J=2.0Hz), 7.24(1H,d,J=2.0Hz).

(Step 8) 2-Bromo-1-[8-(*tert*-butyl)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone



A solution of the 1-[8-(*tert*-butyl)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone (2.61 g, 10.6 mmol) and tetra-*n*-butylammonium tribromide (6.62 g, 13.7 mmol) in acetic acid was stirred at room temperature for 3.5 hours under a nitrogen atmosphere, and then *n*-butylammonium tribromide (1.02 g, 2.12 mmol) was added and stirring was continued for 45 minutes. After distilling off the solvent under reduced pressure, ethyl acetate was added to the residue and the mixture was washed with saturated aqueous sodium hydrogencarbonate (twice) and brine in that order. It was then dried over anhydrous magnesium sulfate, and the solvent was distilled off

under reduced pressure. The residue was subjected to silica gel chromatography (Wakogel-C200, 80 g) and fractionated with hexane-toluene (1:3) to yield the title compound (977 mg, 28.4% yield) as bright golden yellow crystals.

1H-NMR(CDCl3)δ(ppm)

1.33(9H,s), 2.90(3H,s), 3.30(2H,t,J=4.4Hz), 4.33(2H,t,J=4.4Hz), 4.83(2H,s), 7.18(1H,d,J=2.0Hz), 7.28(1H,d,J=2.0Hz).

(Example 21: Final step)

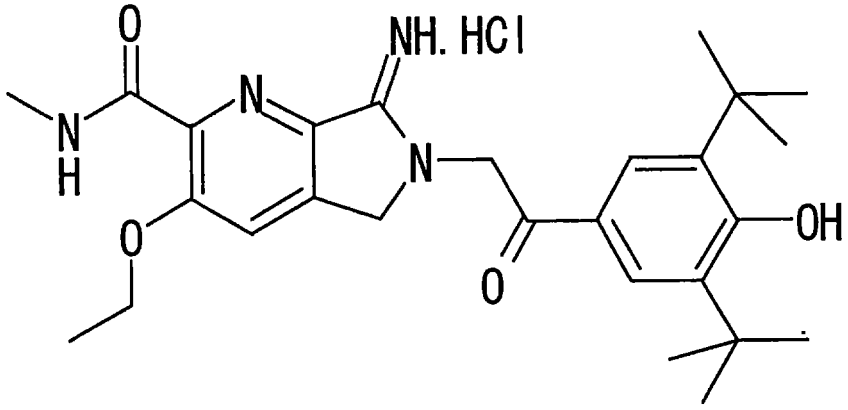
A solution of 3-amino-6-ethoxy-1H-5-isoindolecarboxamide (13 mg, 0.056 mmol) and the 2-bromo-1-[8-(*tert*-butyl)-4-methyl-3,4-dihydro-2H-1,4-benzoxazin-6-yl]-1-ethanone (22 mg, 0.067mmmol) in dimethylformamide (1 ml) was stirred at 50°C for 19 hours under a nitrogen atmosphere. The solvent was distilled off under reduced pressure, and the residue was crystallized from acetonitrile to yield the target compound (19 mg, 61% yield) as bright golden yellow crystals.

1H-NMR(DMSO-d6)δ(ppm)

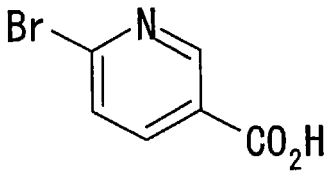
1.37(9H,s), 1.43(3H,t,J=7.2Hz), 2.84(3H,d,J=4.4Hz), 2.92(3H,s), 3.33(2H,t,J=4.4Hz), 4.31(2H,q,J=7.2Hz), 4.36(2H,t,J=4.4Hz), 4.85(2H,s), 5.47(2H,s), 7.18(1H,d,J=2.0Hz), 7.30(1H,d,J=2.0Hz), 7.55(1H,s), 8.21(1H,q,J=4,4Hz), 8.57(1H,s), 9.18(1H,s), 9.83(1H,s).

<Example 22>

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride



(Step 1) 6-Bromonicotinic acid



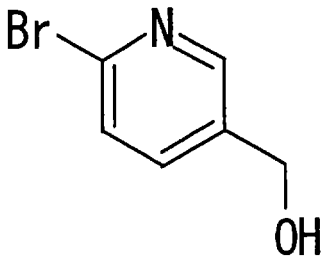
After dissolving 2-bromo-5-picoline (100 g, 0.291 mol) in 1000 ml of water, Aliquat336 (2 ml) was added, and then potassium permanganate (251 g, 0.797 mol) was gradually added over a period of 1 hour and 30 minutes while stirring at 110°C. This mixture was further stirred for an hour, the reaction mixture was filtered through celite without cooling and washed with water, and the filtrate was concentrated to approximately half volume under reduced pressure. After adding 48% hydrobromic acid (~300 ml), the precipitated crystals were filtered, washed with water and dried to yield

the title compound (white crystals 52 g, 44%).

^{1}H-NMR(CDCl3)δ(ppm)

7.64(1H,d,J=8.0Hz), 8.08(1H,d,J=8.0Hz), 9.03(1H,s).

(Step 2) (6-Bromo-3-pyridyl)methanol



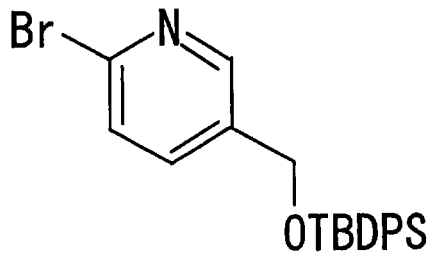
After dissolving 6-bromonicotinic acid (65.7 g, 0.325 mol) in tetrahydrofuran (1600 ml), triethylamine (54 ml, 0.39 mol) and ethyl chloroformate (32.6 ml, 0.341 mol) were added while stirring on ice. The mixture was stirred for 20 minutes while cooling on ice, and the white crystals which precipitated upon filtration were removed and washed with tetrahydrofuran. The filtrate was stirred while cooling on ice, and an aqueous solution (211 ml) of sodium borohydride (18.4 g, 0.488 mol) was gradually added dropwise over a period of 30 minutes. After continued stirring for 1 hour and 20 minutes while cooling on ice, 800 ml of water was added and extraction was performed with ethyl acetate (600 ml x 2), and then after washing the combined organic layers with brine (300 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound (45.5 g,

74.5%). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

4.70(2H,s), 7.46(1H,d,J=8.0Hz), 7.59(1H,d,J=8.0Hz), 8.34(1H,brs).

(Step 3) (6-Bromo-3-pyridyl)methyl [1-(*tert*-butyl)-1,1-diphenylsilyl] ether

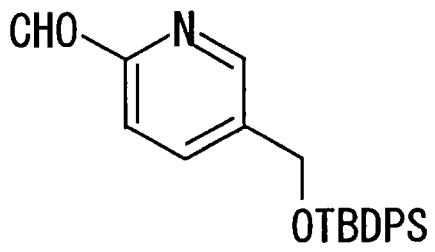


After dissolving the (6-bromo-3-pyridyl)methanol (45.5 g, 0.242 mol) in dimethylformamide (500 ml), *tert*-butyl diphenylsilyl chloride (69 ml, 0.266 mol) and imidazole (18 g, 0.264 mol) were added while stirring at room temperature. The mixture was stirred at room temperature for an additional 17 hours, 500 ml of water was added and extraction was performed with diethyl ether (500 ml x 2), and then after washing the combined organic layers with brine (500 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (light yellow syrup, 76.9 g, 74.3%).

^{1}H-NMR(CDCl3)δ(ppm)

1.08(9H,s), 4.71(2H,s), 7.34-7.47(6H,m),
7.52(1H,d,J=8.0Hz), 7.65(4H,d,J=8.0Hz),
7.71(1H,d,J=8.0Hz), 8.29(1H,s).

(Step 4) 5-({[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarbaldehyde



After dissolving (6-bromo-3-pyridyl)methyl [1-(*tert*-butyl)-1,1-diphenylsilyl] ether (119 g, 0.279 mol) in tetrahydrofuran (1400 ml), n-butyllithium (1.5 M n-hexane solution, 195 ml, 0.293 mol) was added dropwise at -70°C while stirring for a period of 30 minutes. The mixture was stirred for an additional 40 minutes at -70°C, N-formylmorpholine (56.1 ml, 0.558 mol) was added all at once, stirring was continued for 90 minutes, and then saturated aqueous ammonium chloride (700 ml) was added and the temperature was raised to room temperature. Extraction was performed with ethyl acetate (600 ml x 2), and then after washing the combined organic layers with brine (500 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to

yield the title compound (59.5 g, 57%).

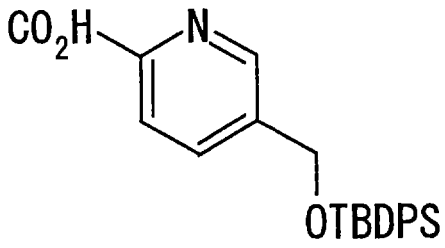
^{1}H-NMR(CDCl3)δ(ppm)

1.08(9H,s), 4.85(2H,s), 7.33-7.78(10H,m),

7.83(1H,d,J=8.0Hz), 7.94(1H,d,J=8.0Hz), 8.72(1H,s),

10.07(1H,s).

(Step 5) 5-({[1-(*tert*-Butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarboxylic acid



After dissolving the 5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarbaldehyde (59.5 g, 0.158 mol) in *t*-butanol (1050 ml) and water (210 ml), NaH_2PO_4-$2H_2O$ (246 g, 1.58 mol), 2-methyl-2-butene (201 ml, 1.90 mol) and $NaClO_2$ (143 g, 1.58 mol) were added in that order while stirring on ice, and then the mixture was further stirred at room temperature for 80 minutes. Water (600 ml) was added to the reaction mixture, extraction was performed with a 1:1 ethyl acetate-tetrahydrofuran mixed solvent (500 ml x 3), and then after washing the combined organic layers with brine (500 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound (53.5 g). This was used without further purification for the

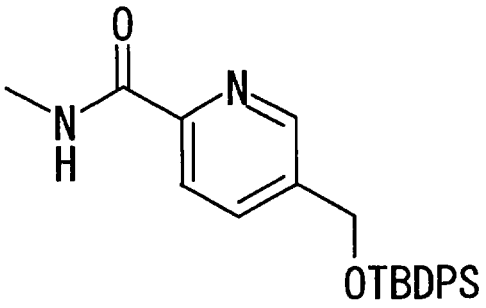
following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.07(9H,s), 4.85(2H,s), 7.33-7.78(10H,m),

7.88(1H,d,J=8.0Hz), 8.18(1H,d,J=8.0Hz), 8.55(1H,s).

(Step 6) N2-Methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarboxamide



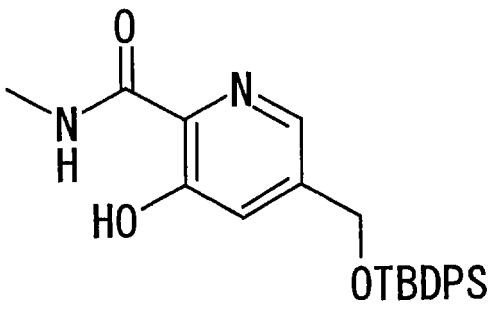
After dissolving 5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarboxylic acid (48.3 g, 0.123 mol) in tetrahydrofuran (615 ml), triethylamine (20.6 ml, 0.148 mol) and ethyl chloroformate (12.9 ml, 0.135 mol) were added while stirring on ice. The mixture was further stirred for 15 minutes while cooling on ice, a 10% aqueous methylamine solution (100 ml) was added, and stirring was continued for 15 minutes while cooling on ice. Brine (400 ml) was added, extraction was performed with a 1:1 ethyl acetate-tetrahydrofuran mixed solvent (400 ml x 5), the extract was dried over anhydrous magnesium sulfate, and then the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent:

dichloromethane-methanol) to yield the title compound (white crystals, 31.9 g, 64.2%).

^{1}H-NMR(CDCl3)δ(ppm)

1.08(9H,s), 3.03(3H,d,J=4.0Hz), 4.80(2H,s), 7.33-7.49(6H,m), 7.65(4H,d,8.0Hz), 7.77(1H,d,J=8.0Hz), 7.99(1H,brs), 8.15(1H,d,J=8.0Hz), 8.27(1H,s).

(Step 7) N2-Methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-hydroxy-2-pyridinecarboxamide



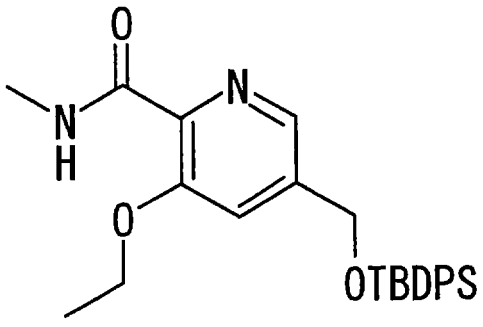
After dissolving the N2-methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-2-pyridinecarboxamide (31.9 g, 78.9 mmol) in tetrahydrofuran (526 ml), n-butyllithium (1.5 M *n*-hexane solution, 132 ml, 198 mmol) was added dropwise at -78°C while stirring over a period of 20 minutes. The mixture was stirred at -78°C for 50 minutes, $B(OMe)_3$ (35.4 ml, 316 mmol) was added, and then stirring was continued for 10 minutes, and at 0°C for 20 minutes. A mixture of 30% aqueous hydrogen peroxide (70 ml), 27% aqueous ammonia and ammonium chloride (28.3 g) was added while stirring on ice, and

stirring was continued at room temperature for 90 minutes. A 10% aqueous citric acid solution was added until the reaction mixture was acidic, extraction was performed with ethyl acetate (250 ml x 2), and then after washing the combined organic layers with brine (300 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (light yellow crystals 17.4 g, 52.5%).

^{1}H-NMR(CDCl3)δ(ppm)

1.09(9H,s), 3.02(3H,d,J=4.0Hz), 4.75(2H,s), 7.31(1H,brs), 7.35-7.74(10H,m), 7.96(1H,brs), 7.97(1H,d,J=1.5Hz), 12.17(1H,s).

(Step 8) N2-Methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-ethoxy-2-pyridinecarboxamide



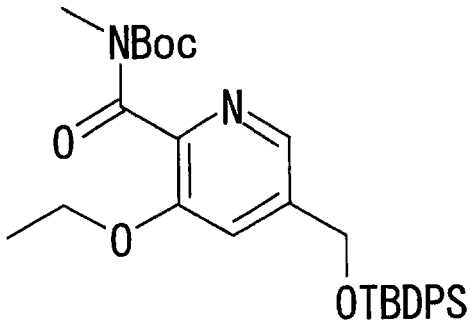
After dissolving N2-methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-hydroxy-2-

pyridinecarboxamide (17.4 g, 41.4 mmol) in dimethylformamide (83 ml), ethyl iodide (3.6 ml, 45.5 mmol) and potassium carbonate (6.3 g, 45.5 mmol) were added while stirring at room temperature. The mixture was stirred at room temperature for an additional 9 hours, water (100 ml) was added and extraction was performed with ethyl acetate (80 ml x 2), and then after washing the combined organic layers with brine (80 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound (22.5 g). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.08(9H,s), 1.49(3H,t,J=7.3Hz), 2.99(3H,d,J=4.0Hz), 4.10(2H,q,J=7.3Hz), 4.80(2H,s), 7.32-7.72(11H,m), 8.09(1H,s).

(Step 9) tert-Butyl N-{[5-({[1-(tert-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-ethoxy-2-pyridyl]carbonyl}-N-methylcarbamate

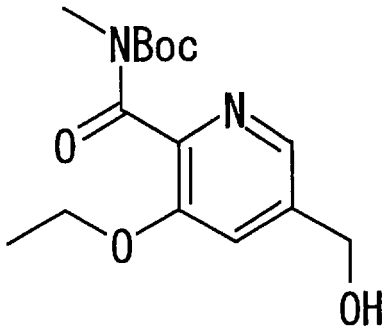


After dissolving the N2-methyl-5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-ethoxy-2-pyridinecarboxamide (crude, 41.4 mmol) in acetonitrile (140 ml), triethylamine (6.9 ml, 49.7 mmol), dimethylaminopyridine (0.51 g, 4.14 mmol) and *tert*-butyl dicarbonate (9.39 g, 43.5 mmol) were added at room temperature while stirring and the mixture was stirred at room temperature for 14 hours. The reaction mixture was concentrated to half volume under reduced pressure, water (100 ml) was added and extraction was performed with ethyl acetate (80 ml x 2), and then after washing the combined organic layers with brine (80 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield a crude product (23.2 g). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.08(9H,s), 1.15(9H,s), 1.39(3H,t,J=7.0Hz), 3.32(3H,s), 4.01(2H,q,J=7.0Hz), 4.77(2H,s), 7.20(1H,s), 7.34-7.75(10H,m), 8.06(1H,s).

(Step 10) <u>*tert*-Butyl N-{[3-ethoxy-5-(hydroxymethyl)-2-pyridyl]carbonyl}-N-methylcarbamate</u>

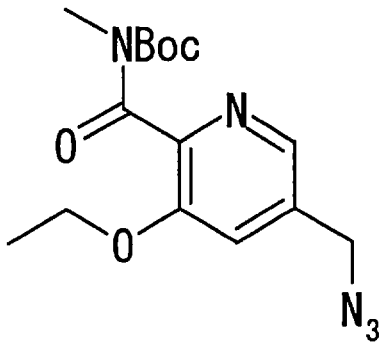


After dissolving *tert*-butyl N-{[5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-ethoxy-2-pyridyl]carbonyl}-N-methyl carbamate (crude, 41.4 mmol) in tetrahydrofuran (120 ml), tris(dimethylamino)sulfur (trimethylsilyl)difluoride (12.5 g, 45.5 mmol) was added while stirring on ice. The mixture was then stirred for an additional 20 minutes while cooling on ice, water (100 ml) was added and extraction was performed with ethyl acetate (80 ml x 3), and then after washing the combined organic layers with brine (100 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (7.9 g, 61.6% 3 step).

^{1}H-NMR(CDCl3)δ(ppm)

1.19(9H,s), 1.39(3H,t,J=7.0), 3.34(3H,s), 4.06(2H,q,J=7.0Hz), 4.74(2H,brs), 7.26(1H,s), 8.07(1H,s).

(Step 11) 1-[(6-{[(*tert*-Butoxycarbonyl)(methyl)amino]carbonyl}-5-ethoxy-3-pyridyl)methyl]-1,2-triazadien-2-ium



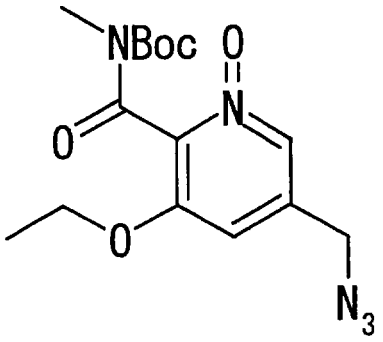
After dissolving the N-{[5-({[1-(*tert*-butyl)-1,1-diphenylsilyl]oxy}methyl)-3-ethoxy-2-pyridyl]carbonyl}-N-methyl carbamate (7.9 g, 25.5 mmol) in toluene (100 ml), diphenylphosphoryl azide (6.0 ml, 28.1 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (4.2 ml, 28.1 ml) were added while stirring on ice, and the mixture was further stirred at room temperature for 5 hours. Water (100 ml) was added and extraction was performed with ethyl acetate (80 ml x 2), and then after washing the combined organic layers with brine (100 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure to yield the title compound (7.85 g). This was used without further purification for the following reaction.

^{1}H-NMR(CDCl3)δ(ppm)

1.18(9H,s), 1.41(3H,t,J=7.0), 3.34(3H,s),

4.07(2H,q,J=7.0Hz), 4.39(2H,s), 7.15(1H,s), 8.09(1H,s).

(Step 12) 5-(Azidomethyl)-2-{[(*tert*-butoxycarbonyl)(methyl)amino]carbonyl}-3-ethoxy-1-pyridiniumolate



After dissolving the 1-[(6-{[(*tert*-butoxycarbonyl)(methyl)amino]carbonyl}-5-ethoxy-3-pyridyl)methyl]-1,2-triazadien-2-ium (crude product, 25.2 mmol) in dichloromethane (120 ml), m-chloroperbenzoic acid (6.92 g, 28.1 mmol) was added at room temperature while stirring and the mixture was stirred at room temperature for 4 hours. The reaction mixture was concentrated under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (9.74 g, 100% up).

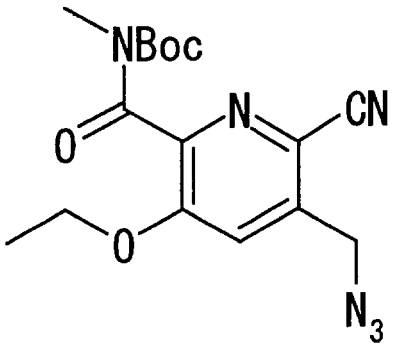
^{1}H-NMR(CDCl3)δ(ppm)

1.30(9H,s), 1.38(3H,t,J=7.0), 3.33(3H,s),

4.10(2H,q,J=7.0Hz), 4.33(2H,s), 6.77(1H,s), 7.83(1H,s).

(Step 13) 1-[(6-{[(*tert*-Butoxycarbonyl)(methyl)amino]carbonyl}-2-cyano-5-

ethoxy-3-pyridyl)methyl]-1,2-triazadien-2-ium

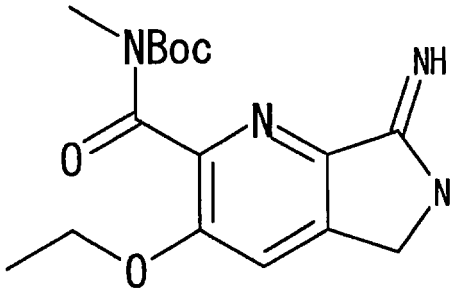


After dissolving 5-(azidomethyl)-2-{[(*tert*-butoxycarbonyl)(methyl)amino]carbonyl}-3-ethoxy-1-pyridiniumolate (9.74 g, 27.7 mmol) in acetonitrile (140 ml), trimethylsilyl cyanide (5.5 ml, 41.6 ml) and dimethylcarbamyl chloride (3.8 ml, 41.6 ml) were added at room temperature while stirring and the mixture was further stirred at 80°C for 24 hours. It was then cooled to room temperature, water (100 ml) was added and extraction was performed with ethyl acetate (80 ml x 2), and then after washing the combined organic layers with brine (100 ml) and drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (faint blue oil, 8.3 g, 83%).

^{1}H-NMR(CDCl3)δ(ppm)

1.28(9H,s), 1.44(3H,t,J=7.0), 3.32(3H,s), 4.17(2H,q,J=7.0Hz), 4.69(2H,s), 7.27(1H,s).

(Step 14) tert-Butyl N-[(7-amino-3-ethoxy-5H-pyrrolo[3,4-b]pyridin-2-yl)carbonyl]-N-methylcarbamate



After dissolving the 1-[(6-{[(tert-butoxycarbonyl)(methyl)amino]carbonyl}-2-cyano-5-ethoxy-3-pyridyl)methyl]-1,2-triazadien-2-ium (8.3 g, 23 mmol) in tetrahydrofuran (100 ml) and water (5 ml), PPh_3 (10.3 g, 39.1 mmol) was added while stirring on ice and the mixture was further stirred at room temperature for 90 minutes. The reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (solvent: ethyl acetate:methanol:27% aqueous ammonia = 3:1:0.1) to yield the title compound (brown solid, 5.63 g, 73.5%).

^{1}H-NMR(DMSO-d_6)δ(ppm)

1.02(9H,s), 1.27(3H,t,J=7.0Hz), 3.18(3H,s),

4.11(2H,q,J=7.0Hz), 4.46(2H,s), 7.72(1H,s).

(Example 22: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

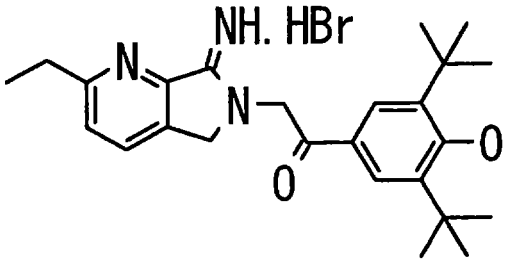
^{1}H-NMR(DMSO-d_6)δ(ppm)

1.35(3H,t,J=7.0Hz), 1.41(18H,s), 2.77(3H,d,J=4.2Hz), 4.25(2H,q,J=7.0Hz), 87(2H,s), 5.52(2H,s), 7.76(2H,s), 7.99(1H,s), 8.07(1H,s), 8.53(1H,brq,J=4.2Hz), 9.40(1H,brs), 9.95(1H,brs).

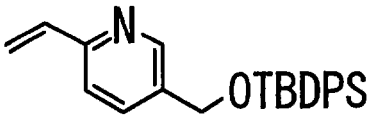
MS:m/e(ESI)481.2(MH+)

<Example 23>

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide



(Step 1) 1-(*tert*-Butyl)-1,1-diphenylsilyl [(6-vinyl-3-pyridyl)methyl] ether



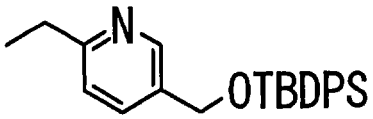
After dissolving 1-(*tert*-butyl)-1,1-diphenylsilyl [(6-chloro-3-pyridyl)methyl] ether (20 g, 52.3 mmol) in toluene (104 ml) and degassing the solution, tetrakis(triphenylphosphine)palladium (3.0 g, 2.6 mmol) and tributylvinyltin (16.5 ml, 56.5 mmol) were added under a nitrogen stream and the mixture was

heated to reflux at 120°C for 7 hours. The reaction mixture was then cooled to room temperature and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (17.46 g) as a colorless oil. (89.3% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.07(9H,s), 4.75(2H,s), 5.46(1H,d,J=10Hz), 6.18(1H,d,J=20Hz), 6.82(1H,dd,J=10Hz,J=20Hz), 7.31(1H,d,J=8.0Hz), 7.35-7.45(6H,m), 7.62(1H,d,J=8.0Hz), 7.66(4H,d,J=7.0Hz), 8.53(1H,s).

(Step 2) 1-(*tert*-Butyl)-1,1-diphenylsilyl [(6-ethyl-3-pyridyl)methyl] ether



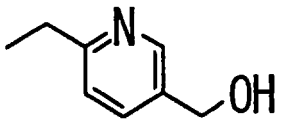
After dissolving 1-(*tert*-butyl)-1,1-diphenylsilyl [(6-vinyl-3-pyridyl)methyl] ether (8 g, 21.4 mmol) in ethyl acetate (80 ml), 10% palladium-carbon (3 g) was added and the mixture was stirred at room temperature for 0.5 hour under a hydrogen stream. The reaction mixture was filtered through celite and concentrated. The title compound (7.81 g) was obtained as a light yellow oil. (97.1% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.07(9H,s), 1.31(3H,t,J=7.6Hz), 2.82(2H,q,J=7.6Hz), 4.74(2H,s), 7.12(1H,d,J=8.0Hz), 7.34-7.48(6H,m),

7.55(1H,d,J=8.0Hz), 7.67(4H,d,J=7.0Hz), 8.45(1H,s).

(Step 3) (6-Ethyl-3-pyridyl)methanol

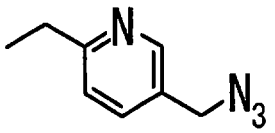


After dissolving the 1-(*tert*-butyl)-1,1-diphenylsilyl [(6-ethyl-3-pyridyl)methyl] ether (7.81 g, 20.8 mmol) in tetrahydrofuran (80 ml), TBAF (31.2 ml, 31.2 mmol) was added and the mixture was stirred at room temperature for 1 hour. The reaction mixture was quenched with water and was extracted with ethyl acetate. After washing the extract with brine, it was dried over anhydrous sodium sulfate and filtered, the filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (2.25 g) as a colorless oil. (78.8% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.28(3H,t,J=7.6Hz), 2.31(1H,s), 2.81(2H,q,J=7.6Hz), 4.67(2H,s), 15(1H,d,J=8.0Hz), 7.63(1H,d,J=8.0Hz), 8.46(1H,s).

(Step 4) (6-Ethyl-3-pyridyl)methyl azide



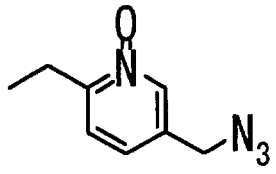
After dissolving (6-ethyl-3-pyridyl)methanol

(2.25 g, 16.4 mmol) in toluene (25 ml), diphenylphosphoryl azide (4.2 ml, 19.6 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (2.9 ml, 19.6 mmol) were added while stirring on ice, and the mixture was further stirred at room temperature for 18 hours. Water was added for treatment and extraction was performed with ethyl acetate. The extract was washed with brine and then dried over sodium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (2.2 g) as a yellow oil. (84.5% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.31(3H,t,J=7.6Hz), 2.84(2H,q,J=7.6Hz), 4.33(2H,s), 7.18(1H,d,J=8.0Hz), 7.56(1H,d,J=8.0Hz), 8.46(1H,s).

(Step 5) 5-(Azidomethyl)-2-ethyl-1-pyridiniumolate



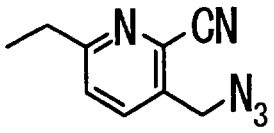
After dissolving the (6-ethyl-3-pyridyl)methyl azide (2.24 g, 13.8 mmol) in methylene chloride (25 ml), m-chloroperbenzoic acid (3.7 g, 15 mmol) was added while stirring on ice, and the mixture was stirred at room temperature for 18 hours. Saturated aqueous sodium hydrogencarbonate was added for

treatment and extraction was performed with methylene chloride. The extract was dried over sodium sulfate and filtered, the filtrate was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate = 1:2 → ethyl acetate-methanol = 4:1). The title compound was obtained (2.16 g) as a light yellow oil. (87.6% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.28(3H,t,J=7.6Hz), 2.92(2H,q,J=7.6Hz), 4.31(2H,s), 7.17(1H,d,J=8.0Hz), 7.24(1H,d,J=8.0Hz), 8.23(1H,s).

(Step 6) 3-(Azidomethyl)-6-ethyl-2-pyridinecarbonitrile



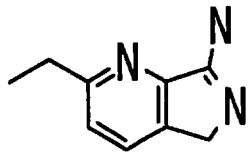
After dissolving 5-(azidomethyl)-2-ethyl-1-pyridiniumolate (2.16 g, 12.1 mmol) in acetonitrile (25 ml), 1.77 ml of trimethylsilylnitrile (13.3 mmol) and 1.23 ml of dimethylcarbamoyl chloride (13.3 mmol) were added under a nitrogen stream and the mixture was stirred at room temperature for 66 hours. Saturated aqueous sodium hydrogencarbonate was added for treatment and extraction was performed with ethyl acetate. The extract was dried over anhydrous sodium sulfate, the filtrate was concentrated under reduced pressure and the residue was purified by silica gel

column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (2.05 g) as a colorless oil. (90.4% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.31(3H,t,J=7.6Hz), 2.87(2H,q,J=7.6Hz), 4.62(2H,s), 7.41(1H,d,J=8.0Hz), 7.77(1H,d,J=8.0Hz).

(Step 7) 2-Ethyl-5H-pyrrolo[3,4-b]pyridine-7-amine



After dissolving 3-(azidomethyl)-6-ethyl-2-pyridinecarbonitrile (1.0 g, 5.34 mmol) in tetrahydrofuran (16 ml)-water (0.8 ml), triphenylphosphine (2.1 g, 8.01 mmol) was added while stirring on ice, and the mixture was further stirred at room temperature for 2.0 hours. The reaction mixture was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: ethyl acetate, ethyl acetate:methanol = 4:1, ethyl acetate:methanol: aqueous ammonia = 2:1:0.1 in this order). The title compound (0.769 g) was obtained as a light green substance. (89.3% yield)

^{1}H-NMR(CDCl3)δ(ppm)

1.33(3H,t,J=7.6Hz), 2.89(2H,q,J=7.6Hz), 4.47(2H,br), 4.56(2H,s), 16(1H,d,J=8.0Hz), 7.73(1H,d,J=8.0Hz).

(Example 23: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

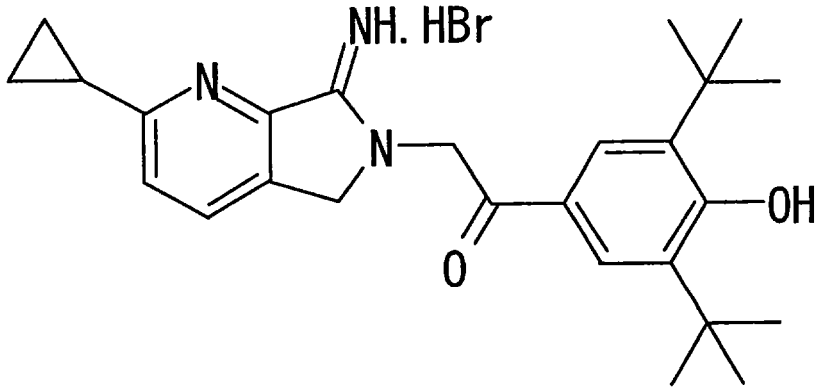
^{1}H-NMR(DMSO-d6)δ(ppm)

1.31(3H,t,J=7.6Hz), 1.42(18H,s), 2.94(2H,q,J=7.6Hz), 4.85(2H,s), 5.56(2H,s), 7.73(1H,d,J=8.0Hz), 7.77(2H,s), 8.18(1H,d,J=8.0Hz), 9.85(1H,s).

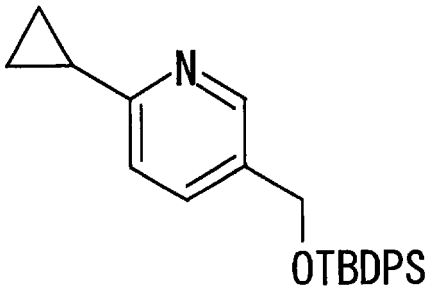
MS:m/e(ESI)408.2(MH+)

<Example 24>

2-(2-Cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide



(Step 1) 1-(*tert*-Butyl)-1,1-diphenylsilyl [(6-cyclopropyl-3-pyridyl)methyl] ether

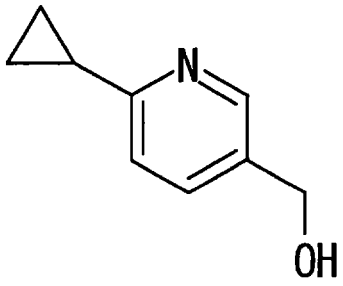


The following procedure was carried out to prepare 1.0 M cyclopropylmagnesium bromide. One third of a solution of cyclopropyl bromide (2.1 ml, 26 mmol) in anhydrous tetrahydrofuran (24 ml) was added all at once to magnesium (0.64 g, 26 mmol atom) prior to vigorous heating to reflux. The remaining two thirds of the solution was slowly added dropwise over a period of 15 minutes, and the reaction mixture was stirred for 30 minutes while heating to reflux. This was cooled to room temperature and used for the following reaction.

$NiCl_2(dppf)_2$ (0.45 g, 0.66 mmol) was added to a solution of 1-(*tert*-butyl)-1,1-diphenylsilyl [(6-chloro-3-pyridyl)methyl] ether (5.0 g, 13 mmol) in tetrahydrofuran (26 ml) at room temperature, after which 1.0 M cyclopropylmagnesium bromide (16 ml) was slowly added dropwise and stirring was continued at room temperature for 5.5 hours. Next, 1.0 M cyclopropylmagnesium bromide (10 ml) was slowly added dropwise over a period of 1.5 hours and stirring was continued for 15 hours. Saturated aqueous NH_4Cl was

added, and then the mixture was stirred for 3 hours and filtered through celite and extraction was performed with ethyl acetate. After drying with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.3 g) as a mixture with impurities. This product was used without further purification for the following reaction.

(Step 2) (6-Cyclopropyl-3-pyridyl)methanol



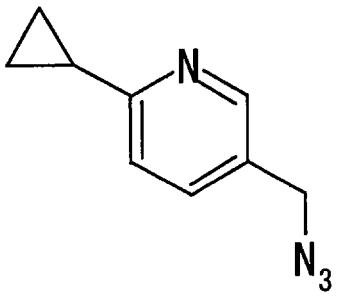
After adding 1.0 M tetra *n*-butylammonium fluoride-tetrahydrofuran (3.7 ml, 3.7 mmol) to a solution of 1-(*tert*-butyl)-1,1-diphenylsilyl [(6-cyclopropyl-3-pyridyl)methyl] ether (1.3 g) in tetrahydrofuran (7 ml) dropwise while cooling on ice, the mixture was stirred for 1 hour. After confirming completion of the reaction by thin layer chromatography, the solvent was distilled off under reduced pressure and the obtained residue was purified by silica gel column chromatography (solvent: n-

hexane-ethyl acetate) to yield the title compound (283 mg, two steps, 14%) as a colorless oil.

^{1}H-NMR(CDCl3)δ(ppm)

0.88-1.07(4H.m), 1.80-1.95(1H.m), 1.99-2.09(1H.m), 4.65(2H.s), 7.11(1H.d.J=8.0Hz), 7.56(1H.brd.J=8.0Hz), 8.39(1H.brs).

(Step 3) (6-Cyclopropyl-3-pyridyl)methyl azide



Diphenylphosphoryl azide (0.49 ml, 2.3 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.34 ml, 2.3 mmol) were added dropwise in that order at room temperature to a solution of (6-cyclopropyl-3-pyridyl)methanol (283 mg, 1.90 mmol) in toluene (4 ml) and the mixture was stirred for 3 hours. After confirming completion of the reaction by thin layer chromatography, it was diluted with ethyl acetate and washed with water and brine. Drying was performed with anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (330 mg, quant.) as a colorless oil.

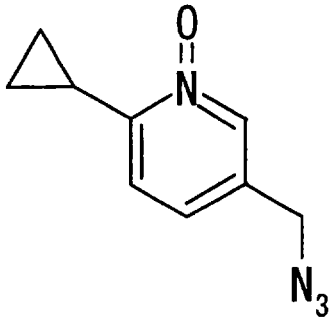
^{1}H-NMR(CDCl3)δ(ppm)

0.80-1.20(4H.s), 1.95-2.11(1H.m), 4.30(2H.s),

7.15(1H.d.J=8.0Hz), 7.50(1H.dd.J=8.0and2.4Hz),

8.38(1H.d.J=2.4Hz).

(Step 4) 5-(Azidomethyl)-2-cyclopropyl-1-pyridinium oxide



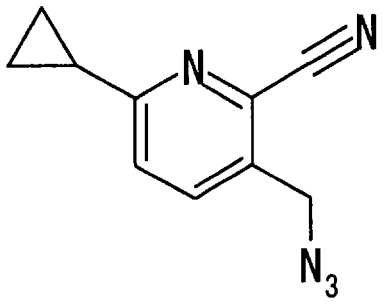
After adding 75% m-chloroperbenzoic acid (560 mg, 2.27 mmol) to a solution of (6-cyclopropyl-3-pyridyl)methyl azide (330 mg, 1.89 mmol) in methylene chloride (4 ml) while cooling on ice, the mixture was stirred for 17 hours while gradually raising the temperature to room temperature. After confirming completion of the reaction by thin layer chromatography, the reaction mixture was directly purified by silica gel column chromatography to yield the title compound (227 mg, 63%) as a colorless oil from the ethyl acetate-methanol (10:1) elution fraction.

^{1}H-NMR(CDCl3)δ(ppm)

0.71-0.89(2H.m), 1.11-1.31(2H.m), 2.63-2.80(1H.m),

4.30(2H.s), 6.87(1H.d.J=8.0Hz), 7.11(1H.brd.J=8.0Hz), 8.26(1H.brs).

(Step 5) 3-(Azidomethyl)-6-cyclopropyl-2-pyridinecarbonitrile



Trimethylsilyl cyanide (0.19 ml, 1.4 mmol) and dimethylcarbamyl chloride (0.13 ml, 1.4 mmol) were added in that order at room temperature to a solution of 5-(azidomethyl)-2-cyclopropyl-1-pyridinium oxide (227 mg, 1.19 mmol) in acetonitrile (4 ml), and the mixture was stirred at room temperature for 95 hours. After confirming completion of the reaction by thin layer chromatography, saturated aqueous sodium hydrogencarbonate was added and the mixture was stirred for 10 minutes. The reaction mixture was diluted with ethyl acetate, the aqueous layer was separated and extraction was performed with ethyl acetate. The collected organic layer was washed with water and brine and dried over anhydrous magnesium sulfate. The solvent was distilled off and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to

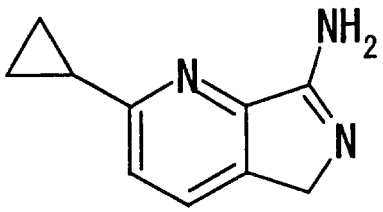
yield the title compound (230 mg, 97%).

^{1}H-NMR(CDCl3)δ(ppm)

1.00-1.20(4H.m), 2.00-2.15(1H.m), 4.58(2H.s),

7.38(1H.d.J=8.4Hz), 7.67(1H.d.J=8.4Hz).

(Step 6) Synthesis of 2-Cyclopropyl-5H-pyrrolo[3,4-b]pyridine-7-amine



Triphenylphosphine (365 mg, 1.39 mmol) was added at room temperature to a solution of the 3-(azidomethyl)-6-cyclopropyl-2-pyridinecarbonitrile (230 mg, 1.15 mmol) in a tetrahydrofuran (4 ml)-H_2O (0.2 ml) mixed solvent and the mixture was stirred for 3 hours. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography, to yield the title compound (180 mg, 90%) as a white amorphous solid from the ethyl acetate-methanol-29% NH_3(aq) (30:10:1) elution fraction.

^{1}H-NMR(CDCl3)δ(ppm)

0.85-1.12(4H.m), 2.10-2.27(1H.m), 4.38(2H.s),

6.19(brs), 7.23(1H.d.J=8.0Hz), 7.79(1H.d.J=8.0Hz).

(Example 24: Final step)

A solution of the 2-cyclopropyl-5H-pyrrolo[3,4-

b]pyridine-7-amine (100 mg, 0.557 mmol) and 2-bromo-1-[3,5-di(*tert*-butyl)-4-hydroxyphenyl]-1-ethanone (227 mg, 0.694 mmol) in dimethylformamide (5 ml) was stirred at room temperature for 17 hours. The solvent was distilled off under reduced pressure and the residue was crystallized from ethyl acetate to yield the target compound (210 mg, 73%) as a colorless amorphous solid.

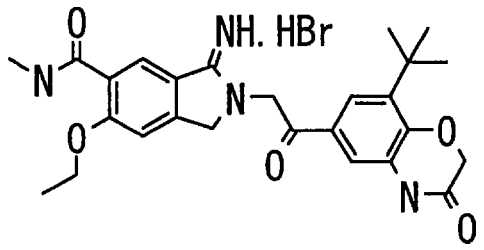
^{1}H-NMR(DMSO-d_6)δ(ppm)

1.03-1.12(4H.m), 1.41(18H.s), 2.26-2.36(1H.m), 4.81(2H.s), 5.53(2H.s), 7.71(1H.d.J=8.0Hz), 7.76(2H.s), 8.09(1H.d.J=8.0Hz), 9.63(1H.brs).

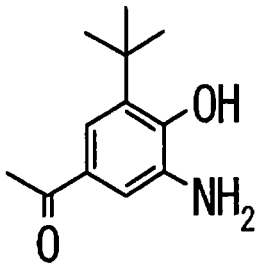
MS:m/e(ESI)420.2(MH+)

<Example 25>

2-[2-(8-*tert*-Butyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



(Step 1) 1-[3-Amino-5-(*tert*-butyl)-4-hydroxyphenyl]-1-ethanone

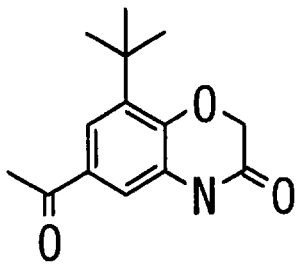


After adding 10% palladium-carbon (50% wet) (100 mg) to a solution of 1-[3-(*tert*-butyl)-4-hydroxy-5-nitrophenyl]-1-ethanone (1.00 g, 4.22 mmol) in ethyl acetate (10 ml) at room temperature, the mixture was hydrogenated for 3 hours under normal pressure. The 10% palladium-carbon was then filtered through celite and the solvent was distilled off under reduced pressure. The residue was subjected to silica gel chromatography (Wakogel-C200, 10 g) to yield the title compound (627 mg, 71.8% yield) as a light red powder from the ethyl acetate-hexane (1:4~1:3) fraction.

1H-NMR(CDCl3)δ(ppm)

1.36(9H,s), 2.42(3H,s), 6.10(2H,s), 7.17(1H,d,J=2.4Hz), 7.21(1H,d,J=2.4Hz).

(Step 2) 6-Acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-3-one

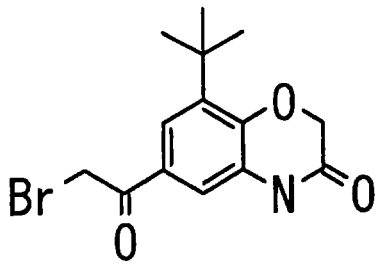


Chloroacetyl chloride (0.14 ml, 1.76 mmol) was added at room temperature to a solution of the 1-[3-amino-5-(*tert*-butyl)-4-hydroxyphenyl]-1-ethanone (300 mg, 1.45 mmol) in a methylene chloride (3 ml)-saturated aqueous sodium hydrogencarbonate (3 ml) mixed solvent, and the resultant mixture was stirred for 30 minutes. After adding ethyl acetate to the reaction mixture for separation, the organic layer was washed with brine. After drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was dissolved in dimethylformamide (6 ml), potassium carbonate (401 mg, 2.90 mmol) was added and the mixture was stirred at 70°C for 7 hours under a nitrogen atmosphere. The solvent was distilled off under reduced pressure, and then ethyl acetate was added to the residue and the mixture was washed with water and brine in that order. After drying over anhydrous magnesium sulfate, the solvent was distilled off under reduced pressure. The residue was subjected to silica gel chromatography (Wakogel-C200, 7 g), and the fraction containing the target compound was obtained from the ethyl acetate-toluene (1:9~1:6) fractions and crystallized from diethyl ether-diisopropyl ether to yield the title compound (102 mg, 28.5% yield) as yellow ochre crystals.

1H-NMR(CDCl3)δ(ppm)

1.36(9H,s), 2.51(3H,s), 4.65(2H,s), 7.40(1H,d,J=2.0), 7.51(1H,d,J=2.0Hz), 10.80(1H,s).

(Step 3) 6-(2-Bromoacetyl)-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-3-one



Tetra-*n*-butylammonium tribromide (64 mg, 0.13 mmol) was added to a solution of the 6-acetyl-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-3-one (30 mg, 0.12 mmol) in a methylene chloride (0.4 ml)-methanol (0.1 ml) mixed solvent under a nitrogen atmosphere, and the mixture was stirred at room temperature for 3 hours. After distilling off the solvent under reduced pressure, the residue was subjected to silica gel chromatography (Wakogel-C200, 1 g) to yield the title compound (36 mg, 91% yield) as light yellow needle-like crystals from the chloroform fraction.

1H-NMR(CDCl3)δ(ppm)

1.38(9H,s), 4.68(2H,s), 4.85(2H,s), 7.43(1H,d,J=2.0Hz), 7.56(1H,d,J=2.0Hz), 10.85(1H,s).

(Example 25: Final step)

A solution of 3-amino-6-ethoxy-1H-5-

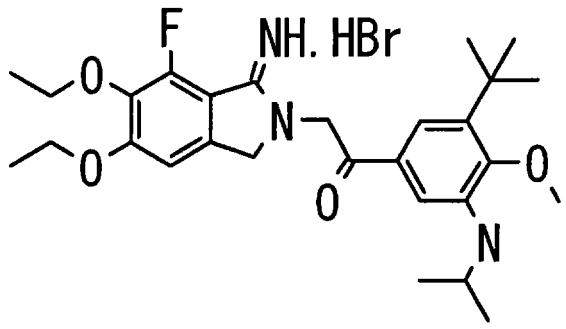
isoindolecarboxamide (72 mg, 0.31 mmol) and the 6-(2-bromoacetyl)-8-(*tert*-butyl)-3,4-dihydro-2H-1,4-benzoxazin-3-one (200 mg, 0.61 mmol) in dimethylformamide (1 ml) was stirred at 70°C for 4 hours under a nitrogen atmosphere. The solvent was distilled off under reduced pressure, the residue was subjected to silica gel chromatography (NAM-200H, 5 g), and the fraction containing the target compound was obtained from the 5% methanol-chloroform~10% methanol-chloroform fractions and recrystallized from acetonitrile-methanol to yield the target compound (87 mg, 50% yield) as light red crystals.

1H-NMR(DMSO-d6)δ(ppm)

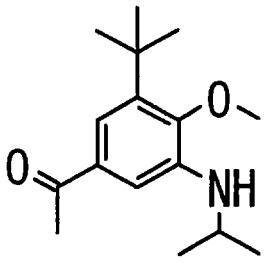
39(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4,4Hz), 4.30(2H,q,J=6.8Hz), 4.72(2H,s), 4.86(2H,s), 5.47(2H,s), 7.44(1H,d,J=2.0Hz), 7.56(2H,s), 8.22(1H,q,J=4.4Hz), 8.58(1H,s), 9.20(1H,s), 9.86(1H,s), 10.95(1H,s).

<Example 26>

1-(3-*tert*-Butyl-5-isopropylamino-4-methoxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-[3-(*tert*-Butyl)-5-(isopropylamino)-4-methoxyphenyl]-1-ethanone



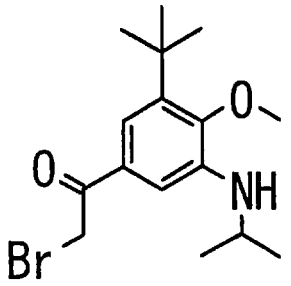
Trimethyl orthoformate (20 ml), p-toluenesulfonic acid (0.5 g, 1.9 mmol) and 3A-molecular sieves (4 g) were added to a solution of 1-[3-amino-5-(*tert*-butyl)-4-methoxyphenyl]-1-ethanone (4 g, 19 mmol) in methanol (20 ml) and the mixture was stirred at room temperature for 13 hours. The reaction mixture was filtered through celite and the solvent was distilled off under reduced pressure. Ethyl acetate was added to the residue, the mixture was washed with brine, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure to yield 5.2 g of 3-(*tert*-butyl)-5-(1,1-dimethoxyethyl)-2-methoxyaniline as a crude product.

Acetone (1.7 ml, 22 mmol), acetic acid (3.2 ml, 56 mmol) and 3A-molecular sieves (2 g) were added to a solution of the compound (5.2 g, 19 mmol) in methanol (6 ml) and the mixture was stirred at room temperature for 3 hours. Sodium cyanoborohydride (1.1 g, 17 mmol) was added to the reaction mixture prior to stirring at room temperature for 2 hours. Ethyl acetate was added to the reaction mixture, washing was performed with saturated sodium hydrogencarbonate water and brine in that order, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1.0 g) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.25(6H,d,J=6.4Hz), 1.40(9H,s), 2.56(3H,s), 3.60~3.72(1H,m), 3.77(3H,s), 7.17(1H,d,J=2.0Hz), 7.31(1H,d,J=2.0Hz).

(Step 2) 2-Bromo-1-[3-(*tert*-butyl)-5-(isopropylamino)-4-methoxyphenyl]-1-ethanone



Triethylamine (0.63 ml, 4.5 mmol) and *tert*-butyl dimethylsilyltrifluoromethanesulfonate (0.6 g, 2.3 mmol) were added to a solution of the 1-[3-(*tert*-butyl)-5-(isopropylamino)-4-methoxyphenyl]-1-ethanone (0.4 g, 1.5 mmol) in tetrahydrofuran (50 ml) while cooling on ice and the mixture was stirred at the same temperature for 30 minutes, after which N-bromosuccinimide (0.53 g, 3.0 mmol) was added and stirring was continued for 30 minutes. Ethyl acetate was added to the reaction mixture, the mixture was washed with brine and the organic layer was dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (410 mg) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.26(6H,d,J=6.4Hz), 1.40(9H,s), 3.30~3.37(1H,m), 3.78(3H,s), 4.42(2H,s), 7.18(1H,d,J=2.0Hz), 7.34(1H,d,J=2.0Hz).

(Example 26: Final step)

Synthesis was performed in the same manner as the final step of Example 3 to yield the target compound as a yellow solid.

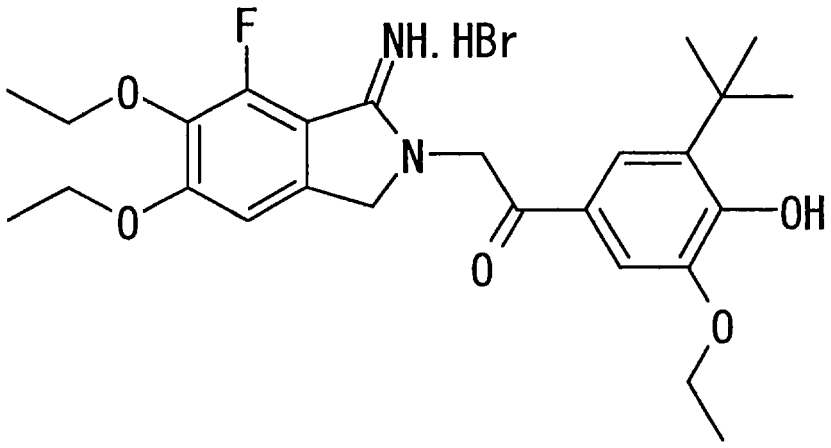
1H-NMR(DMSO-d6)δ(ppm)

1.19(6H,d,J=6.4Hz), 1.29(3H,t,J=7.2Hz), 1.36(9H,s),

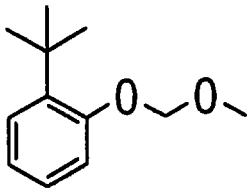
1.40(3H,t,J=7.2Hz), 3.60~3.76(1H,m), 3.71(3H,s), 4.11(2H,q,J=7.2Hz), 4.21(2H,q,J=7.2Hz), 78(2H,s), 4.89(1H,d,J=8.4Hz), 5.45(2H,s), 7.13(1H,s), 7.20(1H,s), 7.33(1H,s).

<Example 27>

1-(3-*tert*-Butyl-5-ethoxy-4-hydroxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 1-(*tert*-Butyl)-2-(methoxymethoxy)benzene



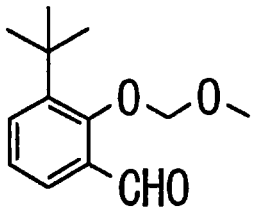
Sodium hydride (214 g, 4.90 mol) and chloromethyl methyl ether (394 g, 4.90) were gradually added to a solution of 2-*tert*-butylphenol (700 g, 4.67 mol) in dimethylformamide (3000 ml) while cooling on ice and the mixture was stirred at 0°C for 2 hours. The

reaction mixture was poured into ice water and extracted with ethyl acetate, and then the organic layer was washed with water and brine in that order and dried over anhydrous magnesium sulfate. The organic layer was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1013 g) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.42(9H,s), 3.52(3H,s), 5.24(2H,s), 6.94(1H,t,J=8.2Hz), 7.11(1H,d,J=8.2Hz), 7.14(1H,t,J=8.2Hz), 7.31(d,1H,J=8.2Hz).

(Step 2) 3-(*tert*-Butyl)-2-(methoxymethoxy)benzaldehyde



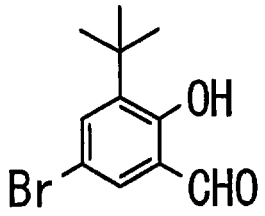
A 2.6 M hexane solution of *n*-BuLi was gradually added to a solution of the 1-(*tert*-butyl)-2-(methoxymethoxy)benzene (1013 g, 4.67 mol) and tetramethylethylenediamine (754 g, 6.5 ml) in dry ether while cooling on ice, and the mixture was stirred at room temperature for 3 hours. After recooling to 0°C, dimethylformamide (1000 ml, 14 mol) was gradually added and the mixture was stirred at

room temperature for 1 hour. The reaction mixture was gradually added to ice water, extraction was performed with ethyl acetate, and the organic layer was washed with water and brine and then dried over anhydrous magnesium sulfate. The organic layer was concentrated under reduced pressure to yield a crude product of the title compound (1247 g) as a red oil.

1H-NMR(CDCl3)δ(ppm)

1.43(9H,s), 3.64(3H,s), 5.03(2H,s), 7.17(1H,t,J=8.2Hz), 7.59(1H,d,J=8.2Hz), 7.64(1H,d,J=8.2Hz), 10.23(1H,s).

(Step 3) 5-Bromo-3-(*tert*-butyl)-2-hydroxybenzaldehyde



Bromine (747 g) was gradually added to a solution of the 3-(*tert*-butyl)-2-(methoxymethoxy)benzaldehyde (1247 g, 4.67 mol) in methanol (4000 ml) while cooling on ice. After stirring at 20°C for 1 hour, the solvent was distilled off under reduced pressure, ethyl acetate was added to the residue, the mixture was washed with water, saturated sodium aqueous hydrogencarbonate and brine in that order and the organic layer was dried over anhydrous magnesium sulfate. The organic layer was concentrated under reduced pressure to yield a crude product of the title

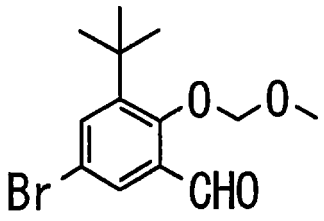
compound (1333 g) as a red oil.

1H-NMR(CDCl3)δ(ppm)

1.42(9H,s), 3.62(3H,s), 5.03(2H,s), 7.64(1H,s),

7.81(1H,s), 10.12(1H,s).

(Step 4) 5-Bromo-3-(*tert*-butyl)-2-(methoxymethoxy)benzaldehyde



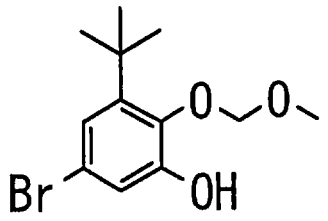
I-PrNEt$_2$ (834 g, 6.46 g) and chloromethyl methyl ether (451 g, 5.60 mol) were gradually added to a solution of the 5-bromo-3-(*tert*-butyl)-2-hydroxybenzaldehyde (1333 g, 4.67 mol) in methylene chloride (4000 ml) while cooling on ice, and the mixture was stirred at room temperature for 2 days. After first distilling off the solvent under reduced pressure, ethyl acetate was added to the residue, washing was performed twice with brine, the organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (1338 g) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

40(9H,s), 3.61(3H,s), 5.02(2H,s), 7.67(1H,s),

7.82(1H,s), 10.13(1H,s).

(Step 5) 5-Bromo-3-(*tert*-butyl)-2-(methoxymethoxy)phenol

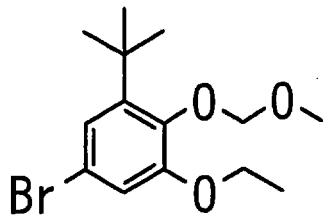


After adding 70% mCPBA (25 g) to a solution of 5-bromo-3-(*tert*-butyl)-2-(methoxymethoxy)benzaldehyde (30 g, 97 mmol) in methylene chloride (200 ml), the mixture was stirred at 50°C for 2 hours. The organic layer was washed with a saturated sodium thiosulfate solution and saturated sodium hydrogencarbonate solution and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (17 g) as a light yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.30(9H,s), 3.68(3H,s), 4.96(2H,s), 6.88(1H,s), 7.02(1H,s), 8.21(1H,s).

(Step 6) 5-Bromo-1-(*tert*-butyl)-3-ethoxy-2-(methoxymethoxy)benzene

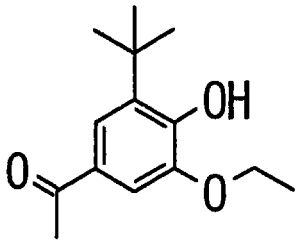


Cesium carbonate (10.05 g, 30.9 mmol) and EtI (2.58 ml, 32.2 mmol) were added to a solution of the 5-bromo-3-(*tert*-butyl)-2-(methoxymethoxy)phenol (7.76 g, 26.8 mmol) in acetonitrile and the mixture was stirred at room temperature for 3 hours. Ethyl acetate was added and the reaction mixture was washed with water and brine in that order. The organic layer was dried over anhydrous magnesium sulfate and then the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (6.5 g) as a yellow oil.

1H-NMR(CDCl3)δ(ppm)

1.39(9H,s), 1.45(3H,t,J=7.2Hz), 3.64(3H,s), 4.00(2H,q,J=7.2Hz), 5.16(2H,s), 6.91(1H,d,J=2.4Hz), 7.04(1H,d,J=2.4Hz).

(Step 7) 1-[3-(*tert*-Butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone



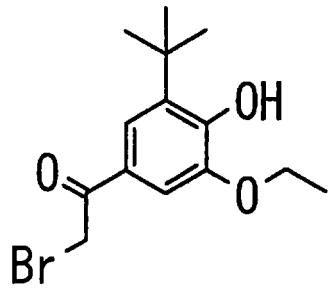
Tributyl(1-ethoxyvinyl)tin (7.77 g, 21.52 mmol)

and $Pd(PPh_3)_4$ (1.18 g, 1.02 mmol) were added to a solution of the 5-bromo-1-(*tert*-butyl)-3-ethoxy-2-(methoxymethoxy)benzene (6.5 g, 20.4 mmol) in toluene (68 ml) and the mixture was stirred at 100°C for 18 hours. The reaction mixture was cooled to room temperature, ethyl acetate was added, the mixture was washed with 20% aqueous KF and filtered through celite, and the organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. A 1 N HCl aqueous solution (15 ml) was added to a solution of the residue in methanol (80 ml), and the mixture was stirred at room temperature for 2 hours. Saturated sodium hydrogencarbonate solution was added to be basic and extraction was performed with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (3.17 g) as colorless crystals.

1H-NMR(CDCl3)δ(ppm)

1.43(9H,s), 1.48(3H,t,J=7.2Hz), 2.56(3H,s), 4.18(2H,q,J=7.2Hz), 6.54(s,1H,), 7.40(1H,s), 7.57(1H,s).

(Step 8) 2-Bromo-1-[3-(*tert*-butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone



Tetra-*n*-butylammonium tribromide (321 mg, 0.666 mmol) was added to a solution of the 1-[3-(*tert*-butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone (150 mg, 0.635 mmol) in methylene chloride-methanol (4 ml:1 ml) and the mixture was stirred at room temperature for 8 hours. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (60 mg) as colorless crystals.

1H-NMR(CDCl3)δ(ppm)

1.43(9H,s), 1.49(3H,t,J=7.2Hz), 4.19(2H,q,J=7.2Hz), 4.41(2H,s), 6.63(1H,s), 7.42(1H,d,J=2.0Hz), 7.60(1H,d,J=2.0Hz).

(Example 27: Final step)

A solution of the 2-bromo-1-[3-(*tert*-butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone (55 mg, 0.174 mmol) and 5,6-diethoxy-4-fluoro-1H-3-isoindoleamine (40 mg, 0.166 mmol) in dimethylformamide was stirred at room temperature for 7 hours. The solvent was distilled off under reduced pressure and the residue was

purified by NAM silica gel (ethyl acetate:methanol) to yield the target compound (62 mg) as colorless crystals.

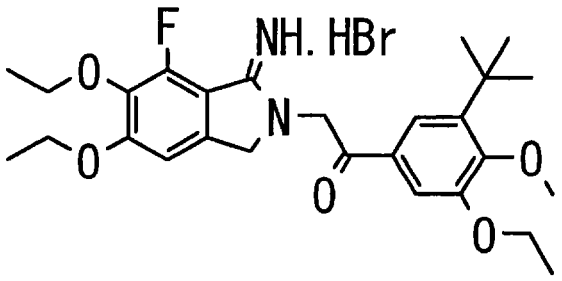
1H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.0Hz), 1.36-1.41(15H,m), 4.08-4.15(4H,m), 4.21(2H,q,J=7.0Hz), 4.78(2H,s), 5.44(2H,s), 7.33(1H,s), 7.42(1H,s), 7.50(1H,s), 9.00(1H,brs), 9.30(1H,brs), 9.44(1H,brs).

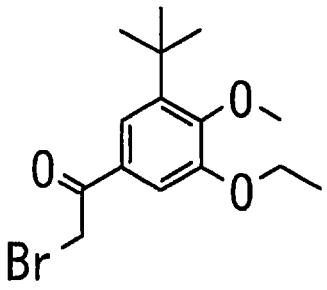
MS:m/e(ESI)473.2(MH+)

<Example 28>

1-(3-*tert*-Butyl-5-ethoxy-4-methoxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



(Step 1) 2-Bromo-1-[3-(*tert*-butyl)-5-ethoxy-4-methoxyphenyl]-1-ethanone



Cesium carbonate (662 mg, 2.03 mmol) and methyl

iodide (0.14 ml, 2.20 mmol) were added to a solution of 1-[3-(*tert*-butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone (400 mg, 1.69 mmol) in acetonitrile and the mixture was stirred at room temperature for 10 hours. Water was added to the reaction mixture, extraction was performed with ethyl acetate, the organic layer was washed with brine and dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure. Tetra-*n*-butylammonium tribromide (841 mg, 1.74 mmol) was added to a solution of the residue in methylene chloride-methanol (8 ml:2 ml) and the mixture was stirred at room temperature for 8 hours. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (491 mg) as a colorless oil.

1H-NMR(CDCl3)δ(ppm)

1.40(9H,s), 1.50(3H,t,J=7.2Hz), 3.97(3H,s), 4.12(2H,q,J=7.2Hz), 4.42(2H,s), 7.46(1H,d,J=2.0Hz), 7.59(1H,d,J=2.0Hz).

(Example 28: Final step)

A solution of 2-bromo-1-[3-(*tert*-butyl)-5-ethoxy-4-methoxyphenyl]-1-ethanone (52 mg, 0.159 mmol) and 5,6-diethoxy-4-fluoro-1H-3-isoindoleamine (33 mg, 0.139 mmol) in dimethylformamide was stirred at room

temperature for 12 hours. After distilling off the solvent under reduced pressure, the residue was purified by NAM silica gel (methylene chloride-methanol) to yield the target compound (40.6 mg) as light orange crystals.

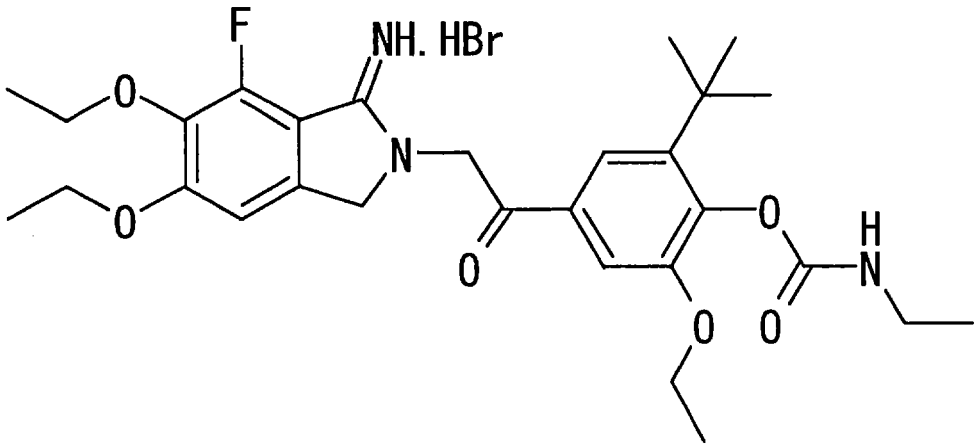
1H-NMR(DMSO-d6)δ(ppm)

1.29(3H,t,J=7.2Hz), 1.36(9H,S), 1.38-1.43(6H,m), 3.89(3H,s), 4.08-4.24(6H,m), 4.79(2H,s), 5.48(2H,s), 7.33(1H,s), 7.51(2H,d,J=5.2Hz), 9.03(1H,brs), 9.26(1H,brs).

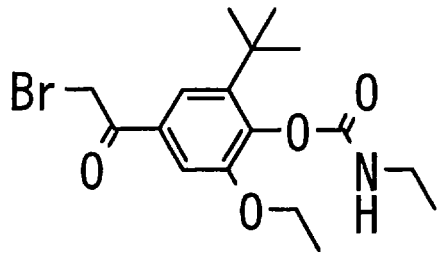
MS:m/e(ESI)487.2(MH+)

<Example 29>

2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-ethoxy-phenyl ethylcarbamate hydrobromide



(Step 1) 4-(2-Bromoacetyl)-2-(*tert*-butyl)-6-ethoxyphenyl N-ethylcarbamate



Triethylamine (0.02 ml, 0.130 mmol) and ethyl isocyanate (0.053 ml, 0.677 ml) were added to a solution of 1-[3-(*tert*-butyl)-5-ethoxy-4-hydroxyphenyl]-1-ethanone (100 mg, 0.423 mmol) in methylene chloride (4.2 ml) and the mixture was stirred at room temperature for 2 days. Ethyl acetate was added, and then the reaction mixture was washed with water, the organic layer was dried over anhydrous magnesium sulfate and the solvent was distilled off under reduced pressure. Tetra-*n*-butylammonium tribromide (214 mg, 444 mmol) was added to a solution of the residue in methylene chloride-methanol (5 ml:1.2 ml) and the mixture was stirred at room temperature for 8 hours. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (142 mg) as colorless crystals.

1H-NMR(CDCl3)δ(ppm)

(Example 29: Final step)

Synthesis was performed in the same manner as the

final step of Example 3 to yield the target compound as a yellow solid.

1H-NMR(DMSO-d6)δ(ppm)

1.08(3H,t,J=7.0Hz), 1.27-1.33(15H,m),

1.40(3H,t,J=6.8Hz), 3.06-3.14(2H,m), 4.03-4.14(4H,m),

4.21(2H,q,J=7.0Hz), 4.80(2H,s), 5.50(2H,s), 7.34(1H,s),

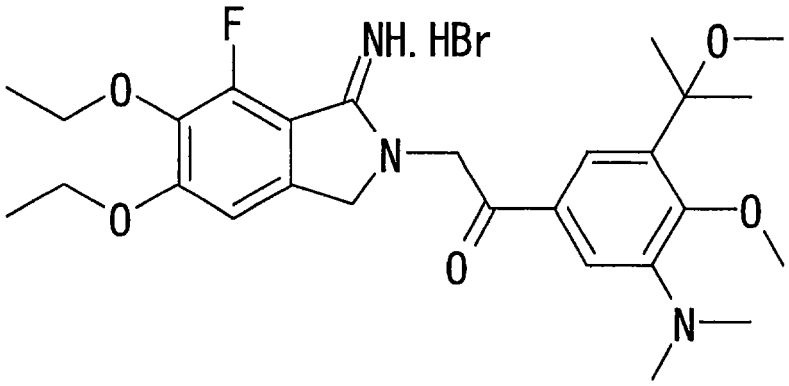
7.51(1H,s), 7.55(1H,s), 7.86(1H,t,J=4.8Hz),

9.02(1H,brs), 9.33(1H,brs).

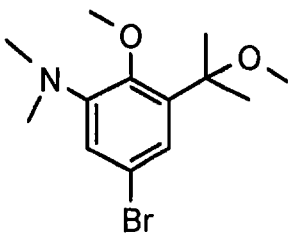
MS:m/e(ESI)544.3(MH+)

<Example 30>

2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-1-[3-dimethylamino-4-methoxy-5-(1-methoxy-1-methyl-ethyl)-phenyl]-ethanone hydrobromide



(Step 1) N-[5-Bromo-2-methoxy-3-(1-methoxy-1-methylethyl)phenyl]-N,N-dimethylamine

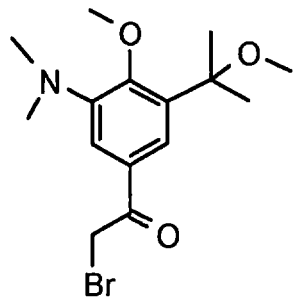


After dissolving 2-[5-bromo-3-(dimethylamino)-2-methoxyphenyl]-2-propanol (410 mg) in 100 mL of methanol-hydrochloric acid, the solution was heated to reflux for 14 hours. The reaction mixture was cooled to room temperature, saturated aqueous sodium hydrogencarbonate was added for neutralization, water was added and extraction was performed with ethyl acetate. The organic layer was washed with brine and then dried over anhydrous magnesium sulfate. After distilling off the solvent under reduced pressure, the residue was purified by silica gel column chromatography (solvent: n-hexane-ethyl acetate) to yield the title compound (370 mg) as an oil.

^{1}H-NMR ($CDCl_3$)

δ: 1.57(3H, s), 1.60(3H, s), 2.77(6H, s), 3.40(3H, s), 3.77(3H, s), 6.95(1H, d, J=2Hz), 7.16(1H, d, J=2Hz).

(Step 2) 2-Bromo-1-[3-(dimethylamino)-4-methoxy-5-(1-methoxy-1-methylethyl)phenyl]-1-ethanone



Synthesis was performed in the same manner as Step 7 of Example 8 to yield the title compound as a light yellow solid.

^{1}H-NMR ($CDCl_3$)

δ: 1.60(6H, s), 2.80(6H, s), 3.23(3H, s), 3.86(3H, s), 4.42(2H, s), 7.52(1H, d, J=2Hz), 7.72(1H, d, J=2Hz).

(Example 30: Final step)

1H-NMR(DMSO-d6)δ(ppm)

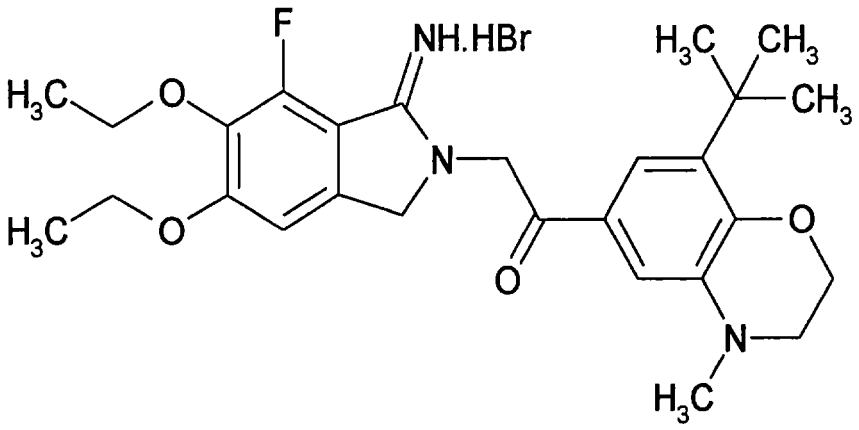
1.29(3H,t,J=7Hz), 1.40(3H,t,J=7Hz), 1.53(6H,s), 2.76(6H,s), 3.16(3H,s), 3.80(3H,s), 4.12(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.80(2H,s), 5.49(2H,s), 7.34(1H,br.s),7.46(1H,br.s), 7.67(1H,br.s), 9.05(1H,br.s), 9.31(1H,br.s).

MS:m/e(ESI)502.2(MH+)

The compounds of the following examples were synthesized by the same method as the final step of Example 3 above, from various 2-imino-dihydropyrrolo[3,4-b~e]pyridine or 1-iminoisoindoline derivatives and various 2-bromo-1-ethanone derivatives, to obtain the respective target compounds as light yellow to yellow solids.

Example 31

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.1Hz), 1.34(9H,s), 1.48(3H,t,J=7.1Hz),

3.23-3.37(2H,m), 2.90(3H,s), 4.12(2H,q,J=7.1Hz),

4.22(2H,q,J=7.1Hz), 4.33(2H,brs), 4.79(2H,s),

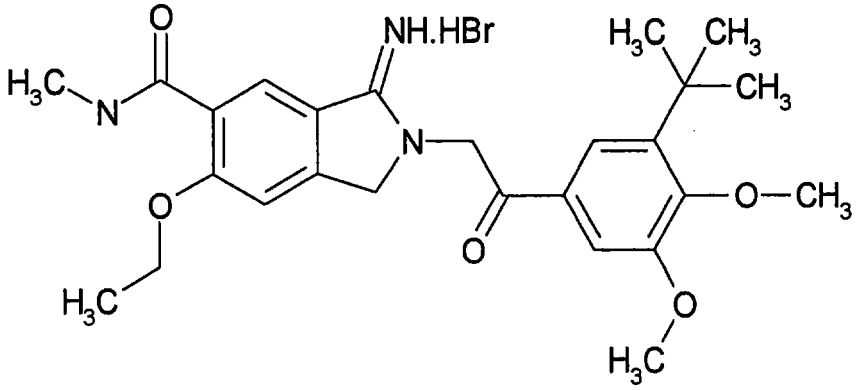
5.46(2H,s), 7.16(1H,s), 7.27(1H,s), 7.33(1H,s),

9.04(1H,brs), 9.32(1H,brs).

MS:m/e(ESI)484.3(MH+)

Example 32

2-[2-(3-*tert*-Butyl-4,5-dimethoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

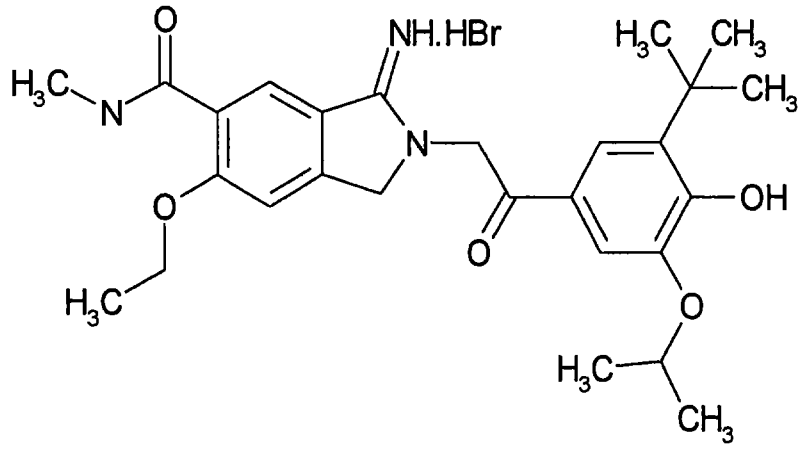


1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 3.89(3H,s), 3.91(3H,s), 4.30(2H,q,J=7Hz), 4.87(2H,s), 5.54(2H,s), 7.55(2H,s), 7.56(1H,s), 8.22(1H,q,J=8Hz), 8.58(1H,s).

Example 33

2-[2-(3-*tert*-Butyl-4-hydroxy-5-isopropoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

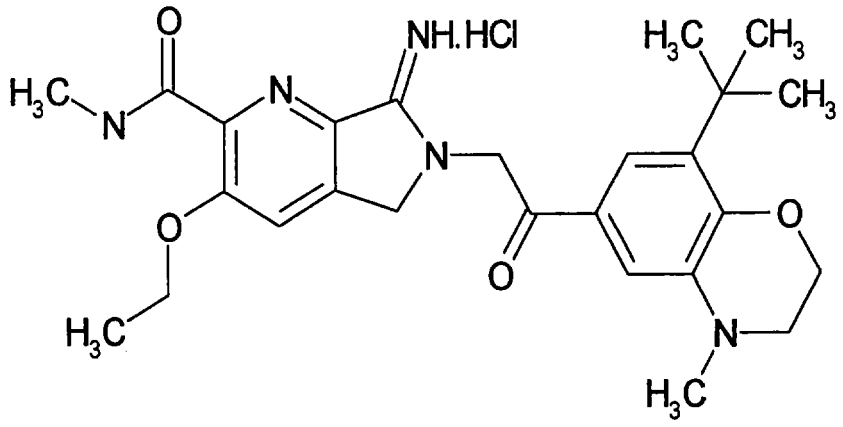


1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=6.0Hz), 1.41(9H,s), 1.44(3H,t,J=7.2Hz), 2.85(3H,d,J=4.4Hz), 4.30(2H,q,J=7.2Hz), 4.67(1H,m), 4.86(2H,s), 5.48(2H,s), 7.49(1H,s), 7.52(1H,s), 7.55(1H,s), 8.22(1H,m), 8.59(1H,s), 9.24(1H,s), 9.87(1H,s).

Example 34

6-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride



1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.38(3H,t,J=6.8Hz), 2.79(3H,d,J=4.0Hz),

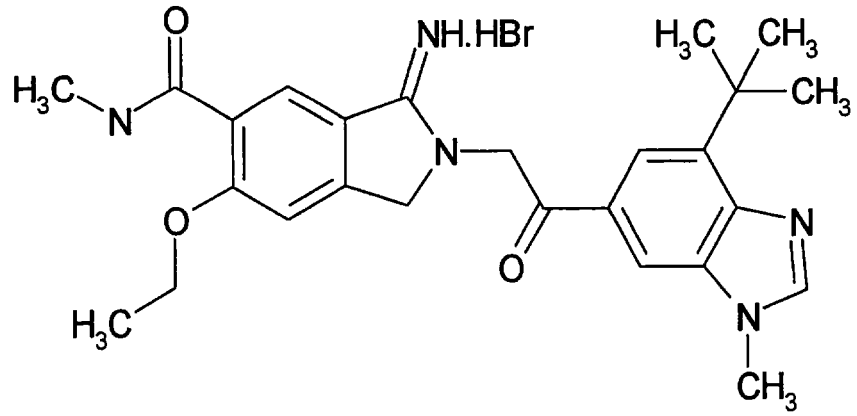
2.93(3H,s), 3.33(2H,s), 4.26(2H,q,J=6.8Hz), 4.36(2H,s),

4.89(2H,s), 5.57(2H,s), 7.20(1H,s), 7.29(1H,s),

8.01(1H,s), 8.59(1H,q,J=4.0Hz), 9.55(1H,s), 9.97(1H,s).

Example 35

2-[2-(7-*tert*-Butyl-3-methyl-3H-benzimidazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=7Hz), 1.55(9H,s), 2.74(3H,d,J=4Hz),

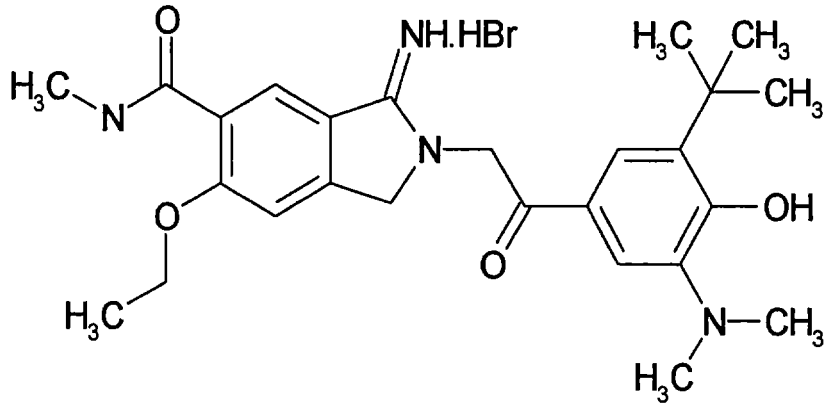
3.94(3H,s), 4.29(2H,q,J=7Hz), 4.89(2H,s), 5.60(2H,s),

7.55(1H,s), 7.71(1H,s), 8.22(1H,q,J=4Hz), 8.23(1H,s), 8.42(1H,s), 8.58(1H,s).

MS:m/e(ESI)462.0(MH+)

Example 36

2-[2-(3-*tert*-Butyl-5-dimethylamino-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

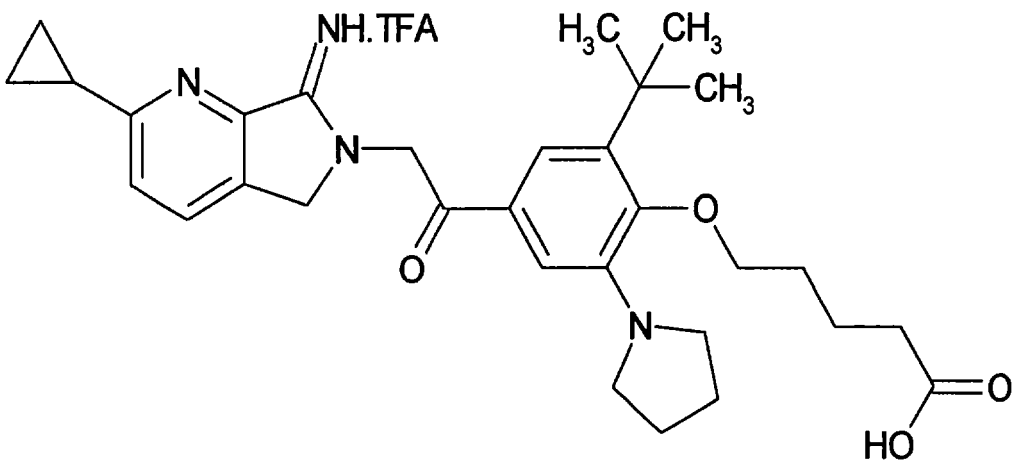


1H-NMR(DMSO-d6)δ:

1.41(12H,m), 2.63(6H,s), 2.84(2H,s), 4.30(2H,q,J=6.8Hz), 4.86(2H,s), 5.47(2H,s), 7.56(1H,s), 7.66(1H,s), 7.71(1H,s), 8.22(1H,s), 8.57(1H,s), 9.17(1H,s), 9.84(1H,s).

Example 37

5-{2-*tert*-Butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate



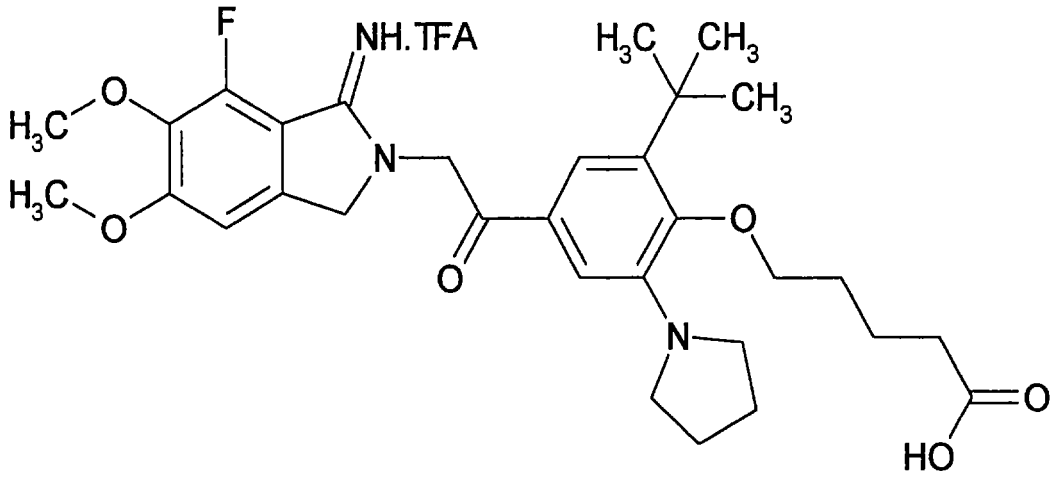
1H-NMR(DMSO-d6)δ:

1.00-1.15(4H,m), 1.38(9H,s), 1.59-1.85(4H,m), 2.23-2.37(3H,m), 3.03-3.20(4H,m), 3.78-3.88(2H,m), 4.81(2H,s), 5.53(2H,s), 7.36(1H,s), 7.46(1H,s), 7.72(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.41-9.49(1H,m), 9.61-9.70(1H,m).

MS:m/e(ESI)533.3(MH+)

Example 38

5-{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate

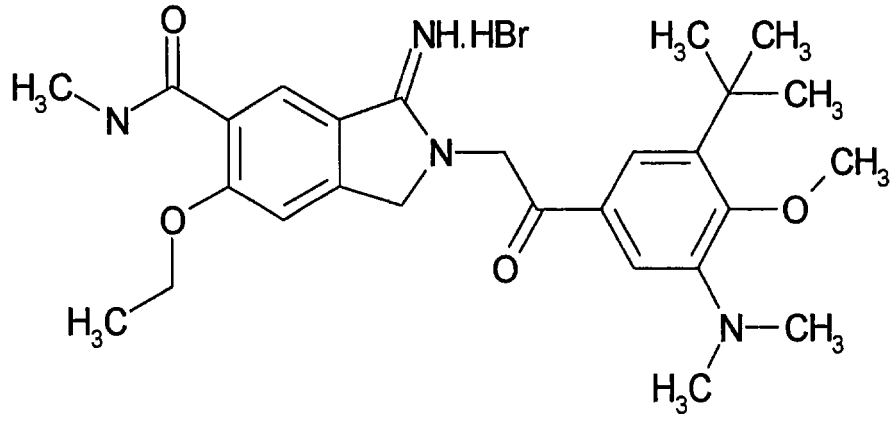


1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.55-1.99(8H,m), 2.17-2.36(2H,m), 2.94-3.20(4H,m), 3.57-4.27(8HandH2O,m), 4.79(2H,s), 5.47(2H,s), 7.36(2H,s), 7.45(1H,s), 9.01-9.11(1H,m), 9.22-9.35(1H,m).

Example 39

2-[2-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



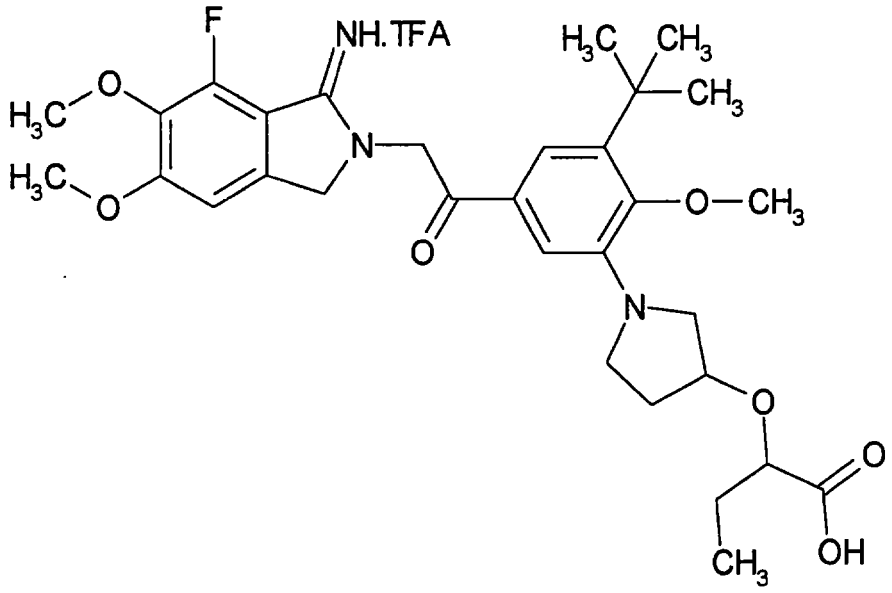
1H-NMR(DMSO-d6)δ:

1.39(12H,m), 2.77(6H,s), 2.84(3H,s), 3.85(3H,s),

4.30(2H,q,J=7.2Hz), 4.86(2H,s), 5.52(2H,s), 7.48(1H,s), 7.56(2H,s), 8.22(1H,s), 8.57(1H,s), 9.18(1H.s), 9.85(1H,s).

Example 40

2-(1-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-pyrrolidin-3-yloxy)-butyric acid trifluoroacetate

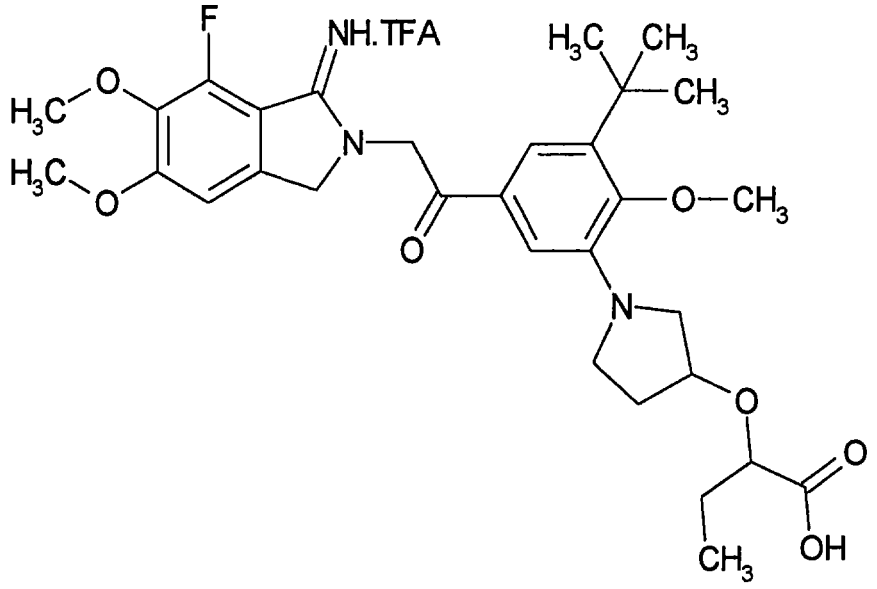


1H-NMR(DMSO-d6)δ:

0.92(3H,t,J=7.6Hz), 1.44(9H,s), 1.61-1.83(2H,m), 2.10-2.24(2H,m), 3.09-3.17(1H,m), 3.19-3.26(1H,m), 3.41-3.56(2H,m), 3.74(3H,s), 3.92(1H,dd,J=7.6and4.8Hz), 3.94(3H,s), 4.02(3H,s), 4.25-4.33(1H,m), 4.85(2H,s), 5.45(2H,s), 7.24(1H,s), 7.46(1H,d,J=2.0Hz), 7.60(1H,d,J=2.0Hz).

Example 41

2-(1-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-pyrrolidin-3-yloxy)-butyric acid trifluoroacetate

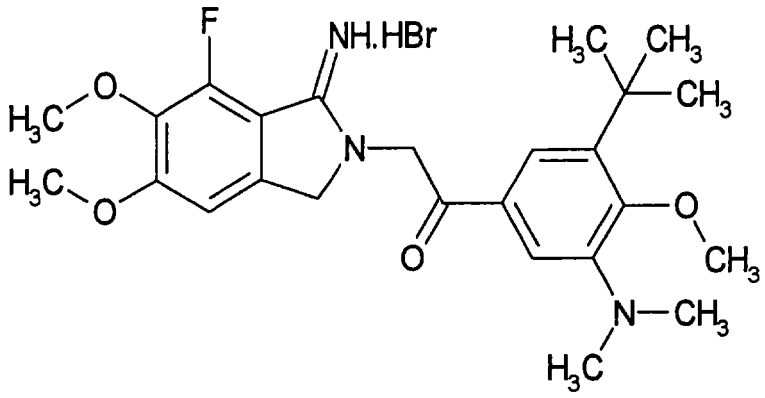


1H-NMR(DMSO-d6)δ:

1.00(3H,t,J=7.6Hz), 1.44(9H,s), 1.63-1.87(2H,m), 2.04-2.19(2H,m), 3.13-3.22(1H,m), 3.22-3.30(1H,m), 3.40-3.57(2H,m), 3.74(3H,s), 3.94(3H,s), 3.98(1H,dd,J=7.6and4.4Hz), 4.02(3H,s), 4.25-4.35(1H,m), 4.86(2H,s), 5.45(2H,s), 7.24(1H,s), 7.46(1H,d,J=2.0Hz), 7.60(1H,d,J=2.0Hz).

Example 42

1-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.75(6H,s), 3.82(3H,s), 3.87(3H,s),

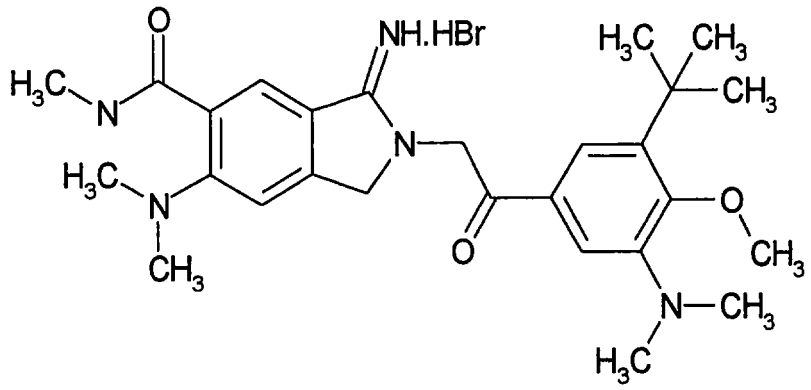
3.95(3H,s), 4.80(2H,s), 5.49(2H,s), 7.37(1H,s),

7.45(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz), 9.06(1H,brs),

9.28(1H,brs).

Example 43

2-[2-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.75(6H,s), 2.77(3H,d,J=4.0Hz), 2.92(6H,s),

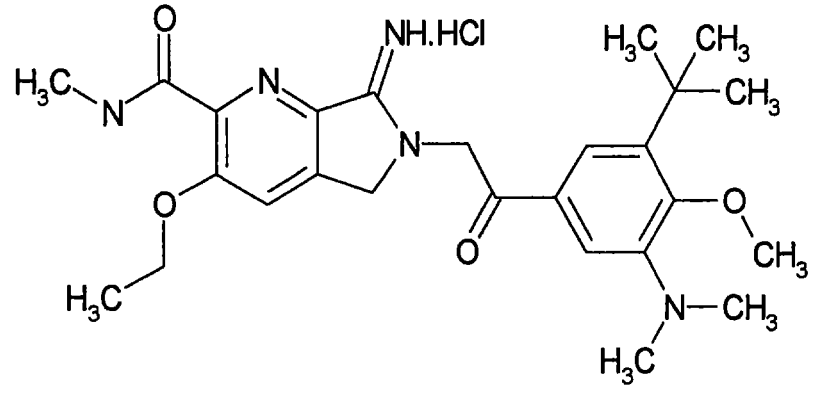
3.82(3H,s), 4.73(2H,s), 5.44(2H,s), 7.15(1H,s),

7.45(1H,s), 7.53(1H,s), 8.06(1H,), 8.36(1H,q,J=4.0Hz),

8.93(1H,brs), 9.49(1H,brs).

Example 44

6-[2-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

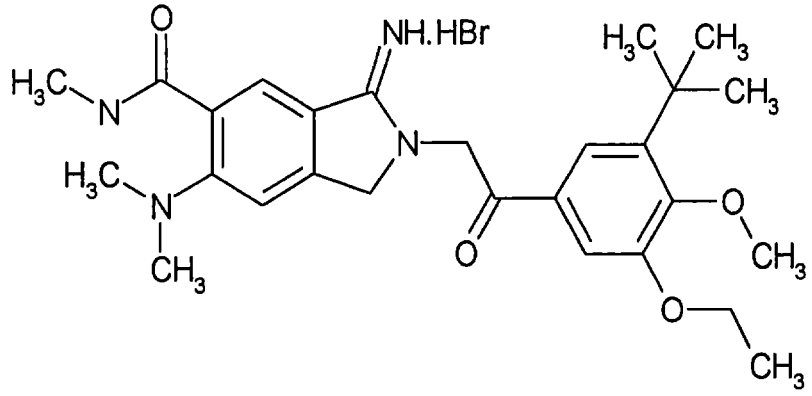


1H-NMR(DMSO-d6)δ:

1.36(3H,t,J=6.8Hz), 1.37(9H,s), 2.76(6H,s), 2.77(3H,d,J=4.0Hz), 3.83(3H,s), 4.24(2H,q,J=6.8Hz), 4.85(2H,s), 5.60(2H,s), 7.48(1H,s), 7.54(1H,s), 8.00(1H,s), 8.57(1H,q,J=4.0Hz), 9.56(1H,brs), 9.97(1H,brs).

Example 45

2-[2-(3-*tert*-Butyl-5-ethoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.36(9H,S), 1.41(3H,t,J=6.8Hz), 2.77(3H,d,J=4.4Hz),

2.92(6H,s), 3.89(3H,s), 4.13(2H,q,J=6.8Hz), 4.74(2H,s),

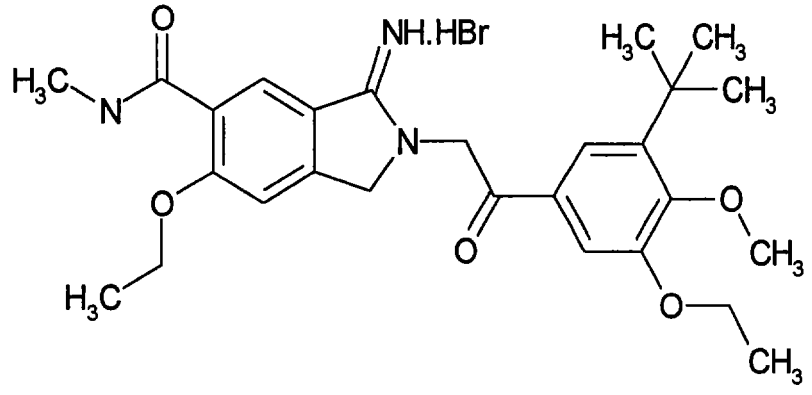
5.45(2H,s), 7.15(1H,s), 7.51(2H,d,J=7.6Hz), 8.07(1H,s),

8.35-8.38(1H,m), 8.94(1H,brs), 9.54(1H,brs).

MS:m/e(ESI)481.2(MH+)

Example 46

2-[2-(3-*tert*-Butyl-5-ethoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

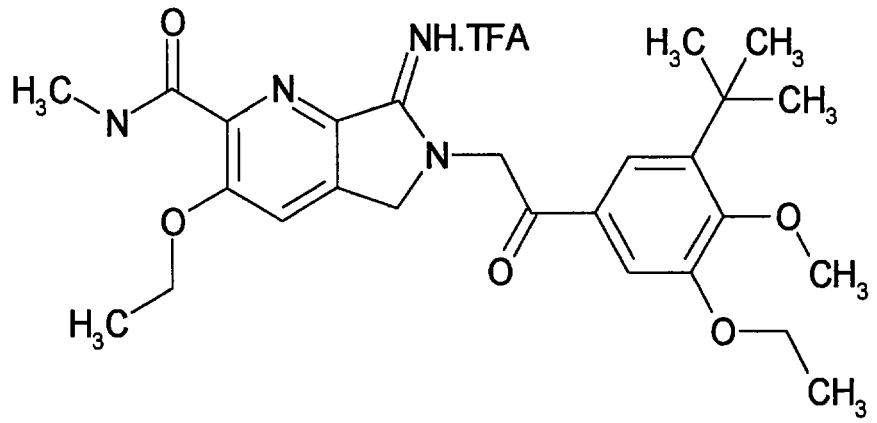
1.36(9H,S), 1.39-1.43(6H,m), 2.82(3H,d,J=4.8Hz),

3.89(3H,s), 4.13(2H,q,J=7.0Hz), 4.28(2H,q,J=7.0Hz),

4.85(2H,s), 5.50(2H,s), 7.51-7.54(3H,m),
8.21(1H,q,J=4.8Hz), 8.56(1H,s), 9.20(1H,brs),
9.85(1H,brs).
MS:m/e(ESI)482.2(MH+)

Example 47

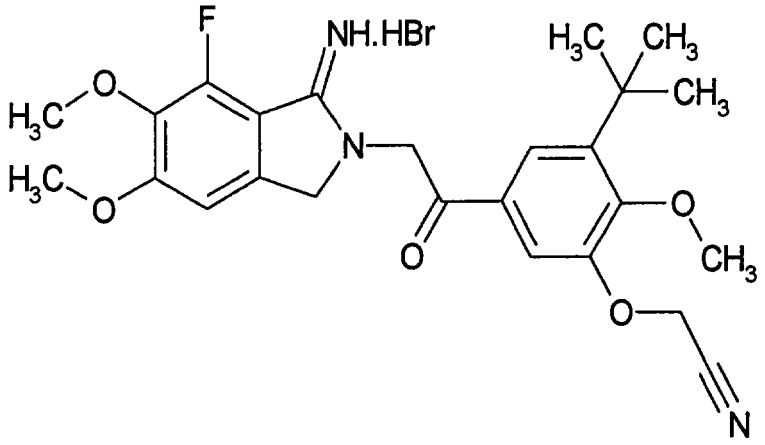
6-[2-(3-*tert*-Butyl-5-ethoxy-4-methoxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate



1H-NMR(DMSO-d6)δ:
1.36(9H,S), 1.40-1.43(6H,m), 2.78(3H,d,J=4.8Hz),
3.90(3H,s), 4.13(2H,q,J=7.0Hz), 4.24(2H,q,J=7.0Hz),
4.89(2H,s), 5.54(2H,s), 7.50-7.52(2H,m), 8.00(1H,s),
8.53(1H,m), 9.42(1H,brs), 9.96(1H,brs).
MS:m/e(ESI)483.1(MH+)

Example 48

{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-acetonitrile hydrobromide



1H-NMR(DMSO-d6)δ:

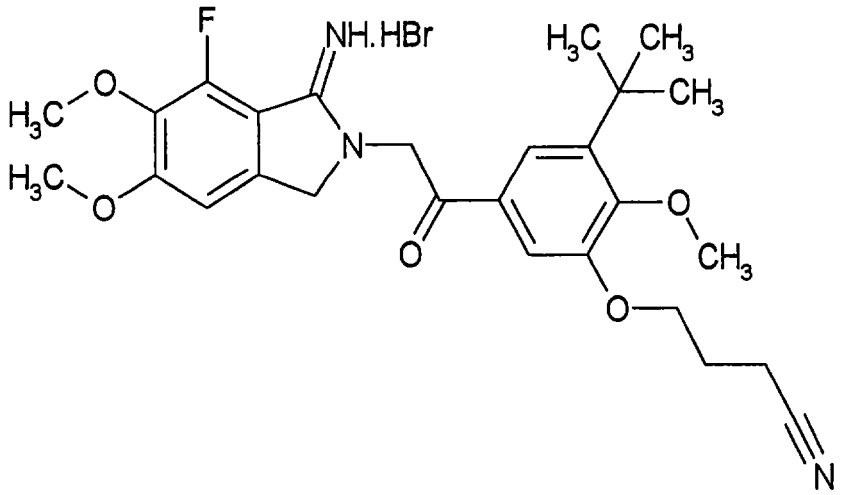
1.37(9H,s), 3.87(3H,s), 3.89(3H,s), 3.95(3H,s),

4.83(2H,s), 5.34(2H,s), 5.51(2H,s), 7.37(1H,s),

7.64(1H,s), 7.70(1H,s), 9.10(1H,brs), 9.37(1H,brs).

Example 49

4-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butyronitrile hydrobromide



1H-NMR(DMSO-d6)δ:

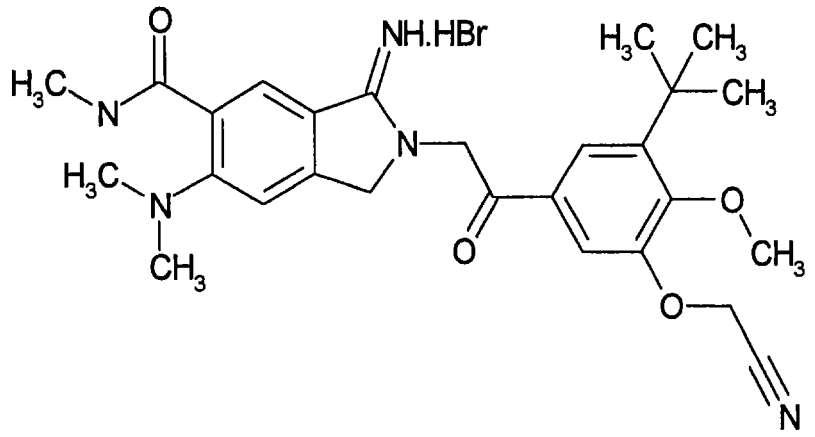
1.37(9H,s), 2.07-2.16(2H,m), 2.67-2.75(2H,m),

3.87(3H,s), 3.90(3H,s), 3.95(3H,s), 4.11-4.18(2H,m),

4.82(2H,s), 5.51(2H,s), 7.37(1H,s), 7.49-7.59(2H,m), 9.00-9.17(1H,brs), 9.27-9.40(1H,m).

Example 50

2-[2-(3-*tert*-Butyl-5-cyanomethoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

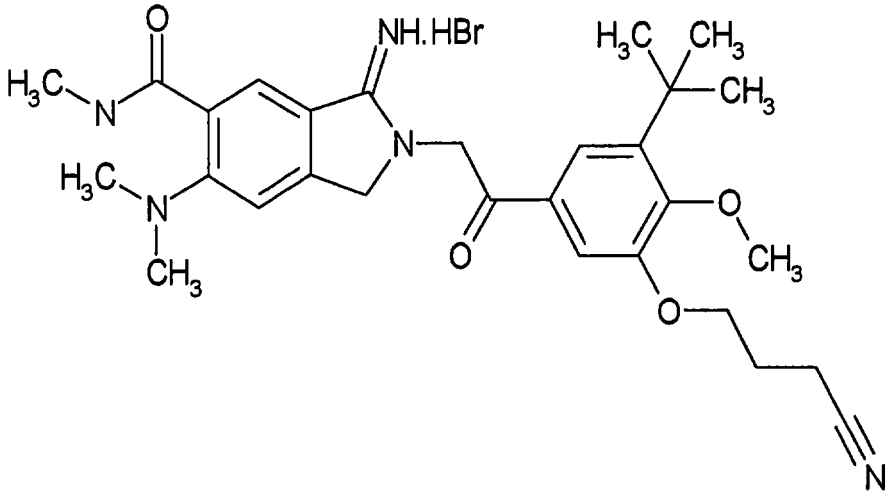


1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.73-2.82(3H,m), 2.91(6H,s), 3.89(3H,s), 4.78(2H,s), 5.33(2H,s), 5.46(2H,s), 7.15(1H,s), 7.65(1H,s), 7.69(1H,s), 8.07(1H,s), 8.31-8.46(1H,m), 8.97(1H,brs), 9.55(1H,brs).

Example 51

2-{2-[3-*tert*-Butyl-5-(3-cyano-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.06-2.17(2H,m), 2.71(2H,t,J=7.6Hz),

2.77(3H,d,J=4.8Hz), 2.91(6H,s), 3.89(3H,s),

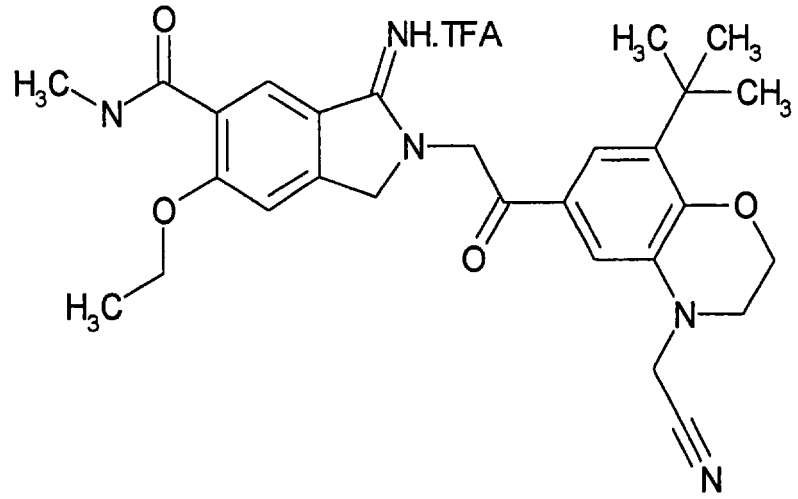
4.24(2H,t,J=6.0Hz), 4.74(2H,s), 5.45(2H,s), 7.15(1H,s),

7.53(1H,s), 7.55(1H,s), 8.07(1H,s), 8.33-8.41(1H,m),

8.95(1H,brs), 9.55(1H,brs).

Example 52

2-[2-(8-*tert*-Butyl-4-cyanomethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate



1H-NMR(DMSO-d6)δ:

1.36-1.43(12H,m), 2.82(3H,d,J=5Hz), 3.30-3.40(2H,m),

4.28(2H,q,J=7Hz), 4.40(2H,m), 4.66(2H,s), 4.85(2H,s),

5.45(2H,s), 7.42-7.45(2H,m), 7,53(1H,s),

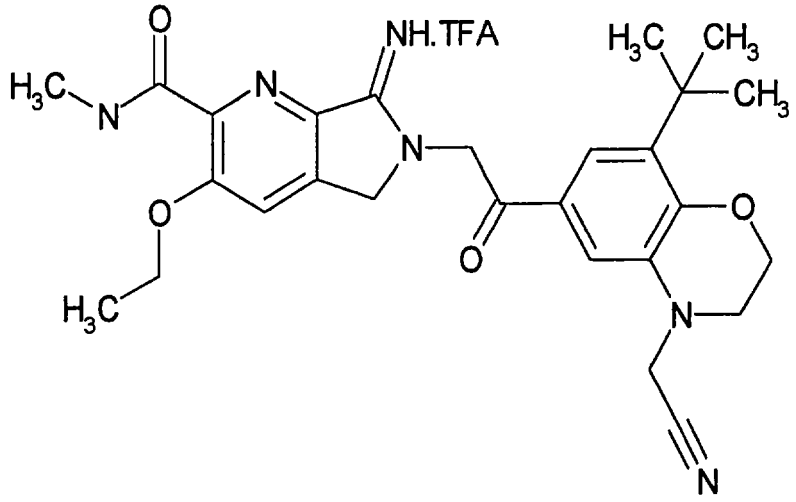
8.21(1H,q,J=5Hz), 8.56(1H,s), 9.22(1H,brs),

9.82(1H,brs).

MS:m/e(ESI)504.3(MH+)

Example 53

6-[2-(8-*tert*-Butyl-4-cyanomethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate



1H-NMR(DMSO-d6)δ:

1.33-1.38(12H,s), 2.78(3H,d,J=5Hz), 3.30-3.40(2H,m),

4.25(2H,q,J=7Hz), 4.40(2H,m), 4.66(2H,s), 4.89(2H,s),

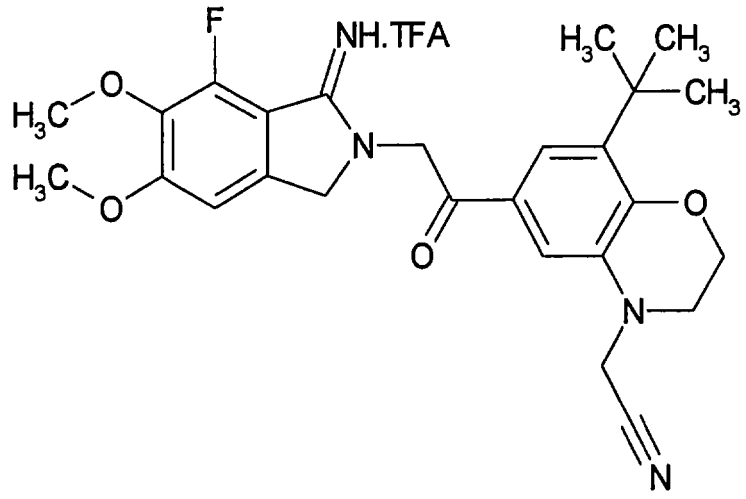
5.49(2H,s), 7.40-7.43(2H,m), 7.99(1H,s),

8.53(1H,q,J=5Hz), 9.46(1H,brs), 9.93(1H,brs).

MS:m/e(ESI)505.3(MH+)

Example 54

{8-*tert*-Butyl-6-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetonitrile trifluoroacetate



1H-NMR(DMSO-d6)δ:

1.36(9H,s), 3.30-3.40(2H,m), 3.87(3H,s), 3.95(3H,s),

4.40(2H,m), 4.66(2H,s), 4.82(2H,s), 5.45(2H,s),

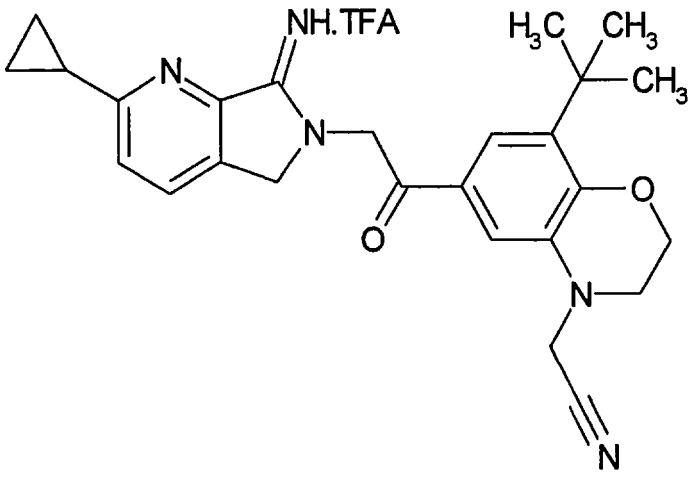
7.36(1H,s), 7.40-7.42(2H,m), 9.06(1H,brs),

9.35(1H,brs).

MS:m/e(ESI)481.3(MH+)

Example 55

{8-*tert*-Butyl-6-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetonitrile trifluoroacetate



1H-NMR(DMSO-d6)δ:

1.06-1.11(4H,m), 1.36(9H,s), 2.32(1H,m), 3.30-3.40(2H,m), 4.40(2H,m), 4.66(2H,s), 4.83(2H,s),

5.51(2H,s), 7.41-7.44(2H,m), 7.72(1H,d,J=8Hz),

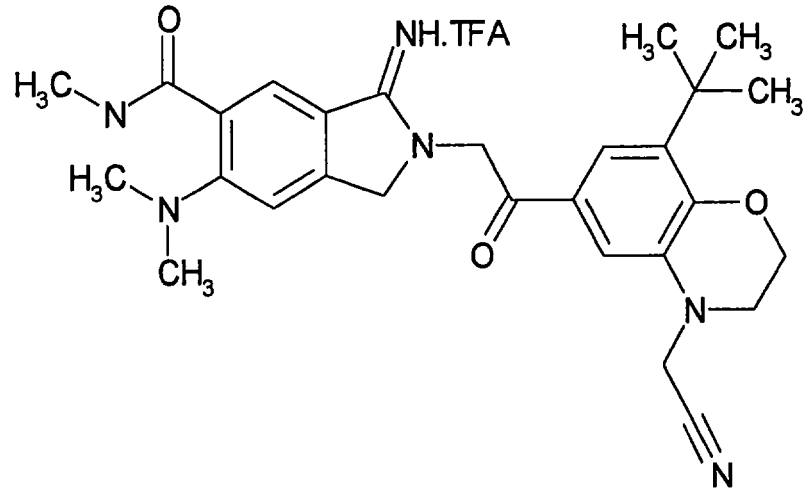
8.09(1H,d,J=8Hz), 9.52,(1H,brs), 9.64(1H,brs).

MS:m/e(ESI)444.3(MH+)

Example 56

2-[2-(8-*tert*-Butyl-4-cyanomethyl-3,4-dihydro-2H-

benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate



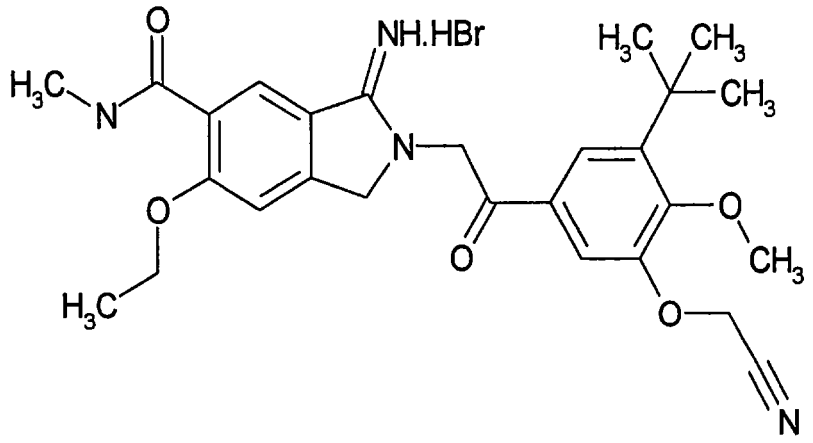
1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.77(3H,d,J=4Hz), 2.91(6H,s), 3.30-3.40(2H,m), 4.40(2H,m), 4.66(2H,s), 4.75(2H,s), 5.41(2H,s), 7.15(1H,s), 7.41-7.43(2H,m), 8.07(1H,s), 8.37(1H,q,J=4Hz), 8.98(1H,brs), 9.53(1H,brs).

MS:m/e(ESI)503.4(MH+)

Example 57

2-[2-(3-*tert*-Butyl-5-cyanomethoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

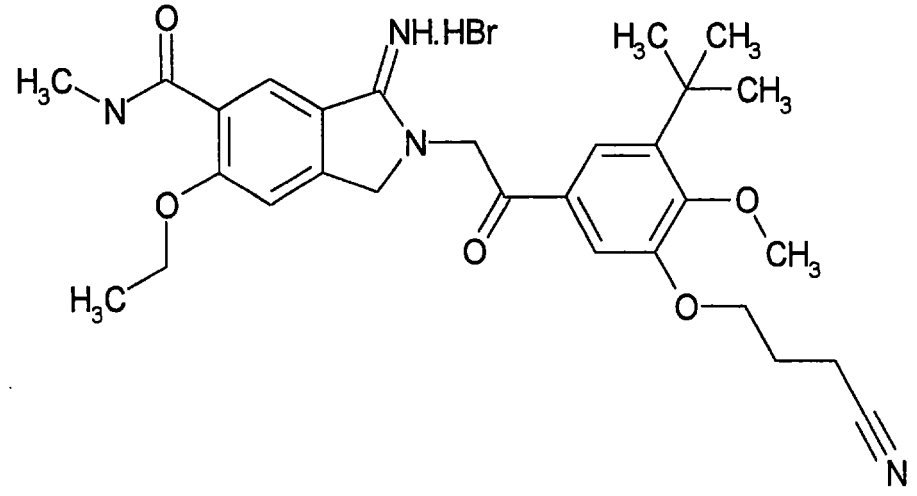


1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=6.8Hz), 2.83(3H,d,J=4.8Hz), 3.89(3H,s), 4.29(2H,q,J=6.8Hz), 4.86(2H,s), 5.34(2H,s), 5.50(2H,s), 7.54(1H,s), 7.65(1H,s), 7.71(1H,s), 8.15-8.30(1H,m), 8.56(1H,s), 9.14-9.26(1H,m), 9.77-9.93(1H,m).

Example 58

2-{2-[3-*tert*-Butyl-5-(3-cyano-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

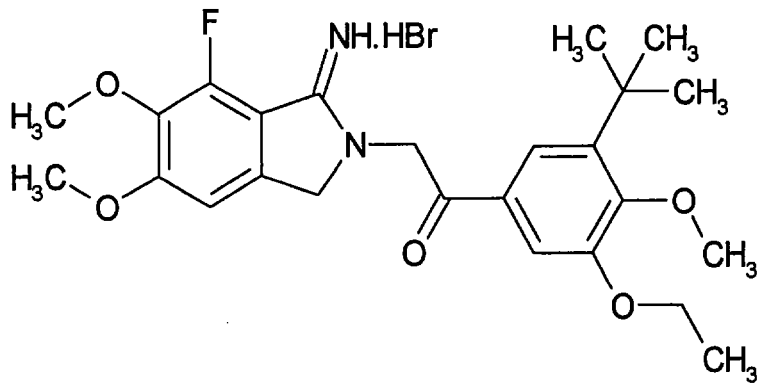


1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.41(3H,t,J=6.8Hz), 2.06-2.17(2H,m), 2.72(2H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 3.90(3H,s), 4.15(2H,t,J=6.0Hz), 4.28(2H,q,J=6.8Hz), 4.85(2H,s), 5.50(2H,s), 7.49-7.62(3H,m), 8.15-8.26(1H,m), 8.56(1H,s), 9.18(1H,brs), 9.85(1H,brs).

Example 59

1-(3-*tert*-Butyl-5-ethoxy-4-methoxy-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



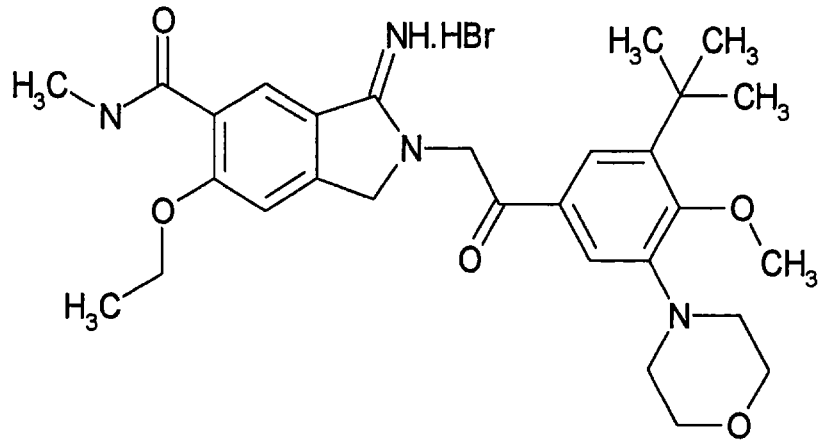
1H-NMR(DMSO-d6)δ:

1.36(9H,S), 1.41(3H,t,J=7.0Hz), 3.87(3H,s), 3.89(3H,s), 3.95(3H,s), 4.13(2H,q,J=7.0Hz), 4.81(2H,s), 5.48(2H,s), 7.36(1H,s), 7.50(1H,s), 7.51(1H,s), 9.03(1H,brs), 9.30(1H,brs).

MS:m/e(ESI)459.1(MH+)

Example 60

2-[2-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



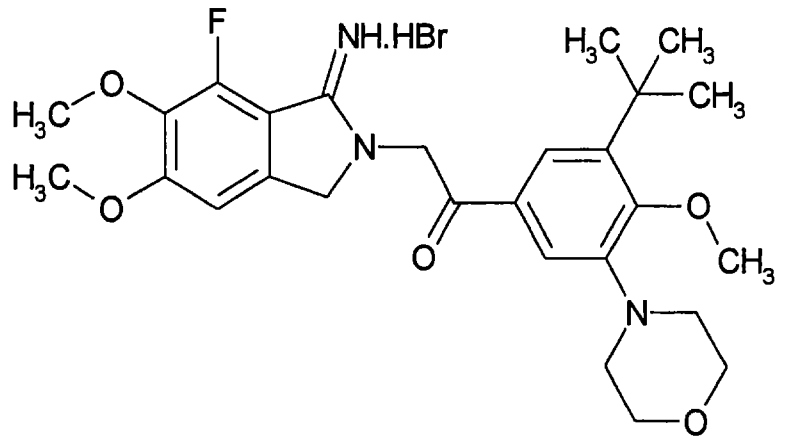
1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.0Hz), 2.94-3.04(4H,m), 3.70-3.86(4H,m), 3.95(3H,s), 4.28(2H,q,J=6.8Hz), 4.85(2H,s), 5.51(2H,s), 7.50(1H,s), 7.54(1H,s), 7.61(1H,s), 8.20(1H,q,J=4.0Hz), 8.56(1H,s), 9.16(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)524.2(MH+)

Example 61

1-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

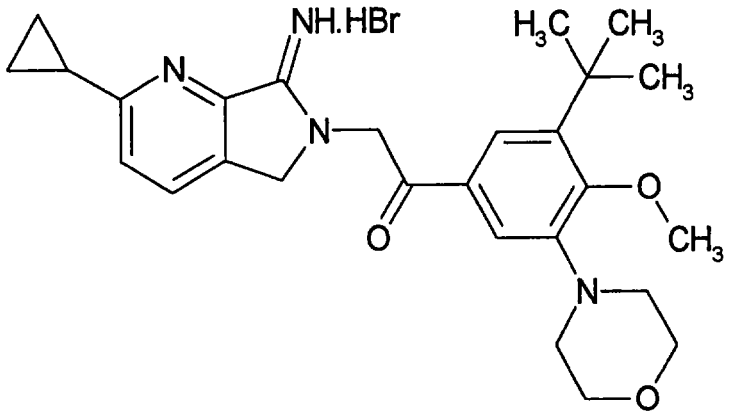


1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.95-3.05(4H,m), 3.74-3.85(4H,m), 3.87(3H,s), 3.95(3H,s), 3.96(3H,s), 4.81(2H,s), 5.51(2H,s), 7.37(1H,s), 7.49(1H,s), 7.60(1H,s).

Example 62

1-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

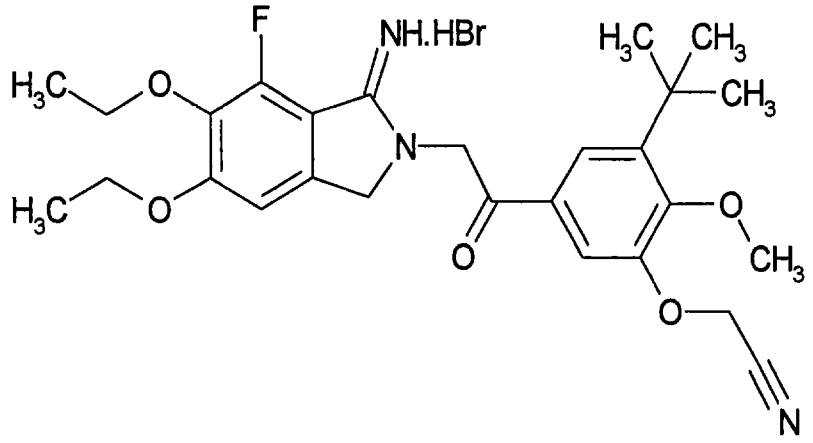


1H-NMR(DMSO-d6)δ:

1.08-1.15(4H,m), 1.37(9H,s), 2.28-2.36(1H,m), 2.94-3.06(4H,m), 3.75-3.86(4H,m), 3.95(3H,s), 4.82(2H,s), 5.56(2H,s), 7.50(1H,s), 7.61(1H,s), 7.72(1H,d,J=8.0Hz), 8.10(1H,d,J=8.0Hz).

Example 63

{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-acetonitrile hydrobromide

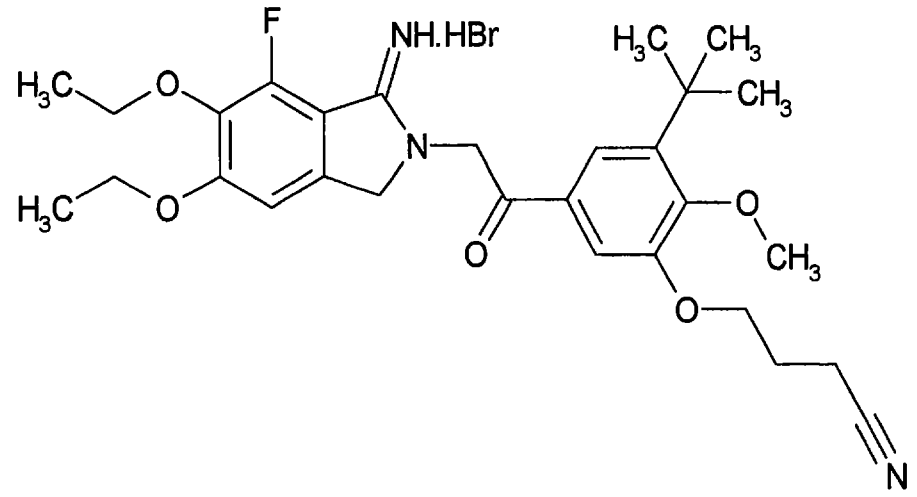


1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.37(9H,s), 1.39(3H,t,J=6.8Hz), 3.89(3H,s), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.81(2H,s), 5.33(2H,s), 5.48(2H,s), 7.34(1H,s), 7.64(1H,s), 7.69(1H,s), 9.00-9.10(1H,m), 9.29-9.37(1H,m).

Example 64

4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butyronitrile hydrobromide

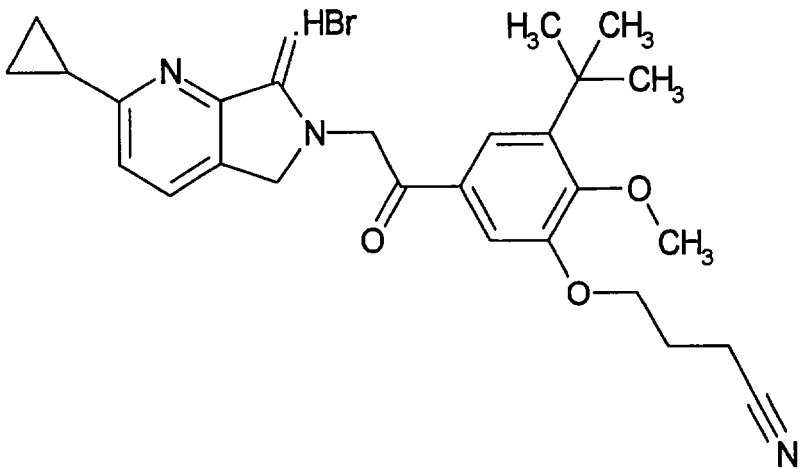


1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.36(9H,s), 1.40(3H,t,J=6.8Hz), 2.07-2.17(2H,m), 2.72(2H,t,J=7.2Hz), 3.90(3H,s), 4.07-4.17(4H,m), 4.21(2H,q,J=6.8Hz), 4.79(2H,s), 5.48(2H,s), 7.33(1H,s), 7.53(1H,s), 7.54(1H,s), 8.96-9.09(1H,m), 9.23-9.36(1H,m).

Example 65

4-{3-*tert*-Butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-methoxy-phenoxy}-butyronitrile hydrobromide



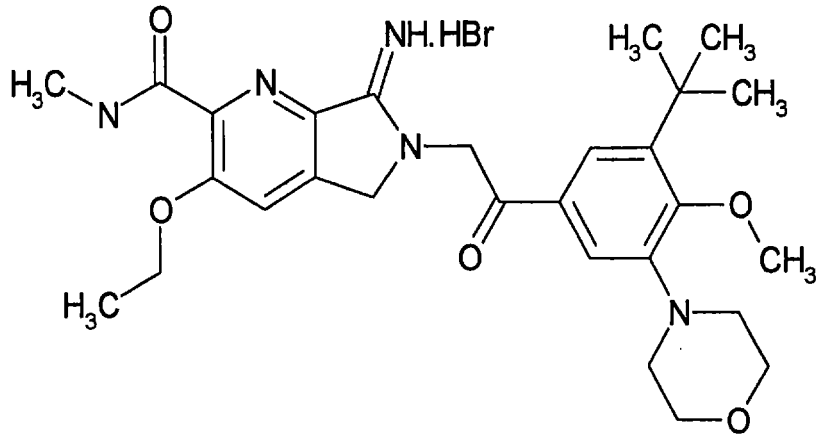
1H-NMR(DMSO-d6)δ:

1.05-1.18(4H,m), 1.36(9H,s), 2.07-2.18(2H,m), 2.28-2.38(1H,m), 2.72(2H,t,J=7.2Hz), 3.89(3H,s), 4.15(2H,t,J=6.0Hz), 4.83(2H,s), 5.56(2H,s), 7.55(2H,brs), 7.72(1H,d,J=8.0Hz), 8.10(1H,d,J=8.0Hz), 9.04-9.55(2H,m).

Example 66

6-[2-(3-*tert*-Butyl-4-methoxy-5-morpholino-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-

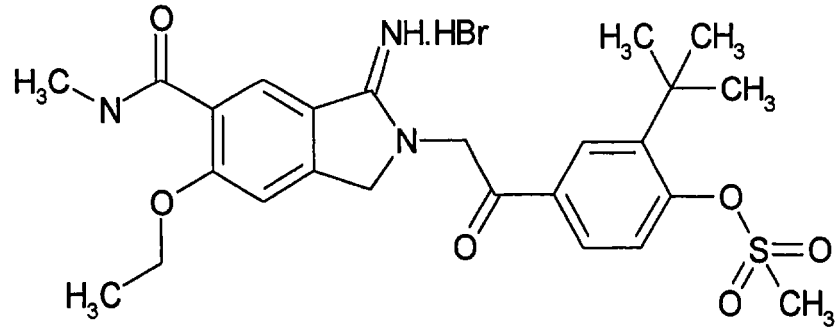
pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrobromide



MS:m/e(ESI)524.2(MH+)

Example 67

2-*tert*-Butyl-4-[2-5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl]-acetyl]-phenyl methanesulfonate hydrobromide



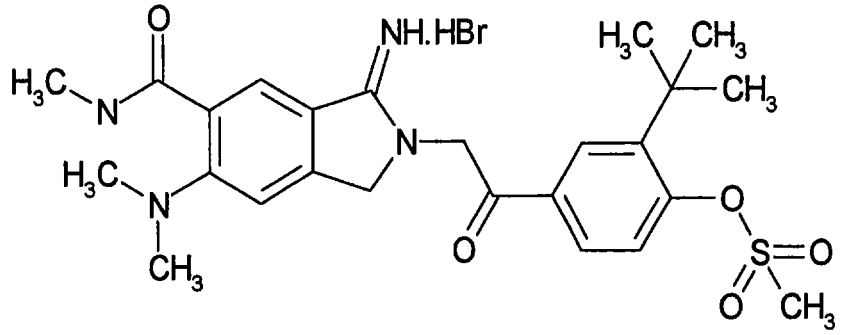
1H-NMR(DMSO-d6)δ:

1.40-1.43(12H,m), 2.82(3H,d,J=4.8Hz), 3.68(3H,s), 4.28(2H,q,J=6.8Hz), 4.86(2H,s), 5.51(2H,s), 7.55(1H,s), 7.70(1H,d,J=8.4Hz), 7.97-8.00(2H,m), 8.19-8.22(1H,m), 8.56(1H,s), 9.20(1H,brs), 9.86(1H,brs).

MS:m/e(ESI)502.1(MH+)

Example 68

2-*tert*-Butyl-4-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl methanesulfonate hydrobromide



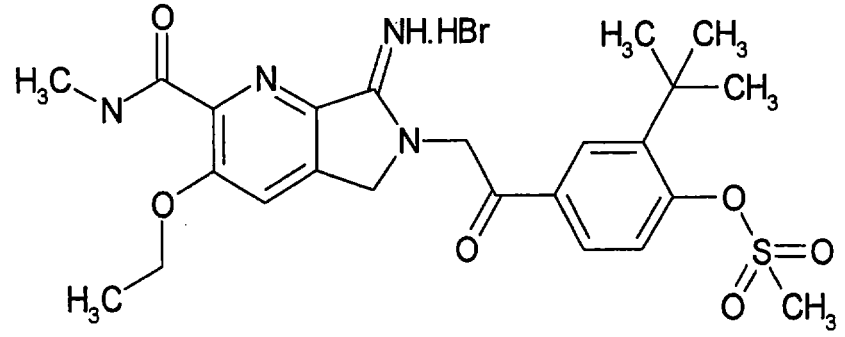
1H-NMR(DMSO-d6)δ:

1.40(9H,S), 2.77(3H,d,J=4.8Hz), 2.92(6H,s), 3.68(3H,s), 4.76(2H,s), 5.46(2H,s), 7.15(1H,s), 7.70(1H,d,J=8.4Hz), 7.95-8.00(2H,m), 8.07(1H,s), 8.34-8.37(1H,m), 8.96(1H,brs), 9.57(1H,brs).

MS:m/e(ESI)501.1(MH+)

Example 69

2-*tert*-Butyl-4-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl methanesulfonate hydrobromide



1H-NMR(DMSO-d6)δ:

1.36(3H,t,J=6.8Hz), 1.41(9H,s), 2.77(3H,d,J=4.4Hz),

3.68(3H,s), 4.24(2H,q,J=6.8Hz), 4.90(2H,s), 5.54(2H,s),

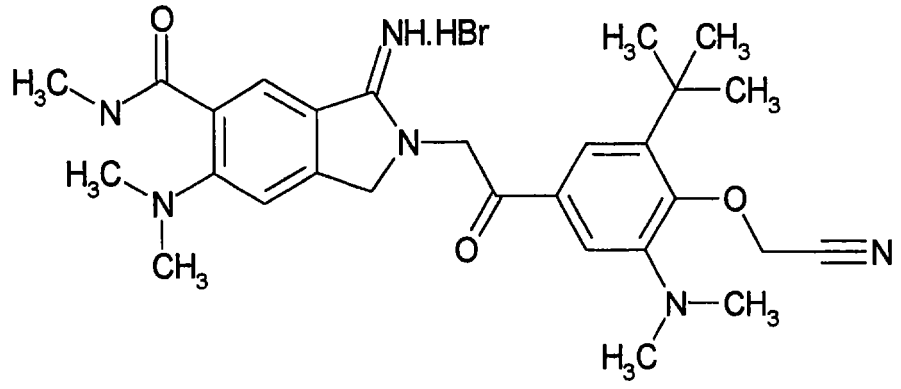
7.70(1H,d,J=8.4Hz), 7.95-8.00(3H,m), 8.52(1H,m),

9.44(1H,brs), 9.99(1H,brs).

MS:m/e(ESI)503.1(MH+)

Example 70

2-[2-(3-*tert*-Butyl-4-cyanomethoxy-5-dimethylamino-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.39(9H,S), 2.71(6H,s), 2.77(3H,d,J=4.4Hz), 2.91(6H,s),

4.74(2H,s), 5.25(2H,s), 5.46(2H,s), 7.15(1H,s),

7.57(1H,s), 7.60(1H,s), 8.06(1H,s), 8.35(1H,m),

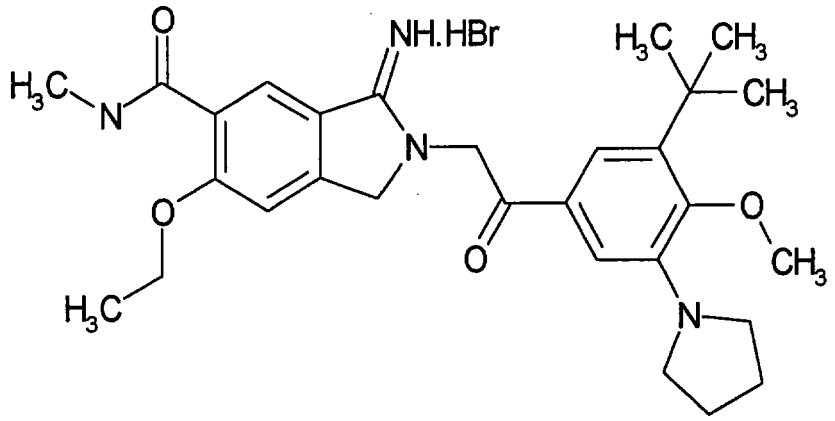
8.92(1H,brs), 9.53(1H,brs).

MS:m/e(ESI)505.2(MH+)

Example 71

2-[2-(3-*tert*-Butyl-4-methoxy-5-(pyrrolidin-1-yl)-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-

isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.38(9H,S), 1.41(3H,t,J=6.8Hz), 1.91(4H,brs),

2.82(3H,d,J=4.0Hz), 3.15(4H,brs), 3.64(3H,s),

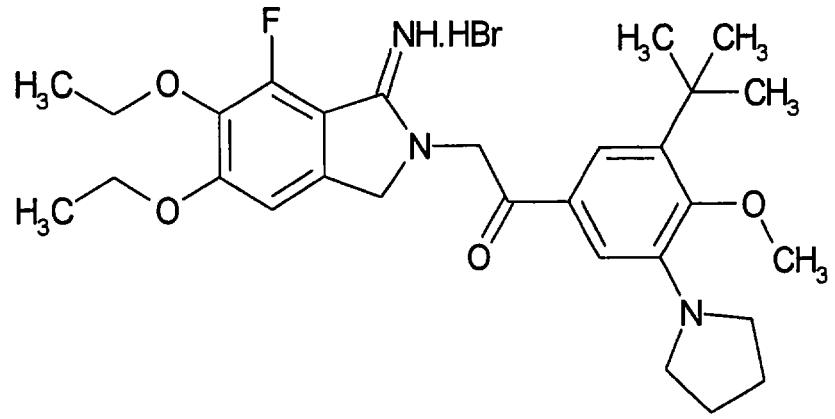
4.27(2H,q,J=7.0Hz), 4.83(2H,s), 5.47(2H,s), 7.35(1H,s),

7.43(1H,s), 7.53(1H,s), 8.18-8.21(1H,m), 8.55(1H,s).

MS:m/e(ESI)507.2(MH+)

Example 72

1-(3-*tert*-Butyl-4-methoxy-5-(pyrrolidin-1-yl)-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



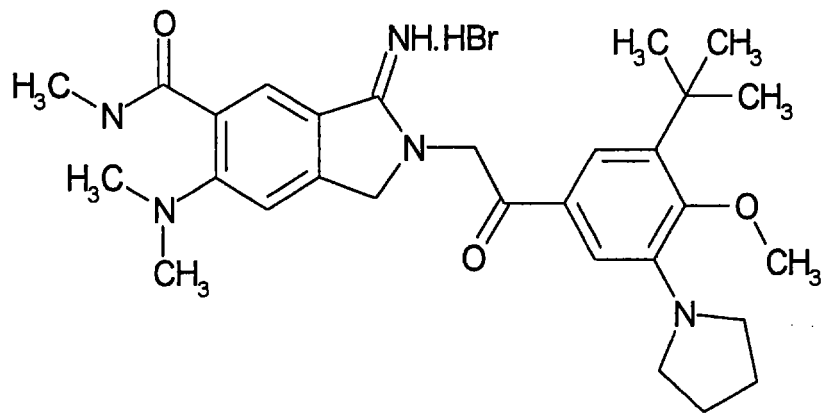
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.37(9H,s), 1.39(3H,t,J=6.8Hz),
1.91(4H,brs), 3.15(4H,brs), 3.64(3H,s),
4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.78(2H,s),
5.46(2H,s), 7.33(1H,s), 7.34(1H,s), 7.42(1H,s),
9.01(1H,brs), 9.23(1H,brs).

MS:m/e(ESI)512.2(MH+)

Example 73

2-[2-(3-*tert*-Butyl-4-methoxy-5-(pyrrolidin-1-yl)-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



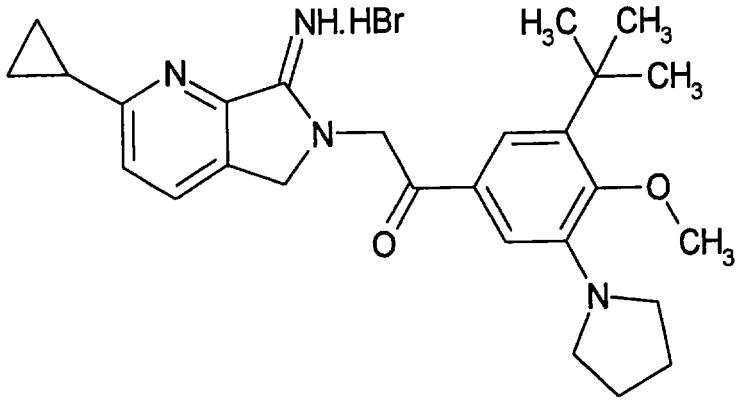
1H-NMR(DMSO-d6)δ:
1.38(9H,s), 1.91(4H,brs), 2.78(3H,d,J=4.4Hz),
2.91(6H,s), 3.15(4H,brs), 3.64(3H,s), 4.72(2H,s),
5.42(2H,s), 7.15(1H,s), 7.35(1H,s), 7.43(1H,s),
8.06(1H,s), 8.35-8.38(1H,m).

MS:m/e(ESI)506.3(MH+)

Example 74

1-(3-*tert*-Butyl-4-methoxy-5-(pyrrolidin-1-yl)-phenyl)-

2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

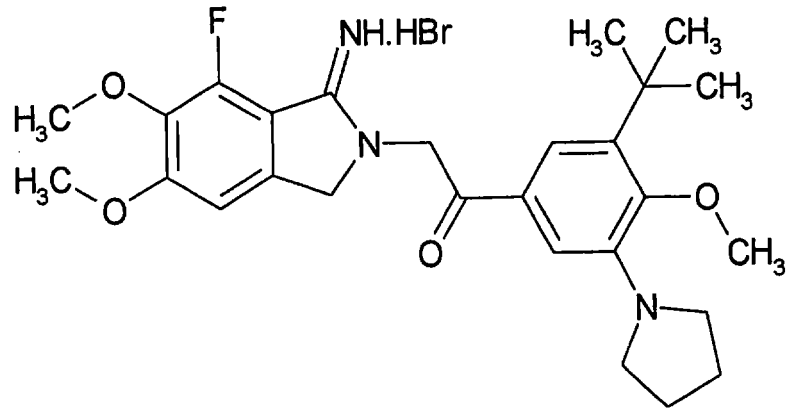


1H-NMR(DMSO-d6)δ:

1.08-1.11(4H,m), 1.38(9H,s), 1.91(4H,brs), 2.29-2.35(1H,m), 3.15(4H,brs), 3.65(3H,s), 4.81(2H,s), 5.56(2H,s), 7.36(1H,s), 7.44(1H,s), 7.72(1H,d,J=8.6Hz), 8.09(1H,d,J=8.6Hz), 9.50(1H,brs), 9.62(1H,brs).

Example 75

1-(3-*tert*-Butyl-4-methoxy-5-(pyrrolidin-1-yl)-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



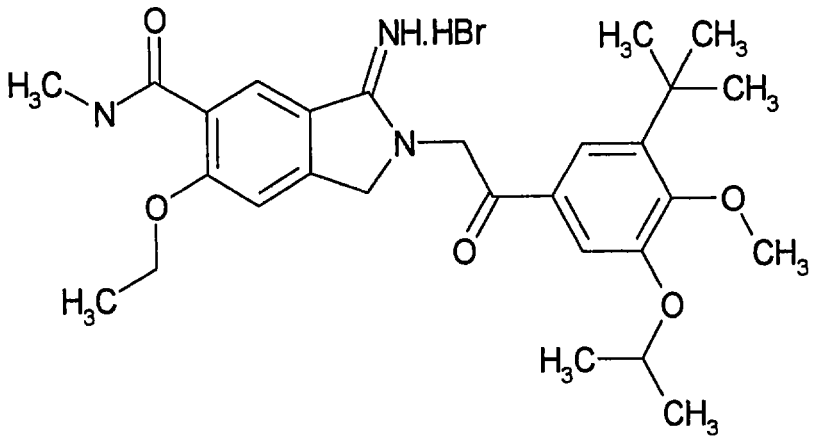
1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.91(4H,brs), 3.15(4H,brs), 3.65(3H,s), 3.87(3H,s), 3.95(3H,s), 4.80(2H,s), 5.48(2H,s), 7.35(1H,s), 7.36(1H,s), 7.43(1H,s), 9.02(1H,brs), 9.23(1H,brs).

MS:m/e(ESI)484.2(MH+)

Example 76

2-[2-(3-*tert*-Butyl-5-isopropoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

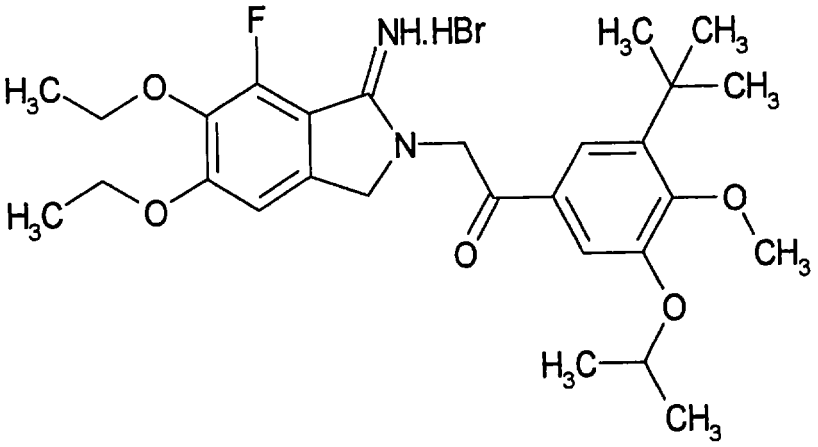


1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=6.4Hz), 1.36(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.4Hz), 3.88(3H,s), 4.28(2H,q,J=6.8Hz), 4.64-4.77(1H,m), 4.85(2H,s), 5.49(2H,s), 7.51(2H,s), 7.54(1H,s), 8.14-8.26(1H,m), 8.56(1H,s), 9.12-9.21(1H,m), 9.79-9.89(1H,m).

Example 77

1-(3-*tert*-Butyl-5-isopropoxy-4-methoxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

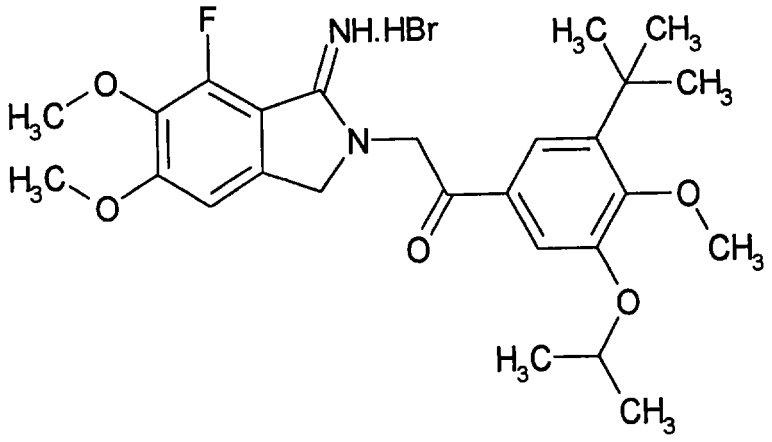


1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.33(6H,d,J=6.0Hz), 1.35(9H,s), 1.39(3H,t,J=6.8Hz), 3.88(3H,s), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.64-4.77(1H,m), 4.80(2H,s), 5.47(2H,s), 7.33(1H,s), 7.50(2H,s), 9.05(1H,brs), 9.29(1H,brs).

Example 78

1-(3-*tert*-Butyl-5-isopropoxy-4-methoxy-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



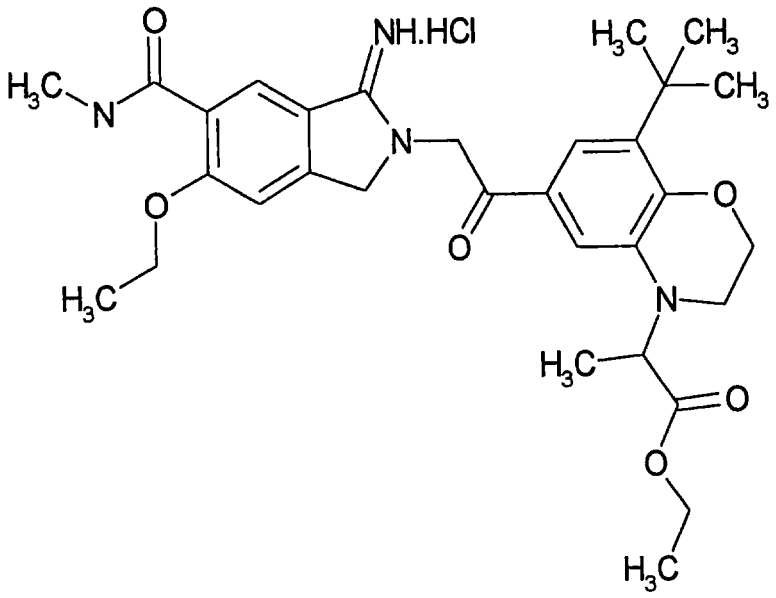
1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=5.6Hz), 1.35(9H,s), 3.87(3H,s), 3.88(3H,s),

3.95(3H,s), 4.64-4.76(1H,m), 4.81(2H,s), 5.48(2H,s), 7.36(1H,s), 7.50(2H,s), 8.99-9.16(1H,m), 9.25-9.40(1H,m).

Example 79

Ethyl 2-{8-*tert*-butyl-6-[2-5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl]-acetyl}-2,3-dihydro-benzo[1,4]oxazin-4-yl}-propanoate hydrochloride

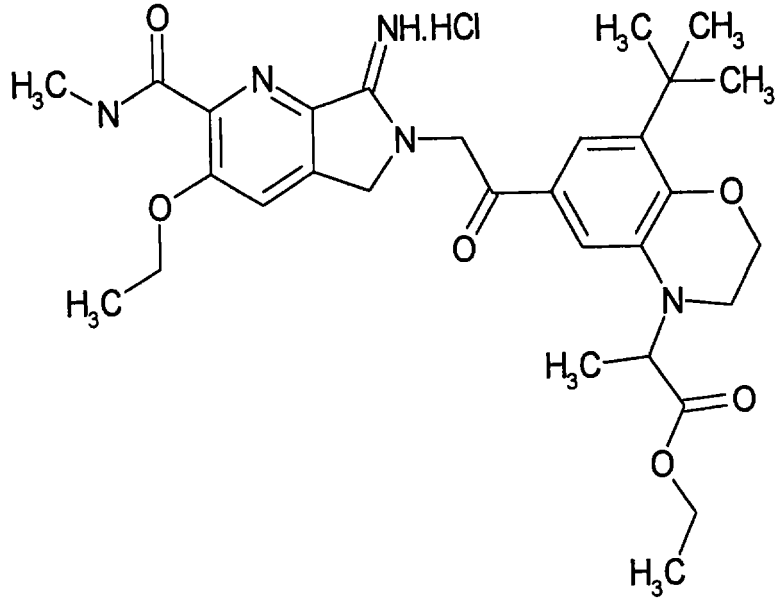


1H-NMR(DMSO-d6)δ:

1.15(3H,t,J=7Hz), 1.30-1.50(15H,m), 2.82(3H,d,J=5Hz), 3.30-3.40(2H,m), 4.09(2H,m), 4.22-4.36(4H,m), 4.71(1H,q,J=6Hz), 4.82(2H,s), 5.38(1H,d,J=18Hz), 5.48(1H,d,J=18Hz), 7.20(1H,brs), 7.28(1H,brs), 7.53(1H,s), 8.21(1H,q,J=5Hz), 8.55(1H,s), 9.21(1H,brs), 9.82(1H,brs).

Example 80

Ethyl 2-{8-*tert*-butyl-6-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-propanoate hydrochloride

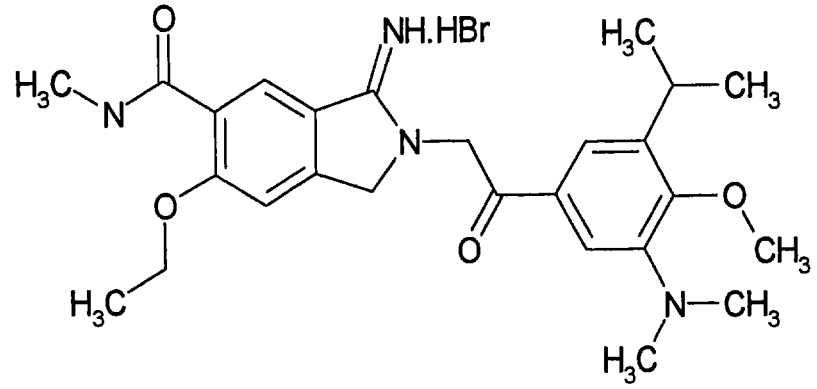


1H-NMR(DMSO-d6)δ:
1.15(3H,t,J=7Hz), 1.32-1.39(12H,m), 1.44(3H,d,J=7Hz),
2.33(1H,m), 2.77(3H,d,J=5Hz), 3.30-3.40(2H,m),
4.09(2H,m), 4.20-4.30(4H,m), 4.71(1H,q,J=7Hz),
4.86(2H,s), 4.82(2H,s), 5.43(1H,d,J=18Hz),
5.52(1H,d,J=18Hz), 7.20(1H,d,J=2Hz), 7.27(1H,d,J=2Hz),
7.98(1H,s), 8.55(1H,q,J=5Hz), 9.47(1H,brs),
9.92(1H,brs).
MS:m/e(ESI)566.2(MH+)

Example 81

2-[2-(3-Dimethylamino-5-isopropyl-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-

5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.20(6H,d,J=7.2Hz), 1.41(3H,t,J=6.8Hz), 2.78(6H,s),

2.81(3H,d,J=4.4Hz), 3.77(3H,s), 4.28(2H,q,J=6.8Hz),

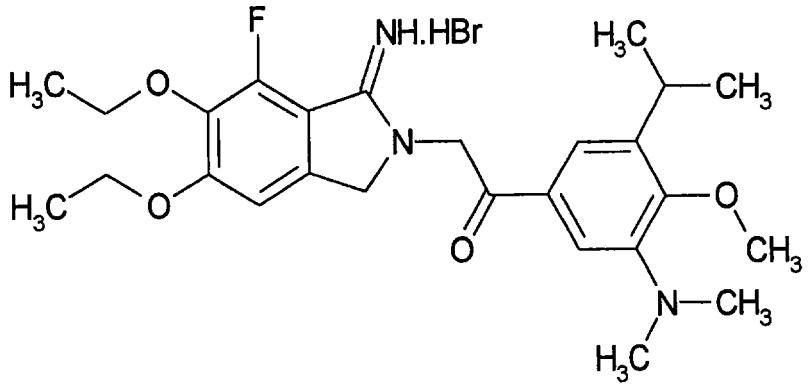
4.84(2H,s), 5.49(2H,s), 7.36(1H,s), 7.51(1H,s),

7.54(1H,s), 8.20(1H,q,J=4.4Hz), 8.56(1H,s),

9.17(1H,brs), 9.84(1H,brs).

Example 82

2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-1-(3-dimethylamino-5-isopropyl-4-methoxy-phenyl)-ethanone hydrobromide



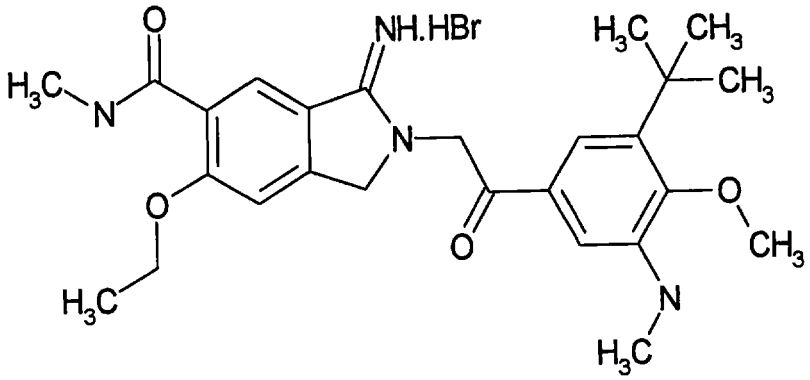
1H-NMR(DMSO-d6)δ:

1.20(6H,d,J=6.8Hz), 1.29(3H,t,J=6.8Hz),

1.39(3H,t,J=6.8Hz), 2.78(6H,s), 3.76(3H,s),
4.11(2H,q,J=6.8Hz), 4.22(2H,q,J=6.8Hz), 4.79(2H,s),
5.47(2H,s), 7.34-7.36(2H,m), 7.52(1H,s).

Example 83

2-[2-(3-*tert*-Butyl-4-methoxy-5-methylamino-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

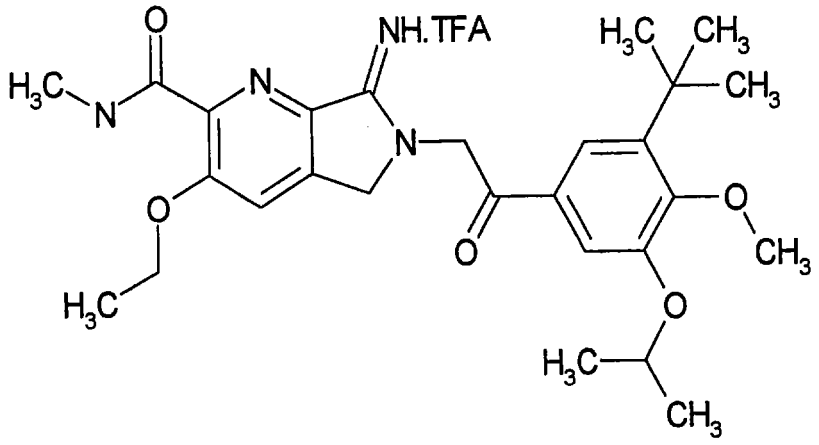


1H-NMR(DMSO-d6)δ:
1.37(9H,s), 1.41(3H,t,J=7.0Hz), 2.76(3H,d,J=5.0Hz),
2.82(3H,d,J=4.4Hz), 3.72(3H,s), 4.28(2H,q,J=7.0Hz),
4.84(2H,s), 5.47(2H,s), 5.51(1H,q,J=5.0Hz), 7.05(1H,s),
7.24(1H,s), 7.54(1H,s), 8.21(1H,q,J=4.4Hz), 8.55(1H,s),
9.17(1H,brs), 9.82(1H,brs).

MS:m/e(ESI)467.3(MH+)

Example 84

6-[2-(3-*tert*-Butyl-5-isopropoxy-4-methoxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate

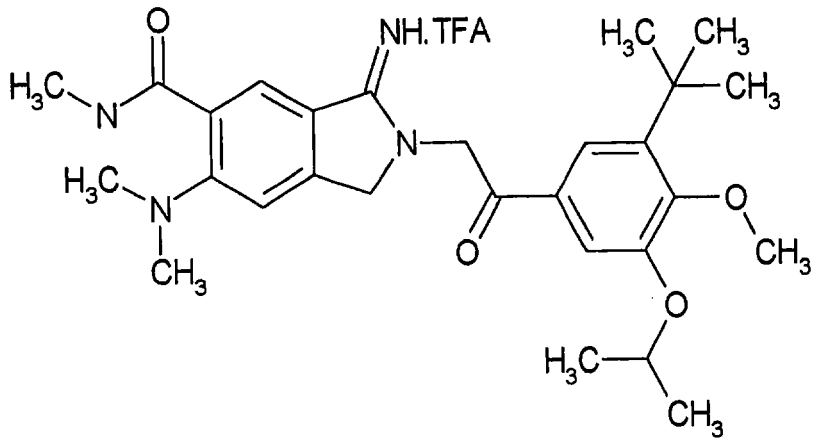


1H-NMR(DMSO-d6)δ:

1.26-1.43(18H,m), 2.77(3H,d,J=4.8Hz), 3.88(3H,s), 4.24(2H,q,J=6.8Hz), 4.64-4.77(1H,m), 4.88(2H,s), 5.52(2H,s), 7.50(2H,s), 7.99(1H,s), 8.47-8.58(1H,m), 9.34-9.46(1H,m), 9.90-10.03(1H,m).

Example 85

2-[2-(3-*tert*-Butyl-5-isopropoxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate



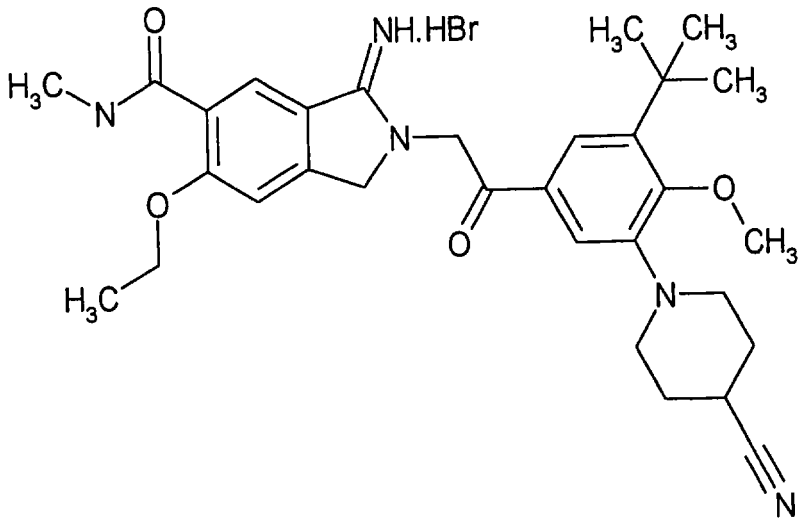
1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=6.0Hz), 1.35(9H,s), 2.77(3H,d,J=4.4Hz),

2.91(6H,s), 3.88(3H,s), 4.63-4.80(3H,m), 5.44(2H,s), 7.15(1H,s), 7.50(2H,s), 8.07(1H,s), 8.31-8.43(1H,m), 8.88-8.99(1H,m), 9.46-9.60(1H,m).

Example 86

2-{2-[3-*tert*-Butyl-5-(4-cyano-piperidin-1-yl)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

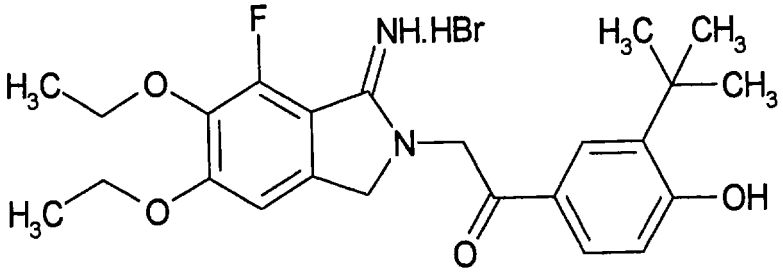
1.36(9H,s), 1.41(3H,t,J=6.8Hz), 1.88-2.13(4H,m), 2.82(3H,d,J=4.4Hz), 2.86-2.98(2H,m), 3.02-3.18(3H,m), 3.93(3H,s), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.49(2H,s), 7.52(1H,d,J=1.6Hz), 7.54(1H,s), 7.61(1H,d,J=1.6Hz), 8.14-8.26(1H,m), 8.56(1H,s), 9.10-9.18(1H,m), 9.81-9.88(1H,m).

MS:m/e(ESI)546.2(MH+)

Example 87

1-(3-*tert*-Butyl-4-hydroxy-phenyl)-2-(5,6-diethoxy-7-

fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



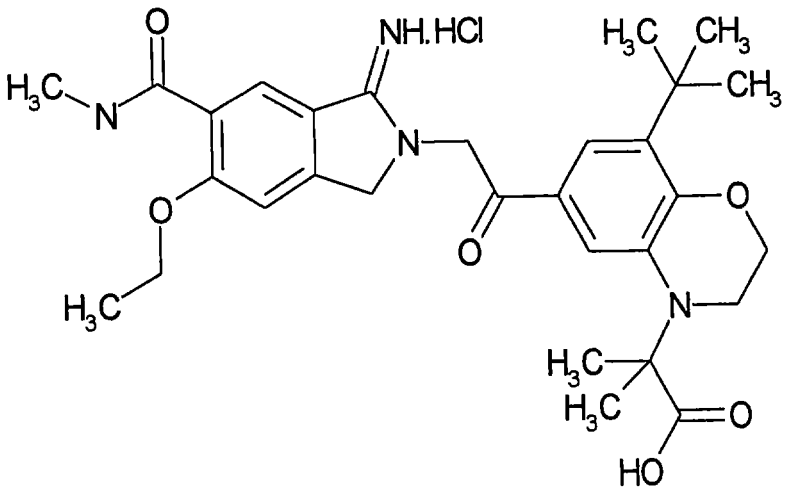
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.37(9H,s), 1.40(3H,t,J=6.8Hz), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.78(2H,s), 5.40(2H,s), 6.95(1H,d,J=8.6Hz), 7.32(1H,s), 7.75(1H,d,J=8.6Hz), 7.80(1H,s), 9.00(1H,brs), 9.30(1H,brs).

MS:m/e(ESI)429.1(MH+)

Example 88

2-{8-*tert*-Butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-2-methyl-propanoic acid hydrochloride



1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.38(3H,t,J=7Hz), 1.48(6H,s),

2.82(3H,d,J=5Hz), 3.30-3.40(2H,m), 4.22-4.40(4H,m),

4.82(2H,s), 5.40(2H,s), 7.08(1H,brs), 7.30(1H,brs),

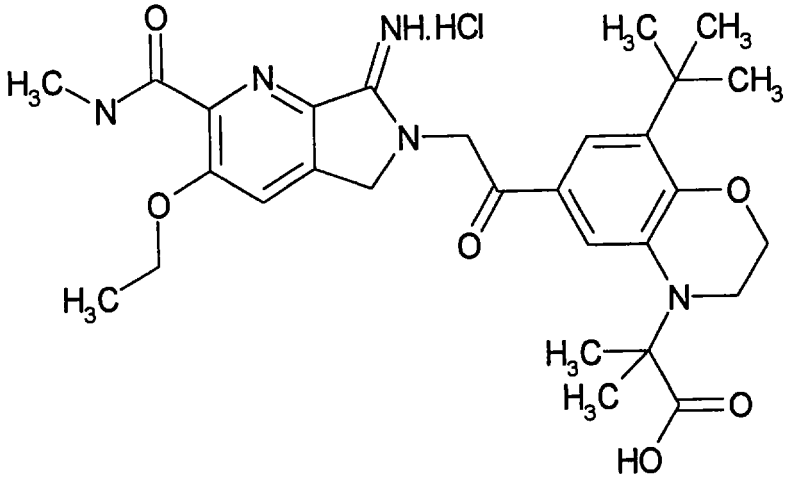
7.52(1H,s), 8.21(1H,q,J=5Hz), 8.55(1H,s), 9.22(1H,brs),

9.83(1H,brs).

MS:m/e(ESI)551.2(MH+)

Example 89

2-{8-*tert*-Butyl-6-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-2-methyl-propanoic acid hydrochloride



1H-NMR(DMSO-d6)δ:

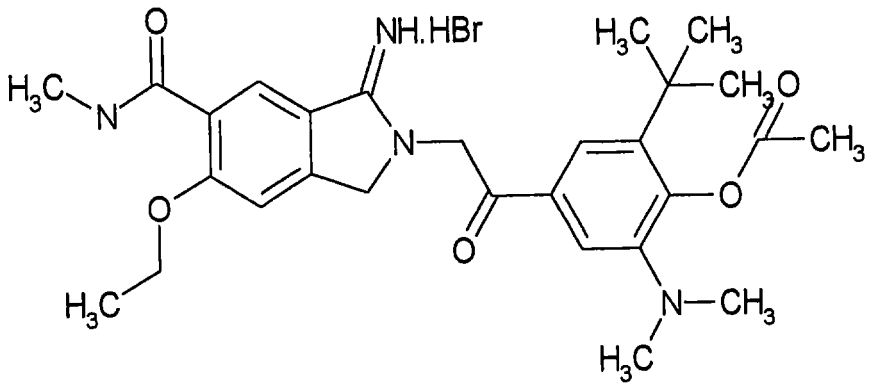
1.30-1.40(12H,m), 1.48(6H,s), 2.77(3H,d,J=5Hz), 3.30-3.40(2H,m), 4.22-4.33(4H,m), 4.85(2H,s), 5.43(2H,s),

7.08(1H,brs), 7.29(1H,brs), 7.98(1H,s),

8.54(1H,q,J=5Hz), 9.45(1H,brs), 9.91(1H,brs).

Example 90

2-*tert*-Butyl-6-dimethylamino-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl acetate hydrobromide

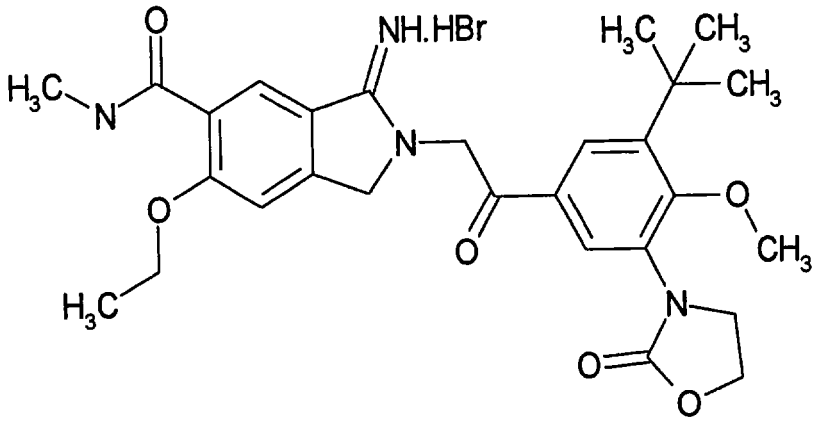


1H-NMR(DMSO-d6)δ:
1.33(9H,s), 1.41(3H,t,J=7.2Hz), 2.33(3H,s), 2.65(6H,s), 2.82(3H,d,J=4.8Hz), 4.27(2H,q,J=7.2Hz), 4.85(2H,s), 5.51(2H,s), 7.54(1H,s), 7.58(1H,s), 7.66(1H,s), 8.19-8.21(1H,m), 8.55(1H,s), 9.17(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)509.2(MH+)

Example 91

2-{2-[3-*tert*-Butyl-4-methoxy-5-(2-oxo-oxazolidin-3-yl)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.4Hz),

3.82(3H,s), 3.93(2H,t,J=7.6Hz), 4.28(2H,q,J=6.8Hz),

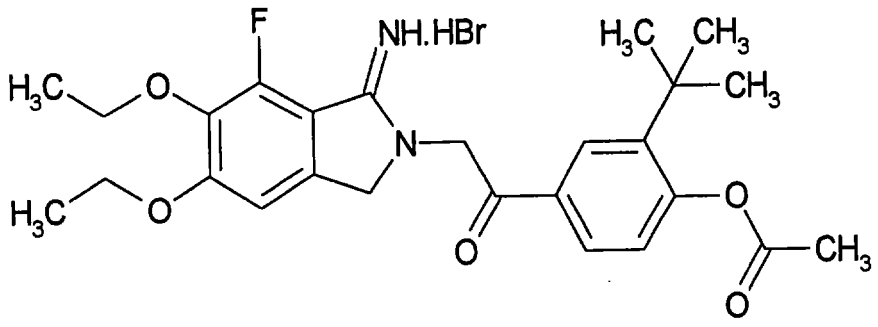
4.54(2H,t,J=7.6Hz), 4.85(2H,s), 5.46(2H,s), 7.54(1H,s),

7.83(1H,d,J=2.0Hz), 7.99(1H,d,J=2.0Hz),

8.20(1H,q,J=4.4Hz), 8.56(1H,s).

Example 92

2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl acetate hydrobromide



1H-NMR(DMSO-d6)δ:

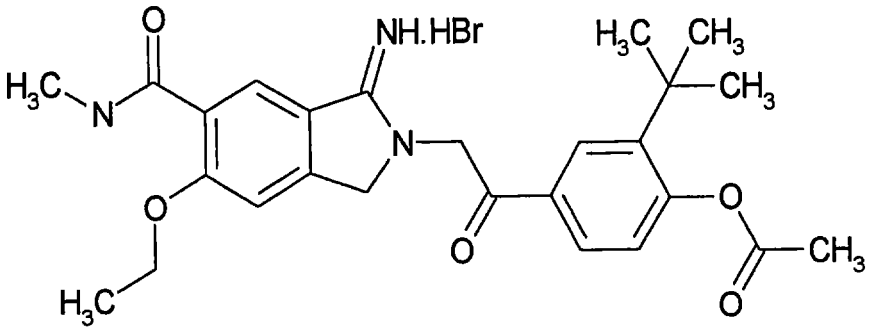
1.29(3H,t,J=7.0Hz), 1.34(9H,s), 1.40(3H,t,J=7.0Hz),

2.37(3H,s), 4.12(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz),

4.81(2H,s), 5.49(2H,s), 7.31-7.34(2H,m),
7.93(1H,d,J=8.4Hz), 7.96(1H,s), 9.02(1H,brs),
9.30(1H,brs).
MS:m/e(ESI)471.1(MH+)

Example 93

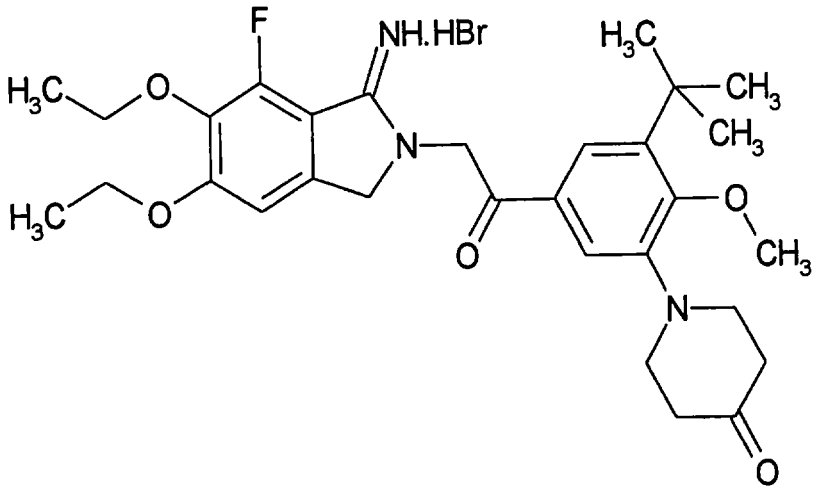
2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl acetate hydrobromide



1H-NMR(DMSO-d6)δ:
1.35(9H,s), 1.42(3H,t,J=7.0Hz), 2.37(3H,s),
2.83(3H,d,J=4.4Hz), 4.28(2H,q,J=7.0Hz), 4.86(2H,s),
5.50(2H,s), 7.33(1H,d,J=8.4Hz), 7.54(1H,s),
7.94(1H,d,J=8.4Hz), 7.97(1H,s), 8.19-8.21(1H,m),
8.56(1H,s), 9.20(1H,brs), 9.82(1H,brs).
MS:m/e(ESI)466.2(MH+)

Example 94

1-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-piperidin-4-one hydrobromide



1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.38(9H,s), 1.39(3H,t,J=6.8Hz),

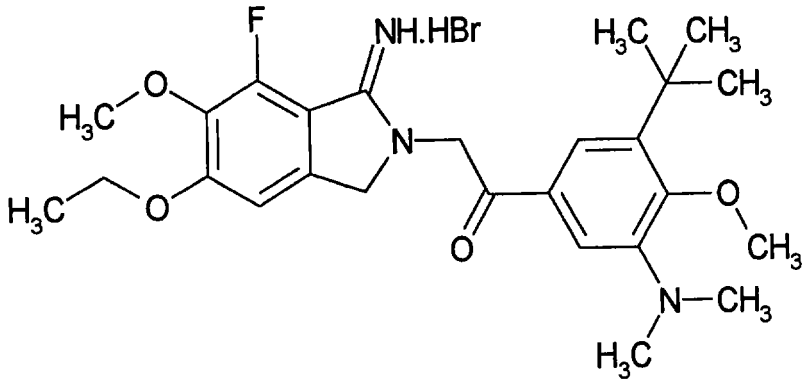
2.48-2.62(4H,m), 3.28-3.45(4H,m), 4.02(3H,s),

4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.79(2H,s),

5.48(2H,s), 7.33(2H,s), 7.56(2H,s), 7.62(2H,s).

Example 95

1-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl)-2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.40(3H,t,J=7.2Hz), 2.75(6H,s), 3.82(3H,s),

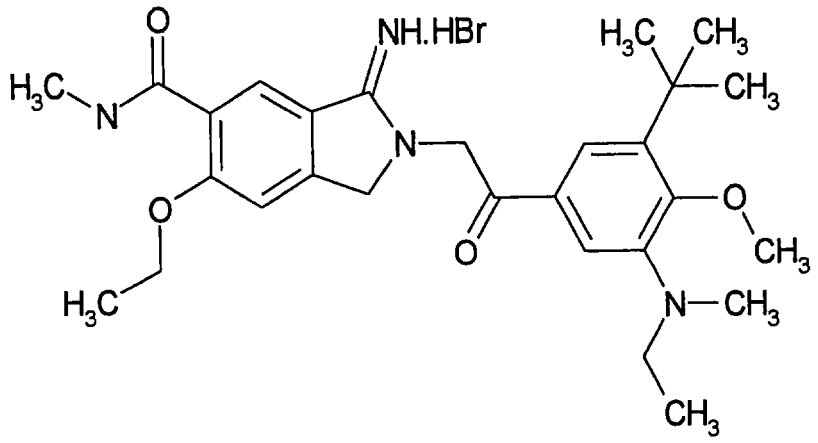
3.87(3H,s), 4.20(2H,q,J=7.2Hz), 4.78(2H,s), 5.48(2H,s),

7.34(1H,s), 7.45(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz).

MS:m/e(ESI)472.2(MH+)

Example 96

2-{2-[3-*tert*-Butyl-5-(ethyl-methyl-amino)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.01(3H,t,J=7.0Hz), 1.37(9H,s), 1.41(3H,t,J=7.0Hz),

2.74(3H,s), 2.82(3H,d,J=4.8Hz), 3.13(2H,q,J=7.0Hz),

3.83(3H,s), 4.28(2H,q,J=7.0Hz), 4.84(2H,s), 5.49(2H,s),

7.48(1H,d,J=2.0Hz), 7.54-7.55(2H,m),

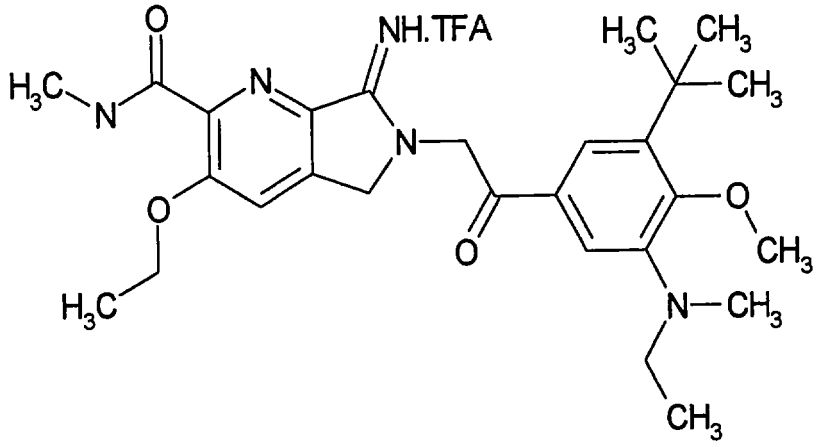
8.21(1H,q,J=4.8Hz), 8.55(1H,s), 9.14(1H,brs),

9.81(1H,brs).

MS:m/e(ESI)495.2(MH+)

Example 97

6-{2-[3-*tert*-Butyl-5-(ethyl-methyl-amino)-4-methoxy-phenyl]-2-oxo-ethyl}-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate



1H-NMR(DMSO-d6)δ:

1.01(3H,t,J=7.0Hz), 1.34-1.37(12H,m), 2.74(3H,s),

2.78(3H,d,J=4.8Hz), 3.13(2H,q,J=7.0Hz), 3.83(3H,s),

4.24(2H,q,J=7.0Hz), 4.87(2H,s), 5.52(2H,s),

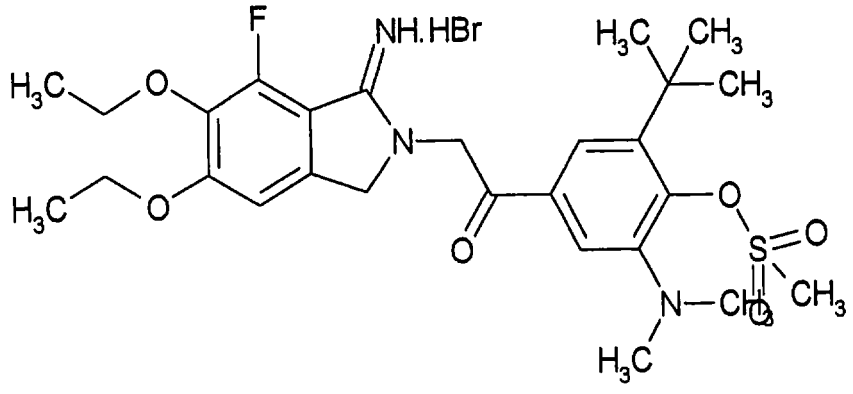
7.47(1H,d,J=2.0Hz), 7.54(1H,d,J=2.0Hz), 7.99(1H,s),

8.53(1H,q,J=4.8Hz), 9.40(1H,brs), 9.92(1H,brs).

MS:m/e(ESI)496.2(MH+)

Example 98

2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-dimethylamino-phenyl methanesulfonate hydrobromide



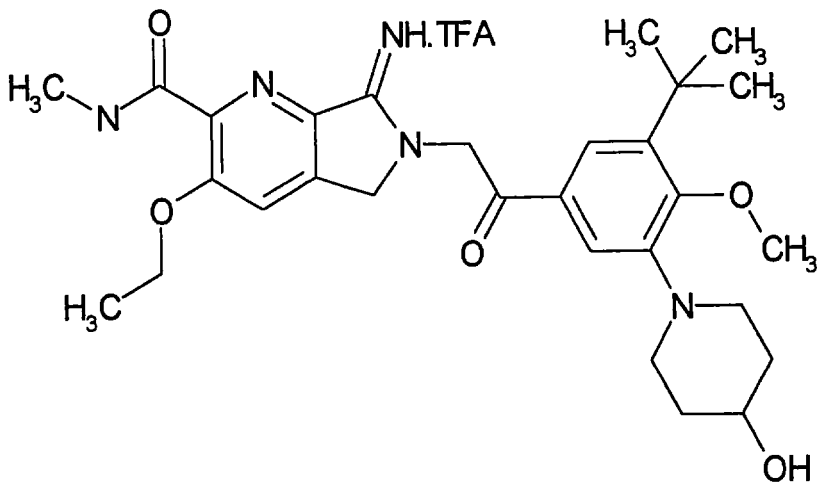
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.40(3H,t,J=7.0Hz), 1.44(9H,s), 2.67(6H,s), 3.73(3H,s), 4.12(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.80(2H,s), 5.51(2H,s), 7.34(1H,s), 7.67(1H,s), 7.75(1H,s).

MS:m/e(ESI)550.1(MH+)

Example 99

6-{2-[3-*tert*-Butyl-5-(4-hydroxy-piperidin-1-yl)-4-methoxy-phenyl]-2-oxo-ethyl}-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate



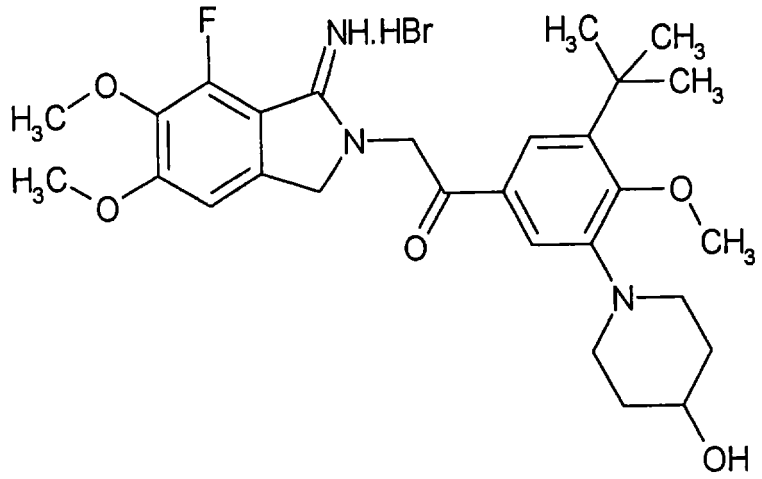
1H-NMR(DMSO-d6)δ:

1.26-1.50(12H,m), 1.50-1.68(2H,m), 1.84-2.03(2H,m), 2.64-2.86(5H,m), 3.12-3.68(3H,m), 3.94(3H,s), 4.23(2H,q,J=6.8Hz), 4.87(2H,s), 5.52(2H,s), 7.44-7.70(2H,m), 7.99(1H,s), 8.41-8.63(1H,m), 9.37(1H,brs), 9.94(1H,brs).

MS:m/e(ESI)538.3(MH+)

Example 100

1-[3-*tert*-Butyl-5-(4-hydroxy-piperidin-1-yl)-4-methoxy-phenyl]-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

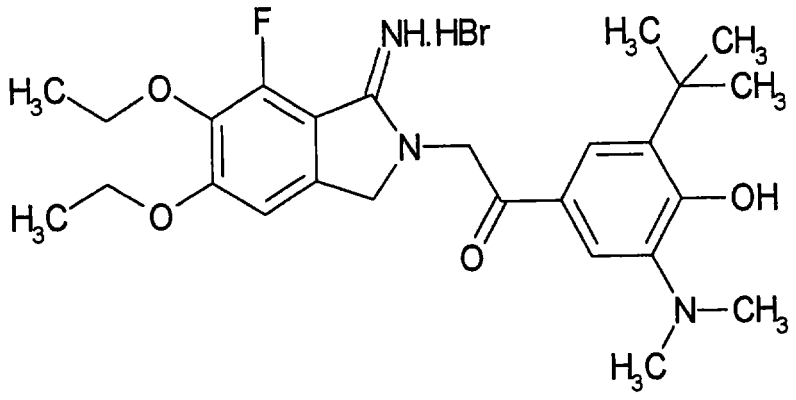


1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.54-1.70(2H,m), 1.84-2.00(2H,m), 2.65-2.80(2H,m), 3.19-3.50(2H,m), 3.55-3.70(1H,m), 3.86(3H,s), 3.93(3H,s), 3.95(3H,s), 4.73(1H,d,J=4.0Hz), 4.80(2H,s), 5.48(2H,s), 7.36(1H,s), 7.51(1H,s), 7.56(1H,s), 8.99-9.40(2H,m).

Example 101

1-(3-*tert*-Butyl-5-dimethylamino-4-hydroxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.38-1.41(12H,m), 2.61(6H,s),

4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.78(2H,s),

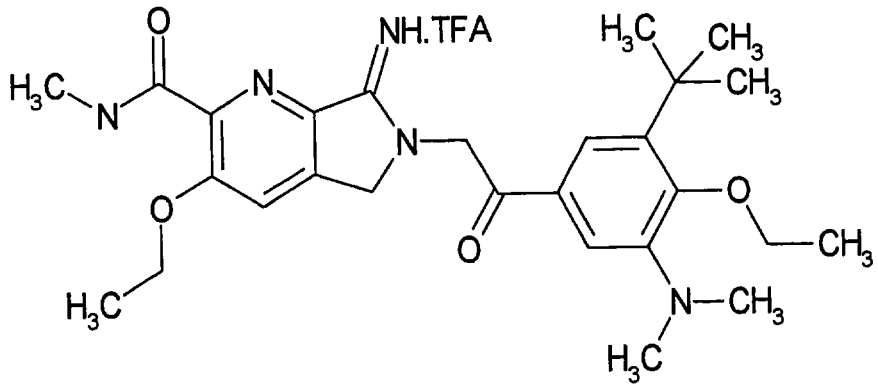
5.44(2H,s), 7.33(1H,s), 7.63(1H,s), 7.68(1H,s),

9.01(1H,brs), 9.26(1H,brs).

MS:m/e(ESI)472.2(MH+)

Example 102

6-[2-(3-*tert*-Butyl-5-dimethylamino-4-ethoxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide trifluoroacetate



1H-NMR(DMSO-d6)δ:

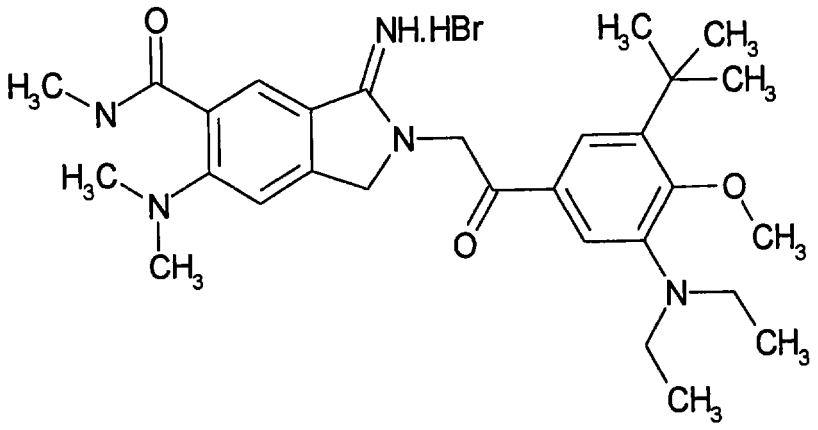
1.34-1.39(15H,m), 2.75(6H,s), 2.78(3H,d,J=4.6Hz),

4.13(2H,q,J=7.0Hz), 4.24(2H,q,J=7.0Hz), 4.87(2H,s),
5.52(2H,s), 7.45(1H,s), 7.55(1H,s), 7.99(1H,s),
8.53(1H,q,J=4.6Hz), 8.55(1H,s), 9.39(1H,brs),
9.92(1H,brs).

MS:m/e(ESI)496.2(MH+)

Example 103

2-[2-(3-*tert*-Butyl-5-dimethylamino-4-methoxy-phenyl]-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



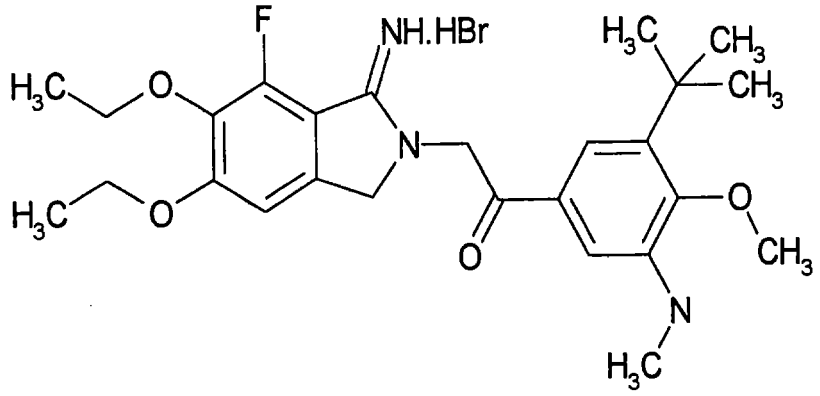
1H-NMR(DMSO-d6)δ:
0.98(6H,t,J=7.0Hz), 1.37(9H,s), 2.78(3H,d,J=4.8Hz),
2.92(6H,s), 3.16(4H,q,J=7.0Hz), 3.85(3H,s), 4.74(2H,s),
5.44(2H,s), 7.15(1H,s), 7.49(1H,d,J=2.0Hz), 7.55(1H,s),
7.55(1H,d,J=2.0Hz), 8.07(1H,s), 8.37(1H,q,J=4.8Hz),
8.92(1H,brs), 9.53(1H,brs).

MS:m/e(ESI)508.2(MH+)

Example 104

1-(3-*tert*-Butyl-4-methoxy-5-methylamino-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-

yl)-ethanone hydrobromide



1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz),

2.76(3H,d,J=5.2Hz), 3.72(3H,s), 4.11(2H,q,J=7.0Hz),

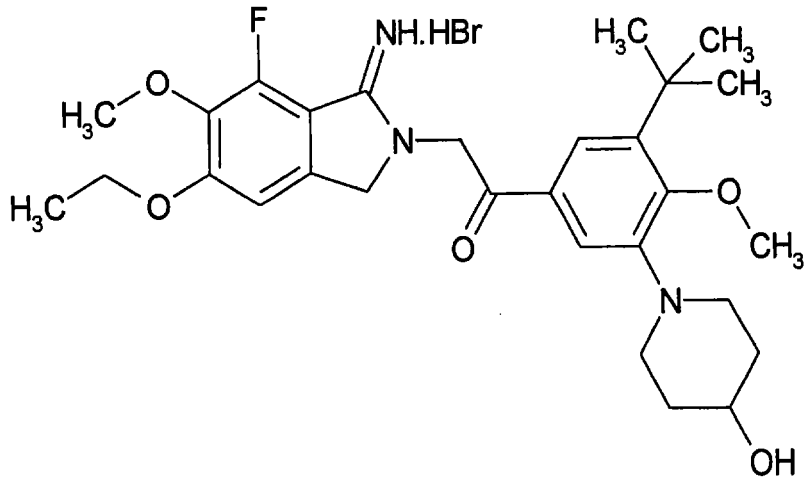
4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.46(2H,s),

5.50(1H,q,J=5.2Hz), 7.04(1H,s), 7.23(1H,s), 7.33(1H,s).

MS:m/e(ESI)472.1(MH+)

Example 105

1-[3-*tert*-Butyl-5-(4-hydroxy-piperidin-1-yl)-4-methoxy-phenyl]-2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl hydrobromide



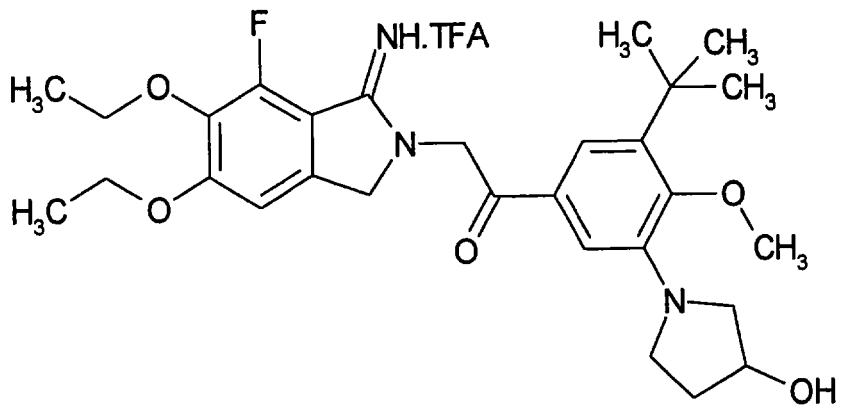
1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.40(3H,t,J=6.8Hz), 1.54-1.68(2H,m), 1.83-1.96(2H,m), 2.64-2.78(2H,m), 3.21-3.48(2H,m), 3.58-3.69(1H,m), 3.87(3H,s), 3.94(3H,s), 4.22(2H,q,J=6.8Hz), 4.73(1H,d,J=4.0Hz), 4.79(2H,s), 5.48(2H,s), 7.34(1H,s), 7.51(1H,s), 7.56(1H,s), 9.00-9.12(1H,m), 9.20-9.34(1H,m).

MS:m/e(ESI)528.2(MH+)

Example 106

1-[3-*tert*-Butyl-5-(3-hydroxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone trifluoroacetate



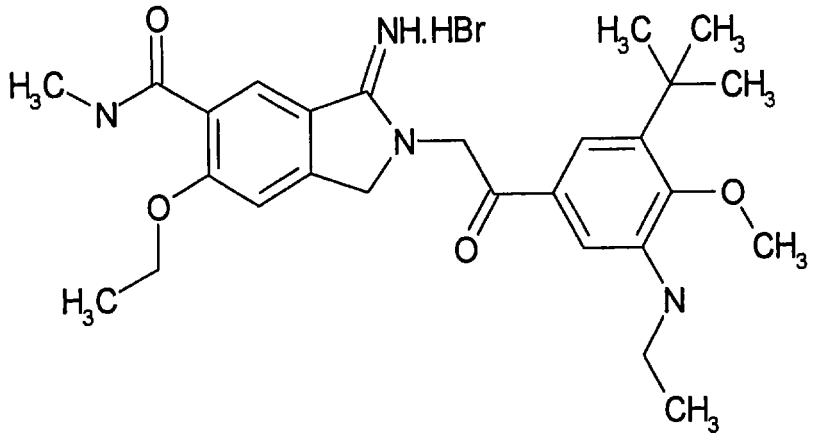
1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.79-1.92(1H,m), 1.98-2.12(1H,m), 2.90-2.99(1H,m), 3.08-3.18(1H,m), 3.20-3.60(2H,m), 3.65(3H,s), 3.89(3H,s), 3.97(3H,s), 4.30-4.43(1H,m), 4.81(2H,s), 5.50(2H,s), 7.34(1H,s), 7.39(1H,s), 7.43(1H,s), 9.08(1H,brs), 9.31(1H,brs).

Example 107

2-[2-(3-*tert*-Butyl-5-ethylamino-4-methoxy-phenyl)-2-

oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



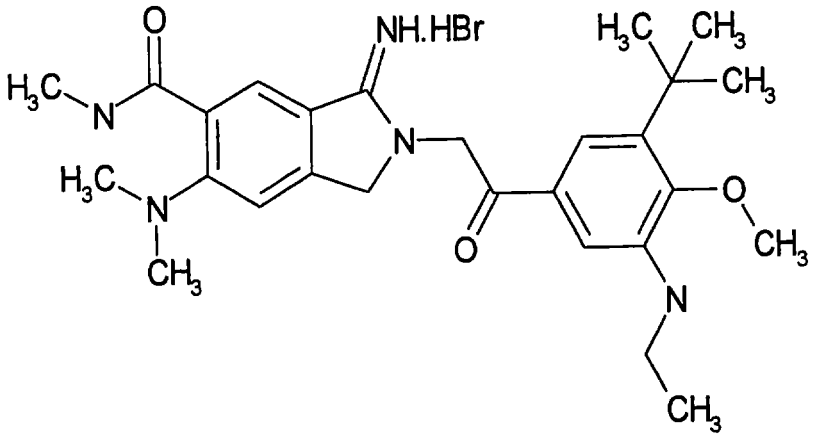
1H-NMR(DMSO-d6)δ:

1.20(3H,t,J=7.0Hz), 1.37(9H,s), 1.41(3H,t,J=7.0Hz), 2.82(3H,d,J=4.8Hz), 3.12-3.17(2H,m), 3.73(3H,s), 4.28(2H,q,J=7.0Hz), 4.83(2H,s), 5.29(1H,t,J=6.0Hz), 5.46(2H,s), 7.11(1H,s), 7.23(1H,s), 7.53(1H,s), 8.21(1H,q,J=4.8Hz), 8.55(1H,s), 9.18(1H,brs), 9.80(1H,brs).

MS:m/e(ESI)481.3(MH+)

Example 108

2-[2-(3-*tert*-Butyl-5-ethylamino-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.20(3H,t,J=7.0Hz), 1.37(9H,s), 2.78(3H,d,J=4.6Hz),

2.92(6H,s), 3.12-3.19(2H,m), 3.72(3H,s), 4.73(2H,s),

5.28(1H,t,J=5.8Hz), 5.42(2H,s), 7.10(1H,s), 7.15(1H,s),

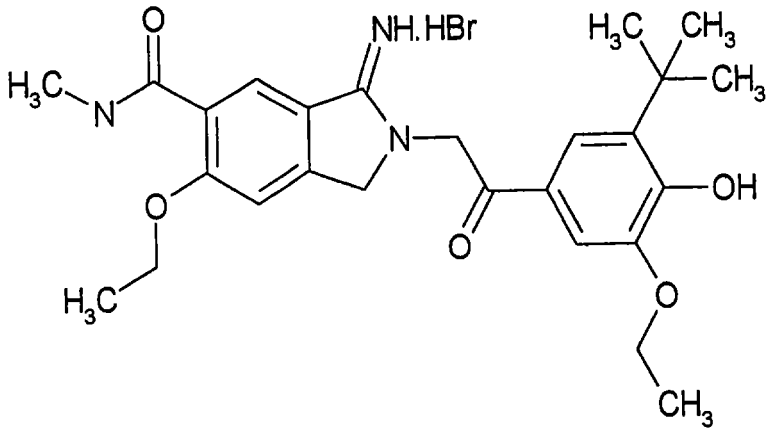
7.23(1H,s), 8.06(1H,s), 8.37(1H,q,J=4.6Hz),

8.92(1H,brs), 9.52(1H,brs).

MS:m/e(ESI)480.3(MH+)

Example 109

2-[2-(3-*tert*-Butyl-5-ethoxy-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



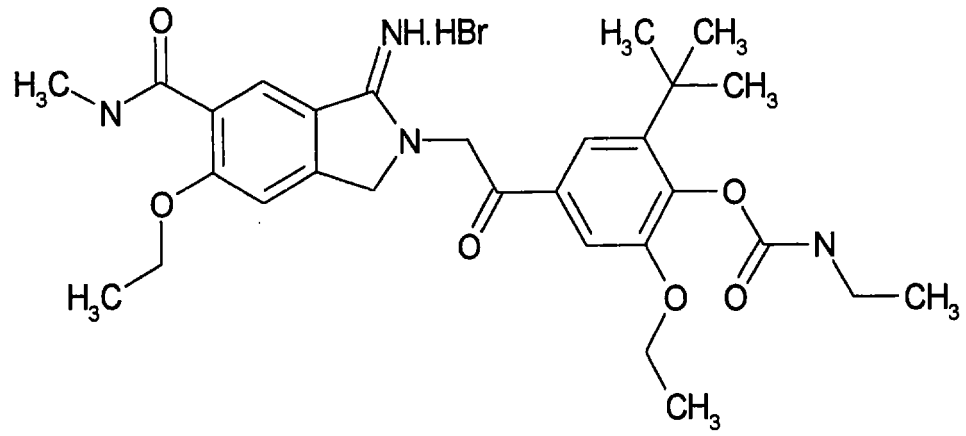
1H-NMR(DMSO-d6)δ:

1.36-1.43(15H,m), 2.82(3H,d,J=4.6Hz),
4.12(2H,q,J=7.0Hz), 4.28(2H,q,J=7.0Hz), 4.83(2H,s),
5.45(2H,s), 7.43(1H,s), 7.51(1H,s), 7.53(1H,s),
8.20(1H,q,J=4.6Hz), 8.55(1H,s).

MS:m/e(ESI)468.2(MH+)

Example 110

2-*tert*-Butyl-6-ethoxy-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl ethylcarbamate hydrobromide



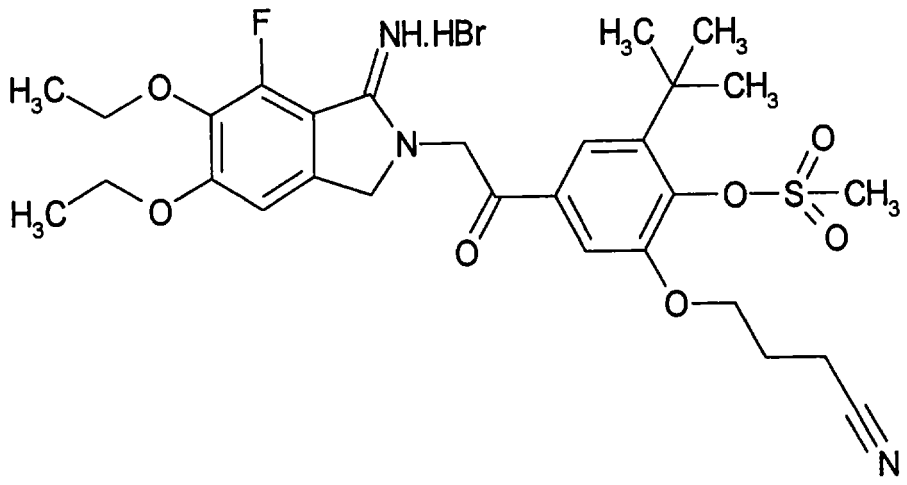
1H-NMR(DMSO-d6)δ:
1.09(3H,t,J=7.0Hz), 1.31(3H,t,J=7.0Hz), 1.34(9H,s),
1.42(3H,t,J=7.0Hz), 2.82(3H,d,J=4.8Hz), 3.05-3.11(2H,m), 4.07(2H,q,J=7.0Hz), 4.28(2H,q,J=7.0Hz),
4.85(2H,s), 5.51(2H,s), 7.52(1H,s), 7.54(1H,s),
7.57(1H,s), 7.86(1H,t,J=6.0Hz), 8.21(1H,q,J=4.8Hz),
8.55(1H,s).

MS:m/e(ESI)539.4(MH+)

Example 111

2-*tert*-Butyl-6-(3-cyano-propoxy)-4-[2-(5,6-diethoxy-7-

fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl methanesulfonate hydrobromide



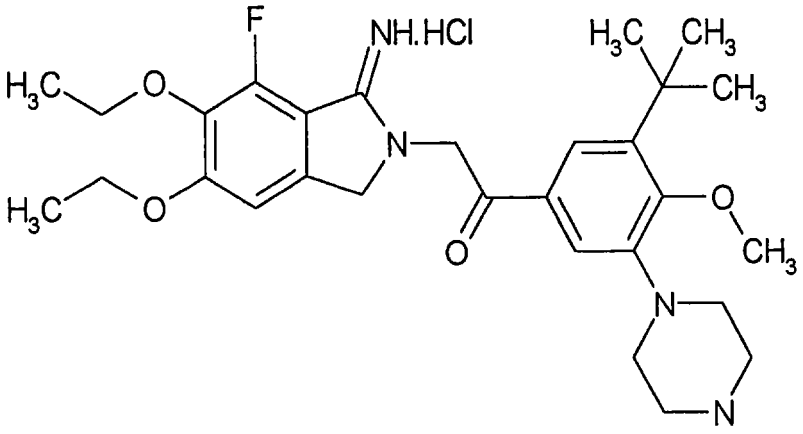
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.40(3H,t,J=7.0Hz), 1.44(9H,s), 2.10-2.17(2H,m), 2.69(2H,t,J=7.2Hz), 3.67(3H,s), 4.12(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.82(2H,s), 5.53(2H,s), 7.35(1H,s), 7.63(1H,s), 7.66(1H,s), 9.08(1H,brs), 9.32(1H,brs).

MS:m/e(ESI)590.2(MH+)

Example 112

1-(3-*tert*-Butyl-4-methoxy-5-piperazin-1-yl-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone dihydrochloride



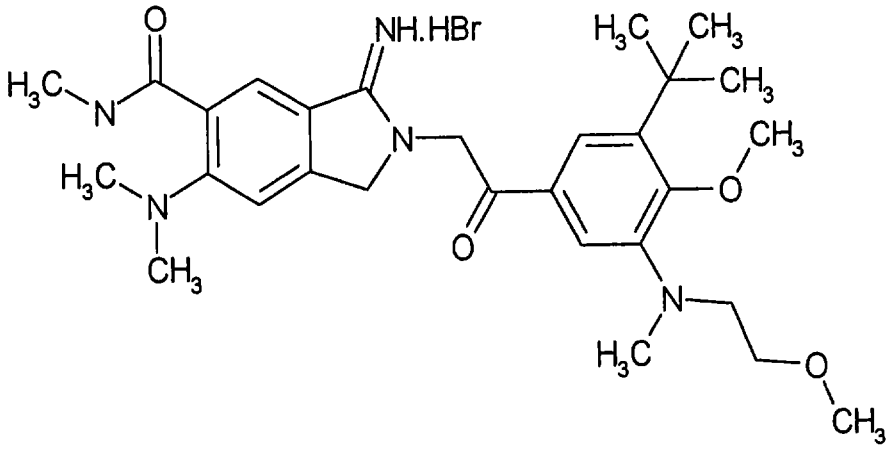
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz), 3.21(4H,brs), 3.32(4H,brs), 3.94(3H,s), 4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.55(2H,s), 7.34(1H,s), 7.50(1H,s), 7.64(1H,s), 9.04-9.16(3H,m), 9.40(1H,brs).

MS:m/e(ESI)527.3(MH+)

Example 113

2-(2-{3-*tert*-Butyl-4-methoxy-5-[(2-methoxyethyl)-methylamino]-phenyl}-2-oxo-ethyl)-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide



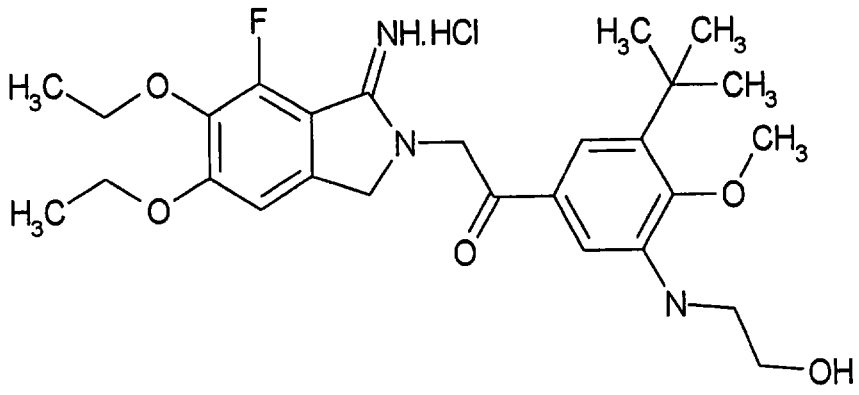
1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.77(3H,d,J=4.0Hz), 2.80(3H,s), 2.91(6H,s), 3.18(3H,s), 3.20-3.48(4H,m), 3.81(3H,s), 4.73(2H,s), 5.43(2H,s), 7.15(1H,s), 7.50(1H,s), 7.53(1H,s), 8.06(1H,s), 8.36(1H,q,J=4.0Hz).

MS:m/e(ESI)524.3(MH+)

Example 114

1-[3-*tert*-Butyl-5-(2-hydroxyethylamino)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride



1H-NMR(DMSO-d6)δ:

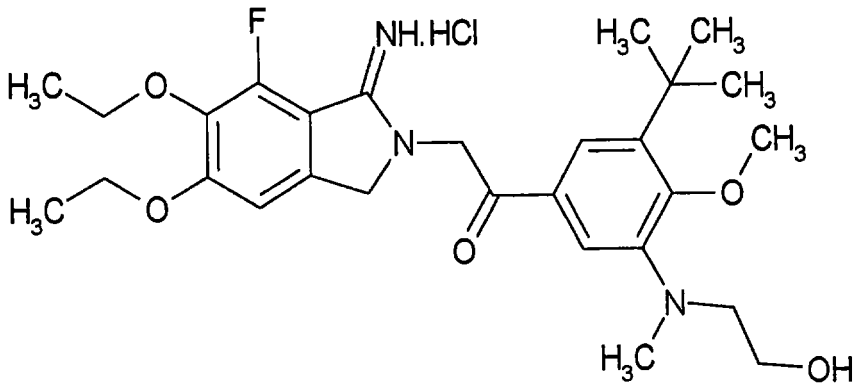
1.38(3H,t,J=6.8Hz), 1.45(9H,s), 1.50(3H,t,J=6.8Hz),

3.44(2H,t,J=5.4Hz), 3.83(2H,t,J=5.4Hz), 3.89(3H,s),
4.18(2H,q,J=6.8Hz), 4.24(2H,q,J=6.8Hz), 4.91(2H,s),
5.49(2H,s), 7.21(1H,s), 7.55(1H,d,J=2.0Hz),
7.66(1H,d,J=2.0Hz).

MS:m/e(ESI)502.3(MH+)

Example 115

1-{3-*tert*-Butyl-5-[(2-hydroxyethyl)-methylamino]-4-methoxy-phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone dihydrochloride

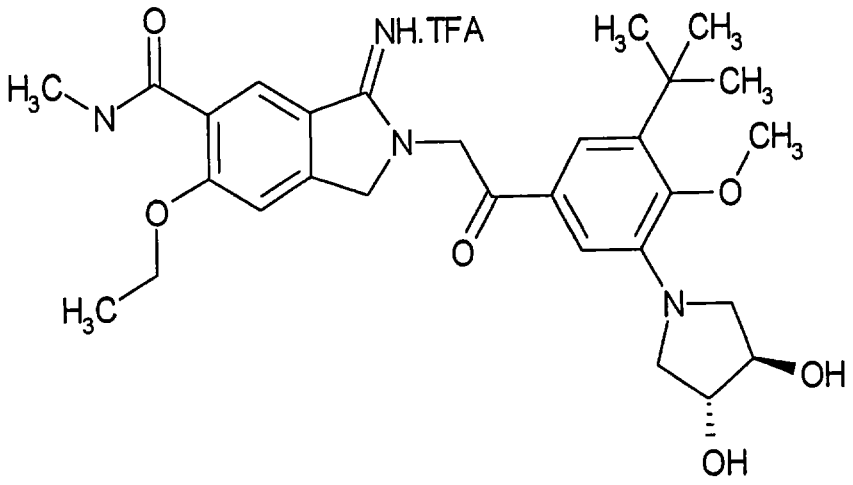


1H-NMR(DMSO-d6)δ:
1.36(3H,t,J=6.8Hz), 1.44(9H,s), 1.49(3H,t,J=6.8Hz),
3.04(3H,brs), 3.38-3.75(4H,m), 3.95(3H,s), 5.49(2H,s),
7.21(1H,s), 7.77-7.95(2H,m).

MS:m/e(ESI)516.4(MH+)

Example 116

2-{2-[3-*tert*-Butyl-5-(3,4-dihydroxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

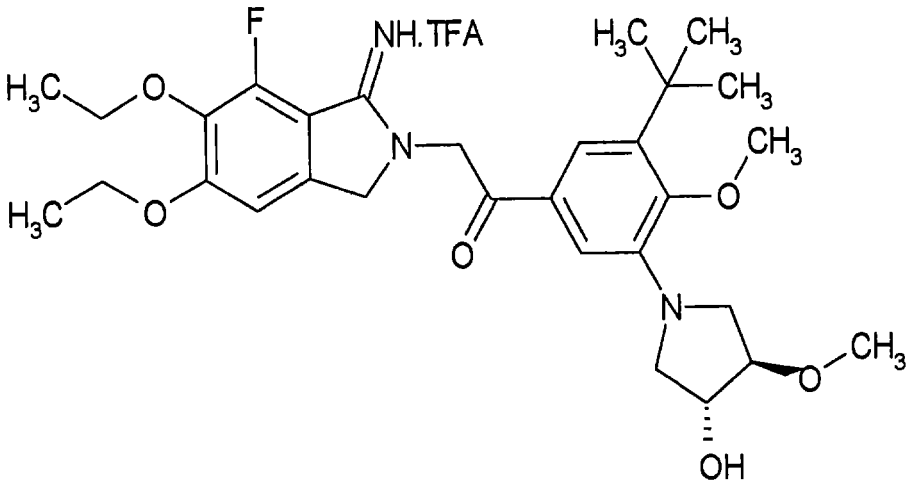


1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.8Hz), 2.88-2.95(2H,m), 3.50-3.59(2H,m), 3.61(3H,s), 4.02(2H,brs), 4.28(2H,q,J=6.8Hz), 4.83(2H,s), 5.37-5.60(2H,m), 7.29(1H,s), 7.38(1H,s), 7.54(1H,s), 8.12-8.28(1H,m), 8.55(1H,s), 9.14(1H,brs), 9.82(1H,brs).

Example 117

1-[3-*tert*-Butyl-5-((3R,4R)-3-hydroxy-4-methoxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone trifluoroacetate

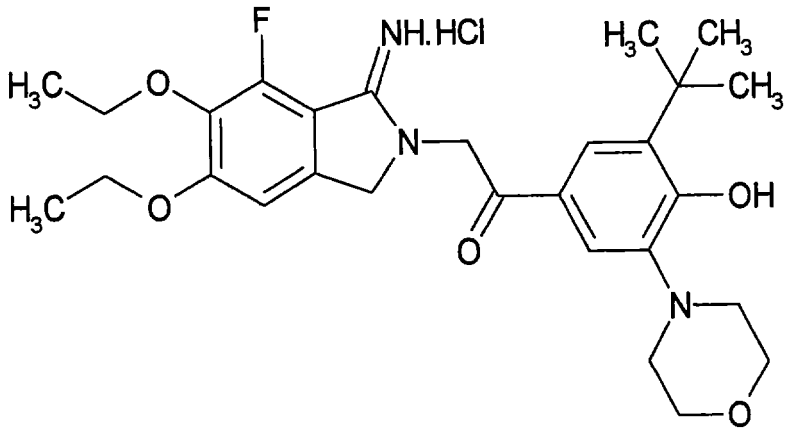


1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(3H,t,J=7.2Hz), 2.91-2.99(1H,m), 3.03-3.12(1H,m), 3.30(3H,s), 3.40-3.58(2H,m), 3.63(3H,s), 3.71-3.79(1H,m), 4.10(2H,q,J=7.2Hz), 4.10-4.30(3H,m), 4.78(2H,s), 5.38-5.60(2H,m), 7.30(1H,s), 7.33(1H,s), 7.41(1H,s), 8.99-9.12(1H,m), 9.20-9.40(1H,m).

Example 118

1-(3-*tert*-Butyl-4-hydroxy-5-morpholino-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride



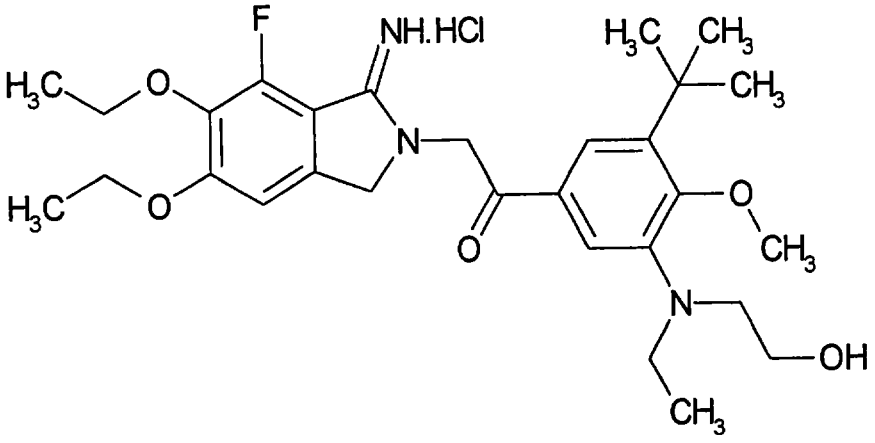
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.38-1.41(12H,m), 2.78-2.79(4H,m), 3.81-3.83(4H,m), 4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.44(2H,s), 7.33(1H,s), 7.67(1H,s), 7.73(1H,s), 9.03(1H,brs), 9.20(1H,brs), 9.28(1H,brs).

MS:m/e(ESI)514.3(MH+)

Example 119

1-{3-*tert*-Butyl-5-[ethyl-(2-hydroxyethyl)-amino]-4-methoxy-phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl hydrochloride



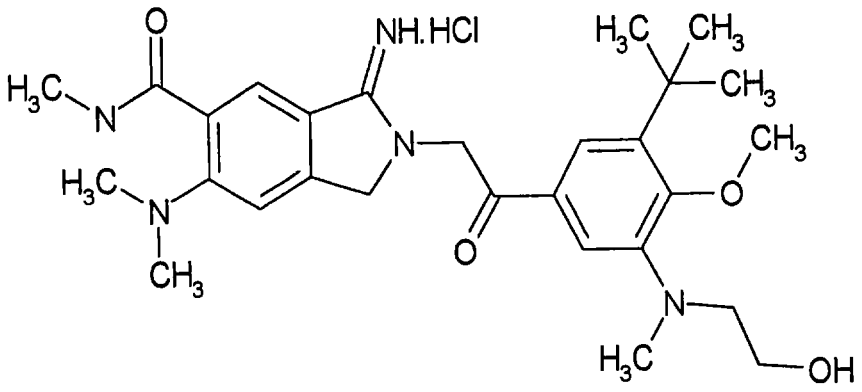
1H-NMR(DMSO-d6)δ:

0.96(3H,t,J=6.4Hz), 1.28(3H,t,J=6.8Hz), 1.37(9H,s), 1.39(3H,t,J=6.8Hz), 3.14-3.26(4H,m), 3.47(2H,t,J=6.0Hz), 3.84(3H,s), 4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.79(2H,s), 5.61(2H,s), 7.33(1H,s), 7.55(1H,s), 7.60(1H,s), 9.10(1H,brs), 9.57(1H,brs).

Example 120

2-(2-{3-*tert*-Butyl-5-[(2-hydroxyethyl)-methylamino]-4-

methoxy-phenyl}-2-oxo-ethyl)-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide dihydrochloride

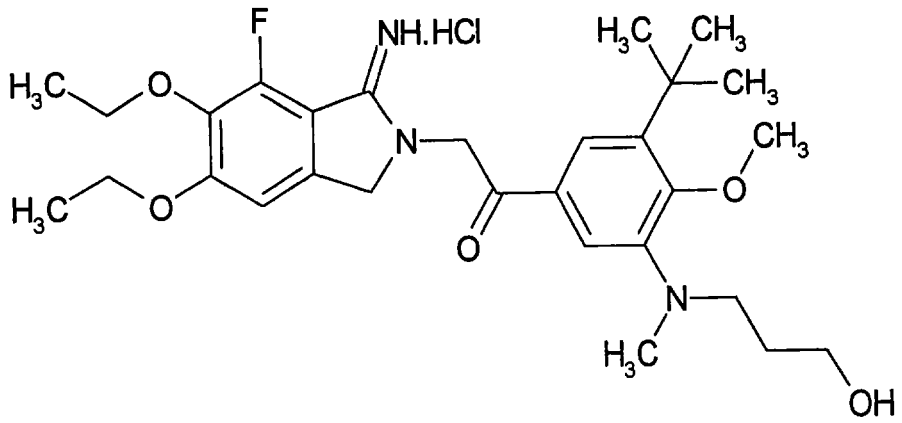


1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.75(3H,d,J=4.0Hz), 2.81(3H,s), 2.91(6H,s), 3.17(2H,t,J=5.6Hz), 3.52(2H,t,J=5.4Hz), 4.73(2H,s), 5.52(2H,s), 7.15(1H,s), 7.53(1H,s), 8.10(1H,s), 8.38(1H,q,J=4.0Hz), 9.17(1H,brs), 9.65(1H,brs).

Example 121

1-{3-*tert*-Butyl-5-[(3hydroxypropyl)-methylamino]-4-methoxy-phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone dihydrochloride



1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=6.8Hz), 1.36(9H,s), 1.39(3H,t,J=6.8Hz),

1.61(2H,t,J=6.4Hz), 2.75(3H,s), 3.14(2H,t,J=6.4Hz),

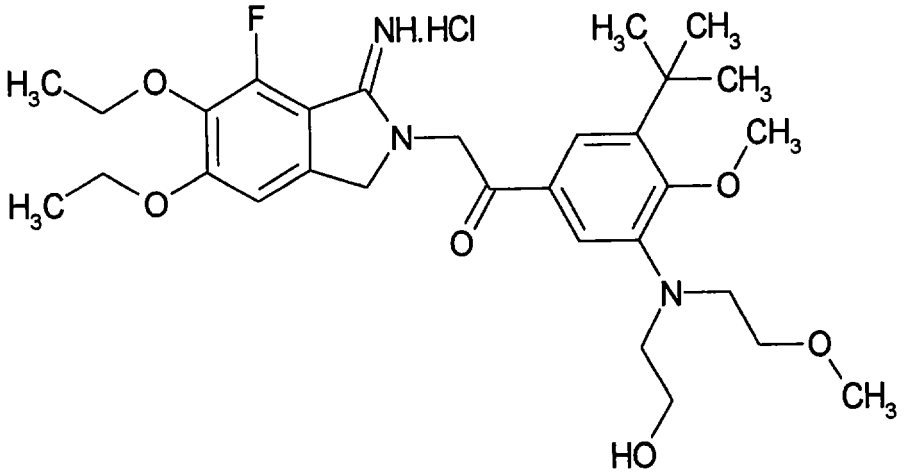
3.38(2H,t,J=6.4Hz), 3.82(3H,s), 4.11(2H,q,J=6.8Hz),

4.20(2H,q,J=6.8Hz), 4.79(2H,s),5.55(2H,s), 7.33(1H,s),

7.51(1H,s), 7.54(1H,s), 9.08(1H,brs), 9.45(1H,brs).

Example 122

1-{3-*tert*-Butyl-5-[(2-hydroxyethyl)-(2-methoxyethyl)-amino]-4-methoxy-phenyl}-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone dihydrochloride



1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.36(9H,s), 1.39(3H,t,J=7.2Hz),

3.15(3H,s), 3.28(2H,t,J=6.0Hz), 3.20-3.78(4H,m),

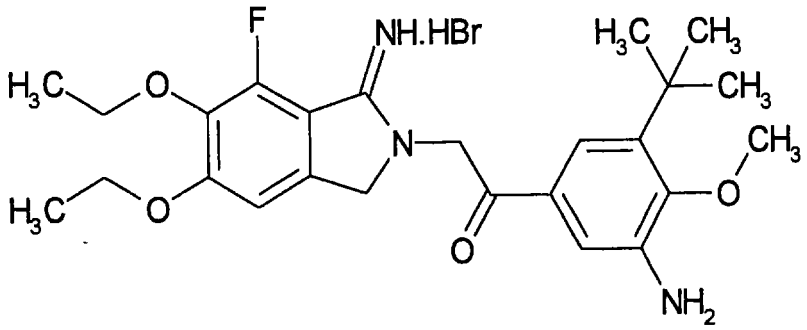
3.46(2H,t,J=6.0Hz), 3.82(3H,s), 4.12(2H,q,J=7.2Hz),

4.21(2H,q,J=7.2Hz), 4.79(2H,s), 5.51(2H,s), 7.33(1H,s),

7.51(1H,s), 7.58(1H,s), 9.06(1H,brs), 9.39(1H,brs).

Example 123

1-(3-Amino-5-*tert*-butyl-4-methoxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



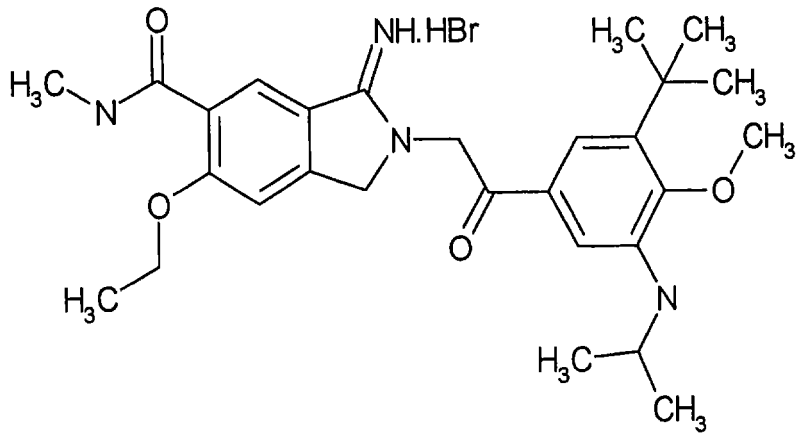
1H-NMR(DMSO-d6)δ:

1.38(3H,t,J=7.2Hz), 1.43(9H,s), 1.50(3H,t,J=7.2Hz), 3.85(3H,s), 4.17(2H,q,J=7.2Hz), 4.24(2H,q,J=7.2Hz), 4.82(2H,s), 5.39(2H,s), 7.19(1H,s), 7.44(1H,d,J=2.0Hz), 7.48(1H,d,J=2.0Hz).

MS:m/e(ESI)458.2(MH+)

Example 124

2-[2-(3-*tert*-Butyl-5-isopropylamino-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

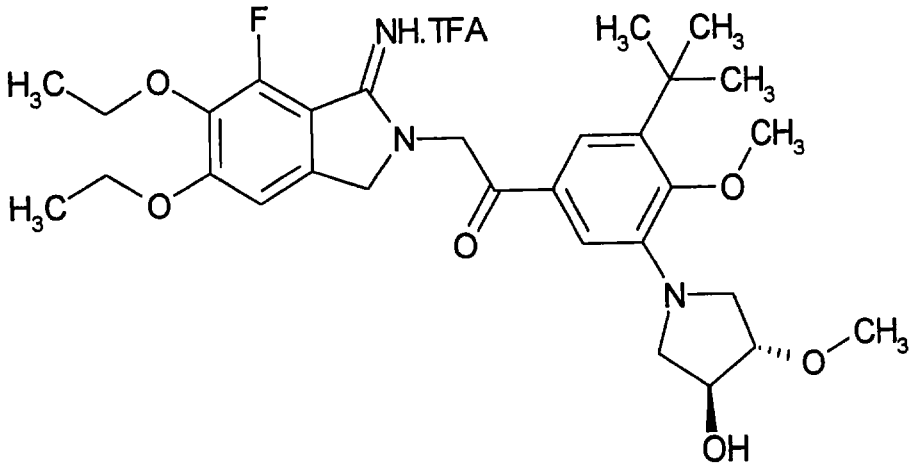


1H-NMR(DMSO-d6)δ:

1.19(6H,d,J=6.0Hz), 1.36(9H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.4Hz), 3.60-3.78(1H,m), 3.71(3H,s), 4.28(2H,q,J=7.2Hz), 4.83(2H,s), 4.90(1H,d,J=6.0Hz), 5.46(2H,s), 7.14(1H,s), 7.22(1H,s), 7.53(1H,s), 8.20(1H,d,J=4.4Hz), 8.55(1H,s).

Example 125

1-[3-*tert*-Butyl-5-((3S,4S)-3-hydroxy-4-methoxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone trifluoroacetate



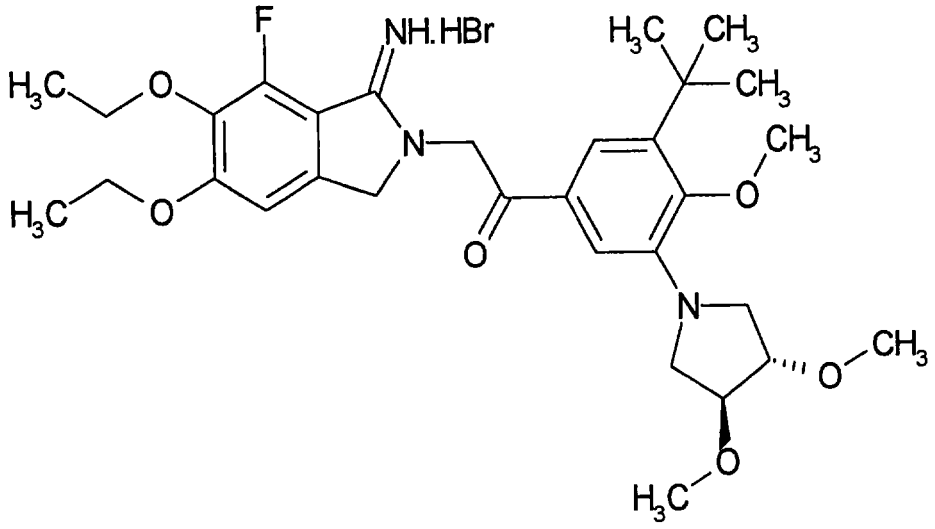
1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(3H,t,J=7.2Hz), 2.91-2.99(1H,m), 3.03-3.12(1H,m), 3.30(3H,s), 3.40-3.58(2H,m), 3.63(3H,s), 3.71-3.79(1H,m), 4.10(2H,q,J=7.2Hz), 4.10-4.30(3H,m), 4.78(2H,s), 5.38-5.60(2H,m), 7.30(1H,s), 7.33(1H,s), 7.41(1H,s), 8.99-9.12(1H,m), 9.20-9.40(1H,m).

MS:m/e(ESI)558.3(MH+)

Example 126

1-[3-*tert*-Butyl-5-((3S,4S)-3,4-dimethoxy-pyrrolidin-1-yl)-4-methoxy-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide



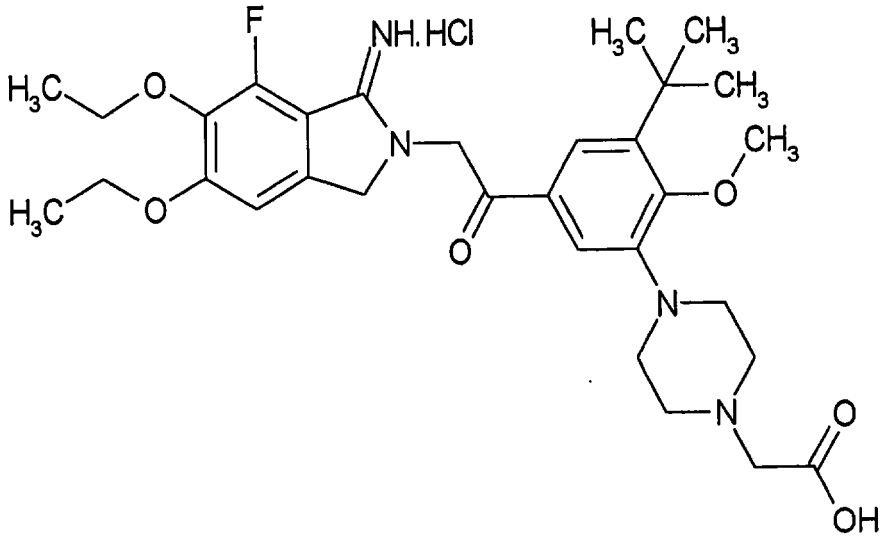
1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(3H,t,J=7.2Hz), 3.03-3.16(2H,m), 3.29(6H,s), 3.36-3.52(2H,m), 3.64(3H,s), 3.91(2H,brs), 4.11(2H,q,J=7.2Hz), 4.21(2H,q,J=7.2Hz), 4.78(2H,s), 5.36-5.62(2H,m), 7.33(2H,s), 7.44(1H,s), 8.95-9.35(2H,m).

MS:m/e(ESI)572.4(MH+)

Example 127

(4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-piperazin-1-yl)-acetic acid dihydrochloride



1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.38(9H,s), 1.40(3H,t,J=7.0Hz),

3.10-3.69(10H,m), 3.93(3H,s), 4.12(2H,q,J=7.0Hz),

4.21(2H,q,J=7.0Hz), 4.22(2H,brs), 4.80(2H,s),

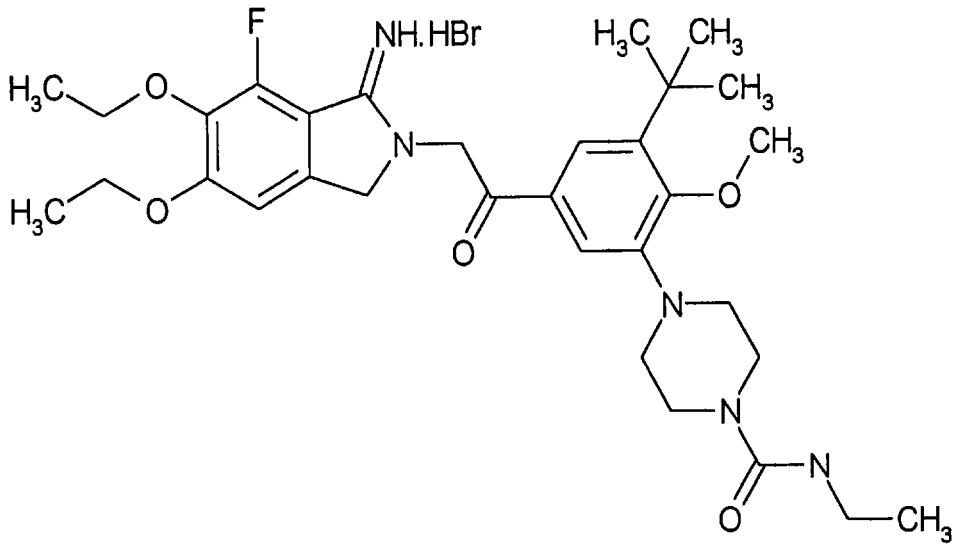
5.54(2H,s), 7.34(1H,s), 7.49(1H,s), 7.64(1H,s),

9.10(1H,brs), 9.40(1H,brs).

MS:m/e(ESI)585.3(MH+)

Example 128

4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-piperazine-1-carboxylic acid ethylamide hydrobromide



1H-NMR(DMSO-d6)δ:

1.01(3H,t,J=7.0Hz), 1.30(3H,t,J=7.0Hz), 1.37(9H,s),

1.40(3H,t,J=7.0Hz), 2.93(4H,brs), 3.02-3.08(2H,m),

3.49(4H,brs), 3.95(3H,s), 4.12(2H,q,J=7.0Hz),

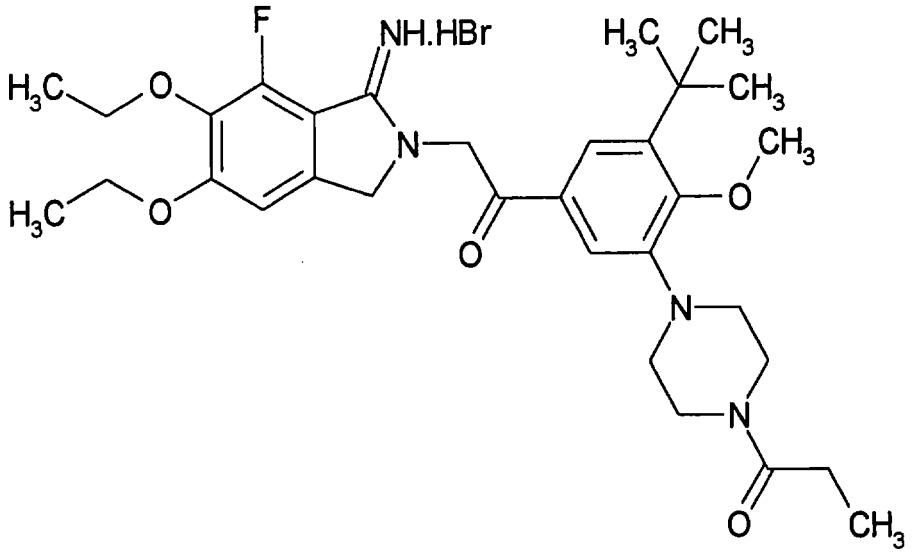
4.22(2H,q,J=7.0Hz), 4.79(2H,s), 5.48(2H,s), 7.34(1H,s),

7.50(1H,s), 7.60(1H,s).

MS:m/e(ESI)598.3(MH+)

Example 129

1-(4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-piperazin-1-yl)-propan-1-one hydrobromide



1H-NMR(DMSO-d6)δ:

1.00(3H,t,J=7.0Hz), 1.29(3H,t,J=7.0Hz), 1.37(9H,s),

1.40(3H,t,J=7.0Hz), 2.36(2H,q,J=7.0Hz), 2.94(2H,brs),

2.98(2H,brs), 3.66(4H,brs), 3.96(3H,s),

4.11(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.79(2H,s),

5.47(2H,s), 7.34(1H,s), 7.50(1H,d,J=2.0Hz),

7.61(1H,d,J=2.0Hz), 9.06(1H,brs), 9.28(1H,brs).

MS:m/e(ESI)583.4(MH+)

Example 130

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.60(18H,s), 4.83(2H,s), 5.50(2H,s), 7.62-7.83(5H,m),

8.05(1H,s), 8.13-8.22(1H,m), 9.21(1H,brs),

9.90(1H,brs).

Example 131

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-5-

methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.88(3H,s), 4.78(2H,s), 5.46(2H,s), 7.24(1H,d,J=8.8Hz), 7.35(1H,s), 7.77(2H,s), 8.10(1H,d,J=8.8Hz), 9.04(1H,brs), 9.71(1H,brs).

MS:m/e(ESI)409.1(MH+)

Example 132

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.10(3H,s), 4.77(2H,s), 5.49(2H,s), 7.59-7.71(2H,m), 7.76(2H,s), 8.01-8.12(1H,s), 8.68(1H,s), 9.19(1H,brs), 9.99(1H,brs), 10.37(1H,s).

MS:m/e(ESI)436.1(MH+)

Example 133

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.12(3H,s), 4.81(2H,s), 5.47(2H,s), 7.69(1H,d,J=8.4Hz), 7.77(2H,s), 8.00-8.20(3H,m), 9.07(1H,brs), 9.76(1H,brs), 10.51(1H,s).

MS:m/e(ESI)436.1(MH+)

Example 134

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 3.11(3H,s), 4.80(2H,s), 5.50(2H,s), 7.53(1H,d,J=8.8Hz), 7.73(1H,d,J=8.8Hz), 7.75(2H,s), 8.08(1H,s), 9.22(1H,brs), 10.02(1H,brs).

MS:m/e(ESI)472.1(MH+)

Example 135

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yl}-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.16(3H,s), 4.81(2H,s), 5.46(2H,s), 7.37(1H,d,J=8.8Hz), 7.50(1H,s), 7.76(2H,s), 8.10(1H,d,J=8.8Hz), 9.07(1H,brs), 9.97(1H,brs).

MS:m/e(ESI)472.1(MH+)

Example 136

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-6-isopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(6H.d.J=6.0Hz), 1.42(18H.s), 4.52-4.70(1H.m), 4.76(2H.s), 5.49(2H.s), 7.33(1H.d.J=8.4Hz), 7.64(1H.d.J=8.4Hz), 7.77(2H.s), 7.82(1H.s.), 9.21(1H.brs), 9.78(1H.brs).

MS:m/e(ESI)437.1(MH+)

Example 137

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-5-isopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(6H.d.J=6.0Hz), 1.42(18H.s), 4.68-4.81(1H.m), 4.77(2H.s), 5.47(2H.s), 7.19(1H.d.J=9.6Hz), 7.32(1H.s), 7.77(2H.s.), 8.02-8.19(3H.m), 9.03(1H.brs), 9.70(1H.brs).

MS:m/e(ESI)437.2(MH+)

Example 138

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(2-methoxy-ethoxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H.s), 3.32(3H.s), 3.71(2H.t.J=4.4Hz), 4.17(2H.t.J=4.4Hz), 4.77(2H.s), 5.51(2H.s), 7.40(1H.d.J=8.4Hz), 7.67(1H.d.J=8.4Hz), 7.78(2H.s), 7.85(1H.m), 8.08(1H.brs), 9.24(1H.brs), 9.80(1H.s).

MS:m/e(ESI)453.2(MH+)

Example 139

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-5-(2-methoxy-ethoxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H.s), 3.30(3H.s), 3.66-3.75(2H.m.), 4.19-4.31(2H.m.), 4.78(2H.s), 5.47(2H.s), 7.24(1H.d.J=8.8Hz), 7.35(1H.s), 7.77(2H.s), 8.07(1H.brs), 8.10(1H.d.J=8.8Hz), 9.06(1H.brs), 9.74(1H.s).

MS:m/e(ESI)453.1(MH+)

Example 140

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yl}-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.48(3H,s), 3.25(3H,s), 4.85(2H,s), 5.51(2H,s), 7.66(1H,d,J=9.0Hz), 7.76(3H,s), 8.10(1H,s), 8.21(1H,d,J=9.0Hz), 9.26(1H,s), 9.94(1H,s).

MS:m/e(ESI)450.2(MH+)

Example 141

N-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.48(3H,s), 3.25(3H,brs), 4.86(2H,s), 5.53(2H,s), 7.75-7.83(2H,m), 8.10(1H,s), 8.16(1H,s), 9.29(1H,s), 9.94(1H,s).

MS:m/e(ESI)450.2(MH+)

Example 142

{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-

ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-urea hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 4.74(2H,s), 5.49(2H,s), 6.12(2H,s), 7.54-7.62(2H,m), 7.77(2H,s), 8.08(1H,s), 8.43(1H,s), 9.07(1H,s), 9.21(1H,s), 9.94(1H,s).

Example 143

{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yl}-urea hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 4.76(2H,s), 5.43(2H,s), 6.19(2H,s), 7.48(1H,d,J=7.7Hz), 7.57(2H,s), 7.97(1H,s), 8.0(1H,d,J=7.7Hz), 8.07(1H,s), 8.98(1H,s), 9.22(1H,s), 9.66(1H,s).

Example 144

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-7-isopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(6H.d.J=7.6Hz), 1.42(18H.s), 4.78(2H.s), 4.87-5.02(1H.m), 5.49(2H.s), 7.26(1H.d.J=8.4Hz), 7.30(1H.d.J=8.4Hz), 7.82(1H.t.J=8.4Hz), 7.77(2H.s), 8.04(1H.brs), 8.08(1H.s), 9.22(1H.brs).

MS:m/e(ESI)437.2(MH+)

Example 145

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H.s), 3.84(3H.s), 4.77(2H.s), 5.52(2H.s), 7.38(1H.d.J=8.4Hz), 7.67(1H.d.J=8.4Hz), 7.78(2H.s), 7.86(1H.s), 8.08(1H.brs), 9.25(1H.brs), 9.85(1H.brs).

MS:m/e(ESI)409.1(MH+)

Example 146

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H.s), 4.85(2H.s), 5.52(2H.s), 7.71(1H.dd.J=8.8 and 8.4Hz), 7.77(2H.s), 7.80-7.88(1H.m.), 8.06(1H.d.J=8.8Hz).

MS:m/e(ESI)397.2(MH+)

Example 147

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H.s), 4.86(2H.s), 5.51(2H.s), 7.52-7.61(1H.m.), 7.69(1H.d.J=8.4Hz), 7.77(2H.s), 8.22-8.31(1H.m.), 9.24(1H.brs), 9.92(1H.brs).

MS:m/e(ESI)397.1(MH+)

Example 148

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-imino-5,7-

dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone dihydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 4.91(2H,s), 5.58(2H,s),

7.75(1H,dd,J=7.1,4.8Hz), 7.78(2H,s), 8.08(2H,s),

8.67(1H,d,J=7.1), 8.94(1H,d,J=4.8Hz), 9.56(1H,s),

10.27(1H,s).

MS:m/e(ESI)380.1(MH+)

Example 149

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(2-methoxy-1,1-dimethyl-ethoxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.22(6H.s), 1.41(18H.s), 3.16(3H.s), 3.91(2H.s),

4.77(2H.s), 5.49(2H.brs), 7.41(1H.d.J=8.0Hz),

7.67(1H.d.J=8.0Hz), 7.77(2H.s), 7.85(1H.s.),

8.09(1H.brs), 9.22(1H.brs), 9.95(1H.brs).

MS:m/e(ESI)481.3(MH+)

Example 150

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[6-(2-hydroxy-1,1-dimethyl-ethoxy)-1-imino-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.23(6H.s), 1.41(18H.s), 3.79(2H.s), 4.75(1H.s),

4.77(2H.s), 5.49(2H.s), 7.39(1H.dd.J=8.4and2.4Hz),

7.66(1H.d.J=8.4Hz), 7.77(2H.s), 7.83(1H.brs.),

8.08(1H.brs), 9.21(1H.brs), 9.75(1H.brs).

MS:m/e(ESI)467.2(MH+)

Example 151

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-6-isobutoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.00(6H.d.J=6.8Hz), 1.41(18H.s), 2.00-2.13(1H.m), 3.81(2H.d.J=6.8Hz), 4.77(2H.s), 5.50(2H.s), 7.38(1H.d.J=8.8Hz), 7.65(1H.d.J=8.0Hz), 7.77(2H.s), 7.84(1H.s.), 8.08(1H.brs), 9.22(1H.brs), 9.78(1H.brs).

MS:m/e(ESI)451.2(MH+)

Example 152

Methyl 2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.92(3H,s), 4.96(2H,s), 5.53(2H,s), 7.77(2H,s), 7.92(1H,d,8.0Hz), 8.09(1H,s), 8.36(1H,d,8.0Hz), 8.91(1H,s), 9.39(1H,s), 10.09(1H,s).

MS:m/e(ESI)437.1(MH+)

Example 153

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 4.92(2H,s), 5.54(2H,s), 7.67(1H,s), 7.78(2H,s), 7.96(1H,d,J=8.0Hz), 8.09(1H,s), 8.20(1H,s), 8.25(1H,d,J=8.0Hz), 8.77(1H,s), 9.34(1H,s), 10.01(1H,s).

MS:m/e(ESI)422.1(MH+)

Example 154

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 4.92(2H,s), 5.54(2H,s), 7.70(1H,s), 7.78(2H,s), 8.10(1H,s), 8.12(1H,d,7.8Hz), 8.21(1H,s), 8.22(1H,s), 8.27(1H,d,7.8Hz), 9.34(1H,s), 10.01(1H,s).

MS:m/e(ESI)422.2(MH+)

Example 155

2-(4or5-Cyano-2-imino-3-propyl-pyrrolidin-1-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 4.98(2H,s), 5.55(2H,s), 7.78(2H,s), 8.02(1H,d,J=8.4Hz), 8.10(1H,s), 8.28(1H,d,J=8.4Hz), 8.67(1H,s), 9.48(1H,s), 10.06(1H,s), B:1.40(18H,s), 4.94(2H,s), 5.55(2H,s), 7.78(2H,s), 8.10,(1H,s), 8.18(1H,d,J=8.4Hz), 8.32(1H,s), 8.38(1H,d,J=8.4Hz), 9.48(1H,s), 10.17(1H,s).

MS:m/e(ESI)404.1(MH+)

Example 156

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-hydroxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H.s), 4.71(2H.s), 5.48(2H.s),

7.20(1H.d.J=8.4Hz), 7.48-7.59(2H.m), 7.77(2H.s),

8.05(1H.brs), 9.12(1H.brs), 9.77(1H.brs), 10.22(1H.s).

MS:m/e(ESI)395.1(MH+)

Example 157

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-hydroxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H.s), 4.72(2H.s), 5.42(2H.s),

7.02(1H.d.J=8.4Hz), 7.07(1H.s), 7.76(2H.s),

8.00(1H.d.J=8.4Hz), 8.05(1H.brs), 8.93(1H.brs),

9.60(1H.brs), 10.78(1H.brs).

MS:m/e(ESI)395.1(MH+)

Example 158

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(2-methoxy-1-methyl-ethoxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.26(3H,d,J=6.0Hz), 1.42(18H,s), 3.29(3H,s), 3.46-3.57(2H,m), 4.60-4.68(1H,m), 4.76(2H,s), 5.51(2H,s),

7.37(1H,dd,J=8.4and2.4Hz), 7.65(1H,d,J=8.4Hz),

7.78(2H,s), 7.87(1H,brs), 8.05(1H,brs), 9.22(1H,brs),

9.79(1H,brs).

MS:m/e(ESI)467.2(MH+)

Example 159

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid dimethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.94(3H,s), 3.03(3H,s), 4.91(2H,s), 5.53(2H,s), 7.77(2H,s), 7.84(1H,d,J=7.8Hz), 7.86(1H,d,J=7.8Hz), 8.10(1H,s), 8.32(1H,s), 9.31(1H,s), 9.93(1H,s).

MS:m/e(ESI)450.2(MH+)

Example 160

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 4.94(2H,s), 5.57(2H,s), 7.77(2H,s), 7.90(1H,d,J=7.1Hz), 8.09(1H,s), 8.33(1H,d,J=7.1Hz), 8.91(1H,s), 9.53(1H,s), 10.13(1H,s), 13.53(1H,s).

MS:m/e(ESI)423.1(MH+)

Example 161

3-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-1,1-dimethyl-urea hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.95(6H,s), 4.75(2H,s), 5.49(1H,s),
7.61(1H,d,J=7.9Hz), 7.64(1H,d,J=7.9Hz), 7.77(2H,s),
8.06(1H,s), 8.48(1H,s), 8.72(1H,s), 9.15(1H,s),
9.88(1H,s).

MS:m/e(ESI)465.2(MH+)

Example 162

2-(6-*tert*-Butyl-1-imino-1,3-dihydro-isoindol-2-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.35(9H,s), 1.41(18H,s), 4.80(2H,s), 5.49(2H,s),
7.69(1H,d,J=8.0Hz), 7.76(2H,s), 7.87(1H,d,J=8.0Hz),
8.30(1H,s), 9.19(1H,brs), 9.83(1H,brs).

Example 163

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yloxy}-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(18H,s), 1.55(3H,d,J=6.8Hz), 4.75(2H,s),
4.90(1H,q,J=6.8Hz), 5.49(2H,s),
7.34(1H,dd,J=8.8and2.4Hz), 7.65(1H,d,J=8.8Hz),
7.73(1H,brs), 7.77(2H,s), 8.09(1H,brs), 9.22(1H,brs),
9.88(1H,brs).

MS:m/e(ESI)467.2(MH+)

Example 164

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-

ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yloxy}-2-methyl-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.59(6H,s), 4.75(2H,s), 5.48(2H,s), 7.27(1H,dd,J=8.4and2.4Hz), 7.65(1H,d,J=8.4Hz), 7.69(1H,d,J=2.4Hz), 7.77(2H,s), 8.08(1H,brs), 9.17(1H,s), 9.93(1H,s).

MS:m/e(ESI)481.2(MH+)

Example 165

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-6-methyl-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.64(3H,s), 4.93(2H,s), 5.58(2H,s), 7.78(2H,s), 8.06(1H,s), 8.09(1H,s), 8.94(1H,s), 9.61(1H,brs), 10.27(1H,brs).

MS:m/e(ESI)394.2(MH+)

Example 166

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.67(3H,s), 4.84(2H,s), 5.63(2H,s), 7.70(1H,d,J=8.0Hz), 7.78(2H,s), 8.08(1H,brs), 8.16(1H,d,J=8.0Hz), 9.63(1H,brs), 9.94(1H,brs).

MS:m/e(ESI)394.1(MH+)

Example 167

1-(7-*tert*-Butyl-3,3-dimethyl-2,3-dihydro-benzofuran-5-yl)-2-(1-imino-6-isopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.30-1.37(21H,m), 4.39(2H,s), 4.59-4.71(1H,m), 4.77(2H,s), 5.48(2H,s), 7.34(1H,d,J=8.8H), 7.65(1H,d,J=8.8Hz), 7.72(1H,s), 7.80(1H,s), 7.82(1H,s), 9.25(1H,brs), 9.79(1H,brs).

MS:m/e(ESI)435.1(MH+)

Example 168

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(3H,t,J=6.8Hz), 1.42(18H,s), 4.11(2H,q,J=6.8Hz), 4.77(2H,s), 5.51(2H,s), 7.36(1H,dd,J=8.4and2.4Hz), 7.66(1H,d,J=8.4Hz), 7.78(2H,s), 7.84(1H,brs), 8.08(1H,s), 9.22(1H,brs), 9.81(1H,s).

MS:m/e(ESI)423.1(MH+)

Example 169

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(3H,t,J=6.8Hz), 1.42(18H,s), 4.16(2H,q,J=6.8Hz), 4.78(2H,s), 5.49(2H,s), 7.21(1H,d,J=8.8Hz), 7.33(1H,s), 7.78(2H,s), 8.05(1H,s), 8.12(1H,d,J=8.8Hz),

9.08(1H,brs), 9.75(1H,brs).

MS:m/e(ESI)423.2(MH+)

Example 170

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-4,7-diisopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.25(6H,d,J=6.0Hz), 1.38(6H,d,J=6.0Hz), 1.42(18H,s), 4.64(1H,qq,J=6.0Hz,6.0Hz), 4.69(2H,s), 4.87(1H,qq,J=6.0Hz,6.0Hz), 5.48(2H,s), 7.24(1H,d,J=9.2Hz), 7.38(1H,d,J=9.2Hz), 7.76(2H,s), 8.05(1H,brs).

Example 171

1-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-3-methyl-urea hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.67(3H,s), 4.74(2H,s), 5.48(2H,s), 7.55(1H,d,J=8.4Hz), 7.59(1H,d,J=8.4Hz), 7.77(2H,s), 8.06(1H,s), 8.44(1H,s), 8.97(1H,s), 9.15(1H,s), 10.40(1H,s).

MS:m/e(ESI)451.2(MH+)

Example 172

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.64(3H,s), 3.88(2H,s), 4.83(2H,s), 5.54(2H,s), 7.70(1H,d,J=8.0Hz), 7.73(1H,d,J=8.0Hz), 7.78(2H,s), 8.02-8.10(1H,br), 8.13(1H,s), 9.94(1H,s).

Example 173

{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.74(2H,s), 4.83(2H,s), 5.55(2H,s), 7.69(1H,d,J=8.0Hz), 7.71(1H,d,J=8.0Hz), 7.78(2H,s), 8.14(1H,s), 9.94(1H,s).

Example 174

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-4-isopropoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36-1.50(24H,m), 4.79(2H,s), 4.87-4.98(1H,m), 5.50(2H,s), 7.26(1H,d,J=7.6Hz), 7.30(1H,d,J=8.4Hz), 7.73(1H,d,J=7.6Hz), 7.77(2H,s), 8.03(1H,brs), 8.07(1H,brs), 9.23(1H,brs).

Example 175

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(1-methoxy-1-methyl-ethyl)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.13(t,J=6.8Hz), 1.41(18H,s), 3.25(3H,s), 3.66(s),
4.12(q,J=6.8Hz), 5.12(2H,s), 5.54(2H,s), 7.78(2H,s),
7.79(1H,d,J=6.8Hz), 7.86(1H,d,J=6.8Hz), 8.39(1H,s).

Example 176

Ethyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-methoxy-acetate hydrobromide

1H-NMR(DMSO-d6)δ:
1.13(3H,t,J=6.8Hz), 1.41(18H,s), 3.38(3H,s),
4.12(2H,q,J=6.8Hz), 4.86(2H,s), 5.12(1H,s), 5.53(2H,s),
7.78(2H,m), 7.79-7.84(2H,s), 8.31(1H,s).

Example 177

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-3-methyl-butyric acid hydrobromide

1H-NMR(DMSO-d6)δ:
0.67(3H,d,J=6.5), 1.04(3H,d,J=6.5), 1.17(1H,t,J=6.5),
1.41(18H,s), 2.25-2.36(1H,m), 4.82(2H,s), 5.54(2H,s),
7.72(1H,d,J=7.0), 7.75(1H,d,J=7.0), 7.77(2H,s),
8.27(1H,s), 10.03(1H,s).
MS:m/e(ESI)479.4(MH+)

Example 178

tert-Butyl 2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-1-imino-2,3-dihydro-1H-isoindole-5-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=6.8Hz), 1.41(18H,s), 1.53(9H,s),
4.14(2H,q,J=6.8Hz), 4.80(2H,s), 5.53(2H,s), 7.78(2H,s),
7.83(1H,s), 8.02(1H,s).

Example 179

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-1-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.39(3H,t,J=6.8Hz), 1.41(18H,s), 4.15(2H,q,J=6.8Hz),
4.80(2H,s), 5.53(2H,s), 7.78(2H,s), 7.87(1H,s),
8.05(1H,s), 9.06(1H,s), 10.05(1H,s).

Example 180

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5,6-diethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.25-1.41(24H,m), 4.08(2H,q,J=6.8Hz),
4,14(2H,q,J=6.8Hz), 4.71(2H,s), 5.44(2H,s), 7.35(1H,s),
7.75(2H,s), 7.81(1H,s), 9.05(1H,brs), 9.59(1H,brs).

Example 181

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(4,7-difluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone trifluoroacetate

1H-NMR(DMSO-d6)δ:
4.77(2H,s), 5.19(2H,s), 7.49(1H,m), 7.60(1H,m),
7.68(2H,s).

Example 182

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[6-(2-hydroxy-1-methyl-ethoxy)-1-imino-1,3-dihydro-isoindol-2-yl]-ethanone trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.25(3H,d,J=6.4Hz), 1.42(18H.s), 3.50-3.63(2H.m), 4.42-4.53(1H.m), 4.76(2H.s), 4.95(1H.t.J=5.6Hz), 5.50(2H.s), 7.36(1H.brd.J=8.8Hz), 7.64(1H.d.J=8.8Hz), 7.78(2H.s), 7.84(1H.brs), 8.08(1H.brs), 9.21(1H.brs), 9.78(1H.s).

MS:m/e(ESI)453.4(MH+)

Example 183

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yloxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.02(3H,t,J=6.8Hz), 1.42(18H,s), 1.86-2.10(2H,m), 4.68-4.83(3H,m), 5.50(2H.s), 7.36(1H,dd,J=8.4and0.8Hz), 7.67(1H,d,J=8.4Hz), 7.77(1H,s), 7.78(2H,s), 8.08(1H,brs), 9.25(1H,brs), 9.87(1H,brs).

MS:m/e(ESI)481.3(MH+)

Example 184

{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-methoxy-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.38(3H,s), 4.83(2H,s), 4.99(1H,s), 5.52(2H,s), 7.77-7.83(2H,m), 7.78(2H,s), 8.07(1H,br), 8.32(1H,s), 9.29(1H,brs), 9.95(1H,brs).

Example 185

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.37(3H,t,J=6.8Hz), 1.41(18H,s), 4.21(2H,q,J=6.8Hz), 4.83(2H,s), 5.46(2H,s), 7.53(1H,s), 7.75(2H,s), 8.49(1H,s), 9.16(1H,br), 9.78(1H,br).

Example 186

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methoxy-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.69(3H,s), 3.18(3H,s), 4.83(2H,s), 5.52(2H,s), 7.78(3H,s), 7.86(1H,d,J=8.0Hz), 8.07(1H,br), 8.41(1H,s), 9.32(1H,s), 9.99(1H,s).

Example 187

N-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-N-methyl-methanesulfonamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.66(3H,s), 3.14(6H,sX2), 4.05(2H,s), 5.47-5.62(2H,m), 7.70(1H,d,J=8.0Hz), 7.81(1H,s),

7.97(1H,s), 8.16(1H,d,J=8.0Hz), 9.57(1H,brs),
9.95(1H.s), 10.01(1H,s).
MS:m/e(ESI)445.2(MH+)

Example 188

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:
1.40(18H,s), 2.82(3H,d,5.3Hz), 4.91(2H,s), 5.55(2H,s),
7.77(2H,s), 7.85(1H,d,J=8.1Hz), 8.03-8.12(1H,br),
8.21(1H,d,J=8.1Hz), 8.70(1H,q,J=5.3Hz), 8.74(1H,s),
10.05(1H,s).

Example 189

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:
1.40(18H,s), 2.81(3H,d,J=5.3Hz), 4.91(2H,s),
5.56(2H,s), 7.79(2H,s), 8.08(1H,s), 8.09(1H,d,=8.1Hz),
8.17(1H,s), 8.31(1H,d,J=8.1Hz), 8.74(1H,q,J=5.3),
9.44(1H,s), 8.74(1H,s), 10.05(1H,s), 10.12(1H,s).

Example 190

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methoxy-propionamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.68(3H,s), 3.18(3H,s), 4.83(2H,s), 5.52(2H,s), 7.34(1H,brs), 7.43(1H,brs), 7.74-7.78(1H,m), 7.77(2H,s), 7.84(1H,d,J=8.0Hz), 8.34(1H,s).

Example 191

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methoxy-N-methyl-propionamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.69(3H,s), 2.58(3H,d,J=4.4Hz), 3.18(3H,s), 4.83(2H,s), 5.52(2H,s), 7.71-7.82(2H,m), 7.85(2H,s), 7.99(1H,brs), 8.31(1H,s).

Example 192

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

0.93(3H,t,J=7.2Hz), 1.41(18H,s), 1.70-1.83(2H,m), 2.89(2H,t,J=7.6Hz), 4.84(2H,s), 5.57(2H,s), 7.71(1H,d,J=8.0Hz), 7.77(2H,s), 8.08(1H,s), 8.17(1H,d,J=8.0Hz), 9.52(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)422.2(MH+)

Example 193

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-sulfonic acid dimethylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.67(6H,s), 4.99(2H,s), 5.55(2H,s), 7.77(2H,s), 8.06(1H,d,J=8.1Hz), 8.16(1H,d,J=8.1Hz), 8.73(1H,s).

MS:m/e(ESI)486.2(MH+)

Example 194

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(methanesulfonyl-methyl-amino)-phenyl]-2-oxo-ethyl}-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid dimethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(18H,s), 2.95(3H,s), 3.03(3H,s), 3.15(6H,s), 4.92(2H,s), 5.52(2H,s), 7.81-7.88(3H,m), 7.97(1H,s), 8.32(1H,s), 9.39(1H,s), 9.95(1H,s), 10.04(1H,s).

MS:m/e(ESI)501.2(MH+)

Example 195

({2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carbonyl}-methyl-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.00(3H,s), 4.20(2H,s), 4.92(2H,s), 5.55(2H,s), 7.77-7.88(2H,m), 7.78(2H,s), 8.09(1H,s), 8.24-8.39(1H,2s), 9.39(1H,br), 9.93-10.03(1H,br).

MS:m/e(ESI)494.3(MH+)

Example 196

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(4-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.25-1.53(21H,m), 4.37(2H,q,J=6.8Hz), 4.80(2H,s), 5.50(2H,s), 7.24-7.31(2H,m), 7.68-7.79(3H,m), 8.07(1H,brs), 8.32(1H,brs), 9.24(1H,brs).

Example 197

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-4-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 4.00(3H,s), 4.80(2H,s), 5.49(2H,s), 7.25(1H,d,J=8.4Hz), 7.29(1H,d,J=7.6Hz), 7.51-7.78(3H,m), 8.06(1H,brs), 8.64(1H,brs), 9.23(1H,brs).

Example 198

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-1-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=6.8Hz), 2.81(3H,d,J=4.8Hz), 4.21(2H,q,J=6.8Hz), 4.80(2H,s), 5.52(2H,s), 7.77(2H,s), 7.91(1H,s), 7.94(1H,s), 8.21-8.23(1H,m).

MS:m/e(ESI)480.3(MH+)

Example 199

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=6.8Hz), 1.42(18H,s), 2.83(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.48(2H,s), 7.54(1H,s), 7.77(2H,s), 8.20(1H,q,J=4.8Hz), 8.55(1H,s), 9.13(1H,br), 9.82(1H,br).

MS:m/e(ESI)480.3(MH+)

Example 200

N-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-N-methyl-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(18H,m), 3.14(6H,s), 4.07-4.15(4H,m), 4.72(2H,s), 5.43(2H,s), 7.36(1H,s), 7.81(2H,s), 7.93(1H,s), 9.08(1H,brs), 9.60(1H,brs).

Example 201

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid ethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.15(3H,t,J=7.0Hz), 1.40(18H,s), 3.27-3.45(2H,m), 4.93(2H,s), 5.53(2H,s), 7.77(2H,s), 7.85(1H,d,J=8.0Hz), 8.01-8.23(1H,m), 8.22(1H,d,J=8.0Hz), 8.70(1H,s), 8.72(1H,s), 9.34(1H,s), 10.01(1H,s).

MS:m/e(ESI)450.3(MH+)

Example 202

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-

carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.70(3H,s), 4.76(2H,s), 5.51(2H,s),

7.61(1H,dd,J=8.4,1.8Hz), 7.67(1H,d,J=8.4Hz),

7.77(2H,s), 8.07(1H,brs), 8.49(1H,brs), 9.20(1H,s),

9.99(1H,brs), 10.12(1H,s).

MS:m/e(ESI)452.3(MH+)

Example 203

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yl}-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.70(3H,s), 4.80(2H,s), 5.48(2H,s),

7.63(1H,dd,J=8.4,1.8Hz), 7.77(2H,s), 7.92(1H,s),

8.09(1H,d,J=8.4Hz), 9.06(1H,brs), 9.74(1H,brs),

10.33(1H,s).

MS:m/e(ESI)452.3(MH+)

Example 204

Ethyl 3-{2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methyl-acrylate

1H-NMR(DMSO-d6)δ:

1.37(3H,t,J=6.8Hz), 1.41(18H,s), 2.08(3H,s),

4.23(2H,q,J=6.8Hz), 4.88(2H,s), 5.22(2H,s), 7.68(1H,s),

7.77(2H,s), 7.83-7.91(2H,m), 8.32(1H,s).

Example 205

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-6-trifluoromethyl-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

4.98(2H,s), 5.56(2H,s), 7.78(2H,s), 8.04(1H,d,J=8.0Hz), 8.20(1H,d,J=8.0z), 8.69(s.1H).

Example 206

3-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2,N-dimethyl-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.05(3H,s), 2.71(3H,d,J=4.4Hz), 4.87(2H,s), 5.53(2H,s), 7.31(1H,s), 7.76-7.80(2H,m), 7.78(2H,s), 8.10(1H,br), 8.30(1H,s).

Example 207

3-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methyl-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.05(3H,s), 4.87(2H,s), 5.53(2H,s), 5.76(1H,s), 7.22(1H,br), 7.34(1H,s), 7.63(1H,brs), 7.77(3H,s), 7.79(1H,d,J=5.2Hz), 8.24(1H,s).

Example 208

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5,6-dichloro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

4.53(2H,s), 5.66(2H,s), 7.55(1H,s), 7.80(1H,s),

7.90(2H,s).

Example 209

1-(7-*tert*-Butyl-3,3-dimethyl-2,3-dihydro-benzofuran-5-yl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(6H,s), 1.34(9H,s), 2.67(3H,s), 4.39(2H,s),

4.85(2H,s), 5.54(2H,brs), 7.711(1H,d,J=8.0Hz),

7.712(1H,s), 7.79(1H,s), 8.16(1H,d,J=8.0Hz),

9.51(1H,brs), 9.95(1H,brs).

MS:m/e(ESI)392.2(MH+)

Example 210

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methoxymethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 3.41(3H,s), 4.67(2H,s), 4.89(2H,s), 5.50-

5.52(2H,m), 7.78(2H,s), 7.85(1H,d,J=8.0Hz),

8.08(1H,brs), 8.29(1H,d,J=8.0Hz), 9.50-9.52(1H,m),

9.99(1H,brs).

MS:m/e(ESI)424.2(MH+)

Example 211

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-

yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.30-1.50(21H,m), 2.50(3H,s), 4.21(2H,q,J=7.2Hz),

4.79(2H,s), 5.49(2H,s), 7.76(3H,sX2), 8.06(1H,s),

9.24(1H,brs), 9.74(1H,brs).

MS:m/e(ESI)438.2(MH+)

Example 212

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(piperidine-1-carbonyl)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.30-1.70(6H,m), 1.40(18H,s), 3.28(2H,m), 3.60(2H,m),

4.88(2H,s), 5.55(2H.s), 7.79(2H,s), 7.81(1H,d,J=8.4Hz),

7.85(1H,d,J=8.4Hz), 8.09(1H,brs), 8.27(1H,s),

9.34(1H,brs), 9.94(1H,brs).

MS:m/e(ESI)490.3(MH+)

Example 213

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyrazin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.72(3H,s), 4.93(2H,s), 5.56(2H,s),

7.77(2H,s), 8.97(1H,s).

MS:m/e(ESI)395.2(MH+)

Example 214

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-

dimethylaminomethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.88(6H,s), 4.64(2H,brs), 4.96(2H,s), 5.58-5.72(2H,m), 7.79(2H,s), 7.95-8.05(1H,m), 8.10(1H,s), 8.37(1H,d,J=8.4Hz), 9.79-9.91(1H,m), 10.03-10.10(1H,m), 10.80-10.96(1H,m).

MS:m/e(ESI)437.2(MH+)

Example 215

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-imino-4-methoxymethyl-3-phenyl-pyrrolidin-1-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.64(3H,s), 4.73(2H,s), 5.54(2H,s), 7.37(1H,d,J=8.4Hz), 7.54-7.67(2H,m), 7.79(2H,s).

MS:m/e(ESI)393.2(MH+)

Example 216

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=7.2Hz), 1.42(18H,s), 2.32(3H,s), 2.58(3H,s), 3.99(2H,t,J=7.2Hz), 4.81(2H,s), 5.52(2H,s), 7.76(2H,s), 8.07(1H,s), 9.37(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)452.2(MH+)

Example 217

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-methoxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 3.27(3H,s), 3.31(2H,s), 3.48(2H,brs), 4.91(2H,s), 5.52(2H,s), 7.77(2H,s), 7.86(1H,d,J=8.0), 8.09(1H,brs), 8.23(1H,d,J=8.0), 8.72(1H,s), 8.77(1H,brs), 9.24(1H,brs), 10.03(1H,brs).

Example 218

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid isopropylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.18(6H,d,J=6.9), 1.40(18H,s), 4.05-4.16(1H,m), 4.91(2H,s), 5.52(2H,s), 7.77(2H,s), 7.85(1H,d,J=8.0), 8.08(1H,s), 8.23(1H,dd,J=8.0,1.1Hz), 8.48(1H,d,J=7.8Hz), 8.68(1H,s), 9.32(1H,brs), 10.00(1H,brs).

MS:m/e(ESI)464.3(MH+)

Example 219

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-sulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 4.95(2H,s), 5.53(2H,s), 7.64(2H,s), 7.77(2H,s), 7.99(1H,d,J=7.9), 8.09(1H,brs),

8.23(1H,d,J=7.9), 8.75(1H,s), 10.14(1H,brs).

Example 220

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-sulfonic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.47(3H), 4.96(2H,s), 5.54(2H,s), 7.72(1H,q,J=4.6Hz), 7.77(2H,s), 8.02(1H,d,J=7.9), 8.09(1H,brs), 8.17(1H,dd,J=7.9,1.2Hz), 8.75(1H,s), 10.14(1H,brs).

Example 221

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2,5-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 1.48(3H,d,J=7.0Hz), 2.67(3H,s), 5.00(1H,q,J=7.0Hz), 5.4(1H,d,J=18.4Hz), 5.6(1H,d,J=18.4Hz), 7.73(1H,d,J=8.0Hz), 7.79(2H,s), 8.05(1H,s), 8.18(1H,d,J=8.0Hz), 9.45(1H,s), 9.93(1H,s).

MS:m/e(ESI)408.2(MH+)

Example 222

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-2-methoxy-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.33(3H,s), 4.77(1H,br), 4.85(2H,s),

5.51(2H,s), 7.39(1H,brs), 7.61(1H,brs), 7.73-7.83(2H,m), 7.86(2H,s), 8.27(1H,s).

Example 223

{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-methoxy-acetic acid hydrazide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 4.35(1H,br), 4.84(3H,s), 4.86(2H,s), 5.52(2H,s), 7.76(4H,s), 8.27(1H,s).

Example 224

1-[3-*tert*-Butyl-4-hydroxy-5-(2-methoxy-ethyl)-phenyl]-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 2.67(3H,s), 2.94(2H,t,J=6.8Hz), 3.27(3H,s), 3.55(2H,t,J=6.8Hz), 4.84(2H,s), 5.46-5.52(2H,m), 7.65-7.74(3H,m), 8.15(1H,d,J=8.0Hz), 9.40(1H,s), 9.46-9.56(1H,m), 9.93(1H,s).

MS:m/e(ESI)396.1(MH+)

Example 225

Methyl 3-*tert*-butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzoate hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 2.67(3H,s), 3.98(3H,s), 4.86(2H,s), 5.58-5.69(1H,m), 7.71(1H,d,J=8.0Hz), 8.05(1H,s),

8.17(1H,d,J=8.0Hz), 8.38(1H,s), 9.99(1H,s),
12.07(1H,s).
MS:m/e(ESI)396.0(MH+)

Example 226

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(methanesulfonyl-methyl-amino)-phenyl]-2-oxo-ethyl}-6-ethoxy-1-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.81(3H,d,J=4.4Hz),
3.13(6H,s), 4.19(2H,q,J=6.8Hz), 4.80(2H,s), 5.48(2H,s),
7.79(1H,s), 7.94(2H,s), 8.04(1H,s), 8.25(1H,br).
MS:m/e(ESI)531.2(MH+)

Example 227

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(methanesulfonyl-methyl-amino)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.81(3H,d,J=4.4Hz),
3.13(6H,s), 4.17(2H,q,J=6.8Hz), 4.83(2H,s), 5.43(2H,s),
7.53(1H,s), 7.80(1H,s), 7.92(1H,s), 8.19(1H,br),
8.56(1H,s).
MS:m/e(ESI)531.2(MH+)

Example 228

2-{2-[3-(Acetyl-methyl-amino)-5-*tert*-butyl-4-hydroxy-

phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.12(3H,s), 2.82(3H,d,J=4.4Hz), 3.10(3H,s), 4.18(2H,q,J=6.8Hz), 4.47(2H,s), 4.82(2H,s), 5.42(2H,s), 7.53(1H,s), 7.82(1H,s), 7.91(1H,s), 8.21(1H,d,J=2.0Hz), 8.54(1H,s), 9.21(1H,brs), 9.83(1H,brs).

Example 229

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[6-(1-hydroxy-propyl)-1-imino-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

0.94(3H,t,J=7.6Hz), 1.77-1.84(2H,m), 4.74(1H,t,J=6.8Hz), 4.89(2H,s), 5.48(2H,s), 7.67-7.78(2H,m), 7.79(1H,d,J=7.6Hz), 7.93(2H,s), 8.13(1H,s).

MS:m/e(ESI)439.2(MH+)3

Example 230

2-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methoxy-propionamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=6.8Hz), 1.41(18H,s), 1.81(3H,s), 3.16(3H,s), 4.87(2H,s), 5.63(2H,s), 7.39(1H,s), 7.54(1H,s), 7.78(2H,s), 7.83(1H,d,J=7.2Hz), 8.08(1H,s), 8.27(1H,d,J=7.2Hz), 9.72(1H,br), 9.78(1H,br).

MS:m/e(ESI)481.1(MH+)

Example 231

N-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.11(3H,s), 2.67(3H,s), 3.10(3H,s), 4.48(2H,s), 4.86(2H,s), 5.55(2H,s), 7.71(1H,d,J=8.0Hz), 7.82(1H,s), 7.92(1H,s), 8.15(1H,d,J=8.0Hz), 9.58(1H,s), 9.95(1H,s).

Example 232

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-4-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=6.9Hz), 1.40(18H,s), 4.26(2H,q,J=6.9Hz), 4.91(2H,s), 5.46(2H,s), 7.55(1H,t,J=8.0Hz), 7.77(2H,s), 8.03(1H,d,J=8.0Hz), 8.08(1H,s), 9.22(1H,s), 9.90(1H,brs).

MS:m/e(ESI)441.2(MH+)

Example 233

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindol-5-yl}-ethyl-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.10(3H,t,J=6.8Hz), 1.42(18H,s), 3.62(3H,s),

3.70(2H,q,J=6.8Hz), 4.86(2H,s), 5.52(2H,s),
7.72(1H,d,J=8.4Hz), 7.78(2H,s), 7.79(1H,d,J=8.4Hz),
8.16(1H,s).

Example 234

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6or7-hydroxymethyl-1-imino-1,3,6,7-tetrahydro-5,8-dioxa-2-aza-cyclopenta[b]naphthalen-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
3.66(2H,brs), 4.05-4.16(2H,m), 4.45(1H,m), 4.68(2H,s),
5.15(1H,t,J=5.0Hz), 5.56(2H,s), 5.46(2H,s), 7.26(1H,s),
7.75(2H,s), 7.77(1H.s).

Example 235

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-6-methyl-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
2.29(3H,s), 2.86(3H,d,J=5.0Hz), 4.78(2H,s), 5.80(2H,s),
7.41(1H,s), 7.81(2H,s), 7.86(1H,s).

Example 236

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(1-methoxy-propyl)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
0.90(3H,t,J=7.6Hz), 1.50(18H,s), 1.61-1.75(2H,m),
3.23(3H,s), 4.25(1H,t,J=7.6Hz), 4.80(2H,s), 5.92(2H,s),

7.32(1H,s), 7.50(1H,d,J=8.8Hz), 7.70(1H,d,J=8.0Hz),
7.98(2H,s), 8.70(2H,brs).

Example 237

N-(2-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-ethyl)-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:
1.398(9H,s), 2.019(3H,s), 2.482(3H,s), 2.84-2.92(1H,m),
2.96-3.02(1H,m), 3.014(3H,s), 3.34-3.42(2H,m),
4.852(2H,s), 5.529(2H,s), 7.64-7.78(3H,m),
8.155(1H,d,J=8.0Hz), 9.50-9.60(2H,m), 9.90-9.99(2H,m).

Example 238

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-ethoxy-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.37(3H,t,J=7.0Hz), 1.42(18H,s), 4.48(2H,q,J=7.0Hz),
4.79(2H,s), 5.54(2H,s), 7.24(1H,d,J=8.8Hz), 7.77(2H,s),
8.13(1H,d,J=8.8Hz), 9.63(1H,s).
MS:m/e(ESI)424.1(MH+)

Example 239

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid dimethylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.15(3H,t,J=7.0Hz), 1.40(18H,s), 2.78(3H,s),

3.00(3H,s), 4.22(2H,q,J=7.0Hz), 4.82(2H,s), 5.47(2H,s), 7.50(1H,s), 7.77(2H,s), 8.02(1H,s), 8.08(1H,brs), 9.67(1H,brs).

MS:m/e(ESI)]494.2(MH+)

Example 240

3-*tert*-Butyl-N-ethyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-N-methyl-benzenesulfonamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.09(3H,t,J=6.8Hz), 1.38(9H,s), 2.63(3H,s), 2.87(3H,s), 3.24(2H,q,J=6.8Hz), 4.86(2H,s), 6.24(2H,s), 7.44(1H,d,J=8.2Hz), 7.82(1H,d,J=8.2Hz), 8.11(1H,s), 8.16(1H,s), 10.08(1H,s), 11.98(1H,brs).

MS:m/e(ESI)459.1(MH+)

Example 241

Ethyl 3-{6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methyl-acrylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(3H,t,J=6.8Hz), 1.41(18H,s), 2.34(3H,s), 4.23(2H,q,J=6.8Hz), 4.88(2H,s), 5.52(2H,s), 7.69(1H,s), 7.73(2H,s), 7.99(1H,d,J=8.4Hz), 8.28(1H,d,J=8.4Hz).

MS:m/e(ESI)492.3(MH+)

Example 242

2-(2-{3-[(Acetyl-methyl-amino)-methyl]-5-*tert*-butyl-4-hydroxy-phenyl}-2-oxo-ethyl)-6-ethoxy-1-imino-2,3-

dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=6.8Hz), 2.12(3H,s), 2.81(3H,d,J=4.8Hz), 3.09(3H,s), 4.21(2H,q,J=6.8Hz), 4.47(2H,s), 4.81(2H,s), 5.52(2H,s), 7.81(1H,s), 7.91(1H,s), 7.94(1H,s), 8.07(1H,s), 8.21-8.25(1H,m).

Example 243

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.82(3H,d,J=4.4Hz), 4.90(2H,s), 5.51(2H,s), 7.74(2H,s), 7.76(1H,d,J=8.8Hz), 8.51(1H,br), 8.54(1H,d,J=5.2Hz).

Example 244

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-hydroxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.41(3H,t,J=6.5Hz), 3.38(2H,dt,J=6.2,6.1Hz), 3.55(2H,dt,J=6.2,6.0Hz), 4.28(2H,q,J=6.5Hz), 4.83(1H,t,J=6.1Hz), 4.85(2H,s), 5.45(2H,s), 7.55(1H,s), 7.76(2H,s), 8.35(1H,t,J=6.0Hz), 8.67(1H,s), 9.84(1H,brs).

MS:m/e(ESI)510.3(MH+)

Example 245

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid dimethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

2.94(3H,s), 3.05(3H,s), 4.94(2H,s), 5.55(2H,s), 7.75(2H,s), 7.96(1H,d,J=10Hz), 8.38(1H,d,J=10Hz).

Example 246

1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-pyrrolidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.380(9H,s), 1.93-2.03(2H,m), 2.34-2.40(2H,m), 2.672(3H,s), 3.500(2H,t,J=7.2Hz,2H), 4.426(2H,s), 4.865(2H,s), 5.570(2H,s), 7.709(2H,d,J=8.0Hz), 7.812(2H,s), 8.164(1H,d,J=7.2Hz), 9.951(1H,s), 10.674(1H,s).

Example 247

N-(1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-ethyl)-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.388(9H,s), 1.473(3H,d,J=6.8Hz,3H), 1.880(2H,m), 2.673(3H,s), 4.863(2H,s), 5.08-5.17(1H,m), 5.46-5.65(2H.m), 7.712(1H,d,J=8.0Hz), 7.760(1H,s), 7.813(1H,s), 8.169(1H,d,J=8.0Hz), 8.948(1H,d,J=7.6Hz).

Example 248

N-(1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-ethyl)-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.362(9H,s), 1.577(3H,d,J=7.2Hz), 2.095(3H,s), 2.673(3H,s), 2.895(3H,s), 4.866(2H,s), 5.54-5.76(3H,m), 7.711(1H,d,J=8.0Hz), 7.806(1H,s), 7.924(1H,s), 8.163(1H,d,J=8.0Hz), 9.577(1H,s), 9.952(1H,s), 11.076(1H,s).

Example 249

N-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.32-1.45(12H,m), 2.11(3H,s), 2.31(3H,s), 2.58(3H,s), 3.11(3H,s), 3.90-4.20(2H and H2O), 4.78(2H,s), 4.84(2H,s), 5.59(2H,s), 7.81(1H,s), 7.93(1H,s), 9.61(1H,s), 9.85(1H,s), 11.28(1H,s).

MS:m/e(ESI)481.2(MH+)

Example 250

N-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenyl}-N-methyl-methanesulfonamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.34-1.42(12H,m), 2.32(3H,s), 2.58(3H,s), 3.15(6H,sX2), 3.99(2H,q,J=6.8Hz), 4.83(1H,s), 5.50(1H,s), 7.81(1H,s), 7.96(1H,s), 9.42(1H,brs), 9.85(1H,brs), 10.03(1H,s).

MS:m/e(ESI)503.2(MH+)

Example 251

1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-pyrrolidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 2.11-2.21(2H,m), 2.41-2.46(2H,m), 2.69(3H,s), 3.65-3.71(2H,m), 4,85(2H,s), 5.48(2H,s), 7.72(1H,d,J=8Hz), 7.74(1H,s), 7.78(1H,s), 8.17(1H,d,J=8Hz).

Example 252

1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-piperidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.373(9H,s), 1.64-1.78(4H,m), 2.34-2.38(2H,m), 2.674(3H,s), 3.43-3.50(2H,m), 4.483(2H,s), 4.863(2H,s), 5.541(2H,s), 7.712(1H,d,J=8.0Hz), 7.822(1H,d,J=2.0Hz), 7.887(1H,d,J=2.0Hz), 8.164(1H,d,J=8.0Hz), 9.940(1H,s).

Example 253

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-dimethylaminomethyl-3-ethoxy-7-imino-4-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone

hydrobromide

1H-NMR(DMSO-d6)δ:

1.25(18H,s), 1.37(3H,t,J=6.8Hz), 2.19(6H,s),

2.26(3H,s), 3.58(2H,s), 4.00(2H,q,J=6.8Hz),

4.55(2H,brs), 4.88-4.92(2H,m), 7.41(2H,s).

MS:m/e(ESI)495.3(MH+)

Example 254

tert-Butyl [2-({2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carbonyl}-amino)-ethyl]-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 1.40(18H,s), 1.42(3H,t,J=7.2Hz), 3.08-3.40(2H,m), 3.60-3.78(2H,m), 4.27(2H,q,J=7.2Hz),

4.84(2H,s), 5.44(2H,s), 6.85-6.94(1H,m), 7.55(1H,s),

7.75(2H,s), 8.29(1H,t,J=5.2Hz), 8.59(1H,s),

9.83(1H,brs).

MS:m/e(ESI)609.3(MH+)

Example 255

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-amino-ethyl)-amide dihydrochloride

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.42(3H,t,J=7.2Hz), 2.96(2H,brt,J=6.4Hz),

3.56(2H,brq,J=6.4Hz), 4.28(2H,q,J=7.2Hz), 4.84(2H,s),

5.53(2H,s), 7.56(1H,s), 7.55(1H,s), 7.77(2H,s),

8.04(3H,brs), 8.47(1H,t,J=5.6Hz), 8.65(1H,s).

Example 256

({2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carbonyl}-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.45(3H,t,J=7.0Hz), 4.05(2H,d,J=5.4Hz), 4.33(2H,q,J=7.0Hz), 4.85(2H,s), 5.47(2H,s), 7.59(1H,s), 7.77(2H,s), 8.07(2H,s), 8.61(1H,t,J=5.4Hz), 8.73(1H,s), 9.15(1H,brs), 9.88(1H,brs).

MS:m/e(ESI)524.2(MH+)

Example 257

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-acetylamino-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.41(3H,t,J=6.8Hz), 3.18-3.37(4H,m), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.46(2H,s), 7.55(1H,s), 7.76(2H,s), 7.96(1H,t,J=5.5Hz), 8.07(1H,brs), 8.31(1H,t,J=5.1Hz), 8.60(1H,s), 9.13(1H,brs), 9.82(1H,brs).

MS:m/e(ESI)551.3(MH+)

Example 258

Ethyl 2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3,6,7-tetrahydro-1H-5,8-dioxa-2-aza-

cyclopenta[b]naphthalene-6-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(3H,t,J=7.2Hz), 1.42(18H,s), 4.25(2H,q,J=7.2Hz),

4.36-5,15(3H,m), 7.30(1H,s), 7.71(1H,s), 7.91(2H,s).

MS:m/e(ESI)509.2(MH+)

Example 259

Methyl {3-*tert*-butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-methylcarbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1,42(9H,s), 2.67(3H,s),3.40(3H,s), 3.79(3H,s),

4.88(2H,s), 5.60(2H,s), 7.68(1H,s), 7.70(1H,d,J=8Hz),

7.80(1H,s), 7.15(1H,d, J=8Hz).

Example 260

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-6-methyl-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

2.42(3H,s), 2.78(3H,s), 4.82(2H,s), 5.50(2H,s),

7.68(1H,s), 7.76(2H,s), 8.06(1H,s), 8.40(1H,d,J=6.0Hz).

Example 261

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-6-methyl-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-methoxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

2.42(3H,s), 3.26(3H,s), 3.43(4H,m), 4.82(2H,s),

5.50(2H,s), 7.66(1H,s), 7.76(2H,s), 8.05(1H,s),
8.48(1H,t,J=6.0Hz).

Example 262

2-{2-[3-(1-Acetylamino-ethyl)-5-*tert*-butyl-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.38(9H,s), 1.42(3H,t,J=6.8Hz), 1.46(3H,d,J=6.4Hz),
1.86(3H,s), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz),
4.84(2H,s), 5.06-5.13(1H,m), 5.36-5.51(2H,m),
7.52(1H,s), 7.74(1H,s), 7.77(1H,s), 8.19(1H,br).
MS:m/e(ESI)509.2(MH+)

Example 263

N-[2-Hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-3-(2-methoxy-ethyl)-benzyl]-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:
2.11(3H,s), 2.68(3H,s), 2.87(2H,t,J=6.8Hz), 3.06(3H,s),
3.22(3H,s), 3.53(2H,t,J=6.8Hz), 4.48(2H,s), 4.87(2H,s),
5.48(2H,s), 7.71(1H,d,J=8.2Hz), 7.78(1H,s), 7.82(1H,s),
8.17(1H,d,J=8.2Hz).
MS:m/e(ESI)425.1(MH+)

Example 264

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindol-5-yl}-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.38-1.42(21H,m), 3.70(3H,s), 4.19(2H,q,J=6.8Hz),

4.75(2H,s), 5.48(2H,s), 7.42(1H,s), 7.77(2H,s),

8.50(1H,s), 8.81(1H,s), 9.07(1H,brs), 9.79(1H,brs).

MS:m/e(ESI)496.2(MH+)

Example 265

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindol-5-yl}-ethyl-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.05(3H,t,J=7.2Hz), 1.33(3H,t,J=7.2Hz), 1.42(18H,s),

3.26(3H,s), 3.43-3.51(2H,m), 4.18(2H,q,J=7.2Hz),

4.18(2H,s), 5.47(2H,s), 7.50(1H,s), 7.77(2H,s),

8.04(1H,s), 9.11(1H,brs), 9.64(1H,brs).

MS:m/e(ESI)542.2(MH+)

Example 266

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid ethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.19(3H,t,J=10Hz), 3.42(2H,q,J=10Hz), 4.99(2H,s),

5.38(2H,s), 7.78(2H,s), 8.35(1H,d,J=10Hz),

8.43(1H,J=10Hz,1H), 8.83(1H,t,J=10Hz).

Example 267

3-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-

yl}-2-methyl-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.33(3H,s), 4.89(2H,s), 5.61(2H,s),

7.27(1H,brs), 7.35(1H,br), 7.68(1H,brs), 7.78(2H,s),

7.86(1H,d,J=8.4Hz), 8.27(1H,d,=8.4Hz), 9.71(1H,br).

MS:m/e(ESI)463.1(MH+)

Example 268

3-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methyl-propionamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.09(3H,d,J=6.4Hz), 1.42(18H,s), 2.83-2.89(2H,m),

3.14-3.20(1H,m), 4.86(2H,s), 5.56(2H,s), 6.75(1H,s),

7.29(1H,s), 7.66(1H,d,J=8.0Hz), 7.77(2H,s),

8.07(1H,br), 8.17(1H,d,J=8.0Hz), 9.47(1H,br),

9.81(1H,br).

MS:m/e(ESI)465.2(MH+)

Example 269

N-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-N-methyl-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.409(9H,s), 2.678(3H,s), 2.737(3H,s), 3.027(3H,s),

4.382(2H,s), 4.866(2H,s), 5.552(2H,s),

7.710(1H,d,J=8.0Hz), 7.804(1H,d,J=2.0Hz),

7.814(1H,d,J=2.0Hz), 8.163(1H,d,J=8.0Hz), 9.944(1H,s).

Example 270

Benzyl {3-*tert*-butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-methylcarbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.400(9H,s), 2.681(3H,s), 2.949(3H,s), 4.533(2H,s), 4.861(2H,s), 5.165(2H,s), 5.504(2H,s), 7.24-7.42(5H,m), 7.716(1H,d,J=8.0Hz), 7.804(1H,s), 8.170(1H,d,J=8.0Hz), 9.952(1H,s).

Example 271

1-(3-*tert*-Butyl-4-hydroxy-5-nitro-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.45(9H,s), 2.64(3H,s), 4.89(2H,s), 5.60(2H,s), 7.73(1H,d,J=8.0Hz), 8.07(1H,d,J=2.0Hz), 8.18(1H,d,J=8.0Hz), 8.52(1H,d,J=2.0Hz), 9.52(1H,s), 10.02(1H,s), 11.50(1H,s).

Example 272

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-4-methyl-2-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

0.95(3H,t,J=7.2Hz), 1.37-1.44(21H,m), 1.71-1.82(2H,m), 2.32(3H,s), 2.83-2.90(2H,s), 3.97(2H,q,J=7.2Hz), 4.81(2H,s), 5.52(2H,s), 7.77(2H,s), 8.08(1H,s),

9.41(1H,brs), 9.71(1H,brs).

MS:m/e(ESI)480.2(MH+)

Example 273

N-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-4-methyl-2-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

0.96(3H,t,J=7.2Hz), 1.37(9H,s), 1.40(3H,t,J=6.8Hz), 1.65-1.82(2H,m), 2.11(3H,s), 2.32(3H,s), 2.81-2.85(2H,m), 3.11(3H,s), 3.98(2H,q,J=6.8Hz), 4.48(2H,s), 4.84(2H,s), 5.47-5.56(2H,m), 7.81(1H,s), 7.92(1H,s), 9.46-9.56(1H,m), 9.72(1H,brs), 11.29(1H,s).

MS:m/e(ESI)509.2(MH+)

Example 274

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-methoxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.42(3H,t,J=7.3Hz), 3.30(3H,s), 3.49(4H,brs), 4.27(2H,q,J=7.3Hz), 4.84(2H,s), 5.48(2H,s), 7.56(1H,s), 7.76(2H,s), 8.07(1H,s), 8.26(1H,brs), 8.65(1H,s), 9.06(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)524.2(MH+)

Example 275

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-

ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (3-methoxy-propyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.40(3H,t,J=7.0Hz),

1.74(1H,tt,J=6.4,6.3Hz), 3.25(3H,s),

3.33(2H,dd,J=6.3,5.7Hz), 3.61(2H,t,J=6.4Hz),

4.25(2H,q,J=7.0Hz), 4.83(2H,s), 5.47(2H,s), 7.53(1H,s),

7.76(2H,s), 8.07(1H,brs), 8.25(1H,t,J=5.7Hz),

8.51(1H,s), 9.12(1H,brs), 9.80(1H,brs).

MS:m/e(ESI)538.3(MH+)

Example 276

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methyl-5-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

0.80(3H,t,J=6.4Hz), 1.42(18H,s), 1.82-1.94(2H,m),

2.04-2.14(2H,m), 2.67(3H,s), 5.03(1H,q,J=2.8),

5.35(1H,d,J=18.8Hz), 5.61(1H,d,18.8Hz),

7.72(1H,d,J=8.0Hz), 7.71(2H,s), 8.16(1H,d,J=8.0Hz),

9.95(1H,s).

MS:m/e(ESI)436.2(MH+)

Example 277

2-(2-{3-[(Acetyl-methyl-amino)-methyl]-5-*tert*-butyl-4-hydroxy-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-hydroxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7.1Hz), 2.12(3H,s), 3.10(3H,s),

3.38(2H,dt,J=5.4,5.2Hz), 3.54(2H,dt,J=5.4,4.9Hz),

4.28(2H,q,J=7.1Hz), 4.48(2H,s), 4.83(1H,t,J=4.9Hz),

4.86(2H,s), 5.47(2H,s), 7.56(1H,s), 7.82(1H,s),

7.90(1H,s), 8.46(1H,t,J=5.2Hz), 8.68(1H,s),

9.87(1H,brs).

MS:m/e(ESI)539.2(MH+)

Example 278

2-{2-[3-(1-Acetylamino-ethyl)-5-*tert*-butyl-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid (2-hydroxy-ethyl)-amide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.42-1.48(6H,m), 1.88(3H,s),

3.38(2H,dt,J=5.5,5.2Hz), 3.54(2H,dt,J=5.4,4.9Hz),

4.27(2H,q,J=6.8Hz), 4.83(1H,t,J=4.9Hz), 4.85(2H,s),

5.13(1H,dq,J=7.0,6.4Hz), 5.40(1H,d,J=18.0Hz),

5.50(1H,d,J=18.0Hz), 7.56(1H,s), 7.75(1H,s),

7.79(1H,s), 8.37(1H,t,J=5.2Hz), 8.67(1H,s),

8.90(1H,d,J=6.4Hz), 9.85(1H,brs).

MS:m/e(ESI)539.2(MH+)

Example 279

N-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methoxymethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.11(3H,s), 3.10(3H,s), 3.41(3H,s),

4.48(2H,s), 4.68(2H,s), 4.91(2H,s), 5.54(2H,s),

7.82(1H,s), 7.85(1H,d,J=8.0Hz), 7.91(1H,s),

8.29(1H,d,J=8.0Hz), 9.58(1H,brs), 10.00(1H,brs),

11.29(1H,s).

MS:m/e(ESI)453.1(MH+)

Example 280

N-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-N-methyl-acetamide hydrochloride

1H-NMR(DMSO-d6)δ:

0.93(3H,t,J=7.2Hz), 1.37(9H,s), 1.72-1.82(2H,m),

2.11(3H,s), 2.86-2.93(2H,m), 3.10(3H,s), 4.48(2H,s),

4.86(2H,s), 5.55(2H,s), 7.72(1H,d,J=8.0Hz), 7.82(1H,s),

7.91(1H,s), 8.17(1H,d,J=8.0Hz), 9.60(1H,brs),

9.85(1H,s), 11.28(1H,s).

MS:m/e(ESI)451.1(MH+)

Example 281

2-{2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-1-imino-2,3-dihydro-1H-isoindol-5-yloxy}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.53(3H,d,J=6,4Hz), 4.75(2H,s), 4.89-

4.98(1H,m), 5.45(2H,s), 7.16(1H,d,J=8.8Hz), 7.22(1H,s),

7.77(2H,s), 8.07(1H,d,J=8.8Hz), 9.07(1H,brs),

9.76(1H,brs).

MS:m/e(ESI)467.2(MH+)

Example 282

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid diethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.06(3H,t,J=10Hz), 1.16(3H,t,J=10Hz),

3.20(2H,q,J=10Hz), 3.49(2H,q,J=10Hz), 4.92(2H,s),

5.53(2H,s), 7.74(2H,s), 7.90(1H,d,J=10Hz),

8.37(1H,d,J=10Hz).

Example 283

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-6-methoxy-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

2.81(3H,d,J=6.0Hz), 3.98(3H,s), 4.84(2H,s), 5.49(2H,s),

7.55(1H,s), 7.76(2H,s), 8.31(1H,brs), 8.59(1H,s).

Example 284

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-6-propoxy-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

0.98(3H,t,J=10Hz), 1.82(2H,m), 2.82(3H,d,J=6.0Hz),

4.20(2H,t,J=10Hz), 4.85(2H,s), 5.46(2H,s), 7.56(1H,s),

7.76(2H,s), 8.31(1H,d,J=6.0Hz), 8.59(1H,s).

Example 285

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-1,3,6,7-tetrahydro-5,8-dioxa-2-aza-cyclopenta[b]naphthalen-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(3H,d,J=7.2Hz), 1.42(18H,s), 3.90-3.98(1H,m), 4.30-4.44(2H,m), 4.69(2H,s), 5.45(2H,s), 7.19-7.27(1H,m), 7.68-7.74(1H,m), 7.77(2H,s), 9.04(1H,brs), 9.64(1H,brs).

MS:m/e(ESI)451.1(MH+)

Example 286

1-{3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-azepan-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.370(9H,s), 1.46-1.59(4H,m), 1.61-1.7(2H,m), 2.54-2.60(2H,m), 2.674(3H,s), 3.54-3.60(2H,m), 4.506(2H,s), 4.865(2H,s), 5.521(2H,s), 7.711(1H,d,J=8.0Hz), 7.811(1H,s), 7.987(1H,s), 8.160(1H,d,J=8.0Hz), 9.920(1H,s).

Example 287

6-Chloro-2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.80(3H,d,J=4.8Hz), 4.90(2H,s),

5.54(2H,s), 7.78(2H,s), 7.99(1H,s), 8.04-8.12(1H,br), 8.29(1H,s), 8.59(1H,q,J=4.4Hz), 9.38(1H,br), 9.95(1H,br).

MS:m/e(ESI)470.1(MH+)

Example 288

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-5,7-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.49(18H,s), 3.91(3H,s),3.99(3H,s), 4.74(2H,s), 5.87(1H,brs), 6.02(2H,s), 6.52(1H,d,J=2Hz), 6.64(1H,d,J=2Hz), 7.46(1H,brs), 8.00(2H,s), 10.75(1H,brs).

MS:m/e(ESI)439.0(MH+)

Example 289

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.41(3H,t,J=7.5Hz), 4.84(2H,s), 5.48(2H,s), 7.54(1H,s), 7.69(1H,brs), 7.77(2H,s), 8.07(1H,s), 8.63(1H,s), 9.15(1H,brs), 9.82(1H,brs).

MS:m/e(ESI)466.1(MH+)

Example 290

1-(3-*tert*-Butyl-4-hydroxy-5-methylaminomethyl-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-

6-yl)-ethanone dihydrochloride

1H-NMR(DMSO-d6)δ:

1.401(9H,s), 2.582(3H,t,J=4.8Hz), 2.667(3H,s), 4.289(3H,s), 4.869(2H,s), 5.627(2H,s), 5.739(1H,s), 7.705(1H,d,J=8.0Hz), 7.870(1H,s), 8.15-8.17(2H,m), 9.188(1H,s), 9.959(1H,s), 10.207(1H,s).

Example 291

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-6-(2-methoxy-ethoxy)-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

2.84(3H,d,J=6.0Hz), 3.76(2H,t,J=10Hz), 4.85(2H,s), 5.46(2H.s), 7.56(1H,s), 7.76(2H,s), 8.31(1H,d,J=6.0Hz), 8.59(1H.s).

Example 292

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(2-oxo-piperidin-1-ylmethyl)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=7.2Hz), 1.64-1.75(4H,m), 2.33-2.37(2H,m), 2.83(3H,d,J=4.8Hz), 3.44-3.49(2H,m), 4.28(2H,q,J=7.2Hz), 4.48(2H,s), 4.85(2H,s), 5.47(2H,s), 7.54(1H,s), 7.82(1H,d,J=2.0Hz), 7.88(1H,d,J=2.0Hz), 8.20(1H,q,J=4.8Hz), 8.56(1H,s), 9.20(1H,br), 9.83(1H,br), 11.55(1H,br).

MS:m/e(ESI)535.2(MH+)

Example 293

2-[2-(3-*tert*-Butyl-5-ethyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.16(3H,t,J=7.6Hz), 1.40(9H,s), 1.41(3H,t,J=7.2Hz), 2.70(2H,q,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=4.8Hz), 4.84(2H,s), 5.45(2H,s), 7.53(1H,s), 7.68(1H,s), 7.70(1H,s), 8.20(1H,q,J=4.8Hz), 8.55(1H,s).

MS:m/e(ESI)452.1(MH+)

Example 294

1-(3-*tert*-Butyl-5-ethyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.15(3H,t,J=7.6Hz), 1.32-1.46(12H,m), 2.31(3H,s), 2.58(3H,s), 2.69(2H,q,J=7.6Hz), 3.99(2H,q,J=7.2Hz), 4.82(2H,s), 5.52(2H,s), 7.68(1H,s), 7.70(1H,s), 9.32(1H,brs), 9.48(1H,s), 9.83(1H,s).

MS:m/e(ESI)424.1(MH+)

Example 295

1-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-piperidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.32-1.44(12H,m), 1.64-1.78(4H,m), 2.32(3H,s), 2.32-2.40(2H,m), 2.58(3H,s), 3.41-3.50(2H,m), 3.95-4.02(2H and AcOEt), 4.48(2H,s), 4.83(2H,s), 5.49(2H,s), 7.82(1H,s), 7.88(1H,s), 9.41(1H,brs), 9.85(1H,brs), 11.56(1H,s).

MS:m/e(ESI)507.2(MH+)

Example 296

Methyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-7-fluoro-3-imino-2,3-dihydro-1H-isoindol-5-yl}-carbamate hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(3H,t,J=7.2Hz), 1.40(18H,s), 3.72(3H,s), 4.25(2H,q,J=7.2Hz), 4.89(2H,s), 5.50(2H,s), 7.76(2H,s), 8.06(1H,s), 8.47(1H,s), 9.28(1H,s), 9.36(1H,brs), 10.07(1H,brs).

MS:m/e(ESI)514.1(MH+)

Example 297

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(4-imino-3a,4,6,6a-tetrahydro-1H-pyrrolo[3,4-d]imidazol-5-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(18H,s), 4.54(2H,s), 5.20(2H,s), 6.34(1H,s), 7.66(2H,s), 7.97(1H,s), 9.42(1H,s), 9.65(1H,s).

MS:m/e(ESI)369.0(MH+)

Example 298

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-

ethyl]-3-imino-6-isopropoxy-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(6H,d,J=6.0Hz), 2.83(3H,d,J=5.0Hz), 4.83(2H,s), 4.86(1H,m), 5.46(2H,s), 7.56(1H,s), 7.76(2H,s), 8.09(1H,d,J=5.0Hz), 8.55(1H,s), 9.79(1H,brs).

Example 299

6-Cyclopropylmethoxy-2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

0.41(2H,bd,J=8.0Hz), 0.60(2H,bd,J=8.0Hz), 2.85(3H,d,J=5.0Hz), 4.15(2H,d,J=8.0Hz), 4.83(2H,s),5.46(2H,s), 7.56(1H,s), 7.76(2H,s), 8.09(1H,d,J=5.0Hz), 8.55(1H.s).

Example 300

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-3-methoxymethyl-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.61(3H,s), 3.43(3H,s), 4.63(3H,s), 4.85(3H,s), 5.58(3H,s), 7.77(2H,s), 8.07(1H,brs), 8.15(1H,s), 9.49-9.53(1H,m), 9.89-9.93(1H,m).

Example 301

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-

carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.41(3H,t,J=6.8Hz), 2.28,(3H,s),

2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s),

5.44(2H,s), 7.53(1H,s), 7.70(1H,s), 8.17-8.23(1H,m),

8.55(1H,s).

MS:m/e(ESI)438.1(MH+)

Example 302

3-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methoxy-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.76(3H,s), 4.89(2H,s), 5.55(2H,s),

6.71(1H,s), 7.65(1H,br), 7.75(2H,s), 7.98(1H,br),

8.27(1H,d,J=8.8Hz), 8.29(1H,d,J=8.0Hz).

MS:m/e(ESI)479.1(MH+)

Example 303

Methyl {2-[2-(3-*tert*-butyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindol-5-yl}-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.25-1.42(12H,m), 2.28(3H,s), 3.70(3H,s),

4.18(2H,q,J=6.8), 4.74(2H,s), 5.40(2H,s), 7.41(1H,s),

7.69(2H,s), 8.50(1H,s), 9.07(1H,brs).

MS:m/e(ESI)454.1(MH+)

Example 304

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-dimethylamino-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 3.08(6H,s), 4.70(2H,s), 5.42(2H,s), 6.92-6.97(2H,m), 7.79(2H,s), 7.95(1H,d,J=9.6Hz), 8.05(1H,s), 8.77(1H,s), 9.42(1H,s).

Example 305

1-(3-*tert*-Butyl-4-hydroxy-5-methyl-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.40(3H,t,J=7.2Hz), 2.28(3H,s), 2.31(3H,s), 2.58(3H,s), 3.99(2H,q,J=7.2Hz), 4.82(2H,s), 5.47(2H,s), 7.70(2H,s), 9.35(1H,s), 9.40(1H,brs), 9.83(1H,brs).

MS:m/e(ESI)410.0(MH+)

Example 306

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.0Hz), 1.40(3H,t,J=7.0Hz), 4.11(2H,q,J=7.0Hz), 4.22(2H,q,J=7.0Hz), 4.77(2H,s), 5.47(2H,s), 7.33(1H,s), 7.76(2H,s), 9.03(1H,brs).

MS:m/e(ESI)485.1(MH+)

Example 307

3-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methoxy-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.74,3.76(3H,each s), 4.85, 4.89(2H,s), 5.56(2H,s), 6.02,6.70(1H,each s), 7.25(1H,br), 7.43(1H,br), 7.56,7.72(1H,each d,J=8.0Hz and J=8.4Hz), 7.74, 7.75(2H,each s).

Example 308

2-[2-(3-Bromo-5-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.4Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.44(2H,s), 7.53(1H,s), 7.76(1H,d,J=2.4Hz), 8.05(1H,2,J=2.0Hz), 8.20(1H,q,J=4.4Hz), 8.55(1H,s), 9.18(1H,br), 9.84(1H,br).

MS:m/e(ESI)504.1(MH+)

Example 309

2-[2-(3-*tert*-Butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.84(2H,s), 5.45(2H,s),

6.98(1H,d,J=8.0Hz), 7.53(1H,s), 7.64-7.71(1H,m), 7.76(1H,dd,J=1.6,8.4Hz), 7.81(1H,d,J=1.6Hz), 8.18-8.22(1H,m), 8.55(1H,s).

MS:m/e(ESI)424.0(MH+)

Example 310

2-(2-{3-*tert*-Butyl-4-hydroxy-5-[(methanesulfonyl-methyl-amino)-methyl]-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(9H,s), 1.45(3H,t,J=7Hz), 2.75(3H,s), 2.85(3H,d,J=6Hz), 3.04(3H,s), 4.30(2H,q,J=7Hz), 3.39(2H,s), 4.87(2H,s), 5.48(2H,s), 7.55(1H,s), 7.81(1H,s), 7.82(1H,s), 8.22(1H,q,J=6Hz), 8.59(1H,s), 9.22(1H,brs), 9.84(1H,brs).

Example 311

3-*tert*-Butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzonitrile hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(9H,s), 2.68(3H,s), 4.82(2H,s), 5.30(2H,s), 7.66(1H,d,J=1Hz), 7.70(1H,d,J=8Hz), 7.81(1H,d,J=1Hz), 8.14(1H,d,J=1Hz).

Example 312

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-4,6-diethoxy-3-imino-2,3-dihydro-1H-isoindole-

5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=7Hz), 1.47(3H,t,J=7Hz), 1.51(18H,s),

3.04(3H,d,J=5Hz), 4.13(2H,q,J=7Hz), 4.38(2H,q,J=7Hz),

4.74(2H,s), 5.88(1H,brs), 5.96(1H,q,J=5Hz), 6.08(2H,s),

6.72(1H,s), 7.52(2H,brs), 7.99(2H,s).

MS:m/e(ESI)524.0(MH+)

Example 313

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(4-imino-1-methyl-4,6-dihydro-1H-pyrrolo[3,4-d]imidazol-5-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

3.79(3H,s), 4.71(2H,s), 5.38(2H,s), 7.76(2H,s),

8.04(1H,s), 8.95(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)383.0(MH+)

Example 314

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-imino-1-methyl-4,6-dihydro-1H-pyrrolo[3,4-d]imidazol-5-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

3.92(3H,s), 4.55(2H,s), 5.40(2H,s), 7.76(2H,s),

8.05(1H,brs), 8.17(1H,s), 9.06(1H,brs), 9.35(1H,brs).

MS:m/e(ESI)383.0(MH+)

Example 315

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[7-imino-3-(1-methoxy-ethyl)-2-methyl-5,7-dihydro-pyrrolo[3,4-

b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(3H,d,J=6.4Hz), 1.42(18H,s), 2.68(3H,s),

3.22(3H,s), 4.74(1H,q,J=6.4Hz), 4.86(2H,brs),

5.55(2H,s), 7.77(2H,s), 8.16(1H,s).

Example 316

6-Ethoxy-2-[2-(7-hydroxy-indan-4-yl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.413(3H,t,J=6.8Hz), 1.92-2.02(2H,m),

2.749(2H,t,J=7.6Hz), 2.826(3H,d,J=4.8Hz),

4.278(2H,t,6.8Hz), 4.823(2H,s), 5.334(2H,s),

6.786(1H,d,J=8.4Hz), 7.516(1H,s), 7.751(1H,d,J=8.4Hz),

8.556(1H,s).

Example 317

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.69(3H,s), 2,92(3H,s), 3.31(2H,t,J=4.4Hz),

4,36(2H,t,J=4.4Hz), 4.85(2H,s), 5.52(2H,s),

7.19(1H,d,J=2.0Hz), 7.30(1H,d,J=2.0Hz),

7.71(1H,d,J=8.0Hz), 8.16(1H,d,J=8.0Hz), 9.75(2H,s).

Example 318

2-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.43(3H,t,J=7.2Hz), 2.84(3H,d,J=4.4Hz), 2.92(3H,s), 3.33(2H,t,J=4.4Hz), 4.31(2H,q,J=7.2Hz), 4.36(2H,t,J=4.4Hz), 4.85(2H,s), 5.47(2H,s), 7.18(1H,d,J=2.0Hz), 7.30(1H,d,J=2.0Hz), 7.55(1H,s), 8.21(1H,q,J=4,4Hz), 8.57(1H,s), 9.18(1H,s), 9.83(1H,s).

Example 319

1-{3-*tert*-Butyl-4-hydroxy-5-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 2.69(3H,s), 2.71(3H,s), 2.97(2H,t,J=5.2Hz), 3.31(3H,s), 3.43(2H,t,J=5.2Hz), 4.86(2H,s), 5.53(2H,s), 7.68(1H,d,J=2.0Hz), 7.72(1H,d,J=8.0Hz), 7.80(1H,d,J=2.0Hz), 8.17(1H,d,J=8.0Hz), 9.18(1H,s), 9.47(1H,s), 9.91(1H,s).

Example 320

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[3-ethoxy-7-imino-4-methyl-2-(2-methyl-propenyl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(3H,t,J=6.8Hz), 1.42(18H,s), 1.99(3H,s),

2.10(1H,d,J=0.8Hz), 2.30(3H,s), 3.93(2H,q,J=6.8Hz),
4.83(2H,s), 5.54(2H,s), 6.53(1H,brs), 7.78(2H,s),
9.48(1H,s).
MS:m/e(ESI)492.1(MH+)

Example 321

1-(3-*tert*-Butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.34-1.43(12H,m), 2.31(3H,s), 2.58(3H,s),
3.99(2H,q,J=7.2Hz), 4.82(2H,s), 5.47(2H,s),
6.96(1H,d,J=8.4Hz), 7.76(1H,dd,J=8.4and2.0Hz),
7.81(1H,d,J=2.0Hz), 9.42(1H,brs), 9.83(1H,brs),
10.62(1H,s).
MS:m/e(ESI)396.0(MH+)

Example 322

N-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.37-1.44(12H,m), 2.32(3H,s), 2.59(3H,s), 2.73(3H,s),
3.02(3H,s), 4.00(2H,q.J=6.8Hz), 4.38(2H,s), 4.83(2H,s),
5.51(2H.s), 7.80(2H,s), 9.26-9.50(2H,m), 9.84(1H,s).
MS:m/e(ESI)517.1(MH+)

Example 323

2-(6-Chloro-5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 1.40(3H,t,J=6.8Hz), 4.25(2H,q,J=6.8Hz), 4.82(2H,s), 5.48(2H,s), 7.58(1H,s), 7.77(2H,s), 8.06(1H,brs), 8.33(1H,s), 9.17(1H,brs), 9.73(1H,brs).

Example 324

tert-Butyl {6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-ethyl-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.19(3H,t,J=7.2Hz), 1.42(18H,s), 1.48(9H,s), 4.02(2H,q,J=7.2Hz), 4.86(2H,s), 5.56(2H,s), 7.78(2H,s), 8.01(1H,d,J=8.6Hz), 8.19(1H,d,J=8.6Hz), 9.68(1H,s).

MS:m/e(ESI)523.2(MH+)

Example 325

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-ethylamino-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=7.2Hz), 1.42(18H,s), 3.41(2H,q,J=7.2Hz), 4.63(2H,s), 5.51(2H,s), 6.84(1H,d,J=8.8Hz), 7.72(1H,d,J=8.8Hz), 7.77(2H,s), 8.06(1H,s), 9.21(1H,s), 9.32(1H,s).

MS:m/e(ESI)423.1(MH+)

Example 326

6-Ethoxy-2-[2-(4-hydroxy-naphthalen-1-yl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.83(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.53(2H,s), 6.98-7.03(1H,m), 7.12-7.18(1H,m), 7.51-7.56(3H,m), 7.59-7.63(1H,m), 8.18-8.27(1H,m), 8.36-8.45(1H,m), 8.57(1H,s).

MS:m/e(ESI)417.9(MH+)

Example 327

6-Ethoxy-3-imino-2-(2-oxo-2-phenyl-ethyl)-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz), 4.88(2H,s), 5.55(2H,s), 7.54(1H,s), 7.61(2H,t,J=7.6Hz), 7.74(1H,t,J=6.8Hz), 8.02(2H,d,J=6.8Hz), 8.20(2H,q,J=6.8Hz), 8.57(1H,s).

MS:m/e(ESI)351.9(MH+)

Example 328

6-Ethoxy-2-[2-(4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.4Hz),
4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.40(2H,s),
6.93(2H,d,J=8.8Hz), 7.52(1H,s), 7.89(2H,d,J=8.8Hz),
8.19-8.21(1H,m), 8.56(1H,s).
MS:m/e(ESI)368.0(MH+)

Example 329

Ethyl 3-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:
1.17(3H,t,J=7.2Hz), 1.39(9H,s), 1.41(3H,t,J=7.2Hz),
2.58(2H,t,J=6.4Hz), 2.82(3H,d,J=4.8Hz),
2.96(2H,t,J=6.4Hz), 4.06(2H,q,J=7.2Hz),
4.28(2H,q,J=7.2Hz), 4.82(2H,s), 7.52(1H,s), 7.70(1H,s),
7.72(1H,s), 8.18(1H,q,J=4.8Hz), 8.54(1H,s).
MS:m/e(ESI)524.1(MH+)

Example 330

2-Acetylamino-3-{6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-propionamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.42(18H,s), 1.86(3H,s), 3.09-3.15(1H,m), 3.27-3.33(1H,m), 4.69-4.73(1H,m), 4.86(2H,s), 5.55(2H,s),
7.09(1H,brs), 7.38(1H,brs), 7.67(1H,d,J=8.0Hz),
7.77(2H,s), 8.16-8.21(2H,m).
MS:m/e(ESI)508.1(MH+)

Example 331

Ethyl 3-{3-*tert*-butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=7.2Hz), 1.38(9H,s), 2.58(2H,t,6.4Hz), 2.68(3H,s), 2.95(2H,t,J=6.4Hz), 4.06(2H,q,J=7.2Hz), 4.83(2H,s), 5.47(2H,s), 7.68-7.74(3H,m), 8.13(1H,d,J=8.0Hz).

MS:m/e(ESI)438.1(MH+)

Example 332

2-[2-(3-Cyclohexyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.20-1.46(5H,m), 1.409(3H,t,J=6.8Hz), 1.66-1.83(5H,m), 2.252(3H.s), 2.822(3H,d,J= 4.8Hz), 2.91-3.01(1H,m), 4.276(2H,q,J=6.8Hz), 4.836(2H,s), 5.425(2H,s), 7.526(1H,s), 7.639(2H,s), 8.18-8.21(1H,m), 8.551(1H,s).

Example 333

1-(3-Cyclohexyl-4-hydroxy-5-methyl-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.22-1.48(5H,m), 1.68-1.85(5H,m), 2.262(3H,s),

2.680(3H,s), 2.93-3.02(1H,m), 4.854(2H,s), 5.496(2H,s), 7.651(2H,s), 7.713(1H,d,J=8.0Hz), 8.159(1H,d,J=8.0Hz).

Example 334

2-[2-(3-Cyclopentyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.409(3H,t,J=6.8Hz), 1.47-1.82(6H,m), 1.93-2.03(2H,m), 2.252(3H,s), 2.822(3H,d,J=4.4Hz), 4.276(2H,q,J=6.8Hz), 4.834(2H,s), 5.424(2H,s), 7.524(1H,s), 7.644(1H,s), 7.659(1H,s), 8.17-8.23(1H,m), 8.549(1H,s).

Example 335

1-(3-Cyclopentyl-4-hydroxy-5-methyl-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.46-1.1.82(6H,m), 1.93-2.03(2H,m), 2.252(3H,s), 2.669(3H,s), 4.839(2H,s), 5.479(2H,s), 7.63-7.68(2H,m), 7.700(1H,d,J=8.4Hz), 8.145(1H,d,J= 8.4Hz).

Example 336

1-(3-Cyclopentyl-4-hydroxy-5-methyl-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.394(3H,t, J= 6.8Hz), 1.47-1.58(2H,m), 1.60-1.82(4H,m), 1.94-2.04(2H,m), 2.250(3H,s), 2.310(3H.s),

2.578(3H,s), 3.988(2H,q,J=6.8Hz), 4.811(2H,s),
5.457(2H,s), 7.645(1H,s), 7.659(1H,s).

Example 337

2-(2-{3-[(2-Benzyloxy-ethyl)-methyl-amino]-5-*tert*-butyl-4-hydroxy-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.40(9H,s), 1.43(3H,t,J=6.8Hz), 2.71(3H,s),
2.84(3H,d,J=4.4Hz), 3.04(2H,t,J=5.2Hz),
3.55(2H,t,J=5.2Hz), 4.30(2H,q,J=6,8Hz), 4.53(2H,s),
4.85(2H,s), 5.46(2H,s), 7.20-7.40(5H,m), 7.55(1H,s),
7.68(1H,d,J=1.6Hz), 7.80(1H,d,J=1.6Hz),
8.21(1H,q,J=4.4Hz), 8.57(1H,s), 9.16(1H,s), 9.24(1H,s),
9.83(1H,s).

Example 338

2-(2-{3-*tert*-Butyl-4-hydroxy-5-[(2-hydroxy-ethyl)-methyl-amino]-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(9H,s), 1.43(3H,t,J=6.8Hz), 2.69(3H,s),
2.84(3H,d,J=4.8Hz), 2.86(2H,t,J=5.2Hz),
3.58(2H,t,J=5,2Hz), 4.29(2H,q,J=6.8Hz), 4.85(2H,s),
5.48(2H,s), 7.55(1H,s), 7.65(1H,d,J=1.6Hz),
7.71(1H,d,J=1.6Hz), 8.21(1H,q,J=4.8Hz), 8.57(1H,s),

9.00-10.00(2H,brs).

Example 339

tert-Butyl 6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-4-methyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(3H,t,6.8Hz), 1.42(18H,s), 1.58(9H,s), 2.37(3H,s), 4.08(2H,q,J=6.8Hz), 4.90(2H,s), 5.54(2H,s), 7.77(2H,s), 8.00-8.12(1H,m), 9.42-9.55(1H,m), 9.98(1H,brs).

MS:m/e(ESI)538.3(MH+)

Example 340

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-4-methyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.34(3H,t,J=7.2Hz), 1.42(18H,s), 2.35(3H,s), 4.11(2H,q,J=7.2Hz), 4.89(2H,s), 5.53(2H,s), 7.77(2H,s), 8.02-8.12(1H,m), 9.42-9.50(1H,m), 9.99(1H,brs).

MS:m/e(ESI)482.2(MH+)

Example 341

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-thiazol-2-yl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.43(18H,s), 4.96(2H,s), 5.62(2H,s), 7.79(2H,s),

8.03(1H,d,J=3.1Hz), 8.09(1H,d,J=3.1Hz),
8.42(1H,d,J=8.1Hz), 8.54(1H,d,J=8.1Hz), 9.90(1H,brs).
MS:m/e(ESI)463.0(MH+)

Example 342

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-sulfonic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.40(18H,s), 1.40(3H,t,J=7.0Hz), 2.47(3H,brs),
4.35(2H,q,J=7.0Hz), 4.87(2H,s), 5.49(2H,s),
7.15(1H,q,J=4.5Hz), 7.67(1H,s), 7.76(2H,s),
8.06(1H,brs), 8.73(1H,s), 9.23(1H,brs), 9.94(1H,brs).
MS:m/e(ESI)516.2(MH+)

Example 343

2-[2-(3-*tert*-Butyl-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.36(9H,s), 1.41(3H,t,J=6.8Hz), 2.83(3H,d,J=4.8Hz),
3.93(3H,s), 4.28(2H,q,J=6.8Hz), 4.85(2H,s), 5.49(2H,s),
7.19(1H,d,J=8.8Hz), 7.54(1H,s), 7.84(1H,d,J=2.4Hz),
7.93(1H,dd,J=2.4,8.8Hz), 8.17-8.23(1H,m), 8.56(1H,s).
MS:m/e(ESI)438.0(MH+)

Example 344

2-[2-(3-*tert*-Butyl-5-chloro-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-

carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.4Hz),

4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.44(2H,s), 7.53(1H,s),

7.74(1H,s), 7.93(1H,s), 8.18-8.22(1H,m), 8.55(1H,s).

MS:m/e(ESI)458.1(MH+)

Example 345

2-{2-[3-*tert*-Butyl-5-(2-dimethylcarbamoyl-ethyl)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=7.2Hz), 2.77-2.90(4H,m),

2.82(3H,d,J=4.8Hz), 2.86(3H,s), 2.97(3H,s),

4.28(2H,q,J=7.2Hz), 4.84(2H,s), 5.42(2H,s), 7.52(1H,s),

7.69(1H,s), 7.73(1H,s), 8,18(1H,q,J=4.8Hz), 8.55(1H,s),

9.16(1H,brs), 9.8(1H,brs), 10.94(1H,brs).

MS:m/e(ESI)523.1(MH+)

Example 346

2-{2-[3-(2-Dimethylcarbamoyl-ethyl)-4-hydroxy-5-methyl-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=7.2Hz), 2.23(3H,s), 2.68(2H,t,J=6.4Hz),

2.80-2.86(2H,m), 2.82(3H,d,J=4.8Hz), 2.85(3H,s),

2.96(3H,s), 4.28(2H,q,J=7.2Hz), 4.82(2H,s), 5.39(2H,s), 7.51(1H,s), 7.67(1H,s), 7.69(1H,s), 8.19(1H,q,J=4.8Hz), 8.54(1H,s).

Example 347

2-{2-[3-*tert*-Butyl-5-(2-ethylcarbamoyl-ethyl)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

0.98(3H,t,J=7.2Hz), 1.37(9H,s), 1.40(3H,t,J=7.2Hz), 2.48-2.53(2H,m), 2.82(3H,d,J=4.8Hz), 2.82-2.88(2H,m), 3.04-3.12(2H,m), 4.28(2H,q,J=7.2Hz), 4.82(2H,s), 5.40(2H,s), 7.52(1H,s), 7.69(1H,s), 7.71(1H,s), 8.17-8.24(2H,m), 8.55(1H,s).

MS:m/e(ESI)523.3(MH+)

Example 348

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-6-methoxy-5-propyl-1,2,3,5-tetrahydro-isoindol-4-one hydrochloride

1H-NMR(DMSO-d6)δ:

0.97(3H,t,J=7Hz), 1.43(18H,s), 1.69(2H,m), 4.07(3H,s), 4.08(2H,t,J=6Hz), 4.56(2H,s), 4.79(2H,s), 6.04(1H,s), 7.79(1H,s), 7.98(2H,s).

MS:m/e(ESI)468.0(MH+)

Example 349

8-*tert*-Butyl-6-[2-5-ethoxy-1-imino-6-methylcarbamoyl-

1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benz

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 1.43(3H,t,J=7Hz), 2.84(3H,d,J=4Hz), 3.72(3H,s), 4.29(2H,q,J=7Hz), 4.34-4.38(1H,m), 4.55-4.60(1H,m), 4.85(2H,s), 5.45(2H,s), 5.50(1H,m), 7.43-7.45(1H,m), 7.51-7.53(1H,m), 7.54(1H,s), 8.21(1H,q,J=4Hz), 8.57(1H,s).

Example 350

8-*tert*-Butyl-6-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4

1H-NMR(DMSO-d6)δ:

1.49(9H,s), 2.69(3H,s), 3.71(3H,s), 4.33-4.38(1H,m), 4.54-4.60(1H,m), 4.86(2H,s), 5.48-5.53(1H,m), 5.51(2H,s), 7.45(2H,s), 7.53(1H,s), 7.72(1H,d,J=8Hz), 8.17(1H,d,J=8Hz).

Example 351

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[5-ethoxy-1-imino-6-(1-methoxy-propyl)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

0.83(3H,t,J=7.2Hz), 1.30-1.42(21H,m), 1.58-1.75(2H,m), 3.20(2H,s), 4.18(2H,q,J=7.2Hz), 4.56(1H,t,J=5.6Hz), 4.78(2H,s), 5.47(2H,s), 7.40(1H,s), 7.77(2H,s), 8.14(1H,s), 9.08(1H,brs), 9.72(1H,brs).

MS:m/e(ESI)495.3(MH+)

Example 352

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

]1.40(3H,t,J=7.2Hz), 1.41(18H,s), 4.25(2H,q,J=7.2Hz), 4.83(2H,s), 5.50(2H,s), 7.77(2H,s), 7.84(1H,d,J=2.4Hz), 8.55(1H,d,J=2.4Hz), 9.83(1H,brs).

MS:m/e(ESI)424.2(MH+)

Example 353

6-Ethoxy-2-[2-(4-hydroxy-3-methyl-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.408(3H,t,J=6.8Hz), 2.184(3H,s), 2.822(3H,d,J=4.8Hz), 4.274(2H,q,J=6.8Hz), 4.836(2H,s), 5.403(2H,s), 6.942(1H,d,J=8.4Hz), 7.519(1H,s), 7.729(1H,d,J=8.4Hz), 7.779(1H,s), 8.17-8.21(1H,m), 8.52-8.56(1H,m).

Example 354

2-(3-Ethoxy-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-1-(4-hydroxy-3-methyl-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.393(3H,t,J= 6.8Hz), 2.184(3H,s), 2.310(3H,s), 2.577(3H,s), 3.986(2H,q,J=6.8Hz), 4.819(2H,s), 5.442(2H,s), 6.944(1H,d,J=8.4Hz),

7.734(1H,dd,J=2.0,8.4Hz), 7.781(1H,s).

Example 355

Methyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.36-1.43(12H,m), 2.82(3H,d,J=4.8Hz), 3.72(3H,s), 4.29(2H,q,J=7.2Hz), 4.83(2H,s), 5.01(2H,s), 5.44(2H,s), 7.09(1H,d,J=8.0Hz), 7.52(1H,s), 7.84-7.90(2H,m), 8.19(1H,q,J=4.8Hz), 8.56(1H,s).

Example 356

2-(2-{3-[(Acetyl-methyl-amino)-methyl]-4-hydroxy-5-methyl-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.411(3H,t,J=6.8Hz), 2.094(3H,s), 2.215(3H,s), 2.824(3H,d,J=4.8Hz), 3.044(3H,s), 4.279(2H,q,J=6.8Hz), 4.482(2H,s), 4.849(2H,s), 5.418(2H,s), 6.942(1H,d,J=8.4Hz), 7.525(1H,s), 7.784(1H,s), 8.16-8.22(1H,m), 8.558(1H,s).

Example 357

N-{5-[2-(3-Ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-3-methyl-benzyl}-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.393(3H,t,J=6.8Hz), 2.093(3H,s), 2.212(3H,s),
2.314(3H,s), 2.579(3H,s), 3.048(3H,s),
3.989(2H,q,J=6.8Hz), 4.483(2H,s), 4.840(2H,s),
5.491(2H,s), 7.801(1H,s), 7.790(1H,s), 9.836(1H,s),
10.792(1H,s).

Example 358

N-{2-Hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-3-methyl-benzyl}-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:
2.093(3H,s), 2.215(3H,s), 2.670(3H,s), 3.044(3H,s),
4.483(2H,s), 4.858(2H,s), 5.488(2H,s),
7.704(1H,d,J=8.0Hz), 7.790(1H,s), 8.150(1H,d,J=8.0Hz).

Example 359

N-{2-Hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-3-methyl-benzyl}-N-methyl-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:
2.226(3H,s), 2.657(3H,s), 2.699(3H,s), 2.968(3H,s),
4.264(2H,s), 4.803(2H,s), 5.402(2H,s),
7.664(1H,d,J=8.0Hz), 7.717(2H,s), 8.114(1H,d,J=8.0Hz).

Example 360

N-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.18(3H,s), 4.83(2H,s), 5.55(2H,s), 7.77(2H,s), 8.22(1H,d,J=8.2Hz), 8.37(1H,d,J=8.2Hz), 10.65(1H,s).

MS:m/e(ESI)437.2(MH+)

Example 361

{2-*tert*-Butyl-4-[2-5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.37-1.43(12H,m), 2.82(3H,d,J=4.8Hz), 4.25-4.30(4H,m), 4.81(2H,s), 5.58(2H,s), 7.46-7.52(1H,m), 7.72-7.80(2H,m), 8.17-8.22(1H,m), 8.52(1H,s), 12.07(1H,brs).

MS:m/e(ESI)480.1(MH+)

Example 362

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(2-oxo-pyrrolidin-1-yl)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.43(9H,s), 1.44(3H,t,J=7Hz), 2.13-2.23(2H,m), 2.42-2.48(2H,m), 2.85(3H,d,J=5Hz), 3.65-3.71(2H,m), 4.30(2H,q,J=7Hz), 4.86(2H,s), 5.45(2H,s), 7.55(1H,s), 7.66(1H,d,J=1Hz), 7.80(1H,d,J=1Hz), 8.21(1H,q,J=5Hz), 8.58(1H,s).

Example 363

2-{2-[3-*tert*-Butyl-4-(2,2-dimethyl-propoxy)-phenyl]-2-

oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.11(9H,s), 1.43(9H,s), 1.44(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 8.85(2H,s), 4.30(2H,q,J=7Hz), 4.87(2H,s), 5.49(2H,s), 7.22(1H,d,J=9Hz), 7.55(1H,s), 7.88(1H,d,J=2Hz), 7.92(1H,dd,J=2Hz,9Hz), 8.21(1H,q,J=5Hz), 8.59(s,1H).

Example 364

3-*tert*-Butyl-5-[2-5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 1.44(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 4.30(2H,q,J=7Hz), 4.57(2H,s), 4.86(1H,s), 5.47(2H,s), 4.55(1H,s), 7.82(2H,s), 8.21(1H,q,J=5Hz), 7.58(1H,s), 7.21(1H,brs), 9.46(1H,brs), 9.84(1H,brs).

Example 365

N-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-2-methyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-ylmethyl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(18H,s), 1.92(3H,s), 2.65(3H,s), 4.39(2H,d,J=6.0Hz), 4.81(2H,s), 5.46(2H,s), 7.69(2H,s), 7.98(1H,s), 8.52(1H,t,J=6.0Hz).

Example 366

Methyl {8-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.4Hz), 3.51(2H,t,J=4.4Hz), 3.66(3H,s), 4.30(6H,m), 4.84(2H,s), 5.43(2H,s), 7.06(1H,s), 7.29(1H,s), 7.54(1H,s), 8.21(1H,q,J=4.4Hz), 8.57(1H,s), 9.19(1H,s), 9.81(1H,s).

Example 367

Benzyl {8-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.44(3H,t,J=6.8Hz), 2.85(3H,d,J=4.4Hz), 3.53(2H,t,J=3.6Hz), 4.30(2H,q,J=6.8Hz), 4.32(2H,t,J=3.6Hz), 4.38(2H,s), 4.84(2H,s), 5.16(2H,s), 5.39(2H,s), 7.10(1H,s), 7.20-7.35(6H,m), 7.56(1H,s), 8.21(1H,q,J=4.4Hz), 8.58(1H,s), 9.20(1H,s), 9.83(1H,s).

Example 368

{8-*tert*-Butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.8Hz), 3.50(2H,t,J=4.4Hz), 4,14(2H,s), 4.30(4H,m), 4.84(2H,s), 5.44(2H,s), 7.07(1H,d,J=1.6Hz), 7.27(1H,d,J=1.6Hz), 7.53(1H,s), 8.21(1H,q,J=4.8Hz), 8.57(1H,s), 9.22(1H,s), 9.82(1H,s), 12.50(1H,s).

Example 369

{8-*tert*-Butyl-6-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 2.69(3H,s), 4.12(2H,s), 4.30(2H,t,J=4.0Hz), 4.85(2H,s), 5.51(2H,s), 7.07(1H,s), 7.27(2H,s), 7.71(1H,d,J=7.6Hz), 8.15(1H,d,J=7.6Hz), 9.85(1H,s).

Example 370

Methyl {4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-ethyl-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.18(t,3H,J=7.2Hz), 1.42(t,3H,J=7.2Hz), 2.70(q,2H,J=7.2Hz), 2.82(d,3H,J=4.8Hz), 3.71(s,3H), 4.29(q,2H,J=7.2Hz), 4.86(s,2H), 5.00(s,2H), 5.43(s,2H), 7.08(d,1H,J=8.0Hz), 7.52(s,1H), 7.78~7.87(m,2H), 8.18(q,1H,J=4.8Hz), 8.57(s,1H).

Example 371

6-Ethoxy-3-imino-2-[2-oxo-2-(3,4,5-trimethoxy-phenyl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid

methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.8Hz), 3.76(3H,s),

3.87(6H,s), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.56(2H,s),

7.32(2H,s), 7.54(1H,s), 8.17-8.23(1H,m), 8.56(1H,s).

MS:m/e(ESI)442.2(MH+)

Example 372

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-d]pyrimidin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.84(3H,s), 4.96(2H,s), 5.59(2H,s),

7.76(2H,s), 9.26(1H,s).

MS:m/e(ESI)395.2(MH+)

Example 373

6-Ethoxy-2-[2-(4-hydroxy-3-isopropyl-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.193(6H,d,J=6.8Hz), 1.410(3H,t,J=6.8Hz),

2.823(3H,d,J=4.8Hz), 3.20-3.30(1H,m),

4.278(2H,q,J=6.8Hz), 4.839(2H,s), 5.412(2H,s),

6.950(1H,d,J=8.4Hz), 7.523(1H,s), 7.735(1H,d,J=8.4Hz),

7.779(1H,s), 8.198(1H,d,J=4.8Hz), 8.552(1H,s).

Example 374

2-[2-(3-Cyclopentyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-

ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.409(3H,t,J=6.8Hz), 1.49-1.84(6H,m), 1.92-2.03(2H,m), 2.821(3H,d,J=4.8Hz), 4.276(2H,q,J=6.8Hz), 4.835(2H,s), 5.413(2H,s), 6.944(1H,d,J=8.4Hz), 7.522(1H,s), 7.727(1H,d,J=8.4Hz), 7.785(1H,s), 8.18-8.21(1H,m), 8.552(1H,s).

Example 375

N-{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(3H,t,J=6.8Hz), 1.37(9H,s), 2.11(3H,s), 3.10(3H,s), 4.16(2H,q,J=6.8Hz), 4.48(2H,s), 4.79(2H,s), 5.43(2H,s), 7.22(1H,d,J=8.8Hz), 7.32(1H,s), 7.82(1H.s), 7.91(1H,s), 8.09(1H,d,J=8.8Hz), 9.10(1H,s), 9.72(1H,s), 11.27(1H,s).

Example 376

6-Ethoxy-2-[2-(3-ethyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.149(3H,t,J=7.6Hz), 1.407(3H,t,6.8Hz), 2.597(3H,q,J=7.6Hz), 2.820(3H,d,J=4.8Hz), 4.273(2H,q,J=6.8Hz), 4.838(2H,s), 5.406(2H,s),

6.946(1H,d,J=8.4Hz), 7.519(1H,s), 7.70-7.78(2H,m), 8.16-8.23(1H,m), 8.549(1H,s).

Example 377

2-[2-(3-Cyclopentyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.415(3H,t,J=6.8Hz), 1.41-1.83(6H,m), 1.92-2.03(2H,m), 2.249(3H,s), 4.273(2H,q,J=6.8Hz), 4.834(2H,s), 5.427(2H,s), 7.522(1H,s), 7.642(1H,s), 7.657(1H,s), 7.693(1h,s), 7.756(1H,s), 8.617(1H,s).

Example 378

N-{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(3H,t,J=6.8Hz), 1.41(9H,s), 2.73(3H,s), 3.02(3H,s), 4.16(2H,q,J=6.8Hz), 4.37(2H,s), 4.79(2H,s), 5.46(2H,s), 7.21(1H,dd,J=2.0,8.8Hz), 7.32(1H,d,J=2.0Hz), 7.80(1H,s), 7.81(1H,s), 8.09(1H,d,J=8.8Hz), 9.10(1H,s), 9.72(1H,s), 12.06(1H,s).

Example 379

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.35-1.44(15H,m), 4.08(2H,q,J=7.2Hz),
4.15(2H,q,J=7.2Hz), 4.72(2H,s), 4.87(2H,s), 5.45(3H,s),
7.07(1H,d,J=8.8Hz), 7.34(1H,s), 7.87(1H,d,J=8.8Hz),
9.13(1H,s), 9.67(1H,s).

MS:m/e(ESI)467.1(MH+)

Example 380

2-[2-(3-*tert*-Butyl-4-carbamoylmethoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.35-1.44(12H,m), 2.82(3H,d,J=5.2Hz),
4.27(2H,q,J=7.2Hz), 4.66(2H,s), 4.85(2H,s), 5.45(2H,s),
7.03(1H,d,J=8.8Hz), 7.33-7.45(2H,m), 7.53(1H,s),
7.85(1H,s), 7.89(1H,d,J=8.8Hz), 8.19(1H,d,J=0.8Hz),
8.55(1H,s).

MS:m/e(ESI)481.2(MH+)

Example 381

6-Ethoxy-2-[2-(4-ethoxy-3-methylcarbamoyl-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(6H,t,J=7.2Hz), 2.82(3H,s), 2.83(3H,s),
4.29(4H,qq,J=6.8Hz,7.2Hz), 4.86(2H,s), 5.49(2H,s),
7.32(1H,d,J=8.4), 7.53(1H,s), 8.07(1H,d,J=8.4),
8.13(1H,s), 8.21(1H,s), 8.35(1H,s), 8.56(1H,s).

MS:m/e(ESI)453.1(MH+)

Example 382

2-Ethoxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-N-methyl-benzamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.67(3H,s), 2.82(3H,d,J=4.4Hz), 4.29(2H,q,J=6.8Hz), 4.87(2H,s), 5.55(2H,s), 7.32(1H,d,J=8.4Hz), 7.70(1H,d,J=8.4Hz), 8.08(1H,d,J=8.4Hz), 8.12-8.17(2H,m), 8.35(1H,s).

Example 383

2-Ethoxy-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-N-methyl-benzamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(6H,t,J=6.8Hz), 2.32(3H,s), 2.58(3H,s), 2.82(3H,d,J=4.4Hz), 4.01(2H,q,J=6.8Hz), 4.29(2H,q,J=6.8Hz), 4.83(2H,s), 5.54(2H,s), 7.32(1H,d,J=8.4Hz), 8.08(1H,J=8.4Hz), 8.13(1H,d,J=4.4Hz), 8.35(1H,s), 9.50(1H,brs), 9.87(1H,brs).

Example 384

2-Ethoxy-5-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-N-methyl-benzamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 4.89(2H,s), 5.54(2H,s),

7.70(1H,dd,J=2.4,9.6Hz), 7.77-7.86(3H,m),
7.89(1H,d,J=9.6Hz), 7.95(1H,d,J=2.4Hz), 7.99(1H,m),
8.08(1H,s), 8.49(2H,d,J=3.2Hz), 9.31(1H,s), 9.82(1H,s).

Example 385

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-5-(pyridin-3-yloxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.44(18H,s), 4.85(2H,s), 5.52(2H,s),
7.51(1H,dd,J=2.4,8.8Hz), 7.55(1H,d,J=2.4Hz), 7.77-7.84(3H,m), 8.00(1H,m), 8.09(1H,m), 8.28(1H,d,J=8.8Hz),
8.46-8.53(2H,m), 9.24(1H,s), 9.22(1H,s).

Example 386

tert-Butyl {2-*tert*-butyl-4-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:
1.37-1.42(12H,m), 1.43(9H,s), 2.32(3H,s), 2.58(3H,s),
3.99(2H,q,J=6.8Hz), 4.83(2H,s), 4.86(2H,s), 5.50(2H,s),
7.05(1H,d,J=8.8Hz), 7.86(1H,d,J=2.0Hz),
7.90(1H,dd,J=8.8and2.0Hz), 9.40-9.47(1H,m), 9.82-9.89(1H,m).
MS:m/e(ESI)510.3(MH+)

Example 387

{2-*tert*-Butyl-4-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-

acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.34-1.67(12H,m), 2.31(3H,s), 2.58(3H,s),

3.99(2H,q,J=6.8Hz), 4.83(2H,s), 4.89(2H,s), 5.50(2H,s),

7.07(1H,d,J=8.8Hz), 7.85(1H,d,J=2.0Hz),

7.89(1H,dd,J=8.8and2.0Hz), 9.40-9.49(1H,m), 9.81-

9.91(1H,m).

MS:m/e(ESI)454.2(MH+)

Example 388

{2-*tert*-Butyl-4-[2-(6-carbamoyl-5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.40(3H,t,J=7.0Hz), 4.27(2H,q,J=7.0Hz),

4.85(2H,s), 4.88(2H,s), 5.46(2H,s), 7.07(1H,d,J=8.4Hz),

7.53(1H,s), 7.69(1H,brs), 7.76(1H,brs), 7.86(1H,s),

7.88(1H,d,J=8.4Hz), 8.63(1H,s), 9.20-9.26(1H,m),

9.85(1H,brs).

MS:m/e(ESI)468.1(MH+)

Example 389

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[7-imino-2-(2-methyl-2H-pyrazol-3-yl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 4.24(3H,s), 4.96(2H,s), 5.62(2H,s),

6.99(1H,s), 7.55(1H,s), 7.79(2H,s), 8.22(1H,d,J=8.0Hz),

8.35(1H,d,J=8.0Hz).

MS:m/e(ESI)460.2(MH+)

Example 390

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(3H,t,J=7.2Hz), 1.42(18H,s), 2.82(3H,d,J=4.4Hz), 4.29(2H,q,J=7.2Hz), 4.99(2H,s), 5.51(2H,s), 7.77(2H,s), 8.29(1H,s), 8.36-8.41(1H,m).

MS:m/e(ESI)498.2(MH+)

Example 391

{2-*tert*-Butyl-4-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 2.68(3H,s), 4.86(2H,s), 4.89(2H,s), 5.55(2H,s), 7.08(1H,d,J=9.2Hz), 7.71(1H,d,J=7.2Hz), 7.86(1H,s), 7.89(1H,d,J=9.2Hz), 8.15(1H,d,J=7.2Hz), 9.57(1H,s), 9.95(1H,s).

MS:m/e(ESI)394.0(MH+)

Example 392

{4-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 3.85(3H,s),
4.28(2H,q,J=7.2Hz), 4.84(2H,s), 4.85(2H,s), 5.46(2H,s),
7.06(1H,d,J=8.0Hz), 7.50(1H,s), 7.53(1H,s),
7.64(1H,d,J=7.8Hz), 8.19(1H,q,J=4.8Hz), 8.56(1H,s),
9.27(1H,s), 9.85(1H,s).
MS:m/e(ESI)456.1(MH+)

Example 393

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-5-methoxy-7-methyl-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(18H,s), 2.63(3H,s), 3.85(3H,s), 4.54(2H,s),
5.48(2H,s), 7.01(1H,d,J=2Hz), 7.17(1H,d,J=2Hz),
7.76(2H,s).
MS:m/e(ESI)423.0(MH+)

Example 394

1-{3-*tert*-Butyl-4-hydroxy-5-[(2-hydroxy-ethyl)-methyl-amino]-phenyl}-2-(5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.38(3H,t,J=7.2Hz), 1.40(9H,s), 2.69(3H,s),
2.86(2H,t,J=4.8Hz), 3.58(2H,t,J=4,8Hz),
4.18(2H,q,J=7.2Hz), 4.78(2H,s), 5.44(2H,s),
7.22(1H,d,J=8.8Hz), 7.33(1H,s),7.65(1H,s), 7.69(1H,s),
8.11(1H,d,J=8,8Hz).

Example 395

2-[2-(8-*tert*-Butyl-4,4-dimethyl-thiochroman-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(6H,s), 1.44(3H,t,J=7Hz), 1.53(9H,s), 1.91-1.97(2H,m), 2.85(3H,d,J=5Hz), 3.08-3.14(2H,m), 4.31(2H,q,J=7Hz), 4.87(2H,s), 5.53(2H,s), 7.56(1H,s), 7.77(1H,s), 7.94(1H,s), 8.22(1H,q, J=5Hz), 8.59(1H,s).

Example 396

2-[2-(8-*tert*-Butyl-4,4-dimethyl-1-oxo-thiochroman-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(3H,s), 1.43(3H,t,J=7Hz), 1.55(3H,s), 1.61(9H,s), 2.80-2.90(2H,m), 2.85(3H,d,J=5Hz), 3.07-3.27(2H,m), 4.61(2H,q,J=7Hz), 4.89(2H,s), 5.45-5.68(2H,m), 7.57(1H,s), 7.86(1H,s), 8.13(1H,s), 8.22(1H,q,J=5Hz), 8.59(1H,s).

Example 397

Ethyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-5-ethoxy-6-methylcarbamoyl-2,3-dihydro-isoindol-1-ylidene}-carbamate

1H-NMR(DMSO-d6)δ:

1.37(3H,t,J=7.2Hz), 1.46(18H,s), 1.55(3H,t,J=6.8Hz), 3.01(3H,t,J=4.8Hz), 4.25(2H,q,J=7.2Hz), 4.32(2H,q,J=7.2Hz), 4.63(2H,s), 5.11(2H,s), 5.80(1H,s),

6.98(1H,s), 7.88(2H,s), 8.82(1H,s).

MS:m/e(ESI)552.3(MH+)

Example 398

2-[2-(3-*tert*-Butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-1-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.42(3H,t,J=6.8Hz), 2.81(1H,d,J=4.4Hz), 4.20(2H,q,J=6.8Hz), 4.80(2H,s), 5.46(2H,s), 6.96(1H,d,J=8.4Hz), 7.77(1H,d,J=8.0Hz), 7.81(1H,s), 7.94(1H,s), 8.01(1H,s), 8.24(1H,d,J=4.4Hz).

MS:m/e(ESI)424.2(MH+)

Example 399

2-[2-(2-*tert*-Butyl-pyridin-4-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.42(3H,t,J=6.8Hz), 2.83(3H,d,J=4.4Hz), 4.28(2H,q,J=6.8Hz), 4.89(2H,s), 5.53(2H,s), 7.55(1H,s), 7.71(1H,d,J=6.4Hz), 7.85(1H,s), 8.20(1H,d,J=4.4Hz), 8.57(1H,s), 8.82(1H,d,J=5.6Hz), 9.24(1H,brs), 9.90(1H,brs).

Example 400

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(pyridin-4-yloxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 4.93(2H,s), 5.55(2H,s),

7.30(2H,d,J=6.8Hz), 7.76-7.83(3H,m),

7.96(1H,d,J=8.4Hz), 8.12(1H,d,J=2.0Hz),

8.52(2H,d,J=6.8Hz).

Example 401

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-5-(pyridin-4-yloxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 4.90(2H,s), 5.54(2H,s),

7.31(2H,d,J=7.2Hz), 7.64(1H,dd,J=2.0,8.4Hz),

7.75(1H,d,J=2.0Hz), 7.80(2H,s), 8.10(1H,s),

8.36(1H,d,J=8.4Hz), 8.51(2H,d,J=7.2Hz), 9.31(1H,s),

10.00(1H,s).

Example 402

2-{2-[8-*tert*-Butyl-4-(2-hydroxy-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.8Hz),

3.43(2H,t,J=6.0Hz), 3.50(2H,t,J=4.0Hz),

3.63(2H,t,J=6.0Hz), 4.25(2H,t,J=4.0Hz),

4.29(2H,q,J=6.8Hz), 4.85(2H,s), 5.50(2H,s), 7.22(2H,s),

7.54(1H,s), 8.22(1H,q,J=4.8Hz), 8.57(1H,s), 9.31(1H,s),

9.88(1H,s).

Example 403

N-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-methanesulfonamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 3.56(3H,s), 4.80(2H,s), 5.59(2H,s), 7.26(1H,d,J=8.8Hz), 7.78(2H,s), 8.08(1H,s), 8.17(1H,d,J=8.8Hz), 9.50(1H,s), 9.65(1H,s), 11.19(1H,s).

MS:m/e(ESI)473.2(MH+)

Example 404

2-[2-(3-Cyclopentyl-5-fluoro-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=7.2Hz), 1.21-1.33(2H,m), 1.52-1.69(2H,m), 1.74-1.80(2H,m), 1.93-2.02(2H,m), 2.82(3H,d,J=4.8Hz), 4.11-4.13(1H,m), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.45(2H,s), 7.53(1H,s), 7.65-7.71(2H,m), 8.19-8.22(1H,m), 8.56(1H,s).

MS:m/e(ESI)454.2(MH+)

Example 405

2-[2-(7-*tert*-Butyl-2-hydroxymethyl-benzofuran-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=6.8Hz), 1.49(9H,s), 2.83(3H,d,J=4.8Hz),

4.29(2H,q,J=7.2Hz), 4.64(2H,d,J=6.0Hz), 4.88(2H,s),

5.85(2H,d,J=6.0Hz), 6.94(1H,s), 7.55(1H,s), 7.77(1H,s),

8.19-8.23(1H,m), 8.24(1H,s), 8.57(1H,s).

MS:m/e(ESI)478.2(MH+)

Example 406

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(1-imino-5-methoxy-7-methoxymethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.50(18H,s), 3.64(3H,s), 3.90(3H,s), 4.75(2H,s),

5.34(1H,s), 6.04(2H,s), 6.68(1H,d,J=2Hz),

6.80(1H,d,J=2Hz), 7.47(1H,brs), 8.00(2H,s).

MS:m/e(ESI)470.0(MH+)

Example 407

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-hydroxy-1-imino-5-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 3.84(3H,s), 4.69(2H,s), 5.43(2H,s),

6.55(1H,s), 6.78(1H,s), 7.75(2H,s), 8.04(1H,s),

8.34(1H,s), 9.10(1H,s), 11.78(1H,s).

MS:m/e(ESI)426.0(MH+)

Example 408

2-{2-*tert*-Butyl-4-[2-(5,6-diethoxy-1-imino-1,3-

dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.32-1.48(15H,m), 4.09(2H,q,J=7.2Hz), 4.15(2H,q,J=7.2Hz), 4.66(2H,s)4.73(2H,s), 5.43(2H,s), 7.03(1H,d,J=8.8Hz), 7.35(1H,s), 7.36-7.44(2H,m), 7.78(1H,s), 7.86(1H,s), 7.90(1H,d,J=8.8Hz), 9.01-9.16(1H,brs), 9.50-9.65(1H,brs).

MS:m/e(ESI)468.2(MH+)

Example 409

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.44(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 3.90(3H,s), 4.30(2H,q,J=7Hz), 4.87(2H,s), 5.51(2H,s), 7.47(1H,s), 7.55(2H,s), 8.21(1H,q,J=5Hz), 8.58(1H,s).

Example 410

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.58(3H,s), 4.69(2H,s), 4.86(2H,s), 5.60(2H,s), 7.78(2H,s), 8.05-8.10(1H,m), 8.20(1H,s), 9.44-9.50(1H,m), 9.85-9.90(1H,m).

Example 411

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[7-imino-2-methyl-3-(tetrahydropyran-2-yloxymethyl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 1.30-1,85(6H,m), 2.63(3H,s), 3.48-3.55(1H,m), 3.75-3.82(1H,m), 4.68(1H,d,J=14.4Hz), 4.79(1H,brs), 4.86(2H,s), 4.88(1H,d,J=14.4Hz), 5.54(2H,s), 7.76(2H,s), 8.20(1H,s), 9.85-9.95(1H,m).

Example 412

2-(3-Aminomethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.74(3H,s), 4.23-4.30(2H,m), 4.90(2H,s), 5.59(2H,s), 7.78(2H,s), 8.09(1H,s), 8.25(1H,brs), 9.55-9.64(1H,m), 9.95-10.02(1H,m).

Example 413

tert-Butyl {6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-2-methyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-3-ylmethyl}-carbamate hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(27H,s), 2.64(3H,s), 4.28-4.32(2H,m), 4.84(2H,s), 5.49(2H,s), 7.55-7.60(1H,m), 7.72(2H,s), 7.97(1H,s).

Example 414

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-

hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(18H,s), 2.67(3H,s), 3.89(1H,brs), 4.08(1H,d,J=12.0Hz), 5.46(2H,dd,J=18.4Hz,18.4Hz), 7.70(1H,d,J=8.0Hz), 7.73(2H,s), 8.15(1H,d,J=8.0Hz).

Example 415

2-[2-(3-*tert*-Butyl-4-carbamoylmethoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.26-1.30(12H,m), 4.15(2H,q,J=7.2Hz), 4.54(2H,s), 4.73(2H,s), 5.33(2H,s), 6.91(1H,d,J=8.8Hz), 7.24-7.31(2H,m), 7.41(1H,s), 7.57(1H,s), 7.65(1H,s), 7.78(1H,d,J=8.8Hz), 8.51(1H,s).

MS:m/e(ESI)467.1(MH+)

Example 416

2-[2-(3-*tert*-Butyl-4-methanesulfonylamino-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39-1.47(12H,m), 2.83(3H,d,J=5.2Hz), 3.26(3H,s), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.50(2H,s), 7.51-7.60(2H,m), 7.84-7.92(1H,m), 7.95-8.03(1H,m), 8.16-8.23(1H,m), 8.57(1H,s), 8.92(1H,brs), 9.21(1H,brs).

MS:m/e(ESI)501.2(MH+)

Example 417

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 2.80(3H,d,J=4.4Hz), 2.94(6H,s), 4.75(2H,s), 5.46(2H,s), 7.17(1H,s), 7.79(2H,s), 8.05(1H,s), 8.10(1H,s), 8.37(1H,m), 8.94(1H,s), 9.54(1H,s).

Example 418

6-Chloro-2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 2.81(3H,d,J=4,4Hz), 5.06(2H,s), 5.52(2H,s), 7.76(2H,s), 8.20(1H,s), 8.64-8.72(1H,m).

MS:m/e(ESI)488.2(MH+)

Example 419

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-6-(1-methyl-piperidin-4-yloxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(9H,s), 1.85-2.22(4H,m), 2.60(3H,s), 2.73-3.12(4H,m), 4.61(1H,m), 4.79(2H,s), 5.51(2H,s), 7.46(1H,ddd,J=2.4,5.2,8.8Hz), 7.70(1H,dd,J=5.2,8.8Hz), 7.80(2H,s), 7.87(1H,dd,J=2.4,5.2Hz), 8.09(1H,s),

9.25(1H,s), 9.76(1H,s).

Example 420

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[1-imino-5-(1-methyl-piperidin-4-yloxy)-1,3-dihydro-isoindol-2-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(9H,s), 1.86(2H,m), 2.14(2H,m), 2.59(3H,s), 2.92(4H,m), 4.78(1H,m), 4.79(2H,s), 5.47(2H,s), 7.29(1H,dd,J=2.0,8.8Hz), 7.44(1H,d,J=2.0Hz), 7.79(2H,s), 8.11(1H,d,J=8.8Hz), 9.06(1H,s), 9.72(1H,s).

Example 421

6-Ethoxy-3-imino-2-[2-oxo-2-(5,6,7,8-tetrahydro-naphthalen-2-yl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.408(3H,t,J=6.8Hz), 1.73-1.78(4H,m), 2.77-2.83(4H,m), 4.276(2H,q,J=6.8Hz), 4.856(2H.s), 5.470(2H,s), 7.276(1H,d,J=7.6Hz), 7.526(1H,s), 7.716(1H,s), 8.17-8.24(1H,m), 8.553(1H,s).

Example 422

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-ethoxy-3-imino-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(3H,t,J=7.0Hz), 1.41(18H,s), 4.44(2H,q,J=7.0Hz), 4.83(2H,s), 5.46(2H,s), 7.17(1H,s), 7.76(2H,s),

9.02(1H,s).

MS:m/e(ESI)424.3(MH+)

Example 423

N-{2-*tert*-Butyl-4-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=7.2Hz), 1.44(9H,s), 2.32(3H,s), 2.59(3H,s), 3.26(3H,s), 3.98(2H,q,J=7.2Hz), 4.85(2H,s), 5.56(2H,s), 7.57(1H,d,J=8.0Hz), 7.88(1H,brd,J=8.0Hz), 8.00(1H,brs), 8.92(1H,brs), 9.40-9.51(1H,m), 9.85-9,94(1H,m).

MS:m/e(ESI)473.2(MH+)

Example 424

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-6-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=7.0Hz), 1.41(18H,s), 4.23(2H,q,J=7.0Hz), 4.78(2H,s), 5.48(2H,s), 7.60(1H,d,J=7.0Hz), 7.75(2H,s), 8.04(1H,d,J=11.0Hz).

Example 425

2-[2-(3-Cyclopentyl-5-ethyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.150(3H,t,J=7.6Hz), 1.408(3H,t,J=6.8Hz), 1.45-

1.84(6H,m), 1.94-2.04(2H,m), 2.662(2H,q,J=7.6Hz), 2.824(3H,d,J=4.4Hz), 4.276(2H,q,J=6.8Hz), 4.835(2H,s), 5.438(2H,s), 7.523(1H,s), 7.628(1H,s), 7.670(1H,s), 8.17-8.23(1H,m), 8.547(1H,d,J=0.8Hz).

Example 426

N-{6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-N-ethyl-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.10(3H,t,J=7.0Hz), 1.34(18H,s), 2.07(3H,s), 3.91(2H,q,J=7.0Hz), 4.81(2H,s), 5.29(2H,s), 7.54(2H,s), 7.85(1H,d,J=8.2Hz), 8.27(1H,d,J=8.2Hz).

MS:m/e(ESI)465.2(MH+)

Example 427

N-{2-*tert*-Butyl-4-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenyl}-methanesulfonamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(9H,s), 2.69(3H,s), 4.88(2H,s), 5.57(2H,s), 7.53-7.58(1H,m), 7.72(1H,d,J=8.0Hz), 7.82-8.00(2H,m), 8.18(1H,d,J=8.0Hz).

Example 428

Methyl 7-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzofuran-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=6.8Hz), 1.51(9H,s), 2.83(3H,d,J=4.8Hz), 3.93(3H,s), 4.29(2H,q,J=6.8Hz), 4.89(2H,s), 5.61(2H,s), 7.55(1H,d,J=1.2Hz), 7.95(1H,d,J=1.2Hz), 7.97(1H,s), 8.18-8.22(1H,m), 8.44(1H,s), 8.58(1H,s).

MS:m/e(ESI)506.2(MH+)

Example 429

tert-Butyl 8-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]dioxine-2or3-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1,43(9H,s), 1.44(3H,t,J=7Hz), 2.84(3H,d,J=5Hz), 4.25-4.35(1H,m), 4.30(2H,q, J=7Hz), 4.51-4.57(1H,m), 4.85(2H,s), 5.30-5.34(1H,m), 5.46(2H,s), 7.46(1H,d,J=3Hz), 7.52(1H,d,J=3Hz), 7.55(1H,s), 8.21(1H,q,J=5Hz), 8.58(s, 1H), 9.22(1H,brs), 9.85(1H,brs).

Example 430

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.45(3H,t,J=7Hz), 3.89(3H,s), 4.30(2H,q,J=7Hz), 4.86(2H,s), 5.50(2H,s), 7.47(1H,s), 7.55(2H,s), 7.71(1H,s), 7.78(1H,s), 8.64(1H,s).

Example 431

2-[2-(3-*tert*-Butyl-4-methanesulfonylamino-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38-1.46(12H,m), 3.27(3H,s), 4.29(2H,q,J=7.2Hz), 4.87(2H,s), 5.51(2H,s), 7.53-7.60(2H,m), 7.68-7.72(1H,m), 7.76-7.81(1H,m), 7.86-7.91(1H,m), 8.00(1H,s), 8.64(1H,s), 8.93(1H,brs), 9.22(1H,brs).

MS:m/e(ESI)487.2(MH+)

Example 432

1-(3-Cyclopentyl-5-ethyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.151(3H,t,J=7.6Hz), 1.393(3H,t,J=6.8Hz), 1.46-1.82(6H,m), 1.94-2.03(2H,m), 2.311(3H,s), 2.579(3H,s), 2.662(2H,q,J=7.6Hz), 3.054(3H,s), 3.988(2H,q,J=6.8Hz), 4.820(2H,s), 5.503(2H,s), 7.630(1H,d,J=2.0Hz), 7.673(1H,d,J=2.0Hz), 9.324(1H,s), 9.454(1H,s).

Example 433

2-[2-(3-*tert*-Butyl-5-cyclopentyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.392(9H,s), 1.37-1.43(3H,m), 1.40-1.84(6H,m), 1.96-2.06(2H,m), 2.822(3H,d,J=4.4Hz), 4.276(2H,q,J=6.8Hz),

4.835(2H,s), 5.473(2H,s), 7.530(1H,s), 7.709(1H,s), 7.690(1H,s), 8.18-8.24(1H,m9, 8.545(1H,s).

Example 434

1-(3-*tert*-Butyl-5-cyclopentyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.391(9H,s), 1.37-1.43(3H,m), 1.40-1.85(6H,m), 1.96-2.07(2H,m), 2.311(3H,s), 2.578(3H,s), 3.987(2H,q,J=7.6Hz), 4.807(2H,s), 5.495(2H,s), 7.683(1H,s), 7.707(1H,s).

Example 435

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-6-fluoro-1-imino-7-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=7.0Hz), 1.41(18H,s), 4.05(3H,d,J=3.0Hz), 4.22(2H,q,J=7.0Hz), 4.71(2H,s), 5.45(2H,s), 7.24(1H,d,J=6.0Hz), 7.75(2H,s), 7.60(1H,d,J=7.0Hz), 7.75(2H,s), 8.04(1H,d,J=11.0Hz).

MS:m/e(ESI)471.2(MH+)

Example 436

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-3-propyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

0.92(3H,t,J=5.0Hz), 1.41(18H,s),
1.67(2H,dd,J=5.3,5.0Hz), 2.77(2H,t,J=5.3Hz),
4.88(2H,s), 5.54(2H,s), 7.78(2H,s), 8.08(1H,brs),
8.12(1H,brs), 8.77(1H,s), 9.40(1H,brs), 10.02(1H,brs).
MS:m/e(ESI)422.2(MH+)

Example 437

2-(2-Amino-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(18H,s), 4.64(2H,s), 5.49(2H,s), 6.53(2H,s),
6.86(1H,d,J=8.6Hz), 7.76(2H,s), 7.78(1H,d,J=8.6Hz),
9.40(1H,s).
MS:m/e(ESI)395.1(MH+)

Example 438

6-Ethoxy-3-imino-2-[2-(4-methoxy-3-trifluoromethyl-phenyl)-2-oxo-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.42(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.02(3H,s),
4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.51(2H,s),
7.49(1H,d,J=8.0Hz), 7.54(1H,s), 8.17(1H,s), 8.20-8.22(1H,m), 8.29(1H,d,J=8.0Hz), 8.57(1H,s).
MS:m/e(ESI)450.1(MH+)

Example 439

2-(2-Biphenyl-3-yl-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-

dihydro-1H-isoindole-5-carboxylic acid methylamide; hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=7z), 2.85(3H,d,J=5Hz), 4.31(2H,q,J=7Hz), 4.92(2H,s), 5.64(2H,s), 7.42-7.48(1H,m), 7.51-7.58(3H,m), 7.71-7.80(3H,m), 8.00-8.08(2H,m), 8.23(1H,q,J=5Hz), 8.27-8.29(1H,m), 8.60(1H,s).

Example 440

6-Ethoxy-3-imino-2-[2-oxo-2-(3-trifluoromethyl-phenyl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.90(2H,s), 5.62(2H,s), 7.56(1H,s), 7.87(1H,t,J=8.4Hz), 8.12(1H,d,J=8.0Hz), 8.19-8.23(1H,m), 8.28(1H,s), 8.31(1H,d,J=8.0Hz), 8.57(1H,s).

MS:m/e(ESI)420.1(MH+)

Example 441

({3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-methyl-amino)-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.43(3H,t,J=7.2Hz), 2.75(3H,s), 2.84(3H,d,J=4.4Hz), 3.71(2H,s), 4.30(2H,q,J=7.2Hz), 4.86(2H,s), 5.47(2H,s), 7.55(1H,s), 7.66(1H,d,J=1.2Hz), 7.84(1H,d,J=1.2Hz), 8.22(1H,q,J=4.4Hz), 8.58(1H,s),

9.22(1H,s), 9.85(1H,s).

Example 442

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 2.80(3H,d,J=4.4Hz), 2.94(6H,s), 3.89(3H,s), 4.76(2H,s), 5.45(2H,s), 7.17(1H,s), 7.45(1H,d,J=2.0Hz), 7.54(1H,J=2.0Hz), 8.09(1H,s), 8.38(1H,m), 8.97(1H,s), 9.54(1H,s), 9.66(1H,s).

Example 443

1-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.20-1.50(12H,m), 2.31(3H,s), 2.58(3H,s), 3.87(3H,s), 3.99(2H,q,J=6.8Hz), 4.83(2H,s), 5.52(2H,s), 7.44(1H,s), 7.53(1H,s), 9.33-9.48(1H,m), 9.67(1H,s), 9.80-9.92(1H,m).

MS:m/e(ESI)426.2(MH+)

Example 444

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-imino-2-methyl-5,7-dihydro-1-oxa-4,6-diaza-s-indacen-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 2.61(3H,s), 4.90(2H,s), 5.55(2H,s),

7.03(1H,s), 7.77(2H,s), 8.40(1H,s), 10.04(1H,brs).

MS:m/e(ESI)434.2(MH+)

Example 445

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.0Hz), 1.40(9H,s), 1.40(3H,t,J=7.0Hz), 4.10(2H,q,J=7.0Hz), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 4.88(2H,s), 5.47(2H,s), 7.06(1H,d,J=8.5Hz), 7.32(1H,s), 7.85(1H,s), 7.88(1H,d,J=8.5Hz).

Example 446

{2-*tert*-Butyl-4-[2-(5-ethoxy-4-fluoro-1-imino-6-methoxycarbonylamino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.33(3H,t,J=7.0Hz), 1.40(9H,s), 3.72(3H,s), 4.25(2H,q,J=7.0Hz), 4.89(2H,s), 4.91(2H,s), 5.47(2H,s), 7.07(1H,d,J=8.0Hz), 7.85(1H,s), 7.89(1H,d,J=8.0Hz), 8.46(1H,s), 9.30(1H,s).

Example 447

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.35(3H,t,J=7.0Hz), 1.41(18H,s), 2.77(3H,d,J=4.2Hz),

4.25(2H,q,J=7.0Hz), 4.87(2H,s), 5.52(2H,s), 7.76(2H,s), 7.99(1H,s), 8.07(1H,s), 8.53(1H,brq,J=4.2Hz), 9.40(1H,brs), 9.95(1H,brs).

MS:m/e(ESI)481.2(MH+)

Example 448

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-diethylamino-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.13(6H,t,J=6.8Hz), 1.42(18H,s), 3.60(4H,q,J=6.8Hz), 4.65(2H,s), 5.50(2H,s), 7.01(1H,d,J=8.8Hz), 7.77(2H,s), 7.84(1H,d,J=8.8Hz), 9.28(1H,s).

MS:m/e(ESI)451.3(MH+)

Example 449

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(3H,t,J=6.8Hz), 1.38(9H,s), 2.82(3H,d,J=4.8Hz), 3.88(2H,s), 4.29(2H,q,J=6.8Hz), 4.99(2H,s), 5.51(2H,s), 7.46(1H,s), 7.53(1H,s), 8.29(1H,s), 8.36-8.43(1H,m).

MS:m/e(ESI)472.2(MH+)

Example 450

{2-*tert*-Butyl-4-[2-(5-ethoxy-4-fluoro-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz),

4.29(2H,q,J=6.8Hz), 4.89(2H,s), 5.00(2H,s), 5.48(2H,s),

7.08(1H,d,J=8.4Hz), 7.86(1H,d,J=2.4Hz),

7.89(1H,dd,J=2.4,8.4Hz), 8.29(1H,s), 8.36-8.41(1H,m),

9.47(1H,s), 10.04(1H,s).

MS:m/e(ESI)500.2(MH+)

Example 451

1-(8-*tert*-Butyl-2,3-dihydro-benzo[1,4]dioxin-6-yl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone; compound with *tert*-butyl acetate

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.44(9H,s), 2.68(3H,s), 4.27-4.32(1H,m),

4.52-4.57(1H,m), 4.86(2H,s), 5.30-5.35(1H,m),

5.53(2H,s), 7.46(2H,d,J=2Hz), 7.52(1H,d,J=2Hz),

7.72(1H,d,J=8Hz), 8.33(1H,d,J=8Hz).

Example 452

Methyl {3-*tert*-butyl-2-hydroxy-5-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 2.69(3H,s), 3.72(3H,s), 4.86(2H,s),

4.93(2H,s), 5.53(2H,s), 7.41(1H,d,J=1Hz),

7.57(1H,d,J=1Hz,), 7.72(1H,d,J=8Hz), 8.17(1H,d,J=8Hz).

Example 453

Methyl {3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-

methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.43(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 3.73(3H,s), 4.30(2H,q,J=7z), 4.86(2H,s), 4.93(2H,s), 5.47(2H,s), 7.42(1H,s), 7.55(1H,s), 7.57(1H,s), 8.21(1H,q,J=5Hz), 8.58(1H,s).

Example 454

1-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 2.69(3H,s), 3.90(3H,s), 4.88(2H,s), 5.58(2H,s), 7.47(1H,d,J=2Hz), 7.55(1H,d,J=2Hz), 7.73(1H,d,J=8Hz), 8.18(1H,d,J=8Hz).

Example 455

Methyl 3-{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.43(3H,t,J=7Hz), 2.52(2H,t,J=8Hz), 2.85(3H,d,J=5Hz), 2.97(2H,t,J=8Hz), 3.62(3H,s), 4.30(2H,q,J=7Hz), 4.85(2H,s), 5.44(2H,s), 7.55(1H,s), 7.71(1H,s), 7.73(1H,s), 8.22(1H,q,J=5Hz), 8.58(1H,s).

Example 456

8-*tert*-Butyl-6-[2-(7-imino-2-methyl-5,7-dihydro-

pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]dioxine-2or3-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.43(9H,s), 2.69(3H,s), 4.31-4.37(1H,m), 4.51-4.57(1H,m), 4.87(2H,s), 5.30-5.35(1H,m), 5.52(2H,s), 7.45(1H,s), 7.52(1H,s), 7.73(1H,d,J=8Hz), 8.17(1H,d,J=8Hz), 9.52(1H,s), 9.97(1H,s).

Example 457

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-imidazol-1-ylmethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(18H,s), 2.64(3H,s), 4.73(2H,s), 5.26(2H,s), 5.47(2H,s), 6.99(1H,s), 7.20(1H,s), 7.50(3H,brs), 7.77(1H,s).

Example 458

6-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.35(3H,t,J=7.0Hz), 1.37(9H,s), 2.77(3H,d,J=4.0Hz), 3.87(3H,s), 4.24(2H,q,J=7.0Hz), 4.88(2H,s), 5.54(2H,s), 7.44(1H,s), 7.52(1H,s), 8.00(1H,s), 8.52(1H,brq,J=4.0Hz), 9.45(1H,brd,J=8.0Hz), 9.67(1H,s), 9.94(1H,brd,J=8.0Hz).

Example 459

{2-*tert*-Butyl-4-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.35(3H,t,J=6.9Hz), 1.39(9H,s), 2.77(3H,d,J=4.0Hz), 4.23(2H,q,J=6.9Hz), 4.83(2H,s), 4.88(2H,s), 5.55(2H,s), 7.05(1H,d,J=7.7Hz), 7.85(1H,s), 7.88(1H,d,J=7.7Hz), 7.98(1H,s), 8.56(1H,brq,J=4.0Hz), 9.95(1H,s).

Example 460

Methyl 2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.42(3H,t,J=7.2Hz), 2.83(3H,d,J=4.8Hz), 3.86(3H,s), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.51(2H,s), 7.54(1H,s), 7.55(1H,d,J=8.0Hz), 7.91(1H,d,J=8.0Hz), 8.06(1H,s), 8.20(1H,q,J=4.8Hz), 8.57(1H,s).

MS:m/e(ESI)466.2(MH+)

Example 461

Isopropenyl {2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-5-ethoxy-4-fluoro-6-methylcarbamoyl-2,3-dihydro-isoindol-1-ylidene}-carbamate

1H-NMR(DMSO-d6)δ:

1.46(3H,t,J=7.2Hz), 1.47(18H,s), 2.07(3H,d,J=0.4Hz),

3.01(3H,d,J=4.4Hz), 4.35(2H,dq,J=1.2,6.8Hz), 4.73(3H,s), 4.90(1H,s), 5.13(2H,s), 5.83(1H,s), 7.88(2H,s), 8.63(1H,s).

MS:m/e(ESI)582.3(MH+)

Example 462

2-[2-(3-*tert*-Butyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.322(9H,s), 1.405(3H,t,J=6.8Hz), 2.90(2H,s), 4.20-4.32(2H,m), 4.869(2H,s), 5.533(2H,s), 7.45-7.58(2H,m), 7.75-7.86(2H,m), 7.972(1H,s), 8.18-8.22(1H,m), 8.547(1H,d,J=1.2Hz).

Example 463

2-[2-(3-*tert*-Butyl-5-ethyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.215(3H,t,J=7.6Hz), 1.317(9H,s), 1.408(3H,t,J=6.8Hz), 2.700(2H,q,J=7.6Hz), 2.821(3H,d,J=4.8Hz), 4,276(2H,q,J=6.8Hz), 4.863(2H,s), 5.517(2h,s), 7.470(1H,s), 7.531(1H,s), 7.612(1H,s), 7.679(1H,s), 7.799(1H,s), 8.19-8.22(1H,m).

Example 464

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-morpholino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-

ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.64(4H,t,J=4.6Hz), 3.72(4H,t,J=4.6Hz), 4.70(2H,s), 5.51(2H,s), 7.26(1H,d,J=8.8Hz), 7.76(2H,s), 7.94(1H,d,J=8.8Hz), 9.45(1H,s).

MS:m/e(ESI)465.2(MH+)

Example 465

tert-Butyl 4-{6-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-piperazine-1-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(27H,s), 3.44(4H,t,J=4.8Hz), 3.68(4H,br), 4.70(2H,s), 5.51(2H,s), 7.27(1H,d,J=8.8Hz), 7.76(2H,s), 7.94(1H,d,J=8.8Hz), 9.46(1H,s).

MS:m/e(ESI)564.4(MH+)

Example 466

6-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-2-ethoxy-5-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-3-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.32-1.48(12H,m), 2.80-2.87(3H,m), 4.58(2H,q,J=6.8Hz), 4.84(2H,s), 5.47(2H,s), 7.77(2H,s), 8.25-8.33(1H,m), 8.93(1H,s), 9.30-9.38(1H,m), 9.95-10.02(1H,m).

MS:m/e(ESI)481.2(MH+)

Example 467

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-piperazin-1-yl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone dihydrochloride

1H-NMR(DMSO-d6)δ:

1.42(18H,s), 3.19(4H,br), 3.93(4H,t,J=4.8Hz), 4.72(2H,s), 5.58(2H,s), 7.35(1H,d,J=8.8Hz), 7.78(2H,s), 8.00(1H,d,J=8.8Hz), 8.07(1H,s), 9.36(2H,br), 9.51(1H,s), 9.60(1H,s).

MS:m/e(ESI)464.2(MH+)

Example 468

tert-Butyl 2-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-2-methyl-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 1.39(9H,s), 1.41(3H,t,J=7.2Hz), 1.65(6H,s), 2.82(3H,d,J=4.8Hz), 4.27(2H,q,J=7.2Hz), 4.84(2H,s), 5.43(2H,s), 6.68(1H,d,J=8.8Hz), 7.52(1H,s), 7.86(1H,d,J=8.8Hz), 7.87(1H,s), 8.19(1H,q,J=4.8Hz), 8.55(1H,s).

MS:m/e(ESI)566.4(MH+)

Example 469

2-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-2-methyl-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.34-1.46(12H,m), 1.66(6H,s), 2.82(3H,d,J=4.8Hz),

4.27(2H,q,J=7.2Hz), 4.84(2H,s), 5.45(2H,s),
6.73(1H,d,J=8.8Hz), 7.53(1H,s), 7.85(1H,d,J=8.8Hz),
7.87(1H,s), 8.19(1H,q,J=4.8Hz), 8.56(1H,s),
9.25(1H,brs), 9.86(1H,brs).

MS:m/e(ESI)510.2(MH+)

Example 470

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-5-ethoxy-4-fluoro-6-methylcarbamoyl-2,3-dihydro-isoindol-1-ylidenecarbamoyloxymethyl acetate

1H-NMR(DMSO-d6)δ:
1.47(3H,t,J=8.2Hz), 1.48(18H,s), 2.18(3H,s),
3.02(3H,d,J=5.2Hz), 4.22(2H,q,J=8.2Hz),
5.13(2H,ABq,J=16,0Hz), 5.86(1H,s), 5.89(2H,s),
7.87(2H,s), 8.46(1H,s).

MS:m/e(ESI)614.3(MH+)

Example 471

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-5-ethoxy-4-fluoro-6-methylcarbamoyl-2,3-dihydro-isoindol-1-ylidenecarbamoyloxymethyl 2,2-dimethyl-propionate

1H-NMR(DMSO-d6)δ:
1.20,1.23(9H,each s), 1.47(18H,s), 1.48(3H,t,J=6.8Hz),
3.02(3H,d,J=4.8Hz), 4.41(2H,q,J=6.8Hz), 4.87(2H,s),
5.63(2H,s), 5.87(1H,s), 5.88(2H,s), 7.87,7.89(1H,each s).

MS:m/e(ESI)656.4(MH+)

Example 472

Methyl 3-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acrylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.34-1.43(12H,m), 2.82(3H,d,J=4.8Hz), 3.67(3H,s), 4.28(2H,q,7.2Hz), 4.86(2H,s), 5.49(2H,s), 7.43(1H,d,J=8.8Hz), 7.54(1H,s), 7.87(1H,d,J=12Hz), 7.92-8.02(3H,m), 8.17-8.23(1H,m), 8.56(1H,s).

MS:m/e(ESI)508.2(MH+)

Example 473

Methyl 3-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(9H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 2.89(2H,t,J=6.4Hz), 3.62(3H,s), 4.28(2H,q,J=7.2Hz), 4.36(2H,t,J=6.4Hz), 4.84(2H,s), 5.45(2H,s), 7.19(1H,d,J=8.8Hz), 7.53(1H,s), 7.83(1H,s), 7.91(1H,d,J=8.8Hz), 8.19(1H,q,J=4.8Hz), 8.55(1H,s).

Example 474

Ethyl {4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,6-dimethoxy-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.19(3H,t,J=7.2Hz), 1.41(3H,t,J=7.2Hz),

2.82(3H,d,J=4.8Hz), 3.85(6H,s), 4.14(2H,q,J=7.2Hz), 4.27(2H,q,J=7.2Hz), 4.69(2H,s), 4.86(2H,s), 5.55(2H,s), 7.31(2H,s), 7.53(1H,s), 8.16-8.23(1H,m), 8.56(1H,s), 9.39(1H,brs), 9.91(1H,brs).

MS:m/e(ESI)514.3(MH+)

Example 475

{2-*tert*-Butyl-4-[2-(1-imino-5,7-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 3.89(3H,s), 3.97(3H,s), 4.71(2H,s), 4.87(2H,s), 5.40(2H,s), 6.75(1H,s), 6.91(1H,s), 7.07(1H,d,J=8.8Hz), 7.85(1H,s), 7.87(1H,d,J=8.8Hz), 8.45(1H,brs), 9.08(1H,brs).

MS:m/e(ESI)441.1(MH+)

Example 476

3-{6-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridin-2-yl}-2-methyl-acrylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.32(3H,d,J=1.2Hz), 3.86(3H,s), 4.54(2H,s), 5.13(2H,s), 7.17-7.21(2H,br), 7.31(1H,s), 7.49(1H,s), 7.56(1H,s), 7.62(1H,d,J=8.0Hz), 8.06(1H,d,J=8.0Hz).

Example 477

1-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-[7-imino-2-methyl-3-(tetrahydropyran-2-yloxymethyl)-5,7-

dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.40-1.90(6H,m), 2.62(3H,s), 3.45-3.55(1H,m), 3.74-3.82(1H,m), 3.88(3H,s), 4.67(1H,d,J=14.0Hz), 4.76-4.81(1H,m), 4.85(2H,s), 4.87(1H,d,J=14.0Hz), 5.50-5.53(2H,m), 7.45(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz), 8.19(1H,s).

Example 478

1-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-(3-hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 2.58(3H,s), 3.88(3H,s), 4.69(2H,s), 4.86(2H,s), 5.57(2H,s), 7.45(1H,d,J=2.0Hz), 7.53(1H,d,J=2.0Hz), 8.20(1H,s).

Example 479

tert-Butyl (2-*tert*-butyl-4-{2-[7-imino-2-methyl-3-(tetrahydropyran-2-yloxymethyl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-acetyl}-phenoxy)-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.44(9H,s), 1.30-1.89(6H,m), 2.63(3H,s), 3.48-3.55(1H,m), 3.75-3.82(1H,m), 4.68(1H,d,J=14.4Hz), 4.79(1H,t,J=1.8Hz), 4.86(2H,s), 4.87(1H,d,J=14.4Hz), 4.88(2H,s), 5.53(2H,s), 7.05(1H,d,J=8.8Hz),

7.86(1H,d,J=2.0Hz), 7.90(1H,dd,J=8.98,2.2Hz),
8.20(1H,s).

Example 480

tert-Butyl {2-*tert*-butyl-4-[2-(3-hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:
1.40(9H,s), 1.44(9H,s), 2.58(3H,s), 4.68(2H,s), 4.84-4.91(2H,m), 4.86(2H,s), 5.55(2H,s), 7.05(1H,d,J=8.8Hz), 7.86(1H,brs), 7.89(1H,d,J=8.8Hz), 8.20(1H,s), 9.53(1H,d,J=7.2Hz), 9.88(1H,d,J=7.2Hz).

Example 481

{2-*tert*-Butyl-4-[2-(3-hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:
1.40(9H,s), 2.58(3H,s), 4.69(2H,s), 4.85-4.93(2H,m), 4.90(2H,s), 5.54(2H,s), 7.08(1H,d,J=8.8Hz), 7.86(1H,d,J=2.0Hz), 7.89(1H,dd,J=8.8,2.0Hz), 8.20(1H,s), 9.51(1H,d,J=8.4Hz), 9.89(1H,d,J=8.4Hz).

Example 482

1-(3-*tert*-Butyl-2-hydroxy-5-{2-[7-imino-2-methyl-3-(tetrahydropyran-2-yloxymethyl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-acetyl}-benzyl)-piperidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.40-1.80(10H,m), 2.30-2.40(2H,m), 3.30-3.3.40(2H,m), 3.42-3.50(2H,m), 4.48(2H,s), 4.68(1H,d,J=14.4Hz), 4.77-4.80(1H,m), 4.88(1H,d,J=14.4Hz), 4.88(2H,s), 5.52(2H,s), 7.83(1H,d,J=1.6Hz), 7.87(1H,d,J=1.6Hz), 8.20(1H,s).

Example 483

1-{3-*tert*-Butyl-2-hydroxy-5-[2-(3-hydroxymethyl-7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzyl}-piperidin-2-one hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.65-1.78(4H,m), 2.30-2.40(2H,m), 2.58(3H,s), 3.40-3.50(2H,m), 4.48(2H,s), 4.61(2H,s), 4.87(2H,s), 5.55(2H,s), 7.82(1H,d,J=2.0Hz), 7.88(1H,d,J=2.0Hz), 8.20(1H,s), 9.52(1H,d,J=9.2Hz), 9.88(1H,d,J=9.2Hz), 11.55(1H,s).

Example 484

1-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.0Hz), 1.37(9H,s), 1.40(3H,t,J=7.0Hz), 3.86(3H,s), 4.11(2H,q,J=7.0Hz), 4.20(2H,q,J=7.0Hz), 4.79(2H,s), 5.45(2H,s), 7.32(1H,s), 7.43(1H,s), 7.52(1H,s).

Example 485

6-[2-(3-*tert*-Butyl-4-methanesulfonylamino-phenyl)-2-

oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(3H,t,J=6.9Hz), 1.42(9H,s), 2.77(3H,d,J=4.0Hz), 3.26(3H,s), 4.25(2H,q,J=6.9Hz), 4.90(2H,s), 5.55(2H,s), 7.56(1H,d,J=8.0Hz), 7.88(1H,d,J=8.0Hz), 8.00(2H,s), 8.52(1H,brq,J=4.0Hz), 8.94(1H,brs), 9.50(1H,brs), 9.98(1H,brs).

Example 486

{4-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-isopropoxy-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28(6H,d,J=6.0Hz), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.60-4.69(1H,m), 4.85(4H,s), 5.44(2H,s), 7.05(1H,d,J=8.8Hz), 7.51(1H,s), 7.53(1H,s), 7.62(1H,d,J=8.8Hz), 8.17-8.23(1H,m), 8.56(1H,s), 9.24(1H,brs), 9.83(1H,brs).

MS:m/e(ESI)483.9(MH+)

Example 487

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.6Hz), 1.42(18H,s), 2.94(2H,q,J=7.6Hz),

4.85(2H,s), 5.56(2H,s), 7.73(1H,d,J=8.0Hz), 7.77(2H,s), 8.18(1H,d,J=8.0Hz), 9.85(1H,s).

MS:m/e(ESI)408.2(MH+)

Example 488

2-[2-(4-Acetyl-piperazin-1-yl)-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.46(18H,s), 2.17(3H,s), 3.69-3.83(8H,br), 4.74(2H,s), 4.85(2H,s), 7.23(1H,d,J=8.8Hz), 7.88(1H,d,J=8.8Hz), 7.89(2H,s).

MS:m/e(ESI)506.3(MH+)

Example 489

6-[2-(3-*tert*-Butyl-4-hydroxy-5-methoxy-phenyl)-2-oxo-ethyl]-2-ethoxy-5-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-3-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.33-1.44(12H,m), 2.80-2.87(3H,m), 3.88(3H,s), 4.58(2H,q,J=6.8Hz), 4.86(2H,s), 5.48(2H,s), 7.45(1H,s), 7.53(1H,s), 8.23-8.36(1H,m), 8.93(1H,s), 9.35-9.44(1H,m), 9.68(1H,s), 9.98-10.07(1H,m).

MS:m/e(ESI)455.2(MH+)

Example 490

6-[2-(3-Cyclopentyl-4-hydroxy-5-methyl-phenyl)-2-oxo-ethyl]-2-ethoxy-5-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-3-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=7.2Hz), 1.46-1.83(6H,m), 1.91-2.03(2H,m), 2.25(3H,s), 2.78-2.89(4H,m), 4.58(2H,q,J=7.2Hz), 4.85(2H,s), 5.42(2H,s), 7.655(1H,s), 7.664(1H,s), 8.20-8.40(1H,m), 8.93(1H,s), 9.35(1H,s), 9.37-9.49(1H,m), 9.95-10.08(1H,m).

MS:m/e(ESI)451.1(MH+)

Example 491

{2-*tert*-Butyl-4-[2-(2-ethoxy-5-imino-3-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.28-1.49(12H,m), 2.84(3H,d,J=4.8Hz), 4.58(2H,q,J=6.8Hz), 4.86(2H,s), 4.89(2H,s), 5.45(2H,s), 7.08(1H,d,J=8.0Hz), 7.86(1H,s), 7.90(1H,d,J=8.0Hz), 8.25-8.39(1H,m), 8.93(1H,s), 9.34-9.45(1H,m), 9.95-10.05(1H,m).

MS:m/e(ESI)483.1(MH+)

Example 492

Methyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=6.8Hz), 2.48(3H,s), 2.82(3H,d,J=4.8Hz), 3.73(3H,s), 3.84(3H,s), 4.28(2H,q,J=6.8Hz), 4.74(2H,s), 4.85(2H,s), 5.52(2H,s),

7.53-7.55(3H,m), 8.20(1H,d,J=4.8Hz), 8.55(1H,s), 9.20(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)526.2(MH+)6

Example 493

2-{2-[3-*tert*-Butyl-4-(2-carbamoyl-ethoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(9H,s), 1.38-1.45(3H,m), 2.58-2.65(2H,m), 2.82(3H,d,J=4.8Hz), 4.23-4.35(4H,m), 4.85(2H,s), 5.47(2H,s), 6.94-7.02(1H,m), 7.18(1H,d,J=8.4Hz), 7.45-7.56(2H,m), 7.83(1H,s), 7.91(1H,d,J=8.4Hz), 8.15-8.25(1H,m), 8.55(1H,s), 9.21(1H,brs), 9.82(1H,brs).

MS:m/e(ESI)495.2(MH+)

Example 494

3-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.41(3H,t,J=7.2Hz), 2.77(2H,t,J=6.0Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.32(2H,t,J=6.0Hz), 4.85(2H,s), 5.48(2H,s), 7.19(1H,d,J=8.8Hz), 7.53(1H,s), 7.84(1H,s), 7.91(1H,d,J=8.8Hz), 8.20(1H,q,J=4.8Hz), 8.56(1H,s), 9.26(1H,brs,), 9.85(1H,brs).

MS:m/e(ESI)496.3(MH+)

Example 495

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=6.8Hz), 2.83(3H,d,J=4.4Hz), 4.66(2H,s), 4.85(2H,s), 5.50(2H,s), 7.52(1H,s), 7.54(1H,s), 7.56(1H,s), 8.20(1H,q,J=5.2Hz), 8.56(1H,s), 9.18(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)512.2(MH+)

Example 496

2-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.36-1.48(12H,m), 1.59(3H,d,J=6.8Hz), 2.82(3H,d,J=4.4Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.08-5.18(1H,m), 5.44(2H,s), 6.95-7.00(1H,m), 7.53(1H,s), 7.80-7.94(2H,m), 8.14-8.26(1H,m), 8.55(1H,s), 9.19(1H,brs), 9.83(1H,brs).

MS:m/e(ESI)496.2(MH+)

Example 497

2-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.06(3H,t,J=7.2Hz), 1.33-1.57(12H,m), 1.94-2.11(2H,m), 2.82(3H,d,J=4.8Hz), 4.27(2H,q,J=6.8Hz), 4.84(2H,s), 5.05(1H,t,J=5.6Hz), 5.44(2H,s), 6.97(1H,d,J=8.4Hz), 7.53(1H,s), 7.78-7.97(2H,m), 8.11-8.26(1H,m), 8.55(1H,s), 9.11-9.24(1H,m), 9.76-9.85(1H,m).

Example 498

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 3.86(3H,s), 3.95(3H,s), 4.79(2H,s), 5.47(2H,s), 7.36(1H,s), 7.75(2H,s).

Example 499

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.1Hz), 1.34(9H,s), 1.48(3H,t,J=7.1Hz), 3.23-3.37(2H,m), 2.90(3H,s), 4.12(2H,q,J=7.1Hz), 4.22(2H,q,J=7.1Hz), 4.33(2H,brs), 4.79(2H,s), 5.46(2H,s), 7.16(1H,s), 7.27(1H,s), 7.33(1H,s), 9.04(1H,brs), 9.32(1H,brs).

MS:m/e(ESI)484.3(MH+)

Example 500

tert-Butyl {2-*tert*-butyl-4-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-

acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.4Hz), 1.40(9H,s), 1.43(9H,s),

2.94(2H,q,J=7.4Hz), 4.85(4H,s), 5.54(2H,s),

7.05(1H,d,J=8.4Hz), 7.73(1H,d,J=8.0Hz),

7.86(1H,d,J=1.8Hz), 7.90(1H,dd,J=8.4Hz,J=1.8Hz),

8.18(1H,d,J=8.0Hz).

MS:m/e(ESI)466.2(MH+)

Example 501

{2-*tert*-Butyl-4-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.4Hz), 1.40(9H,s), 2.94(2H,q,J=7.4Hz),

4.86(2H,s), 4.88(2H,s), 5.54(2H,s), 7.08(1H,d,J=8.6Hz),

7.73(1H,d,J=8.0Hz), 7.86(1H,d,J=1.6Hz),

7.90(1H,dd,J=8.6Hz,J=1.6Hz), 8.18(1H,d,J=8.0Hz),

9.54(1H,s), 9.86(1H,s).

MS:m/e(ESI)410.1(MH+)

Example 502

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-isopropyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(6H,d,J=6.8HZ), 1.42(18H,s), 3.18-3.28(1H,m),

4.84(2H,s), 5.55(2H,s), 7.75(1H,d,J=8.4Hz), 7.77(2H,s),

8.18(1H,d,J=8.4Hz), 9.72(1H,br).

MS:m/e(ESI)422.2(MH+)

Example 503

2-[2-(8-*tert*-Butyl-2,3-dihydro-benzo[1,4]dioxin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 4.31(2H,q,J=7Hz), 4.32-4.43(4H,m), 4.86(2H,s), 5.46(2H,s,), 7.44(1H,s), 7.47(1H,s), 7.54(1H,s), 8.22(1H,q, J=5Hz), 8.58(1H,s).

Example 504

2-[2-(3-*tert*-Butyl-4,5-dimethoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 3.89(3H,s), 3.91(3H,s), 4.30(2H,q,J=7Hz), 4.87(2H,s), 5.54(2H,s), 7.55(2H,s), 7.56(1H,s), 8.22(1H,q,J=8Hz), 8.58(1H,s).

Example 505

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.41(3H,t,J=7.2Hz), 2.33(3H,s), 2.60(3H,s), 2.93(3H,s), 4.01(2H,q,J=7.2Hz), 4.36(2H,t,J=4.4Hz), 4.83(2H,s), 5.51(2H,s), 7.19(1H,d,J=1.6Hz), 7.29(1H,d,J=1.6Hz), 9.20-10.00(2H,brs).

Example 506

3-{2-*tert*-Butyl-4-[2-5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-acrylic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.39-1.46(12H,m), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.53(2H,s), 6.35(1H,d,J=16Hz), 7.54(1H,s), 7.79(1H,d,J=8.0Hz), 7.90(1H,d,J=8.0Hz), 7.99(1H,s), 8.17-8.23(1H,m), 8.27(1H,d,J=16Hz), 8.57(1H,s), 9.26(1H,brs), 9.87(1H,brs).

MS:m/e(ESI)478.2(MH+)

Example 507

7-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methyl-benzofuran-3-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=6.8Hz), 1.49(9H,s), 2.81(3H,s), 2.83(3H,d,J=4.4Hz), 4.29(2H,q,J=6.8Hz), 4.88(2H,s), 5.62(2H,s), 7.55(1H,s), 7.81(1H,s), 8.18-8.24(1H,m), 8.47(1H,s), 8.57(1H,s).

MS:m/e(ESI)566.2(MH+)

Example 508

3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.41(3H,t,J=6.8Hz), 2.83(3H,d,J=4.8Hz), 4.28(2H,q,J=6.8Hz), 4.85(2H,s), 5.49(2H,s), 7.54(1H,s), 7.98(1H,d,J=2.0Hz), 8.12-8.22(1H,m), 8.38(1H,d,J=2.4Hz), 8.56(1H,s).

MS:m/e(ESI)468.2(MH+)

Example 509

3-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 2.55(2H,t,J=8.0Hz), 2.82(3H,d,J=4.8Hz), 3.17(2H,t,J=8.0Hz), 4.28(2H,q,J=7.2Hz), 4.85(2H,s), 5.49(2H,s), 7.48(1H,d,J=8.0Hz), 7.53(1H,s), 7.81(1H,d,J=8.0Hz), 7.93(1H,s), 8.16-8.24(1H,m), 8.56(1H,s), 9.23(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)480.2(MH+)

Example 510

2-{2-*tert*-Butyl-4-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.34-1.47(12H,m), 1.59(3H,d,J=6.4Hz), 2.31(3H,s), 2.58(3H,s), 3.99(2H,q,J=6.8Hz), 4.83(2H,s), 5.13(1H,q,J=6.4Hz), 5.49(2H,s), 6.97(1H,d,J=8.4Hz), 7.86(1H,s), 7.88(1H,d,J=8.4Hz), 9.36-9.45(1H,m), 9.81-9.90(1H,m).

MS:m/e(ESI)468.2(MH+)

Example 511

2-(2-Cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.03-1.12(4H,m), 1.41(18H,s), 2.26-2.36(1H,m), 4.81(2H,s), 5.53(2H,s), 7.71(1H,d,J=8.0Hz), 7.76(2H,s), 8.09(1H,d,J=8.0Hz), 9.63(1H,brs).

MS:m/e(ESI)420.2(MH+)

Example 512

{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 3.85(3H,s), 3.95(3H,s), 4.81(2H,s), 4.88(2H,s), 5.47(2H,s), 7.07(1H,d,J=8.8Hz), 7.35(1H,s), 7.82-7.90(2H,m).

Example 513

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(7-fluoro-1-imino-5,6-

dimethoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 2.90(3H,s), 3.25-3.36(3H,m), 3.86(3H,s), 3.95(3H,s), 4.33(2H,dd,J=5.5,4.1Hz), 4.79(2H,s), 5.44(2H,s), 7.15(1H,s), 7.26(1H,s), 7.35(1H,s).

Example 514

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-imino-2-(pyrrolidin-1-yl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(18H,s), 1.94-2.00(4H,br), 3.45-3.52(4H,br), 4.67(2H,s), 5.50(2H,s), 6.87(1H,d,J=8.8Hz), 7.76(2H,s), 7.86(1H,d,J=8.8Hz), 9.25(2H,s).

MS:m/e(ESI)449.2(MH+)

Example 515

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[2-(ethyl-methyl-amino)-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.10(3H,t,J=7.0Hz), 1.41(18H,s), 3.09(3H,s), 3.67(2H,q,J=7.0Hz), 4.66(2H,s), 5.50(2H,s), 7.04(1H,d,J=8.8Hz), 7.77(2H,s), 8.86(1H,d,J=8.8Hz), 9.32(2H,s).

MS:m/e(ESI)437.2(MH+)

Example 516

2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.53(2H,s), 7.48-7.56(2H,m), 7.89(1H,d,J=8.0Hz), 8.03(1H,s), 8.15-8.23(1H,m), 8.56(1H,s), 9.30(1H,brs), 9.88(1H,brs).

MS:m/e(ESI)452.1(MH+)

Example 517

2-[2-(4-*tert*-Butyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.32(9H,s), 1.42(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.87(2H,s), 5.48(2H,s), 7.54(1H,s), 7.63(2H,d,J=7.2Hz), 7.95(2H,d,J=7.2Hz), 8.18-8.24(1H,m), 8.56(1H,s).

MS:m/e(ESI)408.1(MH+)

Example 518

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.03-1.16(4H,m), 1.35(9H,s), 2.26-2.37(1H,m),

2.91(3H,s), 4.34(2H,brs), 4.82(2H,s), 5.52(2H,brs), 7.17(1H,s), 7.28(1H,s), 7.72(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.42-9.53(1H,m), 9.60-9.71(1H,m).

MS:m/e(ESI)419.1(MH+)

Example 519

2-[2-(3,3-Dimethyl-2,3-dihydro-benzofuran-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(6H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.4Hz), 4.28(2H,q,J=7.2Hz), 4.37(2H,s), 4.85(2H,s), 5.43(2H,s), 6.98(1H,d,J=8.0Hz), 7.53(1H,s), 7.87(1H,d,J=8.0Hz), 7.89(1H,s), 8.14-8.25(1H,m), 8.56(1H,s).

MS:m/e(ESI)422.1(MH+)

Example 520

2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-1-(3,3-dimethyl-2,3-dihydro-benzofuran-5-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.34(9H,s), 1.40(3H,t,J=6.8Hz), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.37(2H,s), 4.79(2H,s), 5.41(2H,s), 6.97(1H,d,J=8.4Hz), 7.33(1H,s), 7.85(1H,d,J=8.4Hz), 7.88(1H,s).

MS:m/e(ESI)427.1(MH+)

Example 521

2-(3-Chloro-2-diethylamino-7-imino-5,7-dihydro-

pyrrolo[3,4-b]pyridin-6-yl)-1-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.15(6H,t,J=7.2Hz), 1.42(18H,s), 3.51(4H,q,J=7.2Hz), 4.73(2H,s), 5.54(2H,s), 7.77(2H,s), 8.20(1H,s), 9.51(1H,s).

MS:m/e(ESI)485.2(MH+)

Example 522

{8-*tert*-Butyl-6-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7.6Hz), 1.35(9H,s), 2.93(2H,q,J=7.6Hz), 3.47(2H,br), 4.01(2H,s), 4.27(2H,br), 4.81(2H,s), 5.50(2H,s), 7.06(1H,s), 7.23(1H,s), 7.70(1H,d,J=8.0Hz), 8.15(1H,d,J=8.0Hz).

MS:m/e(ESI)451.1(MH+)

Example 523

7-Cyano-2-[2-(3,5-di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s),2.86(3H,d,J=4.4Hz),5.17(2H,s),5.54(2H,s),7.76(2H,s),8.69(1H,d,J=1.2Hz),8.88(1H,m),9.05(1H,d,J=1.2Hz).

Example 524

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.34-146(21H,m), 3.87(3H,s), 4.22(2H,q,J=7.0Hz), 4.77(2H,s), 5.47(2H,s), 7.34(1H,s), 7.75(2H,s), 9.03(1H,brs).

Example 525

{2-*tert*-Butyl-4-[2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.30-1.48(12H,m), 3.86(3H,s), 4.22(2H,q,J=7.0Hz), 4.79(2H,s), 4.88(2H,s), 5.49(2H,s), 7.07(1H,d,J=8.7Hz), 7.33(1H,s), 7.82-7.90(2H,m), 9.08(1H,brd), 9.45(brs).

MS:m/e(ESI)473.1(MH+)

Example 526

Methyl 2-{3-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-2-methyl-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.388(3H,t,J=6.8Hz), 1.529(6H,s), 2.810(3H,d,J=4.8Hz), 3.570(3H,s), 4.257(2H,q,J=6.8Hz), 4.852(2H,s), 5.475(2H,s), 7.487(1H,s), 7.54-7.68(2H,m), 7.857(1H,s), 7.91(1H,d,J=8.0Hz), 8.239(1H,q,J=4.8Hz), 8.498(1H,s).

Example 527

{2-*tert*-Butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.40(2H,t,J=7.1Hz), 2.82(3H,d,J=4.7Hz), 4.27(2H,q,J=7.1Hz), 4.37(2H,s), 4.86(2H,s), 5.42(2H,s), 7.27(1H,t,J=8.0Hz), 7.53(1H,s), 7.64(1H,d,J=8.0Hz), 7.79(1H,d,J=8.0Hz), 8.20(1H,brq,J=4.7Hz), 8.57(1H,s), 9.40(1H,brd), 9.94(1H,brd).

MS:m/e(ESI)482.2(MH+)

Example 528

{2-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=6.9Hz), 1.32-1.46(12H,m), 4.11(2H,q,J=6.9Hz), 4.22(2H,q,J=6.7Hz), 4.38(2H,s), 4.82(2H,s), 5.43(2H,s), 7.27(1H,t,J=5.2Hz), 7.32(1H,s), 7.63(1H,d,J=5.2Hz), 7.80(1H,d,J=5.2Hz), 9.11(1H,brs), 9.45(1H,brs).

MS:m/e(ESI)487.2(MH+)

Example 529

3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-benzoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=7.2Hz), 2.83(3H,d,J=4.8Hz),
3.88(3H,s), 4.28(2H,q,J=7.2Hz), 4.85(2H,s), 5.51(2H,s),
7.54(1H,s), 7.98(1H,d,J=2.0Hz), 8.15(1H,d,J=2.4Hz),
8.16-8.22(1H,m), 8.56(1H,s), 9.19(1H,brs),
9.87(1H,brs).
MS:m/e(ESI)482.3(MH+)

Example 530

Methyl 3-*tert*-butyl-2-carboxymethoxy-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoate trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.39(3H,t,J=7.2Hz), 1.41(9H,s), 2.82(3H,d,J=4.4Hz),
3.88(3H,s), 4.28(2H,q,J=7.2Hz), 4.55(2H,s), 4.85(2H,s),
5.53(2H,s), 7.54(1H,s), 8.04(1H,d,J=2.4Hz),
8.16(1H,d,J=3.0Hz), 8.18-8.23(1H,m), 8.55(1H,s),
9.26(1H,brs), 9.89(1H,brs).
MS:m/e(ESI)540.3(MH+)

Example 531

{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-benzoylamino}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.39(9H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz),
3.88(3H,s), 3.96(2H,d,J=5.6Hz), 4.28(2H,q,J=7.2Hz),
4.85(2H,brs), 5.50(2H,brs), 7.54(1H,s), 7.93(1H,s),
8.18-8.22(1H,m), 8.56(1H,s), 8.81(1H,t,J=5.6Hz),

9.23(1H,s), 9.86(1H,s).

MS:m/e(ESI)539.3(MH+)

Example 532

({3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-benzoyl}-methyl-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.36,1.38(9H,each,s), 1.41(3H,t,J=7.2Hz),
2.82(3H,d,J=4.8Hz), 2.92,3.08(3H,each,s),
3.78,3.88(3H,each,s), 3.82,3.92(2H,each,s),
4.28(2H,q,J=7.2Hz), 4.85(2H,brs), 5.51(2H,brs),
7.54(1H,brs), 7.74(1H,brs), 7.91(1H,brs), 8.55(1H,brs),
8.18-8.22(1H,m), 9.24(1H,brs), 9.88(1H,brs).

MS:m/e(ESI)553.4(MH+)

Example 533

5-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-pentanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=7.2Hz), 1.67-1.88(4H,m),
2.31(2H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz),
4.13(2H,t,J=7.2Hz), 4.27(2H,q,J=7.2Hz), 4.85(2H,s),
5.46(2H,s), 7.17(1H,d,J=8.0Hz), 7.53(1H,s), 7.84(1H,s),
7.90(1H,d,J=8.0Hz), 8.20(1H,q,J=4.8Hz), 8.56(1H,s),
9.24(1H,brs), 9.84(1H,brs), 12.05(1H,brs).

MS:m/e(ESI)524.2(MH+)

Example 534

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(5-ethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.20(21H,m), 4.18(2H,q,J=7.2Hz), 4.78(2H,s), 5.36(2H,s), 7.12(1H,d,J=12.0Hz), 7.18(1H,s), 7.64(2H,s).

MS:m/e(ESI)441.2(MH+)

Example 535

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=6.8Hz), 1.82-1.93(4H,m), 2.83(3H,d,J=4.8Hz), 3.04-3.18(4H,m), 4.28(2H,q,J=6.8Hz), 4.40(2H,s), 4.84(2H,s), 5.49(2H,s), 7.41(1H,s), 7.48(1H,s), 7.54(1H,s), 8.13-8.25(1H,m), 8.56(1H,s), 9.15(1H,brs), 9.83(1H,brs).

MS:m/e(ESI)551.4(MH+)

Example 536

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.34-1.43(12H,m), 1.83-1.92(4H,m), 3.07-3.16(4H,m), 4.11(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.78(2H,s), 5.47(2H,s), 7.33(1H,s), 7.39(1H,s), 7.46(1H,s).

MS:m/e(ESI)556.2(MH+)

Example 537

{2-*tert*-Butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.04-1.14(4H,m), 1.38(9H,s), 1.82-1.94(4H,m), 2.27-2.36(1H,m), 3.03-3.18(4H,m), 4.40(2H,s), 4.82(2H,s), 5.55(2H,s), 7.41(1H,s), 7.48(1H,s), 7.72(1H,d,J=8.0Hz), 8.08(1H,d,J=8.0Hz).

MS:m/e(ESI)491.3(MH+)

Example 538

{4-*tert*-Butyl-2-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.25(9H,s), 1.41(3H,t,J=6.7Hz), 2.82(3H,brs), 4.27(2H,q,J=6.7Hz), 4.86(2H,s), 4.91(2H,s), 5.37(2H,s), 7.14(1H,d,J=9.0Hz), 7.50(1H,s), 7.69(1H,brd,J=9.0Hz), 7.83(1H,s), 8.20(1H,brq,J=4.0Hz), 9.32(1H,brs), 9.87(1H,brs).

MS:m/e(ESI)482.2(MH+)

Example 539

{4-*tert*-Butyl-2-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.24-1.32(12H,m), 1.39(3H,t,J=6.7Hz),

4.12(2H,q,J=6.7Hz), 4.22(2H,q,J=6.7Hz), 4.82(2H,s),

4.89(2H,s), 5.37(2H,s), 7.14(1H,d,J=8.3Hz), 7.31(1H,s),

7.69(1H,dd,J=8.3,2.8Hz), 7.83(1H,d,J=2.8Hz),

9.02(1H,brs).

MS:m/e(ESI)487.1(MH+)

Example 540

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-[2-ethyl-7-imino-3-(tetrahydropyran-2-yloxymethyl)-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl]-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7.3Hz), 1.30-1.80(6H,m), 1.42(18H,s),

2.93(2H,q,J=7.3Hz), 3.47-3.55(1H,m), 3.75-3.82(1H,m),

4.69(1H,d,J=13.6Hz), 4.78-4.81(1H,m), 4.86(2H,s),

4.90(1H,d,J=13.6Hz), 5.55(2H,s), 7.77(2H,s),

8.21(1H,s), 9.75-9.82(1H,m).

Example 541

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(2-ethyl-3-hydroxymethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.04(3H,t,J=6.8Hz), 1.42(18H,s), 2.87(2H,q,J=6.8Hz),

4.72(2H,s), 4.86(2H,s), 5.59(2H,s), 7.78(2H,s),

8.07(1H,brs), 8.21(1H,s), 9.53(1H,d,J=8.0Hz),

9.75(1H,d,J=8.0Hz).

Example 542

Ethyl 3-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.165(3H,t,J=7.2Hz), 1.371(9H,s), 1.411(3H,t,J=7.2Hz),

2.67-2.73(2H,m), 2.822(3H,d,J=4.8Hz), 2.96-3.02(2H,m),

3.799(3H,s), 4.058(2H,q,J=7.2Hz), 4.278(2H,q,J=7.2Hz),

4.147(2H,q,J=7.2Hz), 4.851(2H,s), 5.505(2H,s),

7.542(1H,s), 7.779(1H,d,J=2.0Hz), 7.838(1H,d,J=2.0Hz),

8.206(1H,q,J=4.8Hz), 8.558(1H,s).

Example 543

3-{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.371(9H,s), 1.402(3H,t,J=7.2Hz), 2.630(2H,t,J=7.6Hz),

2.814(3H,d,J=3.2Hz), 2.93-2.99(2H,m), 3.802(3H,s),

4.267(2H,q,J=7.2Hz), 4.838(2H,s), 5.600(2H,s),

7.522(1H,s), 7.785(1H,s), 7.848(1H,s), 8.204(1H,s),

8.215(1H,s), 8.573(1H,s), 10.033(1H,d,J=8.4Hz),

12.262(1H,s).

Example 544

2-[2-(8-*tert*-Butyl-4-carbamoylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7.2Hz), 2.84(3H,d,J=4.8Hz), 3.51(2H,t,J=4.0Hz), 3.90(2H,s), 4.31(2H,q,J=7.2Hz), 4.34(2H,t,J=4.0Hz), 4.84(2H,s), 5.43(2H,s), 7.02(1H,d,J=1.6Hz), 7.12(1H,s), 7.27(1H,d,J=1.6Hz), 7.50(1H,s), 7.54(1H,s), 8.22(1H,q,J=4.8Hz), 8.56(1H,s), 9.22(1H,s), 9.81(1H,s).

Example 545

2-[2-(3-*tert*-Butyl-5-hydroxy-4-methoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s,), 1.43(3H,t, J=7.0Hz), 2.85(3H,d, J=5.0Hz), 3.90(3H,s), 4.29(2H,q, J=7.0Hz), 4.85(2H,s), 5.48(2H,s), 7.41(1H,d, J=2.0Hz), 7.45(1H,d, J=2.0Hz), 7.55(1H,s), 8.22(1H,q,J=5.0Hz), 8.58(1H,s), 9.32(1H,brs), 9.91(1H,brs), 10.03(1H,s).

Example 546

{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-

methoxy-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.43(3H,t,J=7Hz), 1.47(9H,s),

2.85(3H,d,J=5Hz), 3.98(3H,s), 4.30(2H,q,J=7Hz),

4.82(2H,s), 4.87(2H,s), 5.51(2H,s), 7.44(1H,d,J=2Hz),

7.56(1H,s), 7.58(1H,d,J=2Hz), 8.22(1H,q,J=5Hz),

8.59(1H,s), 9.25(1H,brs), 9.88(1H,brs).

Example 547

2-{2-[3-*tert*-Butyl-4-(2H-tetrazol-5-ylmethoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.32(9H,s), 1.42(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz),

4.28(2H,q,J=7.2Hz), 4.85(2H,s), 5.48(2H,s), 5.64(2H,s),

7.00(1H,d,J=8.0Hz), 7.33-7.45(2H,m), 7.53(1H,s),

7.86(1H,s), 7.94(1H,d,J=8.0Hz), 8.20(1H,q,J=4.8Hz),

8.56(1H,s), 9.25(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)506.2(MH+)

Example 548

Ethyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.24(3H,t,J=6.4Hz), 1.31-1.50(12H,m), 1.78-1.99(4H,m),

2.82(3H,d,J=4.4Hz), 3.02-3.17(4H,m), 4.22-4.40(4H,m),

4.49(2H,s), 4.84(2H,s), 5.48(2H,s), 7.42(1H,s),

7.49(1H,s), 7.53(1H,s), 8.13-8.28(1H,m), 8.55(1H,s), 9.14(1H,brs), 9.83(1H,brs).

MS:m/e(ESI)579.3(MH+)

Example 549

Ethyl {2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.23(3H,t,J=7.2Hz), 1.29(3H,t,J=7.2Hz), 1.33-1.48(12H,m), 1.82-1.94(4H,m), 3.04-3.16(4H,m), 4.11(2H,q,J=7.2Hz), 4.15-4.30(4H,m), 4.49(2H,s), 4.78(2H,s), 5.48(2H,s), 7.33(1H,s), 7.42(1H,s), 7.48(1H,s).

MS:m/e(ESI)584.3(MH+)

Example 550

2-[2-(3,5-*tert*-Butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(18H,s), 2.85(3H,d,J=4.4Hz), 5.05(2H,s), 5.55(2H,s), 7.79(2H,s), 8.13(1H,dd,J=1.3,9.5Hz), 8.69(1H,d,J=1.3Hz), 8.77(1H,m).

Example 551

{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.70-2.08(4H,m), 2.88-3.21(4H,m),

3.86(3H,s), 3.95(3H,s), 4.39(2H,s), 4.80(2H,s),

5.48(2H,s), 7.36(1H,s), 7.39(1H,s), 7.47(1H,s),

9.07(1H,brs), 9.29(1H,brs).

MS:m/e(ESI)528.1(MH+)

Example 552

{8-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.2Hz), 1.38(9H,s), 1.41(3H,t,J=7.2Hz),

3.50(2H,t,J=4.4Hz), 4.13(2H,q,J=7.2Hz), 4.16(2H,s),

4.22(2H,q,J=7.2Hz), 4.31(2H,t,J=4.4Hz), 4.79(2H,s),

5.44(2H,s), 7.06(1H,d,J=2.0Hz), 7.26(1H,d,J=2.0Hz),

7.33(1H,s), 9.02(1H,s), 9.35(1H,s), 12.71(1H,s).

Example 553

{8-*tert*-Butyl-6-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=7.2Hz), 2.33(3H,s), 2.60(3H,s),

3.50(2H,t,J=4.4Hz), 4.01(2H,q,J=7.2Hz), 4.16(2H,s),

4.31(2H,t,J=4.4Hz), 4.83(2H,s), 5.49(2H,s),

7.07(1H,d,J=1.6Hz), 7.28(1H,d,J=1.6Hz), 9.45(1H,s),

9.84(1H,s), 12.71(1H,s).

Example 554

2-[2-(8-*tert*-Butyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.43(3H,t,J=7.2Hz), 2.84(3H,d,J=4.8Hz), 3.36(2H,t,J=4.4Hz), 4.23(2H,t,J=4.4Hz), 4.29(2H,q,J=7.2Hz), 4.84(2H,s), 5.43(2H,s), 7.14(1H,d,J=2.0Hz), 7.18(1H,d,J=2.0Hz), 7.54(1H,s), 8.22(1H,q,J=4.8Hz), 8.57(1H,s), 9.28(1H,s), 9.88(1H,s).

Example 555

{8-*tert*-Butyl-6-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 3.48(2H,brs), 3.86(2H,s), 3.95(2H,s), 4.12(2H,s), 4.28(2H,brs), 4.78(2H,s), 5.42(2H,s), 7.04(1H,s), 7.24(1H,s), 7.34(1H,s).

MS:m/e(ESI)500.1(MH+)

Example 556

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-fluoro-1-imino-6-methoxy-5-propoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.00(3H,t,J=7.1Hz), 1.41(18H,s), 1.75-1.86(2H,m),

3.87(3H,s), 4.12(2H,t,J=6.4Hz), 4.78(2H,s), 5.47(2H,s), 7.34(1H,s), 7.75(2H,s).

Example 557

{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-6-methoxy-5-propoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

0.99(3H,t,J=7.5Hz), 1.38(9H,s), 1.72-1.86(2H,m), 3.87(3H,s), 4.11(2H,t,J=6.4Hz), 4.78(2H,s), 4.87(2H,s), 5.47(2H,s), 7.07(1H,d,J=8.1Hz), 7.34(1H,s), 7.78-7.92(2H,m), 9.06(1H,brs).

Example 558

2-[2-(3,3-Dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.30(6H,s), 1.40(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.27(2H,q,J=7.2Hz), 4.85(2H,s), 5.44(2H,s), 7.03(1H,d,J=8.0Hz), 7.52(1H,s), 7.90(1H,d,J=8.0Hz), 7.97(1H,s), 8.16-8.24(1H,m), 8.55(1H,s), 10.90(1H,s).

MS:m/e(ESI)435.0(MH+)

Example 559

6-Ethoxy-3-imino-2-[2-oxo-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.30-1.43(9H,m), 2.82(3H,d,J=4.8Hz), 3.19(3H,s), 4.27(2H,q,J=7.2Hz), 4.85(2H,s), 5.45(2H,s), 7.20-7.24(1H,m), 7.52-7.54(1H,m), 7.98-8.02(2H,m), 8.17-8.21(1H,m), 8.56(1H,s).

MS:m/e(ESI)449.1(MH+)

Example 560

{5-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-3,3-dimethyl-2-oxo-2,3-dihydro-indol-1-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(6H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.53(2H,s), 4.86(2H,s), 5.46(2H,s), 7.24(1H,d,J=8.0Hz), 7.58(1H,s), 7.97(1H,d,J=8.0Hz), 8.03(1H,s), 8.17-8.25(1H,m), 8.56(1H,s), 9.25(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)493.1(MH+)

Example 561

2-{3-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-2-methyl-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.410(3H,t,J=6.8Hz), 1.514(9H,s), 2.823(3H,d,J=4.8Hz), 4.279(2H,q,J=6.8Hz), 4.869(2H,s),5.525(2H,s), 7.539(1H,s), 7.582(1H,t,J=7.6Hz), 7.716(1H,d,J=8.4Hz), 7.913(1H,d,J=8.4Hz), 7.924(1H,s), 8.205(1H,q,J=4.8Hz), 8.563(1H,s).

Example 562

Ethyl 4-{3-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-4-methyl-2-pentenoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.182(3H,7.2Hz), 1.405(3H,t,J=7.2Hz), 1.482(6H,s), 2.817(3H,d,J=4.8Hz), 4.098(2H,q,J=7.2Hz), 4.274(2H,q,J=7.2Hz), 4.868(2H,s), 5.529(2H,s), 5.821(1H,d,J=15.6Hz), 7.026(1H,d,J=15.6Hz), 7.539(1H,s), 7.592(1H,t,J=7.6Hz), 7.713(1H,d,J=8.0Hz), 7.900(1H,s), 7.931(1H,d,J=8.0Hz), 8.206(1H,q,J=4.8Hz), 8.55(1H,s).

Example 563

Ethyl 4-{3-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-4-methyl-2-pentenoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.184(3H,t,J=7.2Hz), 1.285(3H,t,J=6.8Hz), 1.390(3H,t,J=6.8Hz), 1.482(6H,s), 4.06-4.14(4H,m), 4.208(2H,q,J=7.2Hz), 4.817(2H,s), 5.511(2H,s), 5.821(1H,d,J=15.6Hz), 7.028(1H,d,J=15.6Hz), 7.335(1H,s), 7.56-7.61(1H,m), 7.705(1H,d,J=8.0Hz), 7.87-7.91(2H,m).

Example 564

Methyl 2-{3-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-2-methyl-

propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.284(3H,t,J=7.2Hz), 1.390(3H,t,J=6.8Hz), 1.548(6H,s), 3.590(3H,s), 4.110(2H,q,J=6.8Hz), 4.208(2H,t,J=7.2Hz), 4.820(2H,s), 5.517(2H,s), 7.341(1H,s), 7.55-7.70(2H,m), 7.85-7.94(2H,m).

Example 565

2-{3-[2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-2-methyl-propanoic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.282(3H,t,J=6.8Hz), 1.387(3H,t,J=6.8Hz), 1.514(6H,s), 4.106(2H,q,J=6.8Hz), 4.205(2H,q,J=6.8Hz), 4.818(2H,s), 5.521(2H,s), 7.23-7.42(2H,m), 7.579(1H,t,J=8.0Hz), 7.705(1H,d,J=8.0Hz), 7.86-7.93(2H,m).

Example 566

8-*tert*-Butyl-6-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-ylmethylene-cyanamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.70(3H,s), 4.05(2H,t,J=5Hz), 4.39(2H,t,J=5Hz), 5.04(2H,s), 6.33(2H,s), 7.49(1H,d,J=8Hz), 7.86(1H,d,J=8Hz), 7.87(1H,d,J=8Hz), 8.43(1H,d,J=8Hz), 9.70(1H,s).

MS:m/e(ESI)431.0(MH+)

Example 567

2-[2-(8-*tert*-Butyl-4-cyanoiminomethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.40(3H,t,J=7Hz), 2.83(3H,d,J=5Hz), 4.00(2H,t,J=5Hz), 4.28(2H,q,J=7Hz), 4.44(2H,t,J=5Hz), 4.82(2H,s), 5.40(2Hs), 7.51(1H,s), 7.70(1H,d,J=2Hz), 8.19(1H,d,J=2Hz), 8.20(1H,s), 8.52(1H,s), 9.44(1H,s).

MS:m/e(ESI)517.0(MH+)

Example 568

8-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-ylmethylene-cyanamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7Hz), 1.36(9H,s), 1.40(3H,t,J=7Hz), 4.00(2H,t,J=5Hz), 4.12(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.43(2H,t,J=5Hz), 4.80(2H,s), 5.43(2H,s), 7.32(1H,s), 7.70(1H,d,J=2Hz), 8.17(1H,d,J=2Hz), 9.43(1H,s).

MS:m/e(ESI)522.0(MH+)

Example 569

4-{3-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-4-methyl-2-pentenoic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.401(3H,t,J=6.8Hz), 1.472(6H,s), 2.814(3H,d,J=4.8Hz),

4.268(2H,q,J=6.8Hz), 4.862(2H,s), 5.565(2H,s),
5.745(1H,d,J=16.0Hz), 6.969(1H,d,J=16.0Hz),
7.528(1H,s), 7.586(1H,t,J=8.0Hz), 7.69-7.73(1H,m),
7.89-7.92(1H,m), 8.209(1H,q,J=4.8Hz), 8.559(1H,s),
9.388(1H,s).

Example 570

4-{3-[2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-4-methyl-2-pentenoic acid hydrochloride

1H-NMR(DMSO-d6)δ:
1.284(3H,t,J=6.8Hz), 1.389(3H,t,J=6.8Hz), 1.472(6H,s),
4.109(2H,q,J=6.8Hz), 4.207(2H,q,J=6.8Hz), 4.817(2H,s),
5.545(2H,s), 5.745(1h,d,J=16.0Hz),
6.970(1h,d,J=16.0Hz), 7.332(1H,s), 7.582(1H,t,J=8.0Hz),
7.69-7.73(1H,m), 7.8707.92(2H,m), 9.081(1H,s),
9.466(1H,s).

Example 571

2-[2-(3-*tert*-Butyl-4-hydroxy-5-methylaminomethyl-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:
1.37-1.42(12H,m), 2.578(3H,d,J=2.8Hz),
2.806(3H,d,J=4.4Hz), 4.258(2H,q,J=6.8Hz), 4.277(2H,s),
4.843(2H,s), 5.567(2H,s), 7.513(1H,s),
7.861(1H,d,J=2.4Hz), 8.154(1H,s), 8.207(1H,q,J=4.4Hz),
8.559(1H,s), 9.248(1H,s), 9.559(1H,s), 10.001(1H,s),

10.227(1H,s).

Example 572

1-(3-*tert*-Butyl-4-hydroxy-5-methylaminomethyl-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.298(3H,t,J=6.8Hz), 1.385(3H,t,J=6.8Hz), 1.396(9H,s), 2.575(3H,s), 4.101(2H,q,J=6.8Hz), 4.201(2H,q,J=6.8Hz), 4.269(2H,s), 4.798(2H,s), 5.519(2H,s), 7.321(1H,s), 7.852(1H,d,J=1.6Hz), 8.092(1H,s), 9.080(1H,s), 9.494(1H,s), 10.179(1H,s).

Example 573

Ethyl N-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl]-acetyl}-phenyl}-succinate hydrobromide

1H-NMR(DMSO-d6)δ:

1.16(3H,t,J=6.8Hz), 1.33(9H,s), 1.40(3H,t,J=6.8Hz), 2.56(2H,d,J=5.6Hz), 2.58(3H,d,J=5.6Hz), 2.80(3H,d,J=6.4Hz), 4.04(2H,q,J=6.8Hz), 4.25(2H,q,J=6.8Hz), 4.85(2H,s), 5.56(2H,s), 7.29(1H,d,J=8.4Hz), 7.53(1H,s), 7.84(1H,d,J=8.4Hz), 7.98(1H,s), 8.19(1H,q,J=5.2Hz), 8.56((1H,s), 9.44(1H,s), 9.98(1H,brs).

MS:m/e(ESI)551.4(MH+)

Example 574

Ethyl N-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-

methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-N-methyl-succinate hydrobromide

1H-NMR(DMSO-d6)δ:

1.13(3H,t,J=7.2Hz), 1.35(9H,s), 1.40(3H,t,J=7.2Hz), 2.13-2.22(4H,m), 2.81(3H,d,J=4.4Hz), 3.08(3H,s), 3.98(2H,q,J=7.2Hz), 4.26(2H,q,J=7.2Hz), 4.13(2H,s), 5.49(3H,s), 7.23(1H,d,J=8.8Hz), 7.51(1H,s), 7.94(1H,d,J=8.8Hz), 8.17-8.21(2H,m), 8.52(1H,brs).

Example 575

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(3-ethoxy-7-imino-2-methoxy-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=8.0Hz), 1.41(18H,s), 4.03(3H,s), 4.18(2H,q,J=8.0Hz), 4.73(2H,s), 5.45(2H,s), 7.68(1H,s), 7.73(2H,s).

Example 576

1-(3-*tert*-Butyl-4-(pyrrolidin-1-yl)-phenyl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.38(3H,t,J=7.2Hz), 1.42(9H,s), 1.88-1.95(4H,m), 2.90-2.98(4H,m), 4.11(2H,q,J=7.2Hz), 4.20(2H,q,J=7.2Hz), 4.79(2H,s), 5.45(2H,s), 7.32(1H,s), 7.65(1H,d,J=8.4Hz), 7.88(dd,J=8.4,2.0Hz), 7.92(1H,d,J=2.0Hz).

Example 577

tert-Butyl {2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.2Hz), 1.39(3H,t,J=7.2Hz), 1.40(18H,s), 4.05(2H,d,J=6.0Hz), 4.11(2H,q,J=7.2Hz), 4.20(2H,q,J=7.2Hz), 4.75(2H,s), 5.36(2H,s), 5.87(1H,t,J=6.0Hz), 6.53(1H,d,J=8.4Hz), 7.30(1H,s), 7.71(1H,dd,J=8.4,2.0Hz), 7.77(1H,d,J=2.0Hz).

Example 578

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.2Hz), 1.40(3H,t,J=7.2Hz), 1.40(9H,s), 4.09(2H,brs), 4.11(2H,q,J=7.2Hz), 4.20(2H,q,J=7.2Hz), 4.78(2H,s), 5.38(2H,s), 6.57(1H,d,J=8.8Hz), 7.32(1H,brs), 7.72(1H,dd,J=8.8,2.0Hz), 8.48-9.03(1H,m), 9.30-9.35(1H,m).

Example 579

1-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.42(3H,t,J=6.8Hz), 2.92(3H,s), 3.89(3H,s), 4.24(2H,q,J=6.8Hz), 4.36(2H,t,J=4.4Hz), 4.80(2H,s), 5.46(2H,s), 7.17(1H,s), 7.28(1H,s), 7.35(1H,s), 9.08(1H,s), 9.26(1H,s).

Example 580

2-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(3H,t,J=6.8Hz), 1.37(9H,s), 2.84(3H,d,J=4.8Hz), 2.93(3H,s), 4.32(2H,q,J=6,8Hz), 4.36(2H,t,4.4Hz), 5.01(2H,s), 5.49(2H,s), 7.19(1H,d,J=2.0Hz), 7.29(1H,d,J=2.0Hz), 8.30(1H,s), 8.41(1H,q,J=4.8Hz), 9.47(1H,s), 10.02(1H,s).

Example 581

2-[2-(3-Dimethylamino-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.4Hz), 3.10(6H,s), 4.29(2H,q,J=6.8Hz), 4.87(2H,s), 5.54(2H,s), 7.25(1H,d,J=8.4Hz), 7.55(1H,s), 7.93(1H,m), 8.23(2H,m), 8.58(1H,s), 9.46(1H,s), 9.95(1H,s).

Example 582

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(7-fluoro-1-

imino-5-isopropoxy-6-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(6H,d,J=6.0Hz), 1.40(18H,s), 3.85(3H,s), 4.74-4.85(3H,m), 5.47(2H,s), 7.36(1H,s), 7.75(2H,s).

Example 583

{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-5-isopropoxy-6-methoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(6H,d,J=6.0Hz), 1.39(9H,s), 3.84(3H,s), 4.72-4.85(3H,m), 4.88(2H,s), 5.45(2H,s), 7.07(1H,d,J=7.9Hz), 7.82-7.92(2H,m).

MS:m/e(ESI)487.2(MH+)

Example 584

{8-*tert*-Butyl-6-[2-(5-ethoxy-7-fluoro-1-imino-6-methoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.38(3H,t,J=7.0Hz), 3.48(2H,brs), 3.86(3H,s), 4.14(2H,s), 4.20(2H,q,J=7.0Hz), 4.28(2H,brs), 4.76(2H,s), 5.44(2H,s), 7.03(1H,s), 7.23(1H,s), 7.32(1H,s), 9.03(1H,brs).

Example 585

{8-*tert*-Butyl-6-[2-(7-fluoro-1-imino-6-methoxy-5-

propoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

0.98(3H,t,J=7.6Hz), 1.34(9H,s), 1.74-1.85(2H,m), 3.48(2H,brt,J=4.3Hz), 3.86(3H,s), 4.08-4.18(4H,m), 4.28(2H,brt,J=4.3Hz), 4.77(2H,s), 5.44(2H,s), 7.04(1H,s), 7.23(1H,s), 7.32(1H,s), 9.03(1H,brs).

Example 586

1-(8-*tert*-Butyl-4-ethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.09(3H,t,J=7.0Hz), 1.30(3H,t,J=7.6Hz), 1.34(9H,s), 2.94(2H,q,J=7.6Hz), 3.35(2H,t,J=4.4Hz), 3.40(2H,q,J=7.0Hz), 4.27(2H,t,J=4.4Hz), 4.84(2H,s), 5.52(2H,s), 7.19(1H,s), 7.21(1H,s), 7.72(1H,d,J=8.0Hz), 8.17(1H,d,J=8.0Hz).

MS:m/e(ESI)421.2(MH+)

Example 587

1-(8-*tert*-Butyl-4-propyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

0.90(3H,t,J=7.2Hz), 1.30(3H,t,J=7.6Hz), 1.34(9H,s), 1.52-1.62(2H,m), 2.94(2H,q,J=7.6Hz),

3.27(2H,t,J=7.4Hz), 3.38(2H,t,J=4.4Hz),

4.25(2H,t,J=4.4Hz), 4.84(2H,s), 5.54(2H,s),

7.15(1H,d,J=2.0Hz), 7.21(1H,d,J=2.0Hz),

7.72(1H,d,J=8.0Hz), 8.17(1H,d,J=8.0Hz).

MS:m/e(ESI)435.2(MH+)

Example 588

1-{3-*tert*-Butyl-5-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-piperidin-2-one hydrobromide

1H-NMR(DMSO-d6)δ:

1.26(3H,t,J=7.2Hz), 1.34(9H,s), 1.68(4H,br),

2.32(2H,br), 2.86(2H,q,J=7.2Hz), 3.25-3.40(2H,mr),

4.40(2H,s), 4.53(2H,s), 5.12(2H,s), 7.48(1H,d,J=8.0Hz),

7.77(1H,br), 7.82(1H,br), 7.96(1H,d,J=8.0Hz).

MS:m/e(ESI)463.2(MH+)

Example 589

N-{3-*tert*-Butyl-5-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-N-methyl-acetamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7.6Hz), 1.37(9H,s), 2.11(3H,s),

2.94(2H,q,J=7.6Hz), 3.10(3H,s), 4.48(2H,s), 4.86(2H,s),

5.51(2H,s), 7.73(1H,d,J=8.2Hz), 7.81(1H,d,J=2.0Hz),

7.90(1H,d,J=2.0Hz), 8.17(1H,d,J=8.2Hz), 9.52(1H,s),

9.85(1H,s), 11.28(1H,s).

MS:m/e(ESI)437.2(MH+)

Example 590

{2-[(Acetyl-methyl-amino)-methyl]-6-*tert*-butyl-4-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.6Hz), 1.40,1.41(9H,each s), 2.02,2.10(3H,each s), 2.80,2.94(3H,each s), 2.92-2.97(2H,m), 4.49,4.52(2H,each s), 4.62,4.70(2H,each s), 4.86,5.55(2H,each s), 7.49,7.53(1H,each s), 7.74(1H,d,J=8.0Hz), 7.84,7.89(1H,each s), 8.18(1H,d,J=8.0Hz), 9.52(1H,brs), 9.89(1H,brs).

Example 591

{2-[(Acetyl-methyl-amino)-methyl]-6-*tert*-butyl-4-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=6.8Hz), 1.40(9H,s), 2.01,2.09(3H,each s), 2.31(3H,s), 2.58,2.79(3H,each s), 2.93,3.14(3H,each s), 3.98(2H,q,J=7.2Hz), 4.48,4.52(2H,each s), 4.61,4.69(2H,each s), 4.82(2H,s), 5.52,5.54(2H,each s), 7.47,7.51(1H,each d,J=2.0Hz), 7.83,7.88(1H,each d,J=2.0Hz), 9.43(1H,s), 9.88(1H,s).

Example 592

{8-*tert*-Butyl-6-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-

benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.00-1.19(4H,m), 1.35(9H,s), 2.23-2.36(1H,m),

4.14(2H,s), 4.20-4.37(2H,m), 4.80(2H,s), 5.49(2H,s),

7.04(1H,s), 7.25(1H,s), 7.70(1H,d,J=8.4Hz),

8.07(1H,d,J=8.4Hz), 9.52(1H,brs), 9.58-9.63(1H,m).

MS:m/e(ESI)463.2(MH+)

Example 593

6-Ethoxy-3-imino-2-[2-oxo-2-(1,2,3,3-tetramethyl-2,3-dihydro-1H-indol-5-yl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.02(3H,s), 1.15(3H,d,J=6.4Hz), 1.27(3H,s),

1.41(3H,t,J=7.2Hz), 2.80(3H,s), 2.82(3H,d,J=4.8Hz),

3.19(1H,q,J=3.4Hz), 4.27(2H,q,J=7.2Hz), 4.82(2H,s),

5.35(2H,s), 6.60(1H,d,J=8.4Hz), 7.52(1H,s), 7.60(1H,s),

7.77(1H,d,J=8.4Hz), 8.20(1H,d,J=4.8Hz), 8.55(1H,brs).

MS:m/e(ESI)449.2(MH+)2

Example 594

2-[2-(5-*tert*-Butyl-furan-3-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(9H,s), 1.43(3H,t,J=7.2Hz), 2.84(3H,d,J=4.4Hz),

4.29(2H,q,J=7.2Hz), 4.86(2H,s), 5.24(2H,s),

6.48(1H,d,J=0.8Hz), 7.54(1H,s), 8.22(1H,m), 8.58(1H,s),

8.63(1H,d,J=0.8Hz).

Example 595

{2,6-Di-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.39-1.42(3H,m), 1.404(18H,s), 2.818(3H,d,J=4.4Hz), 4.266(2H,s), 4.272(2H,q,J=6.8Hz), 4.847(2H,s), 5.572(2H,s), 7.534(1H,s), 7.891(2H,s), 8.214(1H,q,J=4.4Hz), 8.554(1H,s), 9.309(1H,s), 9.309(1H,s), 9.913(1H,s).

Example 596

{2,6-Di-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.285(3H,t,J=6.8Hz), 1.34-1.45(21H,s), 4.110(2H,q,J=6.8Hz), 4.209(2H,q,J=6.8Hz), 4.262(2H,s), 4.796(2H,s), 5.555(2H,s), 7.333(1H,s), 7.878(2H,s), 9.085(1H,s), 9.412(1H,s).

Example 597

1-{3-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-cyclopentanecarboxylic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.386(3H,t,J=6.8Hz), 1.50-1.77(6H,m), 2.37-2.50(2H,m),

2.806(3H,d,J=4.4Hz), 4.256(2H,q,J=6.8Hz), 4.919(2H,s), 4.97-5.04(1H,m), 7.15-7.42(4H,m), 7.478(1H,s), 8.14-8.21(1H,m), 8.534(1H,s).

Example 598

1-{3-[2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-cyclopentanecarboxylic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.264(3H,t,J=6.8Hz), 1.379(3H,t,J=6.8Hz), 1.55-1.77(6H,m), 2.43-2.50(2H,m), 4.075(2H,q,J=6.8Hz), 4.188(2H,q,J=6.8Hz), 4.879(2H,s), 4.95-5.02(1H,m), 7.23-7.40(5H,m).

Example 599

Ethyl 1-{3-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-cyclopentanecarboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.079(3H,t,J=7.2Hz), 1.408(3H,t,J=6.8Hz), 1.60-1.74(4H,m), 1.83-1.94(2H,m), 2.52-2.60(2H,m), 2.821(3H,d,J=4.4Hz), 4.016(2H,q,J=7.2Hz), 4.276(2H,q,J=6.8Hz), 4.871(2H,s), 5.520(2H,s), 7.52-7.72(2H,m), 7.884(1H,s), 7.924(1H,d,J=7.6Hz), 8.215(1H,q,J=4.4Hz), 8.554(1H,s).

Example 600

Ethyl 1-{3-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-

cyclopentanecarboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.079(3H,t,J=7.2Hz), 1.287(3H,t,J=6.8Hz),

1.393(3H,t,J=6.8Hz), 1.60-1.74(4H,m), 1.84-1.94(2H,m),

2.52-2.60(2H,m), 4.016(2H,q,J=6.8Hz),

4.113(2H,q,J=7.2Hz), 4.211(2H,q,J=6.8Hz), 4.822(2H,s),

5.504(2h,s), 7.339(1H,s), 7.582(1H,t,J=8.0Hz),

7.691(1H,d,J=8.0Hz), 7.877(1H,s), 7.911(1H,d,J=7.6Hz).

Example 601

6-Ethoxy-3-imino-2-[2-oxo-2-(1,3,3-trimethyl-2,3-dihydro-1H-indol-5-yl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(6H,s), 1.41(3H,t,J=7.2Hz), 2.82(3H,d,J=4.8Hz),

2.86(3H,s), 3.28(2H,s), 4.28(2H,q,J=7.2Hz), 4.81(2H,s),

5.32(2H,s), 6.57(1H,d,J=8.0Hz), 7.51(1H,s), 7.59(1H,s),

7.76(1H,d,J=8.0Hz), 8.17-8.23(1H,m), 8.54(1H,s),

9.16(1H,brs), 9.72(1H,brs).

Example 602

1-[3-*tert*-Butyl-4-(2H-tetrazol-5-ylmethoxy)-phenyl]-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.26-1.43(15H,m), 4.11(2H,q,J=7.2Hz),

4.21(2H,q,J=7.2Hz), 4.80(2H,s), 5.46(2H,s), 5.63(2H,s),

6.94-7.06(1H,m), 7.31-7.45(3H,m), 9.04(1H,brs),

9.33(1H,brs).

MS:m/e(ESI)511.2(MH+)

Example 603

2-[2-(8-*tert*-Butyl-4-carbamoylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-7-fluoro-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(3H,t,J=7.2Hz), 1.38(9H,s), 2.84(3H,d,J=4.4Hz), 3.51(2H,t,J=4.4Hz), 3.90(2H,s), 4.31(2H,q,J=7.2Hz), 4.34(2H,t,J=4.4Hz), 5.00(2H,s), 5.46(2H,s), 7.01(1H,s), 7.13(1H,s), 7.27(1H,s), 7.52(1H,s), 8.30(1H,s), 8.41(1H,q,J=4.4Hz), 9.47(1H,s), 10.02(1H,s).

Example 604

2-{8-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=6.8Hz), 1.38(9H,s), 1.41(3H,t,J=6.8Hz), 3.51(2H,t,J=4.4Hz), 3.90(2H,s), 4.13(2H.q.J=6.8Hz), 4.22(2H,q,J=6.8Hz), 4.34(2H,J=4.4Hz), 4.79(2H,s), 5.43(2H,s), 7.00(1H,d,J=2.0Hz), 7.13(1H,s), 7.26(1H,d,J=2.0Hz), 7.34(1H,s), 7.51(1H,s), 9.02(1H,s), 9.35(1H,s).

Example 605

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-ethyl]-6-

ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.29(18H,s), 1.41(3H,t,J=7.2Hz), 2.83(3H,d,J=4.4Hz), 2.90(2H,t,J=7.2Hz), 3.93(2H,t,J=7.2Hz), 4.27(2H,q,J=7.2Hz), 4.75(2H,s), 6.81(1H,s), 6.92(2H,s), 7.47(1H,s), 8.18(1H,q,J=4.4Hz), 8.56(1H,s), 9.17(1H,s), 9.71(1H,s).

Example 606

1-[8-*tert*-Butyl-4-(3-hydroxy-propyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-ethanone hydrochloride

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.4Hz), 1.34(9H,s), 1.71(2H,m), 2.94(2H,q,J=7.4Hz), 3.26-3.72(6H,m), 4.26(2H,t,J=4.8Hz), 4.85(2H,s), 5.53(2H,s), 7.21(2H,s), 7.73(1H,d,J=8.0Hz), 8.17(1H,d,J=8.0Hz), 9.55(1H,s), 9.85(1H,s).

MS:m/e(ESI)451

Example 607

2-{2-[8-*tert*-Butyl-4-(3-hydroxy-propyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

0.90(3H,t,J=7.2Hz), 1.30(3H,t,J=7.6Hz), 1.34(9H,s),

1.52-1.62(2H,m), 2.94(2H,q,J=7.6Hz),
3.27(2H,t,J=7.4Hz), 3.38(2H,t,J=4.4Hz),
4.25(2H,t,J=4.4Hz), 4.84(2H,s), 5.54(2H,s),
7.15(1H,d,J=2.0Hz), 7.21(1H,d,J=2.0Hz),
7.72(1H,d,J=8.0Hz), 8.17(1H,d,J=8.0Hz).

Example 608

6-Ethoxy-3-imino-2-[2-oxo-2-(1,4,4-trimethyl-2-oxo-1,2,3,4-tetrahydro-quinolin-6-yl)-ethyl]-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.27(6H,s), 1.41(3H,t,J=7.2Hz), 2.54(2H,s),
2.82(3H,d,J=4.8Hz), 3.29(2H,s), 4.28(2H,q,J=7.2Hz),
4.86(2H,s), 5.49(2H,s), 7.32(1H,d,J=8.0Hz), 7.54(1H,s),
7.89(1H,s), 7.95(1H,d,J=8.0Hz), 8.18-8.24(1H,m),
8.56(1H,s), 9.24(1H,brs), 9.86(1H,brs).

Example 609

{2-[(Acetyl-methyl-amino)-methyl]-6-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.29(3H,t,J=6.8Hz), 1.39(12H,s), 2.01,2.10(3H,each s),
2.80,2,94(3H,each s), 4.11,4.22(2H,each brd,J=6.8Hz),
4.48,4.52(2H,each s), 4.61,4.69(2H,each s), 4.80(2H,s),
5.47(2H,s), 7.33(1H,s), 7.48,7.51(1H,each s),
7.83,7.87(1H,each s), 9.06(1H,s), 9.32(1H,s).

MS:m/e(ESI)572.3(MH+)

Example 610

Methyl {2-[(acetyl-methyl-amino)-methyl]-6-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetate trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3Ht,J=6.8Hz), 1.39(12H,s), 2.01,2.09(3H,each s), 2.80,2.94(3H,each s), 3.75,3.77(3H,each s), 4.11(2H,q,J=7.2Hz), 4.21(2H,q,J=7.2Hz), 4.06(2H,s), 4.64,4.68(2H,each s), 4.79(2H,s), 5.47(2H,s), 7.33(1H,s), 7.47,7.52(1H,each s), 7.83,7.87(1H,each d,J=2.0Hz), 9.06(1H,each s).

MS:m/e(ESI)586.4(MH+)

Example 611

2-[2-(7-*tert*-Butyl-2-cyanoamino-benzoxazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.08(3H,t,J=7Hz), 1.44(9H,s), 2.84(3H,d,J=5Hz), 4.28(2H,q,J=7Hz), 4.84(2H,s), 5.52(2H,s), 5.55(1H,q,J=5Hz), 7.54(1H,s), 7.64(1H,s), 8.21(1H,s), 8.56(1H,s).

Example 612

{8-*tert*-Butyl-6-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-

yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28-1.42(12H,m), 2.78(3H,d,J=4.5Hz),
3.48(2H,brt,J=4.5Hz), 4.15(2H,s), 4.24(2H,q,J=7.0Hz),
4.30(2H,brt,J=4.5Hz), 4.85(2H,s), 5.49(2H,s),
7.03(1H,s), 7.25(1H,s), 7.98(1H,s),
8.54(qH,brq,J=4.5Hz), 9.48(1H,brd,J=7.0Hz),
9.93(1H,brd,J=7.0Hz).

Example 613

1-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-(6-ethoxy-7-fluoro-1-imino-5-methoxy-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7.0Hz), 1.41(18H,s), 3.95(3H,s),
4.10(2H,q,J=7.0Hz), 4.79(2H,s), 5.48(2H,s), 7.36(1H,s),
7.77(2H,s), 8.07(1H,brs), 9.06(1H,brs), 9.28(1H,brs).

Example 614

Methyl {8-*tert*-butyl-6-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 3.49(2H,brs), 3.64(3H,s), 3.86(3H,s),
3.95(3H,s), 4.25-4.34(3H,m), 4.78(2H,s), 5.40(2H,s),
7.03(1H,s), 7.24(1H,s), 7.35(1H,s).

MS:m/e(ESI)514.3(MH+)

Example 615

2-{8-*tert*-Butyl-6-[2-(3-ethoxy-7-imino-2,4-dimethyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=6.4Hz), 2.33(3H,s), 2.60(3H,s), 3.51(2H,s), 3.90(2H,s), 4.00(2H,q,J=6.4Hz), 4.35(2H,s), 4.83(2H,s), 5.48(2H,s), 7.01(1H,s), 7.13(1H,s), 7.27(1H,s), 7.51(1H,s), 9.40(1H,s), 9.81(1H,s).

Example 616

{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzylamino}-acetic acid ditrifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.38(3H,t,J=7.2Hz), 1.41(9H,s), 3.79(2H,brs), 4.12(2H,q,J=7.2Hz), 4.23(2H,q,J=7.2Hz), 4.25(2H,s), 4.80(2H,s), 5.43(2H,s), 7.33(1H,s), 7.84(1H,s), 7.91(1H,s), 9.07(1H,s), 9.37(1H,s).

Example 617

{6-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-4,4-dimethyl-2-oxo-3,4-dihydro-2H-quinolin-1-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.32(6H,s), 1.42(3H,t,J=7.2Hz), 2.57(2H,s), 2.82(3H,d,J=4.8Hz), 4.28(2H,q,J=7.2Hz), 4.77(2H,s), 4.87(2H,s), 5.49(2H,s), 7.25(1H,d,J=8.0Hz), 7.54(1H,s),

7.87-7.94(2H,m), 8.17-8.25(1H,m), 8.57(1H,s),
9.26(1H,brs), 9.87(1H,brs).
MS:m/e(ESI)507.3(MH+)

Example 618

1-(5-*tert*-Butyl-furan-3-yl)-2-(4-ethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.29(9H,s), 1.35(3H,t,J=7.2Hz), 4.20(2H,q,J=7.2Hz),
4.83(2H,s), 5.22(2H,s), 6.48(1H,d,J=0.4Hz), 7.41-7.54(2H,m), 8.61(1H,d,J=0.4Hz).

Example 619

1-(5-*tert*-Butyl-furan-3-yl)-2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:
1.29(9H,s), 1.31(3H,t,J=7.2Hz), 1.42(3H,t,J=7.2Hz),
4.13(2H,q,J=7.2Hz), 4.23(2H,q,J=7.2Hz), 4.82(2H,s),
5.22(2H,s), 6.48(1H,d,J=0.8Hz), 7.34(1H,s),
8.60(1H,d,J=0.8Hz), 9.10(1H,s), 9.41(1H,s).

Example 620

2-[2-(3-*tert*-Butyl-4-hydroxy-5-isopropoxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.33(6H,d,J=6.0Hz), 1.41(9H,s), 1.44(3H,t,J=7.2Hz),
2.85(3H,d,J=4.4Hz), 4.30(2H,q,J=7.2Hz), 4.67(1H,m),

4.86(2H,s), 5.48(2H,s), 7.49(1H,s), 7.52(1H,s), 7.55(1H,s), 8.22(1H,m), 8.59(1H,s), 9.24(1H,s), 9.87(1H,s).

Example 621

2-[2-(3-*tert*-Butyl-5-cyclopentyloxy-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.44(3H,t,J=7.2Hz), 1.58(2H,m), 1.73-2.00(6H,m), 2.85(3H,d,J=4.4Hz), 4.30(2H,q,J=7.2Hz), 4.86(2H,s), 4.87(1H,m), 5.49(2H,s), 7.40(1H,s), 7.52(1H,s), 7.55(1H,s), 8.22(1H,m), 8.60(1H,s), 9.22(1H,s), 9.86(1H,s).

Example 622

Ethyl {3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.167(3H,t,J=6.8Hz), 1.373(9H,s), 1.409(3H,t,J=6.8Hz), 2.822(3H,d,J=4.4Hz), 3.757(3H,s), 3.819(2H,s), 4.102(2H,q,J=6.8Hz), 4.277(2H,q,J=6.8Hz), 4.856(2H,s), 5.494(2H,s), 7.536(1H,s), 7.846(1H,s), 8.215(1H,s), 8.204(1H,s), 8.551(1H,s).

Example 623

Ethyl {3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-

phenyl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.164(3H,t,J=6.8Hz), 1.285(3h,t,J=6.8Hz), 1.370(9H,s), 1.391(3H,t,J=7.2Hz), 3.753(3H,s), 3.817(2H,s), 4.06-4.14(4H,m), 4.207(2H,q,J=7.2Hz), 4.803(2H,s), 5.469(2H,s), 7.344(1H,s), 7.832(2H,s).

Example 624

6-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.38(3H,t,J=6.8Hz), 2.79(3H,d,J=4.0Hz), 2.93(3H,s), 3.33(2H,s), 4.26(2H,q,J=6.8Hz), 4.36(2H,s), 4.89(2H,s), 5.57(2H,s), 7.20(1H,s), 7.29(1H,s), 8.01(1H,s), 8.59(1H,q,J=4.0Hz), 9.55(1H,s), 9.97(1H,s).

Example 625

6-[2-(8-*tert*-Butyl-4-carbamoylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-3-ethoxy-7-imino-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine-2-carboxylic acid methylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.38(12H,s), 2.79(3H,d,J=4.8Hz), 3.91(2H,s), 4.25(2H,q,J=6.8Hz), 4.34(2H,t,J=4.4Hz), 4.89(2H,s), 5.51(2H,s), 7.02(1H,s), 7.14(1H,s), 7.27(1H,s), 7.55(1H,s), 8.00(1H,s), 8.57(1H,q,J=4.8Hz), 9.52(1H,s),

9.94(1H,s).

Example 626

{2-*tert*-Butyl-4-[2-(6-carbamoyl-5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=6.8Hz), 1.83-1.93(4H,m), 3.06-3.16(4H,m), 4.27(2H,q,J=6.8Hz), 4.40(2H,s), 4.84(2H,s), 5.49(2H,s), 7.41(1H,s), 7.48(1H,s), 7.54(1H,s), 7.70(1H,brs), 7.79(1H,brs), 8.62(1H,s), 9.16(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)537.3(MH+)

Example 627

{2-*tert*-Butyl-4-[2-(6-dimethylcarbamoyl-5-ethoxy-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.34(3H,t,J=6.8Hz), 1.38(9H,s), 1.84-1.93(4H,m), 2.78(3H,s), 3.00(3H,s), 3.08-3.15(4H,m), 4.22(2H,q,J=6.8Hz), 4.40(2H,s), 4.83(2H,s), 5.49(2H,s), 7.42(1H,s), 7.48(1H,s), 7.50(1H,s), 8.03(1H,s), 9.13(1H,brs), 9.69(1H,brs).

MS:m/e(ESI)565.4(MH+)

Example 628

{2-*tert*-Butyl-4-[2-(6-ethoxy-7-fluoro-1-imino-5-

methoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=6.7Hz), 1.40(9H,s), 3.93(3H,s), 4.10(2H,q,J=6.7Hz), 4.80(2H,s), 4.88(2H,s), 5.45(2H,s), 7.06(1H,d,J=8.0Hz), 7.34(1H,s), 7.80-7.92(2H,m), 9.06(1H,brs), 9.37(1H,brs).

Example 629

Methyl {8-*tert*-butyl-6-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.30-1.41(12H,m), 2.77(3H,d,J=4.8Hz), 3.48(2H,brs), 3.64(3H,s), 4.20-4.33(6H,m), 4.86(2H,s), 5.44(2H,s), 7.04(1H,s), 7.26(1H,s), 7.98(1H,s), 8.52(1H,q,J=4.8Hz).

Example 630

8-*tert*-Butyl-6-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazine-2-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 2.88(3H,s), 3.23-3.42(2H,m), 3.87(3H,s), 3.95(3H,s), 4.79(2H,s), 5.15(1H,t,J=3.9Hz), 5.45(2H,s), 7.17(1H,s), 7.32(1H,s), 7.35(1H,s).

Example 631

tert-Butyl (acetyl-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-amino)-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1,32(9H,s), 1.42(9H,s), 1.43(3H,t,J=6.8Hz), 1.74(3H,s), 2.82(3H,d,J=4.4Hz), 3.68(1H,d,J=16.8Hz), 4.28(2H,q,J=6.8Hz), 4.49(1H,d,J=16.8Hz), 4.87(2H,s), 5.53(2H,s), 7.54(1H,s), 7.73(1H,d,J=8.0Hz), 7.98(IH,dd,J=8.0,2.0Hz), 8.15(1H,d,J=2.0Hz), 8.21(1H,q,J=4.4Hz), 8.57(1H,s).

Example 632

(Acetyl-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-amino)-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 1.41(3H,t,J=6.8Hz), 1.73(3H,s), 2.82(3H,d,J=4.4Hz), 3.67(1H,d,J=16.8Hz), 4.28(2H,q,J=6.8Hz), 4.56(1H,d,J=16.8Hz), 4.87(2H,s), 5.58(2H,s), 7.54(1H,s), 7.75(1H,d,J=8.0Hz), 7.97(1H,dd,J=8.0,2.0Hz), 8.17(1H,d,J=2.0Hz), 8.21(1H,q,J=4.4Hz), 8.57(1H,s), 9.34-9.40(1H,m), 9.90-9.98(1H,m).

Example 633

tert-Butyl ({2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-methyl-amino)-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=5.2Hz), 1.44(18H,s), 2.59(3H,s),

2.82(3H,d,J=4.8Hz), 3.49(1H,brs), 4.27(2H,q,J=5.2Hz),

4.84(2H,s), 5.49(2H,s), 7.54(1H,s), 7.64(1H,d,J=8.4Hz),

7.90(1H,dd,J=8.4,2.4Hz), 7.94(1H,d,J=2.4Hz),

8.21(1H,q,J=4.8Hz), 8.56(1H,s).

Example 634

{2-*tert*-Butyl-6-diethylamino-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

0.95(6H,t,J=7.2Hz), 1.38(9H,s), 1.41(3H,t,J=7.2Hz),

2.82(3H,d,J=4.0Hz), 3.11(4H,q,J=7.2Hz),

4.28(2H,q,J=7.2Hz), 4.73(2H,s), 4.84(2H,s), 5.48(2H,s),

7.54(2H,s), 7.59(1H,s), 8.20(1H,brs), 8.55(1H,s),

9.17(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)553.3(MH+)

Example 635

({2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-methyl-amino)-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=6.8Hz), 1.44(9H,s), 2.62(3H,s), 2.82(3H,s),

3.83(1H,d,J=8.8Hz), 4.17(1H,d,J=8.8Hz),

4.27(2H,q,J=6.8Hz), 4.84(2H,s), 5.54(2H,s), 6.34(1H,s),

7.66(1H,d,J=8.0Hz), 7.91(1H,dd,J=8.0,1.6Hz),

7.94(1H,d,J=1.6Hz), 8.56(1H,s), 9.29-9.33(1H,m), 9.48-9.92(1H,m).

Example 636

{2-*tert*-Butyl-4-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.85-1.90(4H,m), 2.77(3H,d,J=4.4Hz), 2.91(6H,s), 3.07-3.15(4H,m), 4.39(2H,s), 4.73(2H,s), 5.44(2H,s), 7.17(1H,s), 7.40(1H,s), 7.47(1H,s), 8.06(1H,s), 8.36(1H,brs), 8.90(1H,brs), 9.53(1H,brs).

MS:m/e(ESI)550.4(MH+)

Example 637

2-[2-(3-*tert*-Butyl-4-hydroxy-5-isopropoxy-phenyl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=6.0Hz), 1.41(9H,s), 2.80(3H,d,J=4.4Hz), 2.94(6H,s), 4.68(1H,m), 4.76(2H,s), 5.45(2H,s), 7.17(1H,s), 7.48(1H,s), 7.52(1H,s), 8.10(1H,s), 8.39(1H,m).

Example 638

2-[2-(4-Acetyl-8-*tert*-butyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide

hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.43(3H,t,J=6.8Hz), 2.30(3H,s),

2.84(3H,d,J=4.4Hz), 3.91(2H,t,J=4.8Hz),

4.29(2H,q,J=6.8Hz), 4.48(2H,t,J=4.8Hz), 4.86(2H,s),

5.45(2H,s), 7.55(1H,s), 7.67(1H,s), 8.00(1H,brs),

8.22(1H,q,J=4.4Hz), 8.57(1H,s), 9.22(1H,s), 9.84(1H,s).

Example 639

Ethyl {2-*tert*-butyl-6-diethylamino-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

0.94(6H,t,J=6.8Hz), 1.23(3H,t,J=6.8Hz), 1.37(9H,s),

1.41(3H,t,J=6.8Hz), 2.83(3H,d,J=4.8Hz), 3.05-

3.10(4H,m), 4.17(2H,q,J=6.8Hz), 4.27(2H,q,J=6.8Hz),

4.80(2H,s), 4.84(2H,s), 5.53(2H,s), 7.54(1H,s),

7.55(1H,s), 7.61(1H,s), 8.21(1H,d,J=4.8Hz), 8.56(1H,s),

9.29(1H,brs), 9.90(1H,brs).

MS:m/e(ESI)581.4(MH+)

Example 640

{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzylamino}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=7.2Hz), 1.38(3H,t,J=7.2Hz), 1.41(9H,s),

3.79(2H,brs), 4.12(2H,q,J=7.2Hz), 4.23(2H,q,J=7.2Hz),

4.25(2H,s), 4.80(2H,s), 5.43(2H,s), 7.33(1H,s),
7.84(1H,s), 7.91(1H,s), 9.07(1H,s), 9.37(1H,s).

Example 641

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(ethyl-methanesulfonyl-amino)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.05(3H,t,J=6.8Hz), 1.38(9H,s), 1.41(3H,t.J=6.8Hz),
2.82(3H,d,J=4.8Hz), 3.27(3H,s), 4.28(2H,q,J=6.8Hz),
4.69-4.93(6H,m), 5.52(2H,s), 7.55(1H,s), 7.86(1H,s),
7.89(1H,s), 8.21(1H,d,J=4.4Hz), 8.56(1H,s),
9.24(1H,brs), 9.88(1H,brs).
MS:m/e(ESI)603.3(MH+)

Example 642

{2-(Acetyl-ethyl-amino)-6-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.05(3H,t,J=6.8Hz), 1.33-1.43(12H,m), 1.89(3H,s),
2.82(3H,d,J=4.8), 2.96-3.12(1H,m), 4.08-4.19(1H,m),
4.28(2H,q,J=6.8Hz), 4.48(2H,dd,J=15.2Hz,15.6Hz),
4.86(2H,s), 5.50(2H,s), 7.54(1H,s), 7.81(1H,s),
7.89(1H,s), 8.21(1H,d,J=4.4Hz), 8.56(1H,s),
9.26(1H,brs), 9.88(1H,brs).
MS:m/e(ESI)567.3(MH+)

Example 643

{2-(Acetyl-methyl-amino)-6-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.36-1.43(12H,m), 1.83(3H,s), 2.82(3H,d,J=4.4Hz), 3.15(3H,s), 4.28(2H,q,J=6.8Hz), 4.44(2H,dd,J=15.6Hz,15.6Hz), 4.85(2H,s), 5.48(2H,s), 7.54(1H,s), 7.87(1H,s), 7.95(1H,s), 8.21(1H,d,J=4.4Hz), 8.55(1H,s), 9.23(1H,brs), 9.88(1H,brs).

MS:m/e(ESI)553.3(MH+)

Example 644

{2-*tert*-Butyl-4-[2-(1-imino-6-methylcarbamoyl-5-propoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

0.98(3H,t,J=7.6Hz), 1.23(3H,t,J=7.2Hz), 1.38(9H,s), 1.85-1.90(2H,m), 2.82(3H,d,J=4.8Hz), 3.06-3.12(4H,m), 4.17(2H,q,J=6.4Hz), 4.20(2H,q,J=7.2), 4.49(2H,s), 4.83(2H,s), 5.49(2H,s), 7.42(1H,br), 7.49(1H,br), 7.54(1H,s), 8.52(1H,s), 9.15(1H,brs), 9.83(1H,brs).

Example 645

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-isopropoxy-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.33(6H,d,J=6.0Hz), 1.39(9H,s), 1.44(3H,t,J=7.2Hz), 2.85(3H,d,J=4.8Hz), 4.30(2H,q,J=7.2Hz), 4.64(2H,s), 4.75(1H,m), 4.87(2H,s), 5.53(2H,s), 7.53(1H,d,J=2.0Hz), 7.54(1H,d,J=2.0Hz), 8.22(1H,m), 8.59(1H,s), 9.28(1H,m), 9.89(1H,s).

Example 646

{2-*tert*-Butyl-6-cyclopentyloxy-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.44(3H,t,J=6.8Hz), 1.63(2H,m), 1.69-1.83(4H,m), 1.95(2H,m), 2.85(3H,d,J=4.8Hz), 4.30(2H,q,J=6.8Hz), 4.59(2H,s), 4.87(2H,s), 4.93(1H,m), 5.55(2H,s), 7.48(1H,d,J=2.0Hz), 7.54(1H,d,J=2.0Hz), 8.22(1H,m), 8.59(1H,s), 9.88(1H,s).

Example 647

7-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoxazol-2-yl-cyanamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(3H,t,J=7Hz), 1.48(3H,t,J=7Hz), 1.51(9H,s), 4.20(2H,q,J=7Hz), 4.25(2H,J=7Hz), 4.85(2H,s), 5.52(2H,s), 7.22(1H,s), 7.91(2H,d,J=2Hz), 8.11(2H,J=2Hz).

MS:m/e(ESI)512.0(MH+)

Example 648

Ethyl {2-*tert*-butyl-4-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.23(3H,t,J=6.8Hz), 1.37(9H,s), 1.82-1.91(4H,m), 2.77(3H,d,J=4.4Hz), 2.91(6H,s), 3.04-3.14(4H,m), 4.21(2H,q,J=6.8Hz), 4.49(2H,s), 4.73(2H,s), 5.44(2H,s), 7.15(1H,s), 7.42(1H,s), 7.48(1H,s), 8.06(1H,s), 8.33-8.41(1H,m), 8.93(1H,brs), 9.54(1H,brs).

MS:m/e(ESI)578.3(MH+)

Example 649

Methyl (acetyl-{3-*tert*-butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-amino)-acetate trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.37(9H,s), 2.06(3H,s), 3.67(3H,s), 3.87(3H,s), 3.96(3H,s), 4.40(2H,s), 4.52(2H,s), 4.81(2H,s), 5.41(2H,s), 7.36(1H,s), 7.79(1H,s), 7.94(1H,s), 9.06(1H,s), 9.34(1H,s), 10.90(1H,s).

Example 650

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.33(3H,t,J=7.0Hz), 1.38(9H,s), 2.80(3H,d,J=7.2Hz),

4.26(2H,s), 4.26(2H,q,J=7.0Hz), 4.82(2H,s), 5.38(2H,s), 7.49(1H,d,J=6.0Hz), 7.52(1H,s), 7.73(1H,dd,J=6.0,2.0Hz), 7.77(1H,d,J=2.0Hz), 8.15-8.24(1H,m), 8.55(1H,s), 9.18-9.23(1H,m), 9.78-9.82(1H,m).

Example 651

Ethyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.19(3H,t,J=7.2Hz), 1.40(9H,s), 1.41(3H,t,J=6.8Hz), 2.82(3H,d,J=4.8Hz), 4.12(2H,q,J=7.2Hz), 4.18(2H,d,J=6.4Hz), 4.27(2H,q,J=6.8Hz), 4.82(2H,s), 5.36(2H,s), 5.92(1H,t,J=6.8Hz), 6.57(1H,d,J=8.8Hz), 7.51(1H,s), 7.72(1H,dd,J=8.8,2.0Hz), 8.20(1H,q,J=4.8Hz), 8.54(1H,s).

Example 652

2-[2-(8-*tert*-Butyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4,4Hz), 4.30(2H,q,J=6.8Hz), 4.72(2H,s), 4.86(2H,s), 5.47(2H,s), 7.44(1H,d,J=2.0Hz), 7.56(2H,s), 8.22(1H,q,J=4.4Hz), 8.58(1H,s), 9.20(1H,s), 9.86(1H,s), 10.95(1H,s).

Example 653

2-[2-(8-*tert*-Butyl-4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.44(3H,t,J=6.8Hz), 2.85(3H,d,J=4.8Hz), 3.37(3H,s), 4.30(2H,q,J=6.8Hz), 4.78(2H,s), 4.88(2H,s), 5.56(2H,s), 7.56(1H,s), 7.64(1H,d,J=1.6Hz), 7.66(1H,d,J=1.6Hz), 8.23(1H,q,J=4.8Hz), 8.58(1H,s), 9.24(1H,s), 9.88(1H,s).

Example 654

2-[2-(8-*tert*-Butyl-4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 2.79(3H,d,J=4.8Hz), 2.92(3H,s), 2.93(6H,s), 4.35(2H,t,J=4.4), 4.75(2H,s), 5.43(2H,s), 7.16(1H,s), 7.18(1H,d,J=2.0Hz), 7.29(1H,d,J=2.0Hz), 8.08(1H,s), 8.39(1H,q,J=4.8Hz), 8.99(1H,s), 9.53(1H,s).

Example 655

4-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=7.2Hz), 1.85-1.94(4H,m), 1.97-2.06(2H,m), 2.36-2.44(2H,m), 2.82(3H,d,J=4.8Hz), 3.07-3.16(4H,m), 3.85(2H,t,J=6.8Hz), 4.27(2H,q,J=7.2Hz), 4.83(2H,s), 5.41-5.50(2H,m), 7.36(1H,s), 7.46(1H,s), 7.53(1H,s), 8.16-8.24(1H,m), 8.55(1H,m).

MS:m/e(ESI)579.4(MH+)

Example 656

4-{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.35-1.42(12H,m), 1.82-1.92(4H,m), 1.94-2.08(2H,m), 2.41(2H,t,J=7.2Hz), 3.06-3.16(4H,m), 3.60-3.80(2H,m), 4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.78(2H,s), 5.46(2H,s), 7.33(1H,s), 7.35(1H,d,J=2.4Hz), 7.45(1H,d,J=2.4Hz).

MS:m/e(ESI)584.4(MH+)

Example 657

5-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.41(3H,t,J=6.8Hz), 1.60-1.70(2H,m), 1.75-1.84(2H,m), 1.86-1.94(4H,m), 2.29(2H,t,J=7.2Hz),

2.82(3H,d,J=4.8Hz), 3.08-3.17(4H,m), 3.78-3.92(2H,m), 4.27(2H,q,J=6.8Hz), 4.83(2H,s), 5.47(2H,s), 7.36(1H,s), 7.46(1H,s), 7.53(1H,s), 8.03-8.27(1H,m), 8.55(1H,s), 9.15(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)593.4(MH+)

Example 658

5-{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=6.8Hz), 1.33-1.46(12H,m), 1.60-1.71(2H,m), 1.75-1.84(2H,m), 1.85-1.96(4H,m), 2.29(2H,t,J=7.2Hz), 3.07-3.18(4H,m), 3.76-3.93(2H,m), 4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.78(2H,s), 5.46(2H,s), 7.33(1H,s), 7.35(1H,s), 7.45(1H,s), 9.06(1H,brs), 9.28(1H,brs).

MS:m/e(ESI)598.4(MH+)

Example 659

Ethyl {2-*tert*-butyl-4-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.23(3H,t,J=7.0Hz), 1.26-1.44(12H,m), 1.87(4H,brs), 2.77(3H,s), 3.11(4H,brs), 4.14-4.30(4H,m), 4.49(2H,s), 4.87(2H,s), 5.55(2H,s), 7.42(1H,s), 7.49(1H,s), 8.53(1H,brd), 9.46(1H,brs), 9.97(1H,brs).

Example 660

[2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(2-oxo-pyrrolidin-1-yl)-phenoxy]-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.27-1.46(12H,m), 2.02-2.16(2H,m), 2.42(2H,d,J=8.1Hz), 2.82(3H,d,J=4.5Hz), 3.63(2H,t,J=7.0Hz), 4.27(2H,q,J=6.8Hz), 4.45(2H,s), 4.85(2H,s), 5.45(2H,s), 7.54(1H,s), 7.84(2H,s), 8.17-8.23(1H,m), 8.55(1H,s).

Example 661

[2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(2-oxo-pyrrolidin-1-yl)-phenoxy]-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.26(3H,t,J=7.1Hz), 1.33-1.45(12H,m), 2.04-2.17(2H,m), 2.42(2H,t,J=8.0Hz), 3.63(2H,brt,J=6.2Hz), 4.11(2H,q,J=7.1Hz), 4.21(2H,q,J=7.1Hz), 4.43(2H,s), 4.80(2H,s), 5.45(2H,s), 7.34(1H,s), 7.82(1H,s), 7.83(1H,s).

Example 662

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carbonitrile hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(18H,s), 1.33(3H,t,J=7Hz), 4.18(2H,q,J=7Hz),

4.71(2H,s), 5.39(2H,s), 7.06(1H,s), 7.65(2H,s),
8.53(1H,s).
MS:m/e(ESI)448.0(MH+)

Example 663

7-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-1H-benzimidazol-2-yl-cyanamide hydrochloride

1H-NMR(DMSO-d6)δ:
1.38(3H,t,J=7Hz), 1.45(3H,t,J=7Hz), 1.54(9H,s),
4.18(2H,q,J=7Hz), 4.26(2H,q,J=7Hz), 4.92(2H,s),
5.59(2H,s), 7.23(2H,s), 8.06(1H,s), 8.22(1H,s).
MS:m/e(ESI)511.0(MH+)

Example 664

2-[2-(8-*tert*-Butyl-4-methyl-2-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(9H,s), 1.44(3H,t,J=6.8Hz), 2.77(3H,s),
2.85(3H,d,J=4.8Hz), 3.61(2H,s), 4.30(2H,q,J=6.8Hz),
4.86(2H,s), 5.47(2H,s), 7.56(1H,s), 7.67(1H,d,J=2.0Hz),
7.86(1H,d,J=2.0Hz), 8.22(1H,m), 8.59(1H,s).

Example 665

3-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoylamino}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.42(3H,t,J=6.8Hz), 2.50(2H,t,J=6.8Hz),

3.42(2H,t,J=6.8Hz), 4.28(2H,t,J=6.8Hz), 4.88(2H,s),

5.51(2H,s), 7.32(1H,d,J=8.0Hz), 7.54(1H,s),

7.85(1H,t,J=7.6Hz), 8.00(1H,s), 8.21(1H,d,J=4.8Hz),

8.52(1H,t,J=5.2), 8.57(1H,s), 9.28(1H,brs),

9.87(1H,brs).

MS:m/e(ESI)523.3(MH+)

Example 666

2-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoylamino}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.17-1.44(15H,m), 2.83(3H,d,J=4.4Hz),

4.28(2H,q,J=6.8Hz), 4.39-4.42(1H,m), 4.88(2H,s),

5.51(2H,s), 7.40(1H,d,J=7.6Hz), 7.54(1H,s),

7.88(1H,d,J=9.6Hz), 8.01(1H,s), 8.21(1H,d,J=4.4Hz),

8.57(1H,s), 8.81(1H,d,J=7.6Hz), 9.28(1H,brs),

9.86(1H,brs).

MS:m/e(ESI)523.3(MH+)

Example 667

{2-Cyclopentyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=7.2Hz), 1.52-1.69(4H,m), 1.70-1.80(2H,m),

1.93-2.05(2H,m), 2.82(3H,d,J=4.0Hz),
4.28(2H,q,J=7.2Hz), 4.85(2H,s), 4.87(2H,s), 5.44(2H,s),
7.05(1H,d,J=8.8Hz), 7.53(1H,s), 7.83(1H,s), 7.85(1H,s),
8.21(1H,d,J=4.0Hz), 8.55(1H,s), 9.21(1H,brs),
9.83(1H,brs).
MS:m/e(ESI)494.4(MH+)

Example 668

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-dimethylamino-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.28(3H,t,J=7.2Hz), 1.38(9H,s), 1.40(3H,t,J=7.2Hz),
2.70(6H,s), 4.12(2H,q,J=7.2Hz), 4.21(2H,q,J=7.2Hz),
4.66(2H,s), 4.79(2H,s), 5.49(2H,s), 7.34(1H,s),
7.51(1H,s), 7.57(1H,s), 9.06(1H,brs), 9.30(1H,brs).
MS:m/e(ESI)530.3(MH+)

Example 669

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-diethylamino-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
0.95(6H,t,J=7.2Hz), 1.29(3H,t,J=6.8Hz), 1.37(9H,s),
1.39(3H,t,J=6.8Hz), 3.10(4H,q,J=7.2Hz),
4.13(2H,q,J=6.8Hz), 4.21(2H,q,J=6.8Hz), 4.72(2H,s),
4.79(2H,s), 5.47(2H,s), 7.34(1H,s), 7.52(1H,s),
7.59(1H,s), 9.05(1H,brs), 9.29(1H,brs).

MS:m/e(ESI)558.4(MH+)

Example 670

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.42(3H,t,J=7Hz), 1.95-2.03(2H,m), 2.25-2.31(2H,m), 2.83(3H,d, J=5Hz), 4.03-4.08(2H,m), 4.28(2H,q,J=7Hz), 4.83(2H,s), 5.45(2H,s), 7.43(1H,s), 7.51(1H,s), 7.52(1H,s), 8.20(1H,q,J=5Hz), 8.53(1H,s), 9.17(brs, 1H), 9.46(s, 1H).

Example 671

Ethyl {2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-dimethylamino-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.23(3H,t,J=6.8Hz), 1.29(3H,t,J=7.2Hz), 1.37-1.41(12H,m), 2.67(6H,s), 4.10(4H,q,J=6.8Hz), 4.20(4H,q,J=7.2Hz), 4.73(2H,s), 4.75(2H,s), 5.45(1H,s), 7.31(1H,s), 7.54(1H,s), 7.58(1H,s), 9.07(1H,brs), 9.39(1H,brs).

MS:m/e(ESI)558.4(MH+)

Example 672

Ethyl {2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-

diethylamino-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

0.94(6H,t,J=7.2Hz), 1.23(3H,t,J=7.2Hz),

1.29(3H,t,J=7.2Hz), 1.37(9H,s), 1.39(6H,t,J=7.2Hz),

3.07(4H,q,J=7.2), 4.11(2H,q,J=7.2Hz),

4.20(4H,q,J=7.2Hz), 4.80(4H,s), 5.52(2H,s), 7.34(1H,s),

7.54(1H,s), 7.60(1H,s), 9.07(1H,brs), 9.39(1H,brs).

MS:m/e(ESI)586.3(MH+)

Example 673

{2-*tert*-Butyl-4-[2-(5-ethoxy-6-ethylcarbamoyl-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.13(3H,t,J=7.2Hz), 1.38(9H,s), 1.42(3H,t,J=7.2Hz),

1.85-1.93(4H,m), 3.06-3.15(4H,m), 4.25(2H,q,J=7.2Hz),

4.40(2H,s), 4.84(2H,s), 5.51(2H,s), 7.41(1H,s),

7.48(1H,s), 7.52(1H,s), 8.23(1H,tJ=4.8Hz), 8.51(1H,s),

9.21(1H,brs), 9.85(1H,brs).

MS:m/e(ESI)565.4(MH+)

Example 674

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-propylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

0.93(3H,t,J=7.2Hz), 1.38(9H,s), 1.41(3H,t,J=7.2Hz),

1.49-1.57(2H,m), 1.85-1.92(4H,m), 3.06-3.15(4H,m),

3.21-3.29(2H,m), 4.25(2H,q,J=7.2Hz), 4.40(2H,s),
4.83(2H,s), 5.51(2H,s), 7.41(1H,s), 7.48(1H,s),
7.52(1H,s), 8.22(1H,t,J=4.8Hz), 8.50(1H,s),
9.22(1H,brs), 9.86(1H,brs).

MS:m/e(ESI)579.4(MH+)

Example 675

Ethyl {2-*tert*-butyl-4-[2-(5-ethoxy-6-ethylcarbamoyl-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:
1.13(3H,t,J=7.2Hz), 1.23(3H,t,J=7.2Hz), 1.38(9H,s),
1.41(3H,t,J=7.2Hz), 1.84-1.91(4H,m), 3.06-3.14(4H,m),
4.17-4.28(4H,m), 4.49(2H,s), 4.83(2H,s), 5.52(2H,s),
7.43(1H,s), 7.49(1H,s), 7.52(1H,s), 8.23(1H,t,J=4.8Hz),
8.52(1H,s), 9.24(1H,brs), 9.86(1H,brs).

MS:m/e(ESI)593.4(MH+)

Example 676

Ethyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-propylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-pyrrolidin-1-yl-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:
0.92(3H,t,J=7.2Hz), 1.23(3H,t,J=7.2Hz), 1.38(9H,s),
1.41(3H,t,J=7.2Hz), 1.50-1.58(2H,m), 1.84-1.92(4H,m),
3.07-3.14(4H,m), 3.21-3.28(2H,m), 4.17-4.28(4H,m),
4.49(2H,s), 4.84(2H,s), 5.50(2H,s), 7.43(1H,s),
7.49(1H,s), 7.52(1H,s), 8.22(1H,t,J=4.8Hz), 8.50(1H,s),

9.19(1H,brs), 9.84(1H,brs).

MS:m/e(ESI)607.4(MH+)

Example 677

Ethyl 1-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-5-oxo-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(6H,t,J=7Hz), 1.39(9H,s), 2.29-2.35(1H,m), 2.54-2.75(2H,m), 2.95(1H,dd,J=12,9Hz), 3.20(3H,d,J=5Hz), 4.15-4.28(3H,m), 4.35(2H,q,J=7Hz), 4.54(1H,d,J=19Hz), 5.30(1H,d,J=11Hz), 5.40(1H,d,J=19Hz), 5.33(1H,d,J=11Hz), 7.17(1H,s), 7.20(1H,s), 7.95(1H,d,J=2Hz), 8.17(1H,q,J=5Hz), 8.38(1H,s), 8.78(1H,d,J=2Hz), 9.45(1H,brs), 10.02(1H,br.2), 10.08(1H,brs).

MS:m/e(ESI)579.0(MH+)

Example 678

Ethyl 1-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-5-oxo-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7Hz), 1.41(3H,t,J=7Hz), 1.42(9H,s), 1.54(3H,t,J=7Hz), 2.24-2.31(1H,m), 2.58(1H,ddd,J=14,8,3Hz), 2.66(td,J=14,5Hz), 2.93(1H,ddd,J=14,11,8Hz), 4.16-4.28(7H,m),

4.70(1H,d,J=19Hz), 5.05(1H,d,J=19z), 5.17(1H,d,J=19Hz), 5.32(1H,d,J=19Hz), 6.88(1H,s), 7.93(1H,d,J=2Hz), 8.35(1H,d,J=2Hz), 8.83(1H,s).

MS:m/e(ESI)584.0(MH+)

Example 679

Ethyl 1-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-5-oxo-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.18(3H,t,J=7Hz), 1.42(9H,s), 1.60(3H,t,J=7Hz), 2.32-2.36(1H,m), 2.54-2.67(2H,m), 2.77-2.84(1H,m), 3.16(3H,d,J=5Hz), 3.80(3H,s), 4.11-4.22(2H,m), 4.36(2H,q,J=7Hz), 4.74(1H,d,J=19Hz), 4.75(1H,m), 4.93(1H,d,J=19Hz), 5.69(1H,d,J=18Hz), 6.56(1H,d,J=18Hz), 7.21(1H,s), 7.25(1H,s), 8.05(1H,d,J=2Hz), 8.13(1H,d,J=2Hz), 8.19(1H,q,J=5Hz), 9.48(1H,s).

MS:m/e(ESI)593.0(MH+)

Example 680

Ethyl 1-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-5-oxo-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.18(3H,t,J=7Hz), 1.42(3H,t,J=7Hz), 1.43(9H,s), 1.54(3H,t,J=7Hz), 2.31-2.36(1H,m), 2.54-2.65(2H,m),

2.76-2.84(1H,m), 3.81(3H,s), 4.15-4.23(6H,m),
4.65(1H,d,J=18Hz), 4.74(1H,dt,J=2,6Hz),
4.86(1H,d,J=18Hz), 5.61(1H,d,J=19Hz), 6.87(1H,s),
6.98(1H,brs), 8.03(1H,d,J=2Hz), 8.11(1H,d,J=2Hz).
MS:m/e(ESI)593.0(MH+)

Example 681

2-[2-(3,5-Di-*tert*-butyl-4-hydroxy-phenyl)-2-oxo-ethyl]-7-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.40(3H,t,J=6.8Hz), 1.44(18H,s), 2.86(3H,d,J=4.4Hz),
4.30(2H,q,J=6.8Hz), 4.83(2H,s), 5.50(2H,s), 7.77(2H,s),
7.81(1H,s), 8.34(1H,s), 8.72(1H,m).

Example 682

2-[2-(5-*tert*-Butyl-2-oxo-1,2,3,4-tetrahydro-quinolin-7-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.43(12H,m), 2.45(2H,t,J=7.2Hz), 2.84(3H,d,J=4.8Hz),
3.18(2H,t,J=7.2Hz), 4.30(2H,q,J=6.8Hz), 4.87(2H,s),
5.47(2H,s), 7.41(1H,d,J=1.6Hz), 7.56(1H,s),
7.61(1H,d,J=1.6Hz), 8.23(1H,q,J=4.8Hz), 8.58(1H,s),
9.22(1H,s), 9.86(1H,s), 10.33(1H,s).

Example 683

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-

isoindole-5-carboxamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.42(3H,t,J=6.8Hz), 1.93-2.04(2H,m), 2.28(2H,t,J=7.2Hz), 4.05(2H,t,J=6.8Hz), 4.28(2H,q,J=6.8Hz), 4.84(2H,s), 5.45(2H,s), 6.83(1H,brs), 7.33(1H,brs), 7.44(1H,s), 7.52(1H,s), 7.53(1H,s), 7.70(1H,brs), 7.78(1H,brs), 8.63(1H,s), 9.18(1H,brs), 9.46(1H,s), 9.82(1H,brs).

MS:m/e(ESI)511.3(MH+)

Example 684

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid dimethylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29-1.46(12H,m), 1.93-2.06(2H,m), 2.23-2.33(2H,m), 2.78(3H,s), 2.99(3H,s), 4.01-4.12(2H,m), 4.17-4.28(2H,m), 4.83(3H,s), 5.45(3H,s), 6.83(1H,brs), 7.33(1H,brs), 7.44(1H,s), 7.49(1H,s), 7.52(1H,s), 8.03(1H,s), 9.16(1H,brs), 9.46(1H,brs), 9.67(1H,brs).

MS:m/e(ESI)539.4(MH+)

Example 685

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.93-2.04(2H,m), 2.23-2.33(2H,m),

2.77(3H,d,J=4.4Hz), 2.93(6H,s), 4.01-4.09(2H,m),

4.73(2H,s), 5.40(2H,s), 7.14(1H,s), 7.43(1H,d,J=2.0Hz),

7.51(1H,d,J=2.0Hz), 8.06(1H,s), 8.34-8.39(1H,m),

8.86(1H,brs), 9.44(1H,brs), 9.52(1H,brs).

Example 686

4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenoxy}-butylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=6.8Hz), 1.34-1.46(12H,m), 1.94-2.04(2H,m),

2.24-2.32(2H,m), 4.00-4.08(2H,m), 4.11(2H,q,J=6.8Hz),

4.21(2H,q,J=6.8Hz), 4.78(2H,s), 5.45(2H,s),

6.82(1H,brs), 7.28-7.36(2H,m), 7.42(1H,s), 7.50(1H,s),

9.00-9.08(1H,m), 9.32(1H,brs), 9.46(1H,s).

Example 687

4-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenoxy}-butylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(9H.s), 1.92-2.05(2H,m), 2.23-2.34(2H,m),

3.86(3H,s), 3.95(3H,s), 4.01-4.09(2H,m), 4.81(2H,s),

5.46(2H,s), 6.83(1H,brs), 7.31-7.38(2H,m), 7.42(1H,s),

7.50(1H,s), 9.04-9.11(1H,m), 9.30-9.38(1H,m),

9.46(1H,s).

Example 688

4-{3-*tert*-Butyl-5-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenoxy}-butylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7.2Hz), 1.40(9H,s), 1.94-2.05(2H,m), 2.24-2.34(2H,m), 2.95(2H,q,J=7.2Hz), 4.01-4.11(2H,m), 4.85(2H,s), 5.53(2H,s), 6.82(1H,brs), 7.34(1H,brs), 7.44(1H,s), 7.51(1H,s), 7.73(1H,d,J=8.0Hz), 8.18(1H,d,J=8.0Hz), 9.46(1H,brs), 9.52-9.60(1H,m), 9.82-9.90(1H,m).

Example 689

4-{3-*tert*-Butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenoxy}-butylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.03-1.13(4H,m), 1.41(9H,s), 1.94-2.05(2H,m), 2.24-2.38(3H,m), 4.01-4.09(2H,m), 4.82(2H,s), 5.53(2H,s), 6.83(1H,brs), 7.35(1H,brs), 7.44(1H,s), 7.52(1H,s), 7.72(1H,d,J=8.0Hz), 8.10(1H,d,J=8.0Hz), 9.47(1H,brs), 9.48-9.56(1H,m), 9.62-9.70(1H,m).

Example 690

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-3-imino-6-propoxy-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

0.99(3H,t,J=7.2Hz), 1.41(9H,s), 1.75-1.87(2H,m), 1.93-2.02(2H,m), 2.24-2.32(2H,m), 2.82(3H,d,J=4.4Hz), 4.02-4.08(2H,m), 4.13-4.20(2H,m), 4.83(2H,s), 5.46(2H,s), 6.83(1H,brs), 7.34(1H,brs), 7.42(1H,s), 7.51(1H,s), 7.54(1H,s), 8.15-8.21(1H,m), 8.52(1H,s), 9.18(1H,brs), 9.46(1H,brs), 9.82(1H,brs).

Example 691

{6-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-4,4-dimethyl-3,4-dihydro-2H-quinolin-1-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.26(6H,s), 1.41(3H,t,J=7.2Hz), 1.68-1.74(2H,m), 2.82(3H,d,J=4.8Hz), 3.38-3.46(2H,m), 4.21(2H,s), 4.27(2H,q,J=7.2Hz), 4.83(2H,s), 5.35(2H,s), 6.57(1H,d,J=8.0Hz), 7.52(1H,s), 7.63(1H,d,J=8.0Hz), 7.75(1H,s), 8.20(1H,q,J=4.8Hz), 8.55(1H,s), 9.18(1H,brs), 9.78(1H,brs).

MS:m/e(ESI)493.3(MH+)

Example 692

{6-[2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-4,4-dimethyl-3,4-dihydro-2H-quinolin-1-yl}-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.26(6H,s), 1.29(3H,t,J=7.2Hz), 1.39(3H,t,J=7.2Hz), 1.68-1.74(2H,m), 3.38-3.45(2H,m), 4.07-4.22(4H,m),

4.20(2H,s), 4.77(2H,s), 5.35(2H,s), 6.57(1H,d,J=8.4Hz), 7.31(1H,s), 7.61(1H,d,J=8.4Hz), 7.75(1H,s), 8.99(1H,brs), 9.33(1H,brs).

MS:m/e(ESI)498.3(MH+)

Example 693

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-piperidin-1-yl-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.43(3H,t,J=7Hz), 1.49-1.57(2H,m), 1.63-1.70(4H,m), 2.85(3H,d,J=5Hz), 2.88-2.98(4H,m), 4.30(2H,q,J=7Hz), 4.85(2H,s), 4.87(2H,s), 5.52(2H,s), 7.56(1H,s), 7.58(1H,s), 7.63(1H,s), 8.23(1H,q,J=5Hz), 8.58(1H,s), 9.22(1H,brs), 9.87(1H,brs).

Example 694

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-morpholino-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.43(3H,t,J=7Hz), 2.85(3H,d,J=5Hz), 2.95-3.03(4H,m), 3.61-3.68(4H,m), 4.29(2H,q,J=7Hz), 4.82(2H,s), 4.87(2H,s), 5.52(2H,s), 7.56(1H,s), 7.58(1H,s), 7.63(1H,s), 8.23(1H,q,J=5Hz), 8.57(1H,s), 9.22(1H,brs), 9.87(1H,brs).

Example 695

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-

dihydro-isoindol-2-yl)-acetyl]-6-piperidin-1-yl-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7Hz), 1.38(9H,s), 1.42(3H,t,J=7Hz), 1.50-1.57(2H,m), 1.63-1.71(4H,m), 2.88-2.97(4H,m), 4.13(2H,q,J=7Hz), 4.23(2H,q,J=7Hz), 4.80(2H,s), 4.86(2H,s), 5.50(2H,s), 7.35(1H,s), 7.56(1H,s), 7.62(1H,s), 9.07(1H,brs), 9.32(1H,brs).

Example 696

{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-morpholino-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7Hz), 1.39(9H,s), 1.42(3H,t,J=7Hz), 2.95-3.03(4H,m), 3.71-3.78(4H,m), 4.13(2H,q,J=7Hz), 4.23(2H,q,J=7Hz), 4.80(2H,s), 4.82(2H,s), 5.52(2H,s), 7.35(1H,s), 7.56(1H,s), 7.65(1H,s), 9.07(1H,brs), 9.33(1H,brs).

Example 697

Ethyl 4-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.16(3H,t,J=6.5Hz), 1.32-1.46(12H,m), 1.95-2.08(2H,m), 2.57(2H,t,J=7.0Hz), 2.83(3H,d,J=5.0Hz), 4.00-4.10(4H,m), 4.26(H,q,J=6.5Hz), 4.83(2H,s), 5.45(2H,s),

7.40(1H,brs), 7.48-7.55(2H,m), 8.19(1H,5.0Hz), 8.54(1H,s).

Example 698

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.40(3H,t,J=7.0Hz), 1.94-2.08(2H,m), 2.28(2H,t,J=7.5Hz), 2.82(3H,s), 3.89(3H,s), 4.06(2H,t,J=5.5Hz), 4.26(2H,q,J=7.0Hz), 4.84(2H,s), 5.50(2H,s), 6.80(1H,brs), 7.37(1H,brs), 7.48-7.55(3H,m), 8.17-8.25(1H,m), 8.55(1H,s), 9.25(1H,brs), 9.88(1H,brs).

Example 699

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 1.42(3H,t,J=7.0Hz), 1.94-2.07(2H,m), 2.24-2.31(2H,m), 3.90(3H,s), 4.07(2H,t,J=6.5Hz), 4.27(2H,q,J=7.0Hz), 4.84(2H,s), 5.49(2H,s), 6.80(1H,brs), 7.37(1H,brs), 7.48-7.54(3H,m), 8.63(1H,s).

Example 700

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-dimethylamino-3-imino-2,3-

dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.93-2.08(2H,m), 2.24-2.35(2H,m), 2.76(3H,brs), 2.82(6H,s), 3.89(3H,s), 4.03-4.12(2H,m), 4.74(2H,s), 5.47(2H,s), 6.80(1H,brs), 7.14(1H,s), 7.36(1H,brs), 7.48-7.56(2H,m), 8.07(1H,s), 8.31-8.42(1H,m), 9.01(1H,brs), 9.57(1H,brs).

Example 701

4-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.26(3H,t,J=7.0Hz), 1.34(9H,s), 1.40(3H,t,J=7.0Hz), 1.94-2.07(2H,m), 2.27(2H,t,J=6.5Hz), 3.88(3H,s), 4.02-4.15(4H,m), 4.21(2H,q,J=7.0Hz), 4.79(2H,s), 5.48(2H,s), 7.32(1H,s), 7.50(1H,s), 7.51(1H,s).

Example 702

4-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.35(9H,s), 1.40(3H,t,J=7.0Hz), 1.94-2.08(2H,m), 2.26(2H,t,J=6.5Hz), 3.86(3H,s), 3.89(3H,s), 3.92(3H,s), 4.06(2H,t,J=5.5Hz), 4.80(2H,s), 5.50(2H,s), 6.80(1H,brs), 7.34-7.39(2H,m), 7.50(1H,s), 7.51(1H,s),

9.10(1H,brs), 9.38(1H,brs).

Example 703

4-{3-*tert*-Butyl-5-[2-(2-ethyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-methoxy-phenoxy}-butylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7.5Hz), 1.35(9H,s), 1.94-2.08(2H,m), 2.27(2H,t,J=7.0Hz), 2.94(2H,q,J=7.5Hz), 3.89(3H,s), 4.06(2H,t,J=5.5Hz), 4.85(2H,s), 5.56(2H,s), 6.80(1H,brs), 7.37(1H,brs), 7.50(2H,brs), 7.72(1H,d,J=8.0Hz), 8.18(1H,d,J=8.0Hz), 9.56(1H,brs), 9.88(1H,brs).

Example 704

4-{3-*tert*-Butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-methoxy-phenoxy}-butylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.05-1.12(4H,m), 1.35(9H,s), 1.94-2.07(2H,m), 2.23-2.36(3H,m), 3.89(3H,s), 4.06(2H,t,J=5.5Hz), 4.82(2H,s), 5.55(2H,s), 6.80(1H,brs), 7.36(1H,brs), 7.51(2H,brs), 7.72(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.48-9.55(1H,m), 9.64-9.72(1H,m).

Example 705

2-{2-[3-*tert*-Butyl-5-(3-carbamoyl-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid ethylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.11(3H,t,J=6.0Hz), 1.24-1.45(12H,m), 1.96-2.07(2H,m), 2.22-2.33(2H,m), 3.23-3.39(2H,m), 3.89(3H,s), 4.02-4.12(2H,m), 4.19-4.30(2H,m), 4.83(2H,s), 5.49(2H,s), 6.80(1H,brs), 7.35(1H,brs), 7.51(3H,brs), 8.23(1H,brs), 8.52(1H,s), 9.21(1H,brs), 9.84(1H,brs).

Example 706

Methyl 4-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-1-methyl-1H-benzimidazole-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.54(9H,s), 1.62(3H,t,J=7Hz), 3.21(3H,d,J=5Hz), 4.06(3H,s), 4.37(2H,q,J=7Hz), 4.38(3H,s), 5.04(2H,s), 6.32(2H,s), 7.21(1H,s), 7.25(1H,s), 7.84(1H,d,J=2Hz), 8.22(1H,q,J=5Hz), 8.93(1H,d,J=2Hz), 9.56(1H,s), 10.44(1H,s).

MS:m/e(ESI)520.0(MH+)

Example 707

Ethyl 4-{2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.21(3H,t,J=7Hz), 1.38(9H,s), 1.44(3H,t,J=7Hz), 2.01-2.09(2H,m), 2.48-2.57(2H,m), 2.85(3H,d,J=5Hz), 3.88(3H,s), 4.07-4.13(2H,m), 4.09(2H,q,J=7Hz), 4.30(2H,q,J=7Hz), 4.87(2H,s), 5.55(2H,s), 7.53(1H,s),

7.56(1H,s), 7.58(1H,s), 8.22(1H,q,J=5Hz), 8.58(1H,s), 9.25(1H,brs), 9.87(1H,brs).

Example 708

Ethyl 4-{2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.20(3H,t,J=7Hz), 1.32(3H,t,J=7Hz), 1.38(9H,s), 1.42(3H,t,J=7Hz), 2.00-2.09(2H,m), 2.50-2.56(2H,m), 3.88(3H,s), 4.09(2H,q,J=7Hz), 4.13(2H,q,J=7Hz), 4.23(2H,q,J=7Hz), 4.80(2H,s), 5.71(2H,s), 7.35(1H,s), 7.52(1H,s), 7.56(1H,s).

Example 709

{2-*tert*-Butyl-4-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 2.78(3H,d,J=4.8Hz), 2.92(6H,s), 4.04-4.10(2H,m), 4.72(2H,s), 5.32(2H,s), 6.57(1H,d,J=8.4Hz), 7.14(1H,s), 7.73(1H,dd,J=8.4,2.0Hz), 7.77(1H,d,J=2.0Hz), 8.05(1H,s), 8.36(1H,t,J=4.8Hz), 8.90-8.94(1H,m), 9.45-9.50(1H,m).

Example 710

Ethyl 5-*tert*-butyl-7-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-1H-benzo[d]pyrrolo[2,1-b]oxazole-3a-

carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(3H,J=7Hz), 1.40(9H,s), 1.61(3H,t,J=7Hz),

1.91(1H,m), 2.05(1H,m), 2.27(1H,ddd,J=13,7,6Hz),

2.72(1H,ddd,J=13,7,6Hz), 3.12(3H,d,J=5Hz),

3.44(1H,ddd,J=15,7,6Hz), 3.58(1H,ddd,J=15,7,6Hz),

4.23(1H,dq,J=10,7Hz), 4.25(1H,dq,J=10,7Hz),

4.45(2H,brs), 4.71(1H,d,J=18Hz), 4.99(1H,d,J=18Hz),

5.70(1H,d,J=19Hz), 6.46(1H,d,J=19Hz), 7.34(1h,s),

7.56(1H,s), 7.72(1H,s), 8.30(1H,q,J=5Hz), 9.50(1H,s),

10.19(1H,brs), 10.36(1H,brs).

MS:m/e(ESI)563.0(MH+)

Example 711

Ethyl 3-{4-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-1-methyl-1H-benzimidazol-2-yl}-propanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.20(3H,t,J=7Hz), 1.28(3H,t,J=7Hz), 1.57(9H,s),

3.03(2H,t,J=7Hz), 3.18(2H,t,J=7Hz), 3.19(3H,d,J=5Hz),

3.92(3H,s), 4.17(2H,q,J=7Hz), 4.37(2H,q,J=7Hz),

5.04(2H,s), 6.24(2H,s), 7.20(1H,s), 7.76(1H,s),

8.04(1H,q,J=5Hz), 8.67(1H,s), 9.56(1H,s),

10.21(1H,brs), 10.32(1H,brs).

MS:m/e(ESI)562.0(MH+)

Example 712

{2-*tert*-Butyl-6-dimethylamino-4-[2-(7-fluoro-1-imino-

5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 2.70(6H,s), 3.87(3H,s), 3.95(3H,s), 4.66(2H,s), 4.80(2H,s), 5.49(2H,s), 7.37(1H,s), 7.51(1H,s), 7.57(1H,s), 9.09(1H,brs), 9.31(1H,brs).

MS:m/e(ESI)502.2(MH+)

Example 713

Ethyl {2-(1-amino-1-methyl-ethyl)-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.224(3H,t,J=7.2Hz), 1.401(3H,t,J=6.8Hz), 1.746(6H,s), 2.813(3H,d,J=4.4Hz), 4.188(2H,q,J=7.2Hz), 4.265(2H,q,J=6.8Hz), 4.852(2H,s), 5.097(2H,s), 5.633(2H,s), 7.269(1H,d,J=8.8Hz), 7.514(1H,s), 7.943(1H,s), 8.048(1H,d,J=8.8Hz), 8.18-8.24(1H,m), 8.560(1H,s), 8.587(2H,s), 9.658(1H,s), 9.999(1H,s).

Example 714

Ethyl {2-(1-amino-1-methyl-ethyl)-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenoxy}-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.223(3H,t,J=7.2Hz), 1.283(3H,t,J=6.8Hz), 1.389(3H,t,J=6.8Hz), 1.759(6H,s), 4.103(2H,q,J=7.2Hz), 4.15-4.24(4H,m), 4.816(2H,s), 5.097(2H,s), 5.676(2H,s),

7.263(1H,d,J=8.8Hz), 7.329(1H,s), 7.954(1H,d,J=2.0Hz), 8.034(1H,dd,J=2.0,8.8Hz), 8.668(2H,s), 9.141(1H,s), 9.765(1H,s).

Example 715

Ethyl {2-*tert*-butyl-4-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenylamino}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.31(3H,t,J=7.2Hz), 1.38(9H,s), 2.77(3H,d,J=4.4Hz), 2.92(6H,s), 3.70-3.82(2H,m), 3.87(2H,s), 4.76(2H,s), 5.36(1H,dd,J=5.6,2.0Hz), 5.46(2H,s), 7.15(1H,s), 7.56(1H,d,J=8.0Hz), 7.92(1H,dd,J=8.0,2.4Hz), 8.01(1H,d,J=2.4Hz), 8.07(1H,s), 8.38(1H,q,J=4.4Hz), 11.69(1H,s).

Example 716

2-{2-[3-*tert*-Butyl-4-(3-carbamoyl-propoxy)-5-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36(9H,s), 1.42(3H,t,J=7Hz), 1.93-2.02(2H,m), 2.21-2.28(2H,m), 3.87(3H,s), 4.03-4.10(2H,m), 4.28(2H,q,J=7Hz), 4.85(2H,s), 5.51(2H,s), 6.78(1H,brs), 7.33(1H,brs), 7.51(1H,s), 7.54(1H,s), 7.56(1H,s), 7.70(1H,brs), 7.78(1H,brs), 8.62(1H,s).

Example 717

4-{2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-

1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenoxy}-butylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7Hz), 1.37(9H,s), 1.39(3H,t,J=7Hz), 1.93-2.02(2H,m), 2.22-2.28(2H,m), 3.87(3H,s), 4.03-4.09(2H,m), 4.11(2H,q,J=7Hz), 4.21(2H,q,J=7Hz), 4.80(2H,s), 5.50(2H,s), 6.78(1H,brs), 7.32(1H,brs), 7.34(1H,s), 7.50(1H,s), 7.54(1H,s).

Example 718

2-{2-[3-*tert*-Butyl-4-(3-carbamoyl-propoxy)-5-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.42(3H,t,J=7Hz), 1.93-2.02(2H,m), 2.21-2.28(2H,m), 2.82(3H,d,J=5Hz), 3.87(3H,s), 4.03-4.10(2H,m), 4.28(2H,q,J=7Hz), 4.85(2H,s), 5.51(2H,s), 6.78(1H,brs), 7.32(1H,brs), 7.51(1H,s), 7.55(1H,s), 7.56(1H,s), 8.21(1H,q, J=5Hz), 8.56(1H,s).

Example 719

[2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(3-hydroxy-pyrrolidin-1-yl)-phenoxy]-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.38(9H,s), 1.40(3H,t,J=6.8Hz), 1.78-1.84(1H,m), 1.97-2.05(1H,m), 2.91(1H,brd,J=10.4Hz), 3.04-3.09(1H,m), 3.21-

3.40(2H,m), 4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.32(2H,ABq,J=16.0Hz), 4.34(1H,br), 4.78(2H,s), 5.49(2H,s), 7.33(1H,s), 7.35(1H,s), 7.44(1H,s).

MS:m/e(ESI)572.4(MH+)

Example 720

[2-*tert*-Butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(3-hydroxy-pyrrolidin-1-yl)-phenoxy]-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.08-1.10(4H,m), 1.38(9H,s), 1.77-1.84(1H,m), 1.99-2.06(1H,m), 2.08-2.16(1H,m), 2.90-2.96(1H,m), 3.03-3.09(1H,m), 3.29-3.40(2H,m), 4.35(1H,br), 4.39(2H,ABq,J=15.6Hz), 4.82(2H,s), 5.57(2H,s), 7.37(1H,d,J=2.0Hz), 7.45(1H,d,J=2.4Hz), 7.72(1H,d,J=8.0Hz), 8.10(1H,d,J=8.0Hz), 9.47(1H,brs), 9.66(1H,brs).

MS:m/e(ESI)507.4(MH+)

Example 721

(1-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.38(9H,s), 1.39(3H,t,J=6.8Hz), 1.94-2.01(1H,m), 2.07-2.14(1H,m), 2.94(1H,brd,J=8.0Hz), 3.01-3.17(2H,m), 3.37-3.42(1H,m), 3.97(2H,s), 4.11(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.25(1H,br),

4.78(2H,s), 5.47(2H,d,J=8.0Hz), 7.32(1H,s), 7.57(1H,s), 7.70(1H,s).

MS:m/e(ESI)572.3(MH+)

Example 722

(1-{3-*tert*-Butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.08-1.10(4H,m), 1.39(9H,s), 1.95-2.01(1H,m), 2.10-2.15(1H,m), 2.28-2.33(1H,m), 2.94(1H,brd,J=7.6Hz), 3.01-3.06(1H,m), 3.09-3.14(1H,m), 3.41(1H,br), 4.00(2H,s), 4.27(1H,br), 4.81(2H,s), 4.53(2H,d,J=6.0Hz), 7.58(1H,s), 7.69(1H,s), 7.71(1H,d,J=8.0Hz), 8.09(1H,d,J=8.4Hz).

MS:m/e(ESI)507.3(MH+)

Example 723

Ethyl 4-{2-*tert*-butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.00-1.14(4H,m), 1.17(3H,d,J=6.8Hz), 1.37(9H,s), 1.80-1.97(4H,m), 1.99-2.12(2H,m), 2.26-2.37(1H,m), 2.43-2.55(2H and DMSO,m), 3.05-3.18(4H,m), 3.75-3.93(2H,m), 4.05(2H,q,J=6.8Hz), 4.81(2H,s), 5.54(2H,s), 7.36(1H,s), 7.46(1H,s), 7.71(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz),

9.46(1H,brs), 9.65(1H,brs).

MS:m/e(ESI)547.4(MH+)

Example 724

Ethyl 5-{2-*tert*-butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.05-1.14(4H,m), 1.16(3H,t,J=6.8Hz), 1.38(9H,s), 1.63-2.00(8H,m), 2.27-2.42(3H,m), 3.06-3.19(4H,m), 3.75-3.93(2H,m), 4.04(2H,q,J=6.8Hz), 4.81(2H,s), 5.54(2H,s), 7.36(1H,s), 7.46(1H,s), 7.71(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.45(1H,brs), 9.65(1H,brs).

MS:m/e(ESI)561.4(MH+)

Example 725

Ethyl 4-{2-*tert*-butyl-4-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=6.8Hz), 1.37(9H,s), 1.82-1.96(4H,m), 1.99-2.11(2H,m), 2.44-2.55(2H and DMSO,m), 3.05-3.18(4H,m), 3.78-3.91(5H,m), 3.95(3H,s), 4.05(2H,q,J=6.8Hz), 4.79(2H,s), 5.47(2H,s), 7.35(1H,s), 7.36(1H,s), 7.45(1H,s).

MS:m/e(ESI)584.3(MH+)

Example 726

Ethyl 5-{2-*tert*-butyl-4-[2-(7-fluoro-1-imino-5,6-

dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoate hydrobromide

1H-NMR(DMSO-d6)δ:

1.16(3H,t,J=6.8Hz), 1.37(9H,s), 1.62-1.99(8H,m), 2.32-2.43(2H,m), 3.03-3.20(4H,m), 3.77-3.92(5H,m), 3.95(3H,s), 4.04(2H,q,J=6.8Hz), 4.79(2H,s), 5.47(2H,s), 7.36(2H,s), 7.45(1H,s), 9.08(1H,brs), 9.29(1H,brs).

MS:m/e(ESI)598.4(MH+)

Example 727

Ethyl 4-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=7.2Hz), 1.36(9H,s), 1.41(3H,t,J=6.8Hz), 2.04-2.08(2H,m), 2.48-2.53(2H,m), 2.82(3H,d,J=4.8Hz), 3.89(3H,s), 4.04-4.12(4H,m), 4.28(2H,q,J=7.2Hz), 4.85(2H,s), 5.51(2H,s), 7.50-7.56(2H,m), 8.21(1H,d,J=5.2Hz), 8.55(1H,s).

MS:m/e(ESI)568.3(MH+)

Example 728

Ethyl 4-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=7.2Hz), 1.29(3H,t,J=7.2Hz), 1.36(9H,s), 1.40(3H,t,J=6.8Hz), 2.03-2.08(2H,m), 2.47-2.53(2H,m),

3.88(3H,s), 4.04-4.14(6H,m), 4.21(2H,q,J=6.8Hz), 4.80(2H,s), 5.48(2H,s), 7.34(1H,s), 7.50(1H,d,J=2.0Hz), 7.52(1H,d,J=2.0Hz).

MS:m/e(ESI)573.3(MH+)

Example 729

Ethyl 4-{3-*tert*-butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenoxy}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.17(3H,t,J=7.2Hz), 1.36(9H,s), 2.05-2.08(2H,m), 2.45-2.54(2H,m), 3.87(3H,s), 3.89(3H,s), 3.96(3H,s), 4.04-4.12(4H,m), 4.81(2H,s), 5.51(2H,s), 7.37(1H,s), 7.48-7.54(2H,m).

MS:m/e(ESI)545.3(MH+)

Example 730

Ethyl 4-{8-*tert*-butyl-6-[2-(5-dimethylamino-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(3H,t,J=7.2Hz), 1.34(9H,s), 1.78-1.85(2H,m), 2.38(2H,t,J=7.2Hz), 2.77(3H,d,J=4.8Hz), 2.91(6H,s), 3.32-3.38(4H,m), 4.04(2H,q,J=7.2Hz), 4.23-4.28(2H,m), 4.74(1H,s), 5.44(1H,s), 7.15(1H,s), 7.22(2H,s), 8.08(1H,s), 8.38(1H,d,J=4.8Hz).

MS:m/e(ESI)578.4(MH+)

Example 731

Ethyl 4-{8-*tert*-butyl-6-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-butyrate hydrobromide

1H-NMR(DMSO-d6)δ:

1.15(3H,t,J=7.2Hz), 1.34(9H,s), 1.78-1.84(2H,m), 2.38(2H,t,J=6.8Hz), 3.30-3.38(4H,m), 3.87(3H,s), 3.98(3H,s), 4.04(2H,q,J=7.2Hz), 4.23-4.28(2H,m), 4.80(1H,s), 5.47(1H,s), 7.21(2H,s), 7.36(1H,s).

MS:m/e(ESI)556.3(MH+)

Example 732

4-({3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-methyl-amino)-butyric acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.16(3H,t,J=7.2Hz), 1.41(9H,s), 1.43(3H,t,J=6.8Hz), 1.65(2H,quint,J=7.2Hz), 2.36(2H,t,J=7.2Hz), 2.56(3H,s), 2.84(3H,d,J=4.4Hz), 2.91(1H,t,J=7.2Hz), 4.03(2H,q,J=7.2Hz), 4.29(2H,q,J=6.8Hz), 4.85(2H,s), 5.48(2H,s), 7.55(1H,s), 7.69(1H,s), 7.77(1H,s), 8.22(1H,q,J=4.4Hz), 8.57(1H,s), 9.22(1H,s), 9.86(1H,s).

Example 733

2-[2-(3-*tert*-Butyl-4-hydroxy-5-{[3-(hydroxymethyl-carbamoyl)-propyl]-methyl-amino}-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic

acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.43(3H,t,J=7.2Hz), 1.62(2H,quint,J=7.2Hz),
2.10(2H,t,J=7.2Hz), 2.57(3H,s), 2.84(3H,d,J=4.8Hz),
2.87(2H,t,J=7.2Hz), 4.29(2H,q,J=7.2Hz),
4.47(2H,t,J=6.0Hz), 4.86(2H,s), 5.46(2H,d),
5.51(1H,t,J=6.0Hz), 7.55(1H,s), 7.68(1H,s), 7.75(1H,s),
8.23(1H,q,J=4.8Hz), 8.46(1H,t,J=6.0Hz), 8.57(1H,s),
9.17(1H,s), 9.83(1H,s).

Example 734

2-[2-(7-*tert*-Butyl-2-methyl-benzoxazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.43(3H,t,J=6.8Hz), 1.49(9H,s), 2.72(3H,s),
2.85(3H,d,J=4.4Hz), 4.30(2H,q,J=6.8Hz), 4.90(2H,s),
5.61(2H,s), 7.57(1H,s), 7.85(1H,d,J=1.2Hz),
8.23(1H,q,J=4.4Hz), 8.28(1H,d,J=1.2Hz), 8.59(1H,s),
9.26(1H,s), 9.89(1H,s).

Example 735

Ethyl {5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-1,3,3-trimethyl-2,3-dihydro-1H-indol-2-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.072(6H,s), 1.202(3H,t,J=7.2Hz), 1.401(3H,t,J=6.8Hz),
2.57-2.74(2H,m), 2.815(3H,d,J=4.8Hz),

3.608(1H,t,J=6.4Hz), 4.116(2H,q,J=7.2Hz),
4.265(2H,d,J=6.8Hz), 4.830(2H,s), 5.381(2H,s),
6.608(1H,d,J=8.4Hz), 7.516(1H,s), 7.612(1H,d,J=1.6Hz),
7.785(1H,dd,J=1.6,8.4Hz), 8.213(1H,q,J=4.8Hz),
8.537(1H,s), 9.224(1H,s), 9.814(1H,s).

Example 736

Ethyl {5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-1,3,3-trimethyl-2,3-dihydro-1H-indol-2-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:
1.072(6H,s), 1.203(3H,t,J=7.2Hz), 1.282(3H,t,J=6.8Hz),
1.387(3H,t,J=6.8Hz), 2.57-2.74(2H,m),
3.606(1H,t,J=6.4Hz), 4.07-4.15(4H,m),
4.201(2H,d,J=7.2Hz), 4.778(2H,s), 5.364(2H,s),
6.606(1H,d,J=8.0Hz), 7.312(1H,s), 7.600(1H,d,J=1.6Hz),
7.785(1H,dd,J=1.6,8.0Hz).

Example 737

({2-*tert*-Butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-methyl-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.29(3H,t,J=7.2Hz), 1.39(3H,t,J=6.8Hz), 1.44(9H,s),
2.62(3H,s), 3.50(2H,s), 4.10(2H,q,J=7.2Hz),
4.20(2H,q,J=6.8Hz), 4.80(2H,s), 5.47(2H,s), 7.33(1H,s),
7.65(1H,d,J=8.4Hz), 7.891H,d,J=8.4Hz), 7.93(1H,s),
9.02-9.10(1H,m), 9.23-9.34(1H,m).

Example 738

Ethyl [2-*tert*-butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(3-hydroxy-pyrrolidin-1-yl)-phenoxy]-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.23(3H,t,J=6.8Hz), 1.37(9H,s), 1.41(3H,t,J=6.8Hz), 1.78-1.84(1H,m), 1.98-2.09(1H,m), 2.73-2.77(1H,m), 2.82(3H,d,J=4.4Hz), 2.78-2.84(1H,m), 2.90-2.97(1H,m), 3.03-3.09(1H,m), 4.21(2H,q,J=6.8Hz), 4.27(2H,q,J=6.8Hz), 4.35(1H,br,), 4.60(2H,s), 4.83(2H,s), 5.56(2H,s), 7.40(1H,s), 7.47(1H,s), 7.53(1H,s), 8.21(1H,brs), 8.56(1H,br), 9.36(1H,br).

MS:m/e(ESI)595.5(MH+)

Example 739

Ethyl [2-*tert*-butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(3-hydroxy-pyrrolidin-1-yl)-phenoxy]-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.08-1.10(4H,m), 1.23(3H,t,J=6.8Hz), 1.38(9H,s), 1.77-1.84(1H,m), 1.97-2.05(1H,m), 2.29-2.35(1H,m), 2.93(1H,brd,J=10.0Hz), 3.02-3.09(1H,m), 3.26-3.42(2H,m), 4.21(2H,q,J=6.8Hz), 4.33(1H,brs), 4.49(2H,ABq,J=15.6Hz), 4.82(2H,s), 5.81(2H,s), 7.40(1H,s), 7.46(1H,s), 7.72(1H,d,J=8.4Hz),

8.09(1H,d,J=8.4Hz), 9.60(1H,br), 9.67(1H,br).

MS:m/e(ESI)535.3(MH+)

Example 740

Ethyl [2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(3-hydroxy-pyrrolidin-1-yl)-phenoxy]-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.19(3Ht,J=6.8Hz), 1.29(3H,t,J=6.8Hz), 1.38(9H,brs), 1.39(3H,t,J=6.8Hz), 1.93-2.02(1H,m), 2.10-2.19(1H,m), 2.92(1H,dd,J=4.0,10.0Hz), 2.99-3.04(1H,m), 3.12(1H,dd,J=7.6,15.6Hz), 3.44(1H,dd,J=6.4,10.0Hz), 4.01(1H,q,J=6.8Hz), 4.12(2H,q,J=6.8Hz), 4.15(2H,s), 4.21(2H,q,J=6.8Hz), 4.28(1H,br), 4.78(2H,s), 5.51(2H,s), 7.33(1H,s), 7.59(1H,s), 7.63(1H,s).

MS:m/e(ESI)600.5(MH+)

Example 741

Ethyl (1-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.18(3H,t,J=6.8Hz), 1.39(9H,s), 1.41(3H,t,J=6.8Hz), 1.94-2.02(1H,m), 2.11-2.18(1H,m), 2.82(3H,d,J=3.6Hz), 2.94-2.98(1H,m), 3.03-3.09(1H,m), 3.12-3.19(1H,m), 3.45-3.49(1H,m), 4.11(2H,q,J=6.8Hz), 4.16(2H,s), 4.25(2H,q,J=6.8Hz), 4.83(2H,s), 5.52(2H,s), 7.52(1H,s),

7.62(1H,s), 7.66(1H,s), 8.21(1H,m), 8.56(1H,s), 9.38(1H,be), 9.93(1H,br).

MS:m/e(ESI)595.4(MH+)

Example 742

Ethyl (1-{3-*tert*-butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.08-1.10(4H,m), 1.18(3H,t,J=6.8Hz), 1.38(9H,s), 1.96-2.03(1H,m), 2.12-2.17(1H,m), 2.28-2.34(1H,m), 2.98(1H,brd,J=9.2Hz), 3.06-3.11(1H,m), 3.13-3.19(1H,m), 3.49(1H,dd,J=5.2,9.6Hz), 4.11(2H,q,J=6.8Hz), 4.16(2H,s), 4.30(1H,brs), 4.82(2H,s), 5.58(2H,s), 7.62(1H,s), 7.67(1H,s), 7.71(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.61(1H,brs), 9.66(1H,brs).

MS:m/e(ESI)535.3(MH+)

Example 743

2-{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetoxymethyl 2,2-dimethyl-propionate hydrobromide

1H-NMR(DMSO-d6)δ:

1.15(9H,s), 1.37(9H,s), 1.41(3H,t,J=7.2Hz), 1.84-1.89(4H,m), 2.82(3H,d,J=4.8Hz), 3.06-3.12(4H,m), 4.28(2H,q,J=7.2Hz), 4.58(2H,s), 4.83(2H,s), 5.49(2H,s),

5.83(2H,s), 7.43(1H,s), 7.49(1H,s), 7.53(1H,s), 8.20(1H,q,J=4.8Hz), 8.55(1H,s), 9.15(1H,brs), 9.82(1H,brs).

MS:m/e(ESI)665.4(MH+)

Example 744

2-(5,6-Diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-1-(1,2,3,3-tetramethyl-2,3-dihydro-1H-indol-5-yl)-ethanone hydrobromide

1H-NMR(DMSO-d6)δ:

1.02(3H,s), 1.14(3H,d,J=6.4Hz), 1.21-1.30(9H,m), 1.39(3H,t,J=6.8Hz), 2.79(3H,s), 3.10-3.20(1H,m), 4.10(2H,q,J=6.8Hz), 4.19(2H,q,J=6.8Hz), 4.76(2H,s), 5.33(2H,s), 6.59(1H,d,J=8.4Hz), 7.31(1H,s), 7.60(1H,s), 7.75(1H,d,J=8,4Hz).

MS:m/e(ESI)454.2(MH+)

Example 745

Ethyl {2-*tert*-butyl-4-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-6-morpholino-phenoxy}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.27(3H,t,J=7Hz), 1.31(3H,t,J=7Hz), 1.39(9H,s), 1.42(3H,t,J=7.0Hz), 2.95-3.01(4H,m), 3.69-3.77(4H,m), 4.13(2H,q,J=7z), 4.23(2H,q,J=7Hz), 4.25(2H,q,J=7Hz), 4.81(2H,s), 4.92(2H,s), 5.53(2H,s), 7.35(1H,s), 7.57(1H,s), 7.66(1H,s), 9.08(1H,brs), 9.33(1H,brs).

Example 746

(1-{3-*tert*-Butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.86-1.96(1H,m), 2.02-2.12(1H,m), 2.89-2.95(1H,m), 3.01-3.18(2H,m), 3.36-3.42(1H,m), 3.86(3H,s), 3.95(3H,s), 3.99(2H,brs), 4.23-4.27(1H,m), 4.80(2H,s), 5.47(2H,d,J=7.2Hz), 7.35(1H,s), 7.58(1H,s), 7.70(1H,s).

MS:m/e(ESI)544.4(MH+)

Example 747

Ethyl (1-{3-*tert*-butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetate hydrochloride

1H-NMR(DMSO-d6)δ:

1.19(3H,t,J=6.8Hz), 1.38(9H,s), 1.96-2.02(1H,m), 2.11-2.19(1H,m), 2.94-2.97(1H,m), 3.02-3.09(1H,m), 3.12-3.18(1H,m), 3.47(1H,dd,J=6.0,10.4Hz), 3.86(3H,s), 3.95(3H,s), 4.11(2H,q,J=6.8Hz), 4.27-4.32(1H,m), 4.79(2H,s), 5.52(2H,s), 7.36(1H,s), 7.60(1H,s), 7.65(1H,s), 9.09(1H,s), 9.45(1H,s).

MS:m/e(ESI)572.3(MH+)

Example 748

Methyl 3-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-

benzylamino}-propanoate hydrochloride

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.40(3H,t,J=6.8Hz), 1.41(9H,s), 2.84(2H,t,J=7.2Hz), 3.19-3.27(2H,m), 3.63(3H,s), 4.11(2H,q,J=7.2Hz), 4.21(2H,q,J=7.2Hz), 4.31(2H,brs), 4.80(2H,s), 5,51(2H,s), 7.34(1H,s), 7.86(1H,s), 8.10(1H,s), 9.08(1H,s), 9.13-9.17(1H,m), 9.45(1H,s), 10.20(1H,s).

MS:m/e(ESI)544.3(MH+)

Example 749

1-{3-*tert*-Butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl}-5-oxo-pyrrolidine-2-carboxylic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.38(9H,s), 1.40(3H,t,J=6.8Hz), 1.88-1.98(1H,m), 2.13-2.21(2H,m), 2.28-2.38(1H,m), 3.78-3.84(1H,m), 4.12(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz), 4.23(1H,brs), 4.71(1H,d,J=14.4Hz), 4.78(2H,s), 5.40(2H,s), 7.32(1H,s), 7.69(1H,s), 7.73(1H,s).

MS:m/e(ESI)570.4(MH+)

Example 750

Methyl 1-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl}-5-oxo-pyrrolidine-2-carboxylate hydrochloride

1H-NMR(DMSO-d6)δ:

1.29(3H,t,J=6.8Hz), 1.38(9H,s), 1.40(3H,t,J=6.8Hz),
2.02-2.09(1H,m), 2.32-2.45(3H,m), 3.64(3H,s),
4.12(2H,q,J=6.8Hz), 4.20(2H,q,J=6.8Hz),
4.29(1H,d,J=17.6Hz), 4.39-4.45(1H,m),
4.63(1H,d,J=14.4Hz), 4.79(2H,s), 5.49(2H,d,J=8.4Hz),
7.33(1H,s), 7.72(1H,s), 7.78(1H,s), 9.06(1H,s),
9.46(1H,s), 10.03(1H,s).
MS:m/e(ESI)584.3(MH+)

Example 751

(Acetyl-{3-*tert*-butyl-5-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-hydroxy-benzyl}-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:
1.35(9H,s), 1.96(3H,s), 2.49(2H,s), 3.86(3H,s),
3.95(3H,s), 4.39(2H,s), 4.80(2H,s), 5.47(2H,s),
7.34(1H,s), 7.76(1H,s), 7.88(1H,s), 8.31(1H,s).
MS:m/e(ESI)530.2(MH+)

Example 752

Ethyl (4-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzyl}-piperazin-1-yl)-acetate hydrobromide

1H-NMR(DMSO-d6)δ:
1.16(3H,t,J=7.2Hz), 1.32(9H,s), 1.41(3H,t,J=7.2Hz),
2.35-2.55(8H,m), 2.82(3H,d,J=4.0Hz), 3.18(2H,s),
3.56(2H,s), 4.05(2H,q,J=7.2Hz), 4.28(2H,q,J=7.2Hz),
4.86(2H,s), 5.52(2H,s), 7.54(1H,s), 7.67(1H,s),

7.75(1H,s), 7.87(1H,s), 8.21(1H,d,J=4.0), 8.56(1H,s), 9.28(1H,brs).

MS:m/e(ESI)592.5(MH+)

Example 753

Ethyl {2-*tert*-butyl-4-[2-(5-ethoxy-1-methoxycarbonylimino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-acetate

1H-NMR(DMSO-d6)δ:

1.32(3H,t,J=6.8Hz), 1.41(9H,s), 1.55(3H,t,J=6.8Hz), 1.88-1.95(4H,m), 3.01(3H,d,J=4.8Hz), 3.08-3.25(4H,m), 3.85(3H,s), 4.19-4.35(4H,m), 4.51(2H,s), 4.62(2H,s), 5.10(2H,s), 6.99(1H,s), 7.46(1H,s), 7.56(1H,s), 7.64-7.73(1H,m), 8.81(1H.s).

MS:m/e(ESI)637.4(MH+)

Example 754

2-[2-(7-*tert*-Butyl-2-methoxymethyl-benzoxazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.45(3H,t,J=6.8Hz), 1.50(9H,s), 2.86(3H,d,J=4.4Hz), 3.47(3H,s), 4.31(2H,q,J=6.8Hz), 4.82(2H,s), 4.92(2H,s), 5.63(2H,s), 7.51(1H,s), 7.91(1H,d,J=1.6Hz), 8.23(1H,m), 8.39(1H,d,J=1.6Hz), 8.61(1H,s), 9.30(1H,m), 9.92(1H,m).

Example 755

Ethyl 7-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-

methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoxazole-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=6.8Hz), 1.44(3H,t,J=7.2Hz), 1.52(9H,s), 2.85(3H,d,J=4.4Hz), 4.29(2H,q,J=6.8Hz), 4.49(2H,q,J=7.2Hz), 4.92(2H,s), 5.63(2H,s), 7.57(1H,s), 8.02(1H,s), 8.24(1H,q,J=4.4Hz), 8.57(1H,s), 8.60(1H,s), 9.28(1H,s), 9.91(1H,s).

Example 756

{3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzyloxy}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.33(9H,s), 1.41(3H,t,J=7.2Hz), 2.82(2H,d,J=4.8), 4.13(2H,s), 4.26(2H,q,J=7.2Hz), 4.64(2H,s), 4.87(2H,s), 5.52(2H,s), 7.54(1H,s), 7.75(1H,s), 7.82(1H,s), 7.91(1H,s), 8.21(1H,d,J=4.8Hz), 8.56(1H,s), 9.24(1H,brs), 9.86(1H,brs).

Example 757

2-{2-[3-*tert*-Butyl-5-(3-cyano-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.42(9H,s), 1.44(3H,t,J=7.2Hz), 2.11(2H,m), 2.85(3H,d,J=4.4Hz), 4.12(2H,t,J=5.6Hz),

4.30(2H,q,J=7.2Hz), 4.86(2H,s), 5.49(2H,s), 7.46(1H,s), 7.55(2H,s), 8.22(1H,m), 8.59(1H,s), 9.21(1H,m), 9.86(1H,m).

Example 758

2-(2-{3-*tert*-Butyl-4-hydroxy-5-[3-(2-methoxy-ethoxy)-propoxy]-phenyl}-2-oxo-ethyl)-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.45(9H,s), 1.53(3H,t,J=7.2Hz), 2.11(2H,m), 3.30(3H,s), 3.54(2H,m), 3.61(2H,m), 3.69(2H,t,J=7.2Hz), 4.22(4H,m), 4.36(2H,q,J=7.2Hz), 4.90(2H,s), 5.43(2H,s), 7.48(1H,sz), 7.52(1H,s), 7.67(1H,s), 8.54(1H,s).

Example 759

Ethyl {4-[2-(1-acetoxymethoxycarbonylimino-5-ethoxy-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-*tert*-butyl-6-(pyrrolidin-1-yl)-phenoxy}-acetate

1H-NMR(DMSO-d6)δ:

1.33(3H,t,J=7.2Hz), 1.42(9H,s), 1.55(3H,t,J=7.2Hz), 1.87-1.97(4H,m), 2.15(3H,s), 3.00(3H,d,J=4.8Hz), 3.11-3.22(4H,m), 4.18-4.36(4H,m), 4.51(2H,s), 4.64(2H,s), 5.14(2H,s), 5.88(2H,s), 6.99(1H,s), 7.44(1H,s), 7.50-7.65(2H,m), 8.88(1H,s).

Example 760

Ethyl 1-{3-*tert*-butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-2-

methoxy-phenyl}-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.10(3H,t,J=7Hz), 1.41(9H,s), 1.54(3H,t,J=7Hz), 1.91-2.13(3H,m), 2.45(1H,q,J=7Hz), 3.13(3H,d,J=5Hz), 3.32(1H,br.t,J=7Hz), 3.74(1H,br.t,J=7Hz), 3.75(3H,s), 4.01(1H,qd,J=7,2Hz), 4.02(1H,qd,J=7,2Hz), 4.46(2H,brs), 4.58(1H,t,J=7Hz), 4.86(2H,s), 6.12(2H,s), 7.35(1H,s), 7.61(1H,d,J=2Hz), 7.66(1H,d,J=2Hz), 8.30(1H,m), 9.50(1H,m).

MS:m/e(ESI)579.0(MH+)

Example 761

Ethyl 1-{3-*tert*-butyl-5-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-2-methoxy-phenyl}-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.24(6H,t,J=7Hz), 1.40(9H,s), 1.53(3H,t,J=7Hz), 1.92-2.12(3H,m), 2.42-2.49(1H,), 3.35(1H,t,J=6Hz), 3.71(1H,t,J=6Hz), 3.73(3H,s), 4.01(2H,m), 4.18(4H,q,J=7Hz), 4.60(1H,t,J=6Hz), 4.77(2H,s), 6.09(2H,s), 6.85(1H,s), 7.62(2H,s).

MS:m/e(ESI)584.0(MH+)

Example 762

Ethyl 1-{3-*tert*-butyl-5-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-methoxy-phenyl}-pyrrolidine-2-carboxylate hydrobromide

1H-NMR(DMSO-d6)δ:

1.11(3H,t,J=7Hz), 1.15-1.25(4H,m), 1.40(9H,s), 1.92-2.11(4H,m), 2.15-2.21(1H,m), 2.41-2.49(1H,m), 3.35(1H,t,J=7Hz), 3.71(1H,t,J=7Hz), 3.73(3H,s), 4.01(1H,qd,J=7,4Hz), 4.02(1H,qd,qd,J=7,4Hz), 4.60(1H,t,J=7Hz), 4.82(2H,s), 6.20(2H,s), 7.54(1H,d,J=8Hz), 7.63(1H,d,J=2Hz), 7.64(1H,d,J=2Hz), 7.79(1H,d,J=8Hz).

MS:m/e(ESI)519.0(MH+)

Example 763

Ethyl {4-*tert*-butyl-6-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzimidazol-1-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.24(3H,t,7Hz), 1.41(3H,t,J=7Hz), 1.57(9H,s), 2.84(3H,d,J=5Hz), 4.19(2H,q,J=7H), 4.30(2H,q,J=7Hz), 4.89(2H,s), 5.37(2H,s), 5.54(2H,s), 7.55(1H,s), 7.71(1H,d,=2Hz), 8.21(1H,q,J=5Hz), 8.26(1H,d,J=2Hz), 8.44(1H,s), 8.57(1H,s).

MS:m/e(ESI)534.0(MH+)

Example 764

Ethyl {4-*tert*-butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-benzimidazol-1-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.21(3H,t,J=7Hz), 1.42(3H,t,J=7Hz), 1.55(3H,t,J=7Hz), 1.60(9H,s), 4.18-4.25(4H,m), 4.23(2H,q,J=7Hz),

5.02(2H,s), 5.41(2H,s), 6.14(2H,s), 6.90(1H,s), 7.00(1H,s), 7.98(1H,s), 8.54(1H,brs), 8.99(1H,brs), 10.78(1H,brs).

MS:m/e(ESI)539.0(MH+)

Example 765

Ethyl {4-*tert*-butyl-6-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzimidazol-1-yl}-acetate hydrobromide

1H-NMR(DMSO-d6)δ:

1.12-1.24(4H,m), 1.35(3H,t,J=7Hz), 1.60(9H,s), 2.17-2.24(1H,m), 4.32(2H,q,J=7Hz), 5.05(2H,s), 5.29(2H,s), 6.23(2H,s), 7.31(1H,brs), 7.37(1H,d,J=8Hz), 7.82(1H,d,J=2Hz), 7.84(1H,d,J=8Hz), 8.08(1H,s), 8.85(1H,d,J=2Hz).

MS:m/e(ESI)474.0(MH+)

Example 766

2-{2-[3-*tert*-Butyl-4-(3-carbamoyl-propoxy)-5-methoxy-phenyl]-2-oxo-ethyl}-6-dimethylamino-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.39(9H,s), 1.95-2.04(2H,m), 2.23-2.30(2H,m), 2.79(3H,d,J=5Hz), 2.93(6H,s), 3.89(2H,s), 4.05-4.11(2H,m), 4.76(2H,s), 5.48(2H,s), 6.80(1H,brs), 7.17(1H,s), 7.34(1H,brs), 7.52(1H,s), 7.57(1H,s), 8.09(1H,s), 8.38(1H,q,J=5Hz).

Example 767

2-{2-[7-*tert*-Butyl-2-(2-cyano-ethyl)-benzoxazol-5-yl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=6.8Hz), 1.50(9H,s), 2.85(3H,d,J=4.8Hz), 3.12(2H,t,J=6.4Hz), 3.45(2H,t,J=6.4Hz), 4.31(2H,q,J=6.8Hz), 4.91(2H,s), 5.61(2H,s), 7.56(1H,s), 7.88(1H,d,J=1.2Hz), 8.23(1H,m), 8.37(1H,d,J=1.2Hz), 8.60(1H,s), 9.28(1H,m), 9.90(1H,m).

Example 768

2-{2-[7-*tert*-Butyl-2-(2-carbamoyl-ethyl)-benzoxazol-5-yl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=6.8Hz), 1.49(9H,s), 2.71(2H,t,J=7.2Hz), 2.85(3H,d,J=4.8Hz), 3.23(2H,t,J=7.2Hz), 4.30(2H,q,J=6.8Hz), 4.91(2H,s), 5.60(2H,s), 6.93(1H,s), 7.49(1H,s), 7.56(1H,s), 7.84(1H,d,J=1.6Hz), 8.23(1H,m), 8.28(1H,d,J=1.6Hz), 8.60(1H,s), 9.28(1H,m), 9.91(1H,m).

Example 769

3-{7-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-benzoxazol-2-yl}-propanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=7.2Hz), 1.49(9H,s), 2.85(3H,d,J=4.8Hz),

2.88(2H,t,J=7.6Hz), 3.27(2H,t,J=7.6Hz),
4.30(2H,q,J=7.2Hz), 4.91(2H,s), 5.59(2H,s), 7.56(1H,s),
7.85(1H,d,J=1.2Hz), 8.23(1H,m), 8.31(1H,d,J=1.2Hz),
8.60(1H,s), 9.28(1H,m), 9.90(1H,m).

Example 770

2-{2-[3-*tert*-Butyl-4-hydroxy-5-(3-methylcarbamoyl-propoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(9H,s), 1.44(3H,t,J=7Hz), 1.97-2.06(2H,m), 2.26-2.35(2H,m), 2.58(3H,d, J=5Hz), 2.84(3H,d,J=5Hz), 4.03-4.10(2H,m), 4.29(2H,q,J=7Hz), 4.85(2H,s), 5.48(2H,s), 7.44(1H,s), 7.53(1H,s), 7.55(1H,s), 7.72(1H,q,J=5Hz), 8.22(1H,q,J=5Hz), 8.57(1H,s).

Example 771

2-{2-[3-*tert*-Butyl-5-(3-dimethylcarbamoyl-propoxy)-4-hydroxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(9H,s), 1.43(3H,t,J=7Hz), 1.96-2.06(2H,m), 2.52-2.59(2H,m), 2.83(3H,s), 2.85(3H,d,J=5Hz), 2.98(3H,s), 4.06-4.14(2H,m), 4.30(2H,q,J=7Hz), 4.85(2H,s), 5.48(2H,s), 7.46(1H,s), 7.53(1H,s), 7.55(1H,s), 8.22(1H,q,J=5Hz), 8.58(1H,s).

Example 772

2-{2-[3-*tert*-Butyl-4-methoxy-5-(3-methylcarbamoyl-propoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.43(3H,t,J=7Hz), 1.98-2.08(2H,m), 2.26-2.33(2H,m), 2.57(3H,d,J=5Hz), 2.84(3H,d,J=5Hz), 3.92(3H,s), 4.05-4.12(2H,m), 4.29(2H,q,J=7Hz), 4.86(2H,s), 5.53(2H,s), 7.53(1H,s), 7.56(2H,s), 7.78-7.88(1H,m), 8.22(1H,q,J=5Hz), 8.58(1H,s).

Example 773

2-{2-[3-*tert*-Butyl-5-(3-dimethylcarbamoyl-propoxy)-4-methoxy-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.44(3H,t,J=7Hz), 1.98-2.08(2H,m), 2.45-2.56(2H,m), 2.83(3H,s), 2.85(3H,d,J=5Hz), 2.98(3H,s), 3.92(3H,s), 4.08-4.16(2H,m), 4.30(2H,q,J=7Hz), 4.86(2H,s), 5.52(2H,s), 7.55(3H,s), 8.22(1H,q,J=5Hz), 8.58(1H,s).

Example 774

2-[2-(7-*tert*-Butyl-benzoxazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.43(3H,t,J=6.8Hz), 1.50(9H,s), 2.85(3H,d,J=4.8Hz), 4.31(2H,q,J=6.8Hz), 4.91(2H,s), 5.62(2H,s), 7.57(1H,s), 7.93(1H,s), 8.23(1H,q,J=4.8Hz), 8.45(1H,s), 8.59(1H,s), 8.98(1H,s), 9.26(1H,s), 9.90(1H,s).

Example 775

{5-[2-(5-Ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-7-methoxy-3,3-dimethyl-2,3-dihydro-indol-1-yl}-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.39(6H,s), 1.44(3H,t,J=6.8Hz), 3.76(3H,s), 4.27(2H,s), 4.30(2H,q,J=6.8Hz), 4.85(2H,s), 5.39(2H,s), 7.32(1H,d,J=1.2Hz), 7.42(1H,d,J=1.2Hz), 7.55(1H,s), 8.22(1H,m), 8.58(1H,s), 9.21(1H,m), 9.83(1H,m).

Example 776

2-{2-[3-(3-Carbamoyl-propoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.44(3H,t,J=7Hz), 1.90-2.01(2H,m), 2.21-2.28(2H,m), 2.85(3H,d,J=5Hz), 4.03-4.10(2H,m), 4.30(2H,q,J=7Hz), 4.88(2H,s), 5.03(2H,s), 6.80(1H,brs), 7.29-7.37(2H,m), 7.48-7.57(3H,m), 7.49-7.54(1H,m), 8.23(1H,q,J=5Hz), 8.59(1H,s).

Example 777

{2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-

methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenylamino}-acetic acid hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.44(3H,t,J=6.8Hz), 2.88(3H,s), 3.77(3H,s), 3.99(2H,s), 4.27(2H,q,J=6.8Hz), 4.81(2H,s), 5.32(2H,s), 7.38(1H,dd,J=7.2,1.6Hz), 7.60(1H,d,J=1.6Hz), 8.45(1H,s).

Example 778

({2-*tert*-Butyl-4-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-6-methoxy-phenyl}-methyl-amino)-acetic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.40(3H,t,J=6.4Hz), 1.44(9H,s), 2.67(3H,s), 2.82(3H,d,J=4.8Hz), 3.28(1H,d,J=20Hz), 4.05(1H,d,J=20Hz), 4.28(2H,q,J=6.4Hz), 4.85(2H,s), 5.51(2H,s), 7.47(1H,d,J=2.0Hz), 7.54(1H,s), 7.58(1H,d,J=2.0Hz), 8.20(1H,q,J=4.8Hz), 8.55(1H,s), 9.16-9.20(1H,m), 9.83-9.88(1H,m).

Example 779

2-[2-(7-*tert*-Butyl-3-cyanomethyl-3H-benzimidazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=7Hz), 1.57(9H,s), 2.85(3H,d,J=4Hz), 4.29(2H,q,J=7Hz), 4.91(2H,s), 5.49(2H,s), 5.74(2H,s),

7.56(1H,s), 7.78(1H,d,J=1Hz), 8.22(1H,q,J=4Hz), 8.39(1H,d,J=1Hz), 8.56(1H,s), 8.59(1H,s), 9.28(1H,s), 9.48(1H,s).

MS:m/e(ESI)487.0(MH+)

Example 780

{4-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-benzimidazol-1-yl}-acetonitrile hydrobromide

1H-NMR(DMSO-d6)δ:

1.30(3H,t,J=7Hz), 1.40(3H,t,J=7Hz), 1.55(9H,s), 4.13(2H,q,J=7Hz), 4.22(2H,q,J=7Hz), 4.84(2H,s), 5.48(2H,s), 5.75(2H,s), 7.35(1H,s), 7.77(1H,d,J=2Hz), 8.37(1H,d,J=2Hz), 8.56(1H,s).

MS:m/e(ESI)492.0(MH+)

Example 781

{4-*tert*-Butyl-6-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzimidazol-1-yl}-acetonitrile hydrobromide

1H-NMR(DMSO-d6)δ:

1.05-1.16(4H,m), 1.56(9H,s), 2.30-2.37(1H,m), 4.89(2H,s), 5.65(2H,s), 5.74(2H,s), 7.74(1H,d,J=8Hz), 7.78(1H,d,J=2Hz), 8.12(1H,d,J=8Hz), 8.39(1H,d,J=2Hz), 8.57(1H,s).

MS:m/e(ESI)427.0(MH+)

Example 782

2-{2-[3-Acetylamino-5-*tert*-butyl-4-(3-carbamoyl-

propoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.36-1.43(12H,s), 2.01-2.07(2H,m), 2.13(3H,s), 2.27(2H,t,J=7.2), 2.82(3H,d,J=4.4Hz), 3.87(2H,t,J=6.8Hz), 4.28(2H,t,J=6.8Hz), 4.84(2H,s), 5.46(2H,s), 6.86(1H,s), 7.38(1H,s), 7.54(1H,s), 7.70(1H,d,J=2.0), 8.17-8.23(2H,m), 8.55(1H,s), 9.65(1H,s), 9.83(1H,s).

MS:m/e(ESI)566.3(MH+)

Example 783

2-{2-[3-*tert*-Butyl-4-(3-cyano-propoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.40(9H,s), 1.44(3H,t,J=7.2Hz), 2.17(2H,m), 2.73(2H,t,J=7.2Hz), 2.85(3H,d,J=4.4Hz), 4.23(2H,t,J=7.2Hz), 4.30(2H,q,J=7.2Hz), 4.87(2H,s), 5.48(2H,s), 7.22(1H,d,J=9.2Hz), 7.55(1H,s), 7.87(1H,d,J=2.0Hz), 7.94(1H,dd,J=2.0,9.2Hz), 8.22(1H,m), 8.59(1H,s).

Example 784

2-[2-(3-*tert*-Butyl-5-dimethylamino-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.34(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.4Hz), 2.99(6H,s), 4.29(2H,q,J=6.8Hz), 4.88(2H,s), 5.53(2H,s), 7.06(1H,s), 7.12(1H,s), 7.34(1H,s), 7.56(1H,s), 8.23(1H,q,J=4.4Hz), 8.58(1H,s), 9.24(1H,s), 9.85(1H,s).

Example 785

(1-{3-*tert*-Butyl-5-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-phenyl}-pyrrolidin-3-yloxy)-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.20-1.50(12H,m), 1.93-2.07(1H,m), 2.10-2.23(1H,m), 2.77(3H,d,J=5.1Hz), 2.94-3.05(1H,m), 3.06-3.24(2H,m), 3.43-3.54(1H,m), 4.07(3H,s), 4.14-4.55(5H,m), 4.87(2H,s), 5.56(2H,s), 7.61(1H,s), 7.69(1H,s), 7.99(1H,s), 8.52-8.62(1H,s), 9.54(1H,brs), 9.95(1H,brs).

Example 786

3-(Acetyl-{3-*tert*-butyl-5-[2-(3-ethoxy-7-imino-2-methylcarbamoyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-2-hydroxy-benzyl}-amino)-propanoic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.23-1.46(12H,m), 2.16(3H,s), 2.60-2.83(5H,m), 3.51-3.69(2H,m), 4.15-4.32(2H,m), 4.48(2H,brs), 4.88(2H,brs), 5.57(2H,brs), 7.81(1H,s), 7.93(2H,brs),

7.99(1H,brs), 8.55-8.64(1H,m), 9.97(1H,brs).

Example 787

4-[2-*tert*-Butyl-4-[2-(7-imino-2-methyl-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(2-oxo-piperidin-1-ylmethyl)-phenoxy]-butylamide hydrochloride

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.73(4H,br), 2.02(2H,br), 2.27(2H,t,J=7.6Hz), 2.58(3H,s), 3.14(2H,br), 3.24-3.40(2H,br), 3.83(2H,t,J=6.8Hz), 4.53(2H,s), 4.60(2H,s), 5.15(2H,s), 6.81(1H,s), 7.35(1H,s), 7.46(1H,d,J=8.0Hz), 7.56(1H,d,J=2.0Hz), 7.87(1H,d,J=2.0Hz), 7.95(1H,d,J=8.0Hz).

MS:m/e(ESI)534.3(MH+)

Example 788

2-[2-(7-*tert*-Butyl-3H-benzimidazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.43(3H,t,J=7Hz), 1.54(9H,s), 2.74(3H,d,J=5Hz), 4.29(2H,q,J=7Hz), 4.88(2H,s), 5.59(2H,s), 7.57(1H,s), 7.70(1H,s), 8.16(1H,brs), 8.22(1H,q,J=5Hz), 8.45(1H,s), 8.57(1H,s), 9.23(1H,s), 9.45(1H,s).

MS:m/e(ESI)448.0(MH+)

Example 789

2-[2-(7-*tert*-Butyl-3-methyl-3H-benzimidazol-5-yl)-2-

oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=7Hz), 1.55(9H,s), 2.74(3H,d,J=4Hz), 3.94(3H,s), 4.29(2H,q,J=7Hz), 4.89(2H,s), 5.60(2H,s), 7.55(1H,s), 7.71(1H,s), 8.22(1H,q,J=4Hz), 8.23(1H,s), 8.42(1H,s), 8.58(1H,s).

MS:m/e(ESI)462.0(MH+)

Example 790

2-[2-(7-*tert*-Butyl-3-carbamoylmethyl-3H-benzimidazol-5-yl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.42(3H,t,J=7Hz), 1.58(9H,s), 2.83(3H,d,J=5Hz), 4.29(2H,q,J=7Hz), 4.89(2H,s), 5.13(2H,s), 5.57(2H,s), 7.38(1H,s), 7.55(1H,s), 7.70(1H,d,J=2Hz), 7.82(1H,s), 8.12(1H,d,J=2Hz), 8.22(1H,q,J=5Hz), 8.39(1H,s), 8.58(1H,s), 9.26(1H,d,J=4Hz), 9.85(1H,d,J=4Hz).

MS:m/e(ESI)505.0(MH+)

Example 791

2-{4-*tert*-Butyl-6-[2-(5,6-diethoxy-7-fluoro-1-imino-1,3-dihydro-isoindol-2-yl)-acetyl]-benzimidazol-1-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.28(3H,t,J=7Hz), 1.40(3H,t,J=7Hz), 1.56(9H,s), 4.12(2H,q,J=7Hz), 4.22(2H,q,J=7Hz), 4.84(2H,s),

5.03(2H,s), 5.55(2H,s), 7.36(1H,s), 7.39(1H,s),
7.67(1H,s), 7.82(1H,s), 8.10(1H,s), 8.39(1H,s),
9.04(1H,brs), 9.39(1H,brs).
MS:m/e(ESI)510.0(MH+)

Example 792

2-{4-*tert*-Butyl-6-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-benzimidazol-1-yl}-acetamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.05-1.13(4H,m), 2.33(1H,quint,J=7Hz), 1.57(9H,s),
4.86(2H,s), 5.03(2H,s), 5.62(2H,s), 7.38(1H,s),
7.70(1H,s), 7.73(1H,d,J=8Hz), 7.81(1H,s),
8.10(1H,d,J=8Hz), 8.11(1,s), 8.39(1H,s), 9.53(1H,brs),
9.66(1H,brs).
MS:m/e(ESI)445.0(MH+)

Example 793

2-[2-(3-*tert*-Butyl-5-dimethylamino-4-hydroxy-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:
1.41(12H,m), 2.63(6H,s), 2.84(2H,s),
4.30(2H,q,J=6.8Hz), 4.86(2H,s), 5.47(2H,s), 7.56(1H,s),
7.66(1H,s), 7.71(1H,s), 8.22(1H,s), 8.57(1H,s),
9.17(1H,s), 9.84(1H,s).

Example 794

4-{2-*tert*-Butyl-4-[2-(2-cyclopropyl-7-imino-5,7-

dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.01-1.15(4H,m), 1.37(9H,s), 1.82-2.08(6H,m), 2.28-2.43(3H,m), 2.82-3.42(4H and H_2O,m), 3.78-3.94(2H,m), 4.81(2H,s), 5.53(2H,s), 7.35(1H,s), 7.46(1H,s), 7.68-7.75(1H,m), 8.06-8.12(1H,m), 9.44(1H,brs), 9.66(1H,brs).

MS:m/e(ESI)519.3(MH+)

Example 795

5-{2-*tert*-Butyl-4-[2-(2-cyclopropyl-7-imino-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.00-1.15(4H,m), 1.38(9H,s), 1.59-1.85(4H,m), 2.23-2.37(3H,m), 3.03-3.20(4H,m), 3.78-3.88(2H,m), 4.81(2H,s), 5.53(2H,s), 7.36(1H,s), 7.46(1H,s), 7.72(1H,d,J=8.0Hz), 8.09(1H,d,J=8.0Hz), 9.41-9.49(1H,m), 9.61-9.70(1H,m).

MS:m/e(ESI)533.3(MH+)

Example 796

4-{4-[2-(1-Amino-7-fluoro-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-2-*tert*-butyl-6-(pyrrolidin-1-yl)-phenoxy}-butyric acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.79-1.96(4H,m), 2.01(2H,t,J=6.8Hz), 2.41(2H,t,J=7.2Hz), 3.02-3.20(4H,m), 3.77-3.90(5H,m), 3.95(3H,s), 4.80(2H,s), 5.48(2H,s), 7.35(1H,d,J=2.0Hz), 7.36(1H,s), 7.45(1H,d,J=2.0Hz), 9.03-9.11(1H,m), 9.27-9.34(1H,m).

Example 797

5-{2-*tert*-Butyl-4-[2-(7-fluoro-1-imino-5,6-dimethoxy-1,3-dihydro-isoindol-2-yl)-acetyl]-6-(pyrrolidin-1-yl)-phenoxy}-pentanoic acid trifluoroacetate

1H-NMR(DMSO-d6)δ:

1.38(9H,s), 1.55-1.99(8H,m), 2.17-2.36(2H,m), 2.94-3.20(4H,m), 3.57-4.27(8H and H_2O,m), 4.79(2H,s), 5.47(2H,s), 7.36(2H,s), 7.45(1H,s), 9.01-9.11(1H,m), 9.22-9.35(1H,m).

Example 798

2-{2-[3-*tert*-Butyl-5-(3-cyano-propoxy)-4-(2-hydroxy-ethoxy)-phenyl]-2-oxo-ethyl}-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(9H,s), 1.44(3H,t,J=7.2Hz), 2.13(2H,m), 2.75(2H,t,J=7.2Hz), 2.85(3H,d,J=4.8Hz), 3.80(2H,t,J=7.2Hz), 4.11-4.19(4H,m), 4.30(2H,q,J=7.2Hz), 4.87(2H,s), 5.52(2H,s), 7.76(2H,m), 7.59(1H,s), 8.22(1H,m), 8.59(1H,s), 9.21(1H,m).

Example 799

2,6-Di-*tert*-butyl-4-[1-hydroxy-2-(3-imino-5,6-dimethoxy-3H-benzo[d]isoxazol-2-yl)-vinyl]-phenol hydrobromide

1H-NMR(DMSO-d6)δ:

1.45(18H,s), 3.90(3H,s), 4.07(3H,s), 5.96(1H,s), 6.27(1H,brs), 6.52(1H,s), 7.84(1H,s), 7.98(2H,s), 9.55-9.66(2H,m), 9.80(1H,brs).

MS:m/e(ESI)441.1(MH+)

Example 800

2-[2-(3-*tert*-Butyl-4-hydroxy-5-(pyrrolidin-1-yl)-phenyl)-2-oxo-ethyl]-6-ethoxy-3-imino-2,3-dihydro-1H-isoindole-5-carboxylic acid methylamide hydrobromide

1H-NMR(DMSO-d6)δ:

1.41(12H,m), 1.94(4H,s), 2.84(3H,s), 3.02(4H,s), 4.30(2H,q,6.4Hz), 4.86(2H,s), 5.48(2H,s), 7.56(1H,s), 7.62(1H,s), 7.65(1H,s), 8.23(1H,s), 8.57(1H,s), 9.18(1H,s), 9.84(1H,s).

Example 801

({3-*tert*-Butyl-5-[2-(5-ethoxy-1-imino-6-methylcarbamoyl-1,3-dihydro-isoindol-2-yl)-acetyl]-phenyl}-methyl-amino)-acetic acid hydrochloride

1H-NMR(DMSO-d6)δ:

1.32(9H,s), 1.43(3H,t,J=6.8Hz), 2.84(3H,d,J=4.4Hz), 3.06(3H,s), 4.21(2H,s), 4.30(2H,q,J=6.8Hz), 4.87(2H,s), 5.54(2H,s), 7.01(1H,s), 7.07(1H,s), 7.35(1H,s),