*159159*

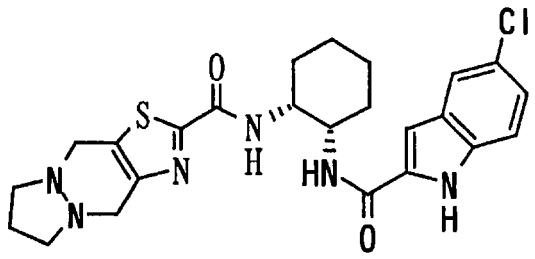
*G00001*

10.36(1H,br.s), 11.75,11.77(1H,each s).

MS (ESI) m/z: 546$(M+H)^+$.

[Example 29]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-4,7,8,10-tetrahydro-6H-pyrazolo[1,2-a]-thiazolo[4,5-d]pyridazine-2-carboxamide hydrochloride:



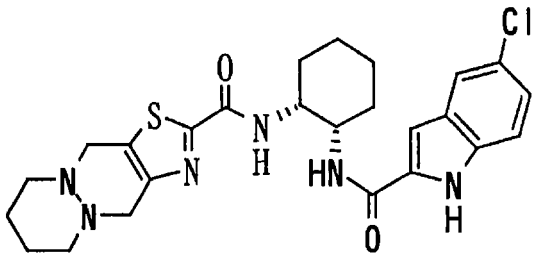
The title compound was obtained from the compound obtained in Referential Example 71 and the compound obtained in Referential Example 44 in a similar manner to Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.50(2H,m), 1.61(4H,br.s), 1.80-2.00(2H,m), 2.27(2H,br.s), 2.80-4.80(10H,m), 7.14(1H,d,J=1.5Hz), 7.17(1H,dd,J=8.5,2.0Hz), 7.41(1H,d,J=8.5Hz), 7.70(1H,d,J=2.0Hz), 8.09(1H,d,J=7.3Hz), 8.44(1H,br.s), 11.81(1H,br.s).

MS (FAB) m/z: 499$(M+H)^+$.

[Example 30]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-4,6,7,8,9,11-hexahydropyridazino[1,2-a]-thiazolo[4,5-d]pyridazine-2-carboxamide hydrochloride:



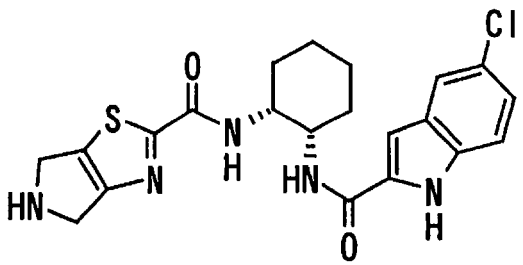
The title compound was obtained from the compound obtained in Referential Example 46 and the compound obtained in Referential Example 71 in a similar manner to Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.55(2H,m), 1.55-2.10(10H,m), 2.80-4.80(10H,m), 7.10-7.25(2H,m), 7.42(1H,d,J=8.8Hz), 7.72(1H,d,J=1.7Hz), 8.12(1H,br.s), 8.41(1H,br.s), 11.83(1H,br.s).

MS (FAB) m/z: 513$(M+H)^+$.

[Example 31]

5-Chloro-N-{(1R*,2S*)-2-[(5,6-dihydro-4H-pyrrolo[3,4-d]-thiazol-2-ylcarbonyl)amino]cyclohexyl}indole-2-carboxamide hydrochloride:



The compound (171 mg) obtained in Referential Example 33 was dissolved in diethyl ether (5 ml) in an argon atmosphere, and the solution was cooled to -78°C, to which n-butyllithium (1.60N hexane solution, 385 μl) was

added dropwise. After the reaction mixture was stirred for 10 minutes at -78°C, and carbon dioxide was blown into the reaction mixture for 20 minutes, it was warmed to room temperature. After the reaction mixture was concentrated under reduced pressure, the residue was dissolved in N,N-dimethylformamide (10 ml). To the solution, were added the compound (184 mg) obtained in Referential Example 71 , 1-hydroxybenzotriazole monohydrate (76 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (215 mg). The resultant mixture was stirred for 3 days. The reaction mixture was concentrated, and methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue to separate an organic layer. The organic layer was dried over anhydrous sodium sulfate, and the solvent was then distilled off under reduced pressure. The resultant residue was purified by column chromatography on silica gel (methanol:methylene chloride = 3:97). After an ethanol solution (5 ml) of hydrochloric acid was added to the thus-obtained product, the mixture was stirred at room temperature for 1 hour, and the reaction mixture was concentrated. Ethyl acetate was added to the residue to solidify it. The resultant powder was collected by filtration to obtain the title compound (31 mg).

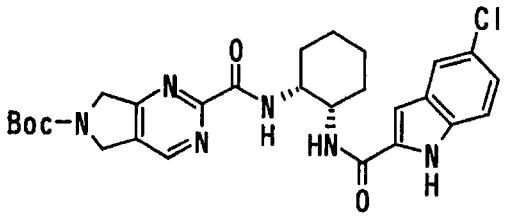
$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.52(2H,m), 1.55-1.80(4H,m), 1.82-2.05(2H,m), 4.22(1H,br.s), 4.28(1H,br.s), 4.38(2H,s), 4.56(2H,s), 7.14-7.20(2H,m), 7.42(1H,d,J=8.6Hz),

7.71(1H,d,J=1.7Hz), 8.10(1H,d,J=7.1Hz), 8.45(1H,d,J=7.8Hz), 10.10-10.50(2H,br), 11.83(1H,br.s).

MS (FAB) m/z: 444$(M+H)^+$.

[Example 32]

tert-Butyl 2-{[((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)amino]carbonyl}-5,7-dihydro-6H-pyrrolo[3,4-d]pyrimidine-6-carboxylate :



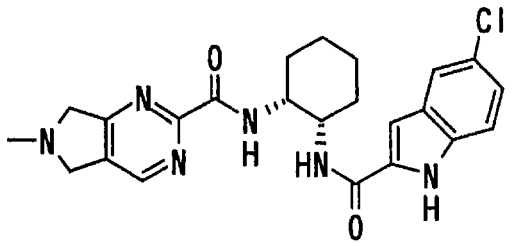

After the compound obtained in Referential Example 50 was hydrolyzed with lithium hydroxide, it was reacted with the compound obtained in Referential Example 71 in a similar manner to Example 2 to obtain the title compound.

$^1$H-NMR ($CDCl_3$) δ: 1.54(9H,s), 1.55-2.30(8H,m), 4.23(1H,br.s), 4.53(1H,br.s), 4.74-4.83(4H,m), 6.99(1H,d,J=1.5Hz), 7.19(1H,dd,J=8.8,2.1Hz), 7.34(1H,d,J=8.8Hz), 7.62(1H,d,J=2.1Hz), 8.11(1H,br.s), 8.48-8.53(1H,br), 8.70-8.76(1H,br), 9.60-9.70(1H,br).

MS (ESI) m/z: 539$(M+H)^+$.

[Example 33]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-6-methyl-6,7-dihydro-5H-pyrrolo[3,4-d]-pyrimidine-2-carboxamide hydrochloride:



Trifluoroacetic acid (1 ml) was added to a solution of the compound (34.0 mg) obtained in Example 32 dissolved in methylene chloride (1 ml) at room temperature, and the mixture was stirred for 1 hour. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in methylene chloride (1 ml), to which triethylamine (17.6 μl), acetic acid (7.21 μl), 35% formalin (8.13 μl) and sodium triacetoxyborohydride (20.1 mg) were added at room temperature. The resultant mixture was stirred for 1 hour. Methylene chloride (10 ml) and saturated aqueous solution (10 ml) of sodium hydrogencarbonate were added to the reaction mixture to separate an organic layer. The organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methanol:methylene chloride = 7:93). A 1N ethanol solution of hydrochloric acid and ethyl acetate were added to the product thus obtained to solidify it, and the resultant solids were collected by filtration to obtain the title compound (8.0 mg).

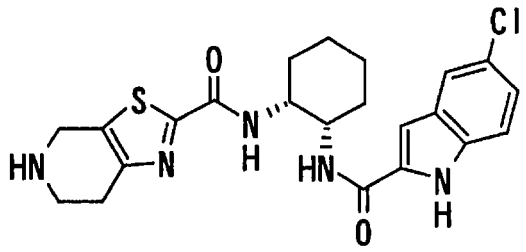
$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.55(2H,m), 1.55-1.75(4H,m), 1.80-

2.05(2H,m), 2.98(3H,br.s), 4.28(2H,br.s), 4.65(4H,br.s), 7.14-7.20(2H,m), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=2.0Hz), 8.17(1H,d,J=6.9Hz),8.65(1H,d,J=8.3Hz), 8.93(1H,s), 11.73(1H,br.s), 11.82(1H,br.s).

MS (FAB) m/z: 453$(M+H)^+$.

[Example 34]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



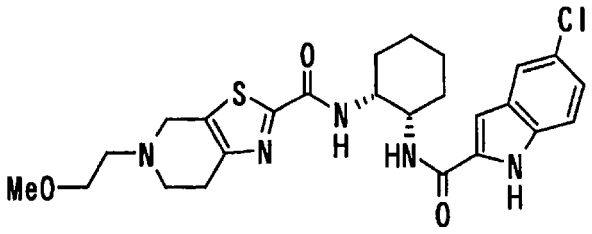
The title compound was obtained by treating a product obtained by the reaction of the compound obtained in Referential Example 71 with the compound obtained in Referential Example 34 with hydrochloric acid in a similar manner to Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.39-1.52(2H,m), 1.62(4H,br.s), 1.86-2.09(2H,m), 3.03(2H,br.s), 3.40-3.47(2H,m), 4.17-4.32(2H,m), 4.44(2H,s), 7.15(1H,s), 7.17(1H,dd,J=8.6,2.0Hz), 7.41(1H,d,J=8.6Hz), 7.71(1H,s), 8.10-8.15(1H,m), 8.40-8.47(1H,m), 9.69(2H,br.s), 11.85(1H,s).

MS (FAB) m/z: 458$(M+H)^+$.

[Example 35]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-5-(2-methoxyethyl)-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide hydrochloride:



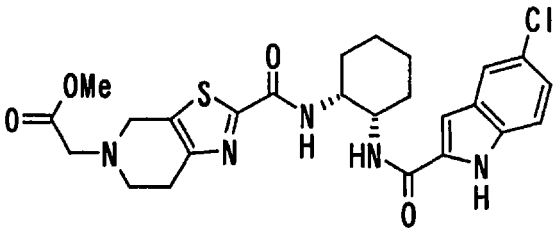
The title compound was obtained from the compound obtained in Example 34 and 2-methoxyethyl bromide in a similar manner to Example 25.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44(2H,br.s), 1.62(4H,br.s), 1.85-2.10(2H,m), 2.76-3.21(6H,m), 3.28(3H,s), 3.64(2H,br.s), 4.00-4.52(4H,m), 7.14(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.70(1H,d,J=2.0Hz), 8.08-8.20(1H,m), 8.36-8.48(1H,m), 11.84(1H,s).

MS (FAB) m/z: 516$(M+H)^+$.

[Example 36]

Methyl 2-[2-{[((1R*,2S*)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}cyclohexyl)amino]carbonyl}-6,7-dihydro-thiazolo[5,4-c]pyridin-5(4H)-yl]acetate hydrochloride:



The title compound was obtained from the compound

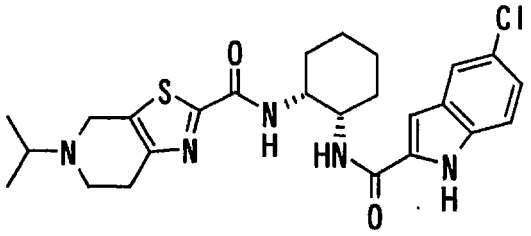
obtained in Example 34 and methyl bromoacetate in a similar manner to Example 25.

$^1$H-NMR ($CDCl_3$) δ: 1.52-1.98(7H,m), 2.17(1H,br.s), 2.87-3.10(4H,m), 3.49(2H,s), 3.76(3H,s), 3.93(1H,d,J=15.4Hz), 3.99(1H,d,J=15.4Hz), 4.22(1H,br.s), 4.45(1H,br.s), 6.86(1H,d,J=1.2Hz), 7.18(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.58-7.63(2H,m), 7.87(1H,br.s), 9.88(1H,br.s).

MS (FAB) m/z: 530$(M+H)^+$.

[Example 37]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



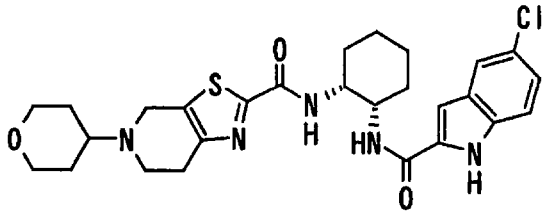

The title compound was obtained from the compound obtained in Example 34 and acetone in a similar manner to Example 24.

$^1$H-NMR (DMSO-$d_6$)δ: 1.18-1.73(8H,m), 1.81-2.10(2H,m), 2.97-3.16(1H,m), 3.20-3.41(2H,m), 3.52-3.80(2H,m), 4.19-4.31(2H,m), 4.34-4.77(2H,m), 7.17(1H,s), 7.18(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.71(1H,d,J=2.0Hz), 8.15(1H,br.s), 8.28-8.51(1H,m), 11.31(1H,br.s), 11.86(1H,s).

MS (FAB) m/z: 500$(M+H)^+$.

[Example 38]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-5-(tetrahydro-2H-pyran-4-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



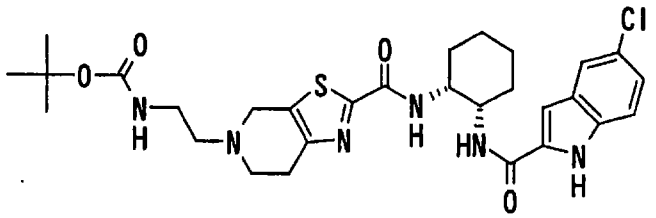
The title compound was obtained from the compound obtained in Example 34 and tetrahydro-4H-pyran-4-one in a similar manner to Example 24.

$^1$H-NMR (DMSO-$d_6$) δ: 1.30-3.56(19H,m), 3.70-4.01(3H,m), 4.17-4.30(2H,m), 4.32-4.80(1H,m), 7.15(1H,s), 7.17(1H,dd,J=8.6,2.0Hz), 7.41(1H,d,J=8.6Hz), 7.71(1H,d,J=2.0Hz), 8.14(1H,br.s), 8.39(1H,br.s), 11.84(1H,s).

MS (FAB) m/z: 542$(M+H)^+$.

[Example 39]

tert-Butyl 2-[2-{[((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)amino]carbonyl}-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl]ethylcarbamate:



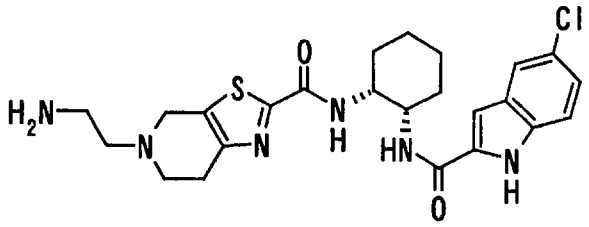
The title compound was obtained from the compound obtained in Example 34 and N-(tert-butoxycarbonyl)aminoacetoaldehyde (J. Org. Chem., 1988, Vol. 53, p.3457) in a similar manner to Example 24.

$^1$H-NMR ($CDCl_3$) δ: 1.44(9H,s), 1.54-1.98(7H,m), 2.10-2.20(1H,m), 2.74(2H,br.s), 2.92(4H,br.s), 3.34(2H,br.s), 3.84(2H,br.s) ,4.21(1H,br.s), 4.45(1H,br.s), 6.86(1H,s), 7.19(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.57-7.63(2H,m), 7.81(1H,br.s), 9.66(1H,br.s).

MS (FAB) m/z: 601$(M+H)^+$.

[Example 40]

5-(2-Aminoethyl)-N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}cyclohexyl)-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (450 mg) obtained in Example 39 was dissolved in methylene chloride (5 ml), and a saturated ethanol solution (30 ml) of hydrochloric acid was added to stir the mixture at room temperature for 1 minute. The reaction mixture was concentrated under reduced pressure, ethyl acetate was added to the residue, and solids deposited were collected by filtration to obtain the title compound (367 mg).

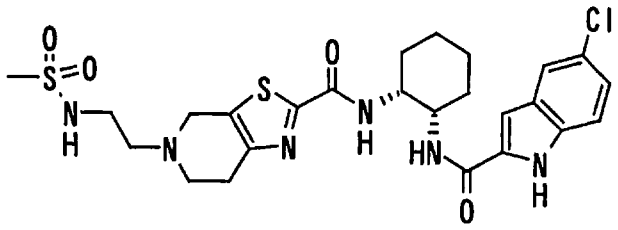
$^1$H-NMR (DMSO-$d_6$) δ: 1.38-1.50(2H,m), 1.61(4H,br.s), 1.85-

2.08(2H,m), 3.00-4.62(12H,m), 7.14(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=2.0Hz), 8.12(1H,d,J=6.6Hz), 8.15-8.68(4H,m), 11.85(1H,s).

MS (FAB) m/z: 501$(M+H)^+$.

[Example 41]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-5-{2-[(methylsulfonyl)amino]ethyl}-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (110 mg) obtained in Example 40 was dissolved in pyridine (3 ml), methanesulfonyl chloride (30 µl) was added, and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and a 85:15 mixed solvent of methylene chloride and methanol, and water were added to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride: methanol = 100:3) to obtain a pale yellow foamy substance. This product was suspended in 1N hydrochloric acid (0.3 ml), and the suspension was concentrated under

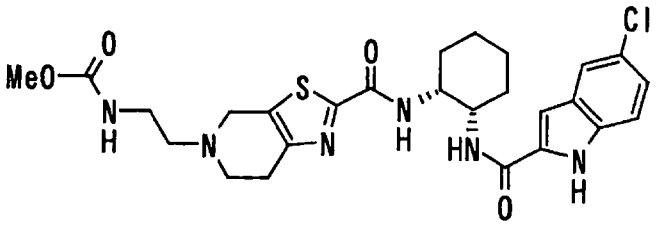
reduced pressure to obtain the title compound (63 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.38-1.50(2H,m), 1.55-1.70(4H,m), 1.86-2.05(2H,m), 2.97(3H,s), 3.02-3.25(2H,m), 3.30-3.60(5H,m), 3.78(1H,br.s), 4.18-4.30(2H,m), 4.45-4.86(2H,m), 7.14(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.40(1H,d,J=8.8Hz), 7.41(1H,br.s), 7.69(1H,d,J=2.0Hz), 8.09(1H,br.s), 8.43(1H,br.s), 11.18(1H,br.s), 11.82(1H,s).

MS (FAB) m/z: 579$(M+H)^+$.

[Example 42]

Methyl 2-[2-{[((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)amino]carbonyl}-6,7-dihydrothiazolo[5,4-c]pyridin-5(4H)-yl]ethylcarbamate hydrochloride:



The compound (144 mg) obtained in Example 40 was dissolved in pyridine (3 ml), triethylamine (138 μl) was added, and the mixture was stirred at room temperature for 5 minutes. A solution prepared by adding triphosgene (49 mg) to tetrahydrofuran (1 ml) containing methanol (20 μl) was added dropwise to this solution. After stirring for 1 hour, the reaction mixture was concentrated under reduced pressure, and the residue was dissolved in a 9:1 mixed solvent of methylene chloride and methanol. Water was

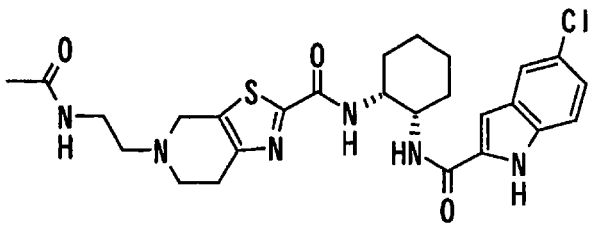
added to the solution to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride: methanol = 100:3) to obtain a colorless foamy substance. This product was suspended in 1N hydrochloric acid (0.2 ml), and the suspension was concentrated under reduced pressure to obtain the title compound (60 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.38-1.50(2H,m), 1.61(4H,br.s), 1.85-2.04(2H,m), 2.80-3.49(8H,m), 3.52(3H,s), 3.62-4.91(4H,m), 7.14(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.37(1H,br.s), 7.40(1H,d,J=8.8Hz), 7.70(1H,s), 8.11(1H,d,J=6.8Hz), 8.40(1H,br.s), 11.05(1H,br.s), 11.82(1H,br.s).

MS (FAB) m/z: 559$(M+H)^+$.

[Example 43]

5-[2-(Acetylamino)ethyl]-N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide hydrochloride:




The compound (90 mg) obtained in Example 40 was dissolved in N,N-dimethylformamide (3 ml), triethylamine

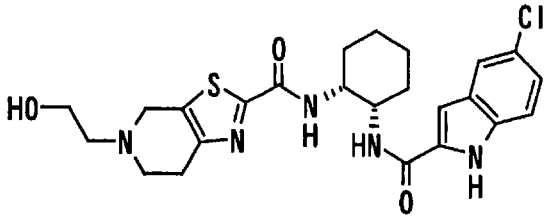
(65 μl) and acetic anhydride (22 μl) were added, and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and methylene chloride and a 0.3N aqueous solution of sodium hydroxide were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride: methanol = 100:3) to obtain a colorless foamy substance. This product was suspended in 1N hydrochloric acid (0.3 ml), and the suspension was concentrated under reduced pressure to obtain the title compound (73 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.39-1.52(2H,m), 1.54-1.70(4H,m), 1.83(3H,s), 1.84-2.06(2H,m), 3.02-3.87(8H,m), 4.16-4.32(2H,m), 4.40-4.52(1H,m), 4.78-4.88(1H,m), 7.14(1H,s), 7.16(1H,d,J=8.6Hz), 7.40(1H,d,J=8.6Hz), 7.70(1H,s), 8.07-8.17(1H,m), 8.22-8.30(1H,m), 8.38-8.52(1H,m), 11.14(1H,br.s), 11.83(1H,s).

MS (FAB) m/z: 543$(M+H)^+$.

[Example 44]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-(2-hydroxyethyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



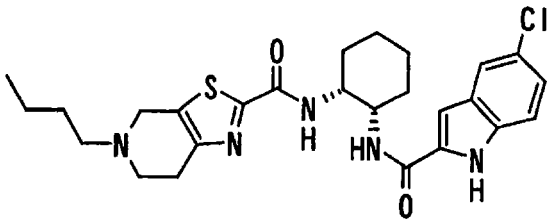
The title compound was obtained from the compound obtained in Example 34 and 2-bromoethanol in a similar manner to Example 25.

$^1$H-NMR (DMSO-$d_6$) δ: 1.37-1.69(6H,m), 1.86-2.03(2H,m), 2.54-2.61(2H,m), 2.75-2.86(4H,m), 3.52-3.59(2H,m), 3.75(2H,s), 4.47(1H,t,J=5.4Hz), 7.12(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.40(1H,d,J=8.8Hz), 7.70(1H,s), 8.05-8.13(1H,m), 8.28-8.35(1H,m), 11.78(1H,s).

MS (FAB) m/z: 502$(M+H)^+$.

[Example 45]

5-Butyl-N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]-amino}cyclohexyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 34 and n-bromobutane in a similar manner to Example 25.

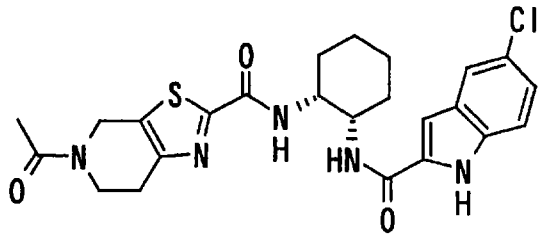
$^1$H-NMR (DMSO-$d_6$) δ: 0.88(3H,t,J=7.2Hz), 1.20-1.70(10H,m),

1.87-2.05(2H,m), 2.55-3.40(8H,m), 4.16-4.30(2H,m), 7.13(1H,s), 7.16(1H,d,J=8.8Hz), 7.40(1H,d,J=8.8Hz), 7.69(1H,s), 8.05-8.14(1H,m), 8.35(1H,br.s), 11.81(1H,s).

MS (FAB) m/z: 514$(M+H)^+$.

[Example 46]

5-Acetyl-N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]-amino}cyclohexyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide:




The compound (100 mg) obtained in Example 34 was dissolved in N,N-dimethylformamide (3 ml), triethylamine (84 μl) and acetic anhydride (29 μl) were added, and the mixture was stirred at room temperature for 3 hours. The reaction mixture was concentrated under reduced pressure, and methylene chloride and 1N hydrochloric acid were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride: methanol = 100:3) to obtain the title compound (86 mg).

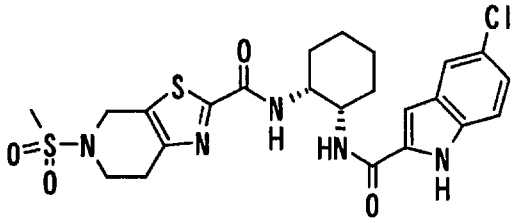
$^1$H-NMR ($CDCl_3$) δ: 1.52-1.85(5H,m), 1.91(2H,br.s), 2.10-2.28(4H,m), 2.77-3.00(2H,m), 3.70-4.00(2H,m), 4.19-

4.38(1H,m), 4.45(1H,br.s), 4.68-4.99(2H,m), 6.85(1H,s), 7.17-7.22(1H,m), 7.30-7.39(1H,m), 7.50-7.84(3H,m), 9.72-10.05(1H,m).

MS (FAB) m/z: 500$(M+H)^+$.

[Example 47]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)-5-(methylsulfonyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide:




The compound (100 mg) obtained in Example 34 was dissolved in pyridine (3 ml), triethylamine (168 μl) and methanesulfonyl chloride (48 μl) were added, and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and methylene chloride and 1N hydrochloric acid were added to the residue to separate an organic layer. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 100:1) to obtain the title compound (79 mg).

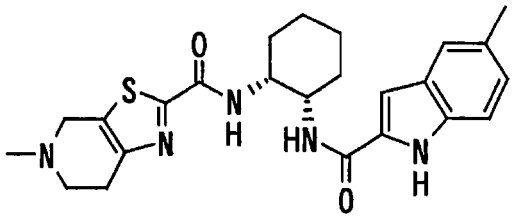
$^1$H-NMR ($CDCl_3$) δ: 1.50-1.82(5H,m), 1.90(2H,br.s), 2.13(1H,br.s), 2.89(3H,s), 2.91-2.98(2H,m), 3.60-3.70(2H,m), 4.30(1H,br.s), 4.44(1H,br.s), 4.58(2H,s),

6.87(1H,s), 7.19(1H,d,J=8.8Hz), 7.34(1H,d,J=8.8Hz), 7.61(3H,br.s), 9.91(1H,br.s).

MS (FAB) m/z: 536$(M+H)^+$.

[Example 48]

5-Methyl-N-((1R*,2S*)-2-{[(5-methylindol-2-yl)carbonyl]-amino}cyclohexyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



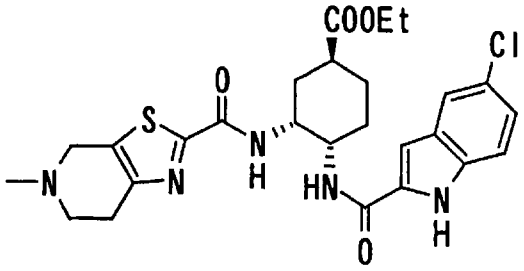
The title compound was obtained from the compound obtained in Referential Example 67 and 5-methylindole-2-carboxylic acid in a similar manner to Example 5.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.50(2H,m), 1.50-1.80(4H,m), 1.85-2.07(2H,m), 2.36(3H,s),2.88(3H,s), 3.12(2H,br.s), 3.53(2H,br.s), 4.15-4.30(2H,m), 4.30-4.80(2H,br), 7.00(1H,dd,J=8.4,1.5Hz), 7.05(1H,d,J=1.5Hz), 7.30(1H,d,J=8.4Hz), 7.38(1H,s), 8.00(1H,d,J=7.3Hz), 8.43(1H,br.s), 11.45(1H,br.s), 11.49(1H,br.s).

MS (FAB) m/z: 452$(M+H)^+$.

[Example 49]

Ethyl (1R*,3S*,4R*)-4-{[(5-chloroindol-2-yl)carbonyl]-amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:




The compound (1.40 g) obtained in Referential Example 91 was suspended in ethanol (8 ml), and a saturated ethanol solution (10 ml) of hydrochloric acid was added at room temperature to stir the mixture for 12 hours. The solvent was distilled off under reduced pressure to obtain ethyl (1R*,3S*,4R*)-3-amino-4-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexanecarboxylate hydrochloride (1.25 g).

The title compound was obtained from the above-described product and the compound obtained in Referential Example 10 in a similar manner to Example 2.

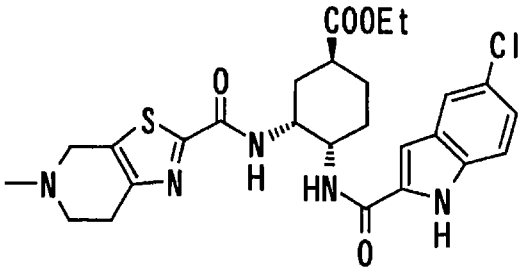
$^1$H-NMR ($CDCl_3$) δ: 1.29(3H,t,J=7.1Hz), 1.52-1.80(2H,m), 2.03-2.37(4H,m), 2.53(3H,s), 2.57-2.71(1H,m), 3.73 and 3.78(total 1H,each d,J=14.4Hz), 4.08-4.17(1H,m), 4.18(2H,q,J=7.2Hz), 4.55-4.65(1H,m), 6.85(1H,br.s), 7.21(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.48(1H,d,J=7.6Hz), 7.63(1H,d,J=2.0Hz), 7.98(1H,d,J=7.6Hz), 9.30(1H,s).

MS (ESI) m/z: 544$(M+H)^+$.

[Example 50]

Ethyl (1S,3R,4S)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-

yl)carbonyl]amino}cyclohexanecarboxylate:



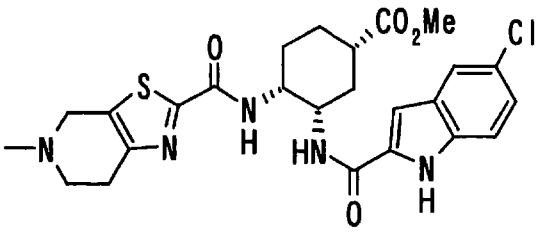

The compound (4.2 g) obtained in Referential Example 97 was suspended in ethanol (25 ml), and a saturated ethanol solution (55 ml) of hydrochloric acid was added at room temperature to stir the mixture for 11 hours. The solvent was distilled off under reduced pressure to obtain colorless solids (4.15 g).

This product (4.15 g) was dissolved in N,N-dimethylformamide (40 ml), and the compound (2.86 g) obtained in Referential Example 10, 1-hydroxybenzotriazole monohydrate (1.72 g) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (2.15 g) were added to this solution at room temperature to stir the mixture for 39 hours. The reaction mixture was concentrated under reduced pressure, and water was added to the residue to conduct extraction with chloroform. The resultant organic layer was washed with saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (chloroform:methanol = 100:1) to obtain the title compound (1.71 g).

$[\alpha]_D$ -94° (C=1.0, chloroform).

[Example 51]

Methyl (1R*,3R*,4S*)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:



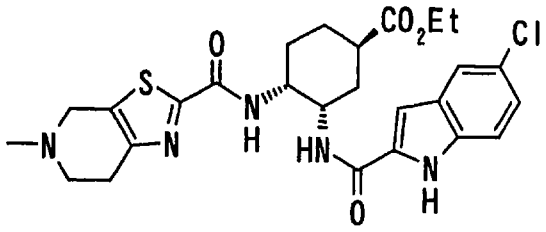

The title compound was obtained by treating the compound obtained in Referential Example 107 with an ethanol solution of hydrochloric acid and then condensing this compound with the compound obtained in Referential Example 10 in a similar manner to Example 49.

$^1$H-NMR (DMSO-$d_6$) δ: 1.55-1.80(3H,m), 1.80-2.20(3H,m), 2.60-2.75(1H,m), 2.92(3H,s), 3.15-3.30(1H,m), 3.30-3.50(4H,m), 3.57(3H,s), 3.55-3.70(1H,m), 4.20-4.30(1H,m), 4.30-4.40(1H,m), 7.02(1H,s), 7.17(1H,dd,J=8.5,2.0Hz), 7.41(1H,d,J=8.5Hz), 7.71(1H,s), 8.20-8.35(1H,m), 8.35-8.45(1H,m), 11.82(1H,br).

MS (FAB) m/z: 530$(M+H)^+$.

[Example 52]

Ethyl (1R*,3S*,4R*)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:



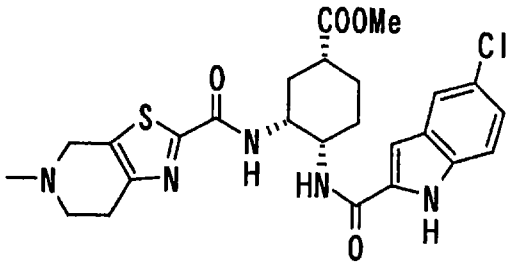
The title compound was obtained by treating the compound obtained in Referential Example 98 with a saturated ethanol solution of hydrochloric acid and then condensing it with 5-chloroindole-2-carboxylic acid in a similar manner to Example 49.

$^1$H-NMR ($CDCl_3$) δ: 1.29(3H,t,J=7.1Hz), 1.82-2.30(6H,m), 2.49(3H,s), 2.62-2.73(1H,m), 3.74-3.85(2H,m), 3.85-3.93(2H,m), 3.71(2H,s), 4.12-4.29(3H,m), 4.49-4.59(1H,m), 6.89(1H,br.s), 7.21(1H,dd,J=8.8, 2.0Hz), 7.32(1H,d,J=8.8Hz), 7.33(1H,br.s), 7.41(1H,br.s), 7.62(1H,br.s), 9.37(1H,s).

MS (ESI) m/z: 544$(M+H)^+$.

[Example 53]

Methyl (1R*,3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]-amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:



The title compound was obtained by treating the

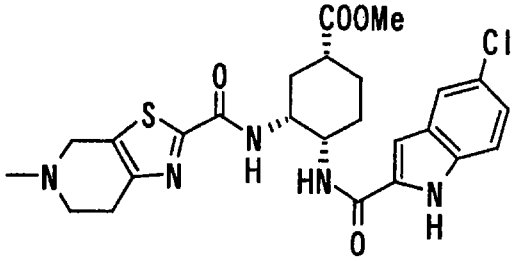
compound obtained in Referential Example 106 with a 4N dioxane solution of hydrochloric acid and then condensing it with 5-chloroindole-2-carboxylic acid in a similar manner to Example 49.

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.80(3H,m), 1.80-2.10(2H,m), 2.15-2.25(1H,m), 2.55-2.70(1H,m), 2.89(3H,s), 3.05-3.20(1H,m), 3.30-3.50(4H,m), 3.55-3.65(1H,m), 3.62(3H,s), 4.20-4.30(1H,m), 4.35-4.45(1H,m), 7.19(1H,dd,J=8.8,1.2Hz), 7.23(1H,s), 7.43(1H,d,J=8.8Hz), 7.73(1H,s), 8.03(1H,d,J=6.8Hz), 8.73(1H,d,J=8.5Hz), 11.15-11.38(1H,br), 11.85(1H,s).

MS (FAB) m/z: 530$(M+H)^+$.

[Example 54]

Methyl (1R,3R,4S)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:




The title compound was obtained by treating the compound obtained in Referential Example 112 a 4N dioxane solution of hydrochloric acid and then condensing it with 5-chloroindole-2-carboxylic acid in a similar manner to Example 49.

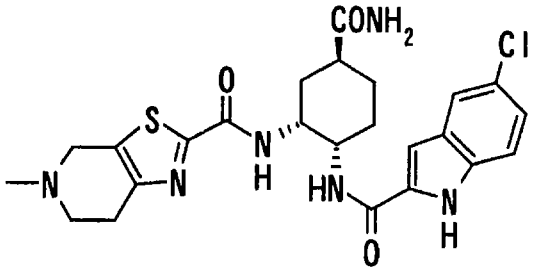
$^1$H-NMR (DMSO-$d_6$) δ: 1.67-1.76(3H,m), 1.88-1.91(1H,m),

2.01(1H,br.s), 2.13-2.22(1H,m), 2.52-2.67(4H,m), 2.86(2H,br.s), 3.04(2H,br.s), 3.33-3.41(1H,m), 3.61(3H,s), 4.22-4.36(3H,m), 7.17-7.22(2H,m), 7.42(1H,d,J=8.8Hz), 7.72(1H,s), 8.00(1H,d,J=6.9Hz), 8.68(1H,d,J=8.6Hz), 11.80(1H,s).

MS (FAB) m/z: 530$(M+H)^+$.

[Example 55]

N-((1R*,2S*,5S*)-5-(Aminocarbonyl)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:




The title compound was obtained by treating the compound obtained in Referential Example 113 with a 4N dioxane solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10.

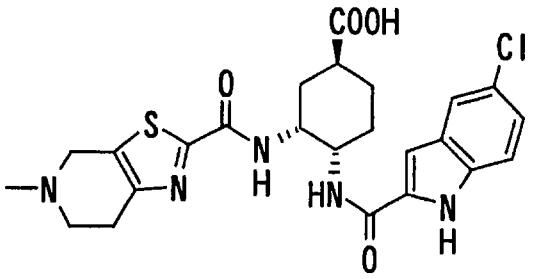
$^1$H-NMR ($CDCl_3$) δ: 0.78-2.40(7H,m), 2.53(3H,s), 2.80-2.89(1H,m), 2.91-3.00(1H,m), 3.68-3.76(2H,m), 4.08-4.19(1H,m), 4.54-4.65(1H,m), 6.80(1H,br.s), 7.21(1H,dd,J=8.4, 1.6Hz), 7.33(1H,d,J=8.4Hz), 7.38-7.43(1H,m), 7.49-7.55(1H,m), 7.63(1H,br.s), 9.14(1H,br.s).

MS (ESI) m/z: 515$(M+H)^+$.

[Example 56]

(1R*,3S*,4R*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-3-

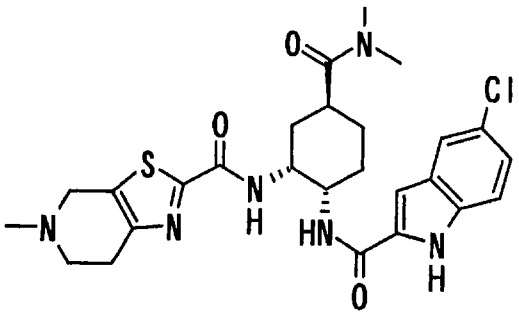
{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylic acid:




The compound (916 mg) obtained in Example 49 was suspended in a mixed solvent of ethanol (10 ml) and tetrahydrofuran (8 ml), and a 1N aqueous solution (3.3 ml) of sodium hydroxide was added at room temperature to stir the mixture for 12 hours at the same temperature. After adding 1N hydrochloric acid (3.3 ml), the solvent was distilled off under reduced pressure, and the residue was washed with water and diethyl ether to obtain the title compound (712 mg).

[Example 57]

N-{(1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




Triethylamine (0.25 ml), dimethylamine hydrochloride

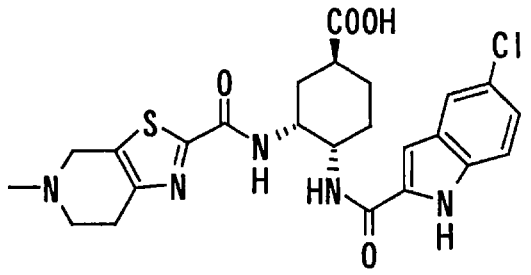
(133 mg), 1-hydroxybenzotriazole monohydrate (53 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (75 mg) were added to a chloroform suspension (10 ml) of the compound (168 mg) obtained in Example 56, and the mixture was stirred for 72 hours. The solvent was distilled off under reduced pressure, and water was added to the residue to conduct extraction with chloroform. The resultant organic layer was washed with saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride: methanol = 93:7). The thus-obtained colorless solids (135 mg) were suspended in ethanol (5 ml), to which 1N ethanol solution (0.5 ml) of hydrochloric acid was added. The mixture was stirred for 2 hours, and the solvent was distilled off to obtain the title compound (112 mg).

$^1$H-NMR (DMSO-$d_6$) $\delta$: 1.42-2.07(6H,m), 2.73-3.70(10H,m), 2.88(3H,s), 2.97(3H,s), 4.03-4.20(1H,m), 4.51-4.67(1H,m), 7.04(1H,br.s), 7.16(1H,br,J=8.8Hz), 7.41(1H,d,J=8.8Hz), 7.68(1H,br.s), 8.32-8.47(2H,m), 10.76(1H,br.s).

MS (ESI) m/z: 543$(M+H)^+$.

[Example 58]

(1S,3R,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylic acid:



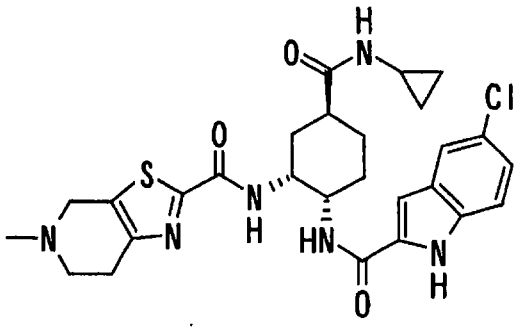
The compound (1.6 g) obtained in Example 50 was suspended in a mixed solvent of ethanol (20 ml) and tetrahydrofuran (15 ml), and a 1N aqueous solution (5.9 ml) of sodium hydroxide was added at room temperature to stir the mixture for 12 hours at the same temperature. After adding 1N hydrochloric acid (5.9 ml), the solvent was distilled off under reduced pressure, and the residue was washed with water and diethyl ether to obtain the title compound (1.19 g).

m.p. 234-236°C.

$[\alpha]_D$ -57° (C=1.0, methanol).

[Example 59]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(cyclopropylamino)carboyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



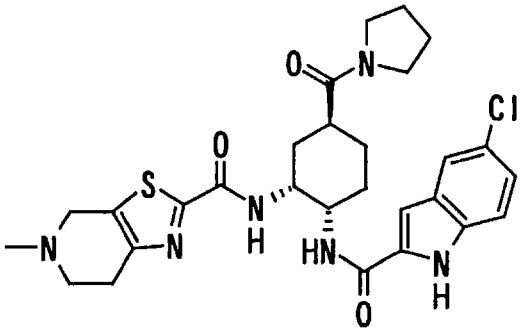
The title compound was obtained from the compound obtained in Example 58 and cyclopropylamine in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 0.32-0.40(2H,m), 0.53-0.63(2H,m), 1.50-2.10(6H,m), 2.25-2.40(1H,m), 2.45-2.70(2H,m), 2.91(3H,s), 3.05-3.80(3H,m), 4.05-4.17(1H,m), 4.30-4.55(2H,m), 4.55-4.80(1H,m), 7.03(1H,d,J=1.5Hz), 7.16(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.68(1H,d,J=2.0Hz), 7.86(1H,br,J=3.4Hz), 8.06(1H,br.s), 8.40(1H,br,J=7.6Hz), 11.20-11.60(1H,br), 11.79(1H,s).

MS (FAB) m/z: 555$(M+H)^+$.

[Example 60]

N-[(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(pyrrolidin-1-ylcarbonyl)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained from the compound obtained in Example 58 and pyrrolidine in a similar manner to Example 57.

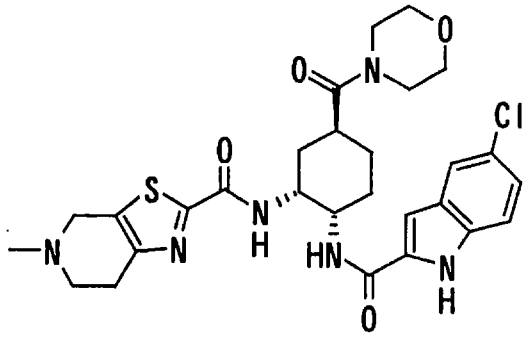
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-2.10(10H,m), 2.75-2.90(2H,m), 2.90(3H,s), 3.10-3.70(H,m), 4.05-4.20(1H,m), 4.25-

4.80(3H,m), 7.05(1H,s), 7.17(1H,d,J=8.7Hz), 7.41(1H,d,J=8.7Hz), 7.69(1H,s), 8.32(1H,br,J=7.6Hz), 8.38(1H,br,J=7.1Hz), 11.22(1H,br.s), 11.78(1H,s).

MS (FAB) m/z: 569$(M+H)^+$.

[Example 61]

N-[(1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(4-morpholinylcarbonyl)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 56 and morpholine in a similar manner to Example 57.

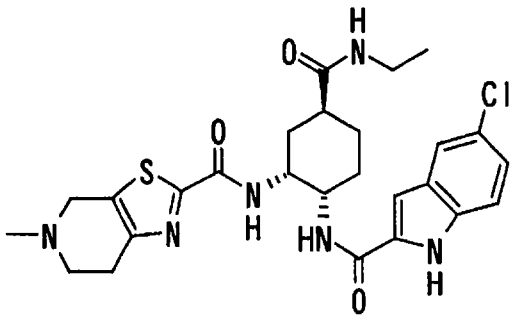
$^1$H-NMR (DMSO-$d_6$) δ: 1.40-2.05(6H,m), 2.75-3.70(18H,m), 4.02-4.17(1H,m), 4.55-4.69(1H,m), 7.05(1H,br.s), 7.17(1H,br,J=8.8Hz), 7.41(1H,d,J=8.8Hz), 7.67(1H,br.s), 8.35(1H,d,J=7.6Hz), 8.40(1H,d,J=7.6Hz), 10.79(1H,br.s).

MS (ESI) m/z: 585$(M+H)^+$.

[Example 62]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(ethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide

hydrochloride:



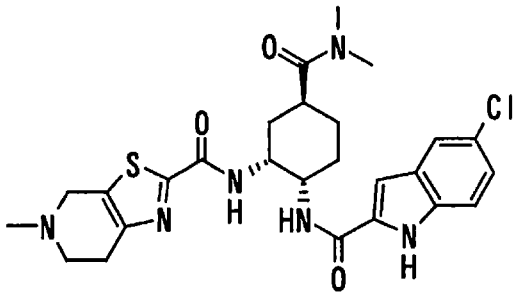
The compound (150 mg) obtained in Example 58 was dissolved in N,N-dimethylformamide (3 ml), to which N-ethylamine hydrochloride (119 mg), 1-hydroxybenzotriazole monohydrate (79 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (112 mg) and triethylamine (326 μl) were added, and the mixture was stirred at room temperature for 4 days. The solvent was distilled off under reduced pressure, and a saturated aqueous solution of sodium hydrogencarbonate was added to the residue to conduct extraction with methylene chloride. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride: methanol = 47:3). The thus-obtained solid was dissolved in methylene chloride, to which 1N ethanol solution (171 μl) of hydrochloric acid was added. The solvent was distilled off under reduced pressure, and methanol and diethyl ether were added to the residue to collect precipitate formed by filtration, thereby obtaining the title compound (74 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 0.99(3H,t,J=7.2Hz), 1.57-2.02(6H,m), 2.33-2.38(1H,m), 2.92(3H,s), 3.01-3.08(2H,m), 3.17-3.20(2H,s), 3.45-3.70(2H,m), 4.10-4.17(1H,m), 4.40-4.69(3H,m), 7.04(1H,d,J=2.0Hz), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=2.0Hz), 7.78-7.81(1H,m), 8.08-8.12(1H,m), 8.40(1H,d,J=8.1Hz), 11.23(1H,br.s), 11.79(1H,br.s).

MS (FAB) m/z: 543$(M+H)^+$.

[Example 63]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (900 mg) obtained in Example 58 was dissolved in N,N-dimethylformamide (50 ml), to which dimethylamine hydrochloride (304 mg), 1-hydroxybenzotriazole monohydrate (262 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (369 mg) and diisopropylethylamine (1.83 ml) were added, and the mixture was stirred at room temperature for 12 hours. The solvent was distilled off under reduced

pressure, and a saturated aqueous solution of sodium hydrogencarbonate was added to the residue to conduct extraction with methylene chloride. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride: methanol = 47:3). The thus-obtained white solids were dissolved in methylene chloride, to which 1N ethanol solution (1.49 ml) of hydrochloric acid was added. The solvent was distilled off under reduced pressure, and methanol and diethyl ether were added to the residue to collect precipitate formed by filtration, thereby obtaining the title compound (777 mg).

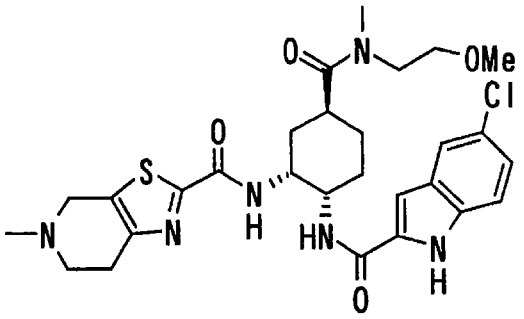
$[\alpha]_D$ = -53.9° (18°C, c = 0.505, methanol).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.70-1.85(3H,m), 1.90-2.05(2H,m), 2.80(3H,s), 2.91(3H,s), 2.95-3.10(1H,m), 2.97(3H,s), 3.10-3.75(4H,m), 4.05-4.15(1H,m), 4.35-4.75(3H,m), 7.05(1H,s), 7.16(1H,dd,J=8.7,2.1Hz), 7.41(1H,d,J=8.6Hz), 7.67(1H,s), 8.30-8.45(2H,m), 11.63(1H,br), 11.78(1H,s).

MS (FAB) m/z: 543$(M+H)^+$.

[Example 64]

N-((1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[(2-methoxyethyl)(methyl)amino]carbonyl}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



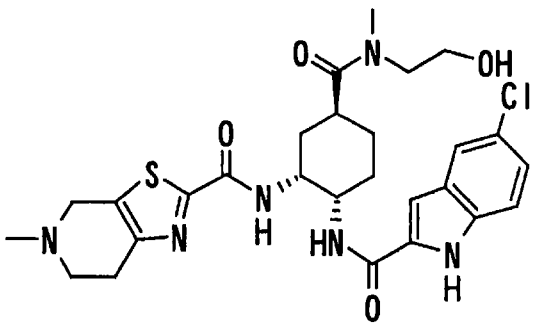
The title compound was obtained from the compound obtained in Example 58 in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.99(6H,m), 2.80,3.01(3H,each s), 2.91(3H,s), 3.03(1H,br.s), 3.16(2H,s), 3.23(3H,s), 3.35-3.67(6H,m), 4.09-4.16(1H,m), 4.43-4.67(3H,m), 7.04-7.06(1H,m), 7.16(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.69(1H,br.s), 8.29-8.41(2H,m), 11.59(1H,br.s), 11.80(1H,br.s).

MS (FAB) m/z: 587$(M+H)^+$.

[Example 65]

N-((1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[(2-hydroxyethyl)(methyl)amino]carbonyl}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound

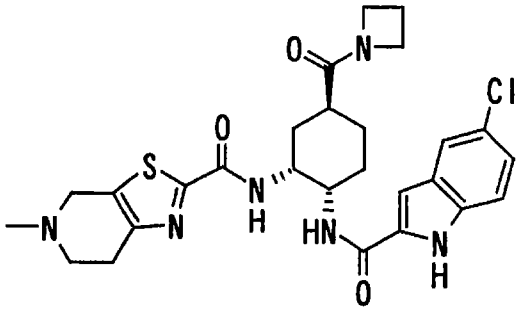
obtained in Example 58 in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.55(1H,m), 1.74-1.84(3H,m), 1.94-1.97(2H,m), 2.67,3.02(3H,each s), 2.91(3H,s), 3.10-3.68(9H,m), 4.11-4.13(1H,m), 4.43-4.66(4H,m), 7.05(1H,s), 7.16(1H,dd,J=8.7,2.0Hz), 7.41(1H,d,J=8.7Hz), 7.68(1H,s), 8.34-8.40(2H,m), 11.47(1H,br.s), 11.79(1H,s).

MS (FAB) m/z: 573$(M+H)^+$.

[Example 66]

N-((1R,2S,5S)-5-(1-Azetidinylcarbonyl)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



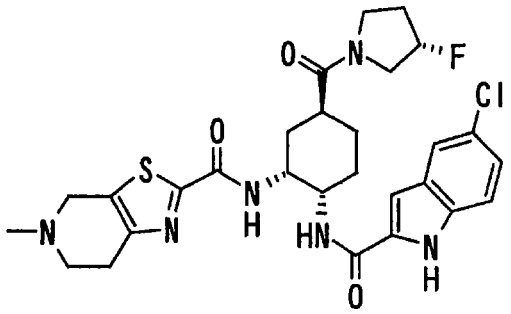
The title compound was obtained from the compound obtained in Example 58 and azetidine hydrochloride in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$)δ: 1.47-1.55(1H,m), 1.65-1.82(3H,m), 1.88-2.01(2H,m), 2.16(2H,quint.,J=7.6Hz), 3.17-3.67(5H,m), 3.82(2H,t,J=7.6Hz), 4.02-4.14(3H,m), 4.43-4.67(3H,m), 7.06(1H,s), 7.17(1H,dd,J=8.7,1.7Hz), 7.41(1H,d,J=8.7Hz), 7.69(1H,br.s), 8.31(1H,d,J=7.6Hz), 8.38(1H,d,J=7.6Hz), 11.41(1H,br.s), 11.80(1H,s).

MS (FAB) m/z: 555$(M+H)^+$.

[Example 67]

N-((1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[(3S)-3-fluoropyrrolidinyl]carbonyl}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinecarboxamide hydrochloride:



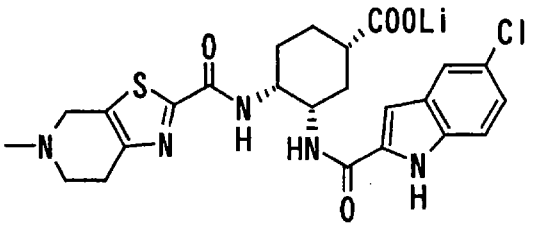
The title compound was obtained from the compound obtained in Example 58 and (S)-3-fluoropyrrolidine (Synlett., 1995, p. 55) in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 1.23-3.77(22H,m), 4.11-4.16(1H,m), 4.58-4.51(1H,m), 5.23-5.42(1H,m), 7.05(1H,s), 7.16(1H,d,J=8.3Hz), 7.42(1H,d,J=8.3Hz), 7.68(1H,s), 8.34-8.37(2H,m), 11.78(1H,s).

MS (FAB) m/z: 587$(M+H)^+$.

[Example 68]

Lithium (1R*,3R*,4S*)-3-{[(5-Chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexanecarboxylate:

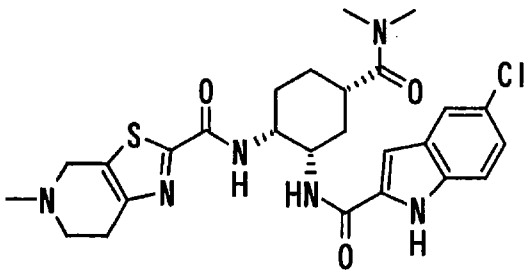


The compound (1.20 g) obtained in Example 51 was dissolved in tetrahydrofuran (32 ml), and lithium hydroxide (60.8 mg) and water (4 ml) were successively added under ice cooling to stir the mixture at room temperature for 14 hours. The solvent was distilled off under reduced pressure to obtain the title compound (1.12 g).

$^1$H-NMR (DMSO-$d_6$) δ: 1.55-1.70(2H,m), 1.70-2.05(4H,m), 2.10-2.20(1H,m), 2.25-2.40(4H,m), 2.50-2.80(4H,m), 3.45-3.65(3H,m), 4.10-4.30(2H,m), 7.00-7.20(2H,m), 7.50-7.65(2H,m).

[Example 69]

N-{(1R*,2S*,4S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound

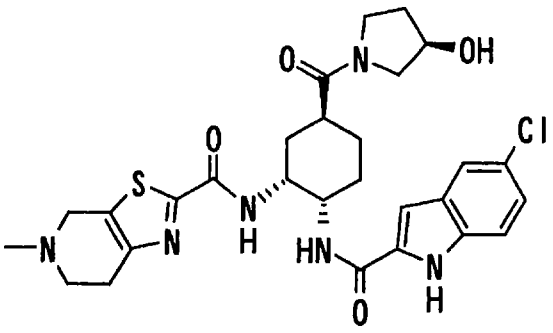
obtained in Example 68 and dimethylamine in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.60(2H,m), 1.65-1.80(2H,m), 1.95-2.10(2H,m), 2.84(3H,s), 2.90-3.05(1H,m), 2.92(3H,s), 3.06(3H,s), 3.15-3.75(4H,m), 4.25-4.75(4H,m), 7.02(1H,d,J=1.5Hz), 7.15(1H,dd,J=8.8,2.1Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=2.1Hz), 8.05(1H,d,J=7.7Hz), 8.63(1H,d,J=7.7Hz), 11.20(1H,br), 11.79(1H,s).

MS (FAB) m/z: 543$(M+H)^+$.

[Example 70]

N-((1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[(3R)-3-hydroxypyrrolidinyl]carbonyl}cyclohexyl-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



1) The compound (1.18 g) obtained in Referential Example 58 was dissolved in methanol (12 ml), 1N hydrochloric acid (240 μl) and palladium hydroxide (221 mg) were added, and hydrogen was introduced to conduct catalytic reduction under normal pressure at room temperature for 4.5 hours. The catalyst was removed by filtration, and the filtrate was concentrated to solid

under reduced pressure to obtain crude (3R)-3-{[tert-butyl(diphenyl)silyl]oxy}pyrrolidine hydrochloride (984 mg).

The thus-obtained product (249 mg), the product (295 mg) obtained in Example 58, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (126 mg) and 1-hydroxybenzotriazole monohydrate (87 mg) were dissolved in N,N-dimethylformamide (10 ml). Diisopropylethylamine (450 µl) was added dropwise to the solution under ice cooling, and the mixture was stirred at room temperature for 12 hours. The solvent was distilled off under reduced pressure, methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The residue was subjected to column chromatography on silica gel (methanol:methylene chloride = 3:97) to obtain N-((1R,2S,5S)-5-[((3R)-3-{[tert-butyl(diphenyl)silyl]oxy}-pyrrolidinyl)carbonyl]-2-{[(5-chloroindol-2-yl)carbonyl]-amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide (248 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.06(9H,s), 1.50-1.60(1H,m), 1.75-2.10(5H,m), 2.20-2.50(2H,m), 2.54(3H,d,J=2.8Hz), 2.60-3.00(5H,m), 3.30-3.80(6H,m), 4.10-4.20(1H,m), 4.40-4.70(2H,m), 6.85(1H,s), 7.15-7.25(1H,m), 7.30-7.50(8H,m), 7.60-7.70(5H,m), 7.90-8.00(1H,m), 9.38(1H,s).

MS (FAB) m/z: 823$(M+H)^+$.

2) The above product (240 mg) was dissolved in pyridine (10 ml), and hydrogen fluoride-pyridine complex (3.0 ml) was added dropwise under ice cooling to stir the mixture at 0°C for 4.5 hours. Ethyl acetate (80 ml) was added to the reaction mixture under ice cooling to dilute it. The diluted reaction mixture was poured into ice. After sodium hydrogencarbonate was added to this solution to alkalify it, liquid separation was conducted. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled under reduced pressure, and the residue was purified by column chromatography on silica gel (methanol:methylene chloride =1:19 → 1:9). The resultant crude purified product was dissolved in methylene chloride and methanol, to which 1N ethanol solution (225 μl) of hydrochloric acid was added to dry it once. Methanol and diethyl ether were added to the residue to solidify it, thereby obtaining the title compound (114 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.60(1H,m), 1.70-2.10(6H,m), 2.75-2.85(1H,m), 2.92(3H,s), 3.10-3.80(8H,m), 4.10-5.10(6H,m), 7.05(1H,d,J=1.7Hz), 7.16(1H,dd,J=8.8,1.7Hz), 7.42(1H,d,J=8.8Hz), 7.68(1H,s), 8.30-8.45(2H,m), 11.10-11.40(1H,m), 11.78(1H,s).

MS (FAB) m/z: 585$(M+H)^+$.

[Example 71]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5,5-

dimethoxycyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide or N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4,4-dimethoxycyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:

The title compound was obtained from the compound obtained in Referential Example 118 and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR ($CDCl_3$) δ: 2.11-2.15(1H,m), 2.21-2.25(1H,m), 2.41-2.43(1H,m), 2.46(3H,s), 2.70-2.75(1H,m), 2.81-2.88(1H,m),3.21(3H,s), 3.24(3H,s), 3.49(1H,s), 3.58(1H,d,J=15.6Hz), 3.71(1H,d,J=15.6Hz), 3.87-3.93(1H,m), 4.26-4.29(1H,m), 6.85(1H,d,J=2.0Hz), 7.19(1H,dd,J=8.5,2.0Hz), 7.30(1H,d,J=8.5Hz), 7.62(1H,s), 9.21(1H,s).

[Example 72]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-oxocyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide or N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4-oxocyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:

The compound (100 mg) obtained in Example 71 was dissolved in chloroform (2 ml), and trifluoroacetic acid (0.5 ml) and water (0.5 ml) were added to stir the mixture at room temperature for 3.5 hours. A saturated aqueous solution of sodium hydrogencarbonate was added to the

reaction mixture to conduct extraction with ethyl acetate. The resultant organic layer was washed with saturated aqueous solution of sodium chloride and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by preparative thin-layer chromatography on silica gel (methylene chloride:methanol = 19:1). The thus-obtained white solids were dissolved in methanol (4 ml), to which a 1N ethanol solution (0.38 ml) of hydrochloric acid was added. The solvent was distilled off under reduced pressure to obtain the title compound (35 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.83-1.90(1H,m), 2.08-2.10(1H,m), 2.28-2.32(1H,m), 2.50-2.59(1H,m), 2.87(3H,s), 2.96(1H,t,J=13.0Hz), 3.06-3.10(2H,m), 3.33-3.36(3H,m), 4.02-4.04(2H,m), 4.55-4.57(2H,m), 7.03(1H,s), 7.15(1H,d,J=8.8Hz), 7.38(1H,d,J=8.8Hz), 7.69(1H,s), 8.43(1H,d,J=8.8Hz), 8.91(1H,d,J=8.8Hz), 11.75(1H,s).

[Example 73]

N-[(1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(hydroxyimino)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide or N-[(1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4-(hydroxyimino)-cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:

The compound (133 mg) obtained in Example 72 was dissolved in a mixed solvent of pyridine (8 ml) and methanol (8 ml), and hydroxylamine hydrochloride (30 mg)

was added to stir the mixture at room temperature for 3 days. The reaction mixture was concentrated, and water was added to the residue to conduct extraction with ethyl acetate. The resultant organic layer was washed with saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride:methanol = 97:3 → 17:3) to obtain the title compound (131 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.43-1.86(3H,m), 1.98-2.03(1H,m), 2.26-2.30(1H,m), 2.45(3H,s), 2.47-2.51(1H,m), 2.67-2.71(1H,m), 2.78-2.86(3H,m), 3.86-3.43(2H,m), 4.16-4.24(2H,m), 6.85(1H,s), 7.16-7.13(1H,m), 7.20-7.24(1H,m), 7.46,7.50(total 1H,s), 7.56-7.64(2H,m), 9.59,9.62(total 1H,s).

[Example 74]

N-((7R*,8S*)-8-{[(5-Chloroindol-2-yl)carbonyl]amino}-1,4-dioxaspiro[4.5]dec-7-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide or N-((7R*,8S*)-7-{[(5-chloroindol-2-yl)carbonyl]amino}-1,4-dioxaspiro-[4.5]dec-8-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:

The title compound was obtained from the compound obtained in Referential Example 120 and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR ($CDCl_3$) δ: 1.69-1.87(6H,m), 2.14-2.17(1H,m), 2.30-2.32(1H,m), 2.47(3H,s), 2.70-2.75(1H,m), 2.81-2.89(2H,m), 3.58(1H,d,J=15.4Hz), 3.72(1H,d,J=15.4Hz), 3.89-3.91(1H,m),3.99(4H,s), 4.37-4.40(1H,m), 6.86(1H,d,J=2.0Hz), 7.19(1H,dd,J=8.8,2.0Hz), 7.30(1H,d,J=8.8Hz), 7.38(1H,d,J=7.3Hz), 7.62(1H,d,J=2.0Hz), 9.15(1H,s).

[Example 75]

N-[(1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(methoxyimino)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide or N-[(1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4-(methoxyimino)-cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide:

1) The compound (2.21 g) obtained in Referential Example 124 was dissolved in methylene chloride (30 ml), and trifluoroacetic acid (6 ml) was added to stir the mixture at room temperature for 1.5 hours. The reaction mixture was concentrated, dried with a vacuum pump and then dissolved in N,N-dimethylformamide (20 ml), to which 5-chloroindole-2-carboxylic acid (500 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (593 mg), 1-hydroxybenzotriazole monohydrate (473 mg) and N-methylmorpholine (2.8 ml) were added. The mixture was stirred at room temperature for 10 hours. Additionally, 5-chloroindole-2-carboxylic acid (242 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (237 mg) and 1-hydroxybenzotriazole monohydrate (189 mg)

were added to stir the mixture for 4 hours. A saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture to conduct extraction with ethyl acetate and with a mixed solvent of ethyl acetate and tetrahydrofuran. The resultant organic layers were washed with saturated aqueous solution of sodium chloride and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride:methanol = 97:3 → 4:1) to obtain N-[(1R*,2S*)-2-amino-5-(methoxyimino)cyclohexyl]-5-chloroindole-2-carboxamide (368 mg) and N-[(1R*,2S*)-2-amino-4-(methoxyimino)-cyclohexyl]-5-chloroindole-2-carboxamide (300 mg).

2) The title compound (mixture of syn and anti isomers at the methoxyimino group) from one of the above-obtained N-[(1R*,2S*)-2-amino-5-(methoxyimino)-cyclohexyl]-5-chloroindole-2-carboxamide or N-[(1R*,2S*)-2-amino-4-(methoxyimino)cyclohexyl]-5-chloroindole-2-carboxamide and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR ($CDCl_3$) δ: 1.84-2.00(3H,m), 2.26-2.56(3H,m), 2.46(3H,s), 2.80-2.83(4H,m), 3.57(1H,q,J=15.4Hz), 3.70(1H,q,J=15.4Hz), 3.84,3.85(total 3H,s), 4.08-4.14(1H,m), 4.26-4.30(1H,m), 6.84(1H,s), 7.17(1H,d,J=8.8Hz), 7.27(1H,d,J=8.8Hz), 7.46-7.48(2H,m), 7.56(1H,m), 9.42,9.55(total 1H,s).

[Example 76]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-hydroxycyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide (Stereoisomer A) or N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4-hydroxycyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide (Stereoisomer A):

1) N-((1R*,2S*)-2-amino-4-{[tert-butyl(diphenyl)silyl]oxy}cyclohexyl)-5-chloroindole-2-carboxamide (Stereoisomer A) and N-((1R*,2S*)-2-amino-5-{[tert-butyl(diphenyl)silyl]oxy}cyclohexyl)-5-chloroindole-2-carboxamide (Stereoisomer A) were obtained by subjecting the ((1R*,2S*)-form obtained in Referential Example 125 to de(tert-butoxycarbonylation) in the same manner as in the step 1) of Example 75 and reacting the formed product with 5-chloroindole-2-carboxylic acid.

2) N-((1R*,2S*)-5-{[tert-Butyl(diphenyl)silyl]oxy}-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer A) or N-((1R*,2S*)-4-{[tert-butyl(diphenyl)silyl]oxy}-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl-5)-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer A) was obtained from the product obtained by the above reaction and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR ($CDCl_3$) $\delta$: 1.06(9H,s), 1.55-1.61(1H,m), 1.85-

1.90(1H,m), 2.18-2.25(1H,m), 2.46(3H,s),
2.51(2H,d,J=7.6Hz), 2.72(1H,m), 3.56(1H,s),
3.57(1H,d,J=15.3Hz), 3.72(1H,d,J=15.3Hz), 3.71-3.81(1H,m),
3.88-3.95(1H,m), 6.78(1H,s), 7.17(1H,dd,J=2.0,8.8Hz),
7.37-7.44(7H,m), 7.59(1H,s), 7.65-7.68(6H,m), 9.30(1H,s).

3) The title compound was obtained from the compound obtained by the above-described reaction in the same manner as in the step 3) of Example 28.

$^1$H-NMR (DMSO-$d_6$) δ: 1.25-1.30(2H,m), 1.45-1.64(2H,m),
1.86(1H,d,J=9.0Hz), 1.98-2.03(1H,m), 2.66-2.73(3H,s),
2.69(2H,m), 2.75-2.79(2H,m), 3.54(1H,d,J=15.6Hz),
3.62(1H,d,J=15.6Hz), 3.96-4.02(2H,m), 4.78(1H,d,J=4.2Hz),
7.00(1H,s), 7.14(1H,dd,J=2.0,8.8Hz), 7.38(1H,d,J=8.8Hz),
7.66(1H,s), 8.20(1H,d,J=7.8Hz), 8.54(1H,d,J=7.8Hz),
11.69(1H,s).

[Example 77]

N-((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-hydroxy-5-methylcyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer A1) or N-((1R*,2S*)-2-{[(5-chloroindol-2-yl)carbonyl]amino}-4-hydroxy-4-methylcyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer A2):

The title compounds were obtained by reacting the compound obtained in Referential Example 128 with the compound obtained in Referential Example 10 in a similar manner to Example 2.

Stereoisomer A1:

$^1$H-NMR (DMSO-$d_6$) δ: 1.24(3H,s), 1.33-1.82(4H,m), 2.34(3H,s), 2.67-3.64(8H,m), 4.02-4.10(2H,m), 4.67(1H,br.s), 7.02(1H,s), 7.13(1H,d,J=8.6Hz), 7.38(1H,d,J=8.6Hz), 7.66(1H,d,J=2.0Hz), 8.21-8.26(1H,br), 8.59(1H,d,J=8.1Hz), 11.73(1H,br.s)

MS (FAB) m/z: 502$(M+H)^+$.

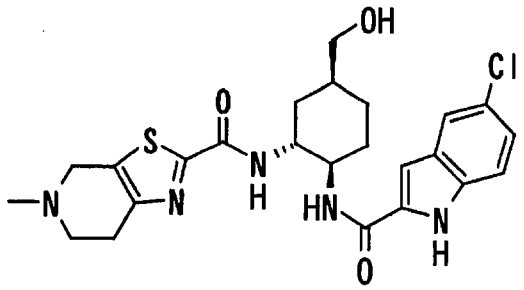
Stereoisomer A2:

$^1$H-NMR (DMSO-$d_6$) δ: 1.25(3H,s), 1.33-1.79(4H,m), 2.33(3H,s), 2.65-3.63(8H,m), 3.88-3.94(1H,m), 4.20-4.25(1H,m), 4.59(1H,br), 7.01(1H,s), 7.13(1H,d,J=7.8Hz), 7.38(1H,d,J=8.6Hz), 7.67(1H,s), 8.29(1H,br), 8.43(1H,d,J=9.3Hz), 11.67(1H,br)

MS (FAB) m/z: 502$(M+H)^+$.

[Example 78]

N-[(1R*,2R*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(hydroxymethyl)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:




The title compound was obtained by treating the compound obtained in Referential Example 129 with an ethanol solution of hydrochloric acid and then condensing

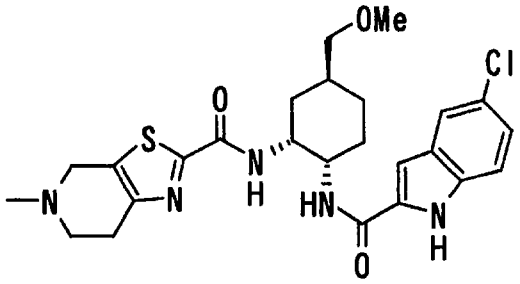
it with the compound obtained in Referential Example 10 in a similar manner to Example 49.

$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.90(5H,m), 2.07-2.26(3H,m), 2.46(3H,s), 2.67-2.95(4H,m), 3.55-3.80(4H,m), 3.80-3.95(1H,m), 4.13-4.25(1H,m), 6.84(1H,br.s), 7.17(1H,dd,J=8.8,2.0Hz), 7.23-7.35(2H,m), 7.43(1H,d,J=7.2Hz), 7.58(1H,br.s), 9.29(1H,s).

MS (ESI) m/z: 502$(M+H)^+$.

[Example 79]

N-[(1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-(methoxymethyl)cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



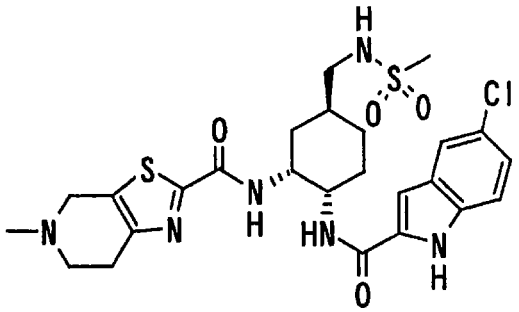

The title compound was obtained by treating the compound obtained in Referential Example 135 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10 in a similar manner to Example 49.

$^1$H-NMR ($CDCl_3$) δ: 1.20-1.38(1H,m), 1.50-1.67(2H,m), 1.88-2.03(2H,m), 2.03-2.14(1H,m), 2.21-2.32(1H,m), 2.53(3H,s), 2.75-2.95(2H,m), 3.20-3.35(2H,m), 3.37(3H,s), 3.73(1H,d,J=16.0Hz), 3.76(1H,d,J=16.0Hz), 4.04-4.13(1H,m), 4.53-

4.62(1H,m), 6.85(1H,d,J=2.0Hz), 7.19(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.54(1H,d,J=7.2Hz), 7.63(1H,d,J=2.0Hz), 8.07(1H,d,J=5.6Hz), 9.49(1H,br.s).

[Example 80]

N-((1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[(methylsulfonyl)amino]methyl}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



1) The compound (437 mg) obtained in Referential Example 137 was dissolved in ethanol (5 ml), and a 4N dioxane solution (5 ml) of hydrochloric acid was added at room temperature to stir the mixture for 13 hours. The solvent was distilled off, and the residue was dissolved in N,N-dimethylformamide (10 ml) , to which triethylamine (0.7 ml), the compound (300 mg) obtained in Referential Example 10, 1-hydroxybenzotriazole monohydrate (162 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (230 mg) were added. The mixture was stirred for 13 hours, and water was added to the reaction mixture to conduct extraction with chloroform. The resultant organic layer was washed with a saturated aqueous solution of sodium hydrogencarbonate and saturated aqueous solution

of sodium chloride and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride: methanol = 97:3) to obtain N- ((1R*,2S*,5S*)-5-(azidomethyl)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (330 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.15-2.08(7H,m), 2.33(3H,s), 2.34-2.95(6H,m), 3.64(2H,s), 4.05-4.17(1H,m), 4.36-4.47(1H,m), 7.02(1H,s), 7.15(1H,dd,J=8.8,2.0Hz), 7.40(1H,d,J=8.8Hz), 7.67(1H,d,J=2.0Hz), 8.02(1H,d,J=7.6Hz), 8.44(1H,d,J=7.6Hz), 11.8(1H,s).

2) The compound (300 mg) obtained by the above reaction was dissolved in ethanol (8 ml), and a catalytic amount of 10% palladium on carbon was added to stir the mixture at room temperature for 168 hours in a hydrogen atmosphere. Insoluble matter was filtered, and the solvent was distilled off. The thus-obtained crude N-((1R*,2S*,5S*)-5-(aminomethyl)-2-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (150 mg) was dissolved in chloroform (6 ml), and triethylamine (0.2 ml) and methanesulfonyl chloride (0.035 ml) were added to stir the mixture for 13 hours. The solvent was distilled off under reduced pressure, and water was added to the residue to conduct extraction with chloroform. The

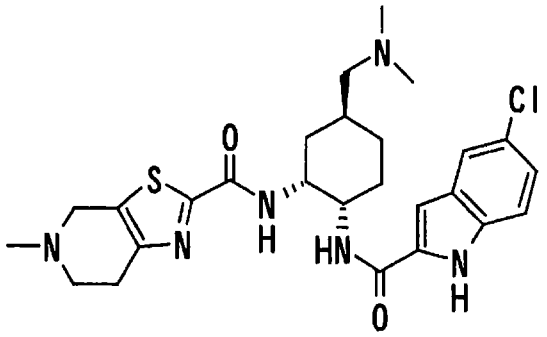
resultant organic layer was washed with a saturated aqueous solution of sodium hydrogencarbonate and saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride: methanol = 24:1) to obtain the title compound (56 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.18-1.34(2H,m), 1.50-1.75(4H,m), 1.90-2.30(4H,m), 2.53(3H,s), 2.78-2.90(2H,m), 2.90-3.05(6H,m), 3.20-3.30(1H,m), 3.68-3.81(2H,m), 3.98-4.08(1H,m), 4.54-4.62(1H,m), 6.10-6.19(1H,m), 6.86(1H,s), 7.19(1H,dd,J=8.8,2.0Hz), 7.35(1H,d,J=8.8Hz), 7.52(1H,d,J=7.6Hz), 7.62(1H,d,J=2.0Hz), 8.21(1H,d,J=5.6Hz), 9.89(1H,s).

MS (ESI) m/z: 579$(M+H)^+$.

[Example 81]

N-{(1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)methyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide trifluoroacetate:



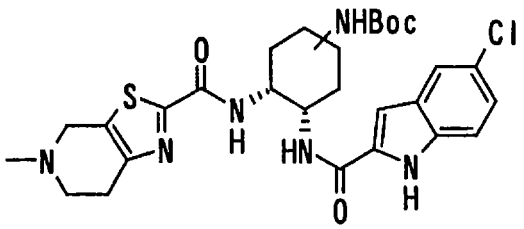
The title compound was obtained from the amine obtained in the step 2) of Example 80 in a similar manner to Example 24.

$^1$H-NMR (DMSO-$d_6$) δ: 1.15-2.22(7H,m), 2.40-2.65(2H,m), 2.68-2.85(6H,m), 2.92-3.08(5H,m), 3.10-3.18(2H,m), 4.08-4.20(1H,m), 4.35-4.51(2H,m), 7.04(1H,s), 7.14-7.20(1H,m), 7.41(1H,d,J=8.8Hz), 7.67(1H,s), 8.25-8.42(2H,m), 9.11(1H,br.s), 9.89(1H,s).

MS (ESI) m/z: 529$(M+H)^+$.

[Example 82]

tert-Butyl (3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]-amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexylcarbamate (Isomer B) and tert-butyl (3R*,4S*)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexylcarbamate (Isomer B):




The compound (Stereoisomer B) (1.79 g) obtained in Referential Example 140 was dissolved in tetrahydrofuran (36 ml), and 10% palladium on carbon (0.40 g) was added to stir the mixture at room temperature for 20 hours in a hydrogen atmosphere. After the catalyst was removed by filtration, the filtrate was concentrated under reduced pressure, and the residue was dissolved in N,N-dimethylformamide (36 ml), to which p-nitrophenyl 5-chloroindole-2-carboxylate (2.02 g) was added to stir the mixture for 16 hours. The reaction mixture was concentrated under reduced pressure, and ethyl acetate and water were added to the residue to collect insoluble matter by filtration. The product was washed with ethyl acetate to obtain crude tert-butyl (3R*,4S*)-3-amino-4-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexylcarbamate (or (3R*,4S*)-4-amino-3-{[(5-chloroindol-2-yl)carbonyl]-amino}cyclohexylcarbamate) (Isomer B1) (1.49 g). The organic layer of the filtrate was washed with water and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride: methanol = 30:1 → 10:1) to obtain tert-butyl

(3R*,4S*)-4-amino-3-{[(5-chloroindol-2-yl)carbonyl]amino}-cyclohexylcarbamate (or tert-butyl (3R*,4S*)-3-amino-4-{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexylcarbamate) (Isomer B2) (0.37 g).

One of the title compounds was obtained from the Isomer B1 and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.25-1.50(1H,m), 1.37(9H,s), 1.50-1.65(1H,m), 1.75-2.20(4H,m),2.37(3H,s), 2.70-3.00(4H,m), 3.60-3.80(3H,m), 4.13(1H,br.a), 4.43(1H,br.s), 6.92(1H,d,J=7.1Hz), 7.05(1H,s), 7.17(1H,dd,J=8.8,2.2Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,s), 8.15(1H,d,J=7.8Hz), 8.37(1H,d,J=7.1Hz), 11.78(1H,s).

MS (FAB) m/z: 587$(M+H)^+$.

The other title compound was obtained from the Isomer B2 in the same manner.

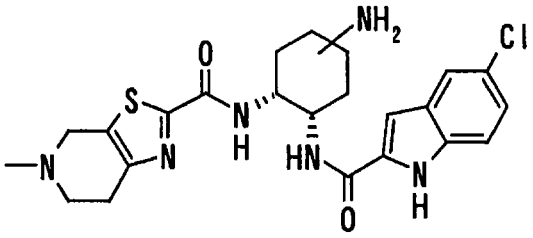
$^1$H-NMR (DMSO-$d_6$) δ: 1.15-1.30(1H,m), 1.35(9H,s), 1.45-1.60(1H,m), 1.65-1.75(1H,m), 1.85-1.95(1H,m), 2.05-2.20(2H,m), 2.34(3H,s), 2.65-2.85(4H,m), 3.55-3.70(3H,m), 4.05-4.14(1H,m),4.40(1H,br.s), 6.80(1H,d,J=7.3Hz), 7.15-7.25(2H,m), 7.43(1H,d,J=8.8Hz), 7.73(1H,d,J=2.0Hz), 8.05(1H,d,J=6.6Hz), 8.51(1H,d,J=8.8Hz), 11.82(1H,s).

MS (FAB) m/z: 587$(M+H)^+$.

[Example 83]

N-((1R*,2S*)-5-Amino-2-{[(5-chloroindol-2-yl)carbonyl]-amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide (or N-((1R*,2S*)-4-amino-2-

{[(5-chloroindol-2-yl)carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide) hydrochloride (Stereoisomer B):



The compound (Stereoisomer B) (1.11 g) synthesized from Isomer B1 in Example 82 was suspended in methylene chloride (20 ml), and an ethanol solution (20 ml) of hydrochloric acid was added to stir the mixture at room temperature for 2 hours. The solvent was distilled off under reduced pressure, and the residue was purified by gel filtration (Sephadex LH-20, methanol) to obtain the title compound (1.05 g).

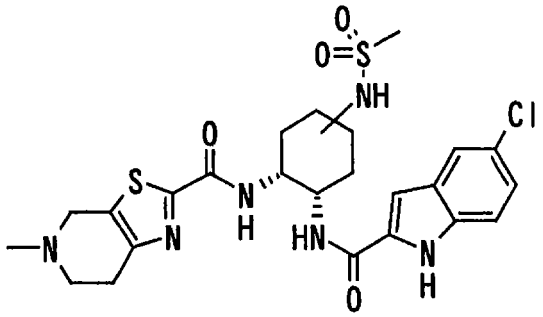
$^1$H-NMR (DMSO-$d_6$) δ: 1.55-1.65(1H,m), 1.75-1.90(2H,m), 1.95-2.20(2H,m), 2.20-2.40(1H,m), 2.90(3H,s), 3.10-3.20(1H,m), 3.20-3.50(3H,m), 3.65-3.75(1H,m), 4.10-4.20(1H,m), 4.35-4.50(1H,m), 4.55-4.65(1H,m), 4.65-4.75(1H,m), 7.07(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.69(1H,s), 8.05-8.30(3H,br), 8.40-8.50(2H,m), 11.70-11.90(2H,m).

MS (FAB) m/z: 487$(M+H)^+$.

[Example 84]

N-{(1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(methylsulfonyl)amino]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide or N-

{(1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-[(methylsulfonyl)amino]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer B):



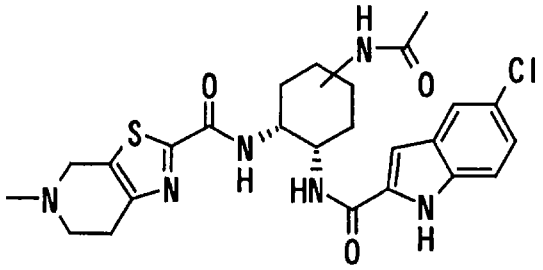
The compound (0.20 g) obtained in Example 83 was suspended in methylene chloride (7 ml), and triethylamine (0.16 ml) and methanesulfonyl chloride (28 µl) were added to stir the mixture at room temperature for 20 hours. After the reaction mixture was diluted with methylene chloride, it was washed with an aqueous solution of sodium hydroxide and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 30:1 → 15:1) to obtain the title compound (67.9 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.55(1H,m), 1.65-1.85(2H,m), 1.90-2.05(2H,m), 2.15-2.25(1H,m), 2.41(3H,s), 2.75-2.95(4H,m), 2.92(3H,s), 3.55-3.80(3H,m), 4.10-4.20(1H,m), 4.45-4.55(1H,m), 7.08(1H,s), 7.15-7.20(2H,m), 7.41(1H,d,J=8.8Hz), 7.69(1H,s), 8.27(1H,d,J=7.3Hz), 8.33(1H,d,J=8.1Hz), 11.77(1H,s).

MS (FAB) m/z: 565 $(M+H)^+$.

[Example 85]

N-((1R*,2S*)-5-(Acetylamino)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide or N-((1R*,2S*)-4-(acetylamino)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (Stereoisomer B):



The compound (Stereoisomer B) (0.20 g) obtained in Example 83 was suspended in methylene chloride (7 ml), and triethylamine (0.16 ml) and acetic anhydride (34 μl) were added to stir the mixture at room temperature for 20 hours. Methylene chloride and an aqueous solution of sodium hydroxide were added to the reaction mixture to separate insoluble matter by filtration. The organic layer of the filtrate was separated and dried over anhydrous sodium sulfate, and the solvent was then distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (methylene chloride:methanol = 15:1 → 10:1) to obtain the title compound (0.12 g).

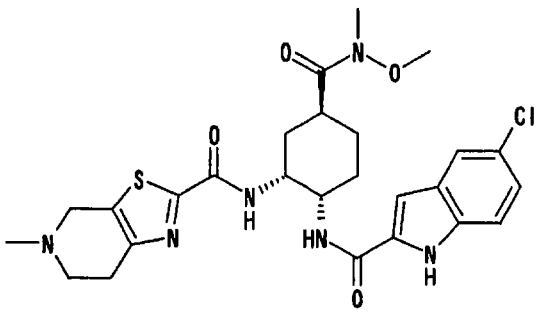
$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.50(1H,m), 1.55-1.70(1H,m),

1.80(3H,s), 1.80-2.05(3H,m), 2.05-2.20(1H,m), 2.47(3H,s), 2.80-3.00(4H,m), 3.75-4.00(3H,m), 4.15-4.30(1H,m), 4.45-4.55(1H,m), 7.07(1H,s), 7.17(1H,dd,J=8.8,1.0Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,s), 7.89(1H,d,J=7.3Hz), 8.24(1H,d,J=8.1Hz), 8.31(1H,d,J=7.3Hz), 11.77(1H,s).

MS (FAB) m/z: 528$(M+H)^+$.

[Example 86]

N-((1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-{[methoxy(methyl)amino]carbonyl}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (250 mg) obtained in Example 58 was dissolved in N,N-dimethylformamide (5 ml), and N,O-dimethylhydroxylamine hydrochloride (142 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (111 mg), 1-hydroxybenzotriazole monohydrate (89 mg) and N-methylmorpholine (213 ml) were added to stir the mixture at room temperature for 19 hours. After the reaction mixture was concentrated, an aqueous solution of sodium hydrogencarbonate was added to the residue to conduct extraction with ethyl acetate. After the resultant organic

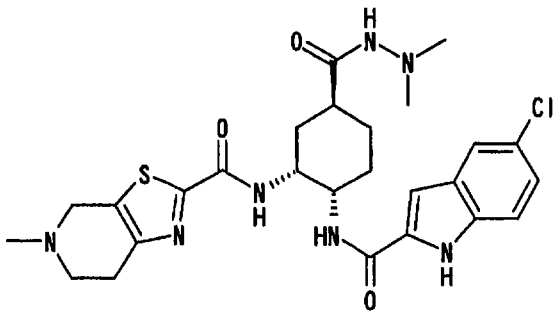
layer was washed with saturated aqueous solution of sodium chloride and dried over anhydrous sodium sulfate, the solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (methylene chloride:methanol = 47:3 → 23:2) to obtain a colorless amorphous solid (179 mg). This prodcut was dissolved in methanol-tetrahydrofuran, and 1N ethanol solution (960 ml) of hydrochloric acid was added to obtain the title compound.

$^1$H-NMR (DMSO-$d_6$) δ: 1.57-1.91(4H,m), 1.96-2.00(1H,m), 2.10-2.21(1H,m), 2.92(3H,s), 2.93-3.03(2H,m), 3.08(3H,s), 3.10-3.28(2H,m), 4.16-4.19(1H,m), 4.50-4.52(1H,m), 4.69(1H,br.s), 7.06(1H,s), 7.17(1H,dd,J=8.8,1.5Hz), 7.42(1H,d,J=8.8Hz), 7.70(1H,s), 8.33(1H,br.s), 8.41(1H,d,J=7.8Hz), 11.81(1H,br.s).

MS (ESI) m/z: 559$(M+H)^+$.

[Example 87]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(2,2-dimethylhydrazino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



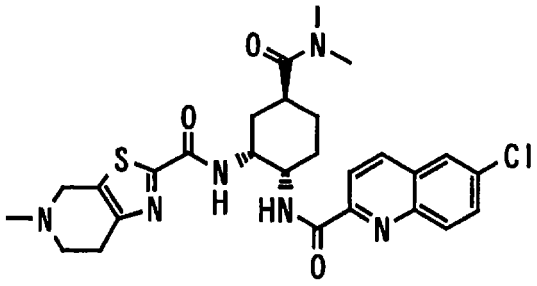
The title compound was obtained from the compound obtained in Example 58 and N,N-dimethylhydrazine in a similar manner to Example 57.

$^1$H-NMR (DMSO-$d_6$) δ: 1.49-1.54(1H,m), 1.76-1.81(2H,m), 1.89-1.93(2H,m), 2.07-2.17(1H,m), 2.33-3.60(14H,m), 4.15-4.19(1H,m), 4.40-4.47(2H,m), 4.70-4.72(1H,m), 7.04(1H,s), 7.17(1H,dd,J=8.5,2.0Hz), 7.42(1H,d,J=8.5Hz), 7.70(1H,s), 8.17-8.22(1H,m), 8.41-8.43(1H,m), 11.80(1H,br.s).

MS (ESI) m/z: 558$(M+H)^+$.

[Example 88]

6-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)-2-quinolinecarboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 145 with an ethanol solution of hydrochloric acid in a similar manner to Example 49 and then condensing it with the compound obtained in Referential Example 10.

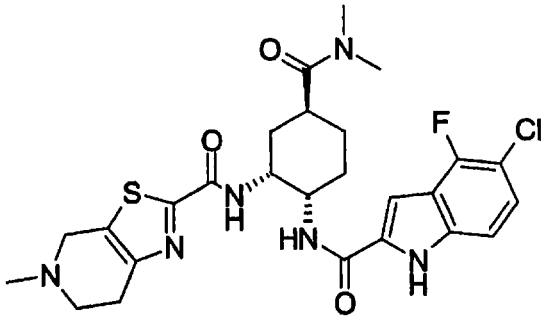
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.75-1.90(3H,m), 1.90-2.00(1H,m), 2.00-2.20(1H,m), 2.80(3H,s), 2.90(3H,s),

2.99(3H,s), 3.10-3.30(5H,m), 3.56(1H,br), 4.10-4.20(1H,m), 4.40-4.70(2H,m), 7.88(2H,s), 8.15(1H,d,J=8.6Hz), 8.22(1H,s), 8.52(1H,d,J=8.6Hz), 8.72(1H,d,J=8.3Hz), 8.89(1H,d,J=8.3Hz).

MS (FAB) m/z: 555$(M+H)^+$.

[Example 89]

N-{(1R,2S,5S)-2-{[(5-Chloro-4-fluoroindol-2-yl)carbonyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



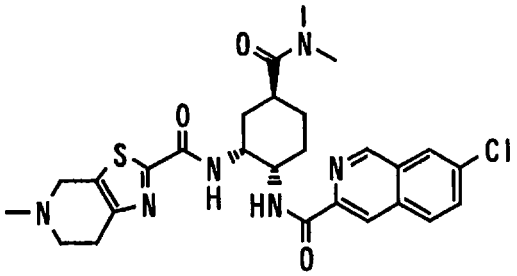
The title compound was obtained by condensing the compound obtained in Referential Example 144 with the compound obtained in Referential Example 274 in a similar manner to Referential Example 91 and treating the resultant compound with a 4N dioxane solution of hydrochloric acid and then with the compound obtained in Referential Example 10.

$^1$H-NMR (DMSO-$d_6$) δ:1.24-1.98(6H,m), 2.33-3.33(6H,m), 2.81(3H,s), 2.90(3H,s), 2.99(3H,s), 4.12(1H,br.s), 4.30-4.70(1H,m), 4.60(1H,br.s), 7.21(1H,s), 7.27(2H,br.s), 8.37(1H,d,J=8.1Hz), 8.43(1H,d,J=7.6Hz), 12.11(1H,s).

MS (FAB) m/z: 561(M+H)$^+$.

[Example 90]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}cyclohexyl)isoquinoline-3-carboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 146 with an ethanol solution of hydrochloric acid in a similar manner to Example 49 and then condensing it with the compound obtained in Referential Example 10.

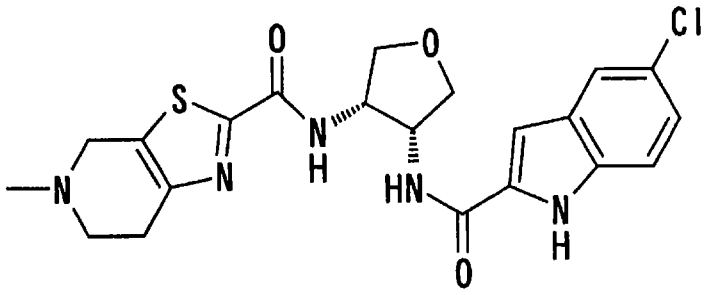
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.65(1H,m), 1.70-1.85(3H,m), 1.95-2.10(1H,m), 2.10-2.20(1H,m), 2.80(3H,s), 2.92(3H,s), 2.96(3H,s), 2.95-3.10(1H,m), 3.10-3.40(3H,m), 3.70-3.80(1H,m), 4.20-4.30(1H,m), 4.40-4.60(2H,m), 4.65-4.80(1H,m), 7.83-7.93(1H,m), 8.26(1H,d,*J*=8.8Hz), 8.38(1H,s), 8.60(1H,s), 8.85-9.00(2H,m), 9.30-9.40(1H,m).

MS (FAB) *m/z*: 555(M+H)$^+$.

[Example 91]

N-((3R$^*$,4S$^*$)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-tetrahydrofuran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo-

[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (0.1 g) obtained in Referential Example 10, 1-hydroxybenzotriazole monohydrate (78 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.2 g) were successively added to a solution of the compound (0.12 g) obtained in Referential Example 172 in N,N-dimethylformamide (20 ml), and the mixture was stirred at room temperature for 1 day. After the reaction mixture was concentrated, and the resultant residue was diluted with chloroform-methanol (9:1) and washed with a saturated aqueous solution of sodium hydrogencarbonate and saturated aqueous solution of sodium chloride, the resultant organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (chloroform:methanol = 95:5) to obtain a free base of the title compound. This product was treated with an ethanol solution of hydrochloric acid to obtain the title compound (0.1 g).

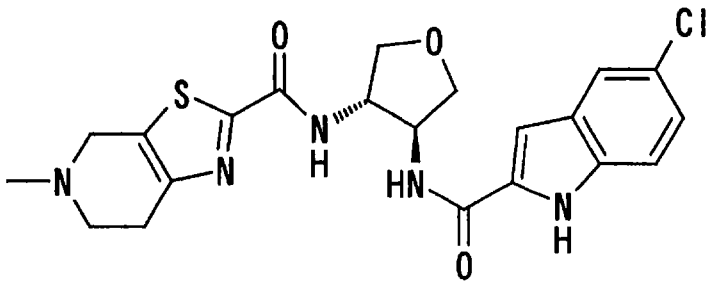
$^1$H-NMR ($CDCl_3$) δ: 2.50(3H,s), 2.70-2.90(4H,m), 3.67(1H,s), 3.70(1H,s), 3.86(1H,dd,J=9.2,6.3Hz), 3.97(1H,dd,J=9.7,4.1Hz), 4.15(1H,dd,J=9.7,5.8Hz),

4.24(1H,dd,J=9.2,7.0Hz), 4.75-4.89(1H,m), 4.92-5.03(1H,m), 6.88(1H,s), 7.20(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.35-7.43(1H,m), 7.58(1H,d,J=2.0Hz), 7.64(1H,d,J=7.1Hz), 9.38(1H,s).

MS (FAB) m/z: 460($M+H^+$).

[Example 92]

N-((3S,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-tetrahydrofuran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide:



The title compound was obtained from the compound obtained in Referential Example 183 in accordance with the processes of Referential Example 172 and Example 91.

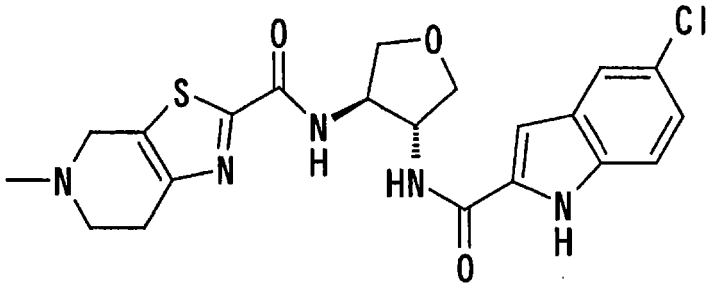
$^1$H-NMR ($CDCl_3$) δ: 2.51(3H,s), 2.83(2H,t,J=5.3Hz), 2.93(2H,t,J=5.3Hz), 3.72(2H,s), 3.78-3.89(2H,m), 4.31(1H,dd,J=9.2,7.3Hz), 4.41-4.56(2H,m), 4.63-4.75(1H,m), 6.88(1H,s), 7.22(1H,dd,J=8.8,2.0Hz), 7.32(1H,d,J=8.8Hz), 7.35-7.46(1H,m), 7.55(1H,d,J=7.1Hz), 7.60(1H,d,J=2.0Hz), 9.38(1H,s).

MS (FAB) m/z: 460($M+H^+$).

[Example 93]

N-((3R,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-tetrahydrofuran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo-

[5,4-c]pyridine-2-carboxamide hydrochloride:

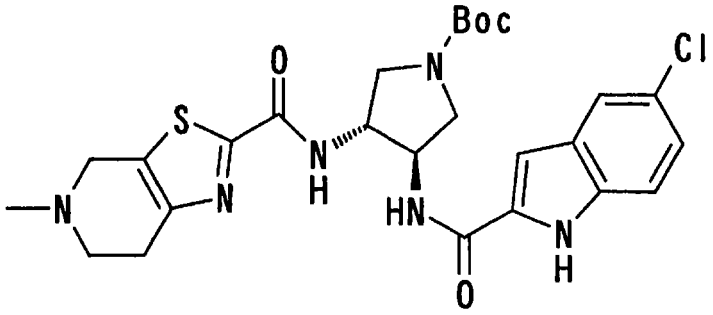


The title compound was obtained from the compound obtained in Referential Example 187 in accordance with the processes of Referential Example 172 and Example 91.

$^1$H-NMR and MS (FAB): The same as those of the enantiomer in Example 92.

[Example 94]

tert-Butyl (3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidine-1-carboxylate:



The title compound was obtained from the compound obtained in Referential Example 193 and the compound obtained in Referential Example 10 in accordance with the process of Example 91.

Melting point: 190-192°C.

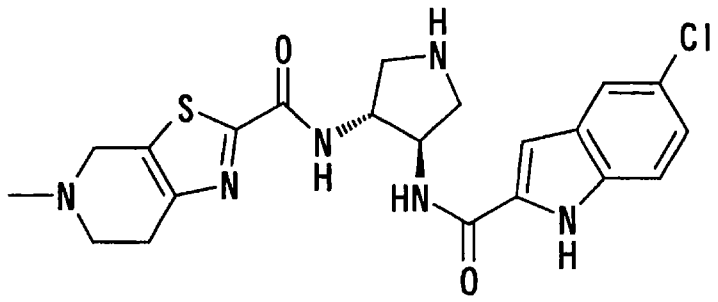
$^1$H-NMR ($CDCl_3$) δ: 1.45(9H,s), 2.46(3H,s), 2.74-2.81(4H,m),

3.24-3.37(2H,m), 3.54-3.70(2H,m), 3.96-4.00(1H,m), 4.15-4.23(1H,m), 4.50-4.65(1H,m), 4.77-4.82(1H,m), 6.79,6.87(total 1H,each s), 7.12-7.95(5H,m), 9.91,9.97(total 1H,each s).

MS (FAB) m/z: 559($M+H^+$).

[Example 95]

N-((3R,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-pyrrolidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (170 mg) obtained in Example 94 was dissolved in methylene chloride (3 ml), and trifluoroacetic acid (2 ml) was added at room temperature to stir the mixture for 1 hour. After concentrating the reaction mixture, chloroform and a saturated aqueous solution of sodium hydrogencarbonate were added. The resultant organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The resultant residue was purified by preparative thin-layer chromatography on silica gel (chloroform:methanol:water = 7:3:1 under layer). A methanol solution of hydrochloric acid was added to the

resultant intended product to obtain the title compound (90 mg) as a hydrochloride (NMR was measured in the form of a free base).

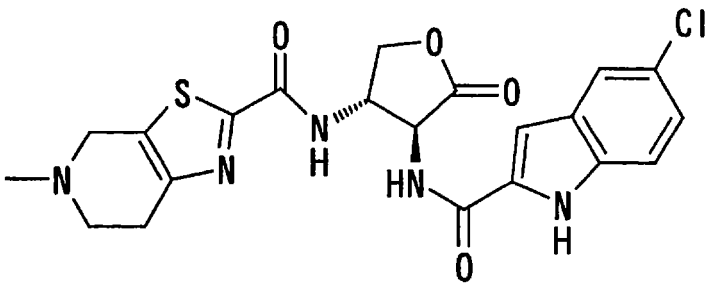
Melting point: 248-250°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 2.44(3H,s), 2.70-2.80(4H,m), 2.97-3.05(2H,m), 3.46-3.68(4H,m), 4.49-4.52(1H,m), 4.60-4.65(1H,m), 6.86(1H,s), 7.05-7.08(1H,m), 7.20(1H,d,J=8.5Hz), 7.44(1H,s), 7.89(2H,br), 10.51(1H,br).

MS (FAB) m/z: 459($M+H^+$).

[Example 96]

N-((3S,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-oxotetrahydrofuran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained by removing the tert-butoxycarbonyl group of the compound obtained in Referential Example 196 in a similar manner to Referential Example 69 and reacting the resultant product with the compound obtained in Referential Example 10 in a similar manner to Example 91.

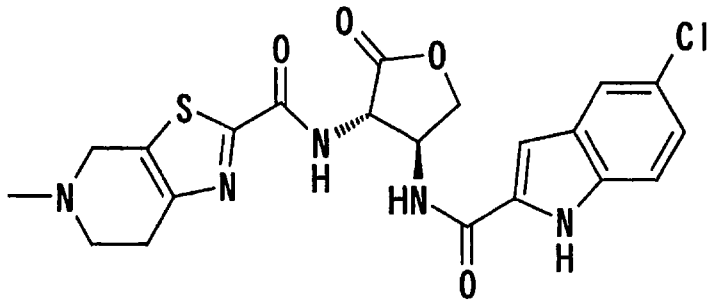
$^1$H-NMR (DMSO-$d_6$) δ: 2.90(3H,s), 3.02-3.17(2H,m), 3.23-3.34(4H,m), 4.20(1H,t,J=8.6Hz), 4.61(1H,t,J=8.6Hz), 4.92-

5.01(1H,m), 5.14-5.26(1H,m), 7.09(1H,s),
7.19(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz),
7.73(1H,d,J=2.0Hz), 9.27(1H,d,J=6.8Hz), 9.35(1H,d,J=6.8Hz),
11.22-11.33(1H,m), 11.89(1H,s).

MS (FAB) m/z: 474($M+H^+$).

[Example 97]

N-((3S,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-2-oxotetrahydrofuran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained by removing the tert-butoxycarbonyl group of the compound obtained in Referential Example 197 in a similar manner to Referential Example 69 and reacting the resultant product with 5-chloroindole-2-carboxylic acid in a similar manner to Example 91.

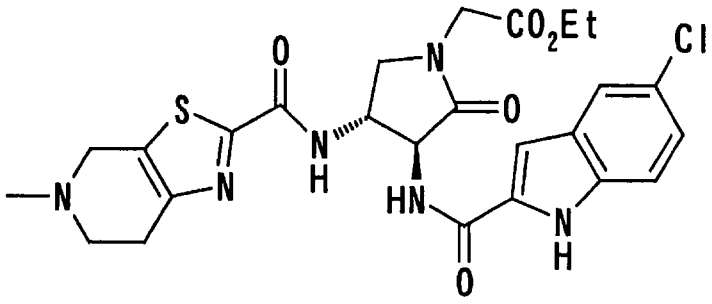
$^1$H-NMR (DMSO-$d_6$) δ: 2.52(3H,s), 2.83(2H,t,J=5.9Hz), 2.91-3.00(2H,m), 3.73(2H,s), 4.23(1H,t,J=8.6Hz), 4.40-4.53(1H,m), 4.96(1H,dd,J=10.8,5.2Hz),
5.16(1H,dd,J=9.2,7.3Hz), 7.01(1H,s),
7.25(1H,dd,J=8.8,2.0Hz), 7.34(1H,d,J=8.8Hz),
7.52(1H,d,J=2.0Hz), 8.01(1H,d,J=5.4Hz), 8.51-

8.63(1H,m),9.22(1H,s).

MS (FAB) m/z: 474($M+H^+$).

[Example 98]

Ethyl (3S,4R)-2-(3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}-2-oxopyrrolidin-1-yl)acetate hydrochloride:




The title compound was obtained from the compound obtained in Referential Example 199 and the compound obtained in Referential Example 10 in a similar manner to Example 91. NMR was measured in the form of a free base.

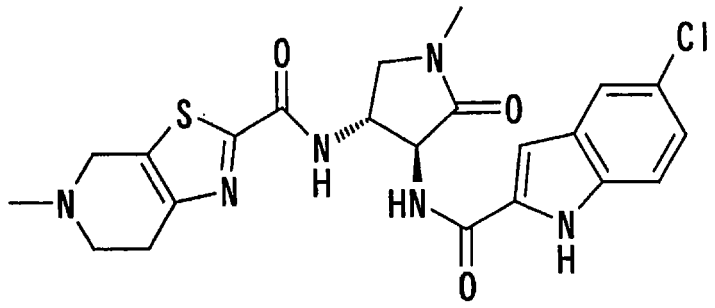
$^1$H-NMR (DMSO-$d_6$) δ: 1.19(3H,t,J=7.1Hz), 2.35(3H,s), 2.71-2.84(2H,m), 2.80-2.90(2H,m), 3.40(1H,d,J=10.3Hz), 3.61(2H,d,J=10.8Hz), 3.84(1H,dd,J=10.3,5.6Hz), 4.01-4.23(4H,m), 4.80-4.94(1H,m), 5.04(1H,t,J=8.6Hz), 7.01(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.40(1H,d,J=8.8Hz), 7.69(1H,d,J=2.0Hz), 8.73(1H,d,J=8.6Hz), 8.90(1H,d,J=8.8Hz), 11.86(1H,s).

MS (FAB) m/z: 559($M+H^+$).

[Example 99]

N-((3R,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-

methyl-5-oxopyrrolidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide:



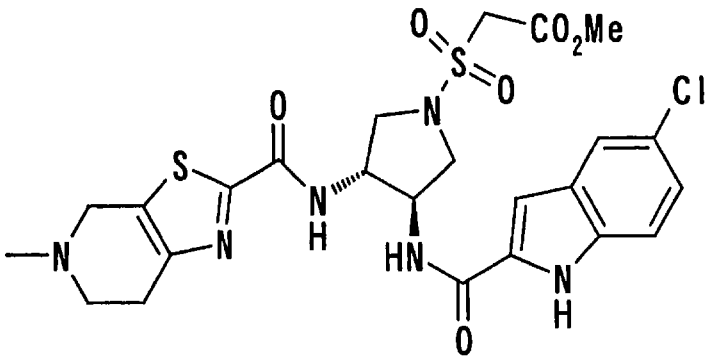
The title compound was obtained from the compound obtained in Referential Example 201 and the compound obtained in Referential Example 10 in a similar manner to Example 91.

$^1$H-NMR ($CDCl_3$) δ: 2.49(3H,s), 2.77-2.82(2H,m), 2.86-2.91(5H,m), 3.69(2H,d,J=1.2Hz), 4.39-4.54(3H,m), 4.93-4.98(1H,m), 6.98(1H,d,J=1.2Hz), 7.05-7.34(3H,m), 7.63(1H,d,J=2.0Hz), 8.11(1H,d,J=7.8Hz), 9.00(1H,s)

MS (FAB) m/z: 487($M+H^+$).

[Example 100]

Methyl 2-[((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)-sulfonyl]acetate:



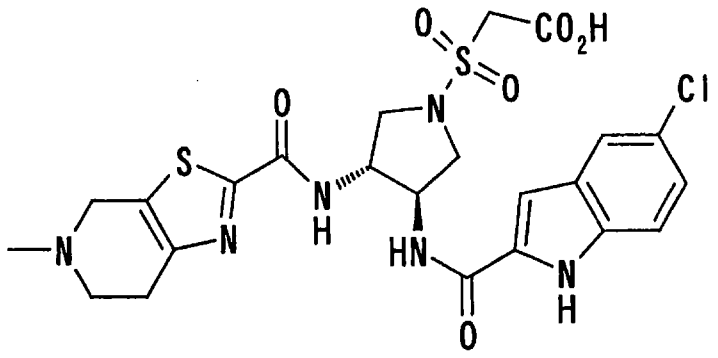
The compound (230 mg) obtained in Example 95 and triethylamine (0.10 ml) were dissolved in methylene chloride (6.9 ml), and the mixture was cooled with ice. Methoxycarbonylmethanesulfonyl chloride (Synthesis, p. 321, 1975) (105 mg) was added, and the resultant mixture was warmed to room temperature and stirred overnight. The reaction mixture was diluted with chloroform, washed with water and saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The resultant residue was purified by preparative thin-layer chromatography on silica gel (chloroform:methanol = 20:1) and powdered with methanol-water to obtain the title compound (150 mg).

$^1$H-NMR ($CDCl_3$) δ: 2.48(3H,s), 2.76-2.86(4H,m), 3.49-3.73(4H,m), 3.87(3H,s), 3.94-3.98(1H,m), 4.08-4.11(1H,m), 4.13(2H,s), 4.69-4.72(1H,m), 4.88-4.91(1H,m), 6.89(1H,s), 7.12-7.15(1H,m), 7.27-7.28(1H,m), 7.50(1H,s), 7.81-7.86(2H,m), 9.92(1H,s).

MS (FAB) m/z: 595($M+H^+$).

[Example 101]

2-[((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)sulfonyl]acetic acid:

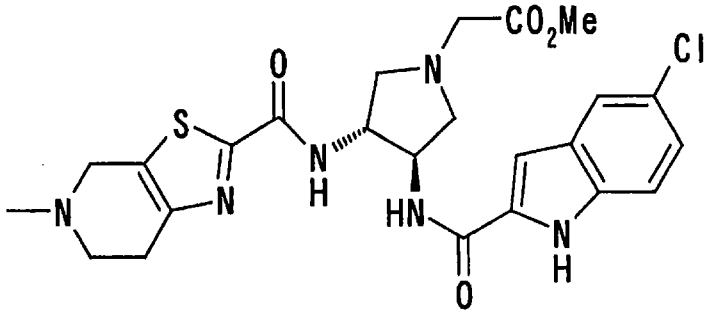


The compound (100 mg) obtained in Example 100 was dissolved in tetrahydrofuran (4 ml)-water (1 ml), and the mixture was cooled with ice. Lithium hydroxide monohydrate (7.8 mg) was added, and the resultant mixture was heated to room temperature and stirred for 4 hours. After the reaction mixture was neutralized with 1N hydrochloric acid, it was concentrated. Deposits were collected by filtration, washed with water and 50% ethanol and dried overnight at 50°C under reduced pressure to obtain the title compound (87 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 2.50(3H,s), 2.92(4H,s), 3.34-3.43(4H,m), 3.76-3.85(2H,m), 4.27(each 1H,AB type d,J=14.5Hz), 4.65-4.71(1H,m), 4.78-4.84(1H,m), 7.14(1H,s), 7.18(1H,d,J=8.8Hz), 7.40(1H,d,J=8.8Hz), 7.72(1H,s), 8.87(1H,d,J=7.8Hz), 9.12(1H,d,J=8.2Hz), 11.83(1H,s).

[Example 102]

Methyl 2-((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)acetate:



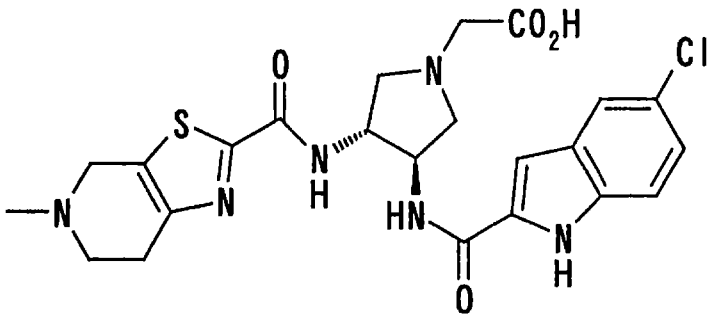

The compound (230 mg) obtained in Example 95 and potassium carbonate (90 mg) were dissolved in N,N-dimethylformamide (4.6 ml), and the mixture was cooled with ice. Methyl bromoacetate (0.062 ml) was added, and the resultant mixture was stirred for 45 minutes. The reaction mixture was diluted with ethyl acetate, washed with water and saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The resultant residue was purified by preparative thin-layer chromatography on silica gel (chloroform:methanol = 10:1) and solidifier with methanol-water to obtain the title compound (190 mg).

$^1$H-NMR ($CDCl_3$) δ: 2.35(2H,s), 2.48(3H,s), 2.73-2.95(4H,m), 3.34-3.42(2H,m), 3.46(2H,q,J=6.5Hz), 3.67(2H,q,J=6.5Hz), 3.75(3H,s), 4.57-4.71(2H,m), 6.91(1H,s), 7.10-7.13(1H,m), 7.31(1H,d,J=9.0Hz), 7.53(1H,s), 7.77(1H,d,J=8.0Hz), 7.87(1H,d,J=6.8Hz), 10.22(1H,s).

MS (FAB) m/z: 531($M+H^+$).

[Example 103]

2-((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)acetic acid:

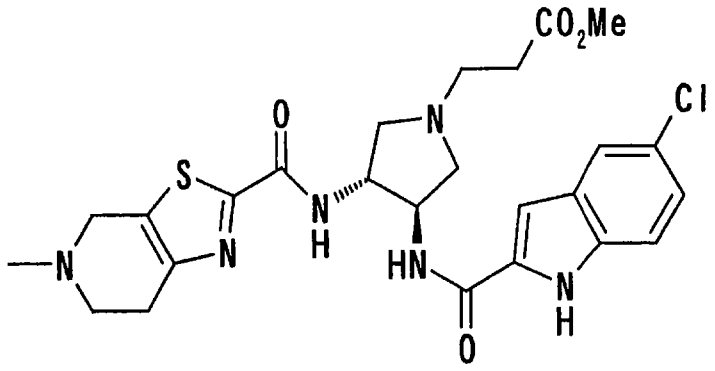


The title compound was obtained from the compound obtained in Example 102 in a similar manner to Example 101.

$^1$H-NMR (DMSO-$d_6$) δ: 2.42(3H,s), 2.69-2.87(6H,m), 3.13(1H,t,J=9.0Hz), 3.22(1H,t,J=9.0Hz), 3.33(each 1H,AB type d,J=6.8Hz), 3.72(2H,s), 4.53-4.60(1H,m), 4.65-4.72(1H,m), 7.16-7.20(2H,m), 7.42(1H,d,J=8.8Hz), 7.70(1H,s), 8.85(1H,d,J=7.5Hz), 9.00(1H,d,J=8.3Hz), 11.79(1H,s).

[Example 104]

Methyl 3-((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)propionate:



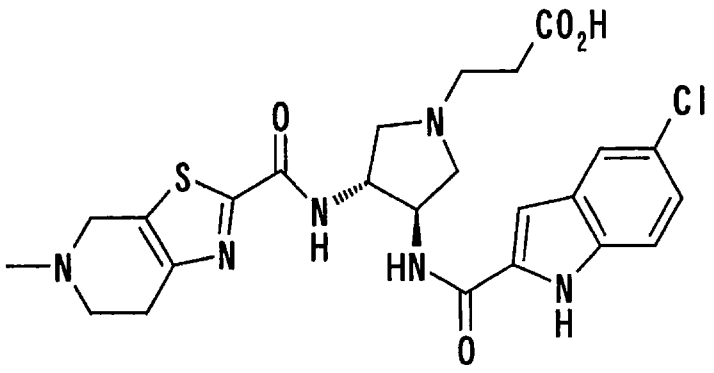
The title compound was obtained from the compound obtained in Example 95 and methyl 3-bromopropionate in a similar manner to Example 102.

$^1$H-NMR ($CDCl_3$) δ: 1.96-2.20(2H,m), 2.49(3H,s), 2.61-2.96(8H,m), 3.17-3.21(2H,m), 3.62-3.72(2H,m), 3.69(3H,s), 4.46-4.49(1H,m), 4.56-4.61(1H,m), 6.87(1H,s), 7.05-7.14(1H,m), 7.32(1H,d,J=9.2Hz), 7.53(1H,s), 7.65-7.71(2H,m), 10.02(1H,s).

MS (FAB) m/z: 545($M+H^+$).

[Example 105]

3-((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)propionic acid:

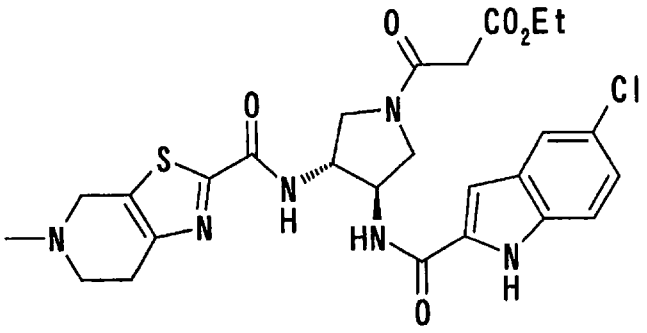


The title compound was obtained from the compound obtained in Example 104 in a similar manner to Example 101.

$^1$H-NMR (DMSO-$d_6$) δ: 2.38(3H,s), 2.39-2.84(10H,m), 2.93(1H,t,J=8.8Hz), 3.05(1H,t,J=8.8Hz), 3.65(2H,s), 4.51-4.56(1H,m), 4.63-4.68(1H,m), 7.16-7.19(2H,m), 7.41(1H,d,J=8.8Hz), 7.69(1H,s), 8.81(1H,d,J=7.8Hz), 8.97(1H,d,J=8.3Hz), 11.75(1H,s).

[Example 106]

Ethyl 3-((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)-3-oxopropionate:

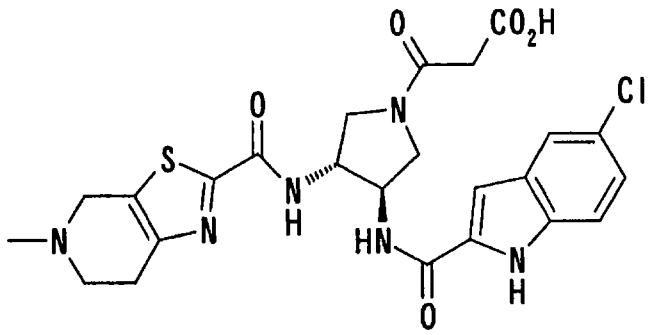



The title compound was obtained from the compound obtained in Example 95 and ethylmalonyl chloride in a similar manner to Example 100.

$^1$H-NMR (DMSO-$d_6$) δ: 1.20(3H,t,J=7.0Hz), 2.37(3H,s), 2.73-2.75(2H,m), 2.82-2.84(2H,m), 3.35-3.38(2H,m), 3.64(2H,s), 3.68-3.83(2H,m), 3.91-4.00(2H,m), 4.10(2H,q,J=7.0Hz), 4.61-4.84(2H,m), 7.13(1H,s), 7.18(1H,dd,J=8.5,2.0Hz), 7.41(1H,d,J=8.5Hz), 7.72(1H,s), 8.73(1H,t,J=9.0Hz), 9.10(1H,d,J=9.0Hz), 11.79(1H,s).

[Example 107]

3-((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)-3-oxopropionic acid:

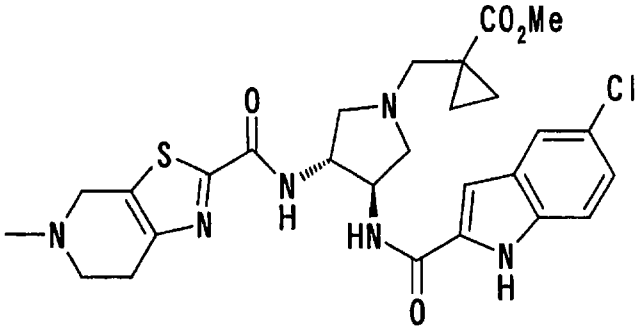


The title compound was obtained from the compound obtained in Example 106 in a similar manner to Example 101.

$^1$H-NMR (DMSO-$d_6$) δ: 2.39(3H,s), 2.77(2H,s), 2.85(2H,s), 3.29-3.55(4H,m), 3.68(2H,s), 3.82-4.01(2H,m), 4.62-4.68(1H,m), 4.77-4.86(1H,m), 7.14(1H,s), 7.18(1H,d,J=8.8Hz), 7.41(1H,d,J=8.8Hz), 7.72(1H,s), 8.75(1H,t,J=8.8Hz), 9.12(1H,d,J=7.8Hz), 11.81(1H,s).

[Example 108]

Methyl 1-[((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)methyl]-cyclopropanecarboxylate:



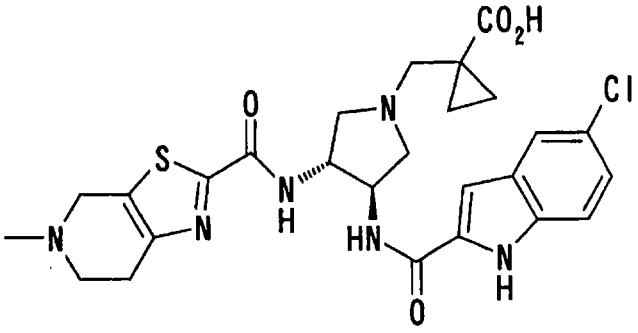
The title compound was obtained from the compound obtained in Example 95 and methyl 1-(bromomethyl)-cyclopropanecarboxylate in a similar manner to Example 102.

$^1$H-NMR ($CDCl_3$) δ: 0.78-0.79(2H,m), 1.24-1.26(2H,m), 2.49(3H,s), 2.62-2.88(6H,m), 3.20-3.28(2H,m), 3.66(3H,s), 3.61-3.75(4H,m), 4.45-4.62(2H,m), 6.86(1H,s), 7.12-7.15(1H,m), 7.24-7.28(1H,m), 7.52(1H,d,J=8.5Hz), 7.54(1H,s), 7.69(1H,d,J=8.0Hz), 10.00(1H,s).

MS (ESI) m/z: 571($M+H^+$).

[Example 109]

1-[((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)methyl]-cyclopropanecarboxylic acid:

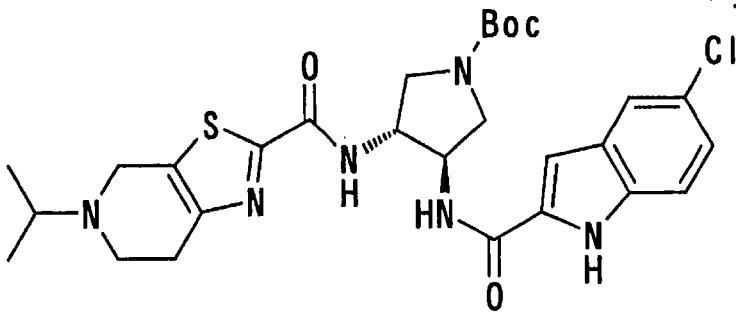


The title compound was obtained from the compound obtained in Example 108 in a similar manner to Example 101.

$^1$H-NMR (DMSO-$d_6$) δ: 0.73-0.78(2H,m), 1.04-1.07(2H,m), 2.37(3H,s), 2.65-2.84(6H,m), 3.11-3.20(4H,m), 3.64(2H,s), 4.59-4.74(2H,m), 7.16(1H,s), 7.17(1H,d,J=8.5Hz), 7.40(1H,d,J=8.5Hz), 7.70(1H,s), 8.84(1H,d,J=7.5Hz), 9.12(1H,d,J=7.5Hz), 11.77(1H,s).

[Example 110]

tert-Butyl (3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}pyrrolidine-1-carboxylate:

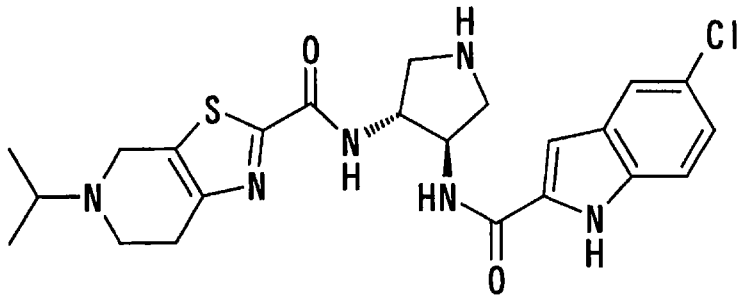


The title compound was obtained from the compound obtained in Referential Example 193 and Referential Example 148 in a similar manner to Example 91.

$^1$H-NMR ($CDCl_3$) δ: 1.12(6H,d,J=6.6Hz), 1.47(9H,s), 2.83-2.88(4H,m), 2.94-2.99(1H,m), 3.20-3.29(1H,m), 3.31-3.42(1H,m), 3.75-3.81(2H,m), 3.98(1H,t,J=8.5Hz), 4.15-4.35(2H,m), 4.50-4.65(1H,m), 6.85,6.91(total 1H,each s), 7.15-7.90(5H,m), 9.41,9.50(total 1H,each s).

[Example 111]

N-((3R,4R)-4-{[(5-chloroindol-2-yl)carbonyl]amino}pyrrolidin-3-yl)-5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:

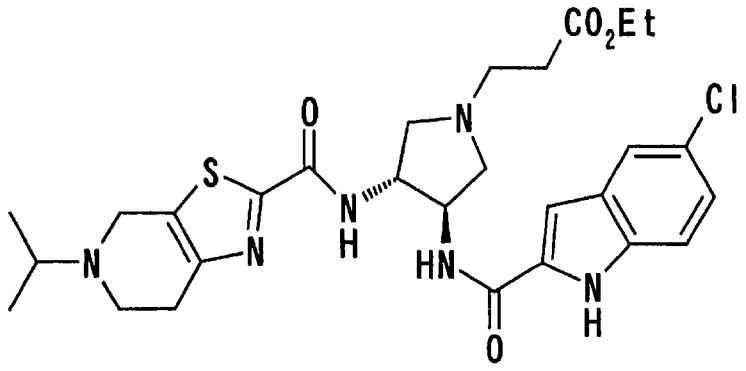


The title compound was obtained from the compound obtained in Example 110 in a similar manner to Example 95.

$^1$H-NMR ($CDCl_3$) δ: 1.13(6H,d,J=6.3Hz), 2.85(4H,br.s), 2.96-3.05(3H,m), 4.51-4.52(1H,m), 4.76-4.80(2H,m), 5.36-5.39(2H,m), 5.53-5.58(1H,m), 7.17-7.19(1H,m), 7.27-7.31(2H,m), 7.57(1H,s), 7.64(2H,br), 9.82(1H,br).

[Example 112]

Ethyl 3-((3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)propionate:



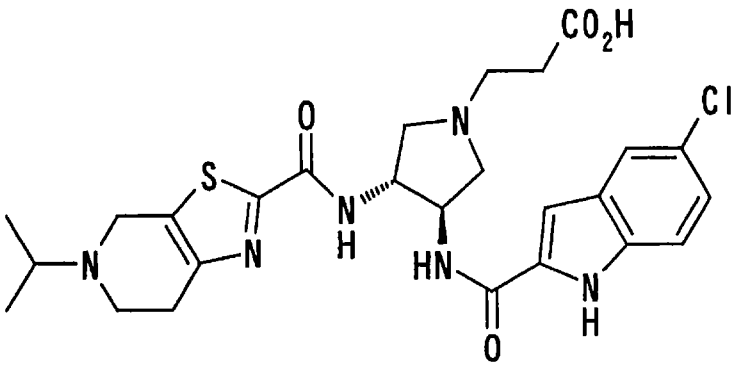

The title compound was obtained from the compound obtained in Example 111 and ethyl 3-bromopropionate in a similar manner to Example 102.

$^1$H-NMR ($CDCl_3$) δ: 1.14(6H,d,J=6.5Hz), 1.26(3H,t,J=7.0Hz), 2.51(3H,t,J=7.0Hz), 2.63(1H,dd,J=9.5,6.5Hz), 2.73-2.91(6H,m), 2.95-3.02(1H,m), 3.22(2H,q,J=7.0Hz), 3.81(each 1H,AB type d,J=14.5Hz), 4.16(2H,q,J=7.0Hz), 4.40-4.45(1H,m), 4.52-4.59(1H,m), 6.88(1H,d,J=2.0Hz), 7.17-7.19(1H,m), 7.30-7.32(2H,m), 7.59(1H,s), 7.62(1H,s), 9.56(1H,s).

MS (FAB) m/z: 587($M+H^+$).

[Example 113]

3-((3R,4R)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-4-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidin-1-yl)propionic acid:

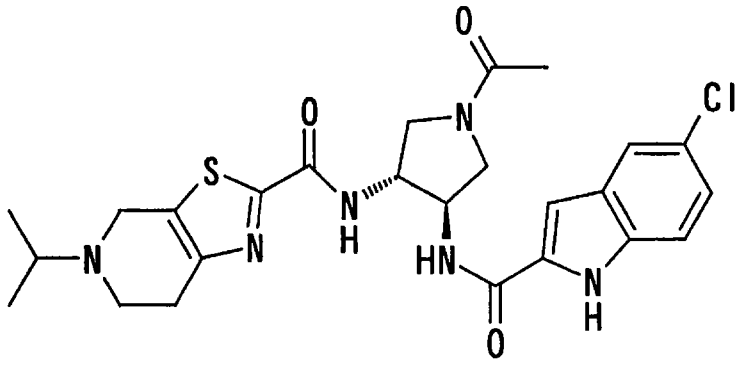


The title compound was obtained from the compound obtained in Example 112 in a similar manner to Example 101.

$^1$H-NMR (DMSO-$d_6$) δ: 1.04(6H,d,J=6.6Hz), 2.40(2H,q,J=7.0Hz), 2.50(4H,s), 2.60-2.74(4H,m), 2.90-2.94(2H,m), 3.02-3.06(1H,m), 3.20-3.35(2H,m), 4.50-4.53(1H,m), 4.61-4.65(1H,m), 7.15-7.18(2H,m), 7.41(1H,d,J=8.8Hz), 7.68(1H,s), 8.78(1H,d,J=7.5Hz), 8.90(1H,d,J=8.0Hz), 11.73(1H,s).

[Example 114]

N-((3R,4R)-1-Acetyl-4-{[(5-chloroindol-2-yl)carbonyl]-amino}pyrrolidin-3-yl)-5-isopropyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound

obtained in Example 111 and acetic anhydride in a similar manner to Example 100.

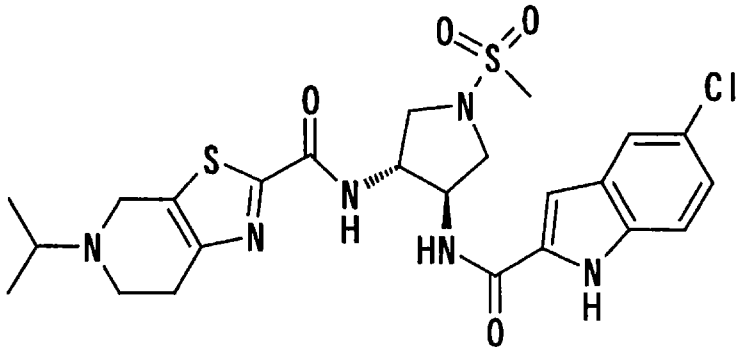
Melting point: 254-258°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.34-1.37(6H,m), 1.96(3H,s), 3.30-3.55(5H,m), 3.66-3.82(3H,m), 3.95(1H,q,J=8.3Hz), 4.45-4.82(4H,m), 7.15(1H,s), 7.18(1H,d,J=9.0Hz), 7.41(1H,d,J=9.0Hz), 7.71(1H,s), 8.75-8.81(1H,m), 9.21(1H,d,J=8.0Hz), 11.32(1H,br), 11.83(1H,d,J=7.3Hz).

MS (FAB) m/z: 529($M+H^+$).

[Example 115]

N-[(3R,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(methylsulfonyl)pyrrolidin-3-yl]-5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 111 and methanesulfonyl chloride in a similar manner to Example 100.

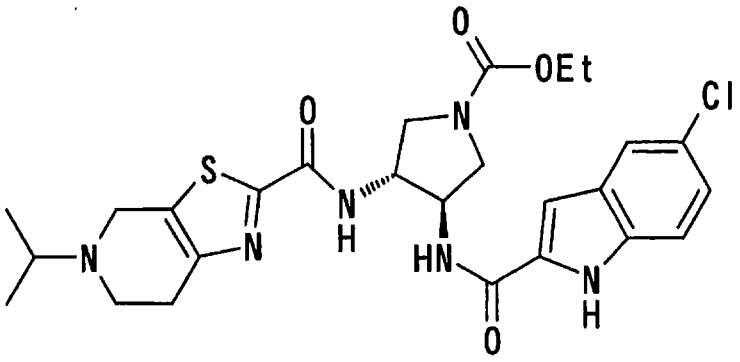
Melting point: 230-235°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.32-1.36(6H,m), 3.32(3H,s), 3.43-3.46(5H,m), 3.68-3.75(4H,m), 4.48(1H,m), 4.62-4.72(2H,m),

4.83(1H,t,J=5.5Hz), 7.14(1H,s), 7.18(1H,d,J=8.6Hz),
7.40(1H,d,J=8.6Hz), 7.72(1H,s), 8.82(1H,br),
9.20(1H,d,J=8.3Hz), 11.30(1H,br), 11.86(1H,d,J=7.5Hz).
MS (FAB) m/z: 565($M+H^+$).

[Example 116]

Ethyl (3R,4R)-3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}pyrrolidine-1-carboxylate hydrochloride:




The title compound was obtained from the compound obtained in Example 111 and ethyl chloroformate in a similar manner to Example 100.

Melting point: 225-228°C (decomposed).

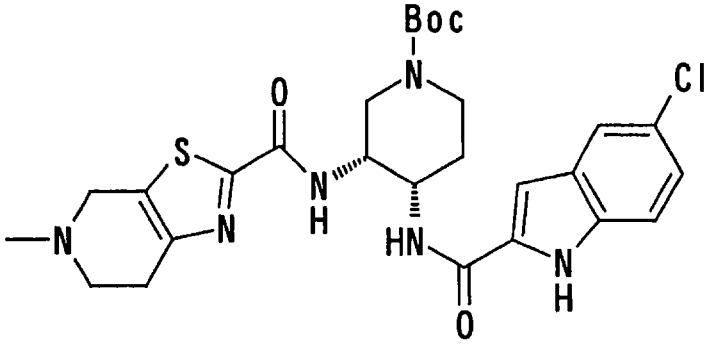
$^1$H-NMR (DMSO-$d_6$) δ: 1.20(3H,t,J=7.0Hz), 1.31-1.37(6H,m), 3.33-3.45(5H,m), 3.66-3.75(4H,m), 4.05(2H,q,J=7.0Hz), 4.45-4.77(4H,m), 7.15(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,d,J=2.0Hz), 8.77(1H,d,J=7.0Hz), 9.20(1H,d,J=8.0Hz), 11.30(1H,br), 11.83(1H,d,J=7.5Hz).

MS (FAB) m/z: 559($M+H^+$).

[Example 117]

tert-Butyl (3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]-

amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate:




The title compound was obtained from the compound obtained in Referential Example 207 and Referential Example 10 in a similar manner to Example 91.

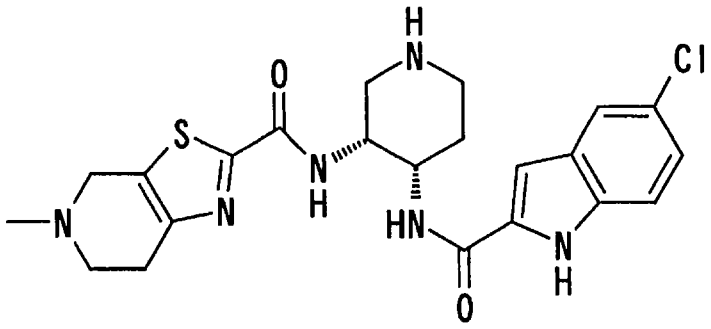
Melting point: 152-154°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 1.53(9H,s), 1.62-1.80(1H,m), 2.23-2.30(1H,m), 2.52(3H,s), 2.75-3.05(5H,m), 3.10-3.25(1H,m), 3.68-3.82(2H,m), 4.15-4.45(4H,m), 6.89(1H,s), 7.19(1H,dd,J=8.8,1.8Hz), 7.32(1H,d,J=8.8Hz), 7.92(1H,d,J=1.8Hz), 7.75(1H,br.s), 8.21(1H,br.s), 9.39(1H,s).

MS (ESI) m/z: 573$(M+H)^+$.

[Example 118]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide dihydrochloride:



The title compound was obtained from the compound obtained in Example 117 in a similar manner to Example 95.

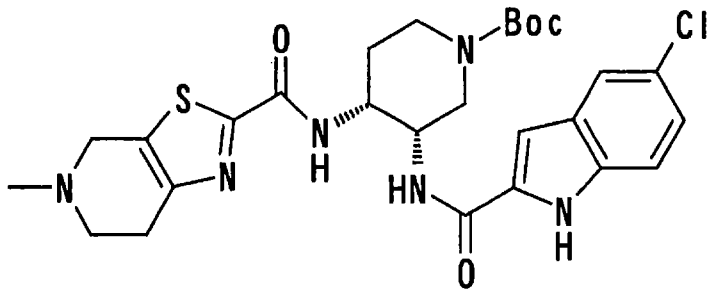
Melting point: 240-258°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.85-2.00(1H,m), 2.05-2.20(2H,m), 2.93(3H,s), 3.05-3.60(7H,m), 3.65-3.75(1H,m), 4.10-4.52(2H,m), 4.60-4.75(2H,m), 7.10-7.21(2H,m), 7.43(1H,d,J=8.6Hz), 7.70(1H,s), 8.50(1H,br.d,J=7.8Hz), 8.90-9.05(2H,m), 9.27(1H,br.s), 11.9(1H,br.d,J=13.4Hz).

MS (ESI) m/z: 473$(M+H)^+$.

[Example 119]

tert-Butyl (3R*,4S*)-3-{[(5-chloroindol-2-yl)carbonyl]-amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate:



The title compound was obtained from the compound obtained in Referential Example 208 and 5-chloroindole-2-carboxylic acid in a similar manner to Example 91.

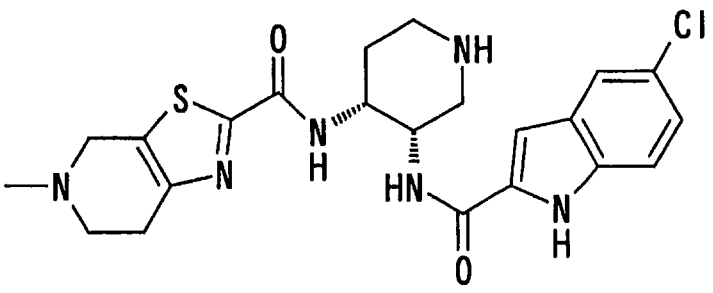
Melting point: 187-189°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 1.48(9H,s), 1.72-1.90(1H,m), 2.00(1H,br.s), 2.00-2.10(1H,m), 2.45(3H,s), 2.60-2.70(2H,m), 2.70-2.80(2H,m), 3.23(1H,t,J=10.8Hz), 3.35-3.50(1H,m), 3.50-3.72(2H,m), 3.90-4.20(2H,m), 4.30-4.40(1H,m), 4.45-4.55(1H,m), 6.85(1H,d,J=1.5Hz), 7.17(1H,dd,J=8.8,1.9Hz), 7.20-7.30(1H,m), 7.33(1H,d,J=8.8Hz), 7.58(1H,d,J=1.9Hz), 10.17(1H,s).

MS (ESI) m/z: 573($M+H^+$).

[Example 120]

N-((3R*,4S*)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-piperidin-4-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide dihydrochloride:




The title compound was obtained from the compound obtained in Example 119 in a similar manner to Example 95.

Melting point: 276-278°C (decomposed).

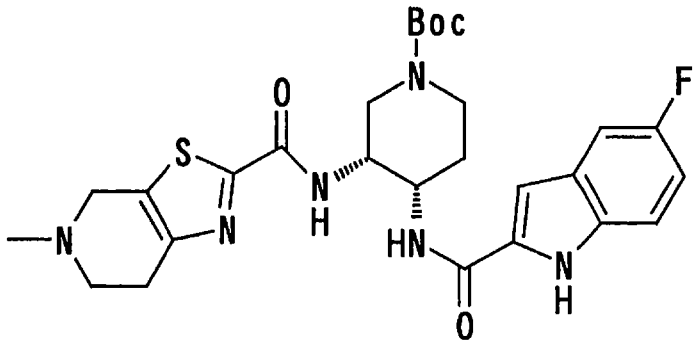
$^1$H-NMR (DMSO-$d_6$) δ: 1.77-1.88(1H,m), 2.40-2.50(2H,m), 2.89(3H,s), 2.90-3.20(4H,m), 3.30-3.50(2H,m),

3.63(1H,br.s), 4.33-4.47(2H,m), 4.62-4.75(2H,m), 7.18(1H,dd,J=8.8,1.9Hz), 7.42(1H,d,J=8.8Hz), 7.48(1H,br.s), 7.71(1H,d,J=1.9Hz), 8.66(1H,br.s), 8.95(1H,d,J=8.1Hz), 9.20-9.30(1H,m), 9.45-9.70(1H,m), 11.61(1H,s), 11.90(1H,s).

MS (ESI) m/z: 473$(M+H)^+$.

[Example 121]

tert-Butyl (3R*,4S*)-4-{[(5-fluoroindol-2-yl)carbonyl]-amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate:



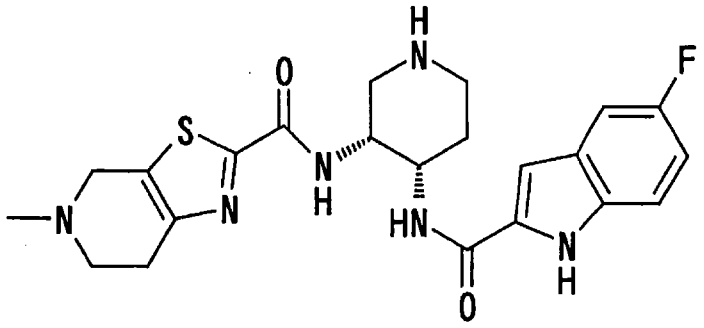

The title compound was obtained from the compound obtained in Referential Example 209 and Referential Example 10 in a similar manner to Example 91.

$^1$H-NMR ($CDCl_3$) δ: 1.53(9H,s), 1.65-1.78(1H,m), 2.23-2.32(1H,br), 2.52(3H,s), 2.78-3.03(5H,m), 3.15-3.24(1H,br), 3.68-3.82(2H,br), 4.16-4.45(4H,br), 6.91(1H,s), 7.02(1H,td,J=9.0,2.7Hz), 7.30(1H,dd,J=9.0,2.7Hz), 7.34(1H,dd,J=9.0,4.4Hz), 7.65-7.90(1H,br), 8.10-8.40(1H,br), 9.31-9.41(1H,br).

MS (ESI) m/z: 557$(M+H^+)$.

[Example 122]

N-((3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide dihydrochloride:



The title compound was obtained from the compound obtained in Example 121 in a similar manner to Example 95.

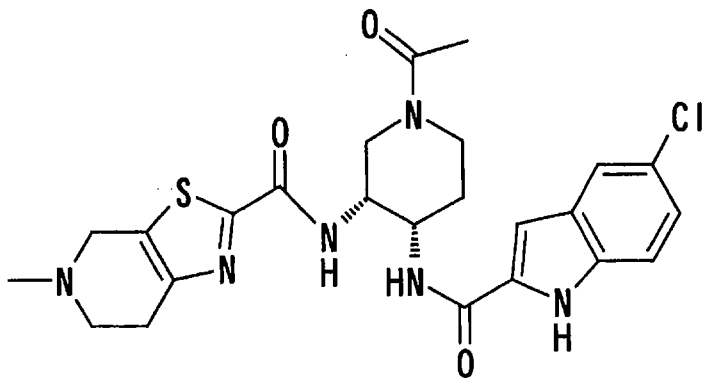
Melting point: 236-245°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.85-1.98(1H,br), 2.06-2.18(1H,br), 2.89(3H,s), 3.05-3.75(8H,s), 4.34-4.54(2H,br), 4.60-4.75(2H,br), 7.04(1H,td,J=9.3,2.4Hz), 7.15(1H,br.s), 7.37-7.44(2H,m), 8.46(1H,d,J=7.8Hz), 8.88-9.00(1H,br), 9.09-9.27(2H,br), 11.55-11.75(1H,br), 11.76-11.84(1H,br).

MS (FAB) m/z: 457($M+H^+$).

[Example 123]

N-((3R*,4S*)-1-Acetyl-4-{[(5-chloroindol-2-yl)carbonyl]-amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and acetic anhydride in a similar manner to Example 100.

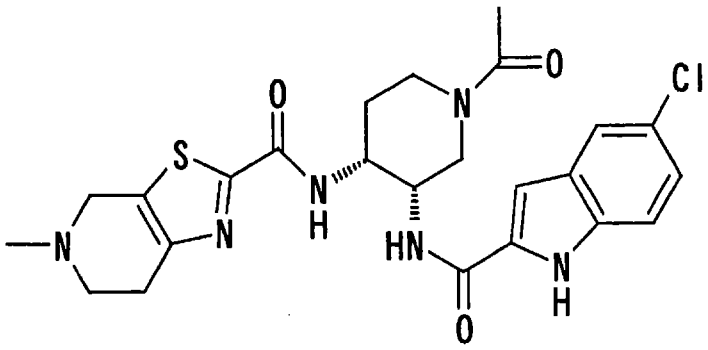
Melting point: 215-225°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.85(1H,m), 1.88,2.06(total 3H,each s), 1.90-2.10(1H,m), 2.91(3H,s), 3.00-3.30(2H,m), 3.30-3.55(2H,m), 3.60-3.90(3H,m), 3.98-4.50(4H,m), 4.65-4.75(1H,m), 7.09(1H,d,J=15.6Hz), 7.17(1H,d,J=8.8Hz), 7.41(1H,d,J=8.8Hz),7.71(1H,s), 8.23-8.53(2H,m), 11.20-11.55(1H,m), 11.85(1H,br.d,J=5.4Hz).

MS (ESI) m/z: 515($M+H^+$).

[Example 124]

N-((3R*,4S*)-1-Acetyl-3-{[(5-chloroindol-2-yl)carbonyl]-amino}piperidin-4-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 120 and acetic anhydride in a similar manner to Example 100.

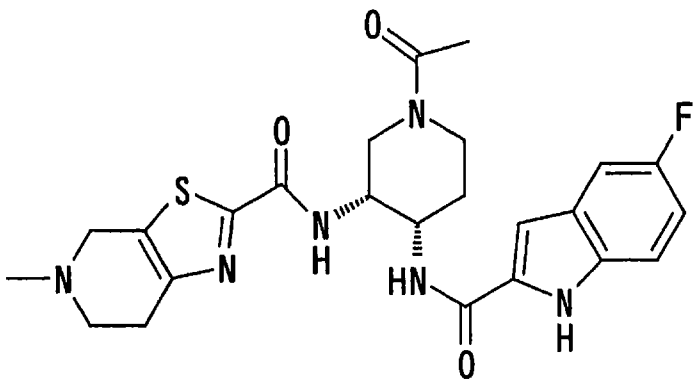
Melting point: 225-250°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.80(1H,m), 1.81,2.05(total 3H,each s), 2.00-2.20(1H,m), 2.70-2.85(1H,m), 2.89(3H,s),3.00-3.20(2H,m), 3.20-3.50(2H,m), 3.64(1H,br.s), 3.78-4.30(2H,m), 4.30-4.50(3H,m), 4.55-4.75(1H,m), 7.05-7.23(2H,m), 7.38-7.48(1H,m), 7.70-7.80(1H,m), 7.79,8.12(total 1H,each d,J=6.8Hz), 8.73,8.83(total 1H,each d,J=8.3Hz), 11.20-11.50(1H,m), 11.89,11.92(total 1H,each s).

MS (FAB) m/z: 515($M+H^+$).

[Example 125]

N-((3R*,4S*)-1-Acetyl-4-{[(5-fluoroindol-2-yl)carbonyl]-amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 122 and acetic anhydride in a similar manner to Example 100.

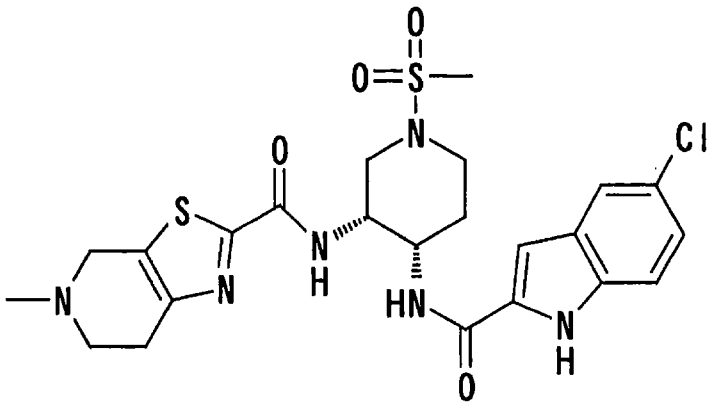
Melting point: 202°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.67-1.85(1H,m), 1.87(1.5H,s), 1.87-2.10(1H,m), 2.06(1.5H,s), 2.88-2.96(3H,br.s), 3.05-3.30(2H,m), 3.32-3.83(5H,br), 3.97-4.33(2H,m), 4.35-4.50(2H,br), 4.67-4.78(1H,br), 7.01-7.14(2H,m), 7.38-7.44(2H,m), 8.25-8.50(2H,m), 10.85-11.15(1H,br), 11.72-11.80(1H,br).

MS (FAB) m/z: 499($M+H^+$).

[Example 126]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(methylsulfonyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and methanesulfonyl chloride in a similar manner to Example 100.

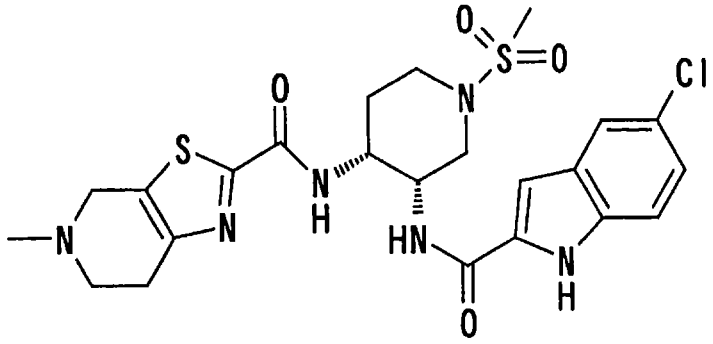
Melting point: 225-230°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.80-1.90(1H,m), 2.05-2.15(1H,m), 2.30-2.80(5H,m), 2.85-3.80(9H,m), 4.20-4.90(4H,m), 7.08(1H,d,J=1.7Hz), 7.18(1H,dd,J=8.7,1.7Hz), 7.42(1H,d,J=8.7Hz), 7.77(1H,s), 8.02-8.20(1H,m), 8.40-8.50(1H,m), 11.00-11.60(1H,m), 11.87(1H,s).

MS (ESI) m/z: 551($M+H^+$).

[Example 127]

N-[(3R*,4S*)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(methylsulfonyl)piperidin-4-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 120 and methanesulfonyl chloride in a similar manner to Example 100.

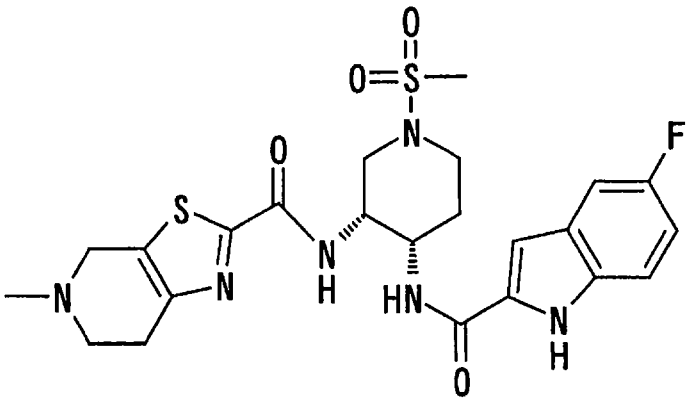
Melting point: 228-245°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.75-1.85(1H,m), 2.25-2.40(1H,m), 2.40-2.60(2H,m), 2.76(3H,br.s), 2.90(3H,s), 2.93-3.05(3H,m), 3.12(1H,d,J=10.6Hz), 3.55-3.80(2H,m), 4.25-4.40(4H,m), 7.17(1H,d,J=1.7Hz), 7.19(1H,dd,J=8.7,2.0Hz), 7.43(1H,d,J=8.7Hz), 7.74(1H,d,J=2.0Hz), 8.03(1H,d,J=6.6Hz), 8.78(1H,d,J=7.4Hz), 10.90-11.20(1H,br.s), 11.89(1H,s).

MS (ESI) m/z: 551($M+H^+$).

[Example 128]

N-[(3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1-(methylsulfonyl)piperazin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 122 and methanesulfonyl chloride in a similar manner to Example 100.

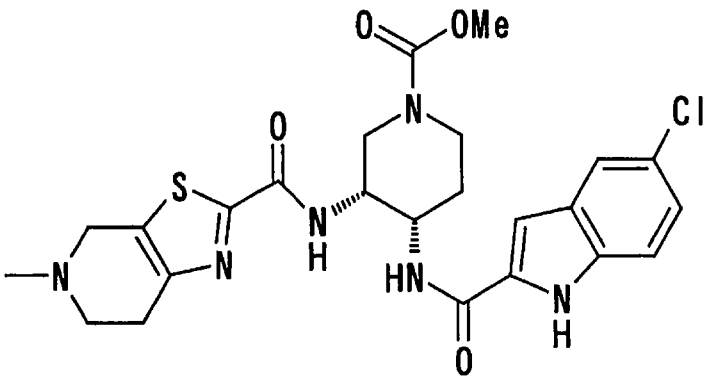
Melting point: 216-250°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.80-1.90(1H,m), 2.01-2.12(1H,m), 2.92(3H,s), 2.94(3H,s), 3.00-3.80(8H,m), 4.28-4.53(3H,m), 4.60-4.80(1H,br), 7.01-7.12(2H,m), 7.37-7.44(2H,m), 8.00-8.18(1H,br), 8.39-8.50(1H,br), 11.00-11.60(1H,br), 11.72-11.80(1H,br).

MS (FAB) m/z: 535($M+H^+$).

[Example 129]

Methyl (3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and methyl chloroformate in a similar manner to Example 100.

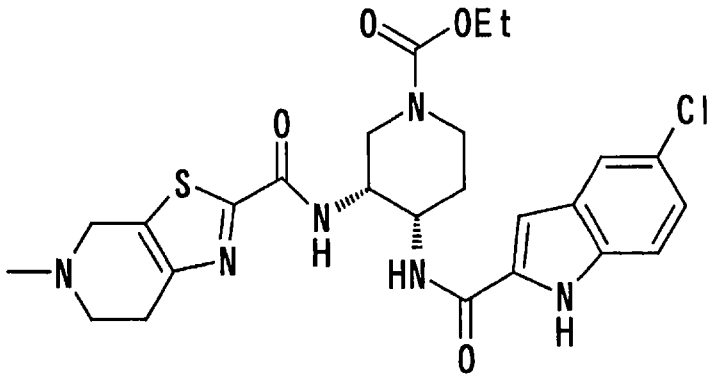
Melting point: 248-253°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.78(1H,m), 1.88-2.03(1H,m), 2.90(3H,s), 3.00-3.80(9H,m), 3.80-3.90(1H,m), 3.95-4.08(1H,m), 4.20-4.70(4H,m), 7.10(1H,s), 7.17(1H,dd,J=8.8,1.8Hz), 7.42(1H,d,J=8.8Hz), 7.71(1H,d,J=1.8Hz), 8.29(1H,br.s), 8.41(1H,d,J=8.1Hz), 11.29(1H,br.s), 11.85(1H,s).

MS (ESI) m/z: 531($M+H^+$).

[Example 130]

Ethyl (3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and ethyl chloroformate in a similar manner to Example 100.

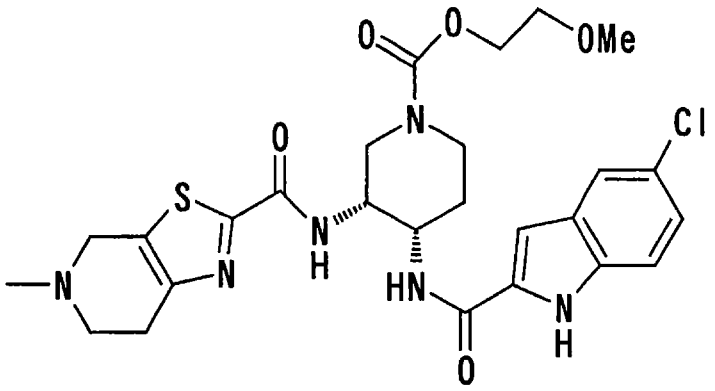
Melting point: 215-225°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.85-1.30(3H,m), 1.65-1.78(1H,m), 1.90-2.03(1H,m), 2.90(3H,s), 3.10-3.40(4H,m), 3.48(1H,br.s), 3.65(1H,br.s), 3.75-4.15(4H,m), 4.25(1H,br.s), 4.32-4.50(2H,m), 4.66(1H,br.s), 7.09(1H,s), 7.18(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,d,J=2.0Hz), 8.23(1H,br.s), 8.45(1H,br.d,J=8.1Hz), 11.50(1H,br.s), 11.86(1H,s).

MS (ESI) m/z: 545($M+H^+$).

[Example 131]

2-Methoxyethyl (3R*,4S*)-4-{[(5-chloroindol-2-yl)-carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and 2-methoxyethyl chloroformate in a similar manner to Example 100.

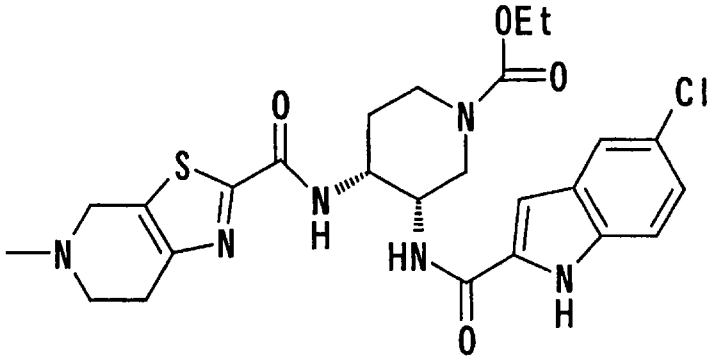
Melting point: 224-226°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.68-1.78(1H,m), 1.90-2.03(1H,m), 2.89(3H,s), 3.00-3.75(11H,m), 3.80-3.90(1H,m), 3.95-4.18(3H,m), 4.20-4.70(4H,m), 7.10(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,d,J=2.0Hz), 8.26(1H,br.s), 8.42(1H,d,J=7.8Hz), 11.30(1H,br.s), 11.86(1H,s).

MS (ESI) m/z: 575($M+H^+$).

[Example 132]

Ethyl (3R*,4S*)-3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate hydrochloride:




The title compound was obtained from the compound obtained in Example 120 and ethyl chloroformate in a similar manner to Example 100.

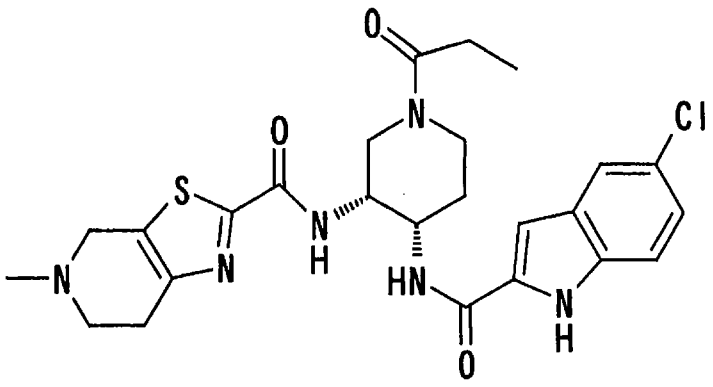
Melting point: 213-225°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.75-1.30(3H,m), 1.60-1.72(1H,m), 2.12-2.25(1H,m), 2.89(3H,s), 2.95-3.20(4H,m), 3.40-3.88(4H,m), 3.90-4.10(2H,m), 4.10-4.30(2H,m), 4.30-4.40(1H,m), 4.40-4.80(1H,m), 7.10(1H,s), 7.18(1H,dd,J=8.8,2.0Hz), 7.43(1H,d,J=8.8Hz), 7.74(1H,s), 8.03(1H,d,J=5.6Hz), 8.79(1H,s), 11.37(1H,s), 11.88(1H,s).

MS (ESI) m/z: 545($M+H^+$).

[Example 133]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-propionylpiperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and propionyl chloride in a similar manner to Example 100.

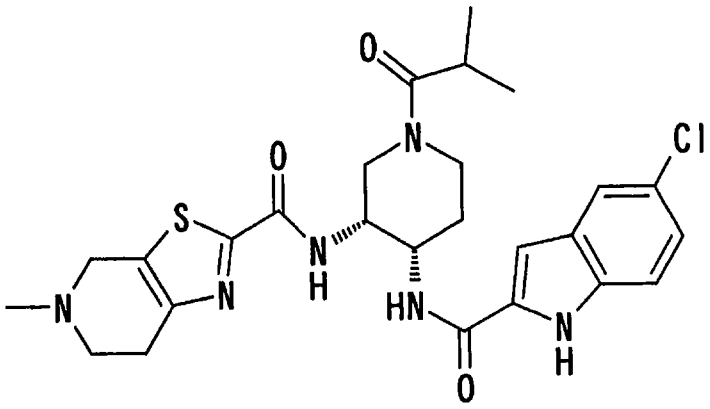
Melting point: 214-228°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.88-1.10(3H,m), 1.70-2.05(2H,m), 2.06-2.60(2H,m), 2.91(3H,s), 3.14(2H,br.s), 3.20-3.90(5H,m), 3.95-4.80(5H,m), 7.09(1H,d,J=11.0Hz), 7.17(1H,dd,J=8.8,1.2Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,s), 8.20-8.50(2H,m), 11.00-11.40(1H,m), 11.86(1H,s).

MS (ESI) m/z: 529($M+H^+$).

[Example 134]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-isobutyrylpiperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and isobutyryl chloride in a similar manner to Example 100.

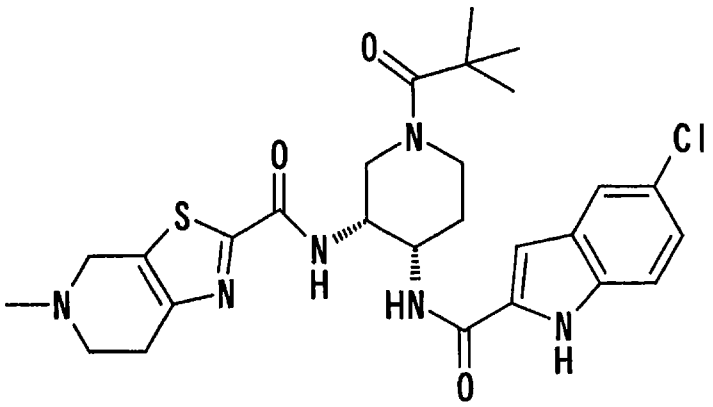
Melting point: 266-272°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.80-1.15(6H,m), 1.70-2.05(2H,m), 2.65-2.80(1H,m), 2.90(3H,s), 2.90-4.80(12H,m), 7.09(1H,d,J=11.0Hz), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,s), 8.00-8.30(1H,m), 8.30-8.50(1H,m), 10.95-11.50(1H,m), 11.86(1H,s).

MS (ESI) m/z: 543($M+H^+$).

[Example 135]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2,2-dimethylpropanoyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and pivaloyl chloride in a similar manner to Example 100.

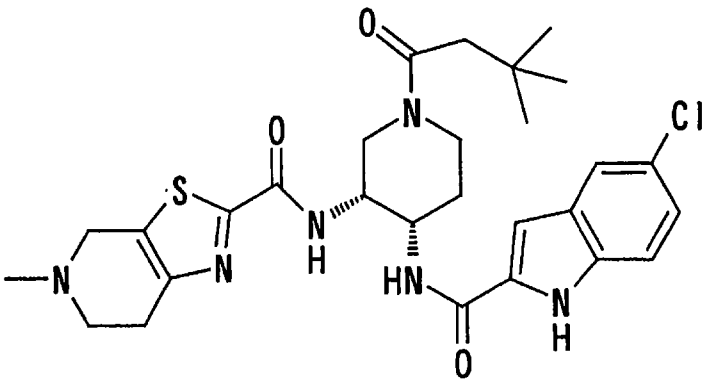
Melting point: 250-255°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.20(9H,s), 1.70-1.81(1H,m), 1.90-2.00(1H,m), 2.88(3H,s), 3.10(2H,br.s), 3.20-3.70(4H,m), 3.95-4.08(1H,m), 4.10-4.20(1H,m), 4.25-4.35(1H,m), 4.35-4.80(3H,m), 7.10(1H,s), 7.16(1H,dd,J=8.8,1.9Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=1.9Hz), 8.06(1H,br.s), 8.38(1H,d,J=7.8Hz), 11.31(1H,br.s), 11.84(1H,s).

MS (ESI) m/z: 557($M+H^+$).

[Example 136]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(3,3-dimethylbutanoyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and tert-butylacetyl chloride in a similar manner to Example 100.

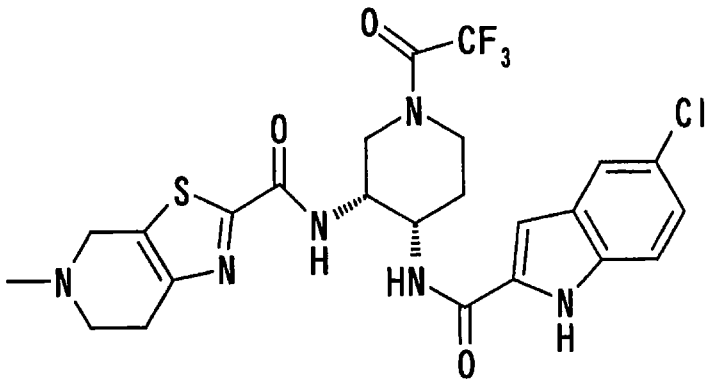
Melting point: 260-265°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.91,1.04(total 9H,each s), 1.68-1.82(1H,m), 1.93-2.40(3H,m), 2.91(3H,s), 3.00-3.20(2H,m), 3.20-4.80(10H,m), 7.08(1H,s), 7.17(1H,dd,J=8.7,1.2Hz), 7.41(1H,d,J=8.7Hz), 7.69(1H,d,J=7.6Hz), 7.93-8.18(1H,m), 8.38-8.45(1H,m), 10.95-11.30(1H,m), 11.80-11.90(1H,m).

MS (ESI) m/z: 571($M+H^+$).

[Example 137]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2,2,2-trifluoroacetyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and trifluoroacetic anhydride in a similar manner to Example 100.

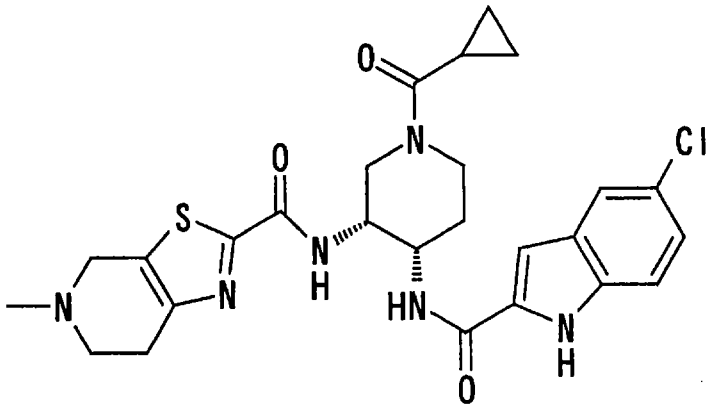
Melting point: 262-267°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.82-1.98(1H,m), 2.05-2.21(1H,m), 2.89(3H,s), 3.05-3.20(2H,m), 3.40-3.75(4H,m), 3.85-3.95(1H,m), 4.00-4.07(1H,m), 4.20-4.70(4H,m), 7.10(1H,s), 7.18(1H,dd,J=8.6,1.9Hz), 7.41(1H,d,J=8.6Hz), 7.72(1H,s), 8.47(1H,dd,J=22.4,7.9Hz), 8.60(1H,br), 11.08(1H,br.s), 11.87(1H,s).

MS (ESI) m/z: 569($M+H^+$).

[Example 138]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(cyclopropylcarbonyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and cyclopropanecarbonyl chloride in a similar manner to Example 100.

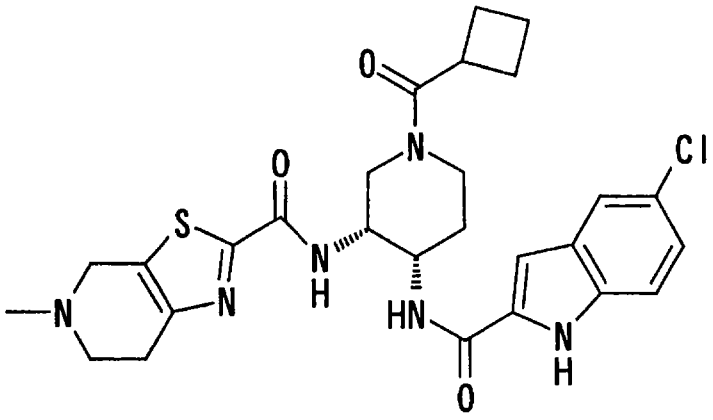
Melting point: 280-286°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.25-0.80(4H,m), 1.65-2.15(4H,m), 2.91(3H,s), 2.90-3.20(3H,m), 3.35-3.70(2H,m), 4.00-4.80(6H,m), 7.06(1H,s), 7.18(1H,d,J=8.8Hz), 7.42(1H,d,J=8.7Hz), 7.71(1H,s), 8.18(1H,br.s), 8.40,8.48(total 1H,each br.s), 11.11(1H,br.s), 11.85(1H,s).

MS (ESI) m/z: 542($M+H^+$).

[Example 139]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(cyclobutylcarbonyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and cyclobutanecarbonyl chloride in a similar manner to Example 100.

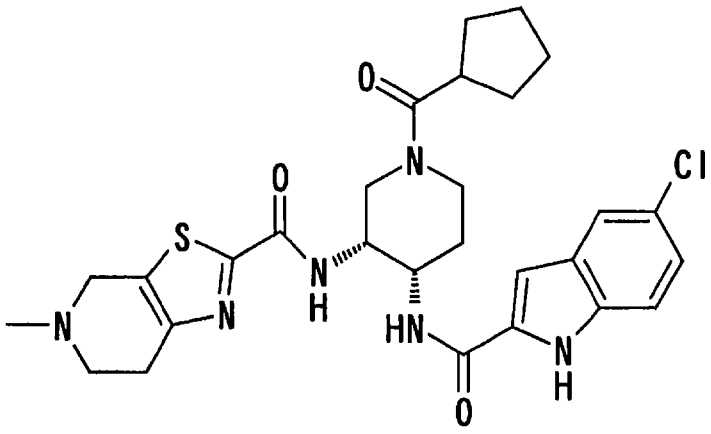
Melting point: 271-275°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-2.30(8H,m), 2.89(3H,s), 3.12(2H,br.s), 3.20-3.75(6H,m), 3.75-3.90(1H,m), 4.05-4.80(4H,m), 7.08(1H,s), 7.15(1H,dd,J=9.0,2.0Hz), 7.39(1H,d,J=9.0Hz), 7.68(1H,d,J=2.0Hz), 8.15(1H,br.s), 8.39(1H,br), 11.19(1H,br.s), 11.84(1H,s).

MS (ESI) m/z: 555($M+H^+$).

[Example 140]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(cyclopentylcarbonyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and cyclopentanecarbonyl chloride in a similar manner to Example 100.

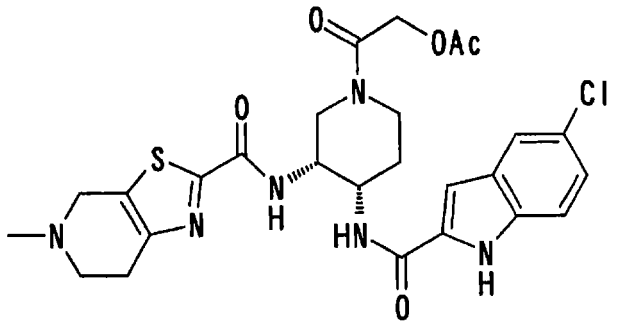
Melting point: 254-260°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.30-2.10(10H,m), 2.90(3H,s), 3.00-3.20(2H,m), 3.20-3.75(5H,m), 3.80-4.80(6H,m), 7.09(1H,s), 7.17(1H,dd,J=8.7,2.0Hz), 7.42(1H,d,J=8.7Hz), 7.71(1H,s), 7.95-8.30(1H,m), 8.35-8.50(1H,m), 11.23(1H,br.s), 11.85(1H,s).

MS (ESI) m/z: 569($M+H^+$).

[Example 141]

2-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidin-1-yl)-2-oxoethyl acetate:



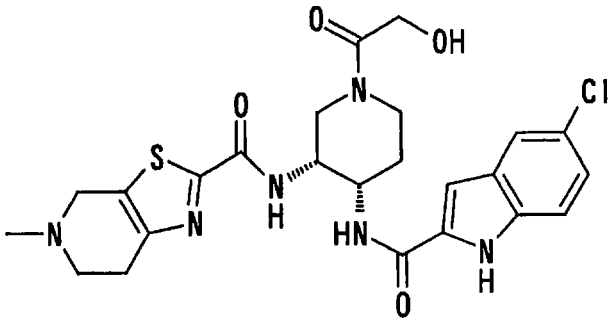
The title compound was obtained from the compound obtained in Example 118 and acetoxyacetyl chloride in a similar manner to Example 100.

$^1$H-NMR ($CDCl_3$) δ: 1.70-2.00(1H,m), 2.05-2.48(3H,m), 2.51(3H,s), 2.70-3.05(4H,m), 3.05-4.10(5H,m), 4.20-4.48(1H,m), 4.50-5.10(4H,m), 6.87(1H,br.s), 7.10-7.82(4H,m), 7.32(1H,d,J=8.8Hz), 8.35(1H,br.s), 9.34,9.45(total 1H,each br.s).

MS (ESI) m/z: 573($M+H^+$).

[Example 142]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-glycoloylpiperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (301.8 mg) obtained in Example 141 was dissolved in tetrahydrofuran (10 ml), and a 1N aqueous solution (0.53 ml) of sodium hydroxide was added to stir the mixture at room temperature for 18 hours. Water was added to the reaction mixture to conduct extraction with methylene chloride. The resultant organic layer was successively washed with water and saturated aqueous solution of sodium chloride and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 20:1 - 10:1), and the solvent was distilled off under reduced pressure. The thus-obtained purified product was dissolved in ethanol (3 ml) and methylene chloride (2 ml), and a 1N ethanol solution of hydrochloric acid to stir the mixture for 30 minutes. The solvent was distilled off under reduced pressure, and the residue was solidified with diethyl ether to obtain the title compound (195 mg).

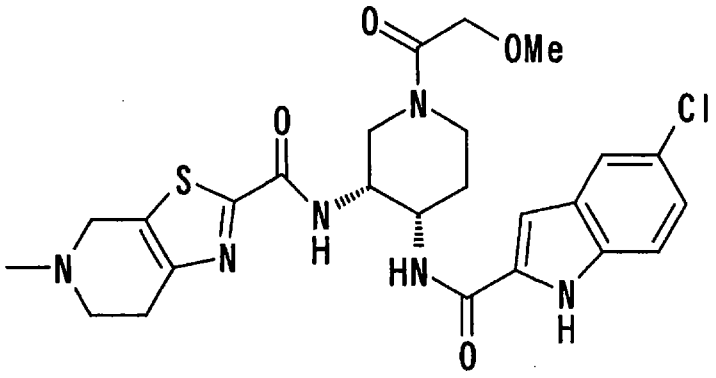
Melting point: 216-230°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.70-1.80(1H,m), 1.88-2.10(2H,m), 2.68(3H,s), 3.18(2H,s), 3.08-3.70(5H,m), 3.80-3.95(1H,m), 4.00-4.25(3H,m), 4.25-4.50(2H,m), 4.50-4.65(1H,m), 7.09(1H,d,J=11.0Hz), 7.17(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.71(1H,s), 8.33(1H,br.s), 8.35-8.50(1H,m), 10.80-11.30(1H,br.s), 11.84(1H,br.s).

[Example 143]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-

methoxyacetyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 in a similar manner to Example 100.

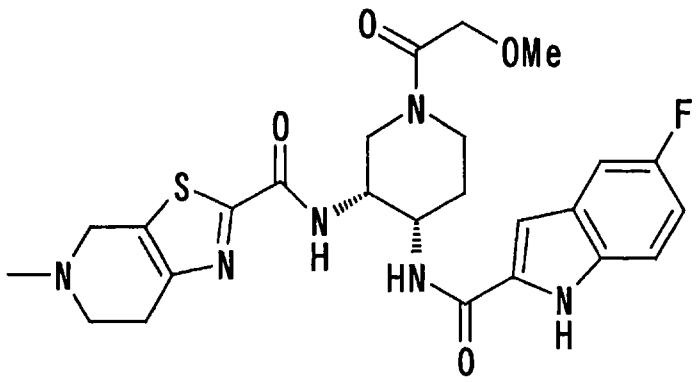
Melting point: 214-228°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.70-1.80(1H,m), 1.85-2.05(1H,m), 2.90(3H,s), 3.00-3.20(2H,m), 3.16(3H,s), 3.22-3.82(7H,m), 3.88-4.80(5H,m), 7.09(1H,d,J=9.0Hz), 7.17(1H,dd,J=8.8,1.9Hz), 7.42(1H,d,J=8.8Hz), 7.70(1H,d,J=1.9Hz), 8.29(1H,br.s),8.40-8.50(1H,m), 11.34(1H,br.s), 11.86(1H,s).

MS (ESI) m/z: 545$(M+H)^+$.

[Example 144]

N-[(3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 122 and methoxyacetyl chloride in a similar manner to Example 100.

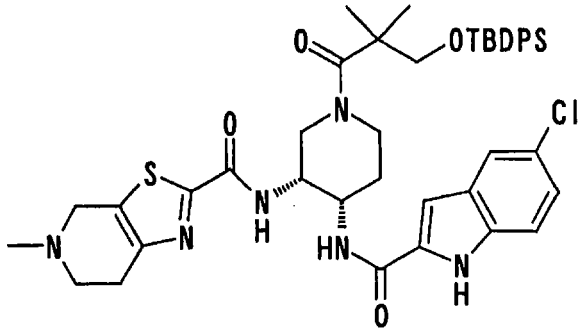
Melting point: 190-208°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.70-1.83(1H,br), 1.85-2.10(1H,m), 2.91(3H,s), 3.00-3.55(10H,m), 3.62-3.85(1H,m), 3.90-4.50(6H,m), 4.63-4.78(1H,br), 7.04(1H,td,J=9.4,2.4Hz), 7.07-7.13(1H,br), 7.37-7.44(1H,m), 8.16-8.49(2H,m), 11.30-11.70(1H,br), 11.72-11.80(1H,br).

MS (FAB) m/z: 529($M+H^+$).

[Example 145]

N-((3R*,4S*)-1-(3-{tert-butyl(diphenyl)silyl}oxy)-2,2-dimethylpropanoyl)-4-{[(5-chloroindol-2-yl)carbonyl]-amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide:



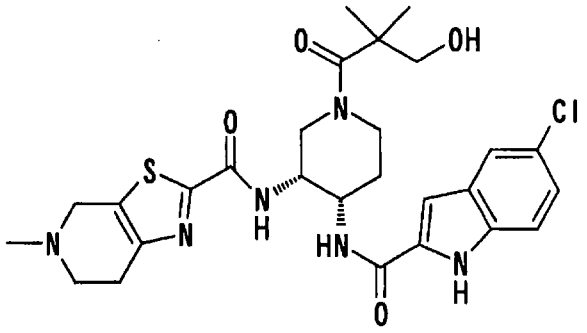

Thionyl chloride (3.0 ml) and a catalytic amount of dimethylformamide were added to a solution of the compound (261 mg) obtained in Referential Example 158 in chloroform (10 ml), and the mixture was stirred overnight at 60°C. The reaction mixture was concentrated under reduced pressure, giving a pale yellow oil. The title compound was obtained from this product and the compound (200 mg) obtained in Example 118 in a similar manner to Example 100.

Melting point: 153°C.

$^1$H-NMR ($CDCl_3$) δ: 1.07(9H,s), 1.39(6H,d,J=3.9Hz), 1.57(1H,br.s), 2.26(1H,d,J=10.7Hz), 2.57(3H,s), 2.86(4H,s), 2.97-3.01(2H,m), 3.78(4H,s), 4.20(1H,br.s), 4.33(1H,d,J=13Hz), 4.42(1H,br.s), 4.67(1H,d,J=13Hz), 6.88(1H,s), 7.20-7.23(1H,m), 7.32-7.46(7H,m), 7.64-7.65(6H,m), 7.86(1H,d,J=6.8Hz), 8.23(1H,s), 9.10(1H,s).

[Example 146]

N-[(3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-1-(3-hydroxy-2,2-dimethylpropanoyl)piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



Tetrabutylammonium fluoride (1 M tetrahydrofuran solution, 0.594 ml) was added to a solution of the compound (241 mg) obtained in Example 145 in tetrahydrofuran (30 ml) under ice cooling, and the mixture was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure, and the resultant residue was dissolved in methylene chloride. The solution was washed with water and saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure. The resultant residue was purified by preparative thin-layer chromatography on silica gel (methylene chloride:methanol = 9:1) to obtain the title compound (116 mg).

Melting point: 220°C (decomposed).

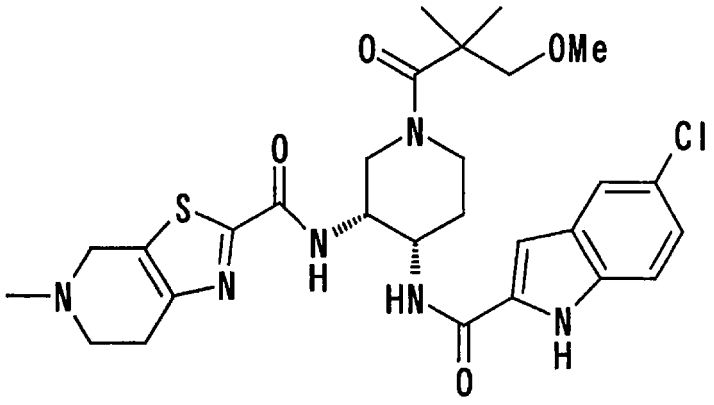
$^1$H-NMR (DMSO-$d_6$) δ: 1.17(6H,d,J=8.3Hz), 1.79(1H,br.s), 1.91-1.97(1H,m), 2.49(3H,s), 2.87(4H,s), 3.35-3.50(4H,m), 3.81(1H,br.s), 3.97(1H,m), 4.10-4.15(1H,m), 4.32(1H,br.s), 4.42(1H,br.s), 4.52(1H,t,J=5.7Hz), 7.10(1H,s), 7.16-7.19(1H,m), 7.42(1H,d,J=8.8Hz), 7.69(1H,s),

8.11(1H,d,J=8.8Hz), 8.37(1H,d,J=7.3Hz), 11.8(1H,s).

MS (FAB) m/z: 573($M+H^+$).

[Example 147]

N-[(3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-1-(3-methoxy-2,2-dimethylpropanoyl)piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:




The title compound was obtained from the compound obtained in Example 118 and the compound obtained in Referential Example 160 in a similar manner to Example 145.

Melting point: 240°C (decomposed).

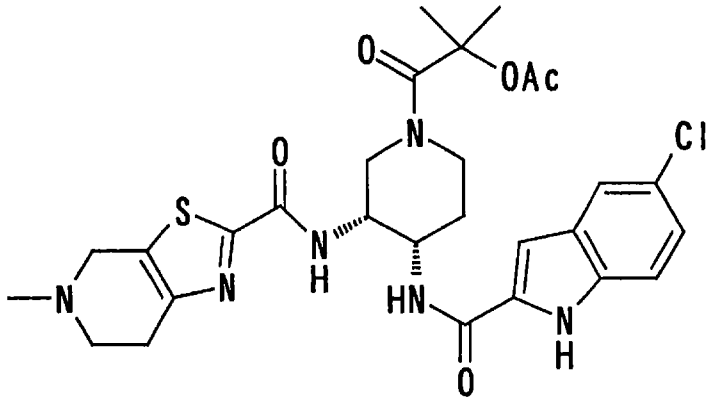
$^1$H-NMR ($CDCl_3$) δ: 1.34(3H,s), 1.37(3H,s), 1.65-1.77(1H,m), 2.33-2.37(1H,m), 2.53(3H,s), 2.82-3.29(6H,m), 3.34(3H,s), 3.41(1H,d,J=9.3Hz), 3.56(1H,d,J=9.3Hz), 3.76(2H,d,J=5.9Hz), 4.26(1H,m),4.44-4.53(2H,m), 4.82(1H,d,J=13.7Hz), 6.88(1H,d,J=1.5Hz), 7.20-7.23(1H,m), 7.33(1H,d,J=8.8Hz), 7.64(1H,d,J=1.5Hz), 7.90(1H,d,J=7.1Hz), 8.22(1H,d,J=5.1Hz), 9.18(1H,s).

MS (FAB) m/z: 587($M+H^+$).

[Example 148]

2-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-3-

{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidin-1-yl)-1,1-dimethyl-2-oxoethyl acetate:



The title compound was obtained from the compound obtained in Example 118 and 2-acetoxyisobutyryl chloride in a similar manner to Example 100.

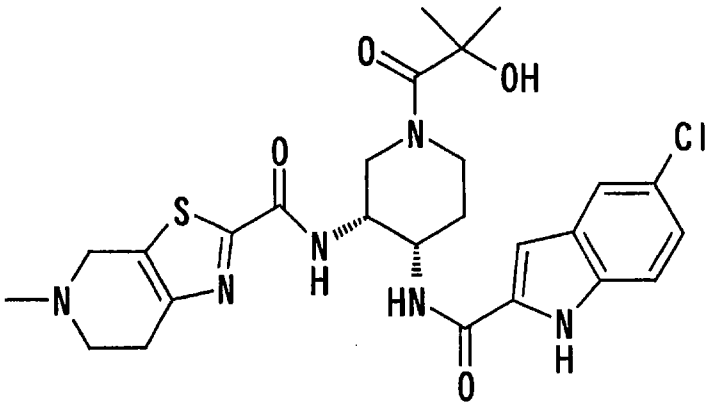
Melting point: 190°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 1.56-1.67(8H,m), 2.08(3H,s), 2.35(1H,d,J=10.5Hz), 2.52(3H,s), 2.82-2.84(2H,m), 2.90-2.96(2H,m), 3.14(1H,br.s), 3.75(2H,s), 4.25(1H,br.s), 4.40-4.47(1H,m), 4.54(1H,br.s), 4.80(1H,br.s), 6.86(1H,s), 7.20-7.33(3H,m), 7.64(1H,d,J=1.7Hz), 7.76(1H,d,J=7.3Hz), 9.11(1H,s).

MS (FAB) m/z: 601($M+H^+$).

[Example 149]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-hydroxy-2-methylpropanoyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



Sodium methoxide (76.8 mg) was added to a solution of the compound (190 mg) obtained in Example 148 in methanol (50 ml), and the mixture was stirred overnight at room temperature. After the reaction mixture was concentrated under reduced pressure, the resultant residue was purified by preparative thin-layer chromatography on silica gel (methylene chloride:methanol = 9:1) to obtain the title compound (130 mg).

Melting point: 190°C (decomposed).

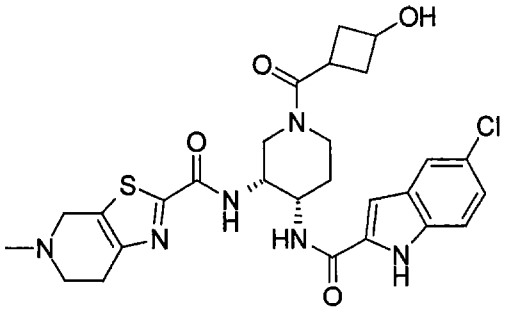
$^1$H-NMR ($CDCl_3$) δ: 1.53(3H,s), 1.56-1.78(5H,m), 2.34(1H,d,J=10.5Hz), 2.53(3H,s), 2.83-2.86(2H,m), 2.91-2.93(2H,m), 3.30(1H,d,J=12.5Hz), 3.75(2H,s), 4.28(1H,d,J=5.6Hz), 4.43(1H,s), 4.65(1H,d,J=13.5Hz), 4.95(1H,d,J=13.5Hz), 6.92(1H,d,J=1.5Hz), 7.20-7.23(1H,m), 7.33(1H,d,J=8.6Hz), 7.65(1H,d,J=2.0Hz), 8.43(1H,d,J=5.6Hz), 9.14(1H,s).

MS (FAB) m/z: 559($M+H^+$).

[Example 150]

N-{(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(3-hydroxycyclobutyl)carbonyl]piperidin-3-yl}-5-methyl-

4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (306 mg) obtained in Example 118, n-methylmorpholine (200 μl), 1-hydroxybenzotriazole monohydrate (87 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (197 mg) were added to a solution of the compound (117 mg) obtained Referential Example 152 in a mixed solvent of tetrahydrofuran (20 ml), methylene chloride (3.0 ml) and N,N-dimethylformamide (2.0 ml), and the mixture was stirred at room temperature for 3 days. The reaction mixture was diluted with methylene chloride, and a saturated aqueous solution of sodium hydrogencarbonate was added to separate the mixture into two layers. The resultant organic layer was washed with saturated aqueous solution of sodium chloride, dried over anhydrous sodium sulfate and then concentrated under reduced pressure. The resultant residue was purified by column chromatography on silica gel (methylene chloride:methanol = 10:1) to obtain a free base (207 mg) of the title compound. The free base was treated with a 1N ethanol solution of hydrochloric acid to obtain the title compound.

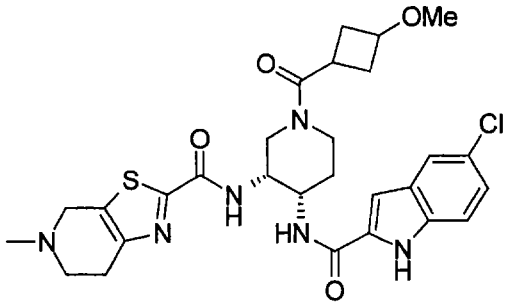
Melting point: 200°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.78-2.10(4H,m), 2.24-2.68(3H,m), 2.75-5.20(14H,m), 2.91(3H,s), 7.08(0.5H,s), 7.09(0.5H,s), 7.18(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.70(1H,d,J=2.0Hz), 8.05-8.28(1H,br), 8.38(0.5H,br.d,J=7.3Hz), 8.43(0.5H,br.d,J=8.3Hz), 10.80-11.25(1H,br), 11.84(1H,br.s).

MS (ESI) m/z: 571($M+H^+$).

[Example 151]

N-{(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(methoxycyclobutyl)carbonyl]piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained from the compound obtained in Example 118 and the compound obtained in Referential Example 154 in a similar manner to Example 150.

Melting point: 191°C (decomposed).

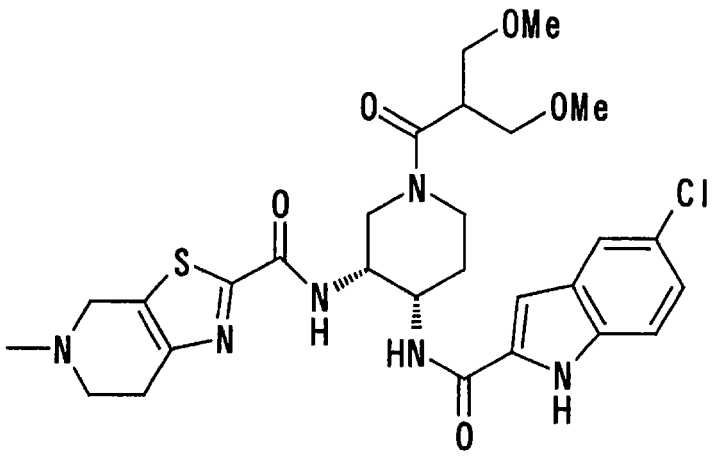
$^1$H-NMR (DMSO-$d_6$) δ: 1.69-2.23(4H,m), 2.25-2.40(1H,m), 2.71-2.84(0.5H,m), 2.89-3.93(9.5H,m), 2.91(3H,s), 3.01(1H,s), 3.14(2H,s), 4.05-4.80(5H,m), 7.09(1H,s), 7.18(1H,d,J=8.4Hz), 7.42(1H,d,J=8.4Hz), 7.70(1H,s), 8.00-8.30(1H,br), 8.36-8.53(1H,m), 11.25-11.75(1H,br),

11.85(1H,br.s).

MS (ESI) m/z: 585($M+H^+$).

[Example 152]

N-{(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[3-methoxy-2-(methoxymethyl)propanoyl]piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained by condensing a carboxylic acid obtained by hydrolysis of the compound obtained in Referential Example 155 with the compound obtained in Example 118 in a similar manner to Example 150.

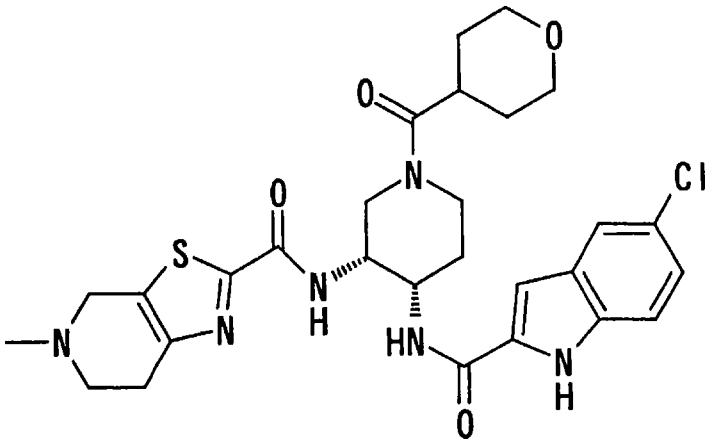
Melting point: 178-184°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.69-1.82(1H,m), 1.84-2.04(1H,m), 2.91(3H,s), 3.00-3.75(17H,m), 3.95-4.55(5H,m), 4.60-4.80(1H,m), 7.10(1H,br.s), 7.18(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.69(0.5H,br.s), 7.71(1H,br.s), 8.18-8.28(1H,br), 8.35-8.50(1H,br), 11.83(1H,br.s).

MS (ESI) m/z: 603($M+H^+$).

[Example 153]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-(tetrahydro-2H-pyran-4-ylcarbonyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and the compound obtained in Referential Example 156 in a similar manner to Example 150.

Melting point: 225-248°C (decomposed).

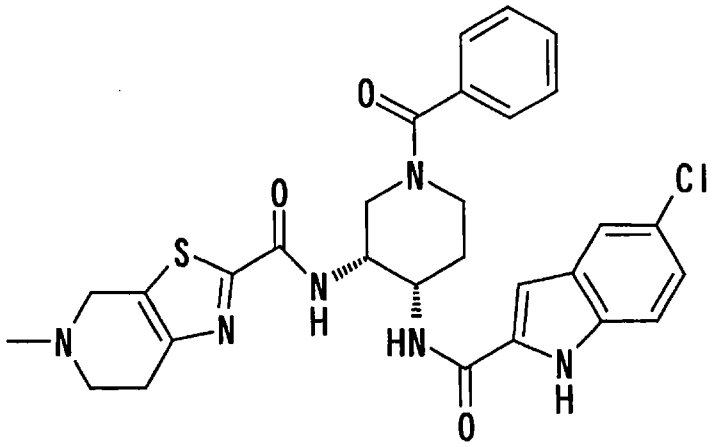
$^1$H-NMR (DMSO-$d_6$) δ: 1.55-1.68(4H,m), 1.70-1.85(1H,m), 1.85-2.05(1H,m), 2.60-2.95(1H,m), 2.89(3H,s), 2.95-3.20(3H,m), 3.20-4.00(9H,m), 4.00-4.80(4H,m), 7.08(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz), 7.71(1H,s), 8.00-8.30(1H,m), 8.35-8.50(1H,m), 11.16(1H,br.s), 11.85(1H,s).

MS (ESI) m/z: 585($M+H^+$).

[Example 154]

N-((3R*,4S*)-1-benzoyl-4-{[(5-Chloroindol-2-yl)carbonyl]amino}piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide

hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and benzoyl chloride in a similar manner to Example 100.

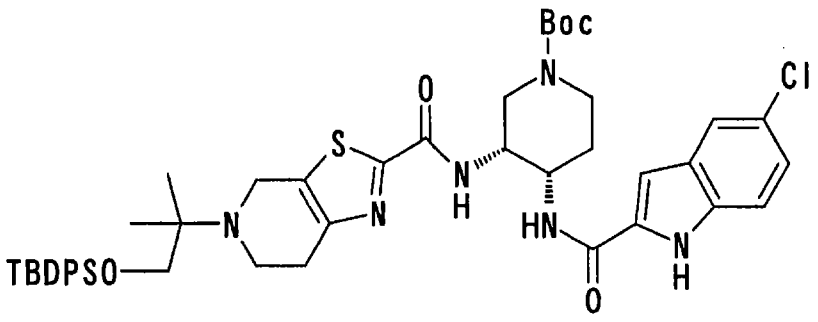
Melting point: 215-225°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.75-1.90(1H,m), 1.90-2.20(1H,m), 2.93(3H,s), 3.10-4.00(8H,m), 4.05-4.80(4H,m), 7.00-7.60(5H,m), 7.08(1H,s), 7.16(1H,dd,J=8.8,1.6Hz), 7.40(1H,d,J=8.8Hz), 7.71(1H,d,J=1.6Hz), 8.31(1H,br.s), 8.46(1H,br.s), 11.39(1H,br.s),11.86(1H,s).

MS (FAB) m/z: 577($M+H^+$).

[Example 155]

tert-Butyl (3R*,4S*)-3-({[5-(2-{[tert-butyl(diphenyl)-silyl]oxy}-1,1-dimethylethyl)-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridin-2-yl]carbonyl}amino)-4-{[(5-chloroindol-2-yl)carbonyl]amino}piperidine-1-carboxylate:



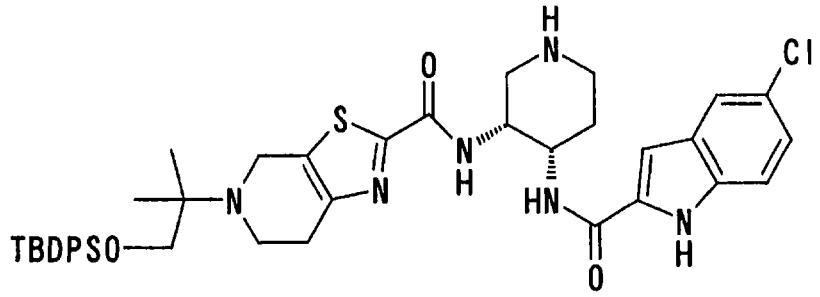

The title compound was obtained from the compound obtained in Referential Example 207 and the compound obtained in Referential Example 42 in a similar manner to Example 91.

$^1$H-NMR (DMSO-$d_6$) δ: 1.00(9H,s), 1.12(6H,s), 1.15-1.50(9H,m), 1.63-1.75(1H,m), 1.82-2.00(1H,m), 2.60-2.80(3H,m), 2.83-2.95(2H,m), 3.12-3.30(1H,m), 3.30(2H,s), 3.58(2H,s), 3.85-4.10(2H,m), 4.19(1H,br.s), 4.37(1H,br.s), 7.04(1H,s), 7.16(1H,d,J=9.0Hz), 7.30-7.50(7H,m), 7.50-7.65(4H,m), 7.70(1H,s), 7.99(1H,d,J=6.8Hz), 8.45(1H,br.s), 11.82(1H,s).

MS(ESI)m/z:869$(M+H)^+$

[Example 156]

5-(2-{[tert-Butyl(diphenyl)silyl]oxy}-1,1-dimethylethyl)-N-((3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-piperidin-3-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide dihydrochloride:



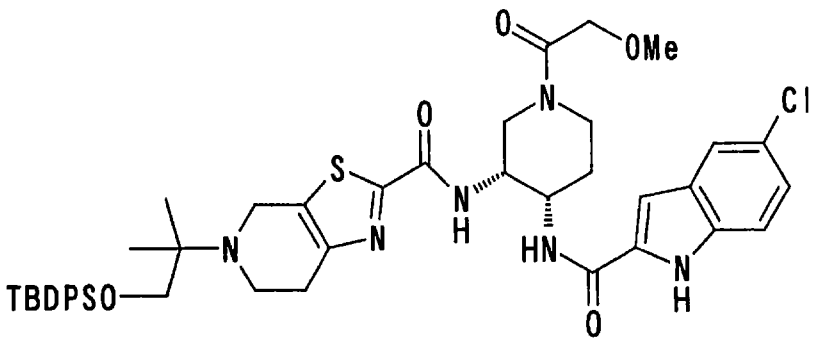

The title compound was obtained by treating the compound obtained in Example 155 in a similar manner to Example 95.

$^1$H-NMR (DMSO-$d_6$) δ: 1.04(9H,s), 1.43, 1.48(total 6H,each s), 1.85-2.00(1H,m), 2.05-2.20(1H,m), 2.95-3.20(2H,m), 3.25-3.60(6H,m), 3.80-3.90(1H,m), 3.95-4.05(1H,m), 4.45-4.55(1H,m), 4.60-4.85(3H,m), 7.10-7.20(2H,m), 7.35-7.55(7H,m), 7.55-7.75(5H,m), 8.52(1H,dd,J=14.4,7.8Hz), 8.93(1H,br), 9.20-9.40(2H,m), 11.30-11.50(1H,m), 11.87,11.92(total 1H,each s).

MS (ESI) m/z: 769($M+H^+$).

[Example 157]

5-(2-{[tert-Butyl(diphenyl)silyl]oxy}-1,1-dimethylethyl)-N-[(3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide:



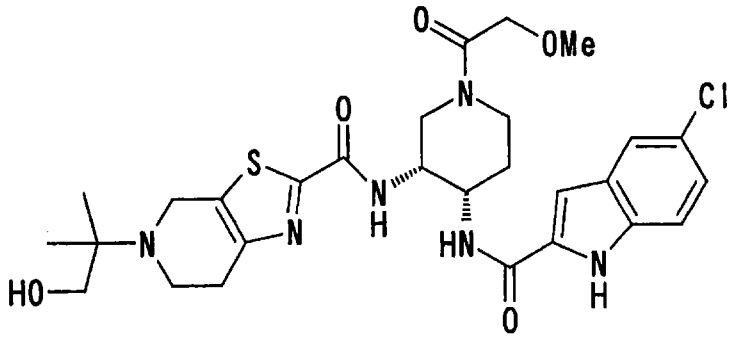

The title compound was obtained from the compound obtained in Example 156 and methoxyacetyl chloride in a similar manner to Example 100.

$^1$H-NMR ($CDCl_3$) δ: 1.07(9H,s), 1.20(6H,s), 1.60-1.85(1H,m), 2.25-2.40(1H,m), 2.36(2H,s), 2.70-3.20(4H,m), 3.20-3.55(4H,m), 3.55-3.70(2H,m), 3.95-4.10(3H,m), 4.10-4.90(4H,m), 6.90(1H,d,J=1.5Hz), 7.15-7.30(2H,m), 7.30-7.50(6H,m), 7.60-7.70(5H,m), 8.15-8.22(1H,m), 8.46(1H,d,J=5.1Hz), 9.28(1H,s).

MS (ESI) m/z: 842($M+H^+$).

[Example 158]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-5-(2-hydroxy-1,1-dimethylethyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 157 in a similar manner to Example 146.

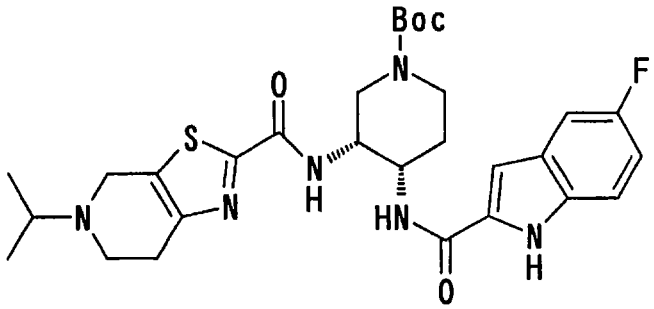
Melting point: 221-232°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.32(3H,s), 1.40(3H,s), 1.70-1.85(1H,m), 1.85-2.10(1H,m), 2.60-3.35(8H,m), 3.40-3.82(3H,m), 3.85-4.05(3H,m), 4.05-4.35(2H,m), 4.50-4.60(1H,m), 4.55-4.80(2H,m), 5.75-5.85(1H,m), 7.08(1H,br.s), 7.17(1H,d,J=8.8Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,s), 8.20-8.35(1H,m), 8.40-8.55(1H,m), 10.00-10.35(1H,m), 11.87(1H,s).

MS (ESI) m/z: 603($M+H^+$).

[Example 159]

tert-Butyl (3R*,4S*)-4-{[(5-fluoroindol-2-yl)carbonyl]-amino}-3-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidine-1-carboxylate:




The title compound was obtained from the compound obtained in Referential Example 209 and the compound obtained in Referential Example 148 in a similar manner to Example 91.

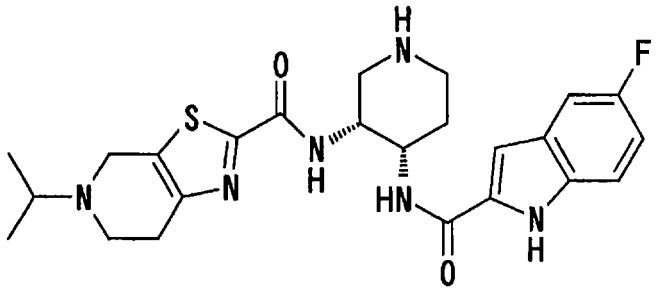
$^1$H-NMR ($CDCl_3$) δ: 1.16(6H,d,J=6.6Hz), 1.53(9H,s), 1.65-1.80(1H,m), 2.23-2.32(1H,m), 2.80-3.10(6H,m), 3.10-

3.25(1H,m), 3.80-3.90(2H,m), 4.00-4.50(4H,m), 6.91(1H,s),6.95-7.05(1H,m), 7.25-7.40(2H,m), 7.74(1H,br.s), 8.21(1H,br.s), 9.30(1H,s).

MS (ESI) m/z: 585($M+H^+$).

[Example 160]

N-((3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-piperidin-3-yl)-5-isopropyl-4,5,6,7-tetrahydrothiazolo-[5,4-c]pyridine-2-carboxamide dihydrochloride:



The title compound was obtained by treating the compound obtained in Example 159 in a similar manner to Example 95.

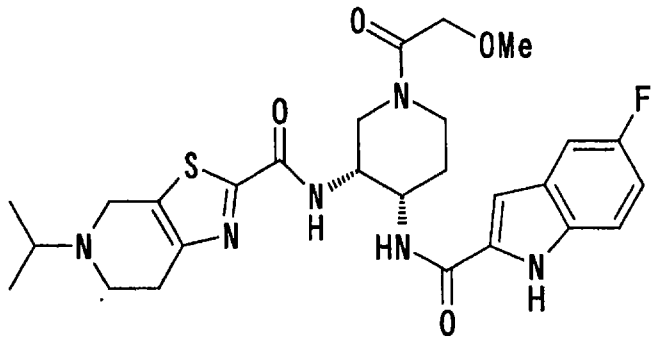
$^1$H-NMR (DMSO-$d_6$) δ: 1.28-1.40(6H,m), 1.85-2.00(1H,m), 2.05-2.20(1H,m), 2.40-2.60(1H,m), 2.95-3.90(8H,m), 4.40-4.55(2H,m), 4.60-4.75(2H,m), 7.00-7.20(2H,m), 7.30-7.50(2H,m), 8.45-8.60(1H,m), 8.85-9.05(1H,m), 9.05-9.50(2H,m), 11.60-11.90(2H,m).

MS (ESI) m/z: 485($M+H^+$).

[Example 161]

N-[(3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide

hydrochloride:



The title compound was obtained from the compound obtained in Example 160 and methoxyacetyl chloride in a similar manner to Example 100.

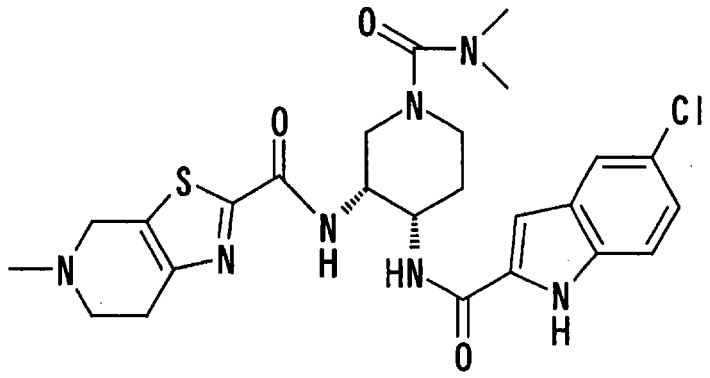
Melting point: 214-228°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.25-1.40(6H,m), 1.68-1.82(1H,m), 1.85-2.10(1H,m), 2.90-3.60(8H,m), 3.60-3.85(2H,m), 3.85-4.40(5H,m), 4.40-4.55(2H,m), 4.60-4.75(1H,m), 7.00-7.15(2H,m), 7.35-7.50(2H,m), 8.15-8.50(2H,m), 10.80-11.30(1H,m), 11.73(1H,d,J=6.6Hz).

MS (ESI) m/z: 557($M+H^+$).

[Example 162]

N-{(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(dimethylamino)carbonyl]piperidin-3-yl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and N,N-dimethylcarbamoyl chloride in a similar manner to Example 100.

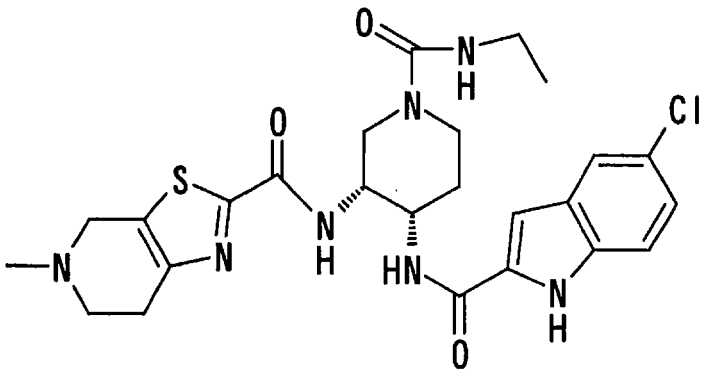
Melting point: 267-270°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.78(1H,m), 1.97-2.10(1H,m), 2.70(6H,s), 2.90(3H,s), 2.95-3.80(8H,m), 4.25-4.80(4H,m), 7.08(1H,s), 7.16(1H,dd,J=8.8,1.8Hz), 7.41(1H,d,J=8.8Hz), 7.70(1H,s), 8.31(1H,br.s), 8.40(1H,d,J=7.3Hz), 11.15-11.60(1H,m), 11.82(1H,s).

MS (ESI) m/z: 544($M+H^+$).

[Example 163]

N-{(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(ethylamino)carbonyl]piperidin-3-yl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and ethyl isocyanate in a similar manner to Example 100.

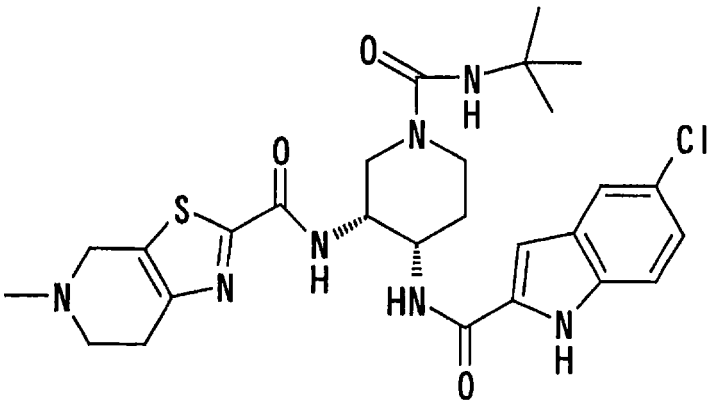
Melting point: 221-235°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 0.98(3H,t,J=7.1Hz), 1.60-1.70(1H,m), 1.80-1.95(1H,m), 2.90(3H,s), 2.95-3.40(6H,m), 3.40-4.00(4H,m), 4.25-4.80(4H,m), 6.60-6.80(1H,m), 7.09(1H,s), 7.16(1H,dd,J=8.8,1.9Hz), 7.41(1H,d,J=8.8Hz), 7.68(1H,d,J=1.9Hz), 8.02(1H,br.s), 8.35(1H,d,J=7.1Hz), 11.20-11.70(1H,m), 11.82(1H,s).

MS(FAB)m/z:544($M+H^+$).

[Example 164]

N-((3R*,4S*)-1-[(tert-Butylamino)carbonyl]-4-{[(5-chloroindol-2-yl)carbonyl]amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 118 and tert-butyl isocyanate in a similar manner to Example 100.

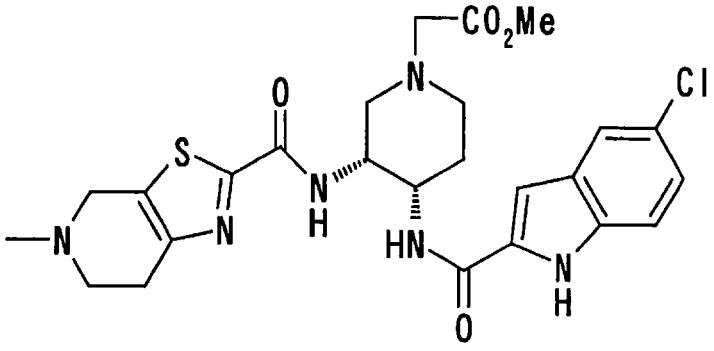
Melting point: 236-238°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.21(9H,s), 1.60-1.70(1H,m), 1.80-1.90(1H,m), 2.87(3H,s), 3.00-3.40(6H,m), 3.49(1H,br.s), 3.80-3.90(1H,m), 3.90-4.00(1H,m), 4.20-4.35(2H,m), 4.47(1H,br.s), 5.90(1H,s), 7.06(1H,s), 7.16(1H,dd,J=8.8,1.9Hz), 7.41(1H,d,J=8.8Hz), 7.67(1H,d,J=1.9Hz), 8.04(1H,d,J=6.8Hz), 8.34(1H,d,J=7.3Hz), 11.22(1H,br.s), 11.79(1H,s).

MS (FAB) m/z: 572($M+H^+$).

[Example 165]

Methyl 2-((3R*,4S*)-4-{[(5-chloroindol-2-yl)carbonyl]-amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidin-3-yl)acetate dihydrochloride:



The title compound was obtained from the compound obtained in Example 118 and methyl bromoacetate in a similar manner to Example 102.

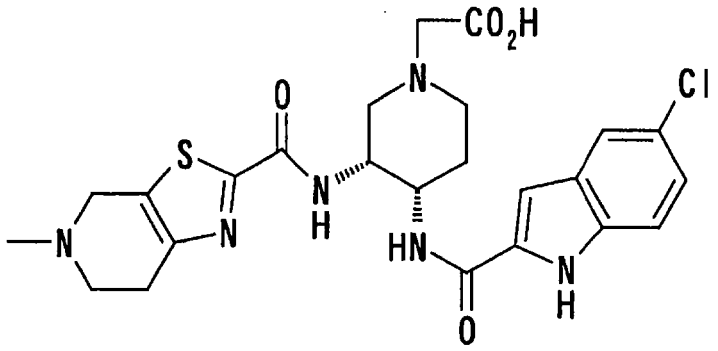
Melting point: 253-255°C (decomposed).

$^1$H-NMR (DMSO-$d_6$, 80°C) δ: 1.95-2.10(1H,m), 2.10-2.25(1H,m), 2.88(3H,s), 3.00-3.73(8H,m), 3.75(3H,s), 3.97-4.15(2H,m), 4.30-4.80(4H,m), 7.08-7.20(2H,m), 7.44(1H,d,J=8.6Hz), 7.63(1H,d,J=2.0Hz), 8.42(1H,d,J=7.3Hz), 8.62(1H,br.s), 11.82(1H,br.s).

MS (ESI) m/z: 545($M+H^+$).

[Example 166]

2-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}piperidin-3-yl)acetic acid hydrochloride:



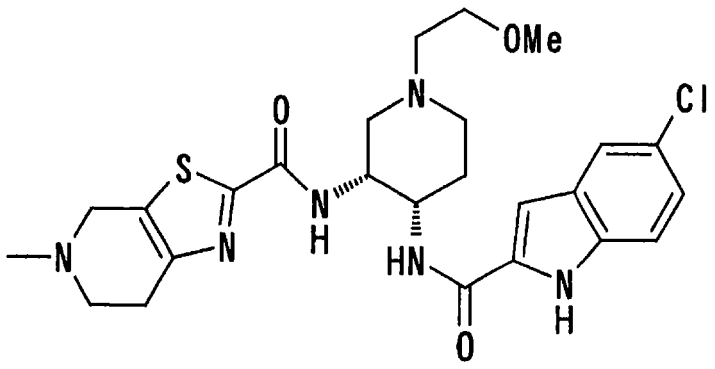
The title compound was obtained by treating the compound obtained in Example 165 in a similar manner to Example 101.

Melting point: 234-240°C (decomposed).

$^1$H-NMR (DMSO-$d_6$) δ: 1.75-1.95(1H,m), 2.05-2.20(1H,m), 2.88(3H,s), 2.95-3.90(10H,m), 4.20-4.70(4H,m), 7.11(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.66(1H,d,J=2.0Hz), 8.46(1H,br.d,J=7.8Hz), 8.65(1H,br.s), 11.60-12.70(2H,br.s), 11.91(1H,br.s).

[Example 167]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-methoxyethyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide dihydrochloride:



The title compound was obtained from the compound obtained in Example 118 and 2-bromoethyl methyl ether in a similar manner to Example 102 (NMR was measured in the form of a free base).

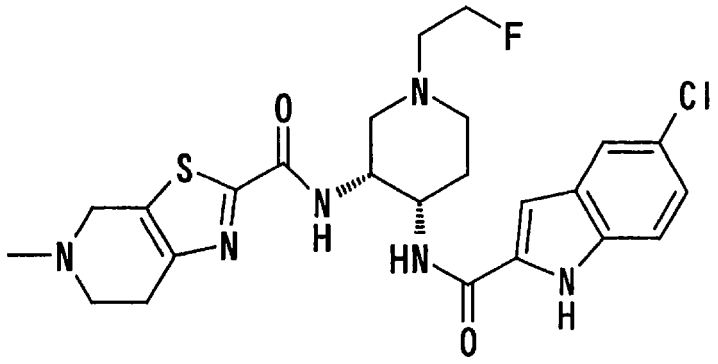
Melting point: 238-242°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 1.75-1.83(2H,m), 2.27-2.39(2H,m), 2.52(3H,s), 2.60-2.66(1H,m), 2.69-2.75(1H,m), 2.81-2.90(2H,m), 2.96-3.07(2H,m), 3.41(3H,s), 3.53-3.60(2H,m), 3.75(each 1H,AB type d,J=15.5Hz), 4.02-4.05(1H,m), 4.40(1H,br), 6.88(1H,d,J=1.5Hz), 7.18-7.21(1H,m), 7.31-7.33(1H,m), 7.63(1H,d,J=1.5Hz), 8.17(1H,d,J=5.0Hz), 8.26(1H,d,J=7.0Hz), 9.30(1H,br.s).

MS (FAB) m/z: 531($M+H^+$).

[Example 168]

N-[(3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-fluoroethyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide dihydrochloride:




The title compound was obtained from the compound obtained in Example 118 and 2-fluoroethyl bromide in a similar manner to Example 102 (NMR was measured in the

form of a free base).

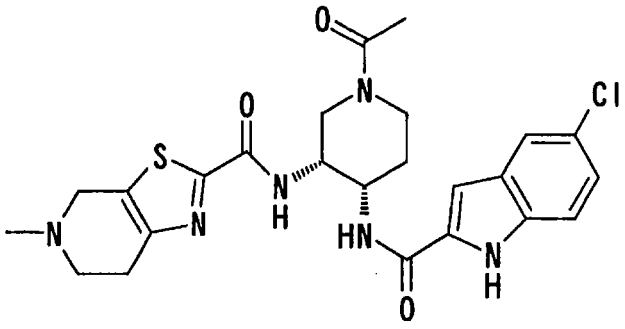
Melting point: 228-233°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 1.77(2H,dq,J=12.5,4.0Hz), 2.28-2.32(1H,m), 2.41(1H,t,J=12.5Hz), 2.52(3H,s), 2.65(1H,d,J=10.5Hz), 2.76-2.81(1H,m), 2.83-2.86(3H,m), 2.98-3.05(3H,m), 3.75(each 1H,AB type d,J=15.5Hz), 4.02-4.08(1H,m), 4.45(1H,br), 4.54-4.59(1H,m), 4.64-4.70(1H,m), 6.87(1H,d,J=1.5Hz), 7.19-7.22(1H,m), 7.32(1H,d,J=8.5Hz), 7.64(1H,d,J=2.0Hz), 8.11(1H,d,J=5.5Hz), 8.20(1H,d,J=7.3Hz), 9.30(1H,br).

MS (FAB) m/z: 519($M+H^+$).

[Example 169]

N-((3R,4S)-1-Acetyl-4-{[(5-chloroindol-2-yl)carbonyl]-amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




A 4N dioxane solution (7.0 ml) of hydrochloric acid was added to a dioxane solution (15 ml) of the compound (630 mg) obtained in Referential Example 214, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure.

The thus-obtained yellow solids (590 mg) and the compound (379 mg) obtained in Referential Example 10 were used to obtain a free base (330 mg) of the title compound in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound (NMR was measured in the form of a free base).

Melting point: 202-222°C (decomposed).

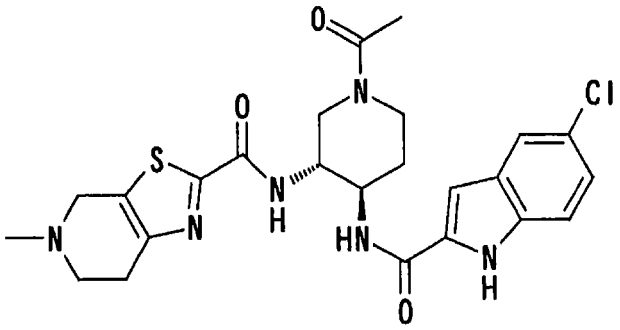
$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.85(1H,m), 1.87,2.06(total 3H,each s), 1.88-2.10(1H,m), 2.37(3H,s), 2.65-2.77(2H,m), 2.79-2.89(2H,m), 2.99-3.09(0.5H,m), 3.30-3.52(2H,m), 3.64(2H,s), 3.70-3.80(0.5H,m), 3.96-4.21(2H,m), 4.27(1H,br.s), 4.35-4.48(1H,m), 7.07,7.11(total 1H,each s), 7.18(1H,d,J=8.8Hz), 7.42(1H,d,J=8.8Hz), 7.71(1H,s), 8.16-8.22(1H,m), 8.37,8.46(total 1H,each d,J=7.8Hz), 11.81,11.83(total 1H,each s).

MS (ESI) m/z: 515($M+H^+$).

$[\alpha]^{25}_D$ = -56.0° (c = 0.50, methanol).

[Example 170]

N-((3R,4R)-1-Acetyl-4-{[(5-chloroindol-2-yl)carbonyl]-amino}piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 219 and Referential Example 10 in a similar manner to Example 169.

Melting point: 221-238°C.

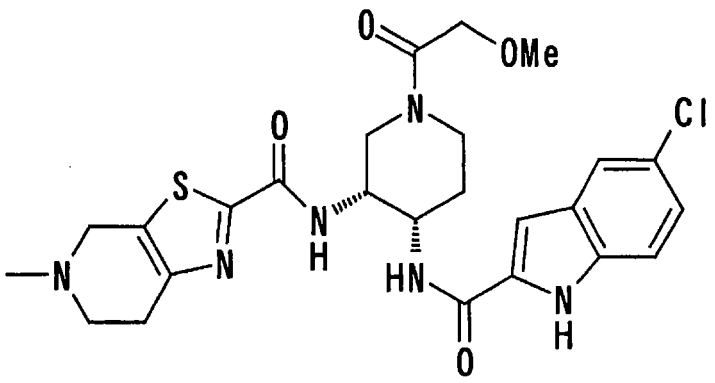
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.56(0.5H,m), 1.60-1.70(0.5H,m), 1.89-2.01(1H,m), 2.05(3H,s), 2.51-2.67(1H,m), 2.88(3H,s), 3.00-3.22(3H,m), 3.31-3.40(3H,m), 3.56-3.67(0.5H,m), 3.78-4.02(1.5H,m), 4.22-4.44(2H,m), 4.56-4.72(1H,m), 7.02(1H,s), 7.15(1H,dd,J=8.8,2.0Hz), 7.37(1H,d,J=8.8Hz), 7.67(1H,d,J=2.0Hz), 8.42(1H,d,J=9.8Hz), 8.67-8.78(1H,m), 11.02-11.14(1H,m), 11.72(0.5H,s), 11.74(0.5H,s).

MS (FAB) m/z: 515($M+H^+$).

$[\alpha]^{25}_D$ = -105.4° (c = 0.58, methanol).

[Example 171]

N-[(3R,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 221 in a similar manner to Example 169.

Melting point: 207-220°C (decomposed).

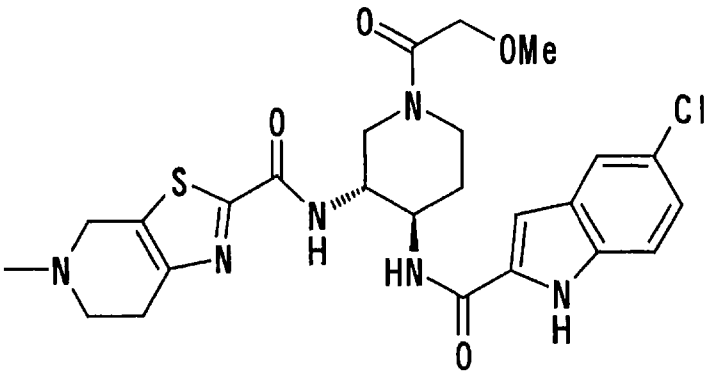
$^1$H-NMR (DMSO-$d_6$) δ: 1.70-1.80(1H,m), 1.85-2.05(1H,m), 2.90(3H,s), 3.00-3.20(2H,m), 3.16(3H,s), 3.22-3.82(7H,m), 3.88-4.80(5H,m), 7.09(1H,d,J=9.0Hz), 7.17(1H,dd,J=8.8,1.9Hz), 7.42(1H,d,J=8.8Hz), 7.70(1H,d,J=1.9Hz), 8.29(1H,br.s), 8.40-8.50(1H,m), 11.20-11.50(1H,m), 11.85(1H,s).

MS (ESI) m/z: 545($M+H^+$).

$[\alpha]^{25}_D$ = -53.4° (c = 0.52, methanol).

[Example 172]

N-[(3R,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-(2-methoxyacetyl)piperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 223 in a similar manner to Example 169.

Melting point: 213-230°C.

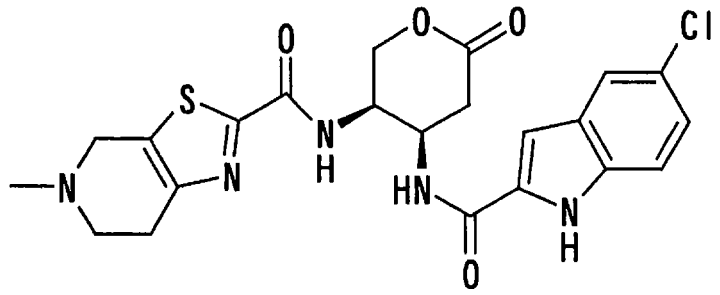
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.56(0.5H,m), 1.61-1.70(0.5H,m), 1.89-2.00(1H,m), 2.05(3H,s), 2.45-2.67(1H,m), 2.88(3H,s), 3.00-3.21(4H,m), 3.32-3.56(7H,m), 3.78-3.89(2H,m), 4.00-4.24(2H,m), 4.26-4.43(2H,m), 7.02(1H,s), 7.13(1H,dd,J=8.8,2.0Hz), 7.37(1H,d,J=8.8Hz), 7.67(1H,d,J=2.0Hz), 8.41(1H,d,J=9.8Hz), 8.74(1H,d,J=9.8Hz), 10.80-10.90(1H,m), 11.72(1H,s).

MS (FAB) m/z: 545($M+H^+$).

$[\alpha]^{25}_D$ = -100.3° (c = 0.51, methanol).

[Example 173]

N-((3R,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-6-oxotetrahydro-2H-pyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



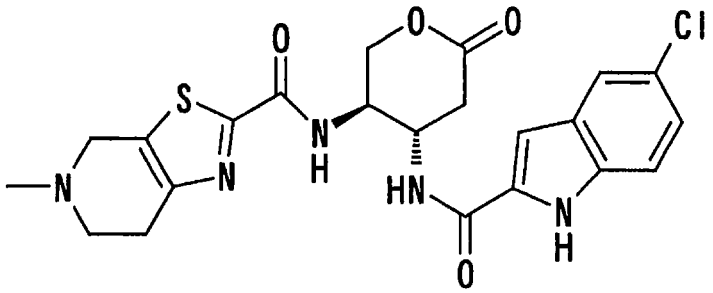
The title compound was obtained from the low-polar compound obtained in Referential Example 176 and the compound obtained in Referential Example 10 in a similar manner to Example 169.

$^1$H-NMR (DMSO-$d_6$) δ: 2.41-2.56(2H,m), 2.91(3H,s), 3.01-3.23(1H,m), 3.24-3.56(5H,m), 3.62-3.67(1H,m), 4.21-4.44(1H,m), 4.56-4.78(2H,m), 7.11(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.22(1H,d,J=8.5Hz), 7.41(1H,d,J=8.8Hz), 7.69(1H,d,J=2.0Hz), 8.40-8.50(1H,m), 11.34-11.56(1H,m), 11.82(1H,s).

MS (FAB) m/z: 488($M+H^+$).

[Example 174]

N-((3R,4S)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-6-oxotetrahydro-2H-pyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



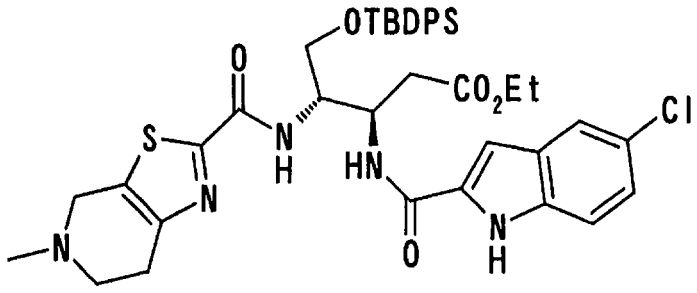
The title compound was obtained from the high-polar compound obtained in Referential Example 176 and the compound obtained in Referential Example 10 in a similar manner to Example 169.

$^1$H-NMR (DMSO-$d_6$) δ: 2.41-2.56(2H,m), 2.91(3H,s), 3.23-3.41(2H,m), 3.43-3.50(2H,m), 3.56-3.67(2H,m), 4.37(1H,dd,J=13.9,7.1Hz), 4.40-4.50(1H,m), 4.56-4.78(2H,m), 7.12(1H,s), 7.17(1H,dd,J=8.8,2.0Hz), 7.41(1H,d,J=8.8Hz), 7.71(1H,d,J=2.0Hz), 8.44(1H,d,J=8.5Hz), 8.15(1H,d,J=8.5Hz), 11.42-11.53(1H,m), 11.79(1H,s).

MS (FAB) m/z: 488($M+H^+$).

[Example 175]

Ethyl (3R,4S)-5-{[tert-butyl(diphenyl)silyl]oxy}-3-{[(5-chloroindol-2-yl)carbonyl]amino}-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-valerate:



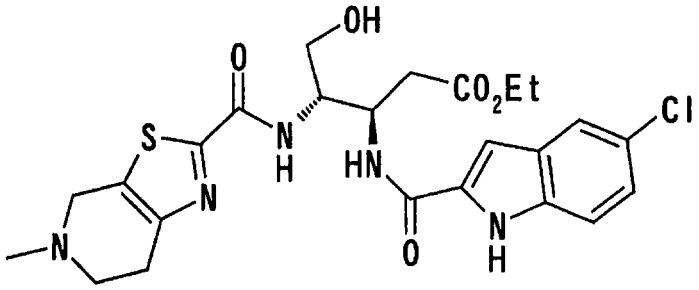

The title compound was obtained from the compound obtained in Referential Example 225 in a similar manner to Example 169.

$^1$H-NMR ($CDCl_3$) δ: 1.09(9H,s), 1.21(3H,t,J=7.4Hz), 2.49(3H,s), 2.65(1H,dd,J=15.9,5.4Hz), 2.67-2.90(5H,m),

3.60(1H,d,J=14.9Hz), 3.72(1H,d,J=14.9Hz), 3.78-3.91(2H,m), 4.00-4.21(2H,m), 4.43-4.50(1H,m), 4.78-4.89(1H,m), 6.81(1H,s), 7.20(1H,dd,J=8.8,2.0Hz), 7.32-7.52(m,7H), 7.63-7.74(6H,m), 7.89-8.01(1H,m), 9.18(1H,s).

[Example 176]

Ethyl (3R,4S)-3-{[(5-chloroindol-2-yl)carbonyl]amino}-5-hydroxy-4-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}valerate:



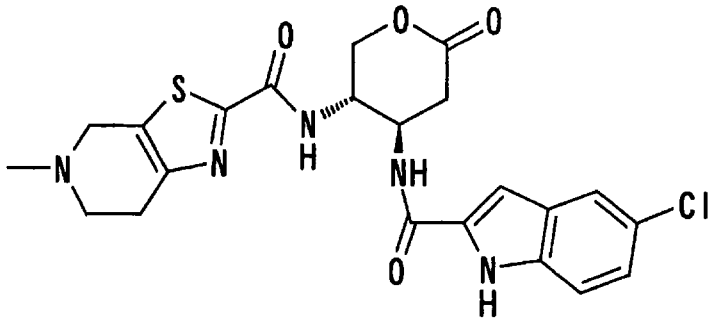

After hydrogen fluoride·pyridine (0.4 ml) was added dropwise to a mixture sulution composed of the compound (0.54 g) obtained in Example 175, pyridine (4.0 ml) and tetrahydrofuran (10 ml) under ice cooling, the reaction mixture was stirred for 18 hours while the temperature thereof was gradually raised to room temperature. The reaction mixture was concentrated, and the resultant residue was purified by column chromatography on silica gel (chloroform:methanol = 9:1) to obtain the title compound (0.31 g).

$^1$H-NMR ($CDCl_3$) δ: 1.20(3H,t,J=7.4Hz), 2.49(3H,s), 2.67-2.90(6H,m), 3.62-3.74(3H,m), 3.78-3.94(1H,m), 4.00-4.20(2H,m), 4.30-4.40(1H,m), 4.80-4.89(1H,m), 6.93(1H,s),

7.23(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz),
7.56(1H,d,J=8.5Hz), 7.61(1H,d,J=2.0Hz), 7.88(1H,d,J=8.5Hz),
9.29(1H,s).

[Example 177]

N-((3S,4R)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-6-oxotetrahydro-2H-pyran-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



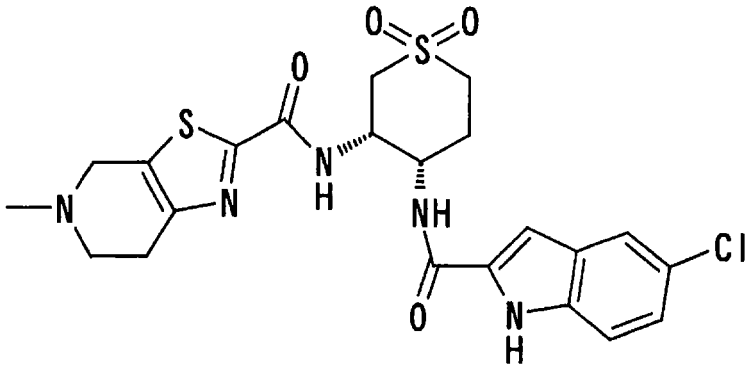
A 4N dioxane solution (20 ml) of hydrochloric acid was added to the compound (0.31 g) obtained in Example 176, and the mixture was heated under reflux for 4 hours. The reaction mixture was concentrated, and the resultant residue was recrystallized from diethyl ether to obtain the title compound (0.23 g).

Melting point: 221-238°C (decomposed).

$^1$H-NMR and MS (FAB): The same as those of the enantiomer in Example 174.

[Example 178]

N-((3R*,4R*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 227 and 5-chloroindole-2-carboxylic acid in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

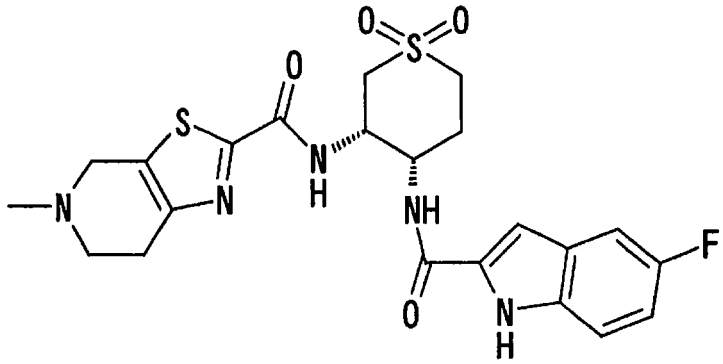
Melting point: 241-244°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.14(1H,br), 2.30-2.34(1H,m), 2.92(3H,s), 3.10-3.18(2H,m), 3.41(4H,br), 3.68(2H,br), 4.44(1H,br), 4.63-4.78(3H,m), 7.16-7.18(1H,m), 7.21(1H,s), 7.43(1H,d,J=8.5Hz), 7.67(1H,d,J=4.6Hz), 8.39(1H,br), 8.94(1H,br), 11.82(1H,br).

MS (ESI) m/z: 522($M+H^+$).

[Example 179]

N-((3R*,4R*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 227 and 5-fluoroindole-2-carboxylic acid in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

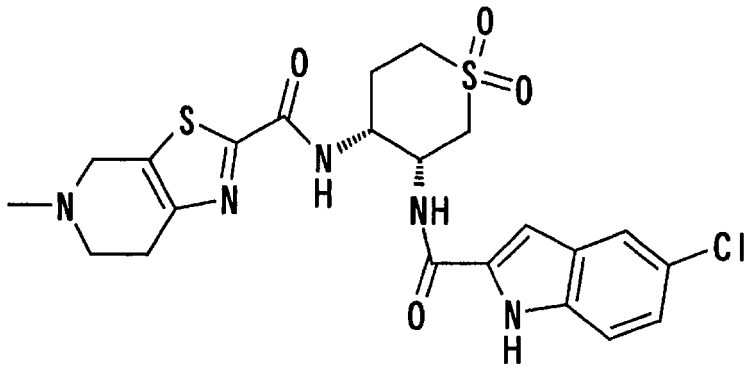
Melting point: 243-245°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.14(1H,br), 2.30-2.33(1H,m), 2.92(3H,s), 3.13(2H,br), 3.51(4H,br), 3.63(2H,br), 4.63(3H,br), 4.78(1H,br), 7.01-7.05(1H,m), 7.21(1H,s), 7.37-7.44(2H,m), 8.36(1H,br), 8.93(1H,d,J=6.8Hz), 11.72(1H,br).

MS (ESI) m/z: 506($M+H^+$).

[Example 180]

N-((3R*,4R*)-3-{[(5-Chloroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-4-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 229 and the compound obtained in Referential Example 10 in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

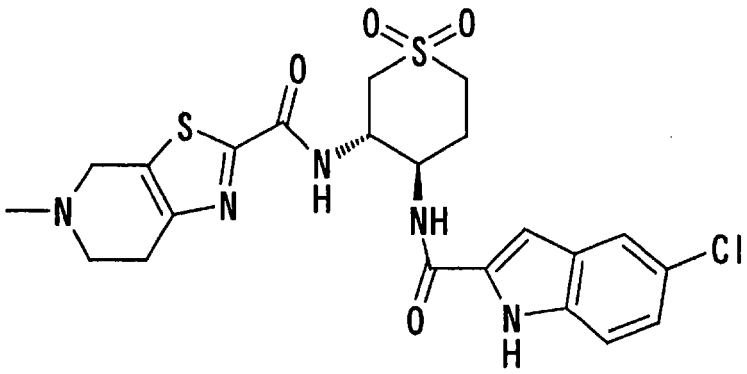
Melting point: 242-247°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.16(1H,br), 2.45(1H,br), 2.93(3H,s), 3.13(2H,br), 3.26(4H,br), 3.69(2H,br), 4.45(1H,br), 4.65-4.77(3H,m), 7.01(1H,s), 7.17(1H,dd,J=8.7,1.4Hz), 7.43(1H,d,J=8.5Hz), 7.69(1H,s), 8.35-8.40(1H,m), 9.04(1H,br), 11.86(1H,s).

MS (ESI) m/z: 522($M+H^+$).

[Example 181]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 231 and 5-chloroindole-2-carboxylic acid in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

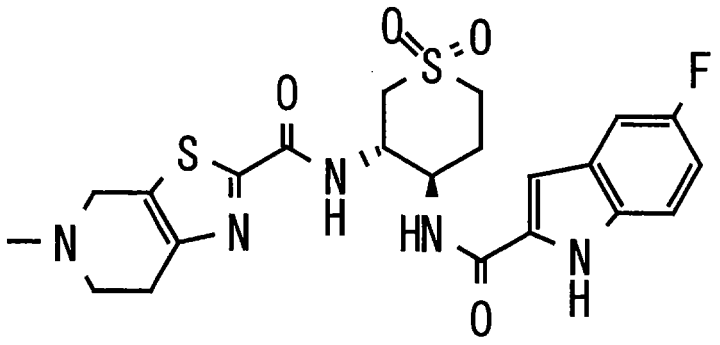
Melting point: 244-249°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.17-2.27(2H,m), 2.90(3H,s), 3.09(1H,br), 3.18-3.21(2H,m), 3.31-3.34(2H,m), 3.60-3.67(3H,m), 4.41-4.49(2H,m), 4.54-4.59(2H,m), 7.04(1H,s), 7.09-7.13(1H,m), 7.39(1H,d,J=8.5Hz), 7.61(1H,d,J=9.9Hz), 8.52-8.56(1H,m), 8.83-8.85(1H,m), 11.65(1H,d,J=11.9Hz).

MS (ESI) m/z: 522($M+H^+$).

[Example 182]

N-((3R*,4S*)-4-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 231 and 5-fluoroindole-2-carboxylic acid in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

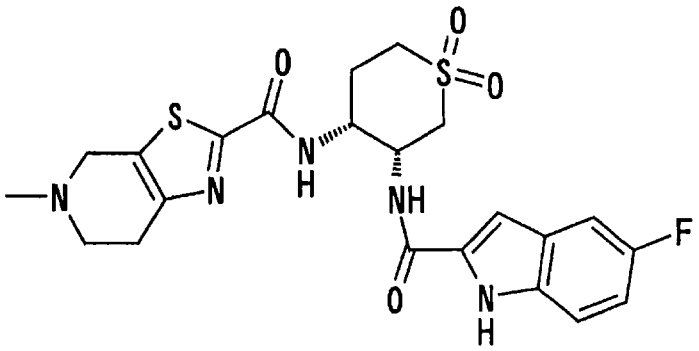
Melting point: 236-241°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.20-2.24(2H,m), 2.89(3H,s), 3.07(1H,br), 3.19-3.22(2H,m), 3.60-3.66(4H,m), 4.43-4.58(5H,m), 6.95-7.00(1H,m), 7.04(1H,s), 7.32-7.38(2H,m), 8.50(1H,d,J=8.5Hz), 8.83(1H,d,J=8.5Hz), 11.59(1H,s).

MS (ESI) m/z: 506($M+H^+$).

[Example 183]

N-((3R*,4R*)-3-{[(5-Fluoroindol-2-yl)carbonyl]amino}-1,1-dioxohexahydro-1-thiopyran-4-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



A free base of the title compound was obtained from the compound obtained in Referential Example 233 and the compound obtained in Referential Example 10 in a similar manner to Example 91. This free base was treated with an ethanol solution of hydrochloric acid to obtain the title compound.

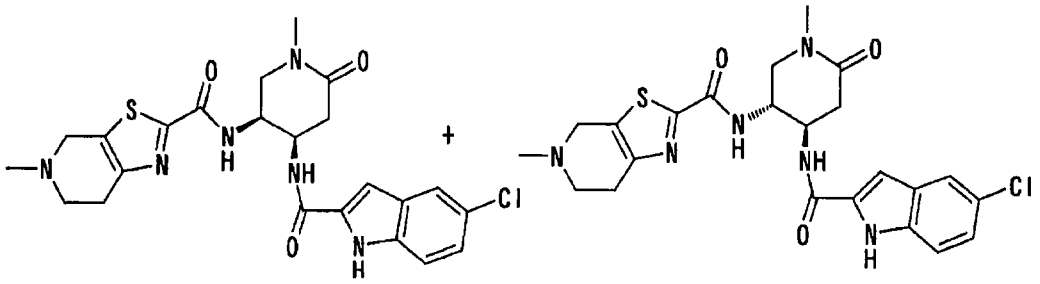
Melting point: 244-249°C.

$^1$H-NMR (DMSO-$d_6$) δ: 2.12-2.18(1H,m), 2.50(1H,br), 2.92(3H,s), 3.17(3H,br), 3.50-3.61(5H,m), 4.45(1H,br), 4.62-4.78(3H,m), 6.98-7.03(2H,m), 7.36-7.42(2H,m), 8.30(1H,br), 9.00(1H,d,J=8.0Hz), 11.74(1H,s).

MS (ESI) m/z: 506($M+H^+$).

[Example 184]

N-((3S,4R)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-1-methyl-6-oxopiperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (low-polar compound) and N-((3R,4R)-4-{[(5-chloroindol-2-yl)carbonyl]amino}-1-methyl-6-oxopiperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (high-polar compound):



Low-polar compound　　High-polar compound

The title compound was obtained from the compound obtained in Referential Example 236 and the compound obtained in Referential Example 10 in a similar manner to Example 169.

Low-polar compound:

Melting poing: 189-203°C (decomposed).

$^1$H-NMR ($CDCl_3$) δ: 2.52(3H,s), 2.59(1H,q,J=8.8Hz), 2.71-2.78(2H,m), 2.89-3.00(2H,m), 3.03(3H,s), 3.12(1H,dd,J=17.6,5.4Hz), 3.43(1H,dd,J=12.7,5.1Hz), 3.70(1H,d,J=15.2Hz), 3.77(1H,d,J=15.2Hz), 3.83(1H,dd,J=12.7,3.9Hz), 4.55-4.67(2H,m), 6.99(1H,s), 7.23(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.65(1H,d,J=2.0Hz), 8.07(1H,d,J=5.1Hz), 8.16(1H,d,J=5.4Hz), 9.43(1H,s).

MS (FAB) m/z: 501($M+H^+$).

High-polar compound:

Melting point:183-195°C (decomposed).

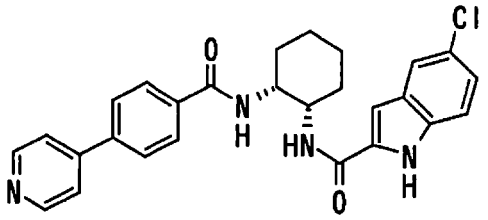
$^1$H-NMR (DMSO-$d_6$) δ: 2.33(3H,s), 2.41-2.50(1H,m), 2.62-2.73(3H,m), 2.75-2.81(1H,m), 2.82(3H,s), 3.21-3.32(2H,m), 3.34-3.50(2H,m), 3.55(1H,d,J=15.4Hz), 3.63(1H,d,J=15.4Hz),

4.30-4.40(0.5H,m), 4.50-4.60(0.5H,m), 7.04(1H,s), 7.15(1H,dd,J=8.8,2.0Hz), 7.38(1H,d,J=8.8Hz), 7.67(1H,d,J=2.0Hz), 8.49(1H,d,J=8.5Hz), 8.71(1H,d,J=8.5Hz), 11.74(1H,s).

MS (FAB) m/z: 501($M+H^+$).

[Example 185]

5-Chloro-N-((1R*,2S*)-2-{[4-(pyridin-4-yl)benzoyl]-amino}cyclohexyl)indole-2-carboxamide hydrochloride:



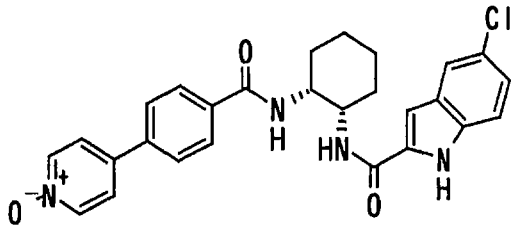
The title compound was obtained from the compound obtained in Referential Example 71 and the compound obtained in Referential Example 237 in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.52(2H,m), 1.60-1.80(4H,m), 1.96-2.10(2H,m), 4.24-4.39(2H,m), 7.15(1H,dd,J=8.8,2.0Hz), 7.21(1H,s), 7.40(1H,d,J=8.8Hz), 7.64(1H,d,J=2.0Hz), 8.06(4H,s), 8.18(1H,J=7.3Hz), 8.34-8.42(3H,m), 8.94(2H,d,J=6.9Hz) ,11.91(1H,s).

MS (FAB)m/z: 473$(M+H)^+$.

[Example 186]

4-(4-{[((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)amino]carbonyl}phenyl)pyridine N-oxide:



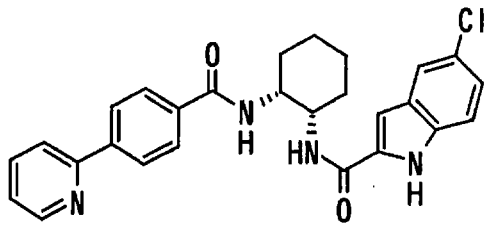
The title compound was obtained from the compound obtained in Referential Example 71 and the compound obtained in Referential Example 240 in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.52(2H,m), 1.60-1.80(4H,m), 1.88-2.00(2H,m), 4.21-4.36(2H,m), 7.12-7.18(2H,m), 7.41(1H,d,J=8.6Hz), 7.66(1H,s), 7.80-7.87(4H,m), 7.91(2H,d,J=8.3Hz), 8.01(1H,d,J=7.6Hz), 8.09(1H,d,J=7.3Hz), 8.27(2H,d,J=6.6Hz), 11.79(1H,s).

MS (FAB) m/z: 489$(M+H)^+$.

[Example 187]

5-Chloro-N-((1R*,2S*)-2-{[4-(pyridin-2-yl)benzoyl]-amino}cyclohexyl)indole-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 71 and 4-(2-pyridyl)benzoic acid (Japanese Patent Application Laid-Open No. 2000-119253) in a similar manner to the process

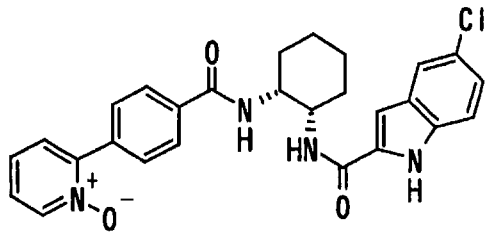
described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.39-1.51(2H,m), 1.60-1.80(4H,m), 1.89-2.00(2H,m), 4.24-4.38(2H,m), 7.12-7.16(2H,m), 7.36-7.39(1H,m), 7.42(1H,d,J=8.8Hz), 7.66(1H,d,J=2.0Hz), 7.87-7.90(1H,m), 7.92(2H,d,J=8.3Hz), 7.98-8.11(3H,m), 8.15(2H,d,J=8.3Hz), 8.69(1H,d,J=4.6Hz), 11.80(1H,s).

MS (FAB) m/z: 473$(M+H)^+$.

[Example 188]

2-(4-{[((1R*,2S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-cyclohexyl)amino]carbonyl}phenyl)pyridine N-oxide:



The title compound was obtained from the compound obtained in Referential Example 71 and the compound obtained in Referential Example 241 in a similar manner to the process described in Example 2.

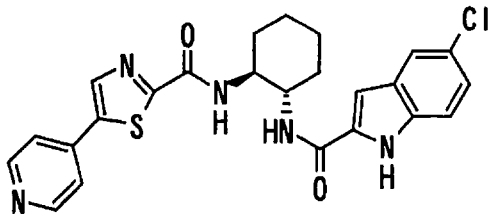
$^1$H-NMR (DMSO-$d_6$) δ: 1.39-1.51(2H,m), 1.60-1.79(4H,m), 1.89-2.00(2H,m), 4.23-4.37(2H,m), 7.12-7.17(2H,m), 7.39-7.43(3H,m), 7.61-7.64(1H,m), 7.67(1H,d,J=2.0Hz), 7.89(4H,s), 8.00-8.06(1H.m), 8.08-8.02(1H,m), 8.32-8.35(1H,m), 11.79(1H,s).

MS (FAB) m/z: 489$(M+H)^+$.

[Example 189]

5-Chloro-N-[(1R*,2R*)-2-({[5-(4-pyridin-2-yl)thiazol-2-

yl]carbonyl}amino)cyclohexyl]indole-2-carboxamide hydrochloride:



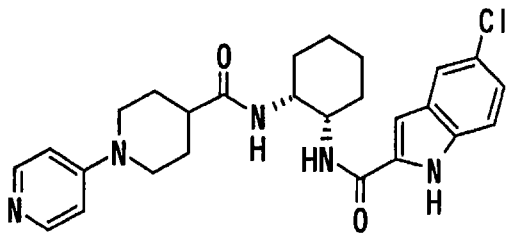
The title compound was obtained from the compound obtained in Referential Example 69 and lithium 5-(4-pyridyl)thiazole-2-carboxylate (Japanese Patent Application Laid-Open No. 2000-143623) in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44(2H,br.s), 1.65(4H,br.s), 1.85-2.06(2H,m), 4.23(1H,br.s), 4.30(1H,br.s), 7.14-7.23(2H,m), 7.41(1H,d,J=8.8Hz), 7.69(1H,s), 8.04-8.13(2H,m), 8.13(1H,d,J=8.8Hz), 8.59(1H,d,J=8.0Hz), 8.75-8.87(3H,m), 11.83(1H,s).

MS (ESI)m/z: 480$(M+H)^+$.

[Example 190]

5-Chloro-N-[(1R*,2S*)-2-({[1-(pyridin-4-yl)piperidin-4-yl]carbonyl}amino)cyclohexyl]indole-2-carboxamide hydrochloride:



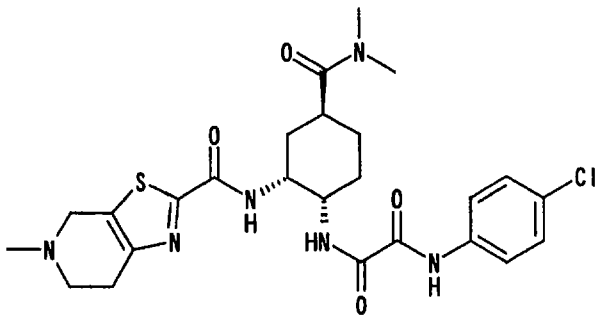
1-(4-Pyridyl)piperidine-4-carboxylic acid (Tetrahedron, 1998, Vol. 44, p.7095) (206 mg) was suspended in methylene chloride (50 ml), and thionyl chloride (144 μl) was added under ice cooling to stir the mixture for 30 minutes. After triethylamine (969 μl) was added to the reaction mixture, the compound (328 mg) obtained in Referential Example 71 was added to stir the mixture at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, water was added to the residue, the mixture was concentrated under reduced pressure, and precipitate deposited was collected by filtration to obtain the title compound (310 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.30-2.00(10H,m), 2.74(1H,br.s), 3.18(2H,q,J=12.3Hz), 4.03(1H,br.s), 4.10-4.25(3H,m), 7.15-7.55(4H,m), 7.42(1H,d,J=8.8Hz), 7.65(1H,s), 7.91(1H,d,J=8.8Hz), 8.20-8.35(3H,m), 11.91(1H,s), 13.47(1H,br.s).

MS (FAB) m/z: 480$(M+H)^+$.

[Example 191]

$N^1$-(4-Chlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



The compound (288 mg) obtained in Referential Example 242 was dissolved in tetrahydrofuran (8.0 ml), lithium hydroxide (46 mg) and water (1.0 ml) were successively added, and the mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure to obtain a crude product (292 mg) of lithium 2-(4-chloroanilino)-2-oxoacetate as a colorless solid. This crude product and the compound obtained in Referential Example 253 were dissolved in N,N-dimethylformamide (15 ml), and 1-hydroxybenzotriazole monohydrate (164 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (251 mg) were added to stir the mixture at room temperature for 64.5 hours. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 47:3). The thus-obtained pale yellow

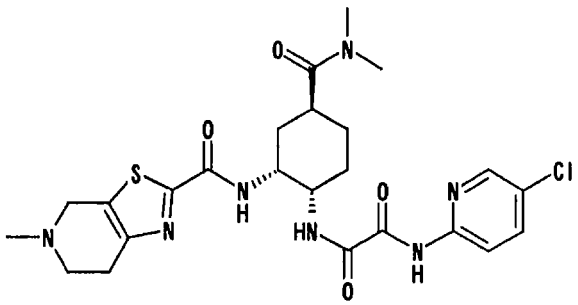
solids were dissolved in methylene chloride, a 1N ethanol solution (0.52 ml) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Methanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain the title compound (245 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.55(1H,m), 1.60-1.80(3H,m), 1.95-2.10(2H,m), 2.79(3H,s), 2.80-3.00(1H,m), 2.92(3H,s), 2.94(3H,s), 3.10-3.40(2H,m), 3.40-3.80(2H,m), 3.95-4.05(1H,m), 4.40-4.80(3H,m), 7.40(2H,d,J=8.8Hz), 7.83(2H,d,J=8.8Hz), 8.75(1H,d,J=7.1Hz), 9.00-9.10(1H,br), 10.81(1H,s), 11.45-11.75(1H,m).

MS (FAB) m/z: 547$(M+H)^+$.

[Example 192]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



The compound (240 mg) obtained in Referential Example 243 was dissolved in tetrahydrofuran (8.0 ml), lithium hydroxide (41 mg) and water (1.0 ml) were successively

added to the solution, and the mixture was stirred at room temperature for 2.5 hours. The reaction mixture was concentrated under reduced pressure to obtain lithium 2-[(5-chloropyridin-2-yl)amino]-2-oxoacetate (249 mg).

On the other hand, 10% palladium on carbon (200 mg) was added to a solution of the compound (293 mg) obtained in Referential Example 252 in methanol (10 ml), and the mixture was stirred at room temperature for 18 hours under a hydrogen atmosphere. After removing palladium on carbon by filtration, the filtrate was concentrated under reduced pressure to obtain a crude product (259 mg) of N-{(1R,2S,5S)-2-amino-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide.

This crude product (259 mg) and the lithium salt (249 mg) prepared above were added to N,N-dimethylformamide (15 ml), and 1-hydroxybenzotriazole monohydrate (166 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (235 mg) were added to stir the mixture at room temperature for 63.5 hours. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol

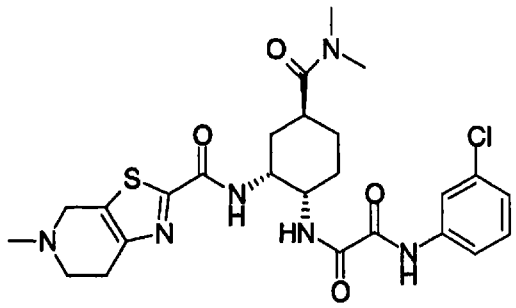
= 93:7). The thus-obtained pale yellow solids were dissolved in methylene chloride, a 1N ethanol solution (0.855 ml) of hydrochloric acid was added to the solution, and the solvent was distilled off under reduced pressure. Methanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain the title compound (209 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.57(1H,m), 1.60-1.80(3H,m), 1.95-2.13(2H,m), 2.79(3H,s), 2.80-3.00(1H,m), 2.92(3H,s), 2.94(3H,s), 3.10-3.40(2H,m), 3.40-3.80(2H,m), 3.95-4.05(1H,m), 4.37-4.80(3H,m), 7.90-8.10(2H,m), 8.45(1H,d,J=2.2Hz), 8.71(1H,d,J=7.6Hz), 9.10-9.30(1H,br), 10.26(1H,s), 11.30-11.60(1H,br).

MS (FAB) m/z: 548$(M+H)^+$.

[Example 193]

$N^1$-(3-Chlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



The compound (222 mg) obtained in Referential Example 270 and 3-chloroaniline (63 µl) were dissolved in N,N-

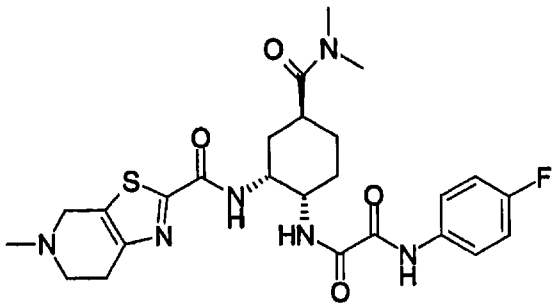
dimethylformamide (10 ml), and 1-hydroxybenzotriazole monohydrate (68 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (144 mg) were added to stir the mixture at room temperature for 40 hours. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 30:1). The thus-obtained pale yellow solids were dissolved in methylene chloride, a 1N ethanol solution (0.50 ml) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Diethyl ether was added to the residue, and precipitate formed was collected by filtration to obtain the title compound (174 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.62(1H,m), 1.65-1.90(3H,m), 1.98-2.20(2H,m), 2.79(3H,s), 2.88-3.10(1H,m), 2.93(3H,s), 2.94(3H,s), 3.15-3.40(2H,m), 3.40-3.90(2H,m), 3.95-4.10(1H,m), 4.40-4.80(3H,m), 7.19(1H,dd,J=9.3,2.0Hz), 7.37(1H,d,J=8.2Hz), 7.77(1H,d,J=8.3Hz), 7.92-8.05(1H,m), 8.75(1H,d,J=7.3Hz), 8.95-9.20(1H,br), 10.87(1H,s), 11.25-11.45(1H,br).

[Example 194]

$N^1$-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-

4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)-$N^2$-(4-fluorophenyl)-ethanediamide hydrochloride:



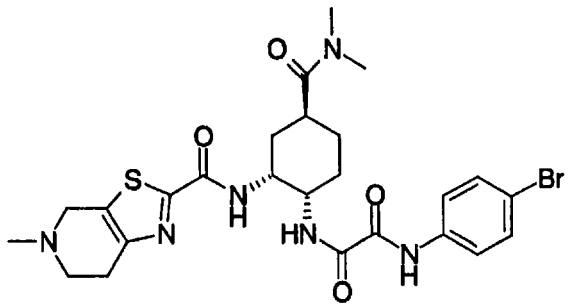
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 254, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-2.13(6H,m), 2.77(3H,s), 2.93(3H,s), 2.97(3H,s), 3.12-3.82(7H,m), 3.93-4.04(1H,m), 4.38-4.46(1H,m), 4.35-4.75(1H,m), 7.11-7.21(2H,m), 7.72-7.84(2H,m), 8.73(1H,d,J=7.6Hz), 8.93-9.02(1H,m), 10.70(1H,s).

MS (FAB) m/z: 531$(M+H)^+$.

[Example 195]

$N^1$-(4-Bromophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



The compound (152 mg) obtained in Referential Example 255 was dissolved in tetrahydrofuran (5.0 ml), a 1N aqueous solution (1.20 ml) of sodium hydroxide and methanol (5.0 ml) were successively added, and the mixture was stirred at room temperature for 2.5 hours. The reaction mixture was concentrated under reduced pressure, and methylene chloride (10 ml) and 1N hydrochloric acid (2.0 ml) were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure to obtain a crude product (280 mg) of 2-(4-bromoanilino)-2-oxoacetic acid as a colorless solid. This crude product and the compound (280 mg) obtained in Referential Example 253 were dissolved in N,N-dimethylformamide (30 ml), and 1-hydroxybenzotriazole monohydrate (90 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (226 mg) were added to stir the mixture at room temperature for a night. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct

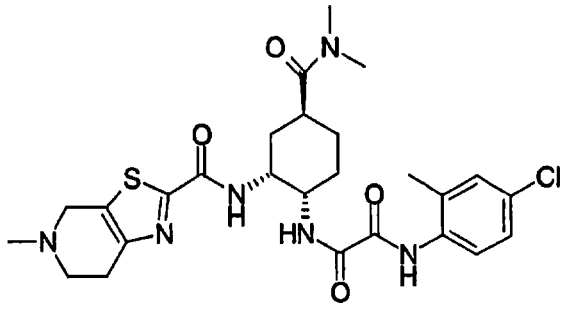
liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 97:3). The thus-obtained pale yellow solids were dissolved in methylene chloride, a 1N ethanol solution (191 μl) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Methanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain the title compound (103 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.43-1.57(1H,m), 1.59-1.80(3H,m), 1.97-2.10(2H,m), 2.79(3H,s), 2.84-2.98(7H,m), 3.18(2H,br.s), 3.39-3.72(2H,m), 3.95-4.05(1H,m), 4.20-4.80(3H,m), 7.53(2H,d,J=8.8Hz), 7.77(2H,d,J=8.8Hz), 8.75(1H,d,J=7.3Hz), 8.97-9.09(1H,m), 10.82(1H,s), 11.11(1H,br.s).

MS (FAB) m/z: 591$(M+H)^+$.

[Example 196]

$N^1$-(4-Chloro-2-methylphenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



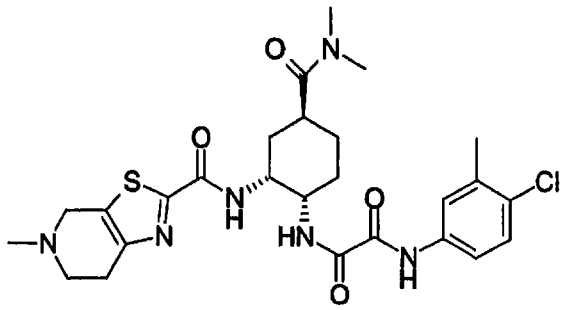
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 256, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

1H-NMR (DMSO-d6) δ: 1.45-1.55(1H,m), 1.60-1.80(3H,m), 2.00-2.10(2H,m), 2.19(3H,s), 2.79(3H,s), 2.80-3.00(7H,m), 3.31(2H,br.s), 3.40-3.70(2H,br), 3.95-4.05(1H,m), 4.35-4.70(3H,m), 7.20-7.30(1H,m), 7.35(1H,d,J=2.5Hz), 7.43(1H,d,J=8.6Hz), 8.76(1H,d,J=6.6Hz), 9.00-9.15(1H,br), 10.19(1H,s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 197]

$N^1$-(4-Chloro-3-methylphenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



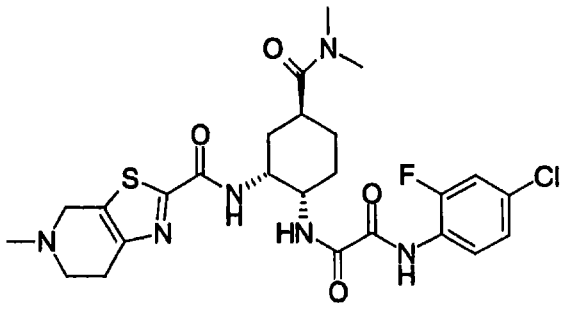
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 257, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.53(1H,m), 1.68-1.80(3H,m), 1.98-2.09(2H,m), 2.29(3H,s), 2.79(3H,s), 2.80-3.00(1H,m), 2.95(6H,s), 3.17-3.19(3H,m), 3.40-3.80(1H,m), 3.93-4.02(1H,m), 4.44-4.56(3H,m), 7.38(1H,d,J=8.8Hz), 7.65(1H,d,J=8.8Hz), 7.74(1H,s), 8.75(1H,d,J=7.8Hz), 8.96(1H,d,J=8.0Hz), 10.69(1H,s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 198]

$N^1$-(4-Chloro-2-fluorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



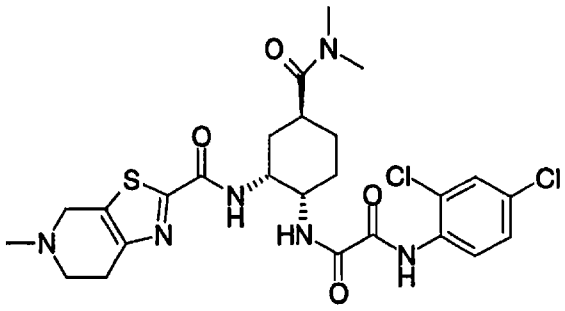
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 258, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.55(1H,m), 1.58-1.80(3H,m), 1.95-2.12(2H,m), 2.77(3H,s), 2.80-3.00(1H,m), 2.91(3H,s), 2.92(3H,s), 3.10-3.40(2H,m), 3.40-3.80(2H,m), 3.95-4.05(1H,m), 4.30-4.80(3H,m), 7.29(1H,d,J=8.5Hz), 7.52(1H,dd,J=10.3,2.0Hz), 7.61(1H,t,J=8.4Hz), 8.72(1H,d,J=6.8Hz), 9.00-9.20(1H,br), 10.38(1H,s), 11.20-11.45(1H,br).

MS (FAB) m/z: 565$(M+H)^+$.

[Example 199]

$N^1$-(2,4-Dichlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



The compound (300 mg) obtained in Referential Example 270 was dissolved in N,N-dimethylformamide (5 ml), and 2,4-dichloroaniline (165 mg), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (260 mg) and 1-hydroxybenzotriazole monohydrate (91 mg) were added to stir the mixture at room temperature for 2 days. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 47:3) to obtain a free base of the title compound. This product was dissolved in methylene chloride, a 1N ethanol solution (108 μl) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. A small amount of methanol was added to the residue, and diethyl ether was added dropwise while irradiating with ultrasonic waves to collect precipitate formed by filtration. This product was washed with diethyl

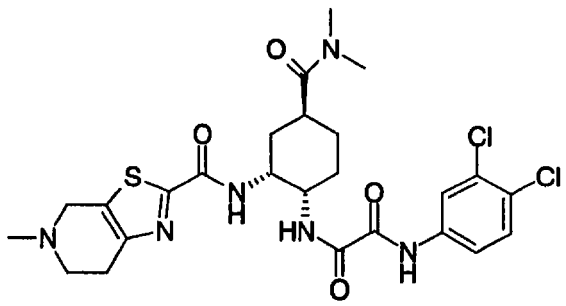
ether to obtain the title compound (60 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.77(4H,m), 2.03-2.12(2H,m), 2.79(3H,s), 2.92-2.96(7H,m), 3.25(2H,br.s), 3.49(1H,br.s), 3.69(1H,br.s), 3.98-4.04(1H,m), 4.40-4.43(1H,m), 4.45(1H,br.s), 4.69(1H,br.s), 7.48(1H,dd,J=8.5,2.4Hz), 7.75(1H,d,J=2.4Hz), 7.89(1H,d,J=8.5Hz), 8.75(1H,d,J=6.8Hz), 9.21(1H,br.s), 10.25(1H,s), 11.55(1H,br.s).

MS (FAB) m/z: 581$(M+H)^+$.

[Example 200]

$N^1$-(3,4-Dichlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



3,4-Dichloroaniline (1.62 g) was dissolved in methylene chloride (20 ml), and triethylamine (1.67 ml) and methyl chlorooxoacetate (1.01 ml) were successively added under ice cooling, and the mixture was stirred at room temperature for 21 hours. Water and methylene chloride were added to the reaction mixture to conduct liquid separation. The resultant water layer was extracted with methylene chloride. Organic layers were combined and dried over anhydrous magnesium sulfate, and the solvent

was distilled off under reduced pressure. The resultant residue was dissolved in ethanol (50 ml), and water (25 ml) and lithium hydroxide monohydrate (629 mg) were successively added to stir the mixture at room temperature for 12.5 hours. Lithium hydroxide monohydrate (629 mg) was additionally added to stir the mixture at room temperature for 5.5 hours. The reaction mixture was concentrated under reduced pressure to solidity. Water and diethyl ether were added to the residue to conduct liquid separation. Hydrochloric acid was added to the resultant water layer to acidify it. Solid formed were collected by filtration to obtain a crude product (1.62 g) of 2-(3,4-dichloroanilino)-2-oxoacetic acid as a colorless solid. This crude product (191 mg) and the compound obtained in Referential Example 253 were dissolved in N,N-dimethylformamide (10 ml), and 1-hydroxybenzotriazole monohydrate (110 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (157 mg) were added to stir the mixture at room temperature for 67 hours. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and ethyl acetate were added to the residue to conduct liquid separation, and the resultant water layer was extracted 3 times with methylene chloride. Organic layers were combined and dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica

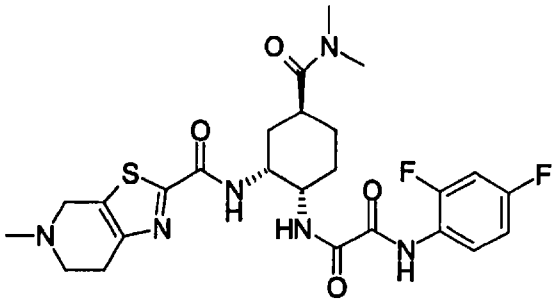
gel (methylene chloride:methanol = 95:5) to obtain the title compound (154 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.77-1.88(1H,m), 1.91-1.95(1H,m), 2.05-2.10(3H,m), 2.51(3H,s), 2.77-2.99(6H,m), 2.95(3H,s), 3.05(3H,s), 3.68(1H,d,J=15.5Hz), 3.74(1H,d,J=15.5Hz), 4.08-4.13(1H,m), 4.69-4.72(1H,m), 7.40(2H,s), 7.41(1H,d,J=7.7Hz), 7.90(1H,s), 8.01(1H,d,J=7.7Hz), 9.27(1H,s).

MS (ESI) m/z: 581$(M+H)^+$.

[Example 201]

$N^1$-(2,4-Difluorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



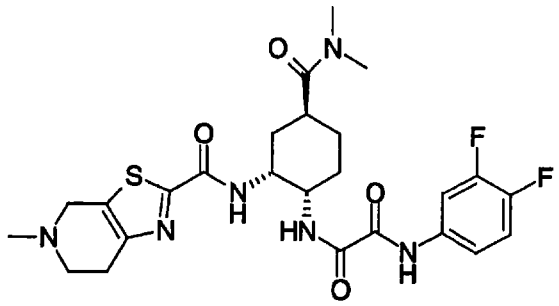
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 259 and condensing the hydrolyzate with the compound obtained in Referential Example 253 in a similar manner to the process described in Example 191.

$^1$H-NMR ($CDCl_3$) δ: 1.55-1.62(1H,m), 1.67-1.98(2H,m), 2.01-2.18(4H,m), 2.52(3H,s), 2.77-3.00(4H,m), 2.95(3H,s),2.99(3H,s), 3.65-3.78(2H,m), 4.06-4.15(1H,m),

4.66-4.73(1H,m), 6.85-6.94(2H,m), 7.38(1H,d,J=8.5Hz), 7.96(1H,d,J=7.3Hz), 8.22-8.29(1H,m), 9.36(1H,br).

[Example 202]

$N^1$-(3,4-Difluorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



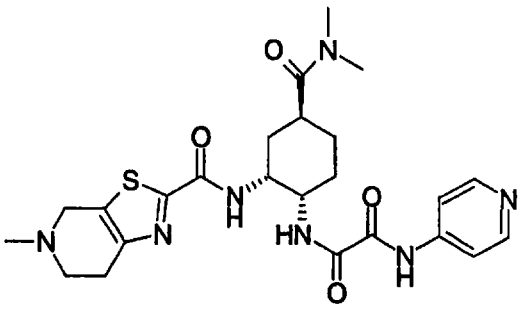
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 260 and condensing the hydrolyzate with the compound obtained in Referential Example 253 in a similar manner to the process described in Example 191.

$^1$H-NMR ($CDCl_3$) δ: 1.56-1.73(1H,m), 1.77-1.99(2H,m), 2.00-2.18(4H,m), 2.52(3H,s), 2.75-3.00(4H,m), 2.95(3H,s), 3.06(3H,s), 3.64-3.79(2H,m), 4.05-4.14(1H,m), 4.68-4.75(1H,m), 7.09-7.21(2H,m), 7.38(1H,d,J=8.8Hz), 7.72(1H,ddd,J=12.0, 7.1,2.6Hz), 7.95(1H,d,J=7.8Hz), 9.22(1H,br).

[Example 203]

$N^1$-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)-$N^2$-(pyridin-4-yl)ethanediamide

hydrochloride:



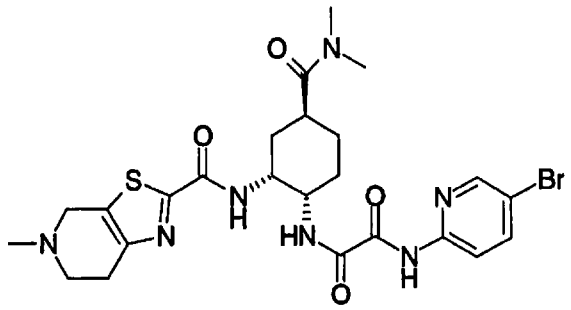
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 261, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ:1.40-2.10(6H,m), 2.77(3H,s), 2.927(3H,s), 2.933(3H,s), 3.05-4.20(8H,m), 4.40-4.55(1H,m), 8.27(2H,d,J=6.8Hz), 8.67(1H,d,J=8.0Hz), 8.71(2H,d,J=6.8Hz), 9.10-9.30(1H,br), 11.81(1H,s).

MS (FAB) m/z: 514$(M+H)^+$.

[Example 204]

$N^1$-(5-Bromopyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



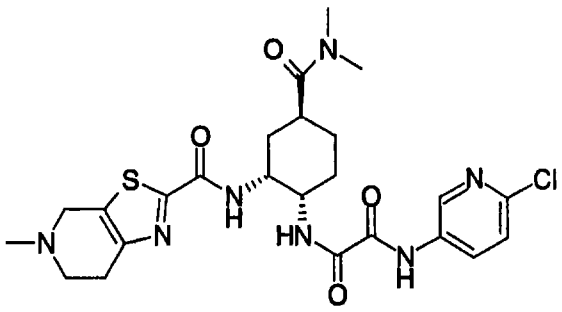
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 262, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 195.

$^1$H-NMR (DMSO-$d_6$) δ: 1.43-1.57(1H,m), 1.61-1.81(3H,m), 1.98-2.15(2H,m), 2.79(3H,s), 2.86(3H,s), 2.89-3.01(4H,m), 3.18(2H,br.s), 3.50(2H,br.s), 3.95-4.05(1H,m), 4.35-4.62(3H,m), 7.97(1H,d,J=9.0Hz), 8.12(1H,dd,J=9.0,2.4Hz), 8.52(1H,d,J=2.4Hz), 8.70(1H,d,J=7.5Hz), 9.18(1H,d,J=7.5Hz), 10.25(1H,br.s).

MS (FAB) m/z: 592$(M+H)^+$.

[Example 205]

$N^1$-(6-Chloropyridin-3-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexyl)ethanediamide hydrochloride:



The compound (200 mg) obtained in Referential Example 263, which was a crude product, was dissolved in methanol (10 ml) to heat the solution to 50°C, and a 1N aqueous solution (3 ml) of sodium hydroxide to stir the mixture for 5 minutes. To this mixture was added 1N hydrochloric acid to adjust the pH to a weak acidity. The solvent was distilled off under reduced pressure to obtain residue containing 2-[(2-chloropyridin-5-yl)amino]-2-oxoacetic acid. This residue and the compound (250 mg) obtained in Referential Example 253 were dissolved in N,N-dimethylformamide (5 ml), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (328 mg) and 1-hydroxybenzotriazole monohydrate (46 mg) were added to stir the mixture at room temperature for 3 days. The solvent was distilled off under reduced pressure, and a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate, the solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene

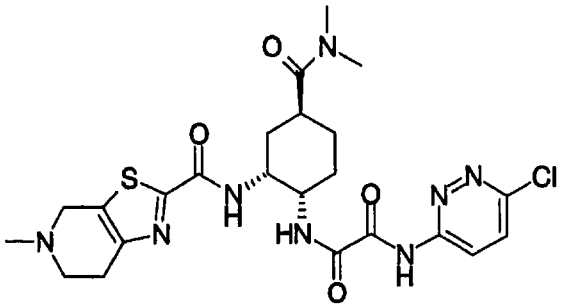
chloride:methanol = 47:3) to obtain a free base of the title compound as a pale yellow solid. This product was dissolved in methylene chloride, a 1N ethanol solution (862 μl) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. A small amount of methanol was added to the residue, and ethyl acetate and diethyl ether were added dropwise while irradiating with ultrasonic waves to collect precipitate formed by filtration. This product was washed with diethyl ether to obtain the title compound (229 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.46-1.75(4H,m), 1.99-2.09(2H,m), 2.79(3H,s), 2.92-2.95(7H,m), 3.12-3.53(3H,m), 3.70(1H,br.s), 3.99-4.06(1H,m), 4.44(2H,br.s), 4.69,4.73(1H,each s), 7.53(1H,d,J=8.5Hz), 8.23-8.25(1H,m), 8.72-8.77(1H,m), 8.85(1H,s), 9.07,9.16(1H,each d,J=8.1Hz), 11.09(1H,d,J=8.1Hz), 11.78(1H,br.s).

MS (FAB) m/z: 548$(M+H)^+$.

[Example 206]

$N^1$-(6-Chloropyridazin-3-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



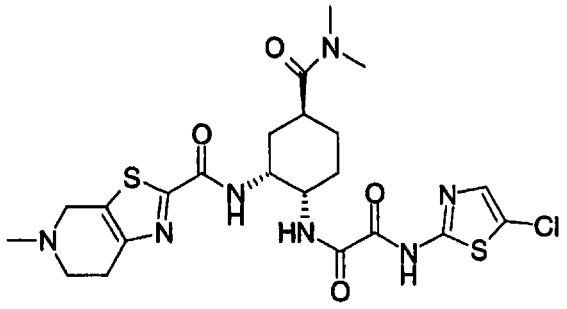
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 264, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44-1.57(1H,m), 1.62-1.80(3H,m), 2.00-2.10(2H,m), 2.79(3H,s), 2.86(3H,br.s), 2.94(3H,s), 2.95-3.01(1H,m), 3.14-3.23(2H,m), 3.45-3.63(2H,m), 3.96-4.08(1H,m), 4.40-4.60(3H,m), 7.97(1H,d,J=9.3Hz), 8.26(1H,d,J=9.3Hz), 8.69(1H,d,J=7.6Hz), 9.20(1H,d,J=7.6Hz), 11.06(1H,s).

MS (FAB) m/z: 549$(M+H)^+$.

[Example 207]

$N^1$-(5-Chlorothiazol-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



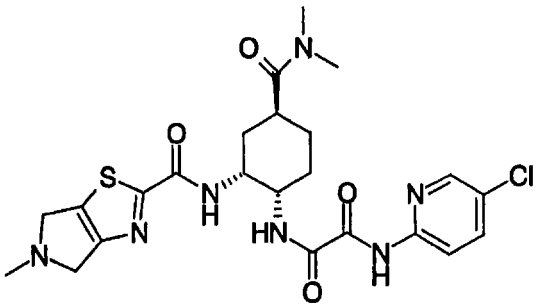
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 265, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-2.10(6H,m), 2.77(3H,s), 2.92(3H,s), 2.93(3H,s), 3.05-4.23(8H,m), 4.32-4.80(2H,m), 7.59(1H,s), 8.63(1H,d,J=7.6Hz), 9.14(1H,d,J=7.6Hz).

MS (FAB) m/z: 554$(M+H)^+$.

[Example 208]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



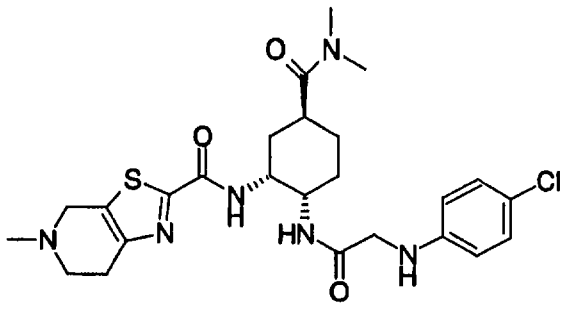
The compound (210 mg) obtained in Referential Example 266 and the compound (350 mg) obtained in Referential Example 272 were dissolved in N,N-dimethylformamide (15 ml), and 1-hydroxybenzotriazole monohydrate (205 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (290 mg) were added to stir the mixture at room temperature for 20 hours. The solvent was distilled off under reduced pressure, and a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate, the solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 20:1). The thus-obtained pale yellow solids were dissolved in methylene chloride, a 1N ethanol solution (0.46 ml) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Methanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain the title compound (248 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.50(1H,m), 1.69-1.76(3H,m), 1.98-2.06(2H,m), 2.79(3H,s), 2.95(3H,s), 2.98-3.05(1H,m), 3.10(3H,s), 3.49-4.62(6H,m), 7.98-8.03(2H,m), 8.45(1H,s), 8.73(1H,d,J=7.6Hz), 9.10(1H,d,J=8.0Hz), 10.30(1H,s).

MS (FAB) m/z: 534$(M+H)^+$.

[Example 209]

N-{(1R,2S,5S)-2-{[2-(4-Chloroanilino)acetyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



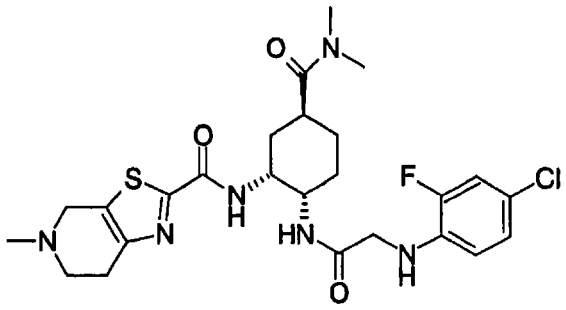
The compound (2.3 g) obtained in Referential Example 267 was dissolved in ethanol (10 ml), and a 1N aqueous solution (20 ml) of sodium hydroxide was added to stir the mixture at room temperature for 2 hours. After 1N hydrochloric acid (20 ml) was added to the reaction mixture, the mixture was diluted with water and stirred for 30 minutes. Insoluble matter deposited was collected by filtration to obtain 2-(4-chloroanilino)acetic acid (1.05 g) as a colorless solid. This solid and the compound (0.25 g) obtained in Referential Example 253 were dissolved in N,N-dimethylformamide (10 ml), and 1-hydroxybenzotriazole monohydrate (0.11 g) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.23 g) were added to stir the mixture at room temperature for 4 days. After the reaction mixture was diluted with chloroform and washed with a saturated aqueous solution of sodium hydrogencarbonate and saturated

aqueous solution of sodium chloride, the resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (chloroform:methanol = 97:3). The thus-obtained pale yellow solid was dissolved in ethanol, a 1N ethanol solution of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Methanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain the title compound (0.15 g).

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.41(1H,m), 1.59-1.80(3H,m), 1.82-1.95(2H,m), 2.76(3H,s), 2.93(3H,s), 2.94(3H,s), 2.99-3.10(1H,m), 3.10-3.22(2H,m), 3.42-3.60(2H,m), 3.60-3.77(2H,m), 3.80-3.90(1H,m), 4.35-4.48(2H,m), 4.68-4.80(1H,m), 6.40(1H,d,J=6.7Hz), 6.44(1H,d,J=6.7Hz), 6.90(1H,d,J=6.7Hz), 7.00(1H,d,J=6.7Hz), 7.70-7.89(1H,m), 8.35-8.42(1H,m), 11.05-11.38(1H,m).

[Example 210]

N-{(1R,2S,5S)-2-{[2-(4-Chloro-2-fluoroanilino)-acetyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:

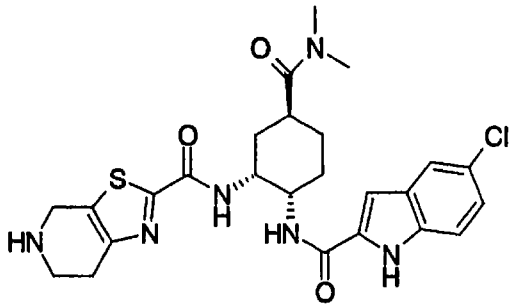


The title compound was obtained by hydrolyzing the compound obtained in Referential Example 268, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 209.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.42(1H,m), 1.55-1.78(3H,m), 1.80-2.00(2H,m), 2.76(3H,s), 2.92(3H,s), 2.94(3H,s), 2.99-3.10(1H,m), 3.10-3.22(2H,m), 3.42-3.60(2H,m), 3.60-3.77(2H,m), 3.85-4.00(1H,m), 4.33-4.48(2H,m), 4.65-4.80(1H,m), 6.41(1H,t,J=8.8Hz), 6.73(1H,dt,J=8.8,1.2Hz), 7.08(1H,dd,J=11.7,1.2Hz), 7.78-7.92(1H,m), 8.35-8.42(1H,m), 11.18-11.50(1H,m).

[Example 211]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



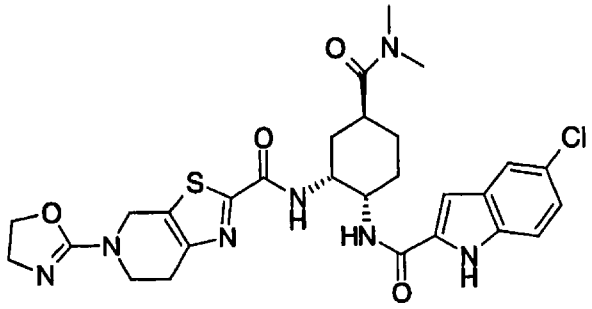
The title compound was obtained by condensing the compound obtained in Referential Example 432 with the compound obtained in Referential Example 34 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.70-2.15(6H,m), 2.80(3H,s), 2.97(3H,s), 2.95-3.15(2H,m), 3.35-3.55(2H,m), 4.05-4.20(1H,m), 4.46(2H,s), 4.50-4.65(1H,m), 7.05(1H,s), 7.16(1H,dd,J=8.8,2.2Hz), 7.41(1H,d,J=8.8Hz), 7.68(1H,s), 8.30-8.45(1H,br), 9.30-9.50(1H,br), 11.78(1H,s).

MS (ESI) m/z: 529$(M+H)^+$.

[Example 212]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-(4,5-dihydrooxazol-2-yl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



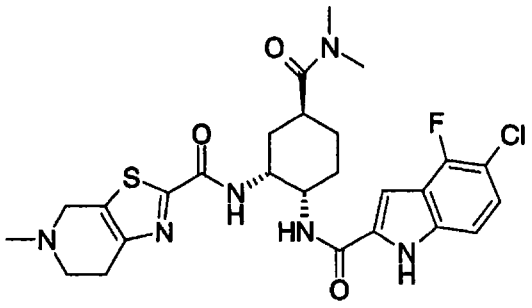
The compound (250 mg) obtained in Example 211 was suspended in methylene chloride, and a saturated aqueous solution of sodium hydrogencarbonate was added to fully stir the mixture. The resultant organic layer was separated and dried over anhydrous magnesium sulfate. Triethylamine (0.5 ml) and bromoethyl isocyanate (43 μl) were then added to stir the mixture at room temperature for 20 hours. A saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture to separate an organic layer. The organic layer was dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 22:3) to obtain the title compound (227 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.50-2.15(4H,m), 2.15-2.40(2H,m), 2.80-3.00(1H,m), 2.97(3H,s), 3.11(3H,s), 3.70-3.95(4H,m), 4.10-4.30(1H,m), 4.30-4.50(2H,m), 4.60-4.70(1H,m), 4.74(2H,s), 6.85(1H,s),7.21(1H,dd,J =8.8,2.2Hz), 7.34(1H,d,J=8.8Hz), 7.50(1H,br.s), 7.62(1H,s), 7.87(1H,br.s), 9.48(1H,br.s).

MS (ESI) m/z: 598$(M+H)^+$.

[Example 213]

N-{(1R,2S,5S)-2-{[(5-Chloro-4-fluoroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (140 mg) obtained in Referential Example 144 was dissolved in N,N-dimethylformamide (10 ml), and the compound (100 mg) obtained in Referential Example 274, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (140 mg) and 1-hydroxybenzotriazole monohydrate (110 mg) were added to stir the mixture at room temperature for 18 hours. The solvent was distilled off under reduced pressure, and the residue was partitioned in water-ethyl acetate, and a water layer was extracted with ethyl acetate. The resultant organic layers were combined, washed with saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methanol:methylene chloride = 1:19), giving tert-butyl (1R,2S,5S)-2-{[(5-chloro-4-

fluoroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexylcarbamate (260 mg).

The thus-obtained powder was dissolved in methylene chloride (5 ml), and a 4N dioxane solution (1.2 ml) of hydrochloric acid was added. After the reaction mixture was stirred at room temperature for 3.5 hours, the solvent was distilled off under reduced pressure. Methylene chloride (10 ml) was added to the residue, and the mixture was concentrated. After this process was repeated 3 times, the residue was dried under reduced pressure to obtain crude N-{(1S,2R,4S)-2-amino-4-[(dimethylamino)carbonyl]-cyclohexyl}-5-chloro-4-fluoroindole-2-carboxamide. This product was dissolved in N,N-dimethylformamide (50 ml), and the compound (150 mg) obtained in Referential Example 10, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (140 mg) and 1-hydroxybenzotriazole monohydrate (110 mg) were added to stir the mixture at room temperature for 18 hours. The solvent was distilled off under reduced pressure, and the residue was partitioned in a mixed solvent of water-ethyl acetate-tetrahydrofuran, and a water layer was extracted with ethyl acetate. The resultant organic layers were combined, washed with saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methanol:methylene chloride = 1:19) to obtain a free base

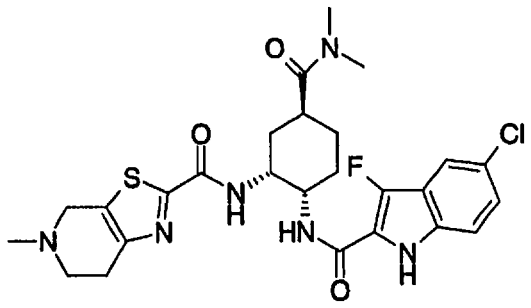
of the title compound (270 mg). This product was dissolved in methylene chloride (10 ml), and a 1N ethanol solution (0.72 ml) of hydrochloric acid was added to stir the mixture at room temperature for 30 minutes. Crystals deposited were collected by filtration to obtain the title compound (200 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.24-1.98(6H,m), 2.33-3.33(6H,m), 2.81(3H,s), 2.90(3H,s), 2.99(3H,s), 4.12(1H, br.s), 4.30-4.70(1H,m), 4.60(1H,br.s), 7.21(1H,s), 7.27(2H,br.s), 8.37(1H,d,J=8.1Hz), 8.43(1H,d,J=7.6Hz), 12.11(1H,s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 214]

N-{(1R,2S,5S)-2-{[(5-Chloro-3-fluoroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (250 mg) obtained in Referential Example 279 was dissolved in methylene chloride (60 ml), and a 4N dioxane solution (1.3 ml) of hydrochloric acid was added. After the reaction mixture was stirred at room temperature for 5.5 hours, a 4N dioxane solution (0.65 ml) of

hydrochloric acid was additionally added, and the mixture was stirred at room temperature for 1 hour. The solvent was distilled off under reduced pressure, methylene chloride (10 ml) was added to the residue, and the mixture was concentrated. This process was repeated 3 times. The residue was dried under reduced pressure, and the thus-obtained crude product was dissolved in N,N-dimethylformamide (50 ml), and the compound (160 mg) obtained in Referential Example 10, 1-(3-dimethylamino-propyl)-3-ethylcarbodiimide hydrochloride (150 mg) and 1-hydroxybenzotriazole monohydrate (120 mg) were added to stir the mixture at room temperature for 18 hours. The solvent was distilled off under reduced pressure, and the residue was partitioned in a mixed solvent of water-ethyl acetate, and a water layer was extracted with ethyl acetate. The resultant organic layers were combined, washed with saturated aqueous solution of sodium chloride and then dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified twice by column chromatography on silica gel (methanol:methylene chloride = 2:23 → 1:9) to obtain a free base (260 mg) of the title compound. This product was dissolved in methylene chloride, and a 1N ethanol solution (0.69 ml) of hydrochloric acid was added to stir the mixture at room temperature for 30 minutes. The solvent was distilled off. The residue was dissolved in methanol, and diethyl ether and hexane were added. The thus-obtained

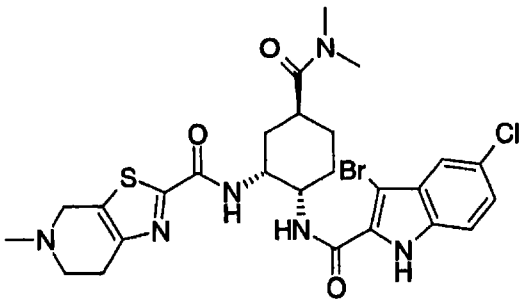
crystals were collected by filtration to obtain the title compound (230 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.56(1H,m), 1.73-1.78(3H,m), 1.94-2.02(2H,m), 2.33-3.55(6H,m), 2.80(3H,s), 2.92(3H,s), 2.98(3H,s), 4.17(1H,br.s), 4.30-4.80(1H,br), 4.62(1H,br.s), 7.25(1H,d,J=8.8,1.7Hz), 7.40(1H,d,J=8.8,1.7Hz), 7.65(1H,d,J=1.7Hz), 7.72(1H,d,J=5.9Hz), 8.74(1H,d,J=8.0Hz), 10.85-11.35(1H,br), 11.71(1H,s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 215]

N-{(1R,2S,5S)-2-{[(3-Bromo-5-chloroindol-2-yl)carbonyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained by treating the compound obtained in Referential Example 282 with a 4N dioxane solution of hydrochloric acid and condensing the-thus treated compound with the compound obtained in Referential Example 10 in a similar manner to the process described in Example 214.

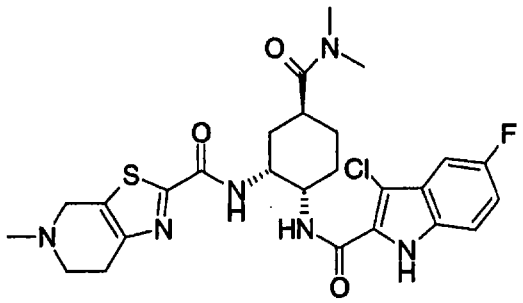
$^1$H-NMR (DMSO-$d_6$) δ: 1.51-2.01(6H,m), 2.33-3.29(7H,m),

2.81(3H,s), 2.88(3H,s), 3.01(3H,s), 4.20(1H,br.s), 4.48(1H,br), 4.70-4.73(1H,m), 7.29(1H,dd,J=8.9,1.8Hz), 7.45-7.49(2H,m), 7.80(1H,d,J=7.6Hz), 8.76(1H,d,J=8.8Hz), 12.31(1H,s).

MS (FAB) m/z: 622$(M+H)^+$.

[Example 216]

N-{(1R,2S,5S)-2-{[(3-Chloro-5-fluoroindol-2-yl)carbonyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



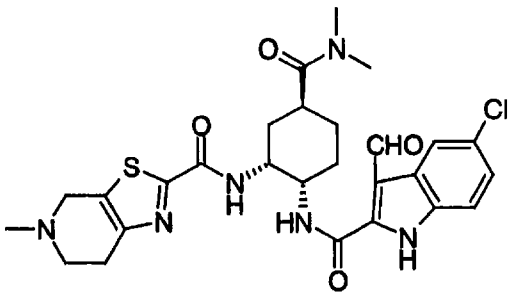
The title compound was obtained from the compound obtained in Referential Example 253 and the compound obtained in Referential Example 284 in a similar manner to the process described in Example 5.

$^1$H-NMR (DMSO-d6) δ: 1.40-1.51(1H,m), 1.75-2.00(5H,m), 2.79(3H,s), 2.92(3H,s), 2.99(3H,s), 3.10-3.21(3H,m), 3.29-3.41(4H,m), 4.11-4.21(1H,m), 4.62-4.75(1H,m), 7.14(1H,dt,J=8.8,2.4Hz), 7.24(1H,dd,J=8.8,2.4Hz), 7.45(1H,dd,J=8.8,4.4Hz), 7.69(1H,d,J=2.5Hz), 8.79(1H,d,J=2.5Hz), 12.10(1H,s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 217]

N-{(1R,2S,5S)-2-{[(5-Chloro-3-formylindol-2-yl)carbonyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 253 and the compound obtained in Referential Example 286 in a similar manner to the process described in Example 5.

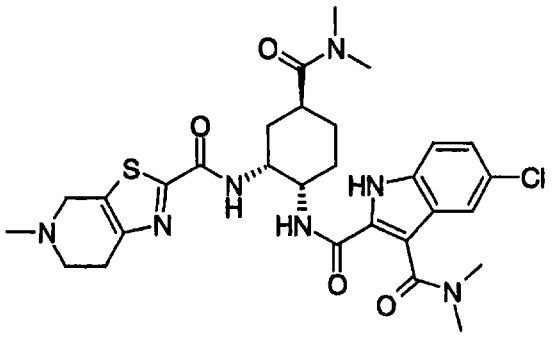
$^1$H-NMR (DMSO-d6) δ: 1.40-1.51(1H,m), 1.75-1.89(4H,m), 1.90-2.01(1H,m), 2.80(3H,s), 2.91(3H,s), 3.03(3H,s), 3.05-3.33(3H,m), 3.60-3.71(1H,m), 4.11-4.21(1H,m), 4.32-4.44(1H,m), 4.62-4.75(2H,m), 7.35(1H,dd,J=8.0,1.4Hz), 7.56(1H,d,J=8.0Hz), 8.21(1H,d,J=1.4Hz), 8.65(1H,t,J=7.4Hz), 9.92(1H,d,J=6.8Hz), 10.15(1H,t,J=9.1Hz), 13.00(1H,dt,J=6.4).

MS (FAB) m/z: 571$(M+H)^+$.

[Example 218]

5-Chloro-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl-$N^3$,$N^3$-dimethylindole-2,3-

dicarboxamide hydrochloride:



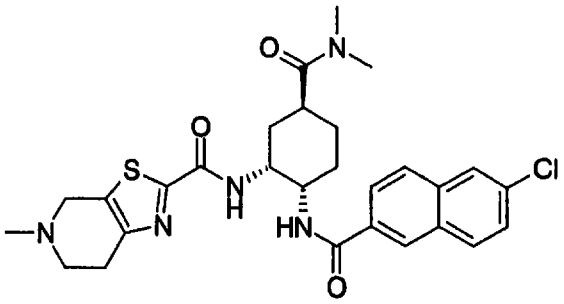
The title compound was obtained from the compound obtained in Referential Example 253 and the compound obtained in Referential Example 289 in a similar manner to the process described in Example 5.

$^1$H-NMR (DMSO-d6) δ: 1.40-1.51(1H,m), 1.75-2.01(5H,m), 2.78(9H,s), 2.93(3H,s), 3.01(3H,s), 3.10-3.33(3H,m), 3.40-3.50(1H,m), 3.65-3.75(1H,m), 4.01-4.09(1H,m), 4.32-4.44(1H,m), 4.62-4.75(2H,m), 7.25(1H,d,J=8.0Hz), 7.40-7.50(2H,m), 8.62(1H,br), 9.08(1H,br), 12.28(1H,br).

MS (FAB) m/z: 614$(M+H)^+$.

[Example 219]

N-{(1R,2S,5S)-2-[(6-Chloro-2-naphthoyl)amino]-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



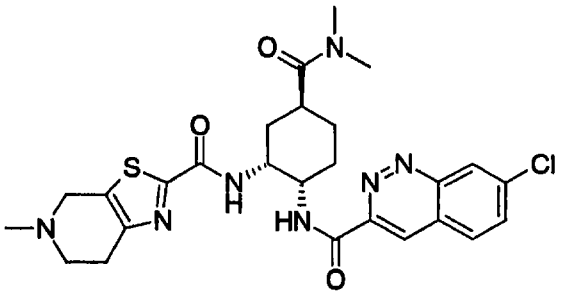
The compound (270 mg) obtained in Referential Example 294 was dissolved in methylene chloride (10 ml), and a 1N ethanol solution (10 ml) of hydrochloric acid was added to stir the mixture for 90 minutes. The solvent was distilled off under reduced pressure, and the resultant residue was dissolved in N,N-dimethylformamide (7 ml). The compound (110 mg) obtained in Referential Example 10, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (100 mg) and 1-hydroxybenzotriazole monohydrate (70 mg) were added to stir the mixture at room temperature for 23 hours. The reaction mixture was concentrated under reduced pressure, and water was added to conduct extraction with ethyl acetate. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified twice by column chromatography on silica gel (methylene chloride: methanol = 20:1 → 10:1). The thus-obtained free base was dissolved in methanol, and a 1N ethanol solution (0.30 ml) of hydrochloric acid was added. The residue was washed with ethyl acetate to obtain the title compound (130 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.70-1.90(3H,m), 1.90-2.10(2H,m), 2.81(3H,s), 2.91(3H,s), 3.00(3H,s), 3.00-3.22(3H,m), 3.53(2H,br), 4.10-4.20(1H,m), 4.30-4.70(3H,m), 7.59(1H,dd,J=8.8,2.2Hz), 7.87(1H,d,J=8.5Hz), 7.96(1H,d,J=8.5Hz), 8.02(1H,d,J=8.8Hz), 8.10(1H,d,J=2.2Hz), 8.33(1H,s), 8.43(1H,d,J=8.1Hz), 8.52(1H,d,J=7.3Hz).

MS(FAB)m/z:554$(M+H)^+$.

[Example 220]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}cyclohexyl)cinnoline-3-carboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 299 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10 in a similar manner to the process described in Example 219.

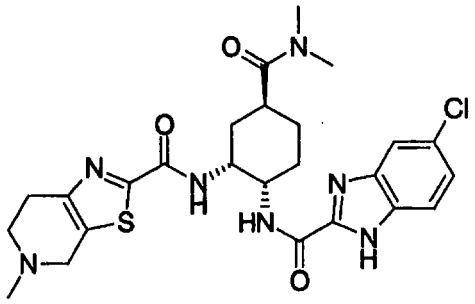
$^1$H-NMR ($CDCl_3$) δ: 1.50-1.65(1H,m), 1.70-1.90(3H,m), 2.05-2.15(1H,m), 2.15-2.30(1H,m), 2.81(3H,s), 2.85-3.05(8H,m), 3.15-3.25(2H,m), 3.40-3.80(1H,m), 4.25-4.80(4H,m), 8.02(1H,dd,J=8.8,2.0Hz), 8.38(1H,d,J=8.8Hz), 8.66(1H,s),

8.91(1H,s), 8.96(1H,d,J=7.3Hz), 9.53(1H,br).

MS (FAB) m/z: 556$(M+H)^+$.

[Example 221]

N-{(1R,2S,5S)-2-{[(5-Chlorobenzimidazol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 300 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10 in a similar manner to the process described in Example 219.

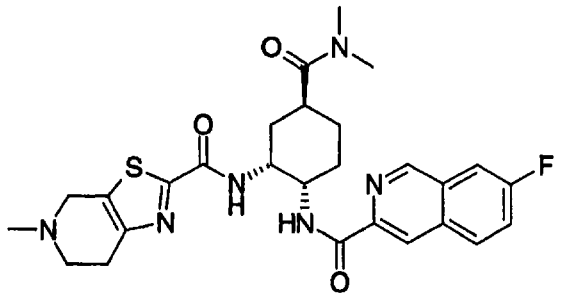
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.60-1.83(3H,m), 2.00-2.20(2H,m), 2.78(3H,s), 2.92(6H,s), 3.00-3.30(3H,m), 3.47(2H,br.s), 4.10-4.75(4H,m), 7.30(1H,d,J=8.8Hz), 7.62(1H,d,J=12.5Hz), 7.63(1H,s), 8.75-8.87(1H,m), 9.09(1H,dd,J=12.5,8.8Hz), 11.20-11.40(1H,m).

MS (FAB) m/z: 546$(M+H)^+$.

[Example 222]

N-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-

yl)carbonyl]amino}cyclohexyl)-7-fluoroisoquinoline-3-carboxamide hydrochloride:



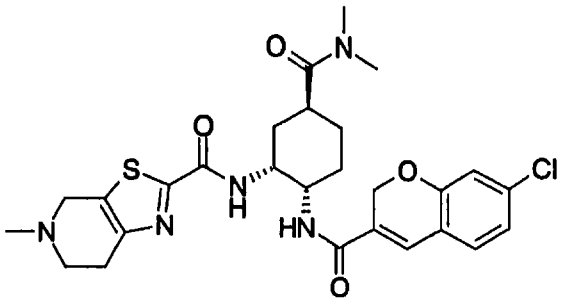
The title compound was obtained from the compound obtained in Referential Example 253 and the compound obtained in Referential Example 304 in a similar manner to the process described in Example 5.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.60(1H,m), 1.70-1.85(3H,m), 1.95-2.05(1H,m), 2.10-2.20(1H,m), 2.80(3H,s), 2.90-3.90(5H,m), 2.93(3H,s), 2.96(3H,s), 4.10-4.75(4H,m), 7.75-7.85(1H,m), 8.00-8.05(1H,m), 8.30-8.35(1H,m), 8.61(1H,s), 8.93(2H,d,J=7.3Hz), 9.31(1H,s).

MS (FAB) m/z: 539$(M+H)^+$.

[Example 223]

N-{(1R,2S,5S)-2-{[(7-Chloro-2H-chromen-3-yl)carbonyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The compound (220 mg) obtained in Referential Example 252 was dissolved in methanol (10 ml), and 10% palladium on carbon (180 mg) was added to stir the mixture at room temperature for 4 hours in a hydrogen atmosphere. After the reaction mixture was filtered, the filtrate was concentrated under reduced pressure, and the residue was dissolved in N,N-dimethylformamide (30 ml). The compound (108 mg) obtained in Referential Example 306, 1-hydroxybenzotriazole monohydrate (78 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (196 mg) were added to stir the mixture at room temperature for a night. The reaction mixture was concentrated under reduced pressure, and methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 100:3) to obtain a pale yellow foamy substance. This foamy substance was dissolved in methylene

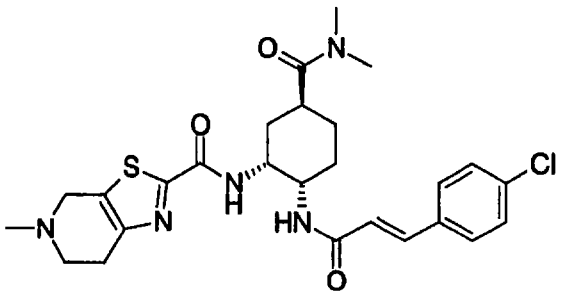
chloride (2 ml), a 1N ethanol solution (363 μl) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. Diethyl ether was added to the residue. Precipitate formed was collected by filtration to obtain the title compound (175 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.52(1H,m), 1.55-1.96(5H,m), 2.78(3H,s), 2.90(3H,s), 2.98(3H,s), 3.01-3.12(1H,m), 3.13-3.28(2H,m), 3.40-3.85(2H,m), 3.92-4.00(1H,m), 4.35-4.80(3H,m), 4.84(1H,d,J=14.5Hz), 4.89(1H,d,J=14.5Hz), 6.92(1H,s), 6.98(1H,dd,J=8.1,1.7Hz), 7.08(1H,s), 7.17(1H,d,J=8.3Hz), 8.12(1H,d,J=8.1Hz), 8.34(1H,d,J=8.1Hz).

MS (FAB) m/z: 558$(M+H)^+$.

[Example 224]

N-{(1R,2S,5S)-2-{[(E)-3(4-Chlorophenyl)-2-propenoyl]-amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:




The title compound was obtained by treating the compound obtained in Referential Example 307 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10 in

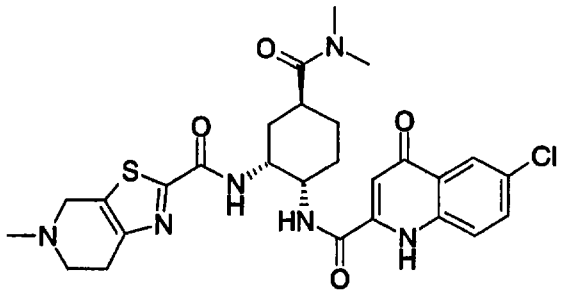
a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.55(1H,m), 1.55-1.90(4H,m), 2.79(3H,s), 2.92(3H,s), 2.99(3H,s), 3.05-3.30(3H,m), 3.40-3.55(1H,m), 3.60-3.75(1H,m), 3.93-4.03(2H,m), 4.35-4.50(1H,m), 4.50-4.60(1H,m), 4.60-4.75(1H,m), 6.65(1H,d,J=15.7 Hz), 7.35(1H,d,J=15.7 Hz), 7.44(1H,d,J=8.6 Hz), 7.55(1H,d,J=8.6 Hz), 8.03(1H,d,J=8.1Hz), 8.34(1H,br.s), 11.25-11.70(1H,br).

MS (ESI) m/z: 530$(M+H)^+$.

[Example 225]

6-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}cyclohexyl)-4-oxo-1,4-dihydroquinoline-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 253 and the compound obtained in Referential Example 309 in a similar manner to the process described in Example 5.

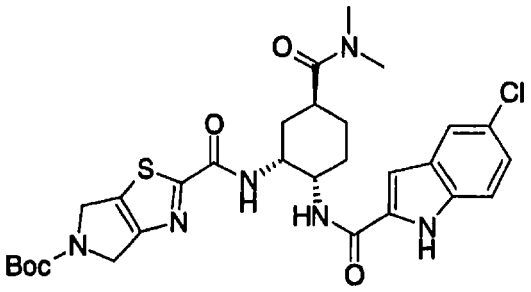
$^1$H-NMR (DMSO-$d_6$) δ: 1.43-1.60(1H,m), 1.65-2.10(3H,m), 2.79(3H,s), 2.92(3H,s), 2.99(3H,s), 3.05-3.20(2H,m), 3.20-3.80(5H,m), 4.08-4.20(1H,m), 4.35-4.50(1H,m), 4.60-

4.70(1H,m), 4.70(1H,d,J=15.6Hz), 6.77(1H,br.s), 7.73(1H,d,J=8.9Hz), 7.94(1H,d,J=8.9Hz), 7.97(1H,d,J=2.2Hz), 8.54(1H,br.s), 8.80-9.00(1H,m), 11.70-12.50(1H,br), 11.70-12.50(1H,br).

MS (ESI) m/z: 571$(M+H)^+$.

[Example 226]

tert-Butyl 2-[({(1R,2S,5S)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-amino)carbonyl]-4,6-dihydro-5H-pyrrolo[3,4-d]thiazole-5-carboxylate:




1) The compound (1.46 g) obtained in Referential Example 310 was dissolved in methylene chloride (10 ml), and an ethanol solution (10 ml) of hydrochloric acid was added at room temperature to stir the mixture for 1 hour. After completion of the reaction, the solvent was distilled off, ethanol was added, the mixture was concentrated, and diisopropyl ether was added to the residue to solidify it. The resultant solids were collected by filtration to obtain N-{(1S,2R,4S)-2-amino-4-[(dimethylamino)carbonyl]cyclohexyl}-5-chloroindole-2-carboxamide hydrochloride.

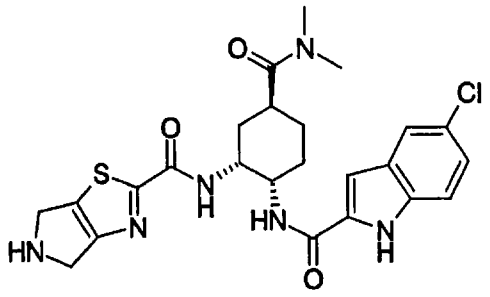
2) This product was dissolved in N,N-dimethylformamide (5 ml), and the compound (1.31 g) obtained in Referential Example 406, 1-hydroxybenzotriazole monohydrate (640 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.36 g) were added to stir the mixture at room temperature for 3 days. The reaction mixture was concentrated, and methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. After the solvent was distilled off under reduced pressure, the residue was purified by column chromatography on silica gel (methanol:methylene chloride = 1:19) to obtain the title compound (1.22 g).

$^1$H-NMR ($CDCl_3$) δ: 1.53(9H,s), 1.70-2.40(6H,m), 2.80-3.20(7H,m), 4.15-4.25(1H,m), 4.55-4.80(5H,m), 6.83(1H,d,J=1.5Hz), 7.20(1H,dd,J=8.8,2.0Hz), 7.33(1H,d,J=8.8Hz), 7.40-7.50(1H,m), 7.61(1H,br.s), 7.72-7.80(1H,m), 9.41(1H,br.s).

MS (ESI) m/z: 615$(M+H)^+$.

[Example 227]

5-Chloro-N-{(1S,2R,4S)-2-[[(5,6-dihydro-4H-pyrrolo[3,4-d]-thiazol-2-yl)carbonyl]amino]-4-[(dimethylamino)carbonyl]-cyclohexyl}indole-2-carboxamide hydrochloride:



The compound (1.22 g) obtained in Referential Example 226 was dissolved in methylene chloride (5 ml), and an ethanol solution (10 ml) of hydrochloric acid was added to stir the mixture for 1 hour. After the reaction mixture was concentrated, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to conduct liquid separation, and the resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off, and the residue was purified by column chromatography on silica gel (methanol:methylene chloride = 1:9) to obtain a free base (636 mg) of the title compound as a colorless glassy solid. The free base (200 mg) was dissolved in a 1N ethanol solution (1 ml) of hydrochloric acid. After the solution was concentrated, ethyl acetate was added to solidfy the residue. The thus-obtained colorless powder was collected by filtration and dried to obtain the title compound (195 mg).

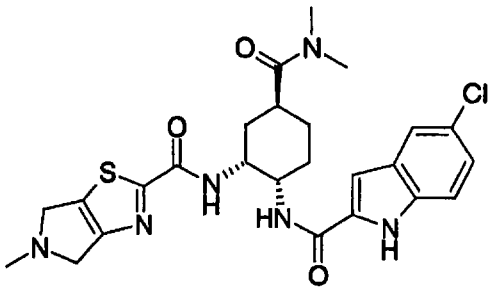
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.70-1.90(3H,m), 1.90-2.05(2H,m), 2.80(3H,s), 2.98(3H,s), 2.98-3.15(1H,m), 4.05-4.20(1H,m), 4.44(2H,br.s), 4.58(3H,br.s), 7.05(1H,d,J=1.5Hz), 7.16(1H,dd, J=8.7,1.8Hz),

7.42(1H,d,J=8.7Hz), 7.68(1H,d,J=1.8Hz), 8.38(1H,d,J=7.8Hz), 8.42(1H,d,J=7.8Hz), 10.45-10.65(2H,br), 11.78(1H,br.s).

MS (FAB) m/z: 515$(M+H)^+$.

[Example 228]

5-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)indole-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 227 and formalin in a similar manner to the process described in Example 18.

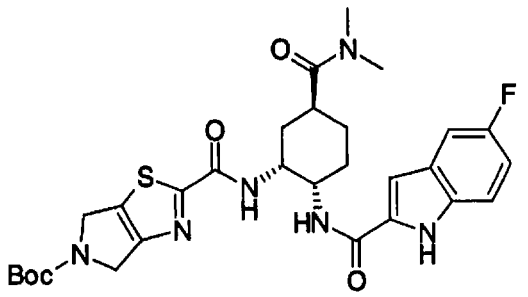
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.65-1.90(3H,m), 1.90-2.05(2H,m), 2.80(3H,s), 2.98(3H,s), 2.98-3.06(1H,m), 3.06(3H,s),4.05-4.20(1H,m), 4.30-5.00(5H,br.s), 7.04(1H,d,J=1.7Hz), 7.17(1H,dd,J=8.8,2.1Hz) ,7.41(1H,d,J=8.8Hz) 7.68(1H,d,J=2.1Hz) 8.36(1H,d,J =7.8Hz), 8.42(1H,d,J=8.1Hz),11.78(1H,br.s),12.14(1H,br.s).

MS (FAB) m/z: 529$(M+H)^+$.

[Example 229]

tert-Butyl 2-{[((1R,2S,5S)-5-[(dimethylamino)carbonyl]-2-{[(5-fluoroindol-2-yl)carbonyl]amino}cyclohexyl)amino]-

carbonyl}-4,6-dihydro-5H-pyrrolo[3,4-d]thiazole-5-carboxylate:



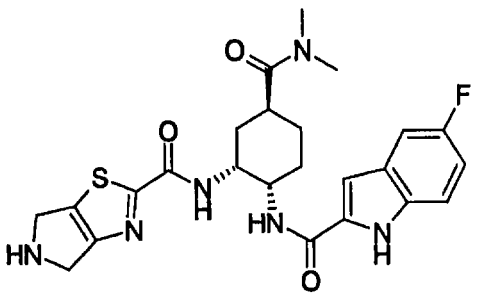
The title compound was obtained from the compound obtained in Referential Example 311 and the compound obtained in Referential Example 406 in a similar manner to the process described in Example 226.

$^1$H-NMR ($CDCl_3$) δ: 1.53(9H,s),1.60-2.40(6H,m),2.80-3.20(7H,m), 4.15-4.25(1H,m),4.55-4.80(5H,m),6.84-6.87(1H,m), 7.01(1H,dt,J=2.4,9.1Hz),7.25-7.30(1H,m), 7.34(1H,dd,J=9.1,4.3Hz),7.42-7.49(1H,m),7.70-7.80(1H,m), 9.37-9.45(1H,m).

MS (ESI) m/z: 599$(M+H)^+$.

[Example 230]

N-{(1S,2R,4S)-2-[[(5,6-Dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino]-4-[(dimethylamino)carbonyl]-5-fluoroindole-2-carboxamide hydrochloride:



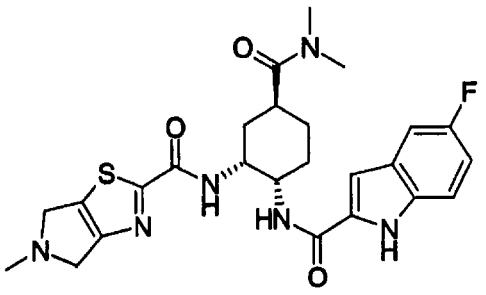
The title compound was obtained from the compound obtained in Example 229 in a similar manner to the process described in Example 227.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m),1.65-1.90(3H,m),1.90-2.10(2H,m),2.80(3H,s),2.97(3H,s),2.98-3.15(1H,m),4.05-4.20(1H,m),4.35-4.50(2H,m),4.58(3H,br.s),6.97-7.10(2H,m), 7.35-7.47(2H,m), 8.34(1H,d,J=7.8Hz),8.41(1H,d,J=8.1Hz), 10.53(2H,br.s),11.68(1H,br.s).

MS (FAB) m/z: 499$(M+H)^+$.

[Example 231]

N-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}-cyclohexyl)-5-fluoroindole-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Example 230 and formalin in a similar manner

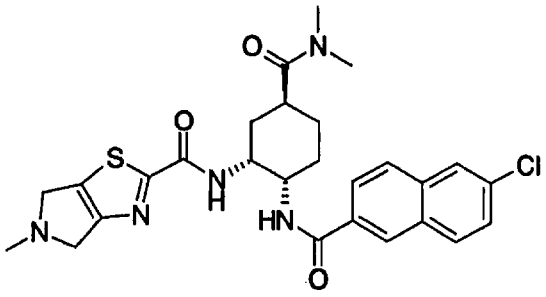
to the process described in Example 18.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m),1.65-1.90(3H,m),1.90-2.10(2H,m),2.80(3H,s),2.90-3.20(7H,m),4.05-4.20(1H, m), 4.30-5.00(5H,br.s),6.95-7.10(2H,m),7.35-7.50(2H,m), 8.33(1H,d,J=7.6Hz),8.41(1H,d,J=8.1Hz),11.67(1H,br.s), 12.37(1H,br.s).

MS (FAB) m/z: 513$(M+H)^+$.

[Example 232]

N-{(1R,2S,5S)-2-[(6-Chloro-2-naphthoyl)amino]-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazole-2-carboxamide hydrochloride:



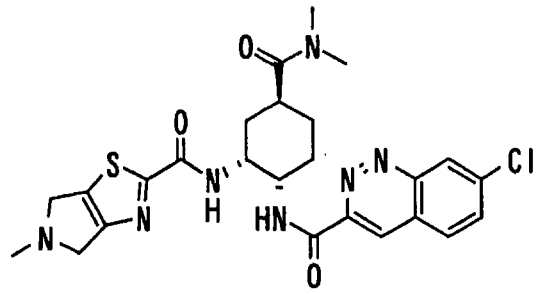
The title compound was obtained from the compound obtained in Referential Example 294 and the compound obtained in Referential Example 293 in a similar manner to the process described in Example 226.

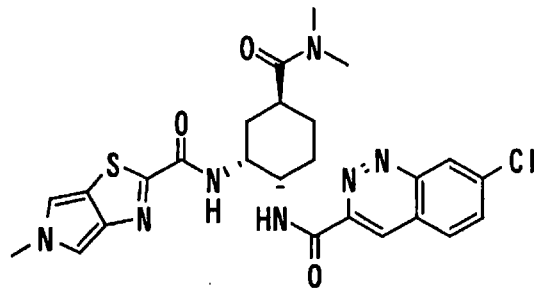
$^1$H-NMR (DMSO-$d_6$) δ: 1.48-1.56(1H,m),1.71-1.84(3H,m), 1.95-2.04(2H,m),2.81(3H,s),3.00(3H,s),3.02(3H,s), 3.06-3.15(2H,m), 4.13-4.14(1H,m),4.52-4.63(4H,m), 7.60(1H,d,J=8.5Hz),7.87(1H,d,J=8.8Hz),7.96(1H,d,J=8.5Hz), 8.01(1H,d,J=8.8Hz),8.10(1H,s),8.32(1H,s), 8.45(1H,d,J=8.1Hz),8.51(1H,d,J=7.3Hz).

MS (FAB) m/z: 540 $(M+H)^+$.

[Example 233]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)-carbonyl]amino}cyclohexyl)cinnoline-3-carboxamide hydrochloride and 7-chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)cinnoline-3-carboxamide:





A 4N dioxane solution (3.0 ml) of hydrochloric acid was added to a suspension of the compound (330 mg) obtained in Referential Example 299 in a mixed solvent of dioxane (3.0 ml) and methylene chloride (3.0 ml), and the mixture was stirred at room temperature for 30 minutes. The solvent was distilled off under reduced pressure, and

the thus-obtained white powder was dissolved in N,N-dimethylformamide (5.0 ml), and the compound (172 mg) obtained in Referential Example 293, 1-hydroxy-benzotriazole monohydrate (130 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (192 mg) were added to stir the mixture at room temperature for 15 hours. The solvent was distilled off under reduced pressure, methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue. The resultant organic layer was washed with saturated saline and then dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 20:1). A 1N ethanol solution (0.35 ml) of hydrochloric acid was added to a solution of the thus-obtained high-polar compound mainly formed in ethanol (4.0 ml), and the solvent was distilled off under reduced pressure. Ethanol and diethyl ether were added to the residue, and precipitate formed was collected by filtration to obtain 7-chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)cinnoline-3-carboxamide hydrochloride (184 mg) a main product.

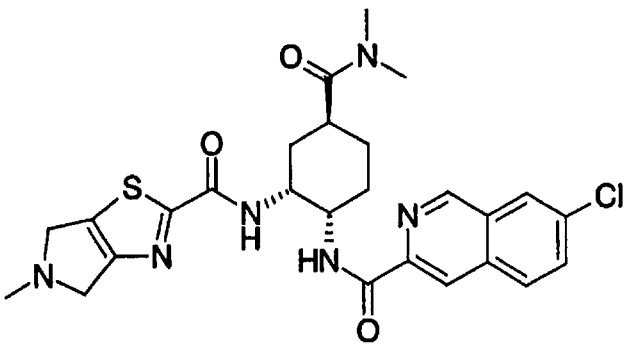
$^1$H-NMR (DMSO-d6) δ: 1.50-1.65(1H,m),1.70-1.90(3H,m),2.03-2.12(1H, m),2.15-2.30(1H,m),2.81(3H,s),2.90-3.05(1H,m), 2.96(3H,s),3.07(3H,s),4.28-4.37(1H, m),4.40-4.95(5H,br),

8.02(1H,d,J=8.8Hz),8.38(1H,d,J=8.8Hz),8.66(1H,s),
8.91(1H,s),8.97(1H,d,J=7.1Hz),9.43-9.57(1H,br),11.75-
11.95(0.5H,br),12.35-11.55(0.5H,br).
MS (FAB) m/z: 542$(M+H)^+$ .

In the purification by the column chromatography on silica gel, low-polar 7-chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)cinnoline-3-carboxamide (98 mg) was also obtained as a by-product.
$^1$H-NMR ($CDCl_3$) δ: 1.90-2.25(6H,m),2.85-3.00(1H,m),
2.95(3H,s),3.05(3H,s),3.91(3H,s),4.43-4.54(1H,m),
4.86-4.95(1H,m),6.70(1H,d,J=1.5Hz),7.19(1H,d,J=1.5Hz),
7.59(1H,d,J=8.8Hz),7.76(1H,d,J=8.8Hz),7.95(1H,d,J=8.8Hz),
8.53(1H,s),8.64(1H,d,J=8.0Hz),8.73(1H,s).
MS (FAB) m/z: 540$(M+H)^+$.

[Example 234]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)-carbonyl]amino}cyclohexyl)isoquinoline-3-carboxamide hydrochloride



The compound (500 mg) obtained in Referential Example 146 was dissolved in an ethanol solution (5 ml) of hydrochloric acid, and the mixture was stirred at room temperature for 30 minutes. The solvent was distilled off under reduced pressure, and the residue was dissolved in N,N-dimethylformamide (7 ml), and the compound (299 mg) obtained in Referential Example 293, 1-hydroxy-benzotriazole monohydrate (71 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (403 mg) were added to the solution to stir the mixture at room temperature for a night. The solvent was distilled off under reduced pressure, a saturated aqueous solution of sodium hydrogencarbonate and methylene chloride were added to the residue to conduct liquid separation. The resultant water layer was extracted with methylene chloride. Organic layers were combined and dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 93:7) to obtain a free base (260 mg) of the title compound as a pale yellow solid. This product was dissolved in methylene chloride, a 1N ethanol solution (961 μl) of hydrochloric acid was added, and the solvent was distilled off under reduced pressure. A small amount of methanol was added to the residue, and diethyl ether was added dropwise to collect precipitate formed by filtration. This product was washed with diethyl ether to

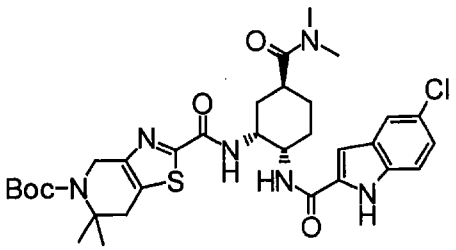
obtain the title compound (260 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.56(1H,m),1.71-1.75(3H,m),
1.95-1.99(1H,m),2.12-2.15(1H,m),2.78(3H,s),2.95(3H,s),
2.98(1H,br.s),3.05(3H,s),4.19-4.22(1H,m),4.44-4.52(3H,m),
4.74-4.88(2H,m),7.87(1H,dd,J=8.8,1.7Hz),8.24(1H,d,J=8.8Hz),
8.36(1H,d,J=1.7Hz),8.58(1H,s),8.90-8.92(2H,m),9.30(1H,s),
12.65-12.75(1H,m).

MS (FAB) m/z: 541$(M+H)^+$.

[Example 235]

tert-Butyl 2-[({(1R,2S,5S)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-amino)carbonyl]-6,6-dimethyl-6,7-dihydrothiazolo[4,5-c]pyridine-5(4H)-carboxylate:




The compound (95.4 mg) obtained in Referential Example 316 was dissolved in diethyl ether (1 ml) in an argon atmosphere, and tert-butyllithium (1.60N pentane solution, 244 μl) was added dropwise at -78°C. After the mixture was stirred for 1 hour at -78°C, carbon dioxide was blown into the reaction mixture for 10 minutes. The reaction mixture was heated to room temperature. After the reaction mixture was concentrated under reduced pressure, the residue was dissolved in N,N-dimethylformamide (5 ml).

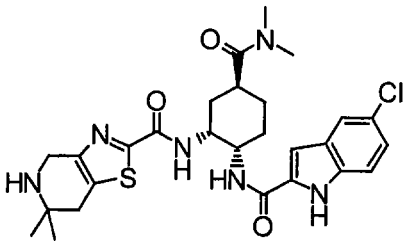
To the solution, were successively added the compound (178 mg) obtained in Referential Example 432 , 1-hydroxybenzotriazole monohydrate (48.0 mg) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (136 mg). The resultant mixture was stirred overnight at room temperature. The reaction mixture was concentrated, and methylene chloride and a saturated aqueous solution of sodium hydrogencarbonate were added to the residue to separate an organic layer. The organic layer was dried over anhydrous sodium sulfate, and the solvent was then distilled off under reduced pressure. The resultant residue was purified by column chromatography on silica gel (methanol:methylene chloride = 1:19) to obtain the title compound (140 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.50(9H,s),1.52(3H,s),1.54(3H,s), 1.70-2.10(4H,m),2.15-2.45(2H,m),2.80-3.20(9H,m), 4.10-4.25(1H,br), 4.60-4.75(3H,m),6.85(1H,br.s), 7.21(1H,dd,J=8.8,1.8Hz),7.34(1H,d,J=8.8Hz), 7.48(1H,d,J=7.3Hz),7.61-7.63(1H,m),7.89(1H,br.s), 9.27(1H,br.s).

MS (ESI) m/z: 657$(M+H)^+$.

[Example 236]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-6,6-dimethyl-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridine-2-carboxamide hydrochloride:



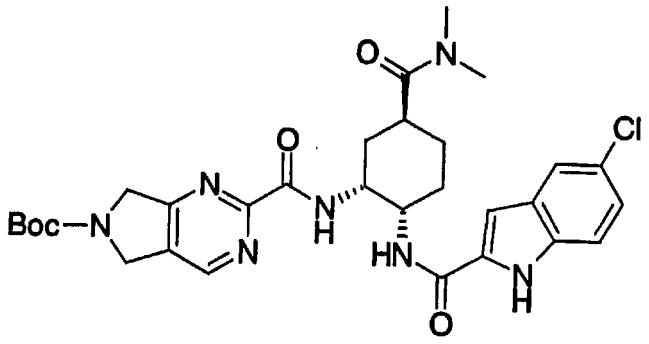
The title compound was obtained from the compound obtained in Example 235 in a similar manner to the process described in Example 227.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40(6H,s),1.45-1.60(1H,m), 1.70-2.05(5H,m),2.81(3H,s),2.95-3.15(6H,m), 4.05-4.20(1H,br),4.25-4.45(2H,m),4.55-4.65(1H,m), 7.06(1H,d,J=1.7Hz),7.17(1H,dd,J=8.8,2.0Hz), 7.42(1H,d,J=8.8Hz),7.68(1H,d,J=2.0Hz),8.34-8.39(2H,m), 9.77(1H,br.s),9.84(1H,br.s),11.79(1H,br.s).

MS (ESI) m/z: 557$(M+H)^+$.

[Example 237]

tert-Butyl 2-[({(1R,2S,5S)-2-{[(5-chloroindol-2-yl)-carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-amino)carbonyl]-5,7-dihydro-6H-pyrrolo[3,4-d]pyrimidine-6-carboxylate:



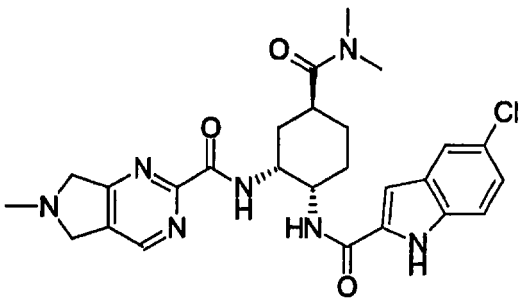
The compound (1.27 g) obtained in Referential Example 50 was dissolved in tetrahydrofuran (48 ml), and lithium hydroxide (117 mg) and water (6.0 ml) were added to stir the mixture at room temperature for 4.5 hours. The reaction mixture was dried to solid under reduced pressure to obtain a crude carboxylic acid lithim salt (1.24 g). This product was condensed with the compound obtained in Referential Example 432 in a similar manner to the process described in the step 2) of Example 226 to obtain the title compound.

$^1$H-NMR ($CDCl_3$) δ: 1.50-1.70(1H,m),1.54(9H,s),1.80-2.10(3H,m),2.25-2.50(2H,m),2.85-2.95(1H,m),2.99(3H,s),3.14(3H,s),4.15-4.25(1H,m),4.65-4.75(1H,m),4.80-4.90(4H,m),6.97(1H,s),7.15-7.25(1H,m),7.30-7.40(1H,m),7.60-7.65(1H,m),8.15-8.25(1H,m),8.40-8.45(1H,m),8.75-8.85(1H,m),9.40-9.45(1H,m).

MS (ESI) m/z: 611(M+H)+.

[Example 238]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-6-methyl-6,7-dihydro-5H-pyrrolo[3,4-d]pyrimidine-2-carboxamide hydrochloride:



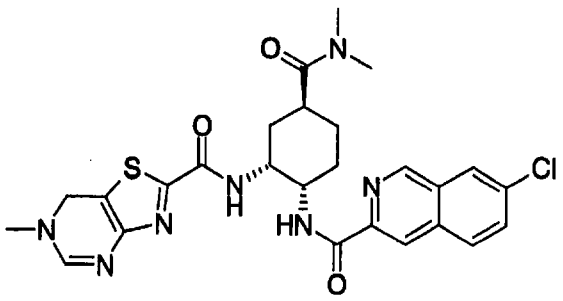
The compound (367 mg) obtained in Example 237 was dissolved in methylene chloride (10 ml), and trifluoroacetic acid (10 ml) was added to stir the mixture at room temperature for 2 hours. The reaction mixture was dried to solid under reduced pressure. The title compound was obtained from the thus-obtained crude product and formalin in a similar manner to the process described in Example 18.

$^1$H-NMR (DMSO-d6) δ: 1.50-1.60(1H,m),1.65-2.10(5H,m), 2.81(3H,s),2.90-3.00(1H,m),2.96(3H,s),3.05(3H,s), 4.10-4.20(1H,m),4.55-4.65(1H,m),4.65-4.90(4H,br), 7.06(1H,s),7.15(1H,dd,J=8.7,2.1Hz), 7.41(1H,d,J=8.8Hz),7.66(1H,d,J=1.7Hz),8.35-8.45(1H,m), 8.57(1H,d,J=8.1Hz),9.00(1H,s),11.80(1H,s), 11.90-12.20(1H,m).

MS (FAB) m/z: 524$(M+H)^+$.

[Example 239]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(6-methyl-6,7-dihydrothiazolo[4,5-d]pyrimidin-2-yl)-carbonyl]amino}cyclohexyl)isoquinoline-3-carboxamide hydrochloride



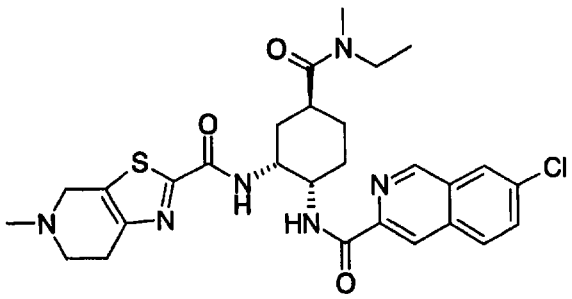
The title compound was obtained by treating the compound obtained in Referential Example 146 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 322 in a similar manner to the process described in Example 49.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.60(1H,m),1.70-1.90(3H,m),1.90-2.15(2H,m),2.81(3H,s),2.95(3H,s),2.90-3.05(1H,m), 3.26(3H,s),4.20-4.55(2H,m),5.00(2H,s),7.91(1H,d,J=8.8Hz), 8.27 (1H,d,J=8.8Hz),8.37(1H,s),8.54(1H,s),8.62(1H,s), 8.79(1H,d,J=8.3Hz),8.94(1H,d,J=8.1Hz),9.32(1H,s).

MS (ESI) m/z: 554$(M+H)^+$.

[Example 240]

7-Chloro-N-((1S,2R,4S)-4-{[ethyl(methyl)amino]carbonyl}-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)isoquinoline-3-carboxamide hydrochloride:



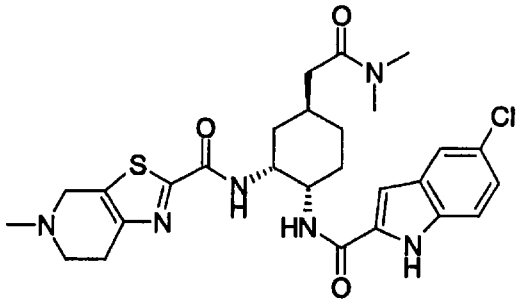
The title compound was obtained from the compound obtained in Referential Example 325 and the compound obtained in Referential Example 10 in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 0.98, 1.04(3H,each t,J=7.1Hz),

1.52-1.60(1H,m),1.74-1.77(3H,m),1.96-2.05(1H,m),
2.15-2.18(1H,m),2.77-2.93(8H,m),3.17-3.32(3H,m),
3.49(1H,br.s),4.22(1H,br.s),4.41-4.45(1H,m),
4.51(1H,br.s),4.69-4.72(1H,m),7.89(1H,d,J=8.7Hz),
8.26(1H,d,J=8.7Hz),8.37(1H,s),8.60(1H,s),8.91-8.98(2H,m),
9.32(1H,d,J=6.6Hz),11.39,11.53(1H,each m).
MS (FAB) m/z: 569$(M+H)^+$.

[Example 241]

N-{(1R*,2S*,5S*)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[2-(dimethylamino)-2-oxoethyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained from the compound obtained in Referential Example 336 and the compound obtained in Referential Example 10 in a similar manner to the process described in Example 2.

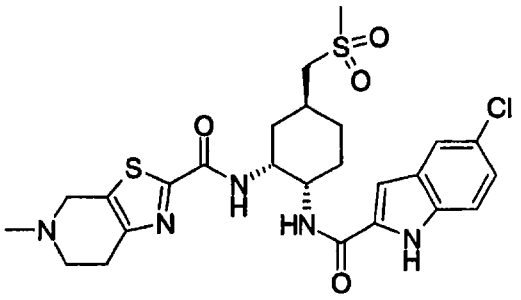
$^1$H-NMR (DMSO-$d_6$) δ: 1.13-1.22(1H,m),1.40-1.46(1H,m),
1.68-1.99(5H,m),2.18-2.29(2H,m),2.80(3H,s),2.92(3H,s),
2.96(3H,s),3.22(2H,br.s),3.49(1H,br.s),3.70(1H,br.s),
4.09-4.16(1H,m),4.42-4.46(2H,m),4.67(1H,br.s),7.03(1H,s),
7.16(1H,dd,J=8.5,1.5Hz),7.42(1H,d,J=8.5Hz),7.67(1H,s),

8.01(1H,d,J=8.5Hz),8.40(1H,d,J=7.8Hz),11.35-11.58(1H,m),
11.76(1H,br.s).

MS (FAB) m/z: 557$(M+H)^+$.

[Example 242]

N-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(methylsulfonyl)methyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



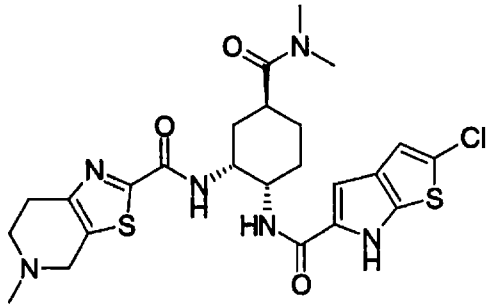
The title compound was obtained by treating the compound obtained in Referential Example 340 with an ethanol solution of hydrochloric acid and then condensing it with the compound obtained in Referential Example 10 in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.40(1H,m),1.55-1.62(1H,m),
1.70-1.76(1H,m),1.88-1.94(1H,m),2.03-2.07(1H,m),
2.13-2.17(1H,m),2.30-2.33(1H,m),2.43-3.48(10H,m),
3.60-3.73(2H,m),4.11-4.16(1H,m),4.40-4.42(2H,m),
4.68-4.73(1H,m),7.05(1H,s),7.16(1H,dd,J=2.0,8.8Hz),
7.41(1H,d,J=8.8Hz),7.68(1H,s),8.26(1H,d,J=7.8Hz),
8.39(1H,d,J=7.8Hz),11.78(1H,br.s).

MS (ESI) m/z: 564$(M+H)^+$.

[Example 243]

N-{(1R,2S,5S)-2-{[(2-Chloro-6H-thieno[2,3-b]pyrrol-5-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



The title compound was obtained by hydrogenation of the compound obtained in Referential Example 252 and then condensing it with the compound obtained in Referential Example 345 in a similar manner to the process described in Example 223.

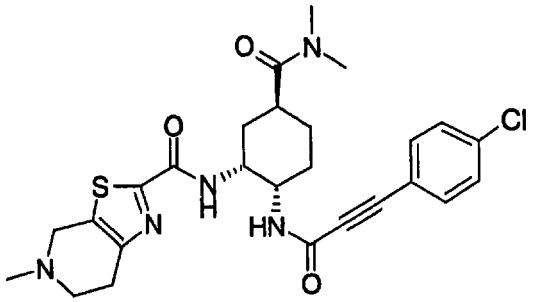
$^1$H-NMR ($CDCl_3$) δ: 1.56-1.66(1H,m),1.76-1.93(2H,m), 2.02-2.06(1H,m),2.19-2.26(1H,m),2.30-2.34(1H,m),2.52(3H,s), 2.79-2.88(3H,m),2.91-2.94(2H,m),2.96(3H,s),3.09(3H,s), 3.69-3.77(2H,m),4.13-4.19(1H,m),4.58-4.61(1H,m),6.72(1H,s), 6.84(1H,s),7.50(1H,d,J=7.3Hz),7.60(1H,d,J=5.8Hz), 10.54(1H,br).

MS (ESI) m/z: 549$(M+H)^+$.

[Example 244]

N-{(1R,2S,5S)-2-{[3-(4-Chlorophenyl)-2-propynoyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide

hydrochloride:



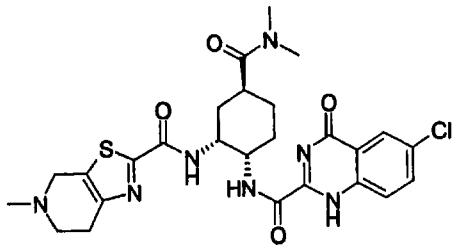
The title compound was obtained by hydrogenation of the compound obtained in Referential Example 252 and then condensing it with the compound obtained in Referential Example 347 in a similar manner to the process described in Example 223.

$^1$H-NMR (DMSO-$d_6$) δ: 1.38-1.50(1H,m),1.58-1.92(4H,m), 2.78(3H,s), 2.90(3H,s),2.97(3H,s),3.01-3.24(3H,m), 3.26-3.80(2H,m),3.90-3.98(1H,m),4.30-4.78(3H,m), 7.51(1H,d,J=8.8Hz),7.57(1H,d,J=8.8Hz),8.34(1H,d,J=8.8Hz), 8.83(1H,d,J=7.8Hz).

MS (FAB) m/z: 528$(M+H)^+$.

[Example 245]

6-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}cyclohexyl)-4-oxo-1,4-dihydroquinazoline-2-carboxamide hydrochloride:



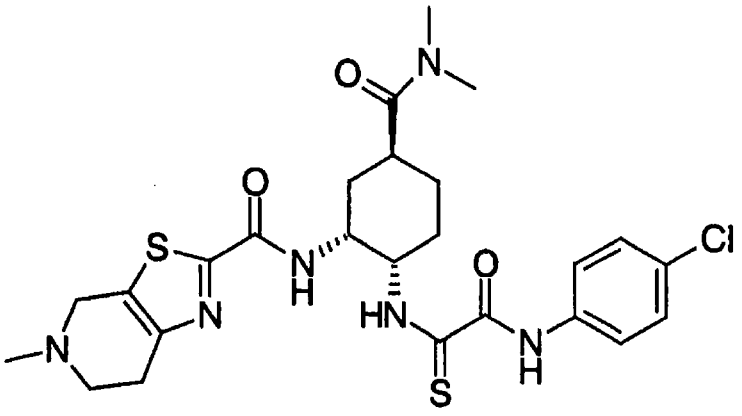
The title compound was obtained by hydrogenation of the compound obtained in Referential Example 252 and then condensing it with the compound obtained in Referential Example 349 in a similar manner to the process described in Example 223.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m),1.70-1.90(3H,m), 1.90-2.20(3H,m),2.80(3H,s),2.93(3H,s),2.97(3H,s), 2.98-3.80(4H,m), 4.05-4.20(2H,m),4.35-4.80(3H,m), 7.63(1H,d,J=8.3Hz),7.90(1H,d,J=7.3Hz),8.75-9.00(2H,m), 11.00-11.50(1H,br),12.53(1H,br.s).

MS (ESI) m/z: 573$(M+H)^+$.

[Example 246]

N-{(1R,2S,5S)-2-{[2-(4-Chloroanilino)-2-oxoethane-thioyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide:



The compound (184 mg) obtained in Referential Example 253 and the compound (150 mg) obtained in Referential Example 351 were dissolved in a mixed solvent of methanol (1 ml)-methylene chloride (4 ml), the solution was heated and stirred at 150°C, and the heating was continued for 5 minutes after distilling off the solvent. After the reaction mixture was allowed to cool, the formed product was purified by column chromatography on silica gel (methylene chloride:methanol = 24:1) to obtain the title compound (59 mg).

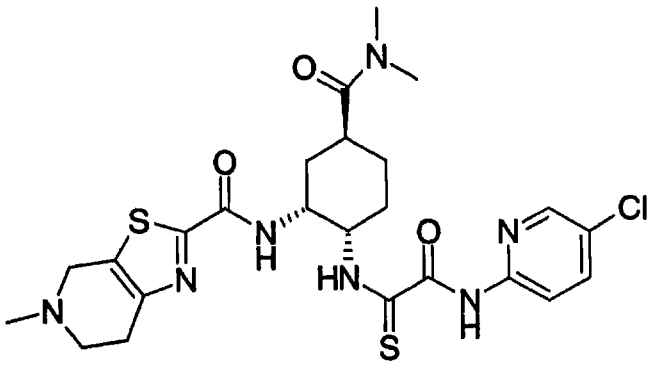
$^1$H-NMR ($CDCl_3$) δ: 1.65-1.90(2H,m), 1.90-2.00(1H,m), 2.00-2.15(2H,m),2.20-2.30(1H,m),2.52(3H,s),2.75-2.95(5H,m), 2.96(3H,s),3.07(3H,s),3.68(1H,d,J=15.2Hz), 3.75(1H,d,J=15.7Hz), 4.45-4,60(1H,m),4.80-4.85(1H,m), 7.31(2H,d,J=8.8Hz),7.44(1H,d,J=8.6Hz),7.60(2H,d,J=8.8Hz), 9.99(1H,d,J=7.6Hz),10.15(1H,s).

MS (ESI) m/z: 563$(M+H)^+$.

[Example 247]

N-{(1R,2S,5S)-2-({2-[(5-Chloropyridin-2-yl)amino]-2-

oxoethanethioyl}amino)-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide:



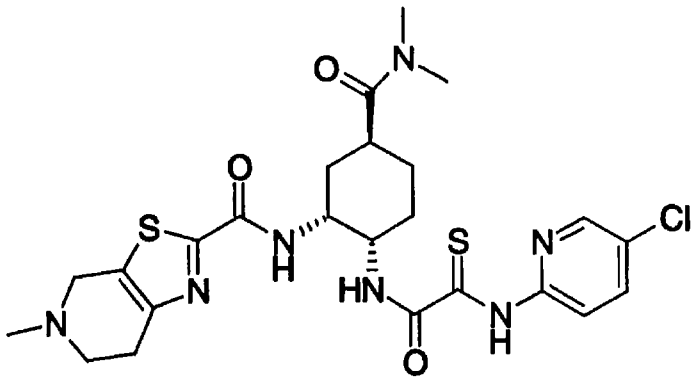
The compound (184 mg) obtained in Referential Example 253 and the compound (150 mg) obtained in Referential Example 353 were dissolved in a mixed solvent of methanol (0.3 ml)-methylene chloride (0.3 ml), the solution was heated and stirred at 150°C, and the heating was continued for 5 minutes after distilling off the solvent. reaction mixture was allowed to cool, the formed product was purifiec by column chromatography on silica gel (methylene chloride:methanol = 24:1) to obtain the title compound (52 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.60-2.00(3H,m),2.00-2.20(2H,m), 2.25-2.40(1H,m),2.53(3H,s),2.80-2.95(5H,m),2.96(3H,s), 3.08(3H,s),3.70(1H,d,J=15.4Hz),3.75(1H,d,J=15.4Hz), 4.45-4,60(1H,m),4.75-4.85(1H,m),7.45(1H,d,J=8.3Hz), 7.67(1H,dd,J=8.8,2.5Hz),8.18(1H,d,J=8.8Hz), 8.31(1H,d,J=2.0Hz),10.06(1H,d,J=6.3Hz),10.56(1H,s).

MS (ESI) m/z: 564$(M+H)^+$.

[Example 248]

N-{(1R,2S,5S)-2-({2-[(5-Chloropyridin-2-yl)amino]-2-thioxoacetyl}amino)-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide:



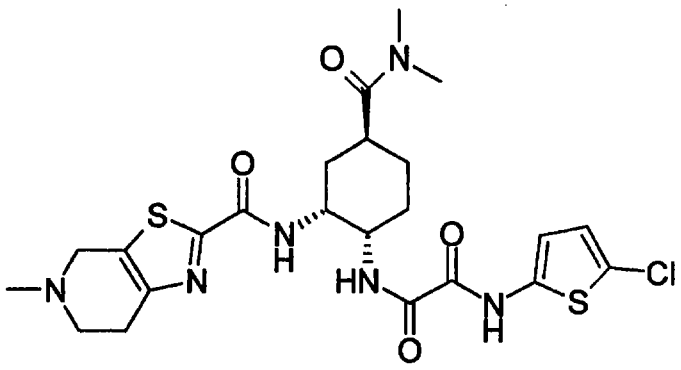
The compound (72 mg) obtained in Referential Example 355 and 2-amino-5-chloropyridine (100 mg) were dissolved in a mixed solvent of methanol (0.2 ml)-methylene chloride (0.2 ml), the solution was heated and stirred at 150°C, and the heating was continued for 8 minutes after distilling off the solvent. After the reaction mixture was allowed to cool, the formed product was purified by preparative thin-layer chromatography on silica gel (methylene chloride:methanol = 23:2) to obtain the title compound (4 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.60-2.00(3H,m),2.00-2.20(3H,m), 2.53(3H,s),2.75-3.00(5H,m),2.95(3H,s),3.05(3H,s), 3.65-3.80(2H,m),4.05-4.15(1H,m),4.70-4.80(1H,m),7.28(1H,d),

7.43(1H,d,J=9.3Hz),7.75(1H,dd,J=8.8,2.7Hz),
8.41(1H,d,J=2.7Hz),9.05(1H,d,J=8.8Hz),11.56(1H,s).
MS (ESI) m/z: 564$(M+H)^+$.

[Example 249]

$N^1$-(5-Chloro-2-thienyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



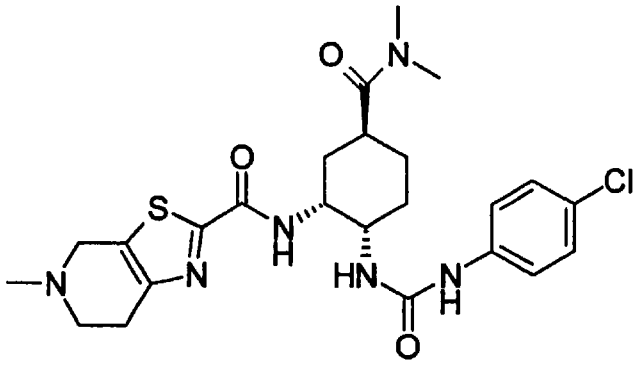
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 356, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ:1.40-1.55(1H,m),1.60-1.85(3H,m),
1.90-2.15(2H,m),2.79(3H,s),2.90-3.15(1H,m),2.92(3H,s),
2.94(3H,s),3.15-3.30(2H,m),3.50-3.80(2H,m),3.95-4.05(1H,m),
4.35-4.90(3H,m),6.90(1H,d,J=4.2Hz),6.94(1H,d,J=4.2Hz),
8.72(1H,d,J=7.3Hz),9.13(1H,br.s),11.21(1H,br.s),
12.32(1H,br.s).

MS (ESI) m/z: 553$(M+H)^+$.

[Example 250]

N-{(1R,2S,5S)-2-{[(4-Chloroanilino)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:

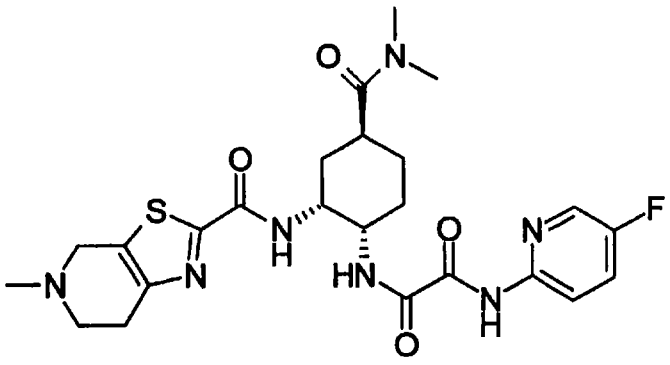


4-Chlorophenyl isocyanate (76.8 mg) was added to a solution of the compound (183 mg) obtained in Referential Example 253 in methylene chloride (20 ml), and the mixture was stirred at room temperature for 24 hours. The solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 20:1 → 10:1) to distil off the solvent. The residue was dissolved in ethanol (2 ml) and methylene chloride (2 ml), a 1N ethanol solution (0.4 ml) of hydrochloric acid was added to stir the mixture at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the residue was solidified with diethyl ether to obtain the title compound (160 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.50(1H,m),1.60-1.90(5H,m),
2.79(3H,s), 2.92(3H,s),3.00(3H,s),3.10-3.60(4H,m),
3.60-3.90(2H,m),4.35-4.80(3H,m),6.26(1H,br.s),
7.23(2H,d,J=9.0Hz),7.37(2H,d,J=9.0Hz),8.53(1H,br.s),
8.72(1H,br.s),11.35,11.67(total 1H,each s).
MS (ESI) m/z: 519$(M+H)^+$.

[Example 251]

$N^1$-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]-amino}cyclohexyl)-$N^2$-(5-fluoropyridin-2-yl)ethanediamide hydrochloride:



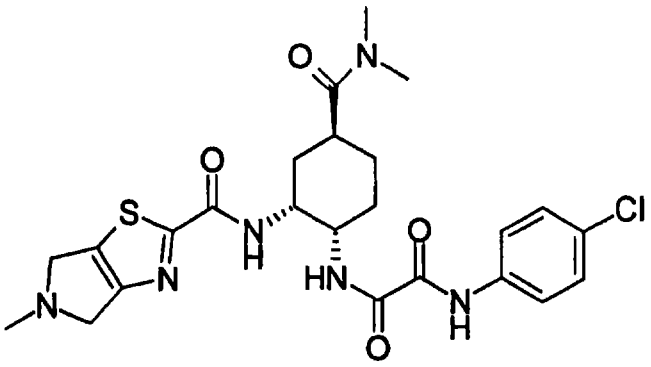
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 357, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.53(1H,m),1.68-1.75(3H,m),
1.99-2.10(2H,m),2.80(3H,s),2.80-3.00(1H,m),2.95(6H,s),
3.18-3.21(2H,m),3.40-3.80(2H,m),3.87-4.82(4H,m),

7.82-7.85(1H,m), 8.01-8.05(1H,m),8.40(1H,d,J=2.9Hz),
8.71(1H,d,J=7.7Hz),9.13(1H,d,J=7.3Hz),10.27(1H,s).
MS (FAB) m/z: 532$(M+H)^+$.

[Example 252]

$N^1$-(4-Chlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]-thiazol-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



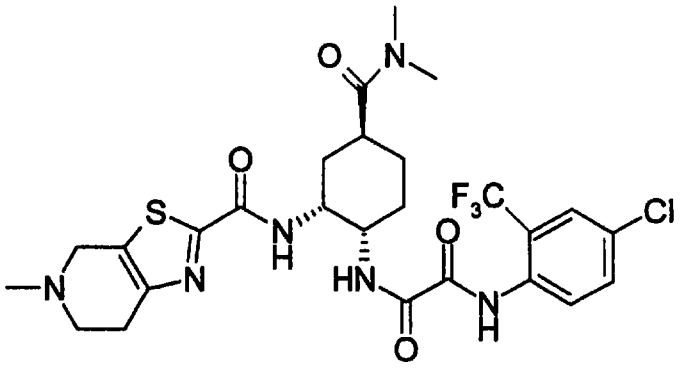
The title compound was obtained from the compound obtained in Referential Example 242 and the compound obtained in Referential Example 272 in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.51(1H,m),1.69-1.75(3H,m),
1.98-2.05(2H,m),2.80(3H,s),2.95(3H,s),2.98-3.04(1H,m),
3.10(3H,s),3.40-4.61(6H,m),7.41(2H,d,J=8.8Hz),
7.81(2H,d,J=8.8Hz),8.76(1H,d,J=7.6Hz),8.95(1H,d,J=8.3Hz),
10.79(1H,s).
MS (FAB) m/z: 533$(M+H)^+$.

[Example 253]

$N^1$-[4-Chloro-2-(trifluoromethyl)phenyl]-$N^2$-((1S,2R,4S)-4-

[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexyl)ethanediamide hydrochloride:



Thionyl chloride (1 ml) was added to a chloroform solution (10 ml) of the compound (269 mg) obtained in Referential Example 359, and the mixture was stirred at 75°C for 30 minutes. The solvent was distilled off under reduced pressure, and the residue was dried. To the residue were added a methylene chloride solution (7 ml) of the compound (286 mg) obtained in Referential Example 253 and pyridine (3 ml) under ice cooling. The mixture was stirred for 2 hours while the temperature of the system was raised to room temperature. A saturated aqueous solution (10 ml) of sodium hydrogencarbonate was added to the reaction mixture to conduct liquid separation. The resultant organic layer was dried over anhydrous sodium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was subjected to column chromatography on silica gel (methylene chloride:methanol = 20:1) and column chromatography on LH-

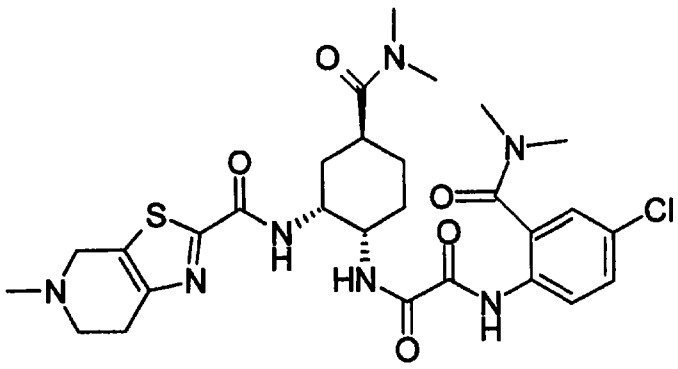
20 (molecular sieve, methanol) to obtain a free base (90 mg) of the title compound as a pale yellow amorphous solid. Methylene chloride (5 ml), ethanol (5 ml) and a 1N ethanol solution (1 ml) of hydrochloric acid were added to thie product, and distilling-off and drying were conducted under reduced pressure to obtain the title compound.

$^1$H-NMR (DMSO-$d_6$) δ: 1.41-1.55(1H,m),1.59-1.80(3H,m), 1.98-2.13(2H,m),2.77(3H,s),2.91(6H,s),3.12-3.26(2H,m), 3.30-3.58(2H,m),3.60-3.78(1H,m),3.94-4.04(1H,m), 4.35-4.63(2H,m),4.64-4.80(1H,m),7.73-7.82(2H,m),7.85(1H,s), 8.68-8.73(1H,m),9.18(1H,br.s),10.31(1H,s).

MS (ESI)m/z: 615(M+H).

[Example 254]

$N^1$-{4-Chloro-2-[(dimethylamino)carbonyl]phenyl}-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by hydrolyzing the compound obtained in Referential Example 362, condensing the hydrolyzate with the compound obtained in Referential

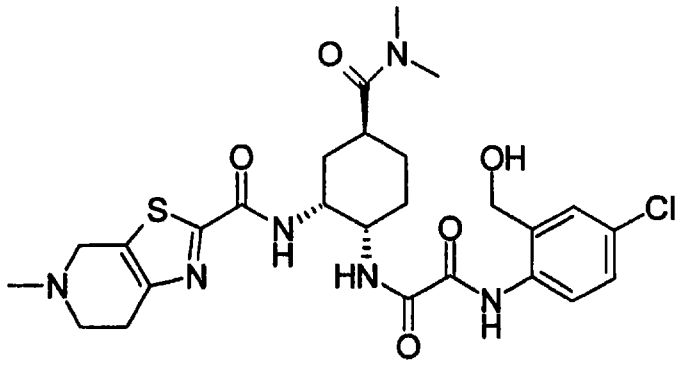
Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.56(1H,m), 1.59-1.82(3H,m), 1.98-2.14(2H,m),2.79(3H,s),2.91(3H,s),2.93(3H,s), 2.95(3H,s),2.98(3H,s),3.10-3.30(4H,m),3.62-3.79(1H,m), 3.92-4.01(1H,m),4.34-4.50(2H,m),4.66-4.79(1H,m), 7.52(1H,d,J=2.4Hz),7.55(1H,dd,J=2.4,8.5Hz), 8.05(1H,d,J=8.5Hz),8.75(1H,br),9.10-9.24(1H,m),10.52(1H,s).

MS (ESI) m/z: 618$(M+H)^+$.

[Example 255]

$N^1$-[4-Chloro-2-(hydroxymethyl)phenyl]-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexyl)ethanediamide hydrochloride:

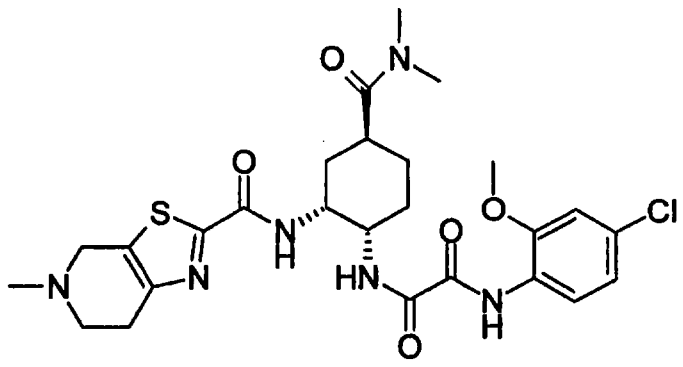



The title compound was obtained by condensing the compound obtained in Referential Example 270 with 4-chloro-2-hydroxymethylaniline and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 199.

$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.57(1H,m),1.58-1.81(3H,m),
1.98-2.14(2H,m),2.79(3H,s),2.93(6H,s),3.12-3.58(4H,m),
3.67-3.80(1H,m),3.94-4.04(1H,m),4.37-4.50(1.5H,m),
4.55(2H,s),4.67-4.80(1H,m),5.77-5.92(0.5H,m),
7.37(1H,dd,J=2.4,8.6Hz),7.42(1H,d,J=2.4Hz),
7.91(1H,d,J=8.6Hz),8.74-8.81(1H,m),9.03-9.19(1H,m),
10.79(1H,s).
MS (ESI) m/z: 577$(M+H)^+$.

[Example 256]

$N^1$-(4-Chloro-2-methoxyphenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by hydrolyzing the compound obtained in Referential Example 364, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

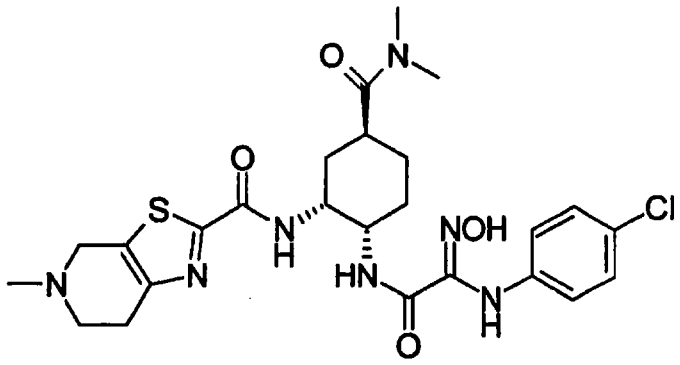
$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.55(1H,m),1.58-1.79(3H,m),1.94-

2.11(2H,m),2.77(3H,s),2.92(6H,s),3.05-3.55(4H,m),3.65-3.75(1H,br),3.90(3H,s),3.91-4.00(1H,m),4.36-4.47(2H,br),4.65-4.77(1H, br), 7.04(1H,dd,J=8.5,2.0Hz), 7.20(1H,d,J=2.0Hz),8.06(1H,d,J=8.5Hz),8.65-8.80(1H,br), 9.10-9.25(1H,br),9.74(1H,s),11.10-11.35(1H,br).

MS (ESI) m/z: 577$(M+H)^+$.

[Example 257]

N-{(1R,2S,5S)-2-{[2-(4-Chloroanilino)-2-(hydroxyimino)acetyl]amino}-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



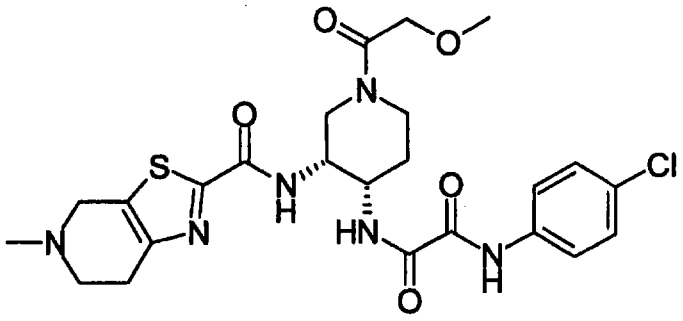
The title compound was obtained by deprotecting the compound obtained in Referential Example 366 by hydrochloric acid treatment, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 214.

$^1$H-NMR (DMSO-$d_6$) δ: 1.41-1.53(1H,m),1.57-1.77(3H,m), 1.88-2.04(2H,m),2.77(3H,s),2.91(6H,s),3.00-3.60(4H,m),

3.65-3.74(1H,br),3.87-3.96(1H,m),4.37-4.48(2H,m),
4.66-4.76(1H,m),6.70(2H,d,J=8.8Hz),
7.04(1H,d,J=8.8Hz),7.10(1H,d,J=8.8Hz),8.40-8.53(2H,m),
8.57-8.66(1H,m), 10.30-10.47(1H,br), 10.66-10.76(1H,br).
MS (ESI) m/z: 562$(M+H)^+$.

[Example 258]

$N^1$-(4-Chlorophenyl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}piperidin-4-yl)ethanediamide hydrochloride:

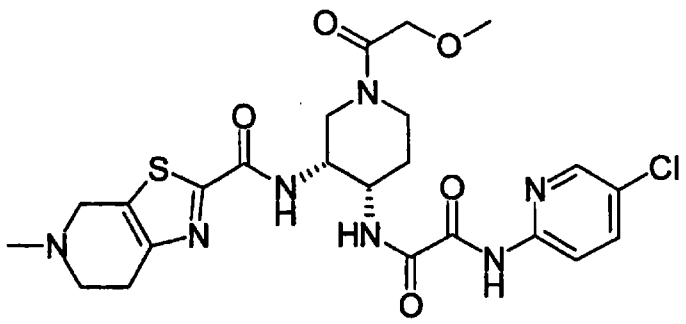


The title compound was obtained by deprotecting the compound obtained in Referential Example 367 by hydrochloric acid treatment, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 214.

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.72(1H,m),1.99-2.22(1H,m),
2.90(3H,s),3.03-4.80(17H,m),7.40(2H,d,J=8.8Hz),
7.83(2H,d,J=8.8Hz),8.56-8.73(1H,br),9.14-9.33(1H,br),
10.83(1H,s),11.20-11.55(1H,br).
MS (ESI) m/z: 549$(M+H)^+$.

[Example 259]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidin-4-yl)ethanediamide hydrochloride:



The title compound was obtained by deprotecting the compound obtained in Referential Example 368 by hydrochloric acid treatment, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 214.

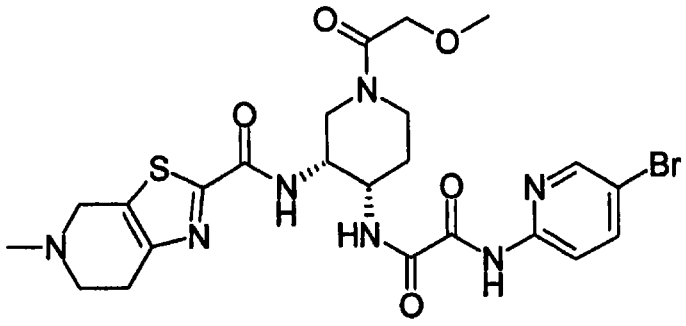
$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.72(1H,m),1.98-2.20(1H,m), 2.90(3H,s),3.00-4.77(17H,m),7.20-7.35(0.8H,br), 7.48-7.56(0.2H,br),7.94-8.07(1H,br),8.40-8.70(1H,br), 8.48-8.70(1H,br),9.23-9.45(1H,br),10.21-10.35(1H,br), 11.30-11.70(1H,br).

MS (ESI) m/z: 550$(M+H)^+$.

[Example 260]

$N^1$-(5-Bromopyridin-2-yl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-

yl)carbonyl]amino}piperidin-4-yl)ethanediamide hydrochloride:



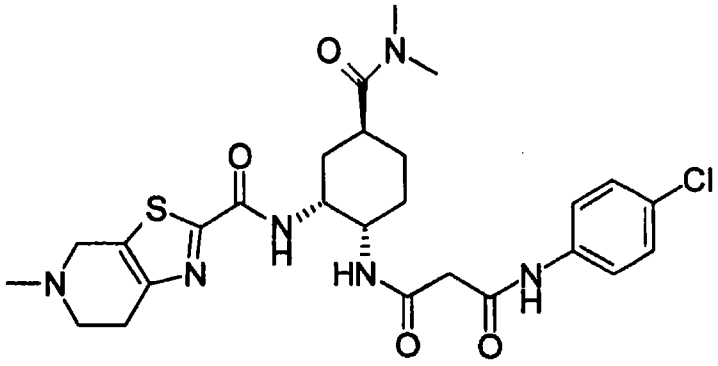
The title compound was obtained by deprotecting the compound obtained in Referential Example 369 by hydrochloric acid treatment, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 214.

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.73(1H,m),1.97-2.20(1H,m), 2.90(3H,s),3.03-3.52(7H,m),3.64-4.07(5H,m),4.10-4.50(4H,m), 4.65-4.78(1H,m),7.28-7.35(0.2H,m),7.97(1H,d,J=8.8Hz), 8.11(1H,dd,J=8.8,2.2Hz),8.51(1H,d,J=2.2Hz),8.55-8.67(1H,m), 9.22-9.41(1H,m),10.20-10.31(0.8H,m),11.25-11.70(1H,br).

MS (ESI) m/z: 594$(M+H)^+$.

[Example 261]

$N^1$-(4-Chlorophenyl)-$N^3$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)malonamide hydrochloride:



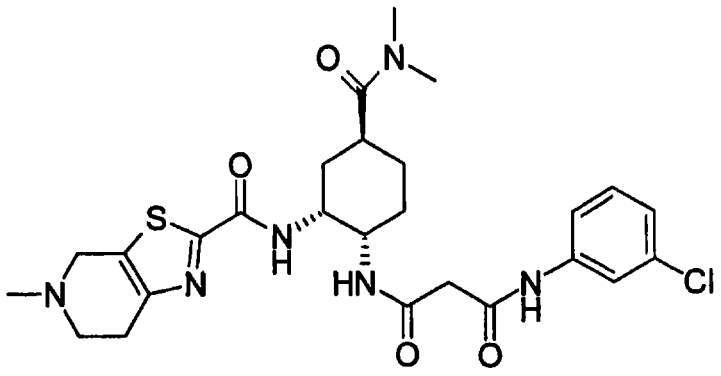
The title compound was obtained by condensing the compound obtained in Referential Example 371 with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 5.

$^1$H-NMR (DMSO-$d_6$) δ: 1.32-1.50(1H,m),1.55-1.87(5H,m), 2.78(3H,m),2.92(3H,s),2.98(3H,s),2.99-3.00(1H,m), 3.05-3.50(5H,m),3.65-3.75(1H,m),3.80-3.92(1H,m), 4.35-4.45(1H,m),4.45-4.55(1H,m),4.65-4.80(1H,m), 7.34(2H,d,J=8.8Hz),7.58(2H,d,J=8.8Hz),8.00-8.10(1H,m), 8.30-8.40(1H,m),10.29(1H,d,J=12.5Hz),12.40(1H,br.s)

MS (FAB) m/z: 561$(M+H)^+$.

[Example 262]

$N^1$-(3-Chlorophenyl)-$N^3$-((1S,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)malonamide hydrochloride:



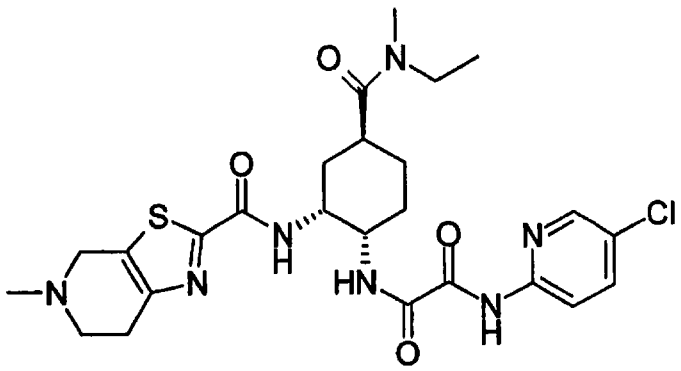
The title compound was obtained by condensing the compound obtained in Referential Example 373 with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 5.

$^1$H-NMR (DMSO-$d_6$) δ: 1.32-1.50(1H,m),1.55-1.90(5H,m), 2.77(3H,s),2.91(3H,s),2.98(3H,s),2.99-3.00(1H,m), 3.05-3.50(5H,m),3.65-3.80(1H,m),3.80-3.90(1H,m), 4.35-4.50(1H,m),4.50-4.60(1H,m),4.65-4.80(1H,m), 7.09(1H,d,J=8.8Hz),7.31(1H,d,J=8.8Hz),7.38(1H,t,J=8.8Hz), 7.79(1H,s),8.00-8.10(1H,m),8.30-8.40(1H,m), 10.28(1H,d,J=12.5Hz), 11.67(1H,br.s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 263]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]carbonyl}-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



10% Palladium on carbon (0.3 g) was added to a solution of the compound (0.33 g) obtained in Referential Example 404 in ethanol (20 ml), and the mixture was stirred at room temperature for 24 hours under a hydrogen atmosphere. After removing insoluble matter by filtration through Celite pad, the filtrate was concentrated under reduced pressure. The resultant residue (0.37 g) was dissolved in N,N-dimethylformamide (20 ml), and the compound (0.3 g) obtained in Referential Example 266, 1-hydroxybenzotriazole monohydrate (0.2 g) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (0.37 g) were successively added to stir the mixture at room temperature for 18 hours. The reaction mixture was concentrated under reduced pressure, and the resultant residue was diluted with a mixed solvent of chloroform-methanol (9:1) and washed with a saturated aqueous solution of sodium hydrogencarbonate and saturated aqueous solution of sodium chloride. After the resultant organic layer was dried over anhydrous sodium sulfate, and the solvent was distilled off under reduced pressure, the

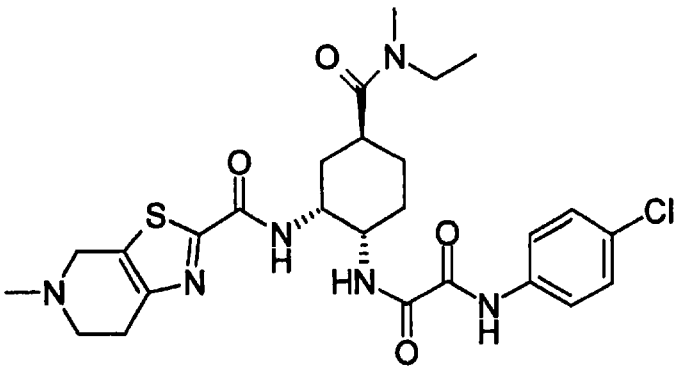
resultant residue was purified by column chromatography on silica gel (chloroform:methanol = 95:5) to concentrate the intended fraction. A 1N ethanol solution of hydrochloric acid was added to form a hydrochloride. This salt was recrystallized from a mixed solvent of methanol and diethyl ether to obtain the title compound (0.28 g).

$^1$H-NMR (DMSO-$d_6$) δ: 0.95(1.5H,t,J=6.9Hz), 1.42(1.5H,t,J=6.9Hz), 1.40-1.52(1H,m),1.60-1.78(3H,m), 1.92-2.11(2H,m),2.74(3H,s),2.90(3H,s),3.10-3.38(5H,m), 3.40-3.52(1H,m),3.68-3.70(1H,m),3.96-4.05(1H,m),4.41(2H,s), 4.70(1H,d,J=15.9Hz),8.00-8.01(2H,m),8.44(1H,s), 8.71(1H,dd,J=10.1,2.2Hz),9.14(0.5H,d,J=7.8Hz), 9.22(0.5H,d,J=8.3Hz),10.24(0.5H,s),10.28(0.5H,s), 11.48(1H,br.s),11.61(1H,br.s).

MS (FAB) m/z: 562$(M+H)^+$.

[Example 264]

$N^1$-(4-Chlorophenyl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]-carbonyl}-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



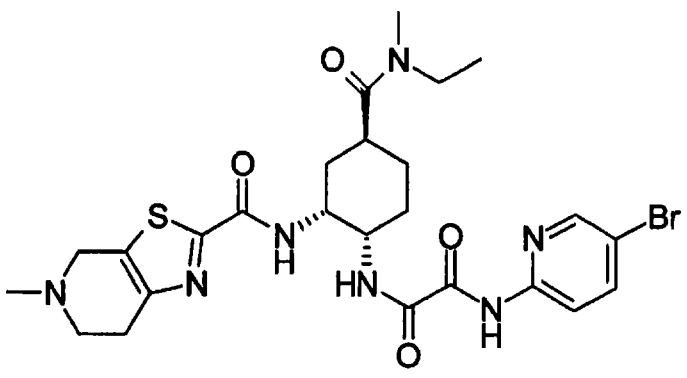
The title compound was obtained by converting the compound obtained in Referential Example 404 into an amine, condensing the amine with the compound obtained in Referential Example 374 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 263.

$^1$H-NMR (DMSO-$d_6$) δ: 0.97(1.5H,t,J=6.9Hz), 1.04(1.5H,t,J=6.9Hz),1.40-1.60(1H,m),1.60-1.80(3H,m), 1.92-2.11(2H,m),2.74(3H,s),2.89(3H,s),3.10-3.32(5H,m), 3.40-3.52(1H,m),3.65-3.80(1H,m),3.90-4.05(1H,m), 4.40(2H,s),4.70(1H,d,J=15.9Hz),7.39(2H,d,J=8.8Hz), 7.82(2H,d,J=8.8Hz),8.75(1H,dd,J=10.1,2.2Hz), 9.00(0.5H,d,J=7.8Hz),9.08(0.5H,d,J=8.3Hz), 10.81(1H,d,J=4.9Hz),11.45(1H,br.s).

MS (FAB) m/z: 561$(M+H)^+$.

[Example 265]

$N^1$-(5-Bromopyridin-2-yl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]carbonyl}-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



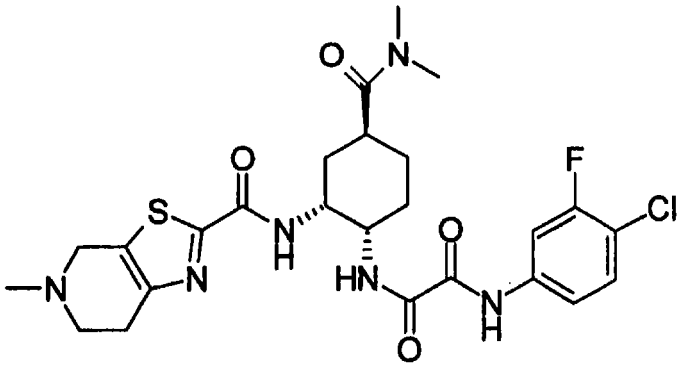
The title compound was obtained by converting the compound obtained in Referential Example 404 into an amine, condensing the amine with the compound obtained in Referential Example 375 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 263.

$^1$H-NMR (DMSO-$d_6$) δ: 1.02(1.5H,t,J=6.9Hz), 1.08(1.5H,t,J=6.9Hz),1.49-1.60(1H,m),1.60-1.86(3H,m), 2.00-2.20(2H,m),2.81(3H,s),2.97(3H,s),3.15-3.42(6H,m), 3.50-3.60(1H,m),3.70-3.82(1H,m),4.48(2H,s), 4.77(1H,d,J=15.9Hz),8.04(1H,d,J=8.8Hz),8.17(1H,d,J=8.8Hz), 8.58(1H,s),8.78(1H,dd,J=10.1,2.2Hz),9.21(0.5H,d,J=7.8Hz), 9.29(0.5H,d,J=8.3Hz),10.29(0.5H,s),10.33(0.5H,s), 11.53(0.5H,br.s),11.65(0.5H,br.s).

MS (FAB) m/z: 607$(M+H)^+$.

[Example 266]

$N^1$-(4-Chlroro-3-fluorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



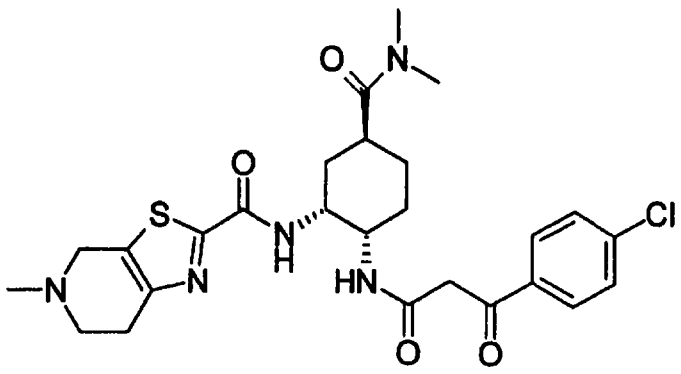
The title compound was obtained by converting the compound obtained in Referential Example 252 into an amine, condensing the amine with the compound obtained in Referential Example 378 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 263.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44-1.52(1H,m),1.65-1.76(3H,m), 2.01-2.07(2H,m),2.77(3H,s),2.93(6H,s),2.94-3.00(1H,m), 3.10-3.38(3H,m),3.68-3.70(1H,m),3.96-4.05(1H,m),4.42(2H,s), 4.70(1H,d,J=15.9Hz),7.56(1H,t,J=8.8Hz),7.68(1H,d,J=8.8Hz), 7.90(1H,dd,J=11.7,1.5Hz),8.73(1H,dd,J=12.5,7.3Hz), 9.06(1H,dd,J=12.5,8.1Hz),11.01(1H,d,J=5.8Hz), 11.30-11.42(1H,m).

MS (FAB) m/z: 565$(M+H)^+$.

[Example 267]

N-{(1R,2S,5S)-2-{[3-(4-Chlorophenyl)-3-oxopropanoyl]amino}-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide:



The title compound was obtained by deprotecting the

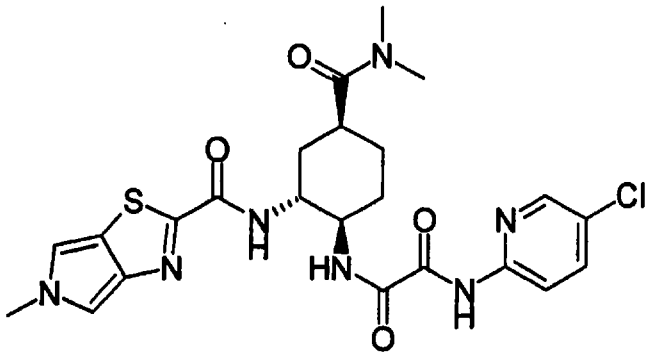
compound obtained in Referential Example 383 by hydrochloric acid treatment, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 214.

$^1$H-NMR ($CDCl_3$)(free base) δ: 1.22-1.32(1H,m),1.49-1.92(3H,m),1.95-2.10(2H,m),2.53(3H,s),2.70-2.79(1H,m),2.80-2.90(2H,m),2.93(6H,s),2.95-3.09(2H,m),3.72(2H,s),3.87(2H,s),4.05-4.19(1H,m),4.60-4.70(1H,m),7.20-7.40(2H,m),7.42(2H,d,J=8.3Hz),7.87(2H,d,J=8.3Hz).

MS (FAB) m/z: 546$(M+H)^+$.

[Example 268]

$N^1$-(5-Chlroropyridin-2-yl)-$N^2$-((1R,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5H-pyrrolo[3,4-d]-thiazol-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



The title compound was obtained by deprotecting the compound obtained in Referential Example 386 by hydrochloric acid treatment, and condensing the deprotected compound with the compound obtained in

Referential Example 293 in a similar manner to the process described in Example 214.

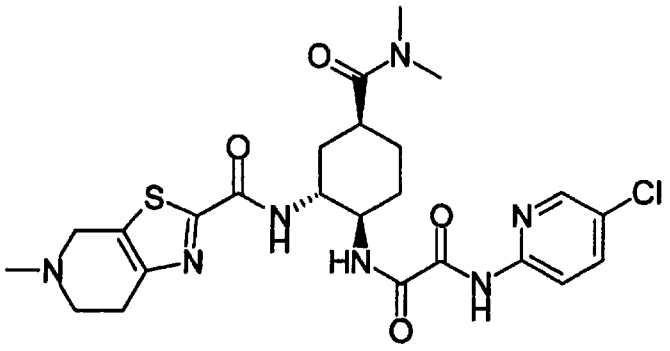
$^1$H-NMR (DMSO-$d_6$) δ:1.00-2.35(7H,m),2.96(3H,s),3.04(3H,s), 3.85-3.95(1H,m),3.88(3H,s),4.60-4.75(1H,m), 6.68(1H,d,J=2.0Hz), 7.17(1H,d,J=2.0Hz),7.20-7.32(1H,m), 7.67(1H,dd,J=8.8,2.8Hz),7.99(1H,d,J=8.4Hz), 8.21(1H,d,J=8.8Hz),8.25(1H,d,J=2.8Hz),9.64(1H,s).

HRMS (FAB) m/z: 532.1520$(M+H)^+$.

(Calculated; $C_{23}H_{27}ClN_7O_4S$: 532.1534).

[Example 269]

$N^1$-[(5-Chlroropyridin-2-yl)amino]-$N^2$-((1R,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



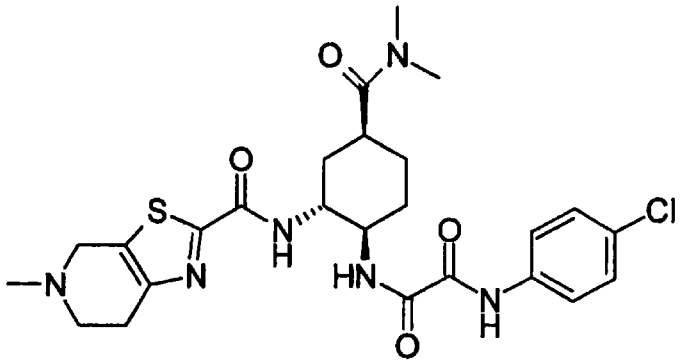
The title compound was obtained by reducing the compound obtained in Referential Example 387 in a similar manner to the process described in Referential Example 253, and condensing the reduction product with the compound obtained in Referential Example 266 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 208.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.98(6H,m), 2.82(3H,s),2.91(3H,s), 2.95(3H,s),2.86-3.92(7H,m),4.30-4.81(2H,m),7.92-8.09(2H,m), 8.39-8.47(1H,m),8.56-8.72(2H,m),10.17(1H,s).

MS (ESI) m/z: 548$(M+H)^+$.

[Example 270]

$N^1$-(4-Chlorophenyl)-$N^2$-((1R,2R,4S)-4-[(dimethylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



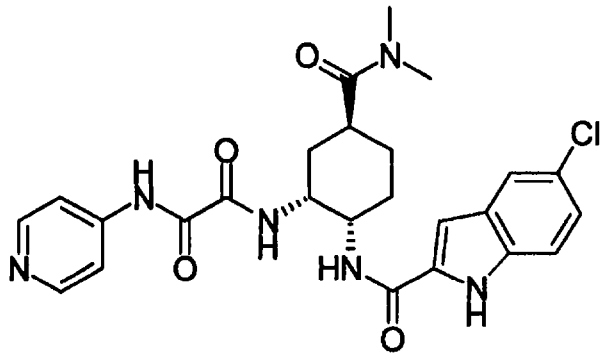
The title compound was obtained by reducing the compound obtained in Referential Example 387 in a similar manner to the process described in Referential Example 253, and condensing the reduction product with the lithium salt obtained by hydrolyzing the compound obtained in Referential Example 242 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.97(6H,m), 2.82(3H,s),2.91(3H,s), 2.98(3H,s),2.83-3.88(7H,m),4.30-4.79(2H,m), 7.37(2H,d,J=8.8Hz), 7.89(2H,d,J=8.8Hz), 8.34(1H,d,J=8.4Hz),8.63(1H,d,J=8.8Hz),10.72(1H,s).

MS (ESI) m/z: 547$(M+H)^+$.

[Example 271]

$N^1$-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-$N^2$-(pyridin-4-yl)-ethanediamide hydrochloride:



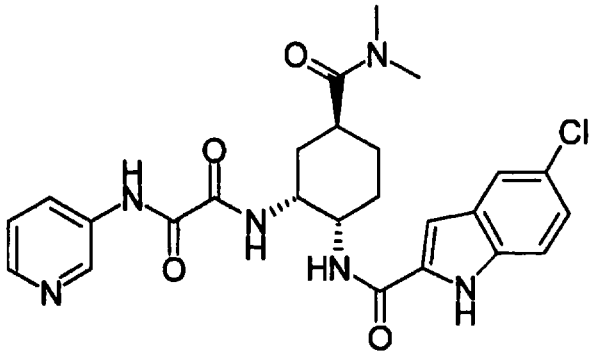
The title compound was obtained by deprotecting the compound obtained in Referential Example 310 by hydrochloric acid treatment, and condensing the deprotected compound with lithium 2-[(pyridin-4-yl)amino]-2-oxoacetate obtained by hydrolyzing the compound obtained in Referential Example 261 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-2.01(6H,m),2.79(3H,s),3.01(3H,s), 3.00-3.18(1H,m),4.02-4.19(1H,m),4.45-4.55(1H,m),7.09(1H,s), 7.13-7.22(1H,m),7.41(1H,d,J=8.4Hz),7.64(1H,br.s), 8.28(2H,d,J=6.8Hz),8.36(1H,d,J=8.0Hz),8.62(1H,d,J=8.8Hz), 8.72(2H,d,J=6.8Hz),11.74(1H,s),11.83(1H,s).

MS (FAB) m/z: 511$(M+H)^+$.

[Example 272]

$N^1$-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-$N^2$-(pyridin-3-yl)-ethanediamide hydrochloride:



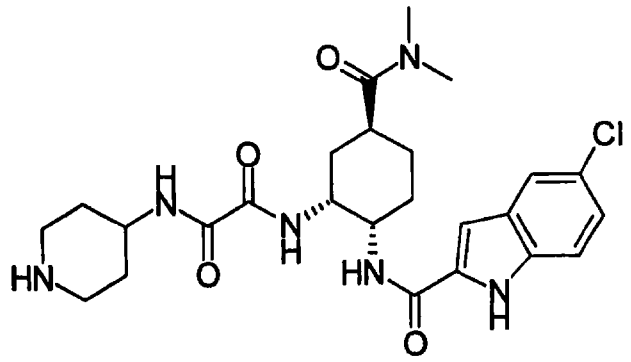
The title compound was obtained by using methyl 2-[(pyridin-3-yl)amino]-2-oxoacetate obtained by condensing 3-aminopyridine with methyl 2-chloro-2-oxoacetate in a similar manner to the process described in Referential Example 242, and the compound obtained in Referential Example 310 as raw materials in a similar manner to the process described in Example 271.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-2.05(6H,m),2.80(3H,s),3.02(3H,s), 2.92-3.15(1H,m),4.02-4.17(1H,m),4.42-4.58(1H,m),7.10(1H,s), 7.12-7.19(1H,m),7.40(1H,d,J=8.4Hz),7.62-7.87(2H,m), 8.36-8.64(4H,m),9.18(1H,s),11.39(1H,s),11.79(1H,s).

MS (FAB) m/z: 511$(M+H)^+$.

[Example 273]

$N^1$-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-$N^2$-(piperidin-4-yl)-ethanediamide hydrochloride:



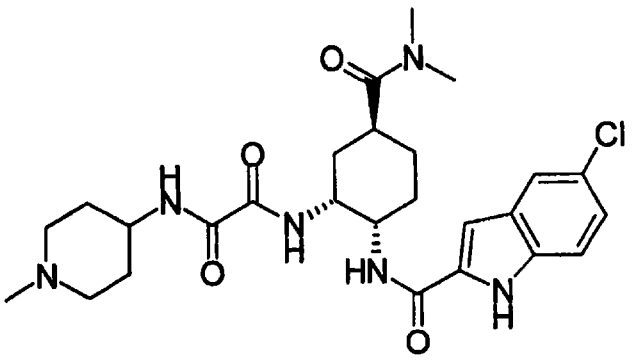
A 4N dioxane solution (8.0 ml) of hydrochloric acid was added to a solution of the compound (400 mg) obtained in Referential Example 389 in ethanol (5.0 ml) at room temperature and the mixture was stirred the same temperature for 5 hours. The solvent was distilled off under reduced pressure, the residue was washed with methylene chloride, and insoluble matter was filterred and washed to obtain the title compound (320 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.38-1.92(10H,m),2.77(3H,s),2.96(3H,s), 2.82-3.35(6H,m),3.88-4.10(2H,m),4.34-4.43(1H,m),7.05(1H,s), 7.11-7.17(1H,m),7.38(1H,d,J=8.8Hz),7.65(1H,s), 8.25(1H,d,J=8.0Hz),8.34(1H,d,J=7.6Hz),8.89(1H,d,J=8.4Hz), 11.75(1H,s).

MS (ESI) m/z: 517$(M+H)^+$.

[Example 274]

$N^1$-{(1R,2S,5S)-2-{[(5-Chloroindol-2-yl)carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-$N^2$-(1-methylpiperidin-4-yl)ethanediamide hydrochloride:



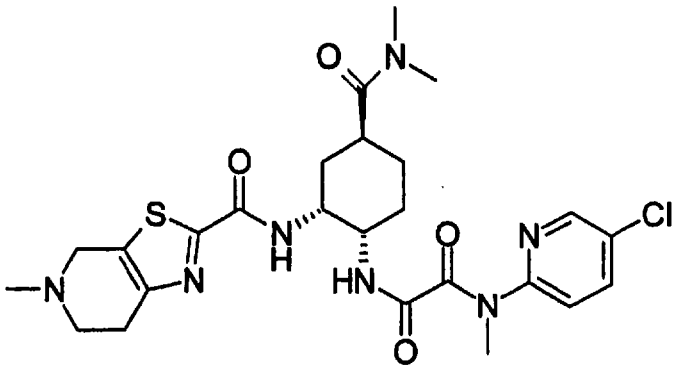
The title compound was obtained by methylating the compound obtained in Example 273 in a similar manner to the process described in Referential Example 9 and treating it with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-2.01(11H,m),2.67(3H,s),2.79(3H,s), 2.98(3H,s),2.85-4.48(7H,m),7.07(1H,s), 7.16(1H,dd,J=8.8,2.0Hz), 7.40(1H,d,J=8.8Hz), 7.68(1H,d,J=2.0Hz), 8.25-8.35(1H,m),8.37(1H,d,J=7.6Hz), 8.90-9.02(1H,m),9.82(1H,br.s),11.78(1H,s).

MS (ESI) m/z: 531$(M+H)^+$.

[Example 275]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)-$N^1$-methylethanediamide hydrochloride:



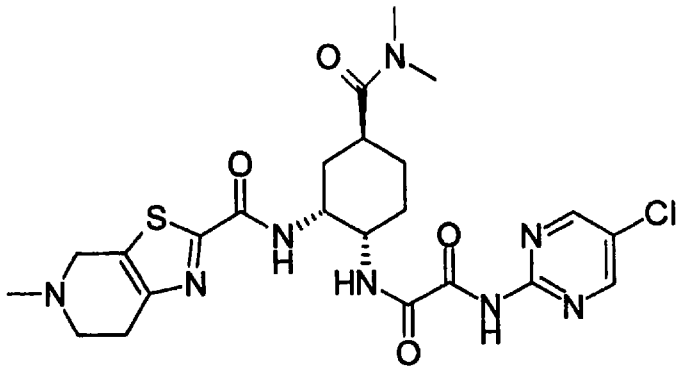
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 390, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.32-1.97(6H,m), 2.42-2.51(1H,m), 2.76(3H,s), 2.91(3H,s),2.93(3H,s),3.27(3H,s), 3.00-4.80(8H,m), 7.45(1H,br.s),7.88-7.97(1H,m), 8.25-8.41(2H,m),8.78-8.91(1H,m).

MS (FAB) m/z: 562$(M+H)^+$.

[Example 276]

$N^1$-(5-Chloropyrimidin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



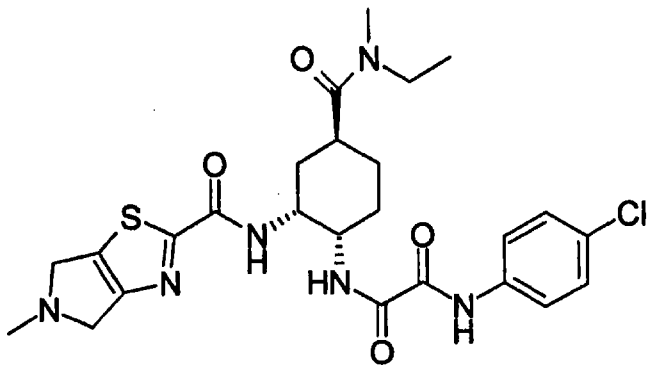
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 391, condensing the hydrolyzate with the compound obtained in Referential Example 253 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 191.

$^1$H-NMR (DMSO-$d_6$) δ: 1.38-2.10(7H,m),2.77(3H,s),2.90(3H,s), 2.93(3H,s), 3.04-4.80(8H,m),8.60-8.70(2H,m),8.82(2H,s), 9.08(1H,br.s),10.64(1H,s),11.57(1H,br.s).

MS (FAB) m/z: 549$(M+H)^+$.

[Example 277]

$N^1$-(4-Chlorophenyl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]-carbonyl}-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]-thiazol-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



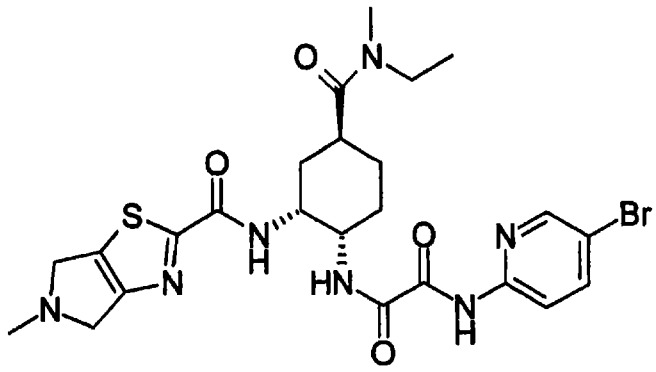
The title compound was obtained by reducing the compound obtained in Referential Example 392 in a similar manner to the process described in Referential Example 253, and condensing the reduction product with the carboxylic acid obtained by hydrolyzing the compound obtained in Referential Example 242 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 195.

$^1$H-NMR (DMSO-$d_6$) δ: 0.96,1.02(3H,each t,J=7.0Hz), 1.47-1.58(1H,m),1.65-1.77(3H,m),1.98-2.08(2H,m), 2.76-2.91(4H,m),3.07(3H,s),3.19-3.41(2H,m),3.98-4.04(1H,m), 4.42(1H,br.s),4.46-4.94(4H,m),7.41(2H,d,J=8.8Hz), 7.83(2H,d,J=8.8Hz),8.74-8.80(1H,m),9.02(1H,d,J=7.3Hz), 10.82(1H,s),12.41(1H,br.s).

MS (FAB) m/z: 547$(M+H)^+$.

[Example 278]

$N^1$-(5-Bromopyridin-2-yl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]carbonyl}-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)-ethanediamide hydrochloride:



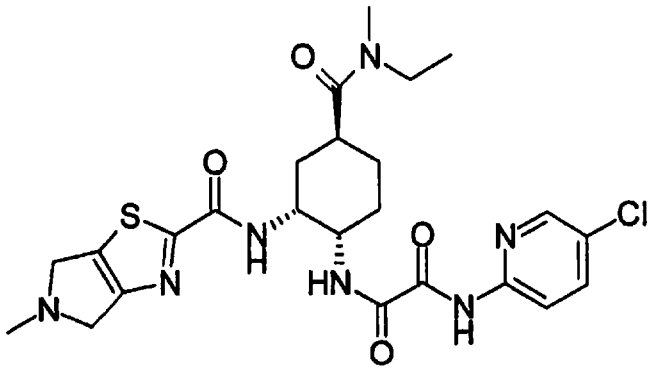
The title compound was obtained from the compound obtained in Referential Example 392 and the compound obtained in Referential Example 262 in a similar manner to the process described in Example 277.

$^1$H-NMR (DMSO-$d_6$) δ: 0.90-1.08(3H,m),1.40-2.13(6H,m), 2.70-3.53(13H,m),3.92-4.08(1H,m),4.35-4.47(1H,m), 7.95(1H,d,J=8.8Hz),8.10(1H,dd,J=8.8,2.4Hz),8.50-8.55(1H,m), 8.68-8.78(1H,m),9.12-9.18(1H,m),10.26(1H,s).

MS (FAB) m/z: 592$(M+H)^+$.

[Example 279]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-{[ethyl(methyl)amino]carbonyl}-2-{[(5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}cyclohexyl)-ethanediamide hydrochloride:



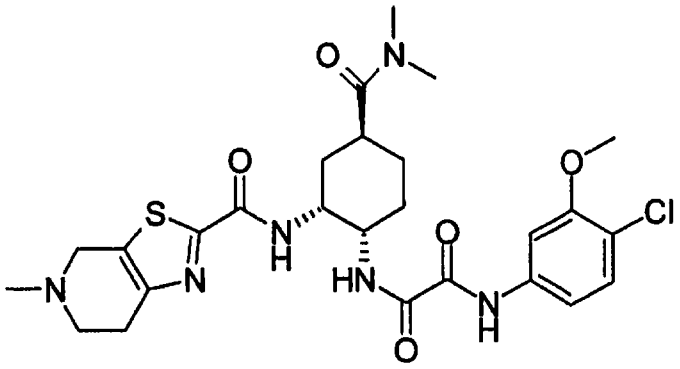
The title compound was obtained from the compound obtained in Referential Example 392 and the compound obtained in Referential Example 243 in a similar manner to the process described in Example 277.

$^1$H-NMR (DMSO-$d_6$) δ: [0.95(t,J=7.0Hz),1.01(t,J=6.8Hz),3H], 1.45-1.72(4H,m),1.96-2.07(2H,m),2.74-2.90(4H,m),3.06(3H,s), 3.18-3.40(2H,m),3.95-4.02(1H,m),4.41(1H,br.s),4.54-4.90(4H,m), 8.00(2H,br.s),8.45(1H,s),8.70-8.75(1H,m), 9.15(1H,br.s),10.27(1H,br.s),12.29(1H,br.s).

MS (ESI) m/z: 548$(M+H)^+$.

[Example 280]

$N^1$-(4-Chloro-3-methoxyphenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



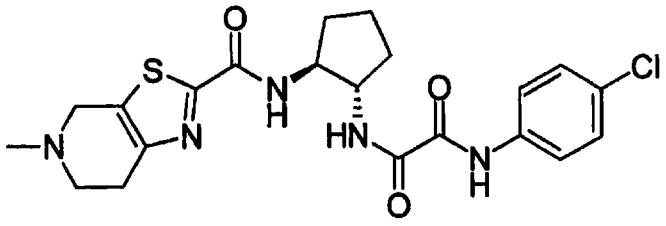
The title compound was obtained by condensing the compound obtained in Referential Example 395 with the compound obtained in Referential Example 10 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.46-1.54(1H,m),1.67-1.77(3H,m), 2.01-2.10(2H,m),2.79(3H,s),2.92-2.98(7H,m),3.21(2H,br.s), 3.49(1H,br.s),3.69(1H,br.s),3.80(3H,s),3.98-4.03(1H,m), 4.42-4.50(2H,m),4.69(1H,br.s),7.37(1H,d,J=8.7Hz), 7.48(1H,dd,J=8.7,2.2Hz),7.72(1H,d,J=2.2Hz), 8.75(1H,d,J=7.3Hz),9.06(1H,br.s),10.77(1H,s), 11.44(1H,br.s).

MS (FAB) m/z: 577$(M+H)^+$.

[Example 281]

$N^1$-(4-Chlorophenyl)-$N^2$-((1R*,2R*)-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclopentyl)ethanediamide hydrochloride:



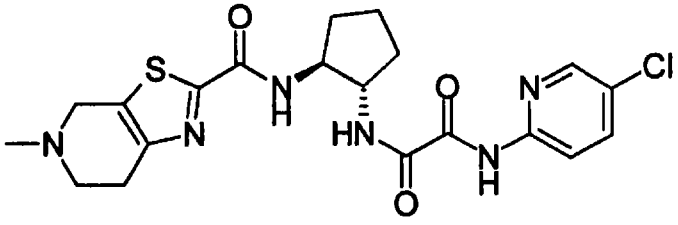
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 242, condensing the hydrolyzate with the compound obtained in Referential Example 62 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 195.

$^1$H-NMR (DMSO-$d_6$) δ: 1.65-1.73(4H,m), 1.91-1.96(2H,m), 2.91(3H,s),3.15(2H,br.s),3.49(1H,br.s),3.66(1H,br.s), 4.32-4.42(3H,m),4.66(1H,br.s),7.40(2H,d,J=8.9Hz), 7.84(2H,d,J=8.9Hz),8.92(1H,d,J=8.5Hz),9.03(1H,d,J=8.3Hz), 10.76(1H,s),11.32(1H,br.s).

MS (FAB) m/z: 462$(M+H)^+$.

[Example 282]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1R*,2R*)-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclopentyl)ethanediamide hydrochloride:



The title compound was obtained by condensing the compound obtained in Referential Example 62 with the

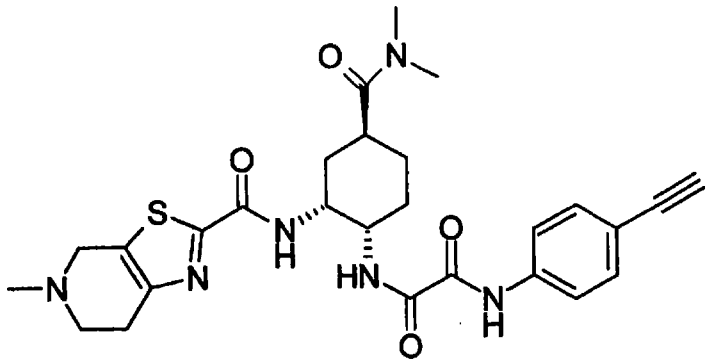
compound obtained in Referential Example 266 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 208.

$^1$H-NMR (DMSO-$d_6$) δ: 1.71(4H,br.s),1.96(2H,br.s),2.90(3H,s), 3.14(1H,br.s),3.21(1H,br.s),3.47(1H,br.s),3.68(1H,br.s), 4.34-4.45(3H,m),4.66(1H,br.s),7.99-8.06(2H,m),8.43-8.44(1H,m), 8.94(1H,d,J=8.3Hz),9.20(1H,d,J=8.5Hz), 10.20(1H,br.s), 11.78(1.1H,br.s).

MS (FAB) m/z: 463$(M+H)^+$.

[Example 283]

$N^1$-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)-$N^2$-(4-ethynylphenyl)ethanediamide:



The title compound was obtained by condensing the compound obtained in Referential Example 252 with the compound obtained in Referential Example 397 in a similar manner to the process described in Example 263.

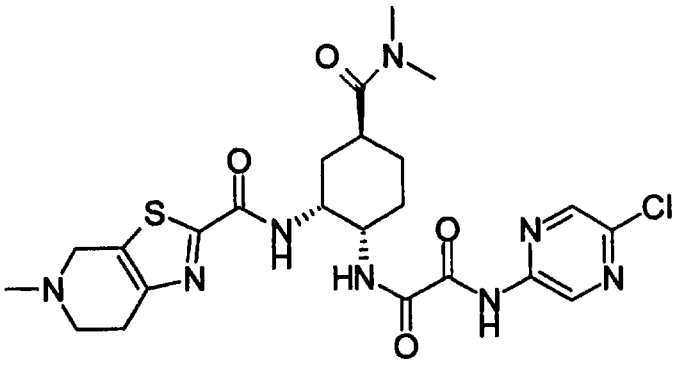
$^1$H-NMR ($CDCl_3$) δ: 1.67-2.16(6H,m),2.51(3H,s),2.76-2.91(5H,m),

2.94(3H,s),3.04(3H,s),3.07(1H,s),[3.65(1H,d,J=15.5Hz),
3.73(1H,d,J=15.5Hz)AB pattern],4.09-4.16(1H,m),4.72-
4.75(1H,m),7.42-7.46(3H,m),7.58(2H,d,J=8.5Hz),
8.02(1H,d,J=8.1Hz),9.36(1H,s).

MS (FAB) m/z: 537$(M+H)^+$.

[Example 284]

$N^1$-(5-Chloropyrazin-2-yl)-$N^2$-((1S,2R,4S)-4-
[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-
tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-
amino}cyclohexyl)ethanediamide hydrochloride:



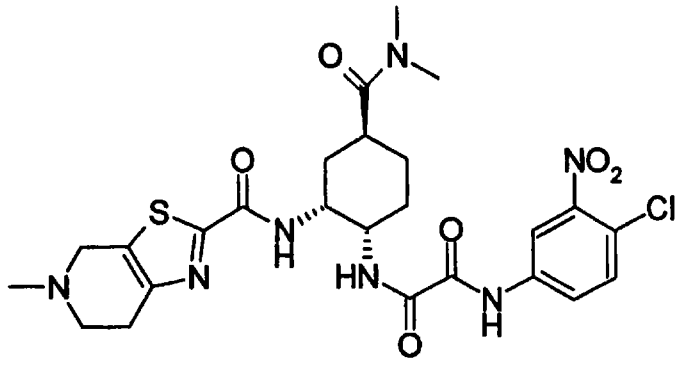
The title compound was obtained by condensing the compound obtained in Referential Example 253 with the compound obtained in Referential Example 399 in a similar manner to the process described in Referential Example 97 and then treating the condensation product with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44-1.52(1H,m),1.65-1.77(3H,m),
2.00-2.10(2H,m),2.77(3H,s),2.91-2.97(7H,m),3.20(2H,br.s),
3.48(1H,br.s),3.68(1H,br.s),3.97-4.02(1H,m),4.40-
4.46(2H,m),

4.68(1H,br.s),8.64(1H,d,J=1.2Hz),8.70(1H,d,J=7.3Hz),
9.02(1H,s),9.21(1H,br.s),10.91(1H,br.s),11.50(1H,br.s).
MS (FAB) m/z: 549$(M+H)^+$.

[Example 285]

$N^1$-(4-Chloro-3-nitrophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



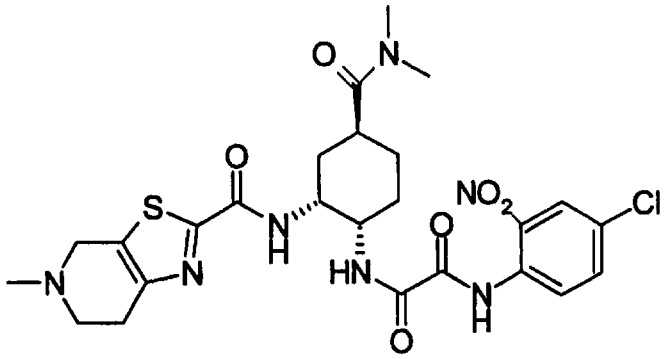
The title compound was obtained by condensing the compound obtained in Referential Example 253 with the compound obtained in Referential Example 400 in a similar manner to the process described in Referential Example 97 and then treating the condensation product with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ:1.44-1.53(1H,m),1.66-1.73(3H,m),
1.97-2.07(2H,m),2.77(3H,s),2.89-3.05(7H,m),3.20(2H,br.s),
3.55(2H,br.s),4.00(1H,br.s),4.44(1H,br.s),4.52(2H,br.s),
7.75(1H,d,J=8.8Hz),8.08(1H,d,J=8.8Hz),8.59(1H,s),
8.71(1H,d,J=7.3Hz),9.07(1H,d,J=8.0Hz),11.24(1H,s),
11.58(1H,br.s).

MS (FAB) m/z: 592$(M+H)^+$.

[Example 286]

$N^1$-(4-Chloro-2-nitrophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



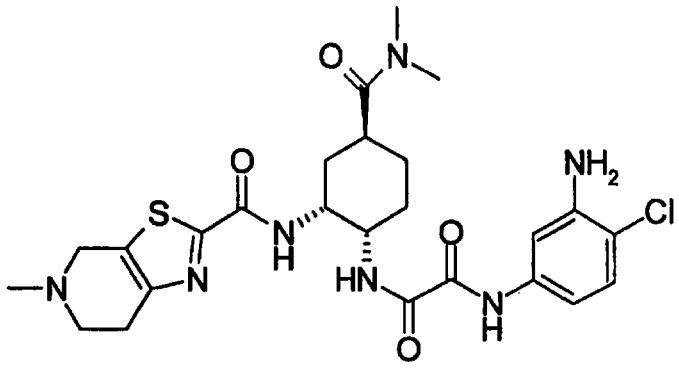
The title compound was obtained by condensing the compound obtained in Referential Example 253 with the compound obtained in Referential Example 401 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 208.

$^1$H-NMR (DMSO-$d_6$) δ: 1.46-1.54(1H,m), 1.66-1.77(3H,m), 2.03-2.10(2H,m),2.79(3H,s),2.90-2.93(7H,m),3.17-3.28(2H,m), 3.49(1H,br.s),3.68(1H,br.s),3.99-4.04(1H,m),4.41(1H,br.s), 4.46(1H,br.s),4.68(1H,br.s),7.89(1H,d,J=9.0Hz),8.20-8.21(2H,m), 8.73(1H,d,J=6.4Hz),9.28(1H,br.s), 11.49(1H,br.s), 11.56(1H,s).

MS (FAB) m/z: 592$(M+H)^+$.

[Example 287]

$N^1$-(3-Amino-4-chlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



The compound (236 mg) obtained in Example 285 was dissolved in ethanol (25 ml), and a catalytic amount of Raney nickel was added to stir the mixture at room temperature for 17 hours under a hydrogen atmosphere. Thereafter, a catalytic amount of Raney nickel was additionally added to stir the mixture for additional 7 hours. The catalyst was removed by filtration, and the solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (methylene chloride:methanol = 23:2) to obtain a pale yellow solid (101 mg). This product was dissolved in methylene chloride, and a 1N ethanol solution (360 µl) of hydrochloric acid. The solvent was distilled off under reduced pressure, a small amount of methanol was added to the residue, and diethyl ether was added dropwise while irradiating with ultrasonic waves to collect precipitate

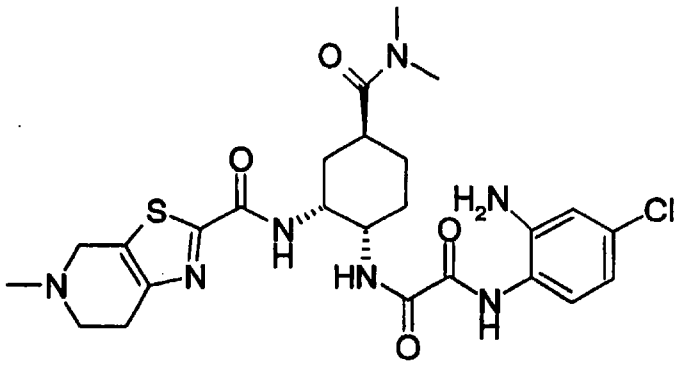
formed. This product was washed with diethyl ether to obtain the title compound (95 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.53(1H,m),1.66-1.73(3H,m), 1.97-2.10(2H,m),2.78(3H,s),2.91-2.94(7H,br.s),3.11-3.19(1H,m),3.29(1H,br.s),3.48(1H,br.s),3.69(1H,br.s), 3.95-4.02(1H,m),4.44(2H,br.s),4.68,4.72(1H,each br.s), 4.86(2.5H,br.s),6.98(1H,dd,J=8.5,1.9Hz),7.14(1H,d,J=8.5Hz), 7.35,7.38(1H,each br.s),8.72-8.77(1H,m),[8.91(d,J=7.8Hz), 8.99(d,J=8.5Hz),1H],10.45,10.47(1H,each br.s), 11.74(1H,br.s).

MS (FAB) m/z: 562$(M+H)^+$.

[Example 288]

$N^1$-(2-Amino-4-chlorophenyl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



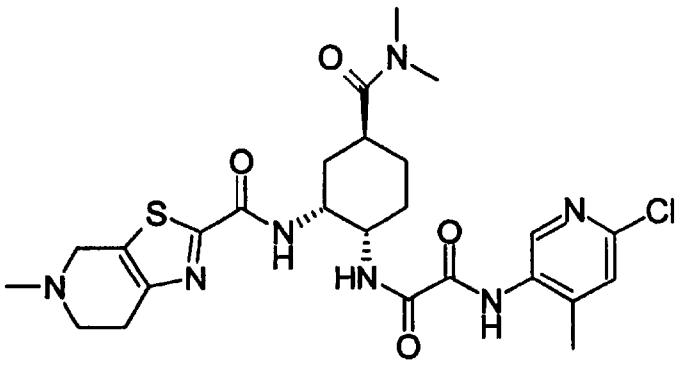
The title compound was obtained from the compound obtained in Example 286 in a similar manner to the process described in Example 287.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.77(4H,m),2.06-2.09(2H,m),

2.78(3H,s),2.92(7H,br.s),3.12-3.19(1H,m),3.26-3.28(1H,m),
3.48(1H,br.s),3.70(1H,br.s),4.00-4.44(5.7H,m),
4.70,4.74(1H,each br.s),6.63-6.66(1H,m),6.85(1H,br.s),
7.18-7.21(1H,m),8.77-8.81(1H,m),[8.97(d,J=7.8Hz),
9.06(d,J=8.1Hz),1H],9.98(1H,s),11.60(1H,br.s).
MS (FAB) m/z: 562$(M+H)^+$.

[Example 289]

$N^1$-(6-Chloro-4-methylpyridin-3-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by condensing the compound obtained in Referential Example 270 with the compound obtained in Referential Example 402 and then treating the condensation product with hydrochloric acid in a similar manner to the process described Example 199.

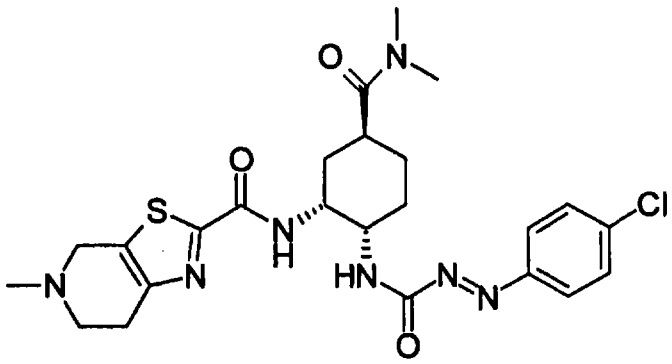
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.54(1H,m),1.65-1.77(3H,m),
2.02-2.08(2H,m),2.22(3H,s),2.79(3H,s),2.89-2.93(7H,m),
3.19(2H,br.s),3.54(2H,br.s),3.99-4.04(1H,m),4.40-
4.42(1H,m), 4.50(2H,br.s),7.49(1H,s),8.32(1H,s),

8.75(1H,d,J=7.1Hz),9.09(1H,d,J=7.3Hz),10.48(1H,s),
11.40(0.9H,br.s).

MS (FAB) m/z: 562$(M+H)^+$.

[Example 290]

N-{(1R,2S,5S)-2-({[(E)-2-(4-Chlorophenyl)diazenyl]-carbonyl}amino)-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



After 10% Palladium on carbon (200 mg) was added to a solution of the compound (700 mg) obtained in Referential Example 252 in tetrahydrofuran (10 ml), and the mixture was stirred at room temperature for 2 days under a hydrogen atmosphere, the reaction mixture was filtered, and the compound obtained in Referential Example 405 (470 mg) was added to a solution of an amine obtained by concentrating the filtrate in formamide (5.0 ml) to stir the mixture at 95°C for 18 hours. After the reaction mixture was concentrated, and a saturated aqueous solution (50 ml) of sodium hydrogencarbonate, water (50 ml) and methylene chloride (30 ml) were added to conduct liquid

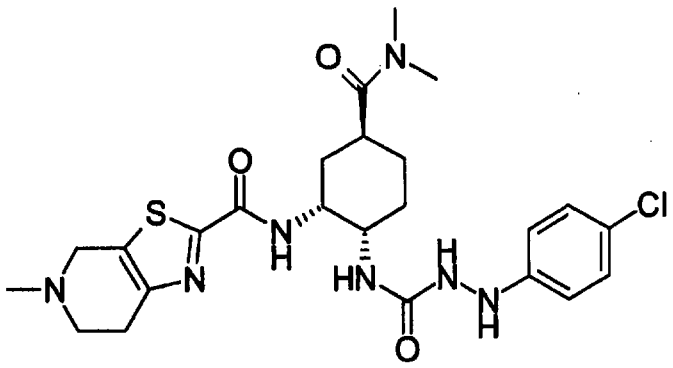
separation, the resultant water layer was extracted with methylene chloride (2 x 20 ml). Organic layere were combined, dried over anhydrous sodium sulfate, concentrated and purified by column chromatography on silica gel (methylene chloride:methanol = 12:1). This purified product was treated with a 1N ethanol solution of hydrochloric acid to obtain the title compound (100 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.60(1H,m),1.65-2.05(5H,m), 2.80(3H,s), 2.91(3H,s),2.99(3H,s),3.00-3.20(2H,m), 3.20-3.32(1H,m),3.43(1H,br.s),3.69(1H,br.s),3.95(1H,br.s), 4.45(1H,br.s),4.60-4.80(2H,m),7.68(2H,d,J=8.7Hz), 7.83(2H,d,J=8.7Hz), 8.41(1H,br.s),8.68(1H,d,J=7.6Hz), 11.40-11.80(1H,br).

MS (ESI) m/z: 532$(M+H)^+$.

[Example 291]

N-{(1R,2S,5S)-2-({[2-(4-Chlorophenyl)hydrazino]-carbonyl}amino)-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained by changing the

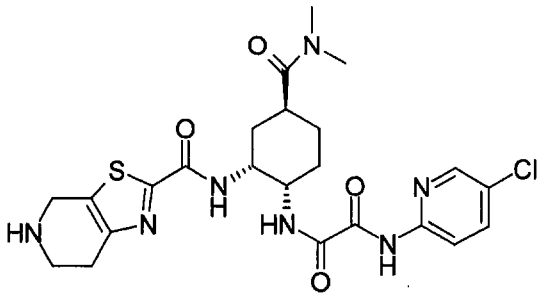
reaction conditions in the reaction described in Example 290 to conditions that stirring was conducted at 40°C for 3 days.

$^1$H-NMR (DMSO-$d_6$) δ: 1.30-1.50(1H,m), 1.50-1.80(3H,m), 1.80-1.97(2H,m),2.76(3H,s),2.80-3.05(2H,m),2.91(6H,s), 3.05-3.30(2H,m),3.47(2H,br.s),4.30-4.50(2H,m), 4.72(1H,t,J=12.8Hz),6.40-6.60(2H,m),6.55-6.70(2H,m), 6.95-7.20(2H,m),7.88(1H,d,J=11.3Hz),8.48-8.65(1H,m), 11.48-11.80(1H,br).

MS (ESI) m/z: 534$(M+H)^+$.

[Example 292]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by condensing the compound obtained in Referential Example 34 with the compound obtained in Referential Example 420 and then treating the condensation product with hydrochloric acid in a similar manner to the process described Example 17.

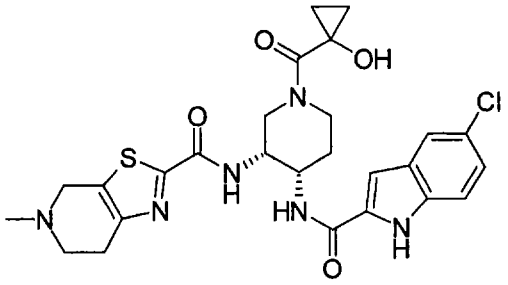
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.55(1H,m),1.60-1.80(3H,m), 1.95-2.10(2H,m),2.78(3H,s),2.85-3.00(4H,m),

3.11(2H,br s),3.40-3.55(2H,m),3.95-4.07(1H,m),4.37-4.45(1H,m),4.48(2H,br s),8.00-8.01(2H,m), 8.10(1H,d,J=7.1Hz), 8.43-8.47(1H,m), 9.16(1H,d,J=7.8Hz),9.43(2H,br s), 10.27(1H,s).

MS (FAB) m/z: 534$(M+H)^+$.

[Example 293]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(1-hydroxycyclopropyl)carbonyl]piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



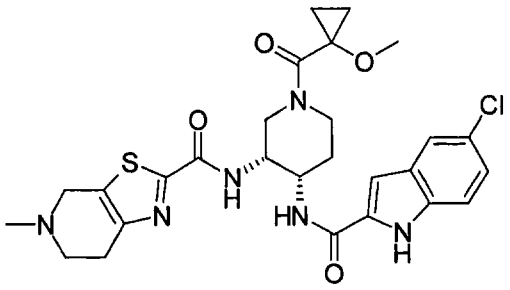
The title compound was obtained by condensing the compound obtained in Example 118 with 1-hydroxy-1-cyclopropanecarboxylic acid and then treating the condensation product with hydrochloric acid in a similar manner to the process described Example 150.

$^1$H-NMR (DMSO-$d_6$) δ: 0.60-0.90(3H,br),0.92-1.03(1H,m), 1.71-1.84(1H,m),1.85-2.03(1H,m),2.91(3H,s), 3.00-3.80(7H,m), 4.05-4.80(5H,m),6.28-6.42(1H,br), 7.09(1H,s), 7.18(1H,dd,J=8.8,1.5Hz), 7.42(1H,d,J=8.8Hz), 7.70(1H,d,J=1.5Hz),8.14-8.29(1H,br),8.41(1H,br d,J=7.6Hz), 11.83(1H,s).

MS (ESI) m/z: 557$(M+H)^+$.

[Example 294]

N-((3R*,4S*)-4-{[(5-Chloroindol-2-yl)carbonyl]amino}-1-[(1-methoxycyclopropyl)carbonyl]piperidin-3-yl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:

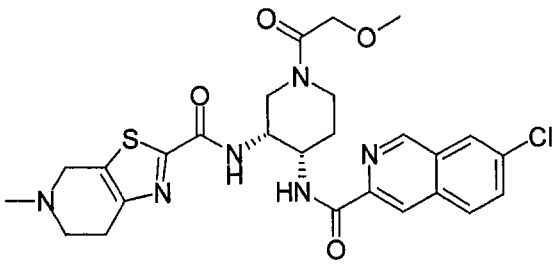


The title compound was obtained by condensing the compound obtained in Example 118 with the compound obtained in Referential Example 409 and then treating the condensation product with hydrochloric acid in a similar manner to the process described Example 150.

$^1$H-NMR (DMSO-$d_6$) δ: 0.65-1.05(4H,m),1.74-1.88(1H,m),1.92-2.10(1H,m),2.91(3H,s),3.00-3.80(10H,m),4.05-4.83(6H,m),7.08(1H,s),7.18(1H,dd,J=8.6,2.0Hz),7.42(1H,d,J=8.6Hz),7.71(1H,d,J=2.0Hz),8.08-8.30(1H,br),8.41(1H,br d,J=7.8Hz),10.60-10.80(0.5H,br),10.85-11.05(0.5H,br),11.84(1H,s).

[Example 295]

7-Chloro-N-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}piperidin-4-yl)-3-isoquinolinecarboxamide hydrochloride:



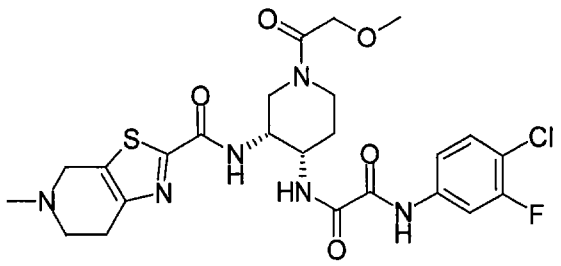
The title compound was obtained by treating the compound obtained in Referential Example 410 with a 4N dioxane solution of hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.80(1H,m),2.13-2.38(1H,m), 2.90(3H,s),3.00-3.87(10H,m),3.89-4.10(2H,m), 4.15-4.58(4H,m), 4.60-4.78(1H,m),7.89(1H,d,J=8.8Hz), 8.25(1H,d,J=8.8Hz),8.37(1H,s),8.61(1H,s),8.70-8.95(1H,m), 9.05-9.29(1H,m),9.36(1H,s),11.20-11.40(0.5H,br), 11.45-11.65(0.5H,br).

MS (ESI) m/z: 557$(M+H)^+$.

[Example 296]

$N^1$-(4-chloro-3-fluorophenyl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}piperidin-4-yl)ethanediamide hydrochloride:



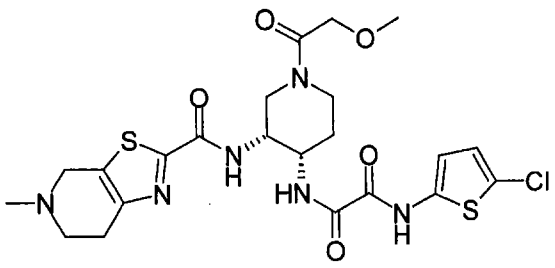
The title compound was obtained by treating the compound obtained in Referential Example 411 with a 4N dioxane solution of hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.72(1H,m),1.98-2.21(1H,m), 2.91(3H,s),3.00-3.52(9H,m),3.56-4.05(3H,m),4.08-4.50(4H,m), 4.60-4.78(1H,br),7.56(1H,t,J=8.8Hz),7.70(1H,d,J=9.0Hz), 7.91(1H,dd,J=8.8,2.3Hz),8.50-8.72(1H,m),9.15-9.35(1H,m), 11.02(1H,s),11.15-11.33(0.5H,br),11.35-11.50(0.5H,br).

MS (FAB) m/z: 567$(M+H)^+$.

[Example 297]

$N^1$-(5-chloro-2-thienyl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}piperidin-4-yl)ethanediamide hydrochloride:



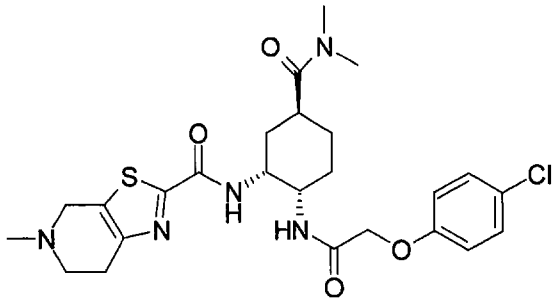
The title compound was obtained by treating the compound obtained in Referential Example 412 with a 4N dioxane solution of hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.60-1.73(1H,m),1.96-2.19(1H,m), 2.91(3H,s),3.04-3.54(9H,m),3.60-4.05(3H,m),4.07-4.34(3H,m), 4.35-4.54(1H,br),4.60-4.80(1H,br),6.89(1H,d,J=4.2Hz), 6.93(1H,d,J=4.2Hz),8.48-8.70(1H,m),9.18-9.40(1H,m), 12.31(1H,s).

MS (ESI) m/z: 555$(M+H)^+$.

[Example 298]

N-{(1R,2S,5S)-2-{[2-(4-Chlorophenoxy)acetyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



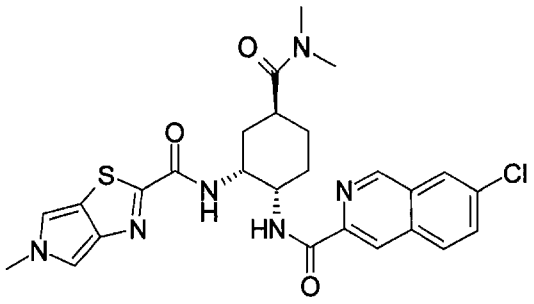
The title compound was obtained by reducing the compound obtained in Referential Example 252, condensing the reduction product with p-chlorophenoxyacetic acid and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 223.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.47(1H,m),1.55-1.90(5H,m), 2.77(3H,s),2.92(3H,s),2.96(3H,s),2.98-3.10(1H,m), 3.10-3.80(3H,m),3.85-3.95(1H,m),4.35-4.50(4H,m), 4.50-4.80(1H,br),6.85(2H,d,J=8.5Hz),7.15-7.35(1H,br), 7.88-8.03(1H,br),8.46(1H,d,J=8.8Hz),11.30-11.65(1H,br).

MS (FAB) m/z: 534$(M+H)^+$.

[Example 299]

7-Chloro-N-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5H-pyrrolo[3,4-d]thiazol-2-yl)carbonyl]amino}-cyclohexyl)-3-isoquinolinecarboxamide hydrochloride:



The title compound was obtained by condensing the

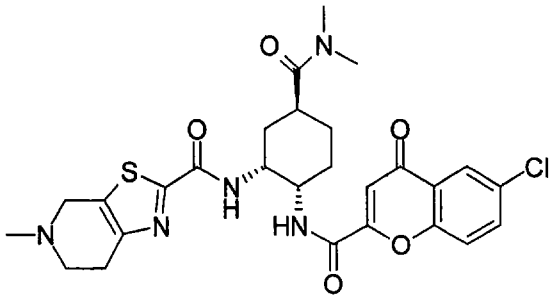
lithium salt of the carboxylic acid obtained by hydrolyzing the compound obtained in Referential Example 413 with a compound obtained by deprotecting the the compound obtained in Referential Example 146 by an acid treatment and treating the condensation product with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ: 1.00-1.11(2H,m),1.45-1.60(1H,m), 1.65-1.85(1H,m),1.95-2.06(1H,m),2.10-2.24(1H,m),2.78(3H,s), 2.87-3.02(1H,m),2.94(3H,s),3.88(3H,s),4.16-4.27(1H,m),4.45-4.56(1H,m),7.03(1H,s),7.55(1H,s), 7.87(1H,br d,J=8.3Hz),8.24(1H,br d,J=8.8Hz),8.33(1H,s), 8.59(1H,s),8.85(1H,br d,J=7.6Hz),9.01(1H,br d,J=7.8Hz), 9.28(1H,s).

MS (ESI) m/z: 539$(M+H)^+$.

[Example 300]

N-{(1R,2S,5S)-2-{[(6-Chloro-4-oxo-4H-chromen-2-yl)-carbonyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained by condensing a compound obtained by treating the compound in Referential Example 417 with a 4N dioxane solution of hydrochloric

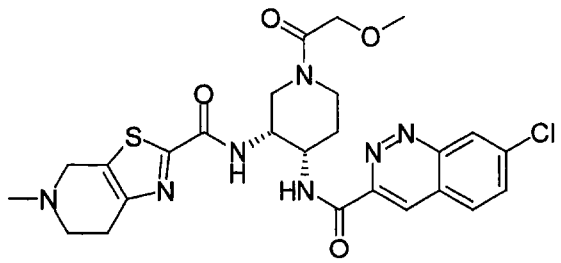
acid with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.40-1.53(1H,m),1.67-2.04(5H,m), 2.40-2.53(1H,m),2.80(3H,s),2.92(3H,s),3.01(3H,s), 3.09-3.22(3H,m),3.66-3.77(1H,m),4.01-4.10(1H,m), 4.34-4.49(1H,m),4.58-4.76(2H,m),6.80(1H,d,J=4.9Hz), 7.59-7.70(1H,m),7.90-8.00(1H,m),7.96(1H,s),8.52-8.60(1H,m), 8.80-8.90(1H,m),11.10-11.25(0.5H,br),11.40-11.55(0.5H,br).

MS (ESI) m/z: 572$(M+H)^+$.

[Example 301]

7-Chloro-N-((3R,4S)-1-(2-methoxyacetyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)-carbonyl]amino}piperidin-4-yl)-3-cinnolinecarboxamide hydrochloride:



The title compound was obtained by condensing a compound obtained by treating the compound obtained in Referential Example 418 with a 4N dioxane solution of hydrochloric acid with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid in a similar manner to the

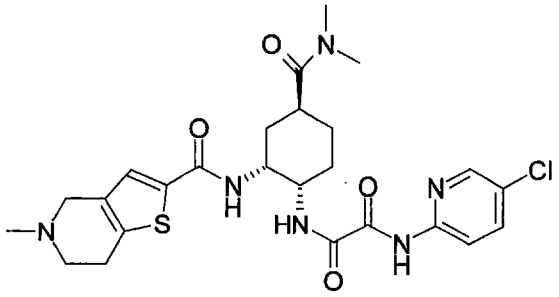
process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.70-1.80(1H,m),1.85-2.05(1H,m),
2.90(3H,s),3.00-3.20(2H,m),3.16(3H,s),3.22-3.82(7H,m),
3.88-4.80(5H,m),7.09(1H,d,J=9.0Hz),7.17(1H,dd,J=8.8,1.9Hz),
7.42(1H,d,J=8.8Hz),7.70(1H,d,J=1.9Hz),8.29(1H,br s),
8.40-8.50(1H,m),11.20-11.50(1H,br m),11.85(1H,s).

MS (ESI) m/z: 558$(M+H)^+$.

[Example 302]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-
[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-
tetrahydrothieno[3,2-c]pyridin-2-yl)carbonyl]amino}-
cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by deprotecting the compound obtained in Referential Example 421 with hydrochloric acid, methylating the deprotected compound in a similar manner to the process described in Example 18 and treating it with hydrochloric acid.

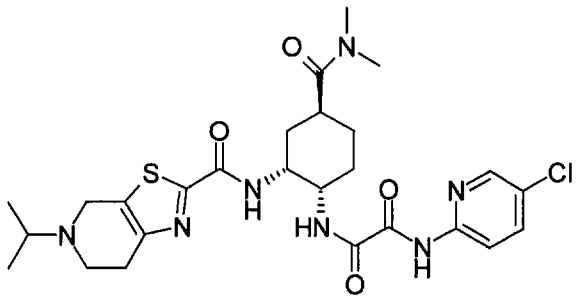
$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.58(1H,m),1.59-1.80(3H,m),
1.83-1.95(1H,m),1.97-2.10(1H,m),2.78(3H,s), 2.89(3H,s),
2.96(3H,s),3.00-3.10(1H,m),3.10-3.20(2H, m),
3.45-3.80(1H, m),3.90-4.00(2H,m),4.00-4.50(3H,m),
7.77(1H,s),7.95-8.05(3H,m),8.44(1H,t,J=1.6Hz),

8.90(1H,d,J=8.6Hz),10.25(1H,s),11.12(1H,br s).

MS (ESI) m/z: 547$(M+H)^+$.

[Example 303]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-isopropyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino-cyclohexyl)ethanediamide hydrochloride:



The title compound was obtained by condensing the compound obtained in Referential Example 418 with the compound obtained in Referential Example 420 and then treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 2.

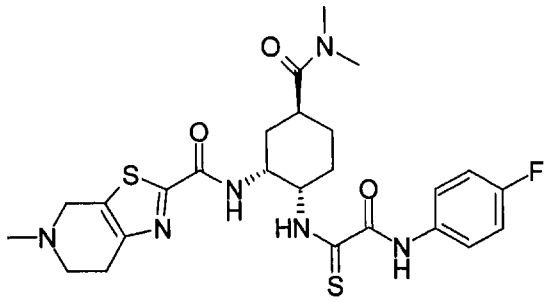
$^1$H-NMR (DMSO-$d_6$) δ: 1.30-1.40(6H,m),1.38-1.58(1H,m),1.59-1.82(3H,m),1.95-2.13(2H,m),2.40-2.65(1H,m),2.49(3H,s),2.87-3.55(4H,m),2.49(3H,s),3.60-3.82(2H,m),3.93-4.04(1H,m),4.37-4.55(2H,m),4.55-4.72(1H,m),7.94-8.10(2H,m),8.43(1H,s),8.64-8.77(1H,m),9.12(1/2H,d,J=7.8Hz),9.24(1/2H,d,J=7.8Hz),10.22(1/2H,s),10.26(1/2H,s),11.25(1/2H,br s),11.44(1/2H,br s).

MS (FAB) m/z: 578$(M+H)^+$.

[Example 304]

N-((1R,2S,5S)-5-[(Dimethylamino)carbonyl]-2-{[2-(4-

fluoroanilino)-2-oxoethanethioyl]amino}cyclohexyl)-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 424 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

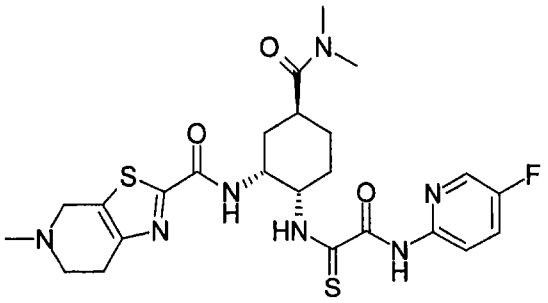
$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m),1.60-1.80(3H,m), 2.00-2.10(1H,m),2.20-2.35(1H,m),2.79(3H,s),2.93(3H,s), 2.95(3H,s),2.95-3.10(1H,m),3.10-3.30(2H,m),3.40-3.60(1H,m), 3.60-3.80(1H,m),4.35-4.50(1H,m),4.50-4.60(1H,m), 4.60-4.80(2H,m), 7.20(2H,t,J=8.8Hz), 7.77(2H,dd,J=9.0,5.1Hz), 8.80(1H,br),10.42(1H,s), 10.93(1H,br), 11.28(1H,br).

MS (ESI) m/z: 547$(M+H)^+$.

[Example 305]

N-[(1R,2S,5S)-5-[(Dimethylamino)carbonyl]-2-({2-[(5-fluoropyridin-2-yl)amino]-2-oxoethanethioyl}amino)-

cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



The title compound was obtained by treating the compound obtained in Referential Example 427 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

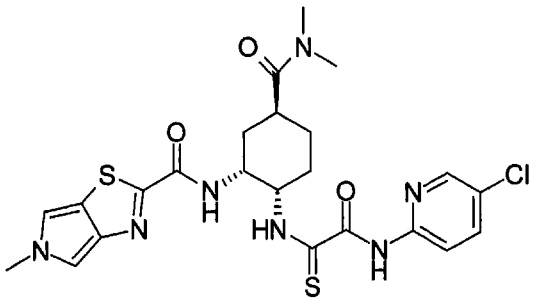
$^1$H-NMR (DMSO-$d_6$) δ: 1.43-1.57(1H,m),1.64-1.87(3H,m), 2.00(1H,br s),2.17-2.34(1H,m),2.78(3H,s),2.90(3H,s), 2.95(3H,s),2.95-3.10(1H,m), 3.10-3.30(2H,m), 3.40-3.60(1H,m), 3.68(1H,br s),4.44(1H,br s),4.45-4.56(1H,m),4.60-4.73(2H,m),7.80-7.90(1H,m),8.08(1H,dd,J=9.1,3.9Hz), 8.41(1H,d,J=2.9Hz),8.79(1H,d,J=6.6Hz),10.49(1H,s), 11.07(1H,br s),11.69(1H,br).

MS (ESI) m/z: 548$(M+H)^+$.

[Example 306]

N-{(1R,2S,5S)-2-({2-[(5-Chloropyridin-2-yl)amino]-2-oxoethanethioyl}amino)-5-[(dimethylamino)carbonyl]-

cyclohexyl}-5-methyl-5H-pyrrolo[3,4-d]thiazole-2-carboxamide:



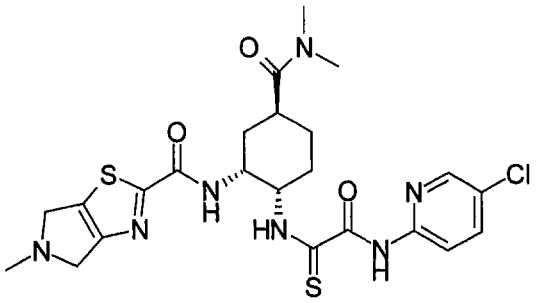
The title compound was obtained by treating the compound obtained in Referential Example 428 with hydrochloric acid to deprotect it and then condensing the deprotected compound with the compound obtained in Referential Example 293 in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.58(1H,m),1.63-1.73(2H,m),1.73-1.87(2H,m),2.00-2.10(1H,m),2.20-2.35(1H,m),2.79(3H,s), 2.95(3H,s),2.96-3.10(1H,m),3.89(3H,s),4.48-4.58(1H,m),4.60-4.70(1H,m),7.05(1H,d,J=1.7Hz), 7.55(1H,d,J=1.7Hz),8.00(1H,dd,J=8.9,2.4Hz), 8.05(1H,d,J=8.9Hz),8.44(1H,d,J=2.4Hz),8.71(1H,d,J=7.3Hz), 10.57(1H,s), 11.13(1H,d,J=7.8Hz).

MS (FAB) m/z: 548$(M+H)^+$.

[Example 307]

N-{(1R,2S,5S)-2-({2-[(5-Chloropyridin-2-yl)amino]-2-oxoethanethioyl}amino)-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-5,6-dihydro-4H-pyrrolo[3,4-d]-thiazole-2-carboxamide hydrochloride:



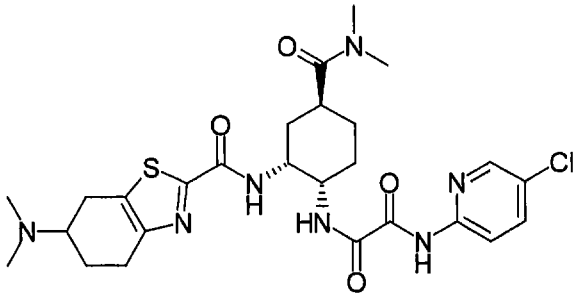
The title compound was obtained by treating the compound obtained in Referential Example 428 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 293 under an argon atmosphere and then subjecting the condensation product to a hydrochloric acid treatment again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.58(1H,m),1.65-1.87(3H,m), 1.97-2.10(1H,m),2.17-2.30(1H,m),2.80(3H,s),2.96(3H,s), 2.98-3.10(1H,m),3.07(3H,s),4.30-5.00(6H,m),8.00-8.10(1H,m), 8.46(1H,d,J=2.4Hz),8.79(1H,t,J=7.3Hz),10.54(1H,s), 11.04(1H,d,J=7.8Hz),12.24(1H,br s).

MS (ESI) m/z: 550$(M+H)^+$.

[Example 308]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-({[6-(dimethylamino)-4,5,6,7-tetrahydrobenzothiazol-2-yl]carbonyl}amino)cyclohexyl]-ethanediamide:



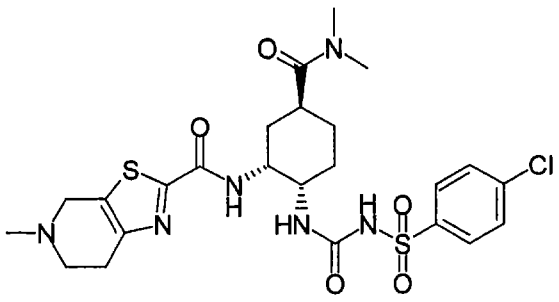
The title compound was obtained by deprotecting the compound obtained in Referential Example 431 with hydrochloric acid, methylating the deprotected compound in a similar manner to the process described in Example 18 and treating it with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ: 1.42-1.58(1H,m),1.59-1.80(3H,m),1.90-2.12(3H,m),2.30-2.45(1H,m),2.70-3.00(11H,m),2.92(3H,s),3.00-3.20(2H,m),3.25-3.45(1H,m),3.63-3.80(1H,m),3.88-4.02(1H,m),4.35-4.47(1H,m),8.02(1H,s),8.42-8.55(1H,m),8.60-8.68(1H,m),8.93(1H,dd,J=14.5,8.2Hz),9.19(1H,dd,J=17.7,8.2Hz),10.28(1H,s),10.91(1H,br s).

MS (ESI) m/z: 576$(M+H)^+$.

[Example 309]

N-{(1R,2S,5S)-2-[({[(4-Chlorophenyl)sulfonyl]amino}-carbonyl)amino]-5[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridine-2-carboxamide hydrochloride:



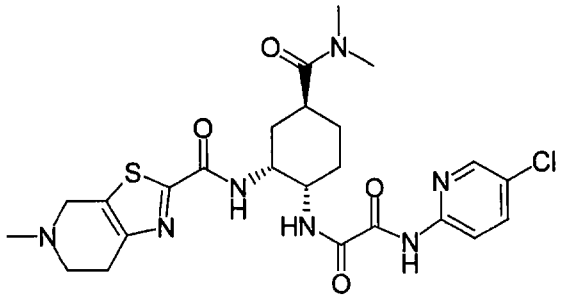
4-Chlorophenylsulfonyl isocyanate (148 μl) was added to a solution of the compound (328.0 mg) obtained in Referential Example 253 in methylene chloride (10 ml), and the mixture was stirred at room temperature for 24 hours. The solvent was distilled off under reduced pressure, and residue was purified by preparative thin-layer column chromatography on silica gel (methylene chloride:methanol = 9:1). The thus-obtained product was dissolved in ethanol (2 ml) and methylene chloride (2 ml), and a 1N ethanol solution (0.25 ml) of hydrochloric acid was added to stir the mixture at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and the residue was solidified with diethyl ether to obtain the title compound (104.3 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.25-1.45(1H,m),1.45-1.80(5H,m), 2.76(3H,s),2.94(3H,s),2.97(3H,s),3.00-3.80(6H,m), 4.35-4.85(3H,m),6.53(1H,brs),7.66(2H,d,J=8.5Hz), 7.86(2H,d,J=8.5Hz),8.50-8.82(1H,m),10.64(1H,br s), 11.10-11.80(1H,br).

MS (ESI) m/z: 583$(M+H)^+$.

[Example 310]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide:



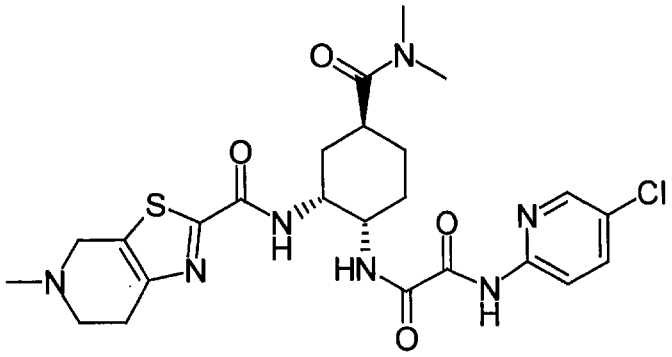
The title compound was obtained from the compound obtained in Referential Example 435 and the compound obtained in Referential Example 10 in a similar manner to Example 2.

$^1$H-NMR ($CDCl_3$) δ: 1.60-1.98(3H,m),2.00-2.16(3H,m), 2.52(3H,s),2.78-2.90(3H,m),2.92-2.98(2H,m),2.95(3H,s), 3.06(3H,s),3.69(1H,d,J=15.4Hz),3.75(1H,d,J=15.4Hz), 4.07-4.15(1H,m),4.66-4.72(1H,m),7.40(1H,d,J=8.8,0.6Hz), 7.68(1H,dd,J=8.8,2.4Hz),8.03(1H,d,J=7.8Hz), 8.16(1H,dd,J=8.8,0.6Hz),8.30(1H,dd,J=2.4,0.6Hz),9.72(1H,s).

MS (ESI) m/z: 548$(M+H)^+$.

[Example 311]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide p-toluenesulfonate monohydrate:



The compound (6.2 g) obtained in Example 310 is dissolved in methylene chloride (120 ml), a 1 mol/L ethanol solution (11.28 ml) of p-toluenesulfonic acid was added to the solution, and the solvent was distilled off. Ethanol (95 ml) containing 15% water was added to the residue, and the mixture was stirred at 60°C to dissolve it. The solution was then cooled to room temperature and stirred for a day. Crystals deposited were collected by filtration, washed with ethanol and dried at room temperature for 2 hours under reduced pressure to obtain the title compound (7.4 g).

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.54(1H,m),1.66-1.78(3H,m),2.03-2.10(2H,m),2.28(3H,s),2.79(3H,s),2.91-3.02(1H,m), 2.93(3H,s),2.99(3H,s),3.13-3.24(2H,m),3.46-3.82(2H,m), 3.98-4.04(1H,m),4.43-4.80(3H,m),7.11(2H,d,J=7.8Hz), 7.46(2H,d,J=8.2Hz),8.01(2H,d,J=1.8Hz),8.46(1H,t,J=1.8Hz), 8.75(1H,d,J=6.9Hz),9.10-9.28(1H,br),10.18(1H,br), 10.29(1H,s).

MS (ESI) m/z: 548$(M+H)^+$.

Elemental analysis: $C_{24}H_{30}ClN_7O_4S \cdot C_7H_8O_3S \cdot H_2O$.

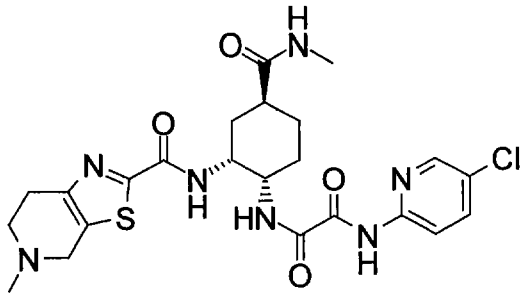
Calculated: C;50.43,H;5.46,N;13.28,Cl;4.80,S;8.69.

Found: C;50.25,H;5.36,N;13.32,Cl;4.93,S;8.79.

mp(decomposed): 245～248°C.

[Example 312]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(methylamino)-carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazoro[5,4-c]-pyridin-2-yl)carbonyl]amino}cyclohexyl)ethanediamide hydrochloride:



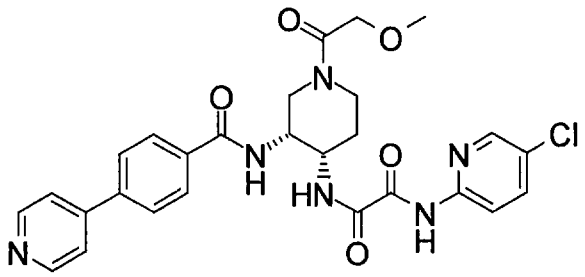
The title compound was obtained by treating the compound obtained in Referential Example 437 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.48-1.61(1H,m), 1.61-1.74(2H,m), 1.74-1.82(1H,m), 1.98-2.12(2H,m), 2.29-2.38(1H,m), 2.53(3H,d,J=4.2Hz), 2.92(3H,s), 3.10-3.40(4H,br), 3.40-3.80(1H,br), 3.97-4.05(1H,m), 4.28-4.34(1H,m), 4.34-4.80(1H,br), 7.70-7.78(1H,m), 7.97-8.07(2H,m), 8.43-8.50(1H,m), 8.49(1H,br.s), 9.27(1H,d,J=7.8Hz), 10.26(1H,br.s), 11.48(1H,br.s).

MS (ESI) m/z: 534[$(M+H)^+$,$Cl^{35}$], 535[$(M+H)^+$,$Cl^{37}$].

[Example 313]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((3R,4S)-1-(2-methoxyacetyl)-3-{[4-(pyridin-4-yl)benzoyl]amino}piperidin-4-yl)ethanediamide hydrochloride:



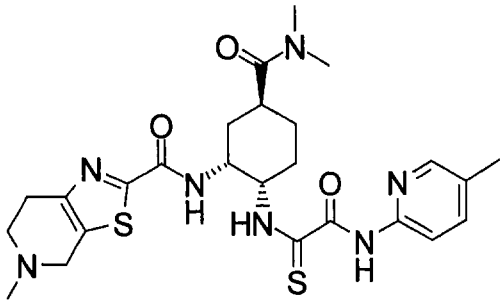
The title compound was obtained by treating the compound obtained in Referential Example 368 with a 4N dioxane solution of hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 237 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.62-1.75(1H,m), 2.00-2.20(1H,m), 2.80-4.40(11H,m), 7.90-8.00(4H,m), 8.05-8.13(2H,m), 8.14-8.43(3H,m), 8.40-8.45(1H,m), 8.87-9.04(3H,m), 10.20-10.50(2H,br).

MS (FAB) m/z: 551[$(M+H)^+$,$Cl^{35}$], 553[$(M+H)^+$,$Cl^{37}$].

[Example 314]

N-{(1R,2S,5S)-5-[(Dimethyamino)carbonyl]-2-({2-[(5-methylpyridin-2-yl)amino]-2-oxoethanethioyl}amino)-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-carboxamide hydrochloride:



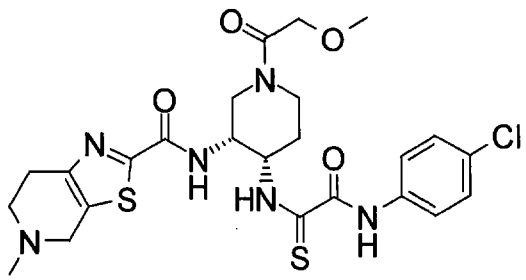
The title compound was obtained by treating the compound obtained in Referential Example 440 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.45-1.60(1H,m), 1.65-1.90(3H,m), 2.00-2.10(1H,m), 2.20-2.40(1H,m), 2.28(3H,s), 2.80(3H,s), 2.91(3H,s), 2.95-3.10(1H,m), 2.96(3H,s), 3.15-3.30(1H,m), 3.32(2H,s), 3.50-3.80(1H,m), 4.45-4.60(2H,m), 4.60-4.80(2H,m), 7.72(1H,d,J=8.5Hz), 7.97(1H,d,J=8.5Hz), 8.23(1H,s), 8.83(1H,d,J=7.3Hz), 10.38(1H,s), 11.06(1H,d,J=7.6Hz), 11.49(1H,br.s).

MS (ESI) m/z: 544$(M+H)^+$.

[Example 315]

N-[(3R,4S)-4-{[2-(4-Chloroanilino)-2-oxoethanethioyl]-amino}-1-(2-methoxyacetyl)pyperidin-3-yl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-carboxamide hydrochloride:



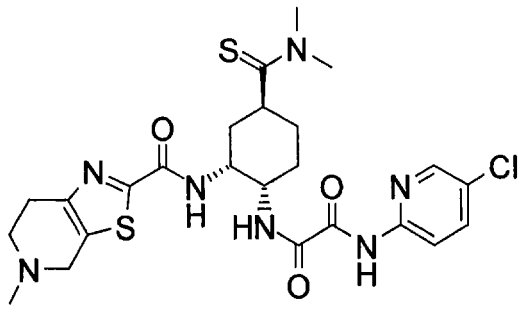
The title compound was obtained by treating the compound obtained in Referential Example 441 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.71-1.82(1H,m), 2.18-2.44(1H,m), 2.89(3H,s), 3.00-4.85(17H,m), 7.41(2H,d,J=8.8Hz), 7.77(2H,d,J=8.8Hz), 8.48-8.73(1H,m), 10.48(1H,br.s), 10.90-11.06(1H,m), 11.45-11.90(1H,br).

MS (ESI) m/z: 565[$(M+H)^+$,$Cl^{35}$], 567[$(M+H)^+$,$Cl^{37}$].

[Example 316]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbothioyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexyl)ethanediamide hydrochloride:



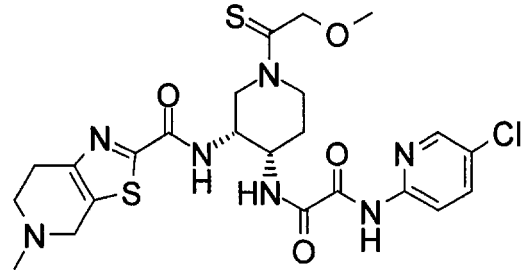
The title compound was obtained by condensing the compound obtained in Referential Example 445 with the compound obtained in Referential Example 10 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 3.

$^1$H-NMR (DMSO-$d_6$) δ: 1.66-2.15(6H,m), 2.93(3H,s), 3.15-3.40(9H,m), 3.49(1H,br.s), 3.71(1H,br.s), 3.97-4.01(1H,m), 4.42(2H,br.s), 4.70(1H,br.s), 8.01(2H,br.s), 8.46(1H,br.s), 8.78(1H,d,J=6.8Hz), 9.24(1H,br.s), 10.28(1H,s), 11.29(1H,br.s).

MS (FAB) m/z: 564[$(M+H)^+$,$Cl^{35}$], 566[$(M+H)^+$,$Cl^{37}$].

[Example 317]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((3R,4S)-1-(2-methoxyethanethioyl)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-piperidin-4-yl)ethanediamide hydrochloride:



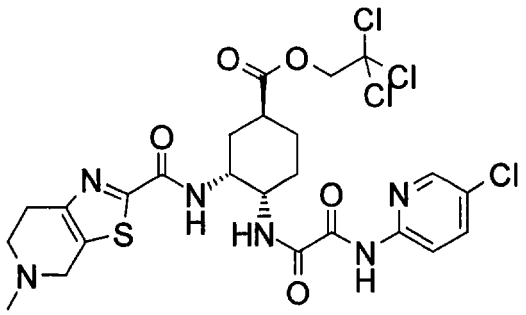
The title compound was obtained by treating the compound obtained in Referential Example 448 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in Referential Example 10 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR (DMSO-$d_6$) δ: 1.74-1.85(1H,m), 2.13-2.35(1H,m), 2.89(3H,s), 2.95-3.98(9H,m), 4.05-5.33(8H,m), 7.95-8.06(2H,m), 8.43(1H,s), 8.48-8.73(1H,br), 9.29-9.45(1H,br), 10.21-10.34(1H,br), 11.45-11.90(1H,br).

MS (ESI) m/z: 566[$(M+H)^+$,$Cl^{35}$], 568[$(M+H)^+$,$Cl^{37}$].

[Example 318]

2,2,2-Trichloroethyl (1S,3R,4S)-4-({2-[(5-Chloropyridin-2-yl)amino]-2-oxoacetyl}amino)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexanecarboxylate:



The title compound was obtained by treating the compound obtained in Referential Example 453 with hydrochloric acid to deprotect it, condensing the deprotected compound with the compound obtained in

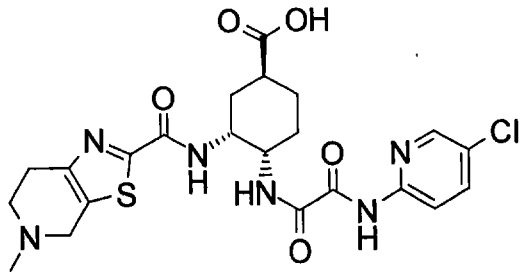
Referential Example 10 and then treating the condensation product with hydrochloric acid again in a similar manner to the process described in Example 219.

$^1$H-NMR ($CDCl_3$) δ: 1.60-1.87(2H,m), 2.04-2.15(2H,m), 2.21-2.32(2H,m), 2.52(3H,s), 2.73-2.89(3H,m), 2.92-2.98(2H,m), 3.71(1H,d,J=15.4Hz), 3.73(1H,d,J=15.4Hz), 4.08-4.16(1H,m), 4.66-4.71(1H,m), 4.72(1H,d,J=12.0Hz), 4.82(1H,d,J=12.0Hz), 7.37(1H,d,J=8.8Hz), 7.69(1H,dd,J=8.8,2.4Hz), 8.05(1H,d,J=8.1Hz), 8.16(1H,d,J=8.8Hz), 8.30(1H,d,J=2.4Hz), 9.69(1H,s).

MS (ESI) m/z: 651[$(M+H)^+$,3x$Cl^{35}$], 653[$(M+H)^+$,2x$Cl^{35}$,$Cl^{37}$], 655[$(M+H)^+$,$Cl^{35}$,2x$Cl^{37}$].

[Example 319]

(1S,3R,4S)-4-({2-[5-Chloropyridin-2-yl]amino}-2-oxoacetyl)amino)-3-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]amino}-cyclohexane carboxylic acid:



The compound (475 mg) obtained in Example 318 was dissolved in tetrahydrofuran (50 ml), zinc (2.85 g) and acetic acid (5.7 ml) were successively added to the solution, and the mixture was stirred at room temperature for 3 hours. Celite 545 (2.85 g) was added to the reaction

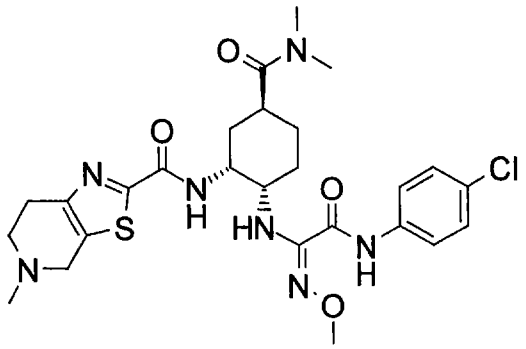
mixture to remove insoluble matter by filtration. After the filtrate was concentrated under reduced pressure, methylene chloride was added to the resultant residue, and a 1N aqueous solution of sodium hydroxide was added with stirring to adjust the pH of the reaction mixture to 7. After an organic layer was separated, saturated saline (50 ml) was added to a water layer to conduct extraction with methylene chloride. The resultant organic layers were combined and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure, and the resultant residue was purified by column chromatography on silica gel (methylene chloride:methanol = 95:5 → 9:1 → 4:1) to obtain the title compound (140 mg).

$^1$H-NMR (DMSO-$d_6$) δ: 1.50-1.80(3H,m), 1.84-1.95(1H,m), 1.95-2.10(1H,m), 2.15-2.30(1H,m), 2.38(3H,s), 2.40-2.50(1H,m), 2.67-2.80(2H,m), 2.80-2.95(2H,m), 3.66(2H,m), 4.03(1H,br.s), 4.33(1H,br.s), 7.97-8.10(2H,m), 8.45(1H,s), 8.53(1H,d,J=6.8Hz), 9.19(1H,d,J=8.3Hz), 10.27(1H,br.s).

MS (FAB) m/z: 521[$(M+H)^+$,$^{35}$Cl], 523[$(M+H)^+$,$^{37}$Cl].

[Example 320]

N-{(1R,2S,5S)-2-{[2-(4-Chloroanilino)-1-methoxyimino-2-oxoethyl]amino}-5-[(dimethylamino)carbonyl]cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-carboxamide hydrochloride:



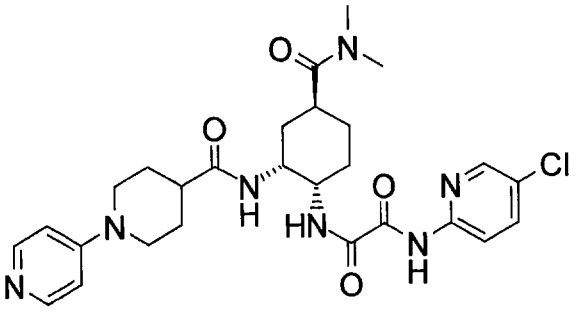
The title compound was obtained by hydrolyzing an ester of the compound obtained in Referential Example 454 in a similar manner to the process described in Example 142, condensing the hydrolyzate with 4-chloroaniline in a similar manner to the process described in Referential Example 143 and then treating the condensation product with hydrochloric acid.

$^1$H-NMR (DMSO-$d_6$) δ: 1.30-1.17(1H,m), 1.50-1.62(1H,m), 1.62-1.75(2H,m), 1.85-2.00(2H,m), 2.76(3H,s), 2.93(6H,br.s), 3.00-3.10(1H,m), 3.18(1H,br.s), 3.27(1H,br.s), 3.49(1H,br.s), 3.71(1H,br.s), 3.76(3H,s), 3.93(1H,br.s), 4.35-4.50(2H,m), 4.66-4.77(1H,m), 6.09(0.5H,d,J=7.8Hz), 6.19(0.5H,d,J=7.8Hz), 7.38(2H,d,J=8.8Hz), 7.71(2H,d,J=8.8Hz), 8.70-8.79(1H,m), 10.28(1H,d,J=11.0Hz), 11.53(0.5H,br.s), 11.45(0.5H,br.s).

MS (FAB) m/z: 576[$(M+H)^+$,$^{35}$Cl], 578[$(M+H)^+$,$^{37}$Cl].

[Example 321]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-[(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-({[1-(pyridin-4-yl)piperidin-4-yl]carbonyl}amino)cyclohexyl]ethanediamide hydrochloride:



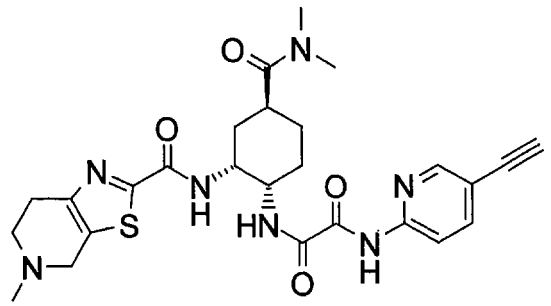
The title compound was obtained by condensing the compound obtained in Referential Example 420 with 1-(pyridin-4-yl)piperidine-4-carboxylic acid (wO96/10022) and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.35-1.49(1H,m), 1.49-1.78(6H,m), 1.78-1.98(3H,m), 2.75-2.90(1H,m), 2.78(3H,s), 3.02(3H,s), 3.03-3.14(1H,m), 3.14-3.28(2H,m), 3.74-3.85(1H,m), 4.13-4.30(3H,m), 7.18(2H,d,J=7.3Hz), 7.99(2H,s), 8.10-8.23(3H,m), 8.41(1H,s), 8.50(1H,d,J=8.1Hz), 10.19(1H,s), 13.73(1H,br.s).

MS (FAB) m/z: 556[$(M+H)^+$,$^{35}$Cl], 558[$(M+H)^+$,$^{37}$Cl].

[Example 322]

$N^1$-((1S,2R,4S)-4-[(Dimethylamino)carbonyl]-2-{[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-amino}cyclohexyl)-$N^2$-(5-ethynylpyridin-2-yl)ethanediamide:



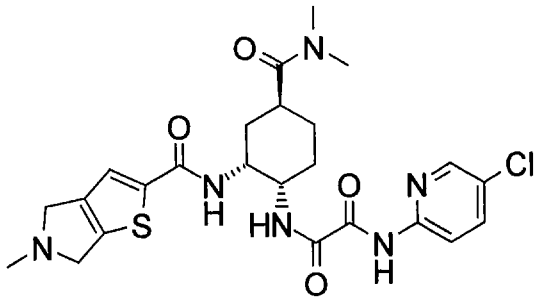
The compound (348 mg) obtained in Referential Example 455 was dissolved in tetrahydrofuran (14 ml), tetrabutylammonium fluoride (1N tetrahydrofuran solution, 628 μl) was added to the solution, and the mixture was stirred at room temperature for 30 minutes. The reaction mixture was decolored with activated carbon (about 1 g) and dried over anhydrous sodium sulfate. After filtration, the solvent was distilled off under reduced pressure, and the residue was purified by column chromatography on silica gel (methylene chloride:methanol = 93:7) and then dissolved in methylene chloride (about 1 ml). Hexane (about 10 ml) was added to the solution, and precipitate formed was collected by filtration to obtain the title compound (116 mg).

$^1$H-NMR ($CDCl_3$) δ: 1.62-2.14(8H,m), 2.52(3H,s), 2.79-2.95(6H,m), 3.05(3H,s), 3.19(1H,s), [AB pattern 3.71(1H,d,J=15.5Hz), 3.74(1H,d,J=15.5Hz)], 4.08-4.14(1H,m), 4.66-4.69(1H,m), 7.41(1H,d,J=8.6Hz), 7.80(1H,dd,J=8.6,2.2Hz), 8.03(1H,d,J=7.6Hz), 8.15(1H,d,J=8.6Hz), 8.46(1H,d,J=2.2Hz), 9.75(1H,s).

MS (ESI) m/z: 538$(M+H)^+$.

[Example 323]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-((1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-{[(5-methyl-5,6-dihydro-4H-thieno[2,3-c]pyrrol-2-yl)carbonyl]amino}cyclohexyl)-ethanediamide:



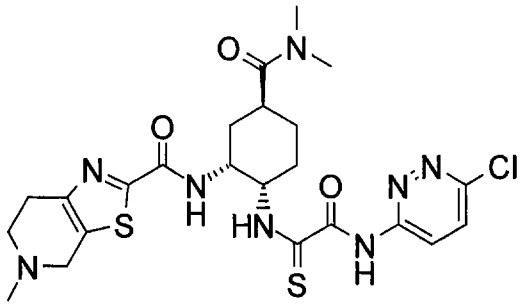
The title compound was obtained by hydrolyzing the compound obtained in Referential Example 456 and condensing the hydrolyzate with the compound obtained in Referential Example 420 in a similar manner to the process described in Example 191.

$^1$H-NMR ($CDCl_3$) δ: 1.80-2.15(6H,m), 2.64(3H,s), 2.76-2.79(1H,m), 2.94(3H,s), 3.03(3H,s), 3.84-3.86(2H,m), 3.94-3.99(3H,m), 4.58-4.59(1H,m), 6.70(1H,d,J=6.3Hz), 7.31(1H,s), 7.70(1H,dd,J=8.8,2.3Hz), 8.15-8.18(2H,m), 8.30(1H,d,J=2.3Hz), 9.72(1H,br.s).

MS (FAB) m/z: 533[$(M+H)^+$,$Cl^{35}$], 535[$(M+H)^+$,$Cl^{37}$].

[Example 324]

N-{(1R,2S,5S)-2-({2-[6-Chloropyridazin-3-yl]amino}-2-oxoethanethioyl)amino}-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]-pyridin-2-carboxamide hydrochloride:



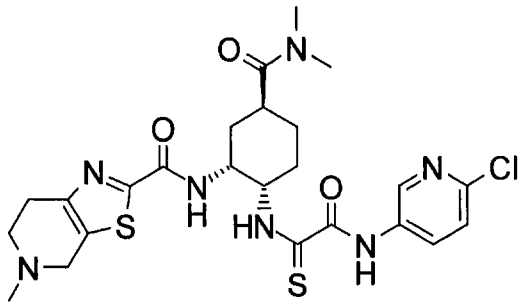
The title compound was obtained by condensing the compound obtained in Referential Example 460 with the compound obtained in Referential Example 10 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 3.

$^1$H-NMR (DMSO-$d_6$) δ: 1.48-1.51(1H,m), 1.71-1.79(3H,m), 2.00(1H,br.s), 2.20-2.23(1H,m), 2.78(3H,s), 2.90(3H,s), 2.96(3H,s), 3.05(1H,br.s), 3.16-3.47(3H,m), 3.69(1H,br.s), 4.43(1H,br.s), 4.53(1H,br.s), 4.69(2H,br.s), 7.97(1H,d,J=9.6Hz), 8.32(1H,d,J=9.6Hz), 8.73(1H,d,J=7.3Hz), 11.08(2H,br.s), 11.61-11.75(1H,m).

MS (FAB) m/z: 565[$(M+H)^+$,$Cl^{35}$], 567[$(M+H)^+$,$Cl^{37}$].

[Example 325]

N-{(1R,2S,5S)-2-({2-[(6-Chloropyridin-3-yl)amino]-2-oxoethanethioyl}amino)-5-[(dimethylamino)carbonyl]-cyclohexyl}-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-carboxamide hydrochloride:



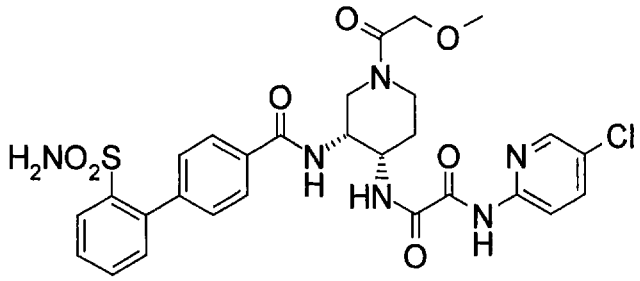
The title compound was obtained by condensing the compound obtained in Referential Example 464 with the compound obtained in Referential Example 10 and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 3.

$^1$H-NMR (DMSO-$d_6$) δ: 1.47-1.55(1H,m), 1.66-1.78(3H,m), 2.02-2.05(1H,m), 2.21-2.33(1H,m), 2.79(3H,s), 2.91(3H,s), 2.95(3H,s), 2.99-3.04(1H,m), 3.21(2H,br.s), 3.45-3.75(2H,br), 4.40-4.75(4H,m), 7.53(1H,d,J=8.6Hz), 8.20(1H,dd,J=8.6,2.6Hz), 8.77(1H,d,J=7.3Hz), 8.80(1H,d,J=2.6Hz), 10.73(1H,s), 10.94(1H,br.d,J=7.6Hz), 11.37(1H,br.s).

MS (FAB) m/z: 564[$(M+H)^+$,$Cl^{35}$], 566[$(M+H)^+$,$Cl^{37}$].

[Example 326]

$N^1$-[(3R,4S)-3-({[2'-(Aminosulfonyl)[1,1'-biphenyl]-4-yl]-carbonyl}amino)-1-(2-methoxyacetyl)piperidin-4-yl]-$N^2$-(5-chloropyridin-2-yl)ethanediamide:



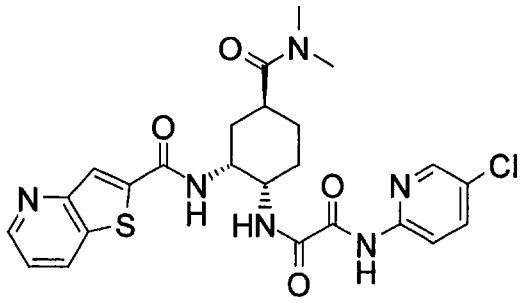
The title compound was obtained by treating the compound obtained in Referential Example 368 with hydrochloric acid to deprotect it and then condensing the deprotected compound with the compound obtained in Referential Example 465 in a similar manner to the process described in Example 219.

$^1$H-NMR ($CDCl_3$) δ: 1.59-1.85(1H,m), 2.09-2.23(1H,m), 2.88-3.13(1H,m), 3.29-3.51(4H,m), 4.06-4.20(4H,m), 4.51-4.78(4H,m), 7.09(0.25H,br.s), 7.30(1H,d,J=7.1Hz), 7.51-7.54(3.75H,m), 7.60(1H,t,J=7.0Hz), 7.69(1H,dd,J=8.9,2.2Hz), 7.94-7.96(2H,m), 8.13-8.22(2H,m), 8.30(1H,d,J=2.2Hz), 8.91(0.75H,br.d,J=5.9Hz), 9.18(0.25H,br.s), 9.70(1H,s).

MS (FAB) m/z: 629[$(M+H)^+$,$Cl^{35}$], 631[$(M+H)^+$,$Cl^{37}$]

[Example 327]

$N^1$-(5-Chloropyridin-2-yl)-$N^2$-{(1S,2R,4S)-4-[(dimethylamino)carbonyl]-2-[(thieno[3,2-b]pyridin-2-yl-carbonyl)amino]cyclohexyl}ethanediamide hydrochloride:



The title compound was obtained by condensing the compound obtained in Referential Example 420 with lithium thieno[3,2-b]pyridin-2-ylcarboxylate (Japanese Patent Application Laid-Open No. 2001-294572) and treating the condensation product with hydrochloric acid in a similar manner to the process described in Example 2.

$^1$H-NMR (DMSO-$d_6$) δ: 1.44-1.57(1H,m), 1.62-1.84(3H,m), 1.86-1.98(1H,m), 2.04-2.19(1H,m), 2.78(3H,s), 2.99(3H,s), 3.11-3.25(1H,m), 3.85-4.10(1H,br), 4.44-4.55(1H,br), 7.51-7.62(1H,m), 7.98(2H,br.s), 8.43(2H,br.s), 8.60(1H,s), 8.66(1H,br.d,J=8.1Hz), 8.81(1H,br.d,J=4.2Hz), 9.05(1H,br.d,J=7.8Hz), 10.24(1H,s).

MS (ESI) m/z: 529[$(M+H)^+$,$Cl^{35}$], 531[$(M+H)^+$,$Cl^{37}$].

[Test Example 1]

Determination of human FXa-inhibiting effect ($IC_{50}$ value):

5% DMSO solutions (10 μl) of each test compound, the concentrations of which were suitably set stepwise, Tris buffer (100 mM Tris, 200 mM potassium chloride, 0.2% BSA, pH 7.4) (40 μl) and 0.0625 U/ml human FXa (Enzyme Research Labolatories, Inc., dissolved and diluted with Tris buffer) (10 μl) were respectively put in wells of a 96-well microplate, and a 750 μM aqueous solution (40 μl) of S-2222 (Chromogenix Co.) was added. Absorbance at 405 nm was measured for 10 minutes at room temperature to determine an increase in absorbance (ΔOD/min). As a control, Tris buffer was used in place of the test

compound.

The percent inhibition (%) calculated using the following equation at the final concentration of the test compound and the final concentration of the test compound were plotted on the axis of ordinate and the axis of abscissa of logarithmic normal probability paper, respectively, to determine the 50 % inhibition dose ($IC_{50}$ value).

Percent inhibition (%) =

[1 - (ΔOD/min of test compound) ÷ (ΔOD/min of control)] x 100

(Result)

In Table 1, it is demonstrated that the compounds according to the present invention have a potent FXa-inhibiting effect.

Table 1

| Compound | Human FXa-inhibiting effect ($IC_{50}$): nM | Compound | Human FXa-inhibiting effect ($IC_{50}$): nM |
|---|---|---|---|
| Ex. 3 | 86 | Ex. 143 | 5.8 |
| Ex. 7 | 83 | Ex. 164 | 4.8 |
| Ex. 11 | 92 | Ex. 191 | 1.2 |
| Ex. 54 | 4.2 | Ex. 192 | 2.0 |
| Ex. 62 | 3.5 | Ex. 194 | 5.0 |
| Ex. 63 | 2.5 | Ex. 204 | 1.5 |
| Ex. 74 | 1.4 | Ex. 246 | 3.1 |
| Ex. 101 | 26 | Ex. 247 | 1.9 |
| Ex. 130 | 4.5 | Ex. 248 | 5.4 |
| Ex. 138 | 4.4 | | |

[Test Example 2]

Determination of anti-FXa activity in rat plasma after oral administration:

(A) Administration and blood collection:

A drug solution (1 mg/ml) obtained by dissolving or suspending a test compound (10 mg) in 0.5% methyl cellulose (MC) was orally administered to rats (10 ml/kg). After 0.5, 1, 2 and 4 hours from the drug administration, the blood (0.5 ml) was collected through the jugular vein using a syringe which is containing a 3.13% (w/v) aqueous solution (50 μl) of trisodium citrate dihydrate (amount of blood collected: 0.45 ml). For rats of a control group,

the same blood collection was conducted after a 0.5% MC solution was administered. Each blood sample was centrifuged at 1500 x g for 10 minutes at 4°C to separate plasma, and the plasma was preserved at -40°C until it was used in the following determination of anti-FXa activity in plasma.

(B) Determination of FXa-inhibiting activity in plasma:

In the determination of anti-FXa activity in plasma, S-2222 was used as a substrate. Tris buffer (100 mM Tris, 200 mM potassium chloride, 0.2% BSA, pH 7.4) (5456 μl), human FXa (2.5 U/ml, 44 μl) and water (550 μl) were mixed. The resultant human FXa solution was used in the following test.

Rat plasma (5 μl) obtained in accordance with the procedure (A) described above was put in wells of a 96-well microplate, and the above-described human FXa solution (55 μl) and a 750 μM aqueous solution (40 μl) of S-2222 were sequentially added. Immediately after that, absorbance at 405 nm was measured at room temperature by means of a spectrophotometer SPECTRAmax 340 or 190 (Molecular Devices Co., U.S.A.), thereby determining a rate of reaction (ΔOD/min).

The anti-FXa activity, i.e., percent inhibition (%) was calculated in accordance with the following equation:

Percent inhibition (%) =

[1 - (ΔOD/min of sample) ÷ (average value of ΔOD/min of the control group)] x 100

(Result)

The compounds described in Examples 63, 191, 192, 194 and 204 exhibited a potent FXa-inhibiting activity of 62 to 96% at an oral dose of 10 mg/kg.

INDUSTRIAL APPLICABILITY

The cyclicdiamine derivatives according to the present invention exhibit a potent inhibitory effect on activated blood coagulation factor X and are useful as medicines, activated blood coagulation factor X inhibitors, anticoagulants, agents for preventing and/or treating thrombosis or embolism, agents for preventing and/or treating thrombotic disease and agents for preventing and/or treating cerebral infarction, cerebral embolism, myocardial infarction, angina pectoris, pulmonary infarction, pulmonary embolism, Buerger's disease, deep venous thrombosis, disseminated intravascular coagulation syndrome, thrombus formation after valve or joint replacement, thrombus formation and reocclusion after angioplasty, systemic inflammatory response syndrome (SIRS), multiple organ dysfunction syndrome (MODS), thrombus formation during extracorporeal circulation, or blood clotting upon blood drawing.

CLAIMS

1. A compound represented by the general formula (1):

$$Q^1\text{-}Q^2\text{-}T^o\text{-}N(R^1)\text{-}Q^3\text{-}N(R^2)\text{-}T^1\text{-}Q^4 \qquad (1)$$

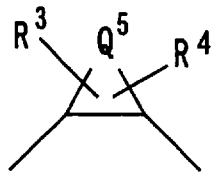
wherein

$R^1$ and $R^2$, independently of each other, represent a hydrogen atom, hydroxyl group, alkyl group or alkoxy group;

$Q^1$ represents a saturated or unsaturated, 5- or 6-membered cyclic hydrocarbon group which may be substituted, a saturated or unsaturated, 5- to 7-membered heterocyclic group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^2$ represents a single bond, a saturated or unsaturated, 5- or 6-membered divalent cyclic hydrocarbon group which may be substituted, a saturated or unsaturated, 5- to 7-membered divalent heterocyclic group which may be substituted, a saturated or unsaturated, divalent bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, divalent bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^3$ represents the following group:




in which $Q^5$ means an alkylene group having 1 to 8 carbon atoms, an alkenylene group having 2 to 8 carbon atoms, or a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or an integer of 1-3, and A means an oxygen atom, nitrogen atom, sulfur atom, -SO-, $-SO_2-$, -NH-, -O-NH-, -NH-NH-, -S-NH-, -SO-NH- or $-SO_2-NH-$, and $R^3$ and $R^4$ are substituents on carbon atom(s), nitrogen atom(s) or a sulfur atom(s) of a ring comprising $Q^5$ and are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, cyano group, cyanoalkyl group, amino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, alkoxyimino group, hydroxyimino group, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylalkylamino group, carboxyalkylamino group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may

have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, carbamoylalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, 3- to 6-membered heterocyclic carbonylalkyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, aryl group, aralkyl group, heteroaryl group, heteroarylalkyl group, alkylsulfonylamino group, arylsulfonylamino group, alkylsulfonylaminoalkyl group, arylsulfonylaminoalkyl group, alkylsulfonylaminocarbonyl group, arylsulfonylaminocarbonyl group, alkylsulfonyl-aminocarbonylalkyl group, arylsulfonylaminocarbonylalkyl group, oxo group, carbamoyloxy group, aralkyloxy group, carboxyalkyloxy group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group,

carboxyalkylsulfonyl group, alkoxycarbonylacyl group, alkoxyalkyloxycarbonyl group, hydroxyacyl group, alkoxyacyl group, halogenoacyl group, carboxyacyl group, aminoacyl group, acyloxyacyl group, acyloxyalkylsulfonyl group, hydroxyalkylsulfonyl group, alkoxyalkylsulfonyl group, 3- to 6-membered heterocyclic sulfonyl group which may be substituted, N-alkylaminoacyl group, N,N-dialkylaminoacyl group, N,N-dialkylcarbamoylacyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkylsulfonyl group which may have a substituent on the alkyl group(s), alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group, or $R^3$ and $R^4$, together with each other, denote an alkylene group having 1 to 5 carbon atoms, alkenylene group having 2 to 5 carbon atoms, alkylenedioxy group having 1 to 5 carbon atoms or carbonyldioxy group;

$Q^4$ represents an aryl group which may be substituted, an arylalkenyl group which may be substituted, an arylalkynyl group which may be substituted, a heteroaryl group which may be substituted, a heteroarylalkenyl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$T^0$ represents a carbonyl or thiocarbonyl group; and

$T^1$ represents a carbonyl group, sulfonyl group, group -C(=O)-C(=O)-N(R')-, group -C(=S)-C(=O)-N(R')-, group -C(=O)-C(=S)-N(R')-, group -C(=S)-C(=S)-N(R')-, in which R' means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group -C(=O)-$A^1$-N(R")-, in which $A^1$ means an alkylene group having 1 to 5 carbon atoms, which may be substituted, and R" means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group -C(=O)-NH-, group -C(=S)-NH-, group -C(=O)-NH-NH-, group -C(=O)-$A^2$-C(=O)-, in which $A^2$ means a single bond or alkylene group having 1 to 5 carbon atoms, group -C(=O)-$A^3$-C(=O)-NH-, in which $A^3$ means an alkylene group having 1 to 5 carbon atoms, group -C(=O)-C(=NO$R^a$)-N($R^b$)-, group -C(=S)-C(=NO$R^a$)-N($R^b$)-, in which $R^a$ means a hydrogen atom, alkyl group or alkanoyl group, and $R^b$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group -C(=O)-N=N-, group -C(=S)-N=N-, group -C(=NO$R^c$)-C(=O)-N($R^d$)-, in which $R^c$ means a hydrogen atom, alkyl group, alkanoyl group, aryl group or aralkyl group, and $R^d$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group -C(=N-N($R^e$)($R^f$))-C(=O)-N($R^g$)-, in which $R^e$ and $R^f$, independently of each other, mean a hydrogen atom, alkyl group, alkanoyl group or alkyl(thiocarbonyl) group, and $R^g$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, or thiocarbonyl group;

a salt thereof, a solvate thereof, or an N-oxide thereof.

2. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 1, wherein the group $Q^4$ in the formula (1) is a group selected from the group consisting of a phenyl group which may be substituted, a naphthyl group which may be substituted, an anthryl group which may be substituted, a phenanthryl group which may be substituted, a styryl group which may be substituted, a phenylethynyl group which may be substituted, a pyridyl group which may be substituted, a pyridazinyl group which may be substituted, a pyradinyl group which may be substituted, a furyl group which may be substituted, a thienyl group which may be substituted, a pyrrolyl group which may be substituted, a thiazolyl group which may be substituted, an oxazolyl group which may be substituted, a pyrimidinyl group which may be substituted, a tetrazolyl group which may be substituted, a thienylethenyl group which may be substituted, a pyridylethenyl group which may be substituted, an indenyl group which may be substituted, an indanyl group which may be substituted, a tetrahydronaphthyl group which may be substituted, a benzofuryl group which may be substituted, an isobenzofuryl group which may be substituted, a benzothienyl group which may be substituted, an indolyl group which may be substituted, an indolinyl group which may be substituted, an isoindolyl group which may be substituted, an isoindolinyl group which may be

substituted, an indazolyl group which may be substituted, a quinolyl group which may be substituted, a dihydroquinolyl group which may be substituted, a 4-oxodihydroquinolyl group (dihydroquinolin-4-on) which may be substituted, a tetrahydroquinolyl group which may be substituted, an isoquinolyl group which may be substituted, a tetrahydroisoquinolyl group which may be substituted, a chromenyl group which may be substituted, a chromanyl group which may be substituted, an isochromanyl group which may be substituted, a 4H-4-oxobenzopyranyl group which may be substituted, a 3,4-dihydro-4H-4-oxobenzopyranyl group which may be substituted, a 4H-quinolizinyl group which may be substituted, a quinazolinyl group which may be substituted, a dihydroquinazolinyl group which may be substituted, a tetrahydroquinazolinyl group which may be substituted, a quinoxalinyl group which may be substituted, a tetrahydroquinoxalinyl group which may be substituted, a cinnolinyl group which may be substituted, a tetrahydrocinnolinyl group which may be substituted, an indolizinyl group which may be substituted, a tetrahydroindolizinyl group which may be substituted, a benzothiazolyl group which may be substituted, a tetrahydrobenzothiazolyl group which may be substituted, a benzoxazolyl group which may be substituted, a benzoisothiazolyl group which may be substituted, a benzoisoxazolyl group which may be substituted, a

benzimidazolyl group which may be substituted, a naphthyridinyl group which may be substituted, a tetrahydronaphthyridinyl group which may be substituted, a thienopyridyl group which may be substituted, a tetrahydrothienopyridyl group which may be substituted, a thiazolopyridyl group which may be substituted, a tetrahydrothiazolopyridyl group which may be substituted, a thiazolopyridazinyl group which may be substituted, a tetrahydrothiazolopyridazinyl group which may be substituted, a pyrrolopyridyl group which may be substituted, a dihydropyrrolopyridyl group which may be substituted, a tetrahydropyrrolopyridyl group which may be substituted, a pyrrolopyrimidinyl group which may be substituted, a dihydropyrrolopyrimidinyl group which may be substituted, a pyridoquinazolinyl group which may be substituted, a dihydropyridoquinazolinyl group which may be substituted, a pyridopyrimidinyl group which may be substituted, a tetrahydropyridopyrimidinyl group which may be substituted, a pyranothiazolyl group which may be substituted,a dihydropyranothiazolyl group which may be substituted, a furopyridyl group which may be substituted, a tetrahydrofuropyridyl group which may be substituted, an oxazolopyridyl group which may be substituted, a tetrahydrooxazolopyridyl group which may be substituted, an oxazolopyridazinyl group which may be substituted, a tetrahydrooxazolopyridazinyl group which may be substituted, a pyrrolothiazolyl group which may

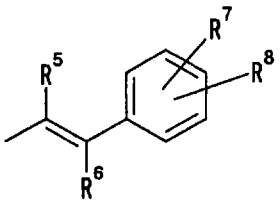
be substituted, a dihydropyrrolothiazolyl group which may be substituted, a pyrrolooxazolyl group which may be substituted, a dihydropyrrolooxazolyl group which may be substituted, a thienopyrrolyl group which may be substituted, a thiazolopyrimidinyl group which may be substituted, a 4-oxo-tetrahydrocinnolinyl group which may be substituted, a 1,2,4-benzothiadiazinyl group which may be substituted, a 1,1-dioxy-2H-1,2,4-benzothiadiazinyl group which may be substituted, a 1,2,4-benzoxadiazinyl group which may be substituted, a cyclopentapyranyl group which may be substituted, a thienofuranyl group which may be substituted, a furopyranyl group which may be substituted, a pyridoxazinyl group which may be substituted, a pyrazoloxazolyl group which may be substituted, an imidazothiazolyl group which may be substituted, an imidazopyridyl group which may be substituted, a tetrahydroimidazopyridyl group which may be substituted, a pyrazinopyridazinyl group which may be substituted, a benzoisoquinolyl group which may be substituted, a furocinnolyl group which may be substituted, a pyrazolothiazolopyridazinyl group which may be substituted, a tetrahydropyrazolothiazolopyridazinyl group which may be substituted, a hexahydrothiazolopyridazinopyridazinyl group which may be substituted, an imidazotriazinyl group which may be substituted, an oxazolopyridyl group which may be

substituted, a benzoxepinyl group which may be substituted, a benzoazepinyl group which may be substituted, a tetrahydrobenzoazepinyl group which may be substituted, a benzodiazepinyl group which may be substituted, a benzotriazepinyl group which may be substituted, a thienoazepinyl group which may be substituted, a tetrahydrothienoazepinyl group which may be substituted, a thienodiazepinyl group which may be substituted, a thienotriazepinyl group which may be substituted, a thiazoloazepinyl group which may be substituted, a tetrahydrothiazoloazepinyl group which may be substituted, a 4,5,6,7-tetrahydro-5,6-tetramethylenethiazolopyridazinyl group which may be substituted, and a 5,6-trimethylene-4,5,6,7-tetrahydrothiazolopyridazinyl group which may be substituted.

3. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 1 or 2, wherein the substituent(s) on the group $Q^4$ are 1 to 3 substituents selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, aminoalkyl groups, a nitro group, hydroxyalkyl groups, alkoxyalkyl groups, a carboxyl group, carboxyalkyl groups, alkoxycarbonylalkyl groups, acyl groups, an amidino group, a hydroxyamidino group, linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, linear, branched or cyclic alkoxy groups having 1

to 6 carbon atoms, amidino groups substituted by a linear, branched or cyclic alkoxycarbonyl group having 2 to 7 carbon atoms, linear, branched or cyclic alkenyl groups having 2 to 6 carbon atoms, linear or branched alkynyl groups having 2 to 6 carbon atoms, linear, branched or cyclic alkoxycarbonyl groups having 2 to 6 carbon atoms, a carbamoyl group, mono- or di-alkylcarbamoyl groups substituted by a linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms on the nitrogen atom, mono- or di-alkylamino groups substituted by a linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, and 5- or 6-membered nitrogen-containing heterocyclic groups.

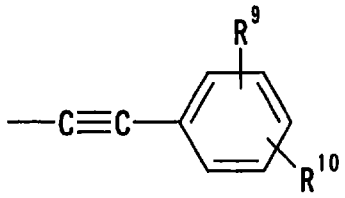
4. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 1, wherein the group $Q^4$ represents any of the following groups:



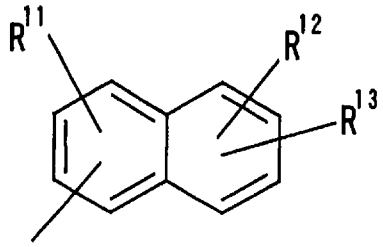
(a)

wherein $R^5$ and $R^6$, independently of each other, represent a hydrogen atom, cyano group, halogen atom, alkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, or phenyl group which may be substituted by a cyano group,

hydroxyl group, halogen atom, alkyl group or alkoxy group, and $R^7$ and $R^8$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;

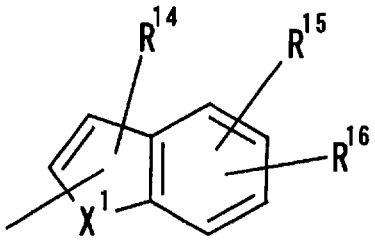

(b)

wherein $R^9$ and $R^{10}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(c)

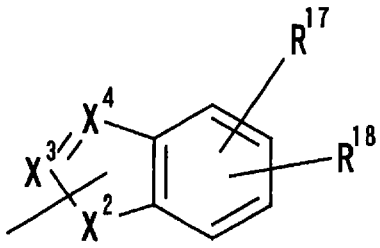
wherein $R^{11}$, $R^{12}$ and $R^{13}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(d)

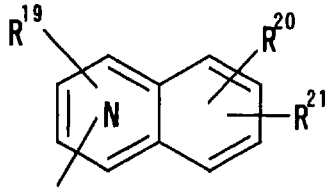
wherein $X^1$ represents $CH_2$, CH, NH, NOH, N, O or S, and $R^{14}$, $R^{15}$ and $R^{16}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group,

alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(e)

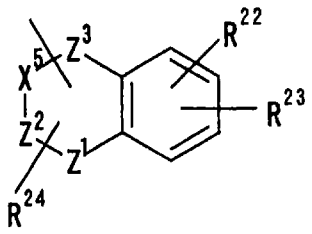
wherein $X^2$ represents NH, N, O or S, $X^3$ represents N, C or CH, $X^4$ represents N, C or CH, and $R^{17}$ and $R^{18}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group, excluding the cases where $X^3$ and $X^4$ are combinations of C and CH, and are both C or CH;



(f)

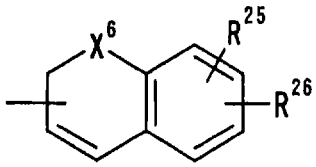
wherein N indicates that 1 or 2 carbon atoms of the ring substituted by $R^{19}$ have been substituted by a nitrogen atom, and $R^{19}$, $R^{20}$ and $R^{21}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group,

amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



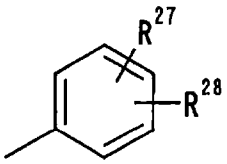
(g)

wherein $X^5$ represents $CH_2$, CH, N or NH, $Z^1$ represents N, NH or O, $Z^2$ represents $CH_2$, CH, C or N, $Z^3$ represents $CH_2$, CH, S, $SO_2$ or C=O, $X^5$-$Z^2$ indicates that $X^5$ and $Z^2$ are bonded to each other by a single bond or double bond, $R^{22}$ and $R^{23}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group, and $R^{24}$ represents a hydrogen atom or alkyl group;



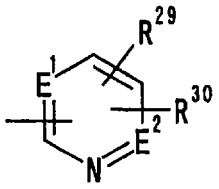
(h)

wherein $X^6$ represents O or S, and $R^{25}$ and $R^{26}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



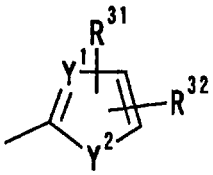
(i)

wherein $R^{27}$ and $R^{28}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(j)

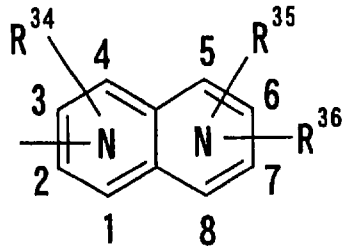
wherein $E^1$ and $E^2$, independently of each other, represent N or CH, and $R^{29}$ and $R^{30}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(k)

wherein $Y^1$ represents CH or N, $Y^2$ represents $-N(R^{33})-$, in which $R^{33}$ means a hydrogen atom or alkyl group having 1 to 6 carbon atoms, O or S, and $R^{31}$ and $R^{32}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-

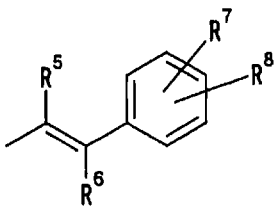
dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group; and



(1)

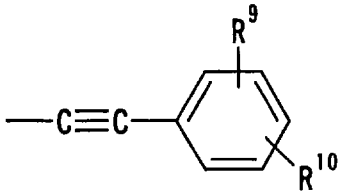
wherein numerals 1 to 8 indicate positions, each N indicates that any one of carbon atoms of positions 1 to 4 and any one of carbon atoms of positions 5 to 8 has been substituted by a nitrogen atom, and $R^{34}$, $R^{35}$ and $R^{36}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group.

5. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 1, wherein the group $Q^4$ represents any of the following groups:



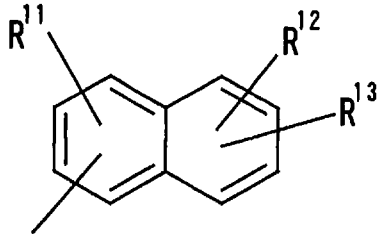
(a)

wherein $R^5$ and $R^6$, independently of each other, represent a hydrogen atom or alkyl group, $R^7$ represents a hydrogen atom, and $R^8$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



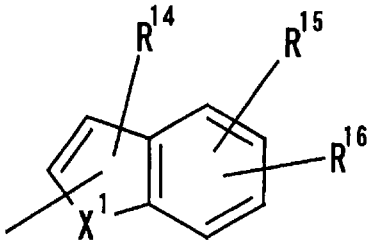
(b)

wherein $R^9$ represents a hydrogen atom, and $R^{10}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



(c)

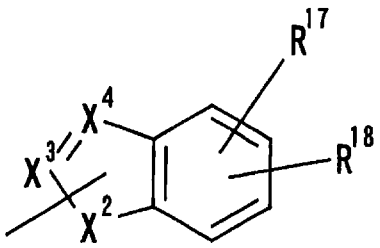
wherein $R^{11}$ are $R^{12}$ both represent hydrogen atoms, and $R^{13}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



(d)

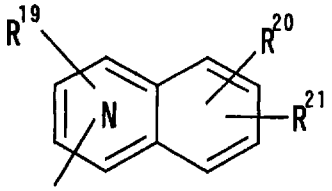
wherein $X^1$ represents NH, NOH, N, O or S, $R^{14}$ represents a hydrogen atom, halogen atom, acyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group or

alkyl group, $R^{15}$ represents a hydrogen atom or halogen atom, and $R^{16}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



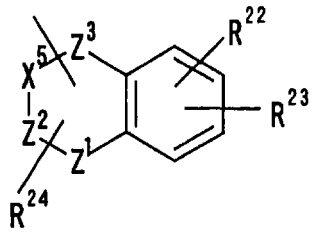
(e)

wherein $X^2$ represents NH, O or S, $X^3$ represents N, C or CH, $X^4$ represents N, C or CH, $R^{17}$ represents a hydrogen atom, and $R^{18}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group, excluding the cases where $X^3$ and $X^4$ are combinations of C and CH, and are both C or CH;



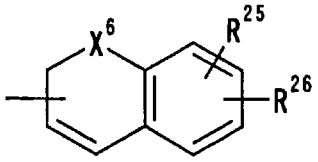
(f)

wherein N indicates that 1 or 2 carbon atoms of the ring substituted by $R^{19}$ have been substituted by a nitrogen atom, $R^{19}$ and $R^{20}$ both represent hydrogen atoms, and $R^{21}$ represents a hydrogen atom, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group or halogenoalkyl group;



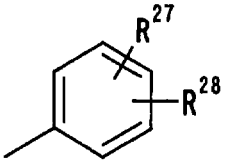
(g)

wherein $X^5$ represents $CH_2$, CH, N or NH, $Z^1$ represents N, NH or O, $Z^2$ represents $CH_2$, CH, C or N, $Z^3$ represents $CH_2$, CH, S, $SO_2$ or C=O, $X^5$-$Z^2$ indicates that $X^5$ and $Z^2$ are bonded to each other by a single bond or double bond, $R^{22}$ represents a hydrogen atom, $R^{23}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group, and $R^{24}$ represents a hydrogen atom;



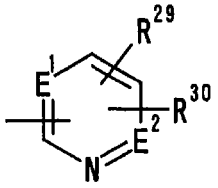
(h)

wherein $X^6$ represents O, $R^{25}$ represents a hydrogen atom, and $R^{26}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



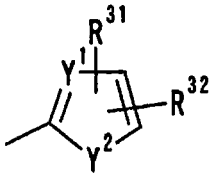
(i)

wherein $R^{27}$ represents a hydrogen atom or halogen atom, and $R^{28}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



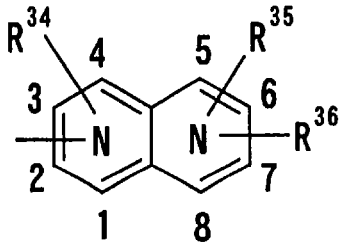
(j)

wherein $E^1$ and $E^2$, independently of each other, represent N or CH, $R^{29}$ represents a hydrogen atom or halogen atom, and $R^{30}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



(k)

wherein $Y^1$ represents CH or N, $Y^2$ represents $-N(R^{33})-$, in which $R^{33}$ means a hydrogen atom or alkyl group having 1 to 6 carbon atoms, O or S, $R^{31}$ represents a hydrogen atom or halogen atom, and $R^{32}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group; and



(l)

wherein numerals 1 to 8 indicate positions, each N indicates that any one of carbon atoms of positions 1 to 4 and any one of carbon atoms of positions 5 to 8 has been substituted by a nitrogen atom, $R^{34}$ represents a hydrogen atom or halogen atom, $R^{35}$ represents a hydrogen

atom or halogen atom, and $R^{36}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group.

6. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 3, wherein the group $Q^4$ in the formula (1) is a 4-chlorostyryl, 4-fluorostyryl, 4-bromostyryl, 4-ethynylstyryl, 4-chlorophenylethynyl, 4-fluorophenylethynyl, 4-bromophenylethynyl, 4-ethynylphenylethynyl, 6-chloro-2-naphthyl, 6-fluoro-2-naphthyl, 6-bromo-2-naphthyl, 6-ethynyl-2-naphthyl, 7-chloro-2-naphthyl, 7-fluoro-2-naphthyl, 7-bromo-2-naphthyl, 7-ethynyl-2-naphthyl, 5-chloroindol-2-yl, 5-fluoroindol-2-yl, 5-bromoindol-2-yl, 5-ethynylindol-2-yl, 5-methylindol-2-yl, 5-chloro-4-fluoroindol-2-yl, 5-chloro-3-fluoroindol-2-yl, 3-bromo-5-chloroindol-2-yl, 3-chloro-5-fluoroindol-2-yl, 3-bromo-5-fluoroindol-2-yl, 5-bromo-3-chloroindol-2-yl, 5-bromo-3-fluoroindol-2-yl, 5-chloro-3-formylindol-2-yl, 5-fluoro-3-formylindol-2-yl, 5-bromo-3-formylindol-2-yl, 5-ethynyl-3-formylindol-2-yl, 5-chloro-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-fluoro-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-bromo-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-ethynyl-3-(N,N-dimethylcarbamoyl)indol-2-yl, 6-chloroindol-2-yl, 6-fluoroindol-2-yl, 6-bromoindol-2-yl, 6-ethynylindol-2-yl, 6-methylindol-2-yl, 5-chlorobenzothiophen-2-yl, 5-fluorobenzothiophen-2-yl, 5-bromobenzothiophen-2-yl, 5-ethynylbenzothiophen-2-yl, 5-methylbenzothiophen-2-yl,

5-chloro-4-fluorobenzothiophen-2-yl, 6-chloro-benzothiophen-2-yl, 6-fluorobenzothiophen-2-yl, 6-bromobenzothiophen-2-yl, 6-ethynylbenzothiophen-2-yl, 6-methylbenzothiophen-2-yl, 5-chlorobenzofuran-2-yl, 5-fluorobenzofuran-2-yl, 5-bromobenzofuran-2-yl, 5-ethynylbenzofuran-2-yl, 5-methylbenzofuran-2-yl, 5-chloro-4-fluorobenzofuran-2-yl, 6-chlorobenzofuran-2-yl, 6-fluorobenzofuran-2-yl, 6-bromobenzofuran-2-yl, 6-ethynylbenzofuran-2-yl, 6-methylbenzofuran-2-yl, 5-chlorobenzimidazol-2-yl, 5-fluorobenzimidazol-2-yl, 5-bromobenzimidazol-2-yl, 5-ethynylbenzimidazol-2-yl, 6-chloroquinolin-2-yl, 6-fluoroquinolin-2-yl, 6-bromoquinolin-2-yl, 6-ethynylquinolin-2-yl, 7-chloroquinolin-3-yl, 7-fluoroquinolin-3-yl, 7-bromoquinolin-3-yl, 7-ethynylquinolin-3-yl, 7-chloroisoquinolin-3-yl, 7-fluoroisoquinolin-3-yl, 7-bromoisoquinolin-3-yl, 7-ethynylisoquinolin-3-yl, 7-chlorocinnolin-3-yl, 7-fluorocinnolin-3-yl, 7-bromocinnolin-3-yl, 7-ethynylcinnolin-3-yl, 7-chloro-2H-chromen-3-yl, 7-fluoro-2H-chromen-3-yl, 7-bromo-2H-chromen-3-yl, 7-ethynyl-2H-chromen-3-yl, 6-chloro-4-oxo-1,4-dihydroquinolin-2-yl, 6-fluoro-4-oxo-1,4-dihydroquinolin-2-yl, 6-bromo-4-oxo-1,4-dihydroquinolin-2-yl, 6-ethynyl-4-oxo-1,4-dihydroquinolin-2-yl, 6-chloro-4-oxo-1,4-dihydroquinazolin-2-yl, 6-fluoro-4-oxo-1,4-dihydroquinazolin-2-yl, 6-bromo-4-oxo-1,4-dihydro-quinazolin-2-yl, 6-ethynyl-4-oxo-1,4-dihydroquinazolin-

2-yl, phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-bromophenyl, 4-ethynylphenyl, 3-chlorophenyl, 3-fluorophenyl, 3-bromo-phenyl, 3-ethynylphenyl, 3-chloro-4-fluorophenyl, 4-chloro-3-fluorophenyl, 4-chloro-2-fluorophenyl, 2-chloro-4-fluorophenyl, 4-bromo-2-fluorophenyl, 2-bromo-4-fluorophenyl, 2,4-dichlorophenyl, 2,4-difluorophenyl, 2,4-dibromophenyl, 4-chloro-3-methylphenyl, 4-fluoro-3-methylphenyl, 4-bromo-3-methylphenyl, 4-chloro-2-methylphenyl, 4-fluoro-2-methylphenyl, 4-bromo-2-methylphenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4-dibromophenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 4-chloro-2-pyridyl, 4-fluoro-2-pyridyl, 4-bromo-2-pyridyl, 4-ethynyl-2-pyridyl, 4-chloro-3-pyridyl, 4-fluoro-3-pyridyl, 4-bromo-3-pyridyl, 4-ethynyl-3-pyridyl, 5-chloro-2-pyridyl, 5-fluoro-2-pyridyl, 5-bromo-2-pyridyl, 5-ethynyl-2-pyridyl, 4-chloro-5-fluoro-2-pyridyl, 5-chloro-4-fluoro-2-pyridyl, 5-chloro-3-pyridyl, 5-fluoro-3-pyridyl, 5-bromo-3-pyridyl, 5-ethynyl-3-pyridyl, 6-chloro-3-pyridazinyl, 6-fluoro-3-pyridazinyl, 6-bromo-3-pyridazinyl, 6-ethynyl-3-pyridazinyl, 5-chloro-2-thiazolyl, 5-fluoro-2-thiazolyl, 5-bromo-2-thiazolyl, 5-ethynyl-2-thiazolyl, 2-chlorothieno[2,3-b]pyrrol-5-yl, 2-fluorothieno[2,3-b]pyrrol-5-yl, 2-bromothieno[2,3-b]-pyrrol-5-yl or 2-ethynylthieno[2,3-b]pyrrol-5-yl group.

7. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of

claims 1 to 6, wherein the group $Q^1$ in the formula (1) is a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted.

8. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 6, wherein the group $Q^1$ in the formula (1) is a thienopyridyl group which may be substituted, tetrahydrothienopyridyl group which may be substituted, thiazolopyridyl group which may be substituted, tetrahydrothiazolopyridyl group which may be substituted, thiazolopyridazinyl group which may be substituted, tetrahydrothiazolopyridazinyl group which may be substituted, pyranothiazolyl group which may be substituted, dihydropyranothiazolyl group which may be substituted, furopyridyl group which may be substituted, tetrahydrofuropyridyl group which may be substituted, oxazolopyridyl group which may be substituted, tetrahydrooxazolopyridyl group which may be substituted, pyrrolopyridyl group which may be substituted, dihydropyrrolopyridyl group which may be substituted, tetrahydropyrrolopyridyl group which may be substituted, pyrrolopyrimidinyl group which may be substituted, dihydropyrrolopyrimidinyl group which may be substituted, oxazolopyridazinyl group which may be substituted, tetrahydrooxazolopyridazinyl group which may be

substituted, pyrrolothiazolyl group which may be substituted, dihydropyrrolothiazolyl group which may be substituted, pyrrolooxazolyl group which may be substituted, dihydropyrrolooxazolyl group which may be substituted, benzothiazolyl group which may be substituted, tetrahydrobenzothiazolyl group which may be substituted, thiazolopyrimidinyl group which may be substituted, dihydrothiazolopyrimidinyl group which may be substituted, benzoazepinyl group which may be substituted, tetrahydrobenzoazepinyl group which may be substituted, thiazoloazepinyl group which may be substituted, tetrahydrothiazoloazepinyl group which may be substituted, thienoazepinyl group which may be substituted, tetrahydrothienoazepinyl group which may be substituted, 4,5,6,7-tetrahydro-5,6-tetramethylenethiazolopyridazinyl group which may be substituted, or 5,6-trimethylene-4,5,6,7-tetrahydrothiazolopyridazinyl group which may be substituted.

9. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 8, wherein the substituent(s) on the group $Q^1$ are 1 to 3 substituents selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, an amidino group, a hydroxyamidino group, $C_1$-$C_6$ alkyl groups, $C_3$-$C_6$ cycloalkyl-$C_1$-$C_6$ alkyl groups, hydroxy-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkoxy groups, $C_1$-$C_6$

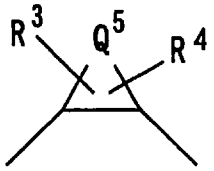
alkoxy $C_1$-$C_6$ alkyl group, a carboxyl group, $C_2$-$C_6$ carboxyalkyl groups, $C_2$-$C_6$ alkoxycarbonyl-$C_1$-$C_6$ alkyl groups, amidino groups substituted by a $C_2$-$C_6$ alkoxycarbonyl group, $C_2$-$C_6$ alkenyl groups, $C_2$-$C_6$ alkynyl groups, $C_2$-$C_6$ alkoxycarbonyl groups, amino $C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylamino-$C_1$-$C_6$ alkyl groups, di($C_1$-$C_6$ alkyl)amino-$C_1$-$C_6$ alkyl groups, $C_2$-$C_6$ alkoxycarbonylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkanoyl groups, $C_1$-$C_6$ alkanoylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylsulfonyl groups, $C_1$-$C_6$ alkylsulfonylamino-$C_1$-$C_6$ alkyl groups, a carbamoyl group, $C_1$-$C_6$ alkylcarbamoyl groups, N,N-di($C_1$-$C_6$ alkyl)carbamoyl groups, $C_1$-$C_6$ alkylamino groups, di($C_1$-$C_6$ alkyl)amino groups, 5- or 6-membered heterocyclic groups containing one of nitrogen, oxygen and sulfur or the same or different two atoms thereof, 5- or 6-membered heterocyclic group-$C_1$-$C_4$ alkyl group, 5- or 6-membered heterocyclic group-amino-$C_1$-$C_4$ alkyl group.

10. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 9, wherein the group $T^1$ in the formula (1) is a carbonyl group, group -C(=O)-C(=O)-N(R')-, group -C(=S)-C(=O)-N(R')-, group -C(=O)-C(=S)-N(R')- or group -C(=S)-C(=S)-N(R')-, in which R' means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group.

11. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 9, wherein the group $T^1$ in the formula (1) is

a group -C(=O)-C(=O)-N(R′)-, group -C(=S)-C(=O)-N(R′)-, group -C(=O)-C(=S)-N(R′)- or group -C(=S)-C(=S)-N(R′)-, in which R′ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group.

12. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 11, wherein the group $Q^3$ in the formula (1) is

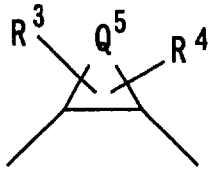



wherein $Q^5$ means an alkylene group having 3 to 6 carbon atoms or a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or 1, and A has the same meaning as defined above, and $R^3$ and $R^4$ are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, amino group, hydroxyimino group, alkoxyimino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-

alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, carbamoylalkyl group, carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), alkylsulfonylamino group, alkylsulfonylaminoalkyl group, oxo group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, carboxyacyl group, alkoxyalkyloxycarbonyl group, halogenoacyl group, N,N-dialkylaminoacyl group, acyloxyacyl group, hydroxyacyl group, alkoxyacyl group, alkoxyalkylsulfonyl group, N,N-dialkylcarbamoylacyl group, N,N-

dialkylcarbamoylalkylsulfonyl group, alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group.

13. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 11, wherein the group $Q^3$ in the formula (1) is

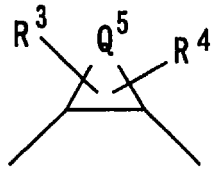



wherein $Q^5$ means a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or 1, and A has the same meaning as defined above, and $R^3$ and $R^4$ are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, amino group, hydroxyimino group, alkoxyimino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the

alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, carbamoylalkyl group, carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), alkylsulfonylamino group, alkylsulfonylaminoalkyl group, oxo group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, carboxyacyl group, alkoxyalkyloxycarbonyl group, halogenoacyl group, N,N-dialkylaminoacyl group, acyloxyacyl group, hydroxyacyl group, alkoxyacyl group, alkoxyalkylsulfonyl group, N,N-dialkylcarbamoylacyl group, N,N-dialkylcarbamoyl-alkylsulfonyl group, alkylsulfonylacyl group,

aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group.

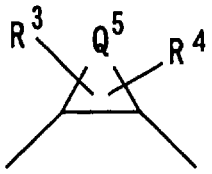
14. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 11, wherein the group $Q^3$ in the formula (1) is




wherein $Q^5$ means an alkylene group having 3 to 6 carbon atoms, and $R^3$ and $R^4$ are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, amino group, hydroxyimino group, alkoxyimino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-

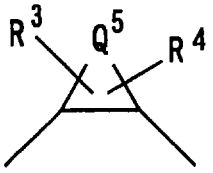
alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, carbamoylalkyl group, carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), alkylsulfonylamino group, alkylsulfonylaminoalkyl group, oxo group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, carboxyacyl group, alkoxyalkyloxycarbonyl group, halogenoacyl group, N,N-dialkylaminoacyl group, acyloxyacyl group, hydroxyacyl group, alkoxyacyl group, alkoxyalkylsulfonyl group, N,N-dialkylcarbamoylacyl group, N,N-dialkylcarbamoyl-alkylsulfonyl group, alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group.

15. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 11, wherein the group $Q^3$ in the formula (1) is




wherein $Q^5$ means an alkylene group having 4 carbon atoms, $R^3$ is a hydrogen atom, and $R^4$ is an N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s).

16. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 11, wherein the group $Q^3$ in the formula (1) is




wherein $Q^5$ means an alkylene group having 4 carbon atoms, $R^3$ is a hydrogen atom, and $R^4$ is an N,N-dimethylcarbamoyl group.

17. The compound according to Claim 1, which is represented by the general formula (1):

$$Q^1\text{-}Q^2\text{-}T^0\text{-}N(R^1)\text{-}Q^3\text{-}N(R^2)\text{-}T^1\text{-}Q^4 \qquad (1)$$

wherein

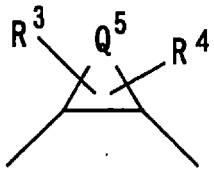
$R^1$ and $R^2$, independently of each other, represent a

hydrogen atom, hydroxyl group, alkyl group or alkoxy group;

$Q^1$ represents a saturated or unsaturated, 5- or 6-membered cyclic hydrocarbon group which may be substituted, a saturated or unsaturated, 5- to 7-membered heterocyclic group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^2$ represents a single bond, a saturated or unsaturated, 5- or 6-membered divalent cyclic hydrocarbon group which may be substituted, a saturated or unsaturated, 5- to 7-membered divalent heterocyclic group which may be substituted, a saturated or unsaturated, divalent bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, divalent bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^3$ represents the following group:




in which $Q^5$ means a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or an integer of 1-3, and A means an oxygen atom, nitrogen

atom, sulfur atom, -SO-, -$SO_2$-, -NH-, -O-NH-, -NH-NH-, -S-NH-, -SO-NH- or -$SO_2$-NH-, and $R^3$ and $R^4$ are substituents on carbon atom(s), nitrogen atom(s) or a sulfur atom(s) of a ring comprising $Q^5$ and are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, cyano group, cyanoalkyl group, amino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, alkoxyimino group, hydroxyimino group, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylalkylamino group, carboxyalkylamino group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic

carbonyl group which may be substituted, carbamoylalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, 3- to 6-membered heterocyclic carbonylalkyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, aryl group, aralkyl group, heteroaryl group, heteroarylalkyl group, alkylsulfonylamino group, arylsulfonylamino group, alkylsulfonylaminoalkyl group, arylsulfonylaminoalkyl group, alkylsulfonylaminocarbonyl group, arylsulfonylaminocarbonyl group, alkylsulfonyl-aminocarbonylalkyl group, arylsulfonylaminocarbonylalkyl group, oxo group, carbamoyloxy group, aralkyloxy group, carboxyalkyloxy group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, alkoxyalkyloxycarbonyl group, hydroxyacyl group, alkoxyacyl group, halogenoacyl group, carboxyacyl group, aminoacyl group, acyloxyacyl group, acyloxyalkylsulfonyl group, hydroxyalkylsulfonyl group, alkoxyalkylsulfonyl group, 3- to 6-membered heterocyclic sulfonyl group which may be substituted, N-alkylaminoacyl group, N,N-dialkylaminoacyl group, N,N-dialkylcarbamoylacyl group

which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkylsulfonyl group which may have a substituent on the alkyl group(s), alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group, or $R^3$ and $R^4$, together with each other, denote an alkylene group having 1 to 5 carbon atoms, alkenylene group having 2 to 5 carbon atoms, alkylenedioxy group having 1 to 5 carbon atoms or carbonyldioxy group;

$Q^4$ represents an aryl group which may be substituted, an arylalkenyl group which may be substituted, an arylalkynyl group which may be substituted, a heteroaryl group which may be substituted, a heteroarylalkenyl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$T^0$ represents a carbonyl or thiocarbonyl group; and

$T^1$ represents a carbonyl group, sulfonyl group or thiocarbonyl group;

a salt thereof, a solvate thereof, or an N-oxide thereof.

18. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 17, wherein the group $Q^1$ is a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may

be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted, and $Q^2$ is a single bond.

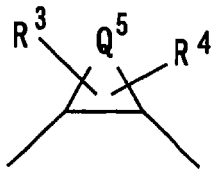
19. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 17 or 18, wherein the group $Q^1$ is a thienopyridyl group which may be substituted, tetrahydrothienopyridyl group which may be substituted, thiazolopyridyl group which may be substituted, tetrahydrothiazolopyridyl group which may be substituted, thiazolopyridazinyl group which may be substituted, tetrahydrothiazolopyridazinyl group which may be substituted, pyranothiazolyl group which may be substituted, dihydropyranothiazolyl group which may be substituted, furopyridyl group which may be substituted, tetrahydrofuropyridyl group which may be substituted, oxazolopyridyl group which may be substituted, tetrahydrooxazolopyridyl group which may be substituted, pyrrolopyridyl group which may be substituted, dihydropyrrolopyridyl group which may be substituted, tetrahydropyrrolopyridyl group which may be substituted, pyrrolopyrimidinyl group which may be substituted, dihydropyrrolopyrimidinyl group which may be substituted, oxazolopyridazinyl group which may be substituted, tetrahydrooxazolopyridazinyl group which may be substituted, pyrrolothiazolyl group which may be substituted, dihydropyrrolothiazolyl group which may be substituted, pyrrolooxazolyl group which may be

substituted, dihydropyrrolooxazolyl group which may be substituted, benzothiazolyl group which may be substituted, tetrahydrobenzothiazolyl group which may be substituted, thiazolopyrimidinyl group which may be substituted, dihydrothiazolopyrimidinyl group which may be substituted, benzoazepinyl group which may be substituted, tetrahydrobenzoazepinyl group which may be substituted, thiazoloazepinyl group which may be substituted, tetrahydrothiazoloazepinyl group which may be substituted, thienoazepinyl group which may be substituted, tetrahydrothienoazepinyl group which may be substituted, 4,5,6,7-tetrahydro-5,6-tetramethylenethiazolopyridazinyl group which may be substituted, or 5,6-trimethylene-4,5,6,7-tetrahydro-thiazolopyridazinyl group which may be substituted.

20. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 19, wherein the substituent(s) on the group $Q^1$ are 1 to 3 substituent(s) selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, an amidino group, a hydroxyamidino group, $C_1$-$C_6$ alkyl groups, $C_3$-$C_6$ cycloalkyl-$C_1$-$C_6$ alkyl groups, hydroxy-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkoxy groups, $C_1$-$C_6$ alkoxy $C_1$-$C_6$ alkyl groups, a carboxyl group; $C_2$-$C_6$ carboxyalkyl groups, $C_2$-$C_6$ alkoxycarbonyl-$C_1$-$C_6$ alkyl groups, amidino groups substituted by a $C_2$-$C_6$ alkoxycarbonyl group, $C_2$-$C_6$ alkenyl groups, $C_2$-$C_6$ alkynyl

groups, $C_2$-$C_6$ alkoxycarbonyl groups, amino $C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylamino-$C_1$-$C_6$ alkyl groups, di($C_1$-$C_6$ alkyl)amino-$C_1$-$C_6$ alkyl groups, $C_2$-$C_6$ alkoxycarbonylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkanoyl groups, $C_1$-$C_6$ alkanoylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylsulfonyl groups, $C_1$-$C_6$ alkylsulfonylamino-$C_1$-$C_6$ alkyl groups, a carbamoyl group, $C_1$-$C_6$ alkylcarbamoyl groups, N,N-di($C_1$-$C_6$ alkyl)carbamoyl groups, $C_1$-$C_6$ alkylamino groups, di($C_1$-$C_6$ alkyl)amino groups, 5- or 6-membered heterocyclic groups containing one of nitrogen, oxygen and sulfur or the same or different two atoms thereof, 5- or 6-membered heterocyclic group-$C_1$-$C_4$ alkyl group, and 5- or 6-membered heterocyclic group-amino-$C_1$-$C_4$ alkyl group.

21. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 20, wherein the group $Q^3$ in the formula (1) is




wherein $Q^5$ means a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or 1, and A has the same meaning as defined above, and $R^3$ and $R^4$ are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, amino group,

hydroxyimino group, alkoxyimino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group, N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, carbamoylalkyl group, carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), alkylsulfonylamino

group, alkylsulfonylaminoalkyl group, oxo group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, carboxyacyl group, alkoxyalkyloxycarbonyl group, halogenoacyl group, N,N-dialkylaminoacyl group, acyloxyacyl group, hydroxyacyl group, alkoxyacyl group, alkoxyalkylsulfonyl group, N,N-dialkylcarbamoylacyl group, N,N-dialkylcarbamoylalkylsulfonyl group, alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group.

22. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 21, wherein the group $Q^4$ in the formula (1) is a group selected from the group consisting of a naphthyl group which may be substituted, an anthryl group which may be substituted, a phenanthryl group which may be substituted, a styryl group which may be substituted, a phenylethynyl group which may be substituted, a thienylethenyl group which may be substituted, a pyridylethenyl group which may be substituted, an indenyl group which may be substituted, an indanyl group which may be substituted, a tetrahydronaphthyl group which may be substituted, a benzofuryl group which may be substituted, an isobenzofuryl group which may be substituted, a

benzothienyl group which may be substituted, an indolyl group which may be substituted, an indolinyl group which may be substituted, an isoindolyl group which may be substituted, an isoindolinyl group which may be substituted, an indazolyl group which may be substituted, a quinolyl group which may be substituted, a dihydroquinolyl group which may be substituted, a 4-oxo-dihydroquinolyl group (dihydroquinolin-4-on) which may be substituted, a tetrahydroquinolyl group which may be substituted, an isoquinolyl group which may be substituted, a tetrahydroisoquinolyl group which may be substituted, a chromenyl group which may be substituted, a chromanyl group which may be substituted, an isochromanyl group which may be substituted, a 4H-4-oxobenzopyranyl group which may be substituted, a 3,4-dihydro-4H-4-oxobenzopyranyl group which may be substituted, a 4H-quinolizinyl group which may be substituted, a quinazolinyl group which may be substituted, a dihydroquinazolinyl group which may be substituted, a tetrahydroquinazolinyl group which may be substituted, a quinoxalinyl group which may be substituted, a tetrahydroquinoxalinyl group which may be substituted, a cinnolinyl group which may be substituted, a tetrahydrocinnolinyl group which may be substituted, an indolizinyl group which may be substituted, a tetrahydroindolizinyl group which may be substituted, a benzothiazolyl group which may be substituted, a

tetrahydrobenzothiazolyl group which may be substituted, a benzoxazolyl group which may be substituted, a benzoisothiazolyl group which may be substituted, a benzoisoxazolyl group which may be substituted, a benzimidazolyl group which may be substituted, a naphthyridinyl group which may be substituted, a tetrahydronaphthyridinyl group which may be substituted, a thienopyridyl group which may be substituted, a tetrahydrothienopyridyl group which may be substituted, a thiazolopyridyl group which may be substituted, a tetrahydrothiazolopyridyl group which may be substituted, a thiazolopyridazinyl group which may be substituted, a tetrahydrothiazolopyridazinyl group which may be substituted, a pyrrolopyridyl group which may be substituted, a dihydropyrrolopyridyl group which may be substituted, a tetrahydropyrrolopyridyl group which may be substituted, a pyrrolopyrimidinyl group which may be substituted, a dihydropyrrolopyrimidinyl group which may be substituted, a pyridoquinazolinyl group which may be substituted, a dihydropyridoquinazolinyl group which may be substituted, a pyridopyrimidinyl group which may be substituted, a tetrahydropyridopyrimidinyl group which may be substituted, a pyranothiazolyl group which may be substituted,a dihydropyranothiazolyl group which may be substituted, a furopyridyl group which may be substituted, a tetrahydrofuropyridyl group which may be substituted, an oxazolopyridyl group which may be

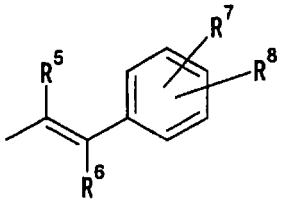
substituted, a tetrahydrooxazolopyridyl group which may be substituted, an oxazolopyridazinyl group which may be substituted, a tetrahydrooxazolopyridazinyl group which may be substituted, a pyrrolothiazolyl group which may be substituted, a dihydropyrrolothiazolyl group which may be substituted, a pyrrolooxazolyl group which may be substituted, a dihydropyrrolooxazolyl group which may be substituted, a thienopyrrolyl group which may be substituted, a thiazolopyrimidinyl group which may be substituted, a 4-oxo-tetrahydrocinnolinyl group which may be substituted, a 1,2,4-benzothiadiazinyl group which may be substituted, a 1,1-dioxy-2H-1,2,4-benzothiadiazinyl group which may be substituted, a 1,2,4-benzoxadiazinyl group which may be substituted, a cyclopentapyranyl group which may be substituted, a thienofuranyl group which may be substituted, a furopyranyl group which may be substituted, a pyridoxazinyl group which may be substituted, a pyrazoloxazolyl group which may be substituted, an imidazothiazolyl group which may be substituted, an imidazopyridyl group which may be substituted, a tetrahydroimidazopyridyl group which may be substituted, a pyrazinopyridazinyl group which may be substituted, a benzoisoquinolyl group which may be substituted, a furocinnolyl group which may be substituted, a pyrazolothiazolopyridazinyl group which may be substituted, a tetrahydropyrazolothiazolopyridazinyl

group which may be substituted, a hexahydrothiazolopyridazinopyridazinyl group which may be substituted, an imidazotriazinyl group which may be substituted, an oxazolopyridyl group which may be substituted, a benzoxepinyl group which may be substituted, a benzoazepinyl group which may be substituted, a tetrahydrobenzoazepinyl group which may be substituted, a benzodiazepinyl group which may be substituted, a benzotriazepinyl group which may be substituted, a thienoazepinyl group which may be substituted, a tetrahydrothienoazepinyl group which may be substituted, a thienodiazepinyl group which may be substituted, a thienotriazepinyl group which may be substituted, a thiazoloazepinyl group which may be substituted, a tetrahydrothiazoloazepinyl group which may be substituted, a 4,5,6,7-tetrahydro-5,6-tetramethylenethiazolopyridazinyl group which may be substituted, and a 5,6-trimethylene-4,5,6,7-tetrahydrothiazolopyridazinyl group which may be substituted.

23. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 21, wherein the substituent(s) on the group $Q^4$ are 1 to 3 substituents selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, aminoalkyl groups, a nitro group, hydroxyalkyl groups, alkoxyalkyl groups, a carboxyl

group, carboxyalkyl groups, alkoxycarbonylalkyl groups, acyl groups, an amidino group, a hydroxyamidino group, linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, linear, branched or cyclic alkoxy groups having 1 to 6 carbon atoms, amidino groups substituted by linear, branched or cyclic alkoxycarbonyl group having 2 to 7 carbon atoms, linear, branched or cyclic alkenyl groups having 2 to 6 carbon atoms, linear or branched alkynyl groups having 2 to 6 carbon atoms, linear, branched or cyclic alkoxycarbonyl groups having 2 to 6 carbon atoms, a carbamoyl group, mono- or di-alkylcarbamoyl groups substituted by a linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms on the nitrogen atom(s), mono- or di-alkylamino groups substituted by linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, and 5- or 6-membered nitrogen-containing heterocyclic groups.

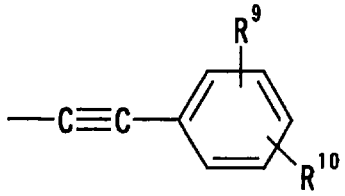
24. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 21, wherein the group $Q^4$ is



(a)

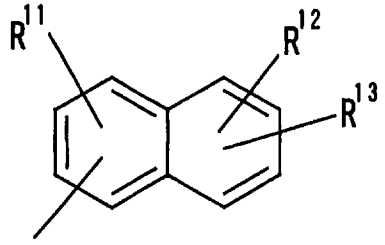
wherein $R^5$ and $R^6$, independently of each other, represent a hydrogen atom, cyano group, halogen atom, alkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group,

carboxyl group, carboxyalkyl group, acyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, or phenyl group which may be substituted by a cyano group, hydroxyl group, halogen atom, alkyl group or alkoxy group, and $R^7$ and $R^8$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



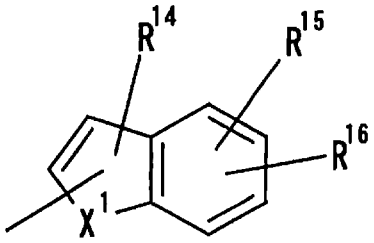
(b)

wherein $R^9$ and $R^{10}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(c)

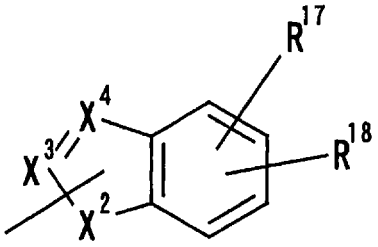
wherein $R^{11}$, $R^{12}$ and $R^{13}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(d)

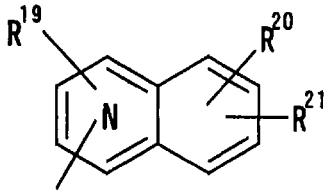
wherein $X^1$ represents $CH_2$, CH, NH, NOH, N, O or S, and $R^{14}$, $R^{15}$ and $R^{16}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group,

alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



(e)

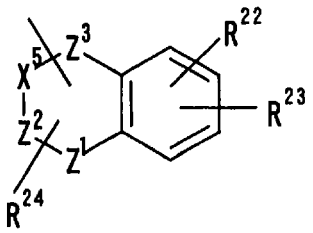
wherein $X^2$ represents NH, N, O or S, $X^3$ represents N, C or CH, $X^4$ represents N, C or CH, and $R^{17}$ and $R^{18}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group, excluding the cases where $X^3$ and $X^4$ are combinations of C and CH, and are both C or CH;



(f)

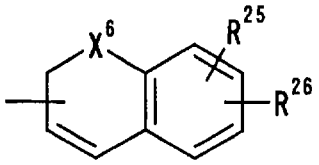
wherein N indicates that 1 or 2 carbon atoms of the ring substituted by $R^{19}$ have been substituted by a nitrogen atom, and $R^{19}$, $R^{20}$ and $R^{21}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group,

amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;



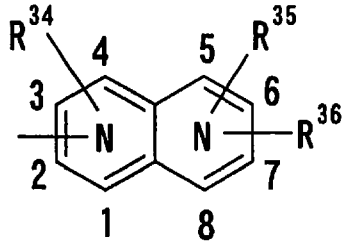
(g)

wherein $X^5$ represents $CH_2$, CH, N or NH, $Z^1$ represents N, NH or O, $Z^2$ represents $CH_2$, CH, C or N, $Z^3$ represents $CH_2$, CH, S, $SO_2$ or C=O, $X^5$-$Z^2$ indicates that $X^5$ and $Z^2$ are bonded to each other by a single bond or double bond, $R^{22}$ and $R^{23}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group, and $R^{24}$ represents a hydrogen atom or alkyl group;



(h)

wherein $X^6$ represents O or S, and $R^{25}$ and $R^{26}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group; or

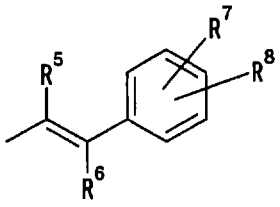


(1)

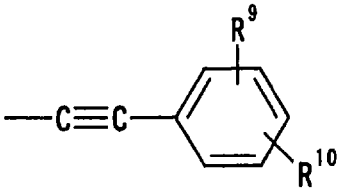
wherein numerals 1 to 8 indicate positions, each N indicates that any one of carbon atoms of positions 1 to 4 and any one of carbon atoms of positions 5 to 8 has been substituted by a nitrogen atom, and $R^{34}$, $R^{35}$ and $R^{36}$, independently of one another, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group,

acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group.

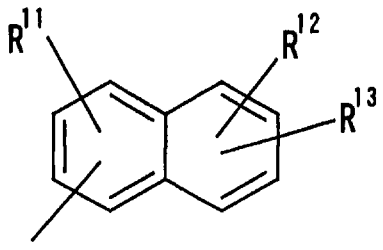
25. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 21, wherein the group $Q^4$ represents any of the following groups:


(a)

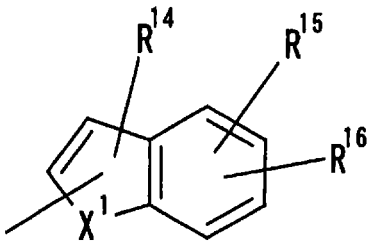
wherein $R^5$ and $R^6$, independently of each other, represent a hydrogen atom or alkyl group, $R^7$ represents a hydrogen atom, and $R^8$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;


(b)

wherein $R^9$ represents a hydrogen atom, and $R^{10}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;

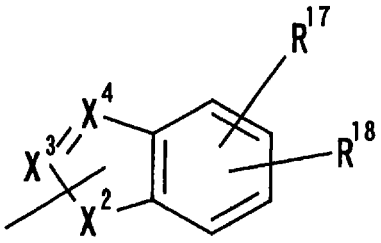

(c)

wherein $R^{11}$ are $R^{12}$ both represent hydrogen atoms, and $R^{13}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



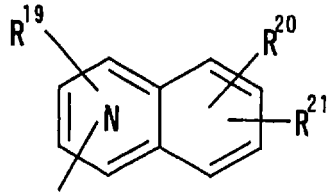

(d)

wherein $X^1$ represents NH, NOH, N, O or S, $R^{14}$ represents a hydrogen atom, halogen atom, acyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group or alkyl group, $R^{15}$ represents a hydrogen atom or halogen atom, and $R^{16}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group;



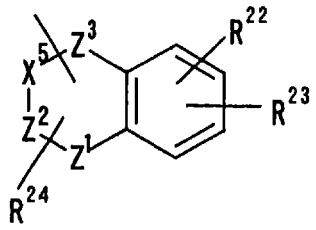

(e)

wherein $X^2$ represents NH, O or S, $X^3$ represents N, C or CH, $X^4$ represents N, C or CH, $R^{17}$ represents a hydrogen atom, and $R^{18}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group, excluding the cases where $X^3$ and $X^4$ are combinations of C and CH, and are both C or CH;



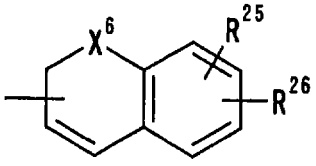
(f)

wherein N indicates that 1 or 2 carbon atoms of the ring substituted by $R^{19}$ have been substituted by a nitrogen atom, $R^{19}$ and $R^{20}$ both represent hydrogen atoms, and $R^{21}$ represents a hydrogen atom, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group or halogenoalkyl group;



(g)

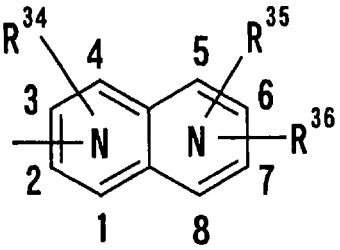
wherein $X^5$ represents $CH_2$, CH, N or NH, $Z^1$ represents N, NH or O, $Z^2$ represents $CH_2$, CH, C or N, $Z^3$ represents $CH_2$, CH, S, $SO_2$ or C=O, $X^5$-$Z^2$ indicates that $X^5$ and $Z^2$ are bonded to each other by a single bond or double bond, $R^{22}$ represents a hydrogen atom, $R^{23}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group, and $R^{24}$ represents a hydrogen atom;



(h)

wherein $X^6$ represents O, $R^{25}$ represents a hydrogen atom,

and $R^{26}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group; or




(1)

wherein numerals 1 to 8 indicate positions, each N indicates that any one of carbon atoms of positions 1 to 4 and any one of carbon atoms of positions 5 to 8 has been substituted by a nitrogen atom, $R^{34}$ represents a hydrogen atom or halogen atom, $R^{35}$ represents a hydrogen atom or halogen atom, and $R^{36}$ represents a hydrogen atom, halogen atom, alkyl group or alkynyl group.

26. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 21, wherein the group $Q^4$ is a 4-chlorostyryl, 4-fluorostyryl, 4-bromostyryl, 4-ethynylstyryl, 4-chlorophenylethynyl, 4-fluorophenylethynyl, 4-bromophenylethynyl, 4-ethynylphenylethynyl, 6-chloro-2-naphthyl, 6-fluoro-2-naphthyl, 6-bromo-2-naphthyl, 6-ethynyl-2-naphthyl, 7-chloro-2-naphthyl, 7-fluoro-2-naphthyl, 7-bromo-2-naphthyl, 7-ethynyl-2-naphthyl, 5-chloroindol-2-yl, 5-fluoroindol-2-yl, 5-bromoindol-2-yl, 5-ethynylindol-2-yl, 5-methylindol-2-yl, 5-chloro-4-fluoroindol-2-yl, 5-chloro-3-fluoroindol-2-yl, 3-bromo-5-chloroindol-2-yl, 3-chloro-5-fluoroindol-2-yl, 3-

bromo-5-fluoroindol-2-yl, 5-bromo-3-chloroindol-2-yl, 5-bromo-3-fluoroindol-2-yl, 5-chloro-3-formylindol-2-yl, 5-fluoro-3-formylindol-2-yl, 5-bromo-3-formylindol-2-yl, 5-ethynyl-3-formylindol-2-yl, 5-chloro-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-fluoro-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-bromo-3-(N,N-dimethylcarbamoyl)indol-2-yl, 5-ethynyl-3-(N,N-dimethylcarbamoyl)indol-2-yl, 6-chloroindol-2-yl, 6-fluoroindol-2-yl, 6-bromoindol-2-yl, 6-ethynylindol-2-yl, 6-methylindol-2-yl, 5-chlorobenzothiophen-2-yl, 5-fluorobenzothiophen-2-yl, 5-bromobenzothiophen-2-yl, 5-ethynylbenzothiophen-2-yl, 5-methylbenzothiophen-2-yl, 5-chloro-4-fluorobenzothiophen-2-yl, 6-chloro-benzothiophen-2-yl, 6-fluorobenzothiophen-2-yl, 6-bromobenzothiophen-2-yl, 6-ethynylbenzothiophen-2-yl, 6-methylbenzothiophen-2-yl, 5-chlorobenzofuran-2-yl, 5-fluorobenzofuran-2-yl, 5-bromobenzofuran-2-yl, 5-ethynylbenzofuran-2-yl, 5-methylbenzofuran-2-yl, 5-chloro-4-fluorobenzofuran-2-yl, 6-chlorobenzofuran-2-yl, 6-fluorobenzofuran-2-yl, 6-bromobenzofuran-2-yl, 6-ethynylbenzofuran-2-yl, 6-methylbenzofuran-2-yl, 5-chlorobenzimidazol-2-yl, 5-fluorobenzimidazol-2-yl, 5-bromobenzimidazol-2-yl, 5-ethynylbenzimidazol-2-yl, 6-chloroquinolin-2-yl, 6-fluoroquinolin-2-yl, 6-bromoquinolin-2-yl, 6-ethynylquinolin-2-yl, 7-chloroquinolin-3-yl, 7-fluoroquinolin-3-yl, 7-bromoquinolin-3-yl, 7-ethynylquinolin-3-yl, 7-

chloroisoquinolin-3-yl, 7-fluoroisoquinolin-3-yl, 7-bromoisoquinolin-3-yl, 7-ethynylisoquinolin-3-yl, 7-chlorocinnolin-3-yl, 7-fluorocinnolin-3-yl, 7-bromocinnolin-3-yl, 7-ethynylcinnolin-3-yl, 7-chloro-2H-chromen-3-yl, 7-fluoro-2H-chromen-3-yl, 7-bromo-2H-chromen-3-yl, 7-ethynyl-2H-chromen-3-yl, 6-chloro-4-oxo-1,4-dihydroquinolin-2-yl, 6-fluoro-4-oxo-1,4-dihydroquinolin-2-yl, 6-bromo-4-oxo-1,4-dihydroquinolin-2-yl, 6-ethynyl-4-oxo-1,4-dihydroquinolin-2-yl, 6-chloro-4-oxo-1,4-dihydroquinazolin-2-yl, 6-fluoro-4-oxo-1,4-dihydroquinazolin-2-yl, 6-bromo-4-oxo-1,4-dihydroquinazolin-2-yl, 6-ethynyl-4-oxo-1,4-dihydroquinazolin-2-yl, 2-chlorothieno[2,3-b]pyrrol-5-yl, 2-fluorothieno[2,3-b]pyrrol-5-yl, 2-bromothieno[2,3-b]-pyrrol-5-yl or 2-ethynylthieno[2,3-b]pyrrol-5-yl group.

27. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 17 to 26, wherein $T^1$ is a carbonyl group.

28. The compound according to Claim 1, which is represented by the general formula (1):

$$Q^1\text{-}Q^2\text{-}T^o\text{-}N(R^1)\text{-}Q^3\text{-}N(R^2)\text{-}T^1\text{-}Q^4 \qquad (1)$$

wherein

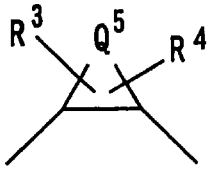
$R^1$ and $R^2$, independently of each other, represent a hydrogen atom, hydroxyl group, alkyl group or alkoxy group;

$Q^1$ represents a saturated or unsaturated, 5- or 6-membered cyclic hydrocarbon group which may be

substituted, a saturated or unsaturated, 5- to 7-membered heterocyclic group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^2$ represents a single bond, a saturated or unsaturated, 5- or 6-membered divalent cyclic hydrocarbon group which may be substituted, a saturated or unsaturated, 5- to 7-membered divalent heterocyclic group which may be substituted, a saturated or unsaturated, divalent bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, divalent bicyclic or tricyclic fused heterocyclic group which may be substituted;

$Q^3$ represents the following group:




in which $Q^5$ means an alkylene group having 1 to 8 carbon atoms, an alkenylene group having 2 to 8 carbon atoms or a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or an integer of 1-3, and A means an oxygen atom, nitrogen atom, sulfur atom, -SO-, $-SO_2-$, -NH-, -O-NH-, -NH-NH-, -S-NH-, -SO-NH- or $-SO_2-NH-$, and $R^3$ and $R^4$ are substituents on carbon atom(s) of a

ring comprising $Q^5$ and are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, cyano group, cyanoalkyl group, amino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, alkoxyimino group, hydroxyimino group, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylalkylamino group, carboxyalkylamino group, alkoxycarbonylamino group, alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, carbamoylalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a

substituent on the alkyl group(s), carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, 3- to 6-membered heterocyclic carbonylalkyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, aryl group, aralkyl group, heteroaryl group, heteroarylalkyl group, alkylsulfonylamino group, arylsulfonylamino group, alkylsulfonylaminoalkyl group, arylsulfonylaminoalkyl group, alkylsulfonylaminocarbonyl group, arylsulfonylaminocarbonyl group, alkylsulfonyl-aminocarbonylalkyl group, arylsulfonylaminocarbonylalkyl group, oxo group, carbamoyloxy group, aralkyloxy group, carboxyalkyloxy group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, alkoxyalkyloxycarbonyl group, hydroxyacyl group, alkoxyacyl group, halogenoacyl group, carboxyacyl group, aminoacyl group, acyloxyacyl group, acyloxyalkylsulfonyl group, hydroxyalkylsulfonyl group, alkoxyalkylsulfonyl group, 3- to 6-membered heterocyclic sulfonyl group which may be substituted, N-alkylaminoacyl group, N,N-dialkylaminoacyl group, N,N-dialkylcarbamoylacyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkylsulfonyl group which may have a substituent on the alkyl group(s), alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl

group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group, or $R^3$ and $R^4$, together with each other, denote an alkylene group having 1 to 5 carbon atoms, alkenylene group having 2 to 5 carbon atoms, alkylenedioxy group having 1 to 5 carbon atoms or carbonyldioxy group;

$Q^4$ represents an aryl group which may be substituted, an arylalkenyl group which may be substituted, an arylalkynyl group which may be substituted, a heteroaryl group which may be substituted, a heteroarylalkenyl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;

$T^0$ represents a carbonyl or thiocarbonyl group; and

$T^1$ represents group -C(=O)-C(=O)-N(R')-, group -C(=S)-C(=O)-N(R')-, group -C(=O)-C(=S)-N(R')-, group -C(=S)-C(=S)-N(R')-, in which R' means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group $-C(=O)-A^1-N(R'')-$, in which $A^1$ means an alkylene group having 1 to 5 carbon atoms, which may be substituted, and R" means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group -C(=O)-NH-, group -C(=S)-NH-, group -C(=O)-NH-NH-, group $-C(=O)-A^2-C(=O)-$, in which $A^2$ means a single bond or alkylene group having 1 to 5 carbon atoms, group $-C(=O)-A^3-C(=O)-NH-$, in which $A^3$

means an alkylene group having 1 to 5 carbon atoms, group $-C(=O)-C(=NOR^a)-N(R^b)-$, group $-C(=S)-C(=NOR^a)-N(R^b)-$, in which $R^a$ means a hydrogen atom, alkyl group or alkanoyl group, and $R^b$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group $-C(=O)-N=N-$, group $-C(=S)-N=N-$, group $-C(=NOR^c)-C(=O)-N(R^d)-$, in which $R^c$ means a hydrogen atom, alkyl group, alkanoyl group, aryl group or aralkyl group, and $R^d$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, group $-C(=N-N(R^e)(R^f))-C(=O)-N(R^g)-$, in which $R^e$ and $R^f$, independently of each other, mean a hydrogen atom, alkyl group, alkanoyl or alkyl(thiocarbonyl) group, and $R^g$ means a hydrogen atom, hydroxyl group, alkyl group or alkoxy group, or thiocarbonyl group,
a salt thereof, a solvate thereof, or an N-oxide thereof.

29. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 28, wherein the group $Q^1$ is a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted, and $Q^2$ is a single bond.

30. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to Claim 28 or 29, wherein the group $Q^1$ is a thienopyridyl group which may be substituted, tetrahydrothienopyridyl group which may be substituted, thiazolopyridyl group which may be

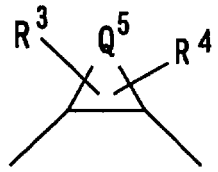
substituted, tetrahydrothiazolopyridyl group which may be substituted, thiazolopyridazinyl group which may be substituted, tetrahydrothiazolopyridazinyl group which may be substituted, pyranothiazolyl group which may be substituted, dihydropyranothiazolyl group which may be substituted, furopyridyl group which may be substituted, tetrahydrofuropyridyl group which may be substituted, oxazolopyridyl group which may be substituted, tetrahydrooxazolopyridyl group which may be substituted, pyrrolopyridyl group which may be substituted, dihydropyrrolopyridyl group which may be substituted, tetrahydropyrrolopyridyl group which may be substituted, pyrrolopyrimidinyl group which may be substituted, dihydropyrrolopyrimidinyl group which may be substituted, oxazolopyridazinyl group which may be substituted, tetrahydrooxazolopyridazinyl group which may be substituted, pyrrolothiazolyl group which may be substituted, dihydropyrrolothiazolyl group which may be substituted, pyrrolooxazolyl group which may be substituted, dihydropyrrolooxazolyl group which may be substituted, benzothiazolyl group which may be substituted, tetrahydrobenzothiazolyl group which may be substituted, thiazolopyrimidinyl group which may be substituted, dihydrothiazolopyrimidinyl group which may be substituted, benzoazepinyl group which may be substituted, tetrahydrobenzoazepinyl group which may be substituted, thiazoloazepinyl group which may be

substituted, tetrahydrothiazoloazepinyl group which may be substituted, thienoazepinyl group which may be substituted, tetrahydrothienoazepinyl group which may be substituted, 4,5,6,7-tetrahydro-5,6-tetramethylenethiazolopyridazinyl group which may be substituted, or 5,6-trimethylene-4,5,6,7-tetrahydro-thiazolopyridazinyl group which may be substituted.

31. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 30, wherein the substituent(s) on the group $Q^1$ are 1 to 3 substituent(s) on the group $Q^1$ are 1 to 3 substituents selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, an amidino group, a hydroxyamidino group, $C_1$-$C_6$ alkyl groups, $C_3$-$C_6$ cycloalkyl-$C_1$-$C_6$ alkyl groups, hydroxy-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkoxy groups, $C_1$-$C_6$ alkoxy-$C_1$-$C_6$ alkyl groups, a carboxyl group, $C_2$-$C_6$ carboxyalkyl groups, $C_2$-$C_6$ alkoxycarbonyl-$C_1$-$C_6$ alkyl groups, amidino groups substituted by a $C_2$-$C_6$ alkoxycarbonyl group, $C_2$-$C_6$ alkenyl groups, $C_2$-$C_6$ alkynyl groups, $C_2$-$C_6$ alkoxycarbonyl groups, amino $C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylamino-$C_1$-$C_6$ alkyl groups, di($C_1$-$C_6$ alkyl)amino-$C_1$-$C_6$ alkyl groups, $C_2$-$C_6$ alkoxycarbonylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkanoyl groups, $C_1$-$C_6$ alkanoylamino-$C_1$-$C_6$ alkyl groups, $C_1$-$C_6$ alkylsulfonyl groups, $C_1$-$C_6$ alkylsulfonylamino-$C_1$-$C_6$ alkyl groups, a carbamoyl group, $C_1$-$C_6$ alkylcarbamoyl groups, N,N-di($C_1$-$C_6$

alkyl)carbamoyl groups, $C_1$-$C_6$ alkylamino groups, di($C_1$-$C_6$ alkyl)amino groups, 5- or 6-membered heterocyclic groups containing one of nitrogen, oxygen and sulfur or the same or different two atoms thereof, 5- or 6-membered heterocyclic group-$C_1$-$C_4$ alkyl group, and 5- or 6-membered heterocyclic group-amino-$C_1$-$C_4$ alkyl group.

32. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 31, wherein the group $Q^3$ is

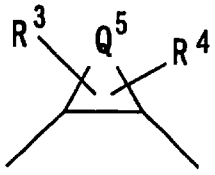



wherein $Q^5$ means an alkylene group having 3 to 6 carbon atoms or a group $-(CH_2)_m-CH_2-A-CH_2-(CH_2)_n-$, in which m and n are independently of each other 0 or 1, and A has the same meaning as defined above, and $R^3$ and $R^4$ are independently of each other a hydrogen atom, hydroxyl group, alkyl group, alkenyl group, alkynyl group, halogen atom, halogenoalkyl group, amino group, hydroxyimino group, alkoxyimino group, aminoalkyl group, N-alkylaminoalkyl group, N,N-dialkylaminoalkyl group, acyl group, acylalkyl group, acylamino group which may be substituted, acylaminoalkyl group, alkoxy group, alkoxyalkyl group, hydroxyalkyl group, carboxyl group, carboxyalkyl group, alkoxycarbonyl group, alkoxycarbonylalkyl group, alkoxycarbonylamino group,

alkoxycarbonylaminoalkyl group, carbamoyl group, N-alkylcarbamoyl group which may have a substituent on the alkyl group, N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s), N-alkenylcarbamoyl group, N-alkenylcarbamoylalkyl group, N-alkenyl-N-alkylcarbamoyl group, N-alkenyl-N-alkylcarbamoylalkyl group, N-alkoxycarbamoyl group, N-alkyl-N-alkoxycarbamoyl group, N-alkoxycarbamoylalkyl group, N-alkyl-N-alkoxycarbamoylalkyl group, carbazoyl group which may be substituted by 1 to 3 alkyl groups, alkylsulfonyl group, alkylsulfonylalkyl group, 3- to 6-membered heterocyclic carbonyl group which may be substituted, 3- to 6-membered heterocyclic carbonyloxyalkyl group which may be substituted, carbamoylalkyl group, carbamoyloxyalkyl group, N-alkylcarbamoyloxyalkyl group, N,N-dialkylcarbamoyloxyalkyl group, N-alkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), N,N-dialkylcarbamoylalkyl group which may have a substituent on the alkyl group(s), alkylsulfonylamino group, alkylsulfonylaminoalkyl group, oxo group, acyloxy group, acyloxyalkyl group, arylsulfonyl group, alkoxycarbonylalkylsulfonyl group, carboxyalkylsulfonyl group, alkoxycarbonylacyl group, carboxyacyl group, alkoxyalkyloxycarbonyl group, halogenoacyl group, N,N-dialkylaminoacyl group, acyloxyacyl group, hydroxyacyl group, alkoxyacyl group, alkoxyalkylsulfonyl group, N,N-

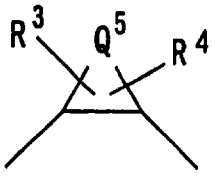
dialkylcarbamoylacyl group, N,N-dialkylcarbamoylalkylsulfonyl group, alkylsulfonylacyl group, aminocarbothioyl group, N-alkylaminocarbothioyl group, N,N-dialkylaminocarbothioyl group or alkoxyalkyl(thiocarbonyl) group.

33. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 31, wherein the group $Q^3$ is




wherein $Q^5$ means an alkylene group having 4 carbon atoms, $R^3$ is a hydrogen atom, and $R^4$ is an N,N-dialkylcarbamoyl group which may have a substituent on the alkyl group(s).

34. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 31, wherein the group $Q^3$ is




wherein $Q^5$ means an alkylene group having 4 carbon atoms, $R^3$ is a hydrogen atom, and $R^4$ is an N,N-dimethylcarbamoyl group.

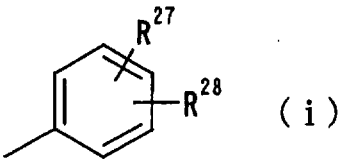
35. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of

claims 28 to 34, wherein the group $Q^4$ is a group selected from a phenyl group which may be substituted, a pyridyl group which may be substituted, a pyridazinyl group which may be substituted, a pyrazinyl group which may be substituted, a furyl group which may be substituted, a thienyl group which may be substituted, a pyrrolyl group which may be substituted, a thiazolyl group which may be substituted, an oxazolyl group which may be substituted, a pyrimidinyl group which may be substituted and a tetrazolyl group which may be substituted,

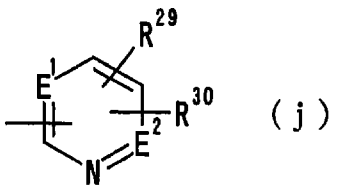
36. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 35, wherein the substituent(s) on the group $Q^4$ are 1 to 3 substituents selected from a hydroxyl group, halogen atoms, halogenoalkyl groups, an amino group, a cyano group, aminoalkyl groups, a nitro group, hydroxyalkyl groups, alkoxyalkyl groups, a carboxyl group, carboxyalkyl groups, alkoxycarbonylalkyl groups, acyl groups, an amidino group, a hydroxyamidino group, linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, linear, branched or cyclic alkoxy groups having 1 to 6 carbon atoms, amidino groups substituted by a linear, branched or cyclic alkoxycarbonyl group having 2 to 7 carbon atoms, linear, branched or cyclic alkenyl groups having 2 to 6 carbon atoms, linear or branched alkynyl groups having 2 to 6 carbon atoms, linear, branched or cyclic alkoxycarbonyl groups having

2 to 6 carbon atoms, a carbamoyl group, mono- or di-alkylcarbamoyl groups substituted by a linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms on the nitrogen atom(s), mono- or di-alkylamino groups substituted by linear, branched or cyclic alkyl groups having 1 to 6 carbon atoms, and 5- or 6-membered nitrogen-containing heterocyclic groups.

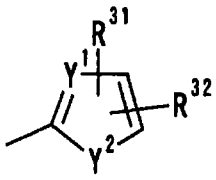
37. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 34, wherein the group $Q^4$ is


(i)

wherein $R^{27}$ and $R^{28}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group;


(j)

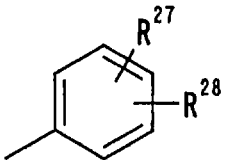
wherein $E^1$ and $E^2$, independently of each other, represent N or CH, and $R^{29}$ and $R^{30}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group; or


(k)

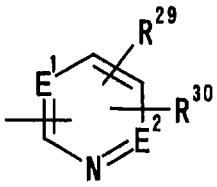
wherein $Y^1$ represents CH or N, $Y^2$ represents $-N(R^{33})-$, in which $R^{33}$ means a hydrogen atom or alkyl group having 1 to 6 carbon atoms, O or S, and $R^{31}$ and $R^{32}$, independently of each other, represent a hydrogen atom, hydroxyl group, nitro group, amino group, cyano group, halogen atom, alkyl group, alkenyl group, alkynyl group, halogenoalkyl group, hydroxyalkyl group, alkoxy group, alkoxyalkyl group, carboxyl group, carboxyalkyl group, acyl group, carbamoyl group, N-alkylcarbamoyl group, N,N-dialkylcarbamoyl group, alkoxycarbonyl group, amidino group or alkoxycarbonylalkyl group.

38. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of

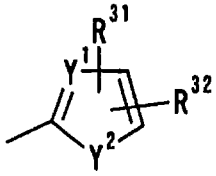
claims 28 to 34, wherein the group $Q^4$ is


(i)

wherein $R^{27}$ is a hydrogen atom or halogen atom, and $R^{28}$ is a hydrogen atom, halogen atom, alkyl group or alkynyl group;


(j)

wherein $E^1$ and $E^2$, independently of each other, represent N or CH, $R^{29}$ is a hydrogen atom or halogen atom, and $R^{30}$ is a hydrogen atom, halogen atom, alkyl group or alkynyl group; or


(k)

wherein $Y^1$ is CH or N, $Y^2$ is $-N(R^{33})-$, in which $R^{33}$ means a hydrogen atom or alkyl group having 1 to 6 carbon atoms, O or S, and $R^{31}$ is a hydrogen atom or halogen atom and $R^{32}$ is a hydrogen atom, halogen atom, alkyl group or alkynyl group.

39. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of

claims 28 to 34, wherein the group $Q^4$ is a phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-bromophenyl, 4-ethynylphenyl, 3-chlorophenyl, 3-fluorophenyl, 3-bromophenyl, 3-ethynylphenyl, 3-chloro-4-fluorophenyl, 4-chloro-3-fluorophenyl, 4-chloro-2-fluorophenyl, 2-chloro-4-fluorophenyl, 4-bromo-2-fluorophenyl, 2-bromo-4-fluorophenyl, 2,4-dichlorophenyl, 2,4-difluorophenyl, 2,4-dibromophenyl, 4-chloro-3-methylphenyl, 4-fluoro-3-methylphenyl, 4-bromo-3-methylphenyl, 4-chloro-2-methylphenyl, 4-fluoro-2-methylphenyl, 4-bromo-2-methylphenyl, 3,4-dichlorophenyl, 3,4-difluorophenyl, 3,4-dibromophenyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 4-chloro-2-pyridyl, 4-fluoro-2-pyridyl, 4-bromo-2-pyridyl, 4-ethynyl-2-pyridyl, 4-chloro-3-pyridyl, 4-fluoro-3-pyridyl, 4-bromo-3-pyridyl, 4-ethynyl-3-pyridyl, 5-chloro-2-pyridyl, 5-fluoro-2-pyridyl, 5-bromo-2-pyridyl, 5-ethynyl-2-pyridyl, 4-chloro-5-fluoro-2-pyridyl, 5-chloro-4-fluoro-2-pyridyl, 5-chloro-3-pyridyl, 5-fluoro-3-pyridyl, 5-bromo-3-pyridyl, 5-ethynyl-3-pyridyl, 6-chloro-3-pyridazinyl, 6-fluoro-3-pyridazinyl, 6-bromo-3-pyridazinyl, 6-ethynyl-3-pyridazinyl, 5-chloro-2-thiazolyl, 5-fluoro-2-thiazolyl, 5-bromo-2-thiazolyl or 5-ethynyl-2-thiazolyl.

40. The compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 28 to 39, wherein the group $T^1$ is a group -C(=O)-C(=O)-N(R')-, group -C(=S)-C(=O)-N(R')-, group -C(=O)-

C(=S)-N(R')- or group -C(=S)-C(=S)-N(R')-.

41. A medicine comprising the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

42. An activated blood coagulation factor X inhibitor comprising the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

43. An anticoagulant comprising the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

44. An agent for preventing and/or treating thrombosis or embolism, comprising the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

45. An agent for preventing and/or treating cerebral infarction, cerebral embolism, myocardial infarction, angina pectoris, pulmonary infarction, pulmonary embolism, Buerger's disease, deep venous thrombosis, disseminated intravascular coagulation syndrome, thrombus formation after valve or joint replacement, thrombus formation and reocclusion after angioplasty, systemic inflammatory response syndrome (SIRS), multiple organ dysfunction syndrome (MODS), thrombus formation during extracorporeal circulation, or blood clotting upon blood drawing, comprising the compound, the salt thereof, the solvate thereof, or the

N-oxide thereof according to any one of claims 1 to 40.

46. A medicinal composition comprising the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40, and a pharmaceutically acceptable carrier.

47. Use of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40 for preparation of a medicine.

48. Use of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40 for preparation of an activated blood coagulation factor X inhibitor.

49. Use of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40 for preparation of an anticoagulant.

50. Use of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40 for preparation of an agent for preventing and/or treating thrombosis or embolism.

51. Use of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40 for preparation of an agent for preventing and/or treating cerebral infarction, cerebral embolism, myocardial infarction, angina pectoris, pulmonary infarction, pulmonary embolism, Buerger's disease, deep venous thrombosis, disseminated

intravascular coagulation syndrome, thrombus formation after valve or joint replacement, thrombus formation and reocclusion after angioplasty, systemic inflammatory response syndrome (SIRS), multiple organ dysfunction syndrome (MODS), thrombus formation during extracorporeal circulation, or blood clotting upon blood drawing.

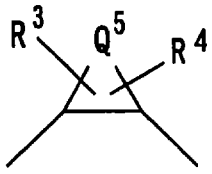
52. A method for treating thrombosis or embolism, which comprises administering an effective amount of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

53. A method for treating cerebral infarction, cerebral embolism, myocardial infarction, angina pectoris, pulmonary infarction, pulmonary embolism, Buerger's disease, deep venous thrombosis, disseminated intravascular coagulation syndrome, thrombus formation after valve or joint replacement, thrombus formation and reocclusion after angioplasty, systemic inflammatory response syndrome (SIRS), multiple organ dysfunction syndrome (MODS), thrombus formation during extracorporeal circulation, or blood clotting upon blood drawing, which comprises administering an effective amount of the compound, the salt thereof, the solvate thereof, or the N-oxide thereof according to any one of claims 1 to 40.

54. A compound represented by the following general formula (4):

$$HN(R^1)-Q^3-N(R^2)-T^1-Q^4 \qquad (4)$$

wherein $R^1$, $R^2$ and $T^1$ have the same meanings as defined in claim 1, $Q^3$ represents the following group:

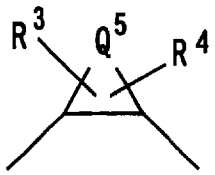



wherein $Q^5$, $R^3$ and $R^4$ have the same meanings as defined in claim 1, and $Q^4$ represents an aryl group which may be substituted, a heteroaryl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;
a salt thereof, a solvate thereof, or an N-oxide thereof.

55. A compound represented by the following general formula (9):

$$Q^1-Q^2-C(=O)-N(R^1)-Q^3-NHR^2 \qquad (9)$$

wherein $Q^2$, $R^1$ and $R^2$ have the same meanings as defined in claim 1, $Q^1$ represents a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted, and $Q^3$ represents the following group:



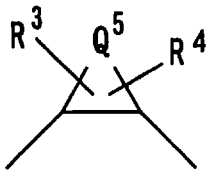

in which $Q^5$, $R^3$ and $R^4$ have the same meanings as defined

in claim 1, a salt thereof, a solvate thereof, or an N-oxide thereof.

56. A compound represented by the following general formula (4):

$$HN(R^1)-Q^3-N(R^2)-T^1-Q^4 \qquad (4)$$

wherein $R^1$, $R^2$ and $T^1$ have the same meanings as defined in claim 17, $Q^3$ represents the following group:

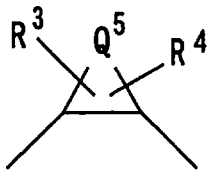



wherein $Q^5$, $R^3$ and $R^4$ have the same meanings as defined in claim 17, and $Q^4$ represents an aryl group which may be substituted, a heteroaryl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;
and a salt thereof, a solvate thereof, or an N-oxide thereof.

57. A compound represented by the following general formula (9):

$$Q^1-Q^2-C(=O)-N(R^1)-Q^3-NHR^2 \qquad (9)$$

wherein $Q^2$, $R^1$ and $R^2$ have the same meanings as defined in claim 17, $Q^1$ represents a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted, and $Q^3$ represents the following group:

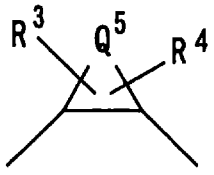


in which $Q^5$, $R^3$ and $R^4$ have the same meanings as defined in claim 17, a salt thereof, a solvate thereof, or an N-oxide thereof.

58. A compound represented by the following general formula (4):

$$HN(R^1)-Q^3-N(R^2)-T^1-Q^4 \qquad (4)$$

wherein $R^1$, $R^2$ and $T^1$ have the same meanings as defined in claim 28, $Q^3$ represents the following group:

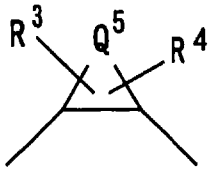


wherein $Q^5$, $R^3$ and $R^4$ have the same meanings as defined in claim 28, and $Q^4$ represents an aryl group which may be substituted, a heteroaryl group which may be substituted, a saturated or unsaturated, bicyclic or tricyclic fused hydrocarbon group which may be substituted, or a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted;
and a salt thereof, a solvate thereof, or an N-oxide thereof.

59. A compound represented by the following general formula (9):

$$Q^1\text{-}Q^2\text{-}C(=O)\text{-}N(R^1)\text{-}Q^3\text{-}NHR^2 \qquad (9)$$

wherein $Q^2$, $R^1$ and $R^2$ have the same meanings as defined in claim 28, $Q^1$ represents a saturated or unsaturated, bicyclic or tricyclic fused heterocyclic group which may be substituted, and $Q^3$ represents the following group:




in which $Q^5$, $R^3$ and $R^4$ have the same meanings as defined in claim 28, a salt thereof, a solvate thereof, or an N-oxide thereof.