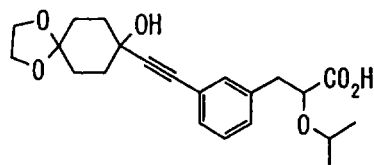


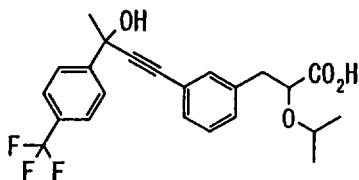
Example 114. 3-3-[2-(8-Hydroxy-1,4-dioxaspiro[4.5]dec-8-yl)-1-ethynyl]phenyl-2-isopropoxypropanoic acid



Using 1,4-dioxaspiro[4.5]decane-8-one, the title compound was obtained in the same manner as described in Example 113b).

MS *m/e*(ESI) 411 (MNa⁺)

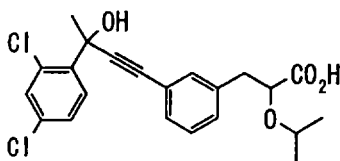
Example 115. 3-(3-3-Hydroxy-3-[4-(trifluoromethyl)phenyl]-1-butynylphenyl)-2-isopropoxypropanoic acid



Using 4-trifluoromethylacetophenone, the title compound was obtained in the same manner as described in Example 113b).

MS *m/e*(ESI) 443 (MNa⁺)

Example 116. 3-3-[3-(2,4-Dichlorophenyl)-3-hydroxy-1-buthynyl]phenyl-2-isopropoxypropanoic acid

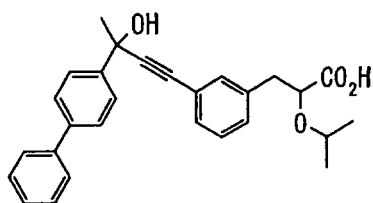


Using 2,4-dichloroacetophenone, the title compound was obtained in the same manner as described in Example 113b).

MS *m/e*(ESI) 443 (MNa⁺)

Example 117. 3-3-[3-Biphenyl-3-hydroxy-1-butynyl]phenyl-2-isopropoxypropanoic acid

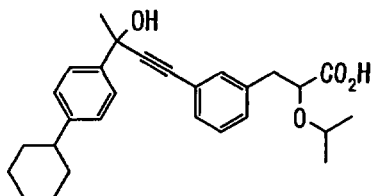




Using 4-phenylacetophenone, the title compound was obtained in the same manner as described in Example 113b).

MS m/e (ESI) 451 (MNa^+)

Example 118. 3-3-[3-(4-cyclohexylphenyl)-3-hydroxy-1-butynyl]phenyl-2-isopropoxypropanoic acid

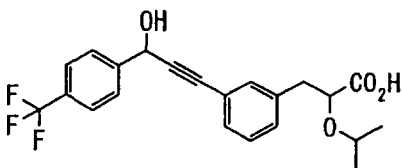


Using 4-cyclohexylacetophenone, the title compound was obtained in the same manner as described in Example 113b).

MS m/e (ESI) 457 (MNa^+)

Example 119.

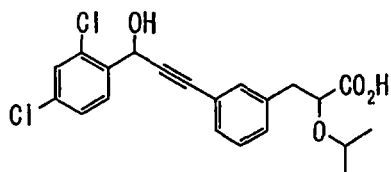
3-(3-3-Hydroxy-3-[4-(trifluoromethyl)phenyl]-1-propynyl)-2-isopropoxypropanoic acid



Using 4-trifluoromethylbenzaldehyde, 1.20 mg of the title compound was obtained in the same manner as described in Example 113b).

MS m/e (ESI) 429 (MNa^+)

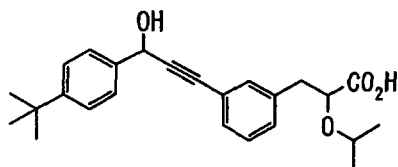
Example 120. 3-(3-Hydroxy-3-[2,4-dichlorophenyl]-1-propynyl)-2-isopropoxypropanoic acid



Using 2,4-dichlorobenzaldehyde, the title compound was obtained in the same manner as described in Example 113b).

MS m/e (ESI) 429 (MNa^+)

Example 121. 3-(3-[4-t-Butylphenyl]-3-hydroxy-1-propynylphenyl)-2-isopropoxypropanoic acid



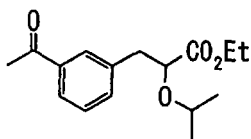
Using 4-*t*-butylbenzaldehyde, the title compound was obtained in the same manner as described in Example 113b).

MS m/e (ESI) 417 (MNa^+)

Example 122. 3-3-[3-(4-Chlorophenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid

Production example 122a) Ethyl

3-(3-acetylphenyl)-2-isopropoxypropanoate



2.037g of Ethyl

2-isopropoxy-3-(3-[(trifluoromethyl)sulfonyl]oxyphenyl)-propanoate, 2.5g of ethyl [1-(1,1,1-tributylstannyl)vinyl]

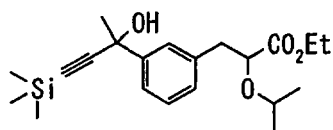
ether, 500 mg of lithium chloride and 186 mg of dichlorobis(triphenylphosphine)palladium were dissolved in 15 ml of dioxane, and the mixture was stirred at 90°C overnight under nitrogen atmosphere. The solution was cooled in ice bath, added with 1N-hydrochloric acid, and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off. The residue was purified by silica gel column chromatography, to give 1.041g of the title compound in the 6:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 0.91 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.25 (t, J=7.2Hz, 3H) 2.59 (s, 3H) 2.94 (dd, J=8.8, 14.0Hz, 1H) 3.08 (dd, J=4.8, 14.0Hz, 1H) 3.50 (Sept, J=6.0Hz, 1H) 4.05 (dd, J=4.8, 8.8Hz, 1H) 4.15-4.22 (m, 2H) 7.38 (t, J=7.6Hz, 1H) 7.47 (dt, J=1.6, 7.6Hz, 1H) 7.82 (dt, J=1.6, 7.6Hz, 1H) 7.87 (dd, J=1.2, 1.6Hz, 1H)

Production example 112b) Ethyl

3-3-[1-hydroxy-1-methyl-3-(1,1,1-trimethylsilyl)-2-propynyl]phenyl-2-isopropoxypropanoate



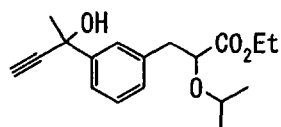
243 mg of Trimethylsilyl acetylene was dissolved in 5 ml of tetrahydrofuran, and 1.43 ml of butyl lithium (1.56 M solution in hexane) and 283 µl of boron trifluoride ether complex were added under nitrogen atmosphere at -78°C, and the mixture was then stirred for 30 minutes. A solution of 345 mg of ethyl

3-(3-acetylphenyl)-2-isopropoxypropanoate in tetrahydrofuran (2ml) was added thereto, and stirring was continued for 30 minutes. A saturated aqueous ammonium chloride was added thereto, and the mixture was extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off. The residue was purified by silica gel column chromatography, to give 256 mg of the title compound in the 6:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 0.21 (s, 9H) 0.94, 0.95 (each d, J=6.4Hz, 3H) 1.15, 1.16 (each d, J=6.0Hz, 3H) 1.24, 1.25 (each t, J=7.2Hz, 3H) 1.74 (s, 3H) 2.35 (s, 1H) 2.93-3.05 (m, 2H) 3.47-3.54 (m, 1H) 4.06 (dd, J=4.8, 8.4Hz, 1H) 4.12-4.19 (m, 2H) 7.18 (d, J=8.0Hz, 1H) 7.26-7.29 (m, 1H) 7.46-7.55 (m, 2H)

Production example 112c) Ethyl 3-3-[1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoate



256 mg of Ethyl

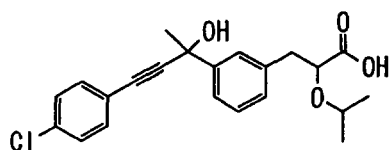
3-3-[1-hydroxy-1-methyl-3-(1,1,1-trimethylsilyl)-2-propynyl]phenyl-2-isopropoxypropanoate was dissolved in 4 ml of tetrahydrofuran, and 0.1 ml of acetic acid and 1 ml of tetrabutylammonium fluoride (1M solution in tetrahydrofuran) were added under ice-cooling, and the mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate, and washed with saturated aqueous sodium bicarbonate and water.

The organic layer was dried over anhydrous magnesium sulfate, filtered and the solvent was distilled off. The residue was purified by silica gel column chromatography, to give 185 mg of the title compound in the 4:1 hexane-ethyl acetate fraction.

^1H NMR (CDCl_3)

δ : 0.94 (d, $J=6.4\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 1.25 (t, $J=7.2\text{Hz}$, 3H) 1.78 (s, 3H) 2.43 (s, 1H) 2.67 (s, 1H) 2.98 (dd, $J=2.0, 8.8\text{Hz}$, 1H) 3.03 (dd, $J=4.8, 13.6\text{Hz}$, 1H) 3.50 (Sept, $J=6.0\text{Hz}$, 1H) 4.06 (ddd, $J=2.8, 4.8, 8.8\text{Hz}$, 1H) 4.14-4.22 (m, 2H) 7.20 (dd, $J=1.2, 7.6\text{Hz}$, 1H) 7.26 (s, 1H) 7.29 (t, $J=7.6\text{Hz}$, 1H) 7.51-7.57 (m, 1H)

Example 112d) 3-3-[3-(4-Chlorophenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid



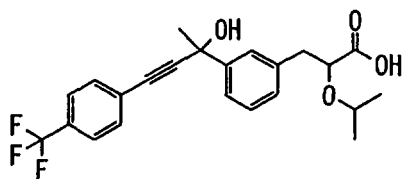
12 mg of Ethyl 3-3-[1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoate, 20 mg of 4-iodochlorobenzene, 5 mg of copper iodide, 5 mg of tetrakis(triphenylphosphine)palladium and 50 μl of triethylamine were dissolved in 0.2 ml of N,N -dimethylformamide, and the mixture was stirred at room temperature for 2 days under nitrogen atmosphere. The reaction mixture was diluted with ethyl acetate and washed with water and 1N hydrochloric acid. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off, to give ethyl 3-3-[3-(4-chlorophenyl)-1-hydroxy-1-methyl-

2-propynyl]phenyl-2-isopropoxypropanoate. This product was dissolved in 0.4 ml of ethanol, and 0.1 ml of 5N-sodium hydroxide was added, and the mixture was kept still at room temperature overnight. The reaction solution was acidified by adding 1N-hydrochloric acid, and extracted with ethyl acetate. The residue was purified by reverse-phase high performance liquid chromatography, to give 4.07 mg of the title compound.

MS m/e (ESI) 409 (MNa^+)

Example 113.

3-3-[3-(4-Trifluoromethylphenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid



Using 4-iodobenzotrifluoride, the title compound was obtained in the same manner as described in Example 112d).

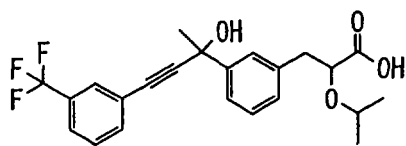
^1H NMR ($CDCl_3$)

δ : 1.06 (d, $J=6.4$ Hz, 3H) 1.15 (d, $J=6.0$ Hz, 3H) 1.87 (s, 3H) 2.27 (s, 1H) 3.00 (ddd, $J=2.4, 8.0, 13.6$ Hz, 1H) 3.17 (dd, $J=3.6, 14.0$ Hz, 1H) 3.52-3.59 (m, 1H) 4.14-4.18 (m, 1H) 7.21 (d, $J=7.6$ Hz, 1H) 7.33 (dd, $J=7.6, 8.8$ Hz, 1H) 7.57-7.61 (m, 6H)

MS m/e (ESI) 443 (MNa^+)

Example 114.

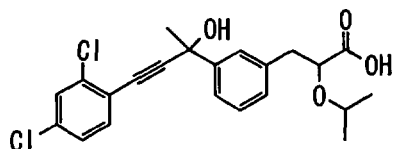
3-3-[3-(3-Trifluoromethylphenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid



Using 3-iodobenzotrifluoride, the title compound was obtained in the same manner as described in Example 112d).

MS m/e (ESI) 443 (MNa^+)

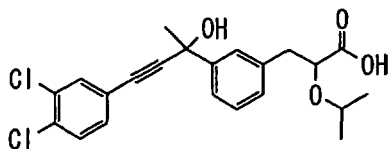
Example 115. 3-3-[3-(2,4-Dichlorophenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid



Using 2,4-dichloriodobenzene, the title compound was obtained in the same manner as described in Example 112d).

MS m/e (ESI) 443 (MNa^+)

Example 116. 3-3-[3-(3,4-Dichlorophenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid



Using 3,4-dichloriodobenzene, the title compound was obtained in the same manner as described in Example 112d).

^1H NMR ($CDCl_3$)

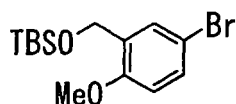
δ : 1.01, 1.02 (each d, $J=6.4$ Hz and 6.0Hz, 3H) 1.15 (d, $J=6.4$ Hz, 3H) 1.85 (s, 3H) 2.05 (s, 1H) 3.01 (dd, $J=8.0$, 14.0Hz, 1H) 3.18 (dd, $J=4.0$, 13.2Hz, 1H) 3.56 (Sept, $J=6.0$ Hz, 1H) 4.17 (dd, $J=3.6$, 7.6Hz, 1H) 7.21 (d, $J=8.0$ Hz, 1H) 7.28-7.35 (m, 2H) 7.40 (d, $J=8.8$ Hz, 1H) 7.54-7.59 (m, 3H)

MS m/e (ESI) 443 (MNa^+)

Example 117. 2-Isopropoxy-3-4-methoxy-3-[(2-(trifluoromethyl)benzyl)oxyimino)methyl]phenylpropanoic acid

Production example 117a)

[(5-Bromo-2-methoxybenzyl)oxy](t-butyl)dimethylsilane

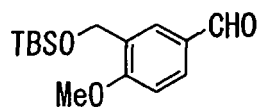


14 g of 2-Methoxybenzyl alcohol was dissolved in 200 ml of N,N-dimethylformamide, and 19.5g of t-butyl chlorodimethylsilane and 13.6 g of imidazole were added. After stirring was continued at room temperature overnight, the solution was diluted with ethyl acetate, and washed successively with 1N hydrochloric acid and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. Then, the resulting crude product was dissolved in 200 ml of acetonitrile, and 21 g of N-bromosuccinimide was added under ice-cooling. After stirring was continued at room temperature for 5 hours, the solvent was evaporated. The residue was dissolved in ethyl acetate, and washed successively with water and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 26 g of the title compound in the 2:1 hexane-diethyl ether fraction.

^1H -NMR ($CDCl_3$)

δ : 0.12 (s, 6H) 0.96 (s, 9H) 3.80 (s, 3H) 4.70 (s, 2H) 6.68 (d, $J=8.4$ Hz, 1H) 7.31 (dd, $J=1.6, 8.4$ Hz, 1H) 7.56 (d, $J=1.6$ Hz, 1H)

Production example 117b) 3-([1-t-Butyl-1,1-dimethylsilyl]oxy)methyl)-4-methoxybenzaldehyde



12g of

[(5-Bromo-2-methoxybenzyl)oxy](t-butyl)dimethylsilane was dissolved in 150 ml of tetrahydrofuran, and the mixture was cooled to -78°C under nitrogen atmosphere. To the mixture was added 28 ml of butyllithium (1.52M solution in hexane), and the mixture was stirred for 30 minutes, and then a solution of 8.3 g of 4-formylmorpholine in 10 ml of tetrahydrofuran was added. After stirring was continued at -78°C for 1 hour, 1N-hydrochloric acid was added thereto. The mixture was extracted with ethyl acetate, and the organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 5.8 g of the title compound in the hexane-ethyl acetate (5:1) fraction.

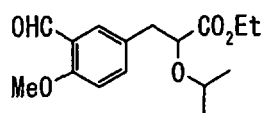
$^1\text{H-NMR}$ (CDCl_3)

δ : 0.12 (s, 6H) 0.93 (s, 9H) 3.91 (s, 3H) 4.76 (s, 2H) 6.94 (d, $J=8.4$ Hz, 1H) 7.80 (dd, $J=1.6, 8.4$ Hz, 1H) 8.01 (d, $J=1.6$ Hz, 1H) 9.90 (s, 1H)

Production example 117c) Ethyl 3-[3-([1-t-butyl-1,1-dimethylsilyl]oxy)methyl)-4-methoxyphenyl]-2-isopropoxypropanoate

1H) 3.85 (s, 3H) 4.00 (dd, J=5.2, 8.4Hz, 1H) 4.11-4.21 (m, 2H) 4.65 (d, J=6.4Hz, 2H) 6.79 (d, J=8.8Hz, 1H) 7.14-7.15 (m, 2H)

Production example 117e) Ethyl 3-[3-(formyl)-4-methoxyphenyl]-2-isopropoxypropanoate

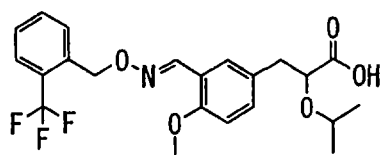


826 mg of Ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate was dissolved in 20 ml of dichloromethane, and 390 mg of N-methylmorpholine N-oxide, 1.4 g of molecular sieve 4A and 49 mg of tetrapropylammonium perruthenate were added, and the mixture was stirred at room temperature overnight. The reaction mixture was filtered through Celite, the filtrate was concentrated, and the residue was purified by silica gel column chromatography, to give 782 mg of the title compound in the 5:1 → 2:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ: 0.95 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.25 (t, J=7.2Hz, 3H) 2.91 (dd, J=8.8, 14.0Hz, 1H) 2.99 (dd, J=4.8, 14.0Hz, 1H) 3.51 (Sept, J=6.0Hz, 1H) 3.91 (s, 3H) 4.02 (dd, J=4.4, 8.4Hz, 1H) 4.11-4.20 (m, 2H) 6.92 (dd, J=2.4, 8.4Hz, 1H) 7.46 (dd, J=2.4, 8.4Hz, 1H) 7.72 (d, J=2.4Hz, 1H) 10.45 (s, 1H)

Example 117f) 2-Isopropoxy-3-(4-methoxy-3-((2-(trifluoromethyl)benzyl)oxyimino)methyl)phenylpropanoic acid



138 mg of Ethyl

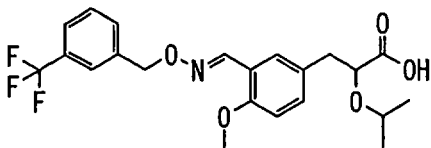
3-[3-(formyl)-4-methoxyphenyl]-2-isopropoxypropanoate was dissolved in 2 ml of ethanol and 0.5 ml of water, and 40 mg of hydroxylamine hydrochloride and 70 ml sodium acetate were added, and the mixture was stirred at room temperature for 15 minutes. The reaction mixture was diluted with ethyl acetate, and washed with water and 1N hydrochloric acid. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off, to give 178 mg of ethyl 3-[3-(hydroxyiminomethyl)-4-methoxyphenyl]-2-isopropoxypropanoate. 12 mg of this compound was dissolved in 0.2 ml of tetrahydrofuran, and 20 mg of 2-trifluoromethylbenzyl bromide and 10 mg sodium hydride were added, and the mixture was stirred at room temperature overnight. To the reaction mixture were added 0.4 ml of ethanol and 0.1 ml of 5N-sodium hydroxide, and the mixture was stirred at room temperature for 4 hours. Then the reaction mixture was neutralized with 1N-hydrochloric acid, extracted with ethyl acetate, and the solvent was concentrated. The residue was purified by reverse-phase high performance liquid chromatography, to give 2.1 mg of the title compound.

MS m/e (ESI) 440 (MH^+)

Example 118.

2-Isopropoxy-3-(4-methoxy-3-([3-(trifluoromethyl)benzyl])-

oxyimino)methyl]phenylpropanoic acid

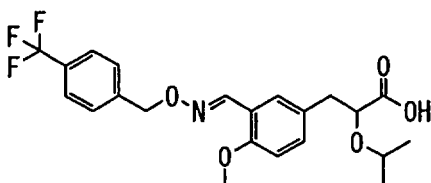


Using 3-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 440 (MH^+)

Example 119. 2-Isopropoxy-3-

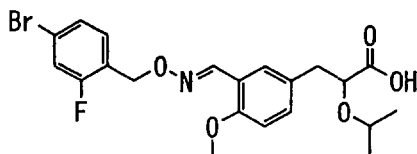
4-methoxy-3-[[4-(trifluoromethyl)benzyl]oxyimino)methyl]-
phenylpropanoic acid



Using 4-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 440 (MH^+)

Example 120. 2-Isopropoxy-3-4-methoxy-3-[[4-bromo-
2-fluorobenzyl]oxyimino)methyl]phenylpropanoic acid

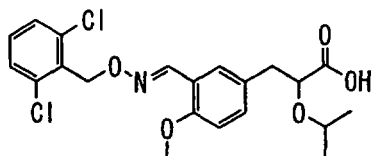


Using 4-bromo-2-fluorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 468 (MH^+)

Example 121. 2-Isopropoxy-3-4-methoxy-

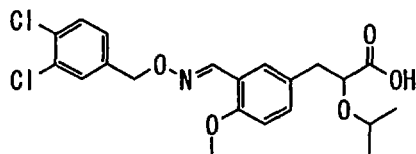
3-[[[2,6-dichlorobenzyl]oxyimino)methyl]phenylpropanoic acid



Using 2,6-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 440 (MH^+)

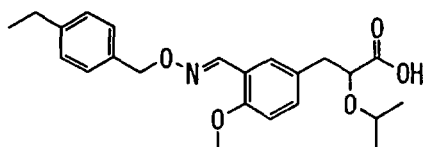
Example 122. 2-Isopropoxy-3-4-methoxy-3-[[[3,4-dichlorobenzyl]oxyimino)methyl]phenylpropanoic acid



Using 3,4-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 440 (MH^+)

Example 123. 2-Isopropoxy-3-4-methoxy-3-[[[4-ethylbenzyl]oxyimino)methyl]phenylpropanoic acid

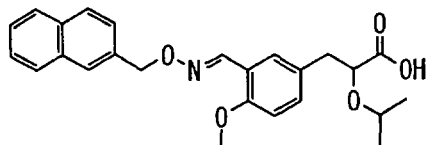


Using 4-ethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 400 (MH^+)

Example 124. 2-Isopropoxy-3-4-methoxy-

3-[[[2-naphtyl]oxyimino)methyl]phenylpropanoic acid

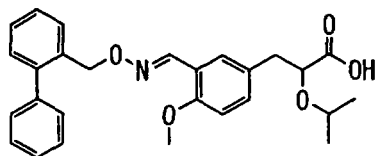


Using 2-bromomethylnaphthalene, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 422 (MH^+)

Example 125. 2-Isopropoxy-3-4-methoxy-

3-[[[2-phenylbenzyl]oxyimino)methyl]phenylpropanoic acid

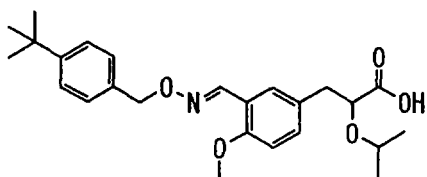


Using 2-phenylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 448 (MH^+)

Example 126. 2-Isopropoxy-3-4-methoxy-

3-[[[4-t-butylbenzyl]oxyimino)methyl]phenylpropanoic acid

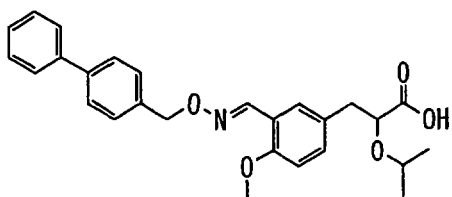


Using 4-t-butylbenzyl chloride, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 428 (MH^+)

Example 127. 2-Isopropoxy-3-4-methoxy-

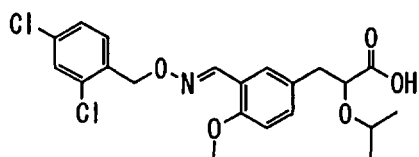
3-[[[4-phenylbenzyl]oxyimino)methyl]phenylpropanoic acid



Using 4-phenylbenzyl chloride, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 448 (MH^+)

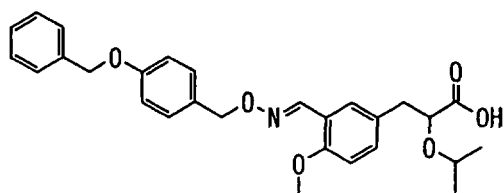
Example 128. 2-Isopropoxy-3-4-methoxy-3-([2,4-dichlorobenzyl]oxyimino)methylphenylpropanoic acid



Using 2,4-dichlorobenzyl chloride, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 440 (MH^+)

Example 129. 2-Isopropoxy-3-4-methoxy-3-([4-benzyloxybenzyl]oxyimino)methylphenylpropanoic acid

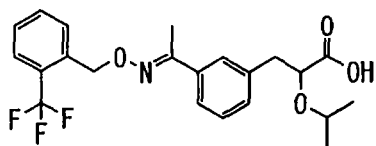


Using 4-benzyloxybenzyl chloride, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 478 (MH^+)

Example 130. 2-Isopropoxy-3-[3-([2-(trifluoromethyl)benzyl]-

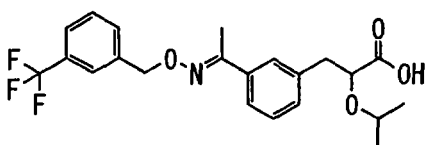
oxyethaneimidoyl)phenyl]propanoic acid



Using ethyl 3-(3-acetylphenyl)-2-isopropanoate and 2-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 424 (MH^+)

Example 131. 2-Isopropoxy-3-[3-([3-(trifluoromethyl)-benzyl]oxyethaneimidoyl)phenyl]propanoic acid

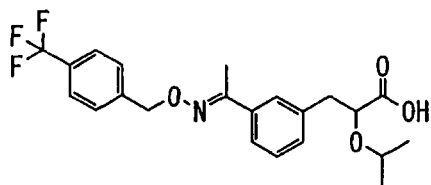


Using 3-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 424 (MH^+)

Example 132.

2-Isopropoxy-3-[3-([4-(trifluoromethyl)benzyl]-oxyethaneimidoyl)phenyl]propanoic acid



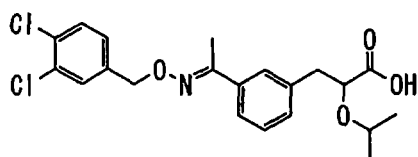
Using 4-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

^1H NMR ($CDCl_3$)

δ : 0.98 (d, $J=6.0$ Hz, 3H) 1.14 (d, $J=6.4$ Hz, 3H) 2.28 (s, 3H) 2.96 (dd, $J=8.0$, 14.0Hz, 1H) 3.15 (dd, $J=3.6$, 14.0Hz, 1H) 3.52 (Sept, $J=6.4$ Hz, 1H) 4.13 (dd, $J=4.0$, 8.4Hz, 1H) 5.29 (s, 2H) 7.23-7.27 (m, 2H) 7.30 (t, $J=7.2$ Hz, 1H) 7.51 (d, $J=7.6$ Hz, 1H) 7.53 (d, $J=6.0$ Hz, 1H) 7.62 (d, $J=8.0$ Hz, 1H)

MS m/e (ESI) 424 (MH^+)

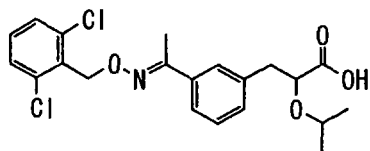
Example 133. 2-Isopropoxy-3-[3-([3,4-(dichloro)benzyl]-oxyethaneimidoyl)phenyl]propanoic acid



Using 3,4-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 424 (MH^+)

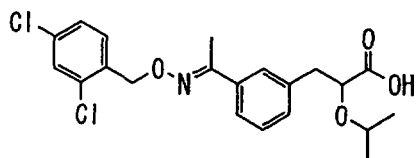
Example 134. 2-Isopropoxy-3-[3-([2,6-(dichloro)benzyl]-oxyethaneimidoyl)phenyl]propanoic acid



Using 2,6-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 424 (MH^+)

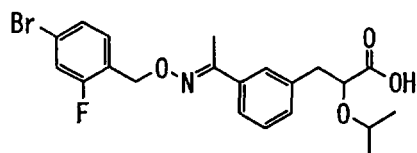
Example 135. 2-Isopropoxy-3-[3-([2,4-(dichloro)benzyl]-oxyethaneimidoyl)phenyl]propanoic acid



Using 2,4-dichlorobenzyl chloride, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 424 (MH^+)

Example 136. 2-Isopropoxy-3-[3-([4-bromo-2-fluorobenzyl]-oxyethaneimidoyl)phenyl]propanoic acid



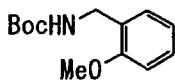
Using 4-bromo-2-fluorobenzyl bromide, the title compound was obtained in the same manner as described in Example 117f).

MS m/e (ESI) 452 (MH^+)

Example 137.

3-[3-(((Benzyloxy)carbonyl)amino)methyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid

Production example 137a) t-Butyl N-(2-methoxybenzyl)carbamate



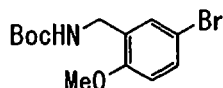
13.0 g of 2-methoxybenzylamine was dissolved in 80 ml of tetrahydrofuran, and a solution of 16 g of t-butyl dicarbonate in tetrahydrofuran (20 ml) was added. After stirring was continued at room temperature for 1 hour, the solvent was evaporated. The residue was dissolved in ethyl acetate, and successively washed with 1N hydrochloric acid and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated, to give 19.0 g of the title compound.

¹H-NMR(CDCl₃)

δ : 1.45 (s, 9H) 3.84 (s, 3H) 4.27-4.33 (m, 2H) 5.01 (br, 1H) 6.84 (d, J=8.8Hz, 1H) 6.94 (t, J=8.8Hz, 1H) 7.23-7.29 (m, 2H)

Production example 137b)

t-Butyl N-(5-bromo-2-methoxybenzyl)carbamate



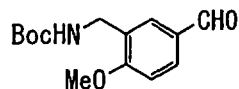
6.04g of t-Butyl N-(2-methoxybenzyl)carbamate was dissolved in 50 ml of acetonitrile, and 4.6 g of N-bromosuccinimide was added. After stirring was continued at room temperature for 3 hours, the solvent was evaporated. The residue was dissolved in ethyl acetate, and washed successively with water and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was washed with a mixed solution of methyl t-butyl ether and hexane, to give 6.97g of the title compound.

¹H-NMR(CDCl₃)

δ : 1.45 (s, 9H) 3.62 (s, 3H) 4.26 (d, J=6.4Hz, 2H) 4.97 (br, 1H) 6.72 (d, J=8.8Hz, 1H) 7.34 (dd, J=2.8, 11.2Hz) 7.35 (s, 1H)

Production example 137c)

t-Butyl N-(5-formyl-2-methoxybenzyl)carbamate



1.015g of t-Butyl N-(5-bromo-2-methoxybenzyl)carbamate, 45 mg of dichlorobis(triphenylphosphine)palladium (II), 330 mg of sodium formate and 17 mg of triphenylphosphine were dissolved

in anhydrous N,N-dimethylformamide, and the mixture was stirred at 110°C for 2 hours under carbon monoxide atmosphere. The reaction mixture was diluted with ethyl acetate, and washed with water and saturated aqueous sodium bicarbonate. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 640 mg of the title compound in the hexane-ethyl acetate (3:1) fraction.

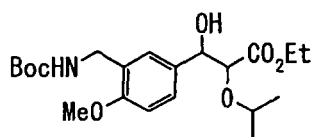
¹H-NMR (CDCl₃)

δ : 1.45 (s, 9H) 3.94 (s, 3H) 4.36 (d, J=6.0Hz, 2H) 5.00 (br, 1H) 6.98 (d, J=8.4Hz, 1H) 7.80-7.83 (m, 2H) 9.88 (s, 1H)

Production example 137d) Ethyl

3-(3-[t-butoxycarbonylamino]methyl-4-methoxyphenyl)-

3-hydroxy-2-isopropoxypropanoate



Under nitrogen atmosphere, 80 ml of sodium hexamethyldisilazane (1M solution in tetrahydrofuran) was diluted with 40 ml of tetrahydrofuran, and the mixture was cooled to -78°C, and a solution of 11.68 g of ethyl 2-isopropoxyacetate in tetrahydrofuran (10 ml) was added. After stirring was continued for 30 minutes, a solution containing 10.73 g of t-butyl N-(5-formyl-2-methoxybenzyl)carbamate in tetrahydrofuran (10 ml) was added. After stirring for another 1 hour, 100 ml of saturated aqueous ammonium chloride was added. The reaction

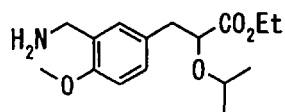
solution was poured into 400 ml of water and 500 ml of ethyl acetate for separation, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography (elution solvent: hexane-ethyl acetate), to give 12.8 g of the title compound (mixture of erythro form and threo form) as a colorless oil.

¹H-NMR(CDCl₃)

δ : 0.99 (d, J=6.1Hz, 3H) 1.15 (d, J=6.1Hz, 3H) 1.19 (t, J=7.6Hz, 3H) 1.44 (s, 9H) 2.91 (d, J=5.2Hz, 1H) 3.43 (sept, J=6.1Hz, 1H) 3.83 (s, 3H) 4.03 (d, J=6.3Hz, 1H) 4.12 (q, J=7.6Hz, 2H) 4.29 (d, J=6.6Hz, 2H) 4.86 (dd, J=5.2, 6.3Hz, 1H) 4.99 (t, J=6.6Hz, 1H) 6.81 (d, J=8.7Hz, 1H) 7.23-7.29 (m, 2H)
 δ : 1.11 (t, J=6.9Hz, 3H) 1.17 (d, J=6.1 Hz, 3H) 1.19 (d, J=6.1 Hz, 3H) 1.44 (s, 9H) 3.00 (d, J=4.4Hz, 1H) 3.63 (sept, J=6.1Hz, 1H) 3.83 (s, 3H) 3.95 (d, J=5.9Hz, 1H) 4.08 (q, J=6.9Hz, 2H) 4.29 (d, J=6.6Hz, 2H) 4.80 (dd, J=4.4, 5.9Hz, 1H) 4.99 (t, J=6.6Hz, 1H) 6.81 (d, J=8.7Hz, 1H) 7.23-7.29 (m, 2H)

Production example 137e) Ethyl

3-[3-(aminomethyl)-4-methoxyphenyl]-2-isopropoxypropanoate



24.7 g of Ethyl 3-(3-[(t-butoxycarbonyl)amino]methyl-4-methoxyphenyl)-3-hydroxy-2-isopropoxypropanoate (mixture of erythro form and threo form) was dissolved in 400 ml of trifluoroacetic acid, and 96 ml of triethylsilane was added, and the mixture was stirred for 38 hours. The solvent was

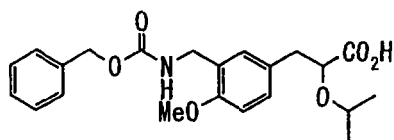
evaporated, and the residue was dissolved in 300 ml of 3N hydrochloric acid and 200 ml of hexane. The aqueous layer was washed with 100 ml of hexane, basified with 5N sodium hydroxide solution, and extracted with dichloromethane (200 ml×4). The organic layers were combined and dried over anhydrous magnesium sulfate, to give 13.0 g of the title compound as a pale yellow oil.

¹H-NMR (CDCl₃)

δ : 0.96 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.25 (t, J=7.2Hz, 3H) 2.88 (dd, J=8.8, 13.6Hz, 1H) 2.95 (dd, J=4.8, 13.6Hz, 1H) 3.50 (sept, J=6.0Hz, 1H) 3.84 (s, 3H) 4.00 (dd, J=4.8, 8.8Hz, 1H) 4.15-4.21 (m, 2H) 4.32 (s, 2H) 6.83 (d, J=8.0Hz, 1H) 7.14 (d, J=2.0Hz, 1H) 7.20 (dd, J=2.0, 8.0Hz, 1H)

Example 137f)

3-[3-(((Benzyloxy)carbonyl)amino)methyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid



4.327 g of Ethyl

3-[3-(aminomethyl)-4-methoxyphenyl]-2-isopropanoate was dissolved in 30 ml of ethyl acetate and 10 ml of water, and 2 g of sodium hydrogen carbonate and 2 ml of benzylchloroformate were added, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was diluted with ethyl acetate, washed with water and saturated brine, dried over anhydrous

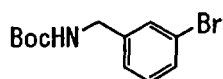
magnesium sulfate, filtered, and the solvent was distilled off, to give ethyl 3-[3-({[(benzyloxy)carbonyl]amino)methyl}-4-methoxyphenyl]-2-isopropoxypropanoate. This product was dissolved in 60 ml of ethanol and 15 ml of 5N-sodium hydroxide, and the mixture was kept still at room temperature for 1 hour. The reaction mixture was acidified with 1N-hydrochloric acid, and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off, to give 4.75 g of the title compound.

MS m/e (ESI) 401 (MH⁺)

Example 138.

2-Isopropoxy-3-(3-({[(3-(trifluoromethyl)benzyl]-oxy)carbonyl]amino)methyl}phenyl)propanoic acid

Production example 138a) t-Butyl N-(3-bromobenzyl)carbamate

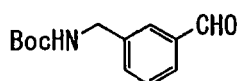


26.25g of 3-Bromobenzylamine hydrochloride was suspended in 250 ml of dichloromethane, and the mixture was cooled to 0°C. 33.5 g of N,N-diisopropylethylamine and 28.3 g of t-butyl dicarbonate were added. After stirring was continued at room temperature overnight, the reaction mixture was diluted with ethyl acetate. The solution was washed with water and saturated brine, dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off, to give 31.28 g of the title compound.

¹H-NMR (CDCl₃)

δ : 1.45 (s, 9H) 4.28 (d, J=6.0Hz, 2H) 4.87 (brs, 1H) 7.20 (m, 2H) 7.38 (m, 1H) 7.43 (brs, 1H)

Production example 138b) t-Butyl N-(3-formylbenzyl)carbamate



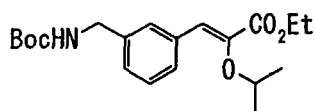
8.58 g of t-Butyl N-(3-bromobenzyl)carbamate was dissolved in 100 ml of tetrahydrofuran, and the mixture was cooled to -78°C under nitrogen atmosphere. 41 ml of butyl lithium (1.56 M solution in hexane) was added. After stirring was continued for 30 minutes, 6.91 g of N-formylmorpholine was added. After stirring was continued at -78°C for 30 minutes, 1N-hydrochloric acid was added, and the mixture was extracted with ethyl acetate. The solution was dried over anhydrous magnesium sulfate, filtered, and the solvent was distilled off, and the residue was purified by silica gel column chromatography, to give 4.762 g of the title compound in the 3:1 $\rightarrow$ 3:2 hexane-ethyl acetate fraction.

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

δ : 1.44 (s, 9H) 4.40 (d, J=6.0Hz, 2H) 4.95 (br, 1H) 7.50 (m, 1H) 7.56-7.59 (m, 1H) 7.78-7.80 (m, 1H) 7.80 (s, 1H) 10.01 (s, 1H)

Production example 138c) Ethyl

(E,Z)-3-(3-([(t-butoxycarbonyl)amino]methyl)phenyl)-2-isopropoxy-2-propenoate

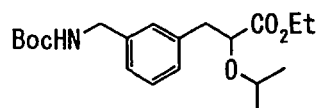


Using t-butyl N-(3-formylbenzyl)carbamate and ethyl 2-(diethoxyphosphoryl)-2-isopropoxyacetate, the title

compound was obtained in the same manner as described in Production example 46a).

Production example 138d) Ethyl

3-(3-([(t-butoxycarbonyl)amino]methyl)phenyl)-
2-isopropoxypropanoate



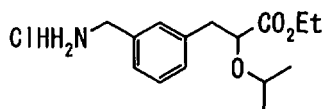
Using ethyl

(E,Z)-3-(3-([(t-butoxycarbonyl)amino]methyl)phenyl)-2-isopropoxy-2-propenoate, the title compound was obtained in the same manner as described in Production example 46b).

¹H-NMR(CDCl₃)

δ : 0.95 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.24 (t, J=7.2Hz, 3H) 1.46 (s, 9H) 2.93 (dd, J=8.4, 14.0Hz, 1H) 3.07 (dd, J=4.8, 14.0 Hz, 1H) 3.49 (sept, J=6.4Hz, 1H) 4.04 (dd, J=4.8, 8.4Hz, 1H) 4.12-4.19 (m, 2H) 4.30 (d, J=5.2Hz, 2H) 4.80 (br, 1H) 7.12-7.16 (m, 3H) 7.23 (d, J=8.0Hz, 1H)

Production example 138e) Ethyl 3-[3-(ammoniomethyl)phenyl]-
2-isopropoxypropanoate chloride



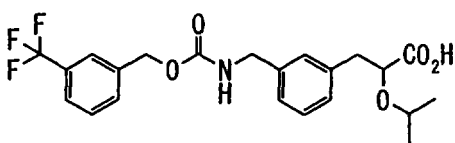
4.67 g of Ethyl 3-(3-([(t-butoxycarbonyl)amino]methyl)phenyl)-2-isopropoxypropanoate was dissolved in 50 ml of trifluoroacetic acid, and the mixture was kept still at room temperature overnight. The solvent was concentrated and dried, and concentrated by adding 10 ml of 4N-hydrogen chloride ethyl acetate solution, to give 6.931 g of the title compound.

¹H-NMR (CDCl₃)

δ : 0.97 (d, J=6.0Hz, 3H) 1.10 (d, J=6.0Hz, 3H) 1.25 (t, J=7.2Hz, 3H) 2.87 (m, 2H) 3.52 (m, 1H) 4.10 (t, J=6.0Hz, 2H) 4.50 (q, J=7.2Hz, 2H) 7.20 (m, 2H) 7.34 (m, 1H)

Example 138f)

2-Isopropoxy-3-(3-([([3-(trifluoromethyl)benzyl]oxy)-
carbonyl)amino]methyl)phenyl)propanoic acid

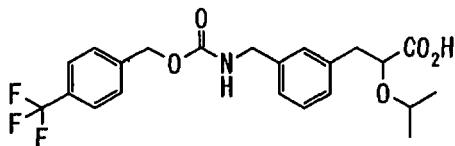


20 mg of Ethyl 3-[3-(ammoniomethyl)phenyl]-2-isopropoxypropanoate chloride was dissolved in 0.5 ml of N,N-dimethylformamide which was saturated in advance with carbon dioxide by adding dry ice, and 150 mg of cesium carbonate and 200 mg of tetrabutylammonium iodide were added, and the mixture was stirred at room temperature for 30 minutes. 40 mg of 3-trifluoromethylbenzyl bromide was added, and stirring was continued at room temperature for 3 hours. To the reaction mixture was added ethyl acetate, and the mixture was washed with water. The solvent was concentrated, and the residue was treated with 0.4 ml of ethanol and 0.1 ml of 5N-sodium hydroxide, and the mixture was kept still at room temperature for 30 minutes. The solution was neutralized with 1N-hydrochloric acid, and extracted with ethyl acetate. The solvent was distilled off, and the residue was purified by reverse-phase high performance liquid chromatography, to give 1.09 mg of the title compound.

MS m/e (ESI) 440(MH⁺)

Example 139.

2-Isopropoxy-3-(3-({([4-(trifluoromethyl)benzyl]oxy)-
carbonyl)amino]methyl}phenyl)propanoic acid



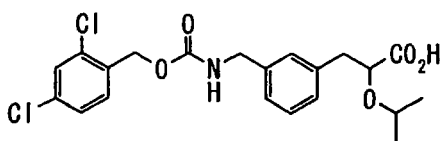
Using 4-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

δ : 1.01 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.95 (dd, J=8.0, 14.4Hz, 1H) 3.12 (dd, J=1.6, 14.8 Hz, 1H) 3.54 (sept, J=6.4Hz, 1H) 4.13 (dd, J=4.0, 8.0Hz, 1H) 4.38 (d, J=6.4Hz, 2H) 5.11 (br, 1H) 5.19 (s, 2H) 7.15-7.19 (m, 3H) 7.25-7.30 (m, 1H) 7.48 (d, J=8.8Hz, 2H) 7.62 (d, J=8.4Hz, 2H)

MS m/e (ESI) 440(MH⁺)

Example 140.

2-Isopropoxy-3-(3-({([2,4-dichlorobenzyl]oxy)carbonyl)-
amino]methyl}phenyl)propanoic acid

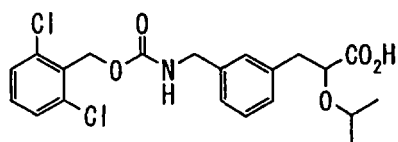


Using 2,4-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 440(MH⁺)

Example 141.

2-Isopropoxy-3-(3-({([2,6-dichlorobenzyl]oxy)carbonyl)-
amino]methyl}phenyl)propanoic acid

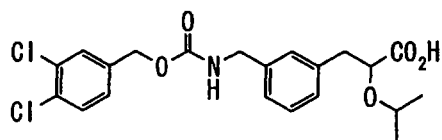


Using 2,6-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 440 (MH^+)

Example 142.

2-Isopropoxy-3-(3-(((3,4-dichlorobenzyl)oxy)carbonyl)-4-amino]methyl)phenyl)propanoic acid

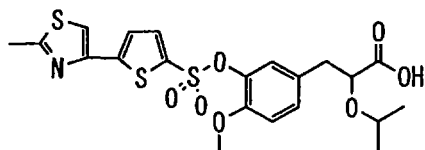


Using 3,4-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 440 (MH^+)

Example 143.

2-Isopropoxy-3-[4-methoxy-3-({[5-(2-methyl-1,3-thiazol-4-yl)-2-thienyl]sulfonyl}oxy)phenyl]propanoic acid

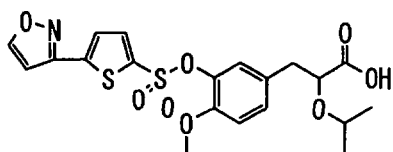


15 mg of Ethyl 3-(3-hydroxy-4-methoxyphenyl)-2-isopropoxypropanoate and 25 mg of 5-(2-methyl-1,3-thiazol-4-yl)-2-thiophenesulfonyl chloride were dissolved in 0.4 ml of dichloromethane, and 50 μ l of triethylamine was added, and the mixture was kept still at room temperature overnight. To the

reaction mixture was added ethyl acetate and the mixture was washed with water. The solvent was concentrated, and the residue was treated with 0.4 ml of ethanol and 0.1 ml of 5N-sodium hydroxide, and the mixture was kept still at room temperature for 30 minutes. The reaction mixture was neutralized with 1N-hydrochloric acid, extracted with ethyl acetate. The solvent was distilled off, and the residue was purified by reverse-phase high performance liquid chromatography, to give 5.8 mg of the title compound. MS *m/e*(ESI) 498 (MH⁺)

Example 144.

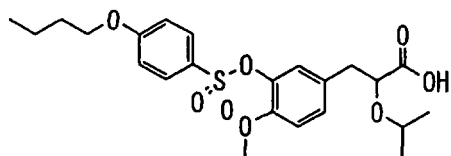
2-Isopropoxy-3-[3-([5-(3-isoxazolyl)-2-thienyl]sulfonyl)-oxy)phenyl]propanoic acid



Using 5-(3-isoxazolyl)-2-thiophenesulfonyl chloride, the title compound was obtained in the same manner as described in Example 143.

MS *m/e*(ESI) 468 (MH⁺)

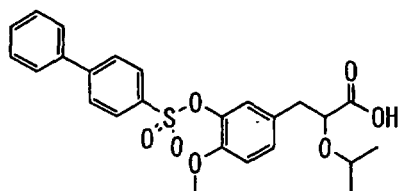
Example 145. 3-(3-([(4-Butoxyphenyl)sulfonyl]oxy)phenyl)-2-isopropoxypropanoic acid



Using 4-butoxybenzenesulfonyl chloride, the title compound was obtained in the same manner as described in Example 143.

MS m/e (ESI) 467 (MH⁺)

Example 146. 3-(3-([4-Biphenylsulfonyl]oxy)phenyl)-2-isopropoxypropanoic acid



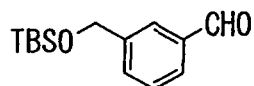
Using 4-biphenylsulfonyl chloride, the title compound was obtained in the same manner as described in Example 143.

MS m/e (ESI) 471 (MH⁺)

Example 147. 2-Isopropoxy-3-{3-([4-(trifluoromethyl)anilino]carbonyl)oxy)methyl}phenyl}propanoic acid

Production example 147a)

3-([1-(t-Butyl)-1,1-dimethylsilyl]oxy)methyl)benzaldehyde



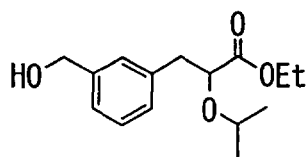
14 g of 3-Bromobenzyl alcohol was dissolved in 200 ml of N,N-dimethylformamide, and 15 g of t-butylchlorodimethyl silane and 10 g of imidazole were added. After stirring was continued at room temperature overnight, the solution was diluted with ethyl acetate, and washed successively with 1N hydrochloric acid and saturated brine. After drying the organic layer over anhydrous magnesium sulfate, the solvent was evaporated. The residue was purified by silica gel column chromatography, and 21 g of [(3-bromobenzyl)oxy](t-butyl)dimethylsilane was

obtained in the 4:1 hexane-ethyl acetate fraction. Then, the obtained 21 g of [(3-bromobenzyl)oxy](t-butyl)dimethylsilane was dissolved in 300 ml of tetrahydrofuran, and the mixture was cooled to -78°C under nitrogen atmosphere. 55 ml of butyllithium (1.52 M solution in hexane) was added thereto, and the mixture was stirred for 30 minutes. A solution of 11.5 g of 4-formylmorpholine solution in 20 ml of tetrahydrofuran was added. After stirring was continued at -78°C for 1 hour, 1N-hydrochloric acid was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 14.7 g of the title compound in the 4:1 hexane-ethyl acetate fraction.

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 0.12 (s, 6H) 0.93 (s, 9H) 4.81 (s, 2H) 7.49-7.53 (m, 1H) 7.60-7.62 (m, 1H) 7.77 (d, $J=7.6\text{Hz}$, 1H) 7.87 (s, 1H) 10.02 (s, 1H)

Production example 147b) Ethyl 3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate



600 mg of Sodium hydride was suspended in 20 ml of tetrahydrofuran, and a solution of 4.2 g diethyl 2-isopropoxyphosphonoacetate in 25 ml tetrahydrofuran was added under ice-cooling. After stirring was continued at room

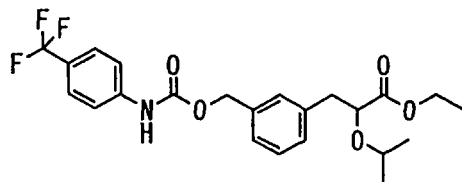
temperature for 30 minutes, a solution of 3.0 g of 3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)benzaldehyde in 25 ml of tetrahydrofuran was added. After stirring was continued at room temperature for 15 hours, to the reaction mixture was added 1N hydrochloric acid, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 3.4 g of ethyl (E,Z)-3-[3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)-phenyl]-2-isopropoxy 2-propenoate in the 4:1 hexane-ethyl fraction. Then the obtained 3.4 g of ethyl (E,Z)-3-[3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)-phenyl]-2-isopropoxy-2-propenoate was dissolved in 30 ml of tetrahydrofuran, and 13.5 ml tetrabutylammonium fluoride (1M solution in tetrahydrofuran) was added. After stirring was continued at room temperature overnight, the reaction mixture was diluted with ethyl acetate, and the organic layer was washed with water and saturated brine, and dried over anhydrous magnesium sulfate. The solvent was evaporated, and then the obtained crude product was dissolved in 25 ml of ethanol, and 0.30 g of 10% palladium carbon was added, and the mixture was stirred for 5 hours under hydrogen atmosphere. The catalyst was filtered off and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 1.1 g of the title compound in the 3:1 hexane-ethyl acetate fraction.

¹H-NMR(CDCl₃)

δ : 0.95 (d, J=6.4Hz, 3H) 1.15 (d, J=6.4Hz, 3H) 1.24 (t, J=6.8Hz, 3H) 2.95 (dd, J=8.8, 13.6Hz, 1H) 3.02 (dd, J=5.2, 13.6Hz, 1H) 3.50 (sept, J=6.4Hz, 1H) 4.05 (dd, J=5.2, 8.8Hz, 1H) 4.14-4.20 (m, 2H) 4.67(s, 2H) 7.17-7.30 (m, 4H)

Production example 147c) Ethyl

2-isopropoxy-3-{3-[[{4-(trifluoromethyl)anilino}carbonyl]-oxy)methyl]phenyl}propanoate



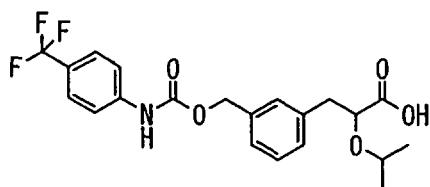
A suspension in tetrahydrofuran (2.0 ml) containing 100 mg of ethyl 3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate, 150 mg of α,α,α-trifluoro-*p*-tolylisocyanate and 35 μl of pyridine was stirred at room temperature for 14 hours. The solvent was removed, and the residue was treated with dichloromethane. After filtering off insoluble substances, the residue was purified by silica gel column chromatography, to give 149 mg of the title compound.

¹H-NMR(CDCl₃)

δ : 0.93 (d, J=6.0Hz, 3H) 1.14 (d, J=6.0Hz, 3H) 1.23 (t, J=7.2Hz, 3H) 2.95 (dd, J=8.8, 13.6Hz, 1H) 3.02 (dd, 4.8, 13.6Hz, 1H) 3.49 (sept, J=6.0Hz, 2H) 4.06 (dd, J=4.8, 8.8Hz, 1H) 4.12-4.23 (m, 2H) 5.19 (s, 2H) 7.00 (br s, 1H) 7.22-7.32 (m, 4H) 7.51 (d, J=8.8Hz, 2H) 7.56 (d, J=8.8Hz, 2H)

Example 147d)

2-Isopropoxy-3-{3-[[{4-(trifluoromethyl)anilino]carbonyl}-oxy)methyl]phenyl}propanoic acid



To 149 mg of Ethyl 2-isopropoxy-3-{3-[[{4-(trifluoromethyl)anilino]carbonyl}-oxy)methyl]phenyl}propanoate were added 4 ml of ethanol and 1.0 ml of 5N sodium hydroxide aqueous solution, and the mixture was stirred at room temperature for 20 hours. After the reaction solution was diluted with water, pH was adjusted to 5 with 5N hydrochloric acid, and the solution was diluted with ethyl acetate and saturated aqueous ammonium chloride. The organic layer was washed with saturated aqueous ammonium chloride, dried over anhydrous sodium sulfate, and concentrated. The residue was purified by silica gel column chromatography, to give 26 mg of the title compound.

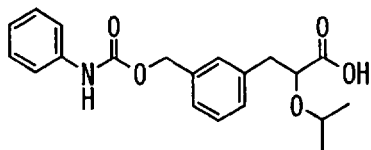
¹H-NMR(CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.99 (dd, J=7.6, 14.0Hz, 1H) 3.15 (dd, 4.0, 14.0Hz, 1H) 3.50-3.60 (m, 1H) 4.15 (dd, J=4.0, 7.6Hz, 1H) 5.20 (s, 2H) 6.93 (br s, 1H) 7.16-7.35 (m, 4H) 7.51 (d, J=8.8Hz, 2H) 7.57 (d, J=8.8Hz, 2H)

MS *m/e* (ESI) 426 (MH⁺)

Example 148. 3-(3-[[{4-(Anilinocarbonyl)oxy)methyl}phenyl]-

2-isopropoxypropanoic acid



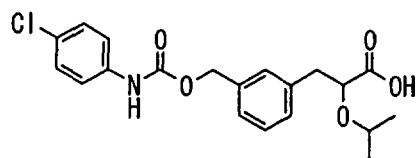
A suspension in tetrahydrofuran (0.6 ml) containing 20 μ l of ethyl 3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate, 20 μ l of phenylisocyanate and 5 μ l of pyridine was stirred at room temperature for 11 hours. After the solvent was distilled off, the residue was treated with 0.4 ml of ethanol and 0.1 ml of 5N sodium hydroxide aqueous solution, and the mixture was stirred at room temperature for 1.5 hours. The reaction solution was diluted with water, and neutralized with 5N hydrochloric acid. The mixture was extracted with ethyl acetate and concentrated. Then, a half volume of the residue was purified by HPLC using a reverse-phase column and an elution solvent of water-acetonitrile-trifluoroacetic acid system, to give 6.02 mg of the title compound.

MS m/e (ESI) 358 (MH^+)

Example 149.

3-[3-({[(4-Chloroanilino)carbonyl]oxy)methyl}phenyl)-

2-isopropoxypropanoic acid



Using ethyl

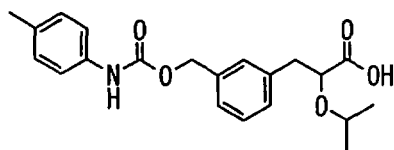
3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and

4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 392 (MH⁺)

Example 150.

2-Isopropoxy-3-(3-([(4-toluidinocarbonyl)oxy]methyl)-phenyl)propanoic acid



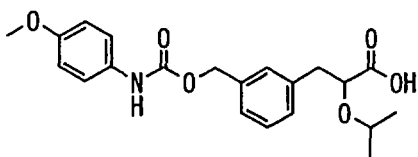
Using ethyl

3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 372 (MH⁺)

Example 151.

2-Isopropoxy-3-[3-([(4-methoxyanilino)carbonyl]oxy)-methyl)phenyl]propanoic acid



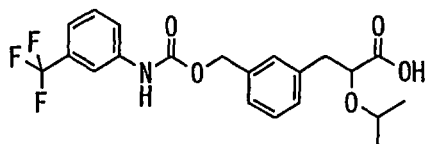
Using ethyl

3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 388 (MH⁺)

Example 152.

2-Isopropoxy-3-{3-[[3-(trifluoromethyl)anilino]carbonyl]-oxy)methyl}phenyl}propanoic acid



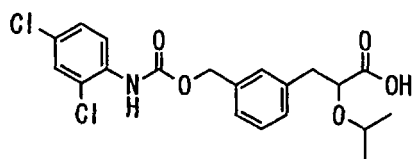
Using ethyl

3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 426 (MH⁺)

Example 153.

3-[3-({[(2,4-Dichloroanilino)carbonyl]oxy)methyl}phenyl]-2-isopropoxypropanoic acid



Using ethyl

3-[3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

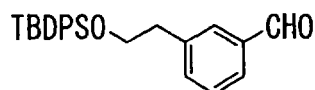
MS *m/e* (ESI) 426 (MH⁺)

Example 154.

2-Isopropoxy-3-{3-[2-({[4-(trifluoromethyl)anilino]carbonyl}oxy)ethyl]phenyl}propanoic acid

Production example 154a)

3-(2-{{[1-(*t*-Butyl)-1,1-diphenylsilyl]oxy}ethyl}benzaldehyde



3-Bromophenethyl alcohol was dissolved in 110 ml of N,N-dimethylformamide, and 16 ml of t-butyl chlorodiphenyl silane and 8.3g of imidazole were added. After stirring was continued at room temperature overnight, the solution was diluted with ethyl acetate, and washed successively with 1N hydrochloric acid and saturated brine. After drying the organic layer over anhydrous magnesium sulfate, the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 22.1 g of [(3-bromophenethyl)oxy] (t-butyl)diphenyl silane in the 4:1 hexane-ethyl acetate fraction. Then, the obtained 22.1g of [(3-bromophenethyl)oxy] (t-butyl)diphenyl silane was dissolved in 200 ml of tetrahydrofuran, and the mixture was cooled to -78°C under nitrogen atmosphere. 37 ml of Butyllithium (1.52 M solution in hexane) was added thereto, and the mixture was stirred for 30 minutes, and then 10 ml of 4-formylmorpholine was added. After stirring was continued at -78°C for 1 hour, 1N-hydrochloric acid was added, and the mixture was extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 17 g of the title compound in the 4:1 hexane-ethyl acetate fraction.

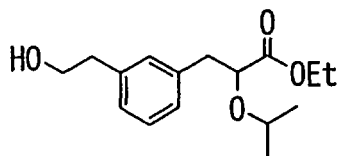
$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 0.12 (s, 6H) 0.93 (s, 9H) 4.81 (s, 2H) 7.49–7.53 (m, 1H) 7.60–7.62 (m,

1H) 7.77 (d, J=7.6Hz, 1H) 7.87 (s, 1H) 10.02 (s, 1H)

Production example 154b)

Ethyl 3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate



Using

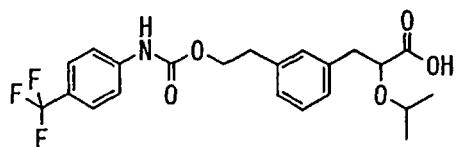
3-(2-([1-(t-butyl)-1,1-diphenylsilyl]oxy)ethyl)benzaldehyde and diethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 147b).

¹H-NMR (CDCl₃)

δ : 0.95 (d, J=6.4Hz, 3H) 1.15 (d, J=6.4Hz, 3H) 1.24 (t, J=6.8Hz, 3H) 2.84 (t, J=6.4Hz, 2H) 2.93 (dd, J=8.4, 14.0Hz, 1H) 2.99 (dd, J=4.8, 14.0Hz, 1H) 3.50 (sept, J=6.4Hz, 1H) 3.84 (br, 2H) 4.05 (dd, J=4.8, 8.4Hz, 1H) 4.14-4.20 (m, 2H) 7.08-7.13 (m, 3H) 7.22 (d, J=7.6Hz, 1H)

Example 154c)

2-Isopropoxy-3-{3-[2-([4-(trifluoromethyl)anilino]-carbonyl)oxy)ethyl]phenyl}propanoic acid



Using ethyl

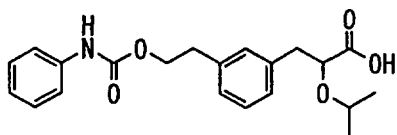
3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and α,α,α-trifluoro-p-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

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

δ : 1.18 (d, $J=6.0\text{Hz}$, 3H) 1.21 (d, $J=6.0\text{Hz}$, 3H) 2.87-2.99 (m, 1H) 3.09 (d, $J=5.2\text{Hz}$, 2H) 3.76 (sept, $J=6.0\text{Hz}$, 1H) 4.14-4.23 (m, 1H) 4.26 (t, $J=5.2\text{Hz}$, 1H) 4.46-4.53 (m, 1H) 7.09-7.15 (m, 3H) 7.25 (t, $J=7.2\text{Hz}$, 1H) 7.53 (d, $J=9.0\text{Hz}$, 2H) 7.56 (d, $J=9.0\text{Hz}$, 2H) 7.67 (br s, 1H)

MS m/e (ESI) 440 (MH^+)

Example 155. 3-(3-{2-[(Anilinocarbonyl)oxy]ethyl}phenyl)-2-isopropoxypropanoic acid



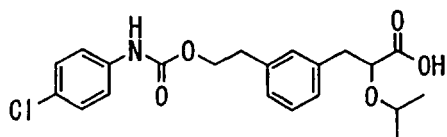
Using ethyl

3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 372 (MH^+)

Example 156.

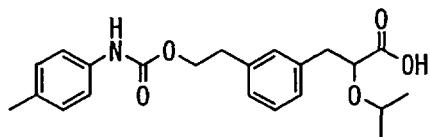
3-[3-(2-{[(4-Chloroanilino)carbonyl]oxy}ethyl)phenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 406 (MH⁺)

Example 157. 2-Isopropoxy-3-(3-(2-[(4-toluidinocarbonyl)-oxy]ethyl)phenyl)propanoic acid



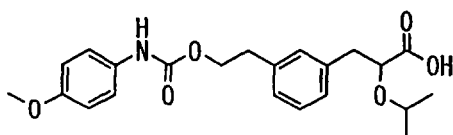
Using ethyl

3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 386 (MH⁺)

Example 158.

2-Isopropoxy-3-[3-(2-[(4-methoxyanilino)carbonyl]oxy)-ethyl)phenyl]propanoic acid



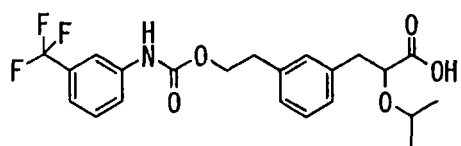
Using ethyl

3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 402 (MH⁺)

Example 159.

2-Isopropoxy-3-{3-[2-([3-(trifluoromethyl)anilino]-carbonyl]oxy)ethyl]phenyl}propanoic acid



Using ethyl

3-[3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

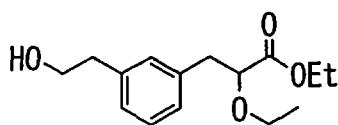
MS *m/e* (ESI) 440 (MH^+)

Example 160.

2-Ethoxy-3-{3-[2-([4-(trifluoromethyl)anilino]carbonyl)-oxy)ethyl]phenyl}propanoic acid

Production example 160a)

Ethyl 2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate



Using

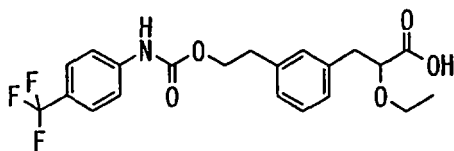
3-(2-{[1-(*t*-butyl)-1,1-diphenylsilyl]oxy)ethyl)benzaldehyde and diethyl 2-ethoxyphosphono acetate, the title compound was obtained in the same manner as described in Production example 147b).

^1H -NMR($CDCl_3$)

δ : 1.13 (t, $J=6.8$ Hz, 3H) 1.22 (t, $J=7.2$ Hz, 3H) 2.97 (t, $J=6.8$ Hz, 2H) 3.05 (dd, $J=5.2, 14.0$ Hz, 1H) 3.11 (dd, $J=8.4, 14.0$ Hz, 1H) 3.31 (dq, $J=6.8, 8.8$ Hz, 1H) 3.59 (dq, $J=6.8, 8.8$ Hz, 1H) 3.87 (dt, $J=1.6, 6.8$ Hz, 2H) 4.06 (dd, $J=5.2, 8.4$ Hz, 1H) 4.17 (q, $J=7.2$ Hz, 2H) 7.16-7.25 (m, 4H)

Example 160b)

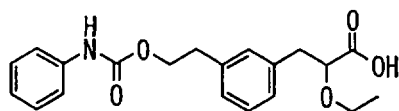
2-Ethoxy-3-{3-[2-({[4-(trifluoromethyl)anilino]carbonyl}-oxy)ethyl]phenyl}propanoic acid



A suspension in tetrahydrofuran (0.6 ml) containing 14 mg of ethyl 2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate, 20 μ l of α,α,α -trifluorotolylisocyanate and 5 μ l of pyridine was stirred at room temperature for 11 hours. After the solvent was distilled off, the residue was treated with 0.4 ml of ethanol and 0.1 ml of 5N sodium hydroxide aqueous solution, and the mixture was stirred at room temperature for 1.5 hours. The reaction solution was diluted with water, and neutralized with 5N hydrochloric acid. The mixture was extracted with ethyl acetate, and concentrated. Then, a half volume of the residue was purified by HPLC using a reverse-phase column and an elution solvent of water-acetonitrile-trifluoroacetic acid system, to give 7.8 mg of the title compound.

MS m/e (ESI) 426 (MH^+)

Example 161. 3-(3-{2-[(Anilinocarbonyl)oxy]ethyl}phenyl)-2-ethoxypropanoic acid



Using ethyl

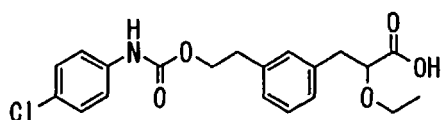
2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and

phenylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 358 (MH⁺)

Example 162.

3-[3-(2-([(4-Chloroanilino)carbonyl]oxy)ethyl)phenyl]-
2-ethoxypropanoic acid



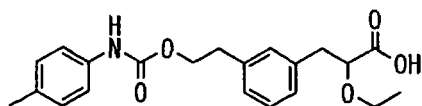
Using ethyl

2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 392 (MH⁺)

Example 163.

2-Ethoxy-3-(3-{2-[(4-toluidinocarbonyl)oxy]ethyl}phenyl)-
propanoic acid



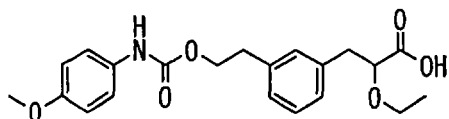
Using ethyl

2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 372 (MH⁺)

Example 164.

2-Ethoxy-3-[3-(2-([(4-methoxyanilino)carbonyl]oxy)ethyl)-
phenyl]propanoic acid



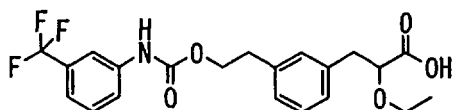
Using ethyl

2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 388 (MH⁺)

Example 165.

2-Ethoxy-3-[3-[2-([3-(trifluoromethyl)anilino]carbonyl)-oxy)ethyl]phenyl]propanoic acid



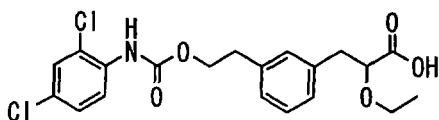
Using ethyl

2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 426 (MH⁺)

Example 166.

3-[3-(2-([2,4-Dichloroanilino]carbonyl)oxy)ethyl]phenyl]-2-ethoxypropanoic acid



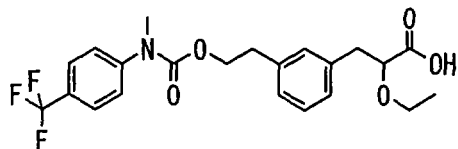
Using ethyl

2-ethoxy-3-[3-(2-hydroxyethyl)phenyl]propanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 160b).

MS *m/e* (ESI) 426 (MH⁺)

Example 167.

2-Ethoxy-3-{3-[2-({[methyl-4-(trifluoromethyl)anilino]-
carbonyl}oxy)ethyl]phenyl}propanoic acid



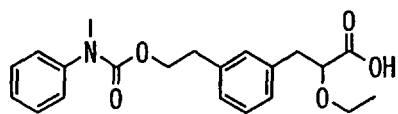
To a solution of another half amount of the residue in dimethylsulfoxide (0.5 ml) prior to HPLC purification in synthesis of

2-ethoxy-3-{3-[2-({[4-(trifluoromethyl)anilino]carbonyl}oxy)ethyl]phenyl}propanoic acid were added 0.1 ml of methyl iodide and 10 ml sodium hydride in oil under ice-cooling, and the mixture was stirred for 12 hours while gradually raising the temperature to room temperature. The reaction solution was diluted with water and extracted with ethyl acetate. After concentrating the organic layer, the residue was treated with 0.4 ml of ethanol and 0.1 ml of 5N aqueous sodium hydroxide, and the mixture was stirred at room temperature for 1 hour. The reaction solution was diluted with water and neutralized with 5N hydrochloric acid. After extracting with ethyl acetate and concentration, the residue was purified by HPLC using a reverse-phase column and an elution solvent of water-acetonitrile-trifluoroacetic acid system, to give 3.4 mg of the title compound.

MS *m/e* (ESI) 440 (MH⁺)

Example 168.

2-Ethoxy-3-[3-(2-([(methylanilino) carbonyl]oxy)ethyl)-phenyl]propanoic acid

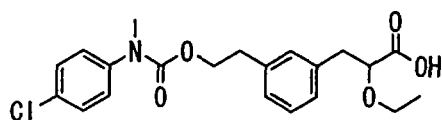


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 372 (MH⁺)

Example 169.

3-{3-[2-([[4-Chloro(methyl) anilino] carbonyl]oxy)ethyl]-phenyl}-2-ethoxypropanoic acid

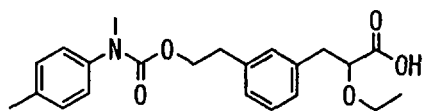


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 406 (MH⁺)

Example 170.

3-[3-(2-([(4-Dimethylanilino) carbonyl]oxy)ethyl)phenyl]-2-ethoxypropanoic acid

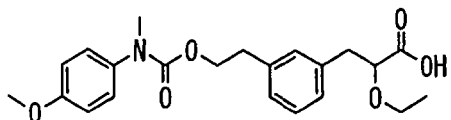


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 386 (MH⁺)

Example 171.

2-Ethoxy-3-{3-[2-([[4-methoxy(methyl) anilino] carbonyl]oxy)-ethyl]phenyl}propanoic acid

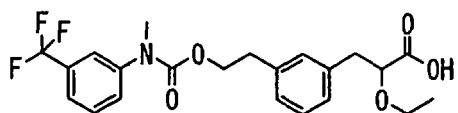


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 402 (MH⁺)

Example 172.

2-Ethoxy-3-{3-[2-({[methyl-3-(trifluoromethyl)anilino]-carbonyl}oxy)ethyl]phenyl}propanoic acid

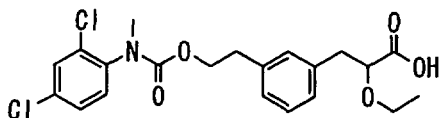


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 440 (MH⁺)

Example 173.

3-{3-[2-({[2,4-Dichloro(methyl)anilino]carbonyl}oxy)ethyl]phenyl}-2-ethoxypropanoic acid

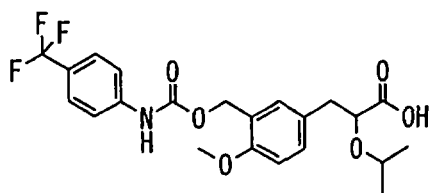


The title compound was obtained in the same manner as described in Example 167.

MS *m/e* (ESI) 440 (MH⁺)

Example 174.

2-Isopropoxy-3-{4-methoxy-3-[({[4-(trifluoromethyl)anilino]carbonyl}oxy)methyl]phenyl}propanoic acid

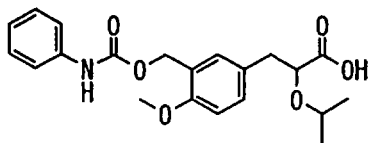


Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 456 (MH^+)

Example 175.

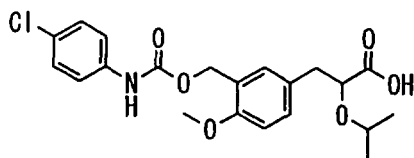
3-(3-([(Anilinocarbonyl)oxy]methyl)-4-methoxyphenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 388 (MH^+)

Example 176. 3-[3-([(4-Chloroanilino)carbonyl]oxy)methyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid



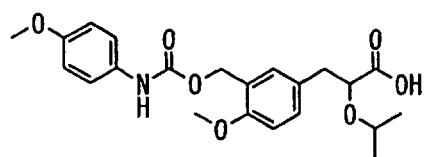
Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 422 (MH⁺)

Example 177.

2-Isopropoxy-3-[4-methoxy-3-({[(4-methoxyanilino) carbonyl]-oxy)methyl}phenyl]propanoic acid

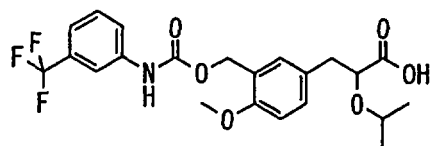


Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 418 (MH⁺)

Example 178.

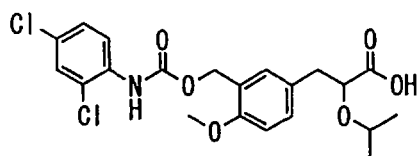
2-Isopropoxy-3-[4-methoxy-3-({[3-(trifluoromethyl)-anilino]carbonyl}oxy)methyl]phenyl]propanoic acid



Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 456 (MH⁺)

Example 179. 3-[3-({[(2,4-Dichloro)carbonyl]oxy)methyl}-4-methoxyphenyl]-2-isopropoxypropanoic acid



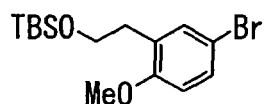
Using ethyl 3-[3-(hydroxymethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 456 (MH⁺)

Example 180.

2-Isopropoxy-3-[4-methoxy-3-(2-{{(3-methoxyanilino)-carbonyl]oxy}ethyl)phenyl]propanoic acid

Production example 180a) [(5-Bromo-2-methoxyphenethyl)oxy]-(*t*-butyl)dimethylsilane

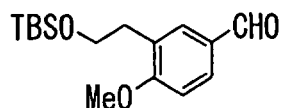


Using 2-methoxyphenethyl alcohol, the title compound was obtained in the same manner as described in Production example 117a).

¹H-NMR(CDCl₃)

δ : 0.07 (s, 6H) 0.88 (s, 9H) 2.82 (t, J=6.8Hz, 2H) 3.79 (t, J=6.8Hz, 2H) 3.81 (s, 3H) 6.73 (d, J=8.4Hz, 1H) 7.26-7.30 (m, 1H)

Production example 180b) 3-(2-{{[1-(*t*-Butyl)-1,1-dimethylsilyl]oxy}ethyl)-4-methoxybenzaldehyde

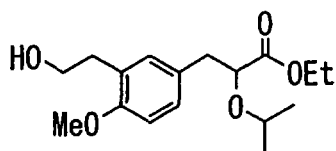


Using [(5-bromo-2-methoxyphenethyl)oxy](t-butyl)-dimethylsilane, the title compound was obtained in the same manner as described in Production example 117b).

¹H-NMR(CDCl₃)

δ : 0.07 (s, 6H) 0.88 (s, 9H) 2.93 (t, J=6.8Hz, 2H) 3.83 (t, J=6.8Hz, 2H) 3.94 (s, 3H) 6.98 (d, J=8.4Hz, 1H) 7.74 (d, J=2.4Hz, 1H) 7.78 (dd, J=2.4, 8.4Hz, 1H) 7.26-7.30 (m, 1H) 9.90 (s, 1H)

Production example 180c) Ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate



Using 3-(2-([1-(t-butyl)-1,1-dimethylsilyl]oxy)ethyl)-4-methoxybenzaldehyde and diethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 147b).

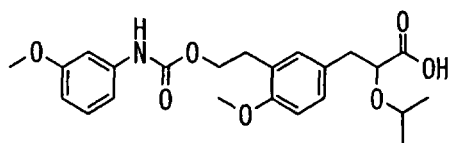
¹H-NMR(CDCl₃)

δ : 0.98 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.24 (t, J=6.8Hz, 3H) 2.85-2.95 (m, 4H) 3.51 (sept, J=6.0Hz, 1H) 3.78-3.84 (m, 2H) 3.80 (s, 3H) 4.01 (dd, J=4.8, 8.0Hz, 1H) 4.14-4.20 (m, 2H) 6.78 (d, J=8.4Hz, 1H) 7.04 (d, J=2.0Hz, 1H) 7.08 (dd, J=2.0, 8.4Hz, 1H)

Example 180d)

2-Isopropoxy-3-[4-methoxy-3-(2-[(3-methoxyanilino)-

carbonyl]oxy)ethyl)phenyl]propanoic acid

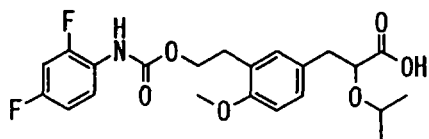


Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 432 (MH⁺)

Example 181.

3-[3-(2-{[(2,4-Difluoroanilino)carbonyl]oxy)ethyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid

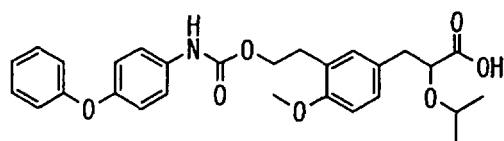


Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 438 (MH⁺)

Example 182.

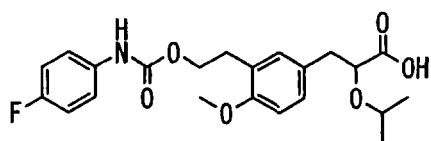
2-Isopropoxy-3-[4-methoxy-3-(2-{[(4-phenoxyanilino)carbonyl]oxy)ethyl)phenyl]propanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-phenoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 494 (MH⁺)

Example 183. 3-[3-(2-((4-Fluoroanilino)carbonyl)oxy)ethyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid

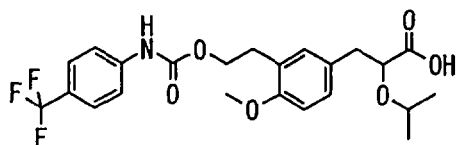


Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-fluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 420 (MH⁺)

Example 184.

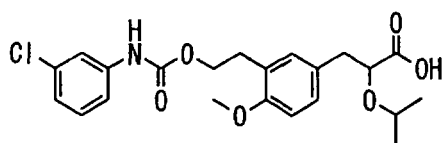
2-Isopropoxy-3-{4-methoxy-3-[2-((4-(trifluoromethyl)-anilino)carbonyl)oxy)ethyl]phenyl}propanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 470 (MH⁺)

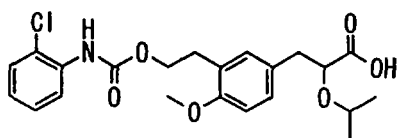
Example 185. 3-[3-(2-[[(3-Chloroanilino) carbonyl]oxy)ethyl]-4-methoxyphenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 436 (MH⁺)

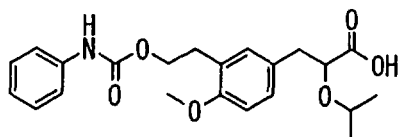
Example 186. 3-[3-(2-[[(2-Chloroanilino) carbonyl]oxy)ethyl]-4-methoxyphenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 436 (MH⁺)

Example 187. 3-(3-(2-[(Anilinocarbonyl)oxy]ethyl)-4-methoxyphenyl)-2-isopropoxypropanoic acid

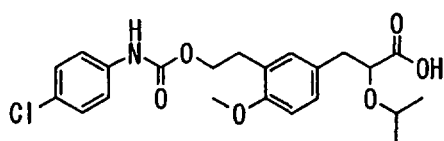


Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and aniline isocyanate, the title compound was obtained in the same manner as described in Example 148.

2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 402 (MH^+)

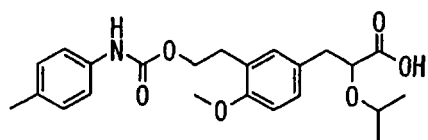
Example 188. 3-[3-(2-([(4-Chloroanilino)carbonyl]oxy)ethyl)-4-methoxyphenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 436 (MH^+)

Example 189. 2-Isopropoxy-3-(4-methoxy-3-{2-[(4-toluidinocarbonyl)oxy]ethyl}phenyl)propanoic acid



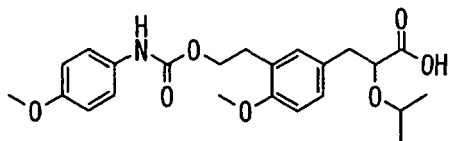
Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 416 (MH^+)

Example 190.

2-Isopropoxy-3-[4-methoxy-3-(2-([(4-methoxyanilino)-

carbonyl)oxy)ethyl)phenyl]propanoic acid

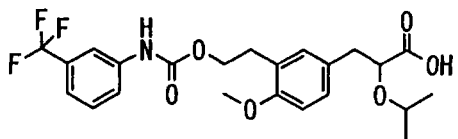


Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 432 (MH⁺)

Example 191.

2-Isopropoxy-3-{4-methoxy-3-[2-({[3-(trifluoromethyl)-anilino]carbonyl)oxy)ethyl]phenyl]propanoic acid



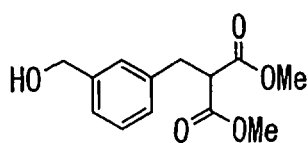
Using ethyl 3-[3-(2-hydroxyethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 470 (MH⁺)

Example 192. Dimethyl 2-{3-[2-({[4-(trifluoromethyl)anilino]-carbonyl)oxy)methyl]benzyl}malonate

Production example 192a)

Dimethyl 2-[3-(hydroxymethyl)benzyl]malonate



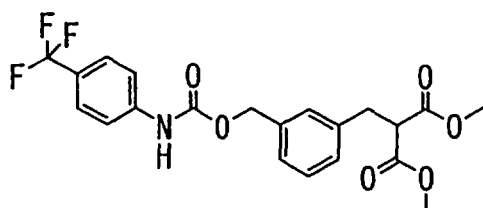
1.5 g of 3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)-benzaldehyde and 1.6 g of dimethyl malonate were dissolved in 20 ml of toluene, and 90 μ l of piperidine and 52 μ l of acetic acid were added thereto, and the mixture was heated at reflux using Dean-Stark equipment. After 9 hours, the solvent was evaporated, and the residue was purified by silica gel column chromatography, to give 5.8g of dimethyl 2-([3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)phenyl]methylene)malonate in the 4:1 hexane-ethyl acetate fraction. Then, the obtained 5.8g of dimethyl 2-([3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)-methyl)phenyl]methylene)malonate was dissolved in a mixture of 3 ml methanol and 15 ml of 1,4-dioxane, and 0.20 g of 10% palladium carbon was added thereto, and the mixture was stirred for 5 hours under hydrogen atmosphere. The catalyst was filtered off, and the solvent was evaporated. Then, the obtained crude product was dissolved in 12 ml of tetrahydrofuran, and 8.0 ml of tetrabutyl ammonium fluoride (1 M solution in tetrahydrofuran) was added thereto. After stirring was continued at room temperature overnight, the reaction mixture was diluted with ethyl acetate, and the organic layer was washed with water and saturated brine. After drying over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was purified by silica gel column, to give 0.95 g of the title compound in the 2:1 hexane-ethyl

acetate(2:1) fraction.

¹H-NMR(CDCl₃)

δ : 3.23 (d, J=8.0Hz, 2H) 3.68 (t, J=8.0Hz, 1H) 3.70 (s, 6H) 4.66 (d, J=4.4Hz, 2H) 7.11-7.30 (m, 4H)

Example 192b) Dimethyl 2-{3-[2-({[4-(trifluoromethyl)-anilino]carbonyl}oxy)methyl]benzyl}malonate



A suspension containing 63 mg of dimethyl 2-[3-(hydroxymethyl)benzyl]malonate, 47 mg of α,α,α-trifluoro-*p*-tolylisocyanate and 30 μl of pyridine in tetrahydrofuran (2.0 ml) was stirred at room temperature for 19 hours. After the solvent was distilled off, the residue was treated with dichloromethane. After filtering off insoluble substances and concentrating the filtrate, the residue was purified by HPLC using a reverse-phase column and an elution solvent of water-acetonitrile-trifluoroacetic acid system, to give 71 mg of the title compound.

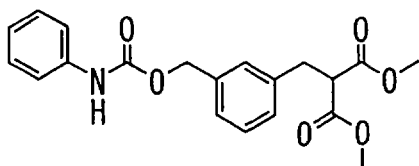
¹H-NMR(CDCl₃)

δ : 3.24 (d, J=8.0Hz, 2H) 3.68 (t, J=8.0Hz, 1H) 3.70 (s, 6H) 5.18 (s, 2H) 7.17-7.31 (m, 4H) 7.50-7.59 (m, 4H)

MS *m/e* (ESI) 440 (MH⁺)

Example 193.

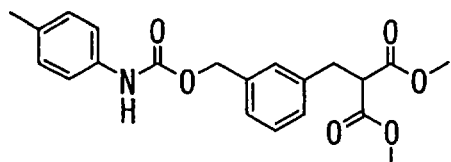
Dimethyl 2-(3-({[anilinocarbonyl]oxy)methyl}benzyl)malonate



Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 372 (MH^+)

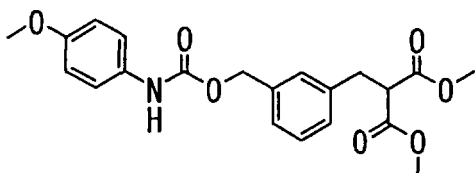
Example 194. Dimethyl 2-[3-([(4-toluidinocarbonyl)oxy]-methyl)benzyl]malonate



Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 386 (MH^+)

Example 195. Dimethyl 2-[3-([(4-methoxyanilino)carbonyl]-oxy)methyl)benzyl]malonate



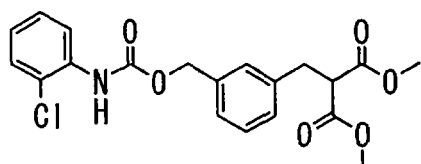
Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 402 (MH^+)

Example 196. Dimethyl 2-[3-([(3-methoxyanilino)carbonyl]-

oxy)methyl)benzyl]malonate

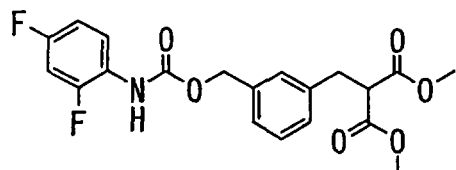
Example 199. Dimethyl 2-[3-({[(2-chloroanilino)carbonyl]oxy}-methyl)benzyl]malonate



Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 406 (MH⁺)

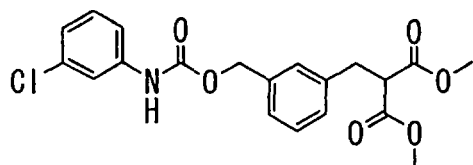
Example 200. Dimethyl 2-[3-({[(2,4-difluoroanilino)carbonyl]-oxy)methyl)benzyl]malonate



Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 408 (MH⁺)

Example 201. Dimethyl 2-[3-({[(3-chloroanilino)carbonyl]oxy}-methyl)benzyl]malonate



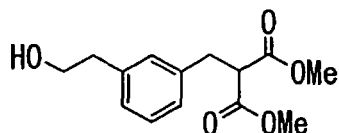
Using dimethyl 2-[3-(hydroxymethyl)benzyl]malonate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 406 (MH^+)

Example 202. Dimethyl 2-{3-[2-({[4-(trifluoromethyl)anilino]-carbonyl}oxy)ethyl]benzyl}malonate

Production example 202a)

Dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate

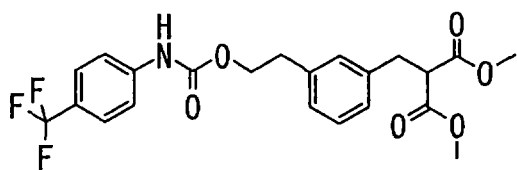


Using 3-(2-({[1-(*t*-butyl)-1,1-diphenylsilyl]oxy}ethyl)-benzaldehyde and dimethyl malonate, the title compound was obtained in the same manner as described in Production example 192a).

^1H -NMR ($CDCl_3$)

δ : 2.83 (t, $J=6.4$ Hz, 2H) 3.21 (d, $J=8.0$ Hz, 2H) 3.67 (t, $J=8.0$ Hz, 1H) 3.70 (s, 6H) 3.84 (t, $J=6.4$ Hz, 2H) 7.06-7.10 (m, 3H) 7.21-7.25 (m, 1H)

Example 202b) Dimethyl 2-{3-[2-({[4-(trifluoromethyl)-anilino]carbonyl}oxy)ethyl]benzyl}malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

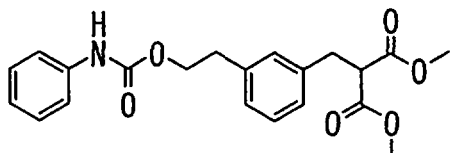
^1H -NMR ($CDCl_3$)

δ : 2.93 (t, $J=6.4$ Hz, 2H) 3.23 (d, $J=7.6$ Hz, 2H) 3.69 (t, $J=7.6$ Hz, 1H) 3.70 (s, 6H) 4.35 (t, $J=6.4$ Hz, 2H) 7.06-7.11 (m, 3H) 7.25 (t, $J=7.2$ Hz, 1H)

7.52-7.56 (m, 4H)

MS *m/e* (ESI) 454 (MH⁺)

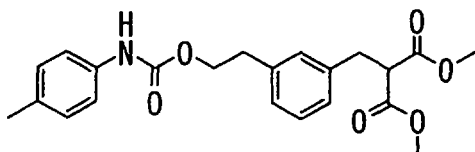
Example 203. Dimethyl 2-(3-{2-[(anilinocarbonyl)oxy]ethyl}-benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 386 (MH⁺)

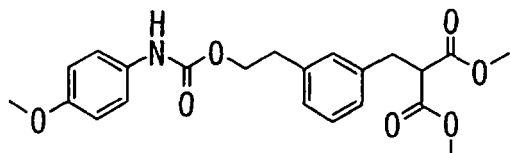
Example 204. Dimethyl 2-(3-{2-[(4-toluidinocarbonyl)oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 400 (MH⁺)

Example 205. Dimethyl 2-(3-{2-[(4-methoxyanilinocarbonyl)oxy]ethyl}benzyl)malonate

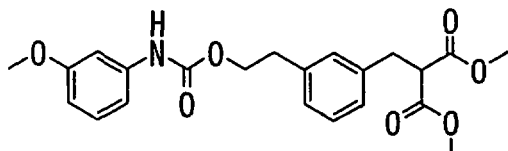


Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and

4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 416 (MH⁺)

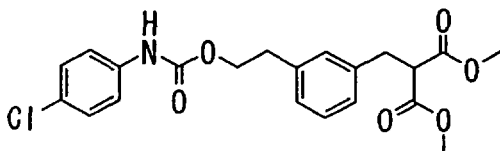
Example 206. Dimethyl 2-(3-{2-[(3-methoxyanilinocarbonyl)-oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 416 (MH⁺)

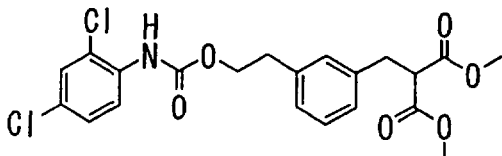
Example 207. Dimethyl 2-(3-{2-[(4-chloroanilinocarbonyl)-oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 420 (MH⁺)

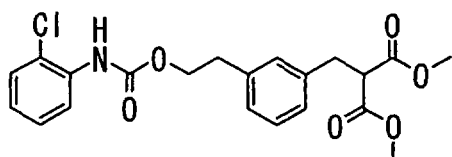
Example 208. Dimethyl 2-(3-{2-[(2,4-dichloroanilinocarbonyl)-oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 454 (MH⁺)

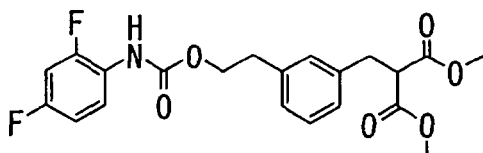
Example 209. Dimethyl 2-(3-{2-[(2-chloroanilinocarbonyl)oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 420 (MH⁺)

Example 210. Dimethyl 2-(3-{2-[(2,4-difluoroanilinocarbonyl)oxy]ethyl}benzyl)malonate

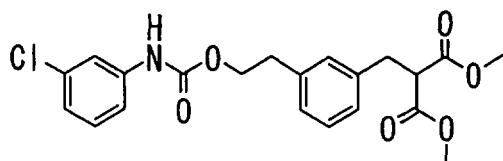


Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 422 (MH⁺)

Example 211. Dimethyl

2-(3-{2-[(3-chloroanilinocarbonyl)oxy]ethyl}benzyl)malonate



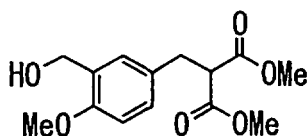
Using dimethyl 2-[3-(2-hydroxyethyl)benzyl]malonate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 420 (MH⁺)

Example 212. Dimethyl 2-(3-([(anilinocarbonyl)oxy]methyl)-4-methoxybenzyl)malonate

Production example 212a)

Dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate

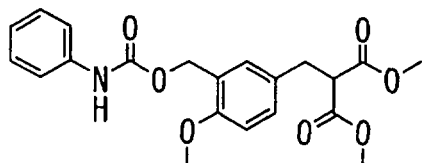


Using 3-([(1-(*t*-butyl)-1,1-dimethylsilyl]oxy)methyl)-4-methoxybenzaldehyde and dimethyl malonate, the title compound was obtained in the same manner as described in Production example 192a).

¹H-NMR (CDCl₃)

δ : 3.16 (d, *J*=8.0Hz, 2H) 3.68 (t, *J*=8.0Hz, 1H) 3.70 (s, 6H) 3.84 (s, 3H) 4.64 (d, *J*=6.0Hz, 2H) 6.79 (d, *J*=9.2Hz, 1H) 7.09-7.11 (m, 2H)

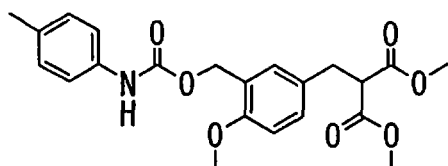
Example 212b) Dimethyl 2-(3-([(anilinocarbonyl)oxy]methyl)-4-methoxybenzyl)malonate



Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 402 (MH⁺)

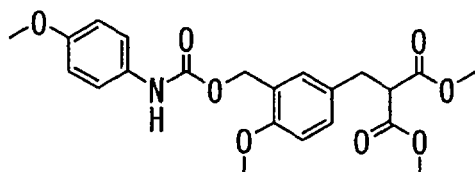
Example 213. Dimethyl 2-(4-methoxy-3-([(4-toluidinocarbonyl)oxy]methyl)benzyl)malonate



Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 416 (MH⁺)

Example 214. Dimethyl 2-[4-methoxy-3-([(4-methoxyanilino)-carbonyl]oxy)methyl)benzyl]malonate

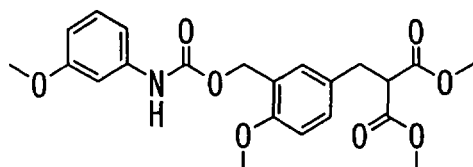


Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 432 (MH⁺)

Example 215. Dimethyl 2-[4-methoxy-3-([(3-methoxyanilino)-

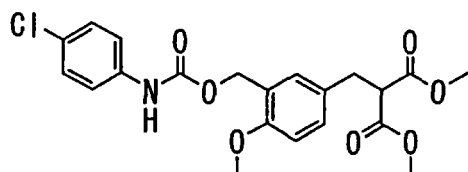
carbonyl]oxy)methyl)benzyl]malonate



Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 432 (MH⁺)

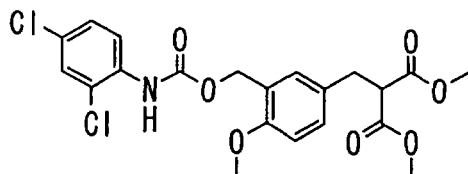
Example 216. Dimethyl 2-[3-(((4-chloroanilino)carbonyl)oxy)methyl)-4-methoxybenzyl]malonate



Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 436 (MH⁺)

Example 217. Dimethyl 2-[3-(((2,4-dichloroanilino)carbonyl)oxy)methyl)-4-methoxybenzyl]malonate

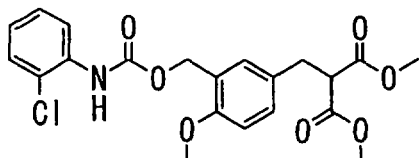


Using dimethyl 2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and

2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 470 (MH⁺)

Example 218. Dimethyl 2-[3-(((2-chloroanilino)carbonyl)oxy)methyl)-4-methoxybenzyl]malonate

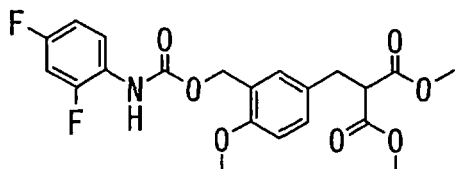


Using dimethyl

2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 436 (MH⁺)

Example 219. Dimethyl 2-[3-(((2,4-difluoroanilino)carbonyl)oxy)methyl)-4-methoxybenzyl]malonate

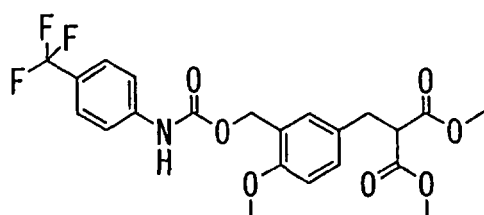


Using dimethyl 2-[3-(hydroxymethyl)-

4-methoxybenzyl]malonate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 438 (MH⁺)

Example 220. Dimethyl 2-[3-(((2,4-difluoroanilino)carbonyl)oxy)methyl)-4-methoxybenzyl]malonate



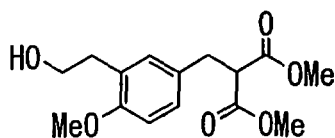
Using dimethyl

2-[3-(hydroxymethyl)-4-methoxybenzyl]malonate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 470 (MH^+)

Example 221. Dimethyl 2-(3-{2-[(anilinocarbonyl)oxy]ethyl}-4-methoxybenzyl)malonate

Production example 221a) Dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate

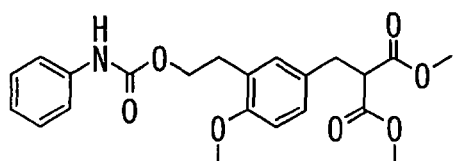


Using 3-(2-{[1-(*t*-butyl)-1,1-dimethylsilyl]oxy}ethyl)-4-methoxybenzaldehyde and dimethyl malonate, the title compound was obtained in the same manner as described in Production example 192a).

^1H -NMR ($CDCl_3$)

δ : 2.86 (t, $J=6.4$ Hz, 2H) 3.14 (d, $J=8.0$ Hz, 2H) 3.62 (t, $J=8.0$ Hz, 1H) 3.70 (s, 6H) 3.80 (s, 3H) 3.81 (t, $J=6.4$ Hz, 2H) 6.77 (d, $J=8.4$ Hz, 1H) 6.98 (d, $J=2.4$ Hz, 1H) 7.04 (dd, $J=2.4, 8.4$ Hz, 1H)

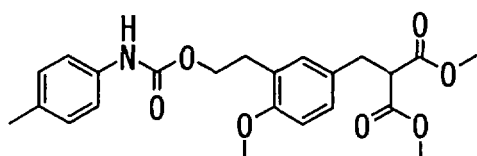
Example 221b) Dimethyl 2-(3-{2-[(anilinocarbonyl)oxy]ethyl}-4-methoxybenzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 416 (MH^+)

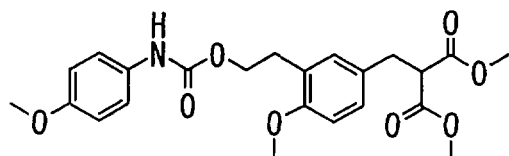
Example 222. Dimethyl 2-(4-methoxy-3-{2-[(4-toluidinocarbonyl)oxy]ethyl}benzyl)malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 430 (MH^+)

Example 223. Dimethyl 2-[4-methoxy-3-(2-{[(4-methoxyanilino)-carbonyl]oxy}ethyl)benzyl]malonate

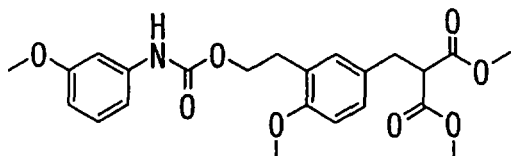


Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in

Example 192b).

MS m/e (ESI) 446 (MH^+)

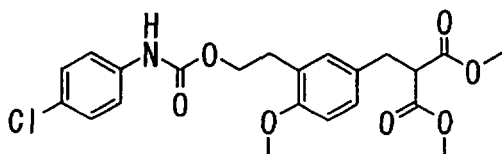
Example 224. Dimethyl 2-[4-methoxy-3-(2-([(3-methoxyanilino)-carbonyl]oxy)ethyl)benzyl]malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 446 (MH^+)

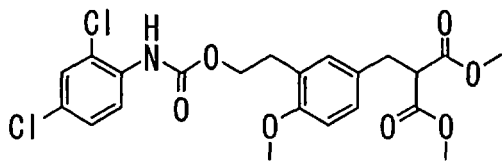
Example 225. Dimethyl 2-[3-(2-([(4-chloroanilino)carbonyl]-oxy)ethyl)-4-methoxybenzyl]malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 450 (MH^+)

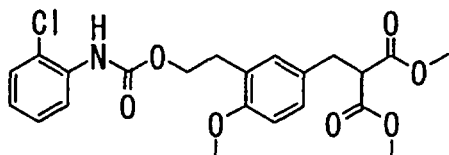
Example 226. Dimethyl 2-[3-(2-([(2,4-dichloroanilino)-carbonyl]oxy)ethyl)-4-methoxybenzyl]malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 484 (MH⁺)

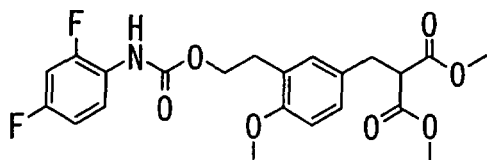
Example 227. Dimethyl 2-[3-(2-(((2-chloroanilino)carbonyl)oxy)ethyl)-4-methoxybenzyl]malonate



Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 450 (MH⁺)

Example 228. Dimethyl 2-[3-(2-(((2,4-difluoroanilino)carbonyl)oxy)ethyl)-4-methoxybenzyl]malonate

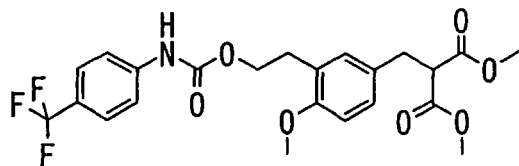


Using dimethyl 2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 452 (MH⁺)

Example 229. Dimethyl

2-{4-methoxy-3-[2-({[4-(trifluoromethyl)anilino]carbonyl}-oxy)ethyl]benzyl}malonate



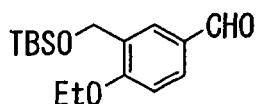
Using dimethyl

2-[3-(2-hydroxyethyl)-4-methoxybenzyl]malonate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 484 (MH⁺)

Example 230. Dimethyl 2-(3-({[anilinocarbonyl]oxy)methyl}-4-ethoxybenzyl)malonate

Production example 230a) 3-({[1-(*t*-butyl)-1,1-dimethylsilyl]-oxy)methyl}-4-ethoxybenzaldehyde



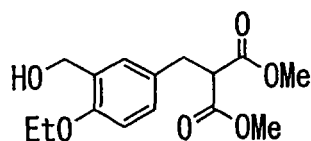
Using 2-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Production example 117a) followed by Production example 117b).

¹H-NMR(CDCl₃)

δ : 0.12 (s, 6H) 0.93 (s, 9H) 1.40 (t, *J*=6.8Hz, 3H) 4.11 (q, *J*=6.8Hz, 2H) 4.74 (s, 2H) 6.90 (d, *J*=8.4Hz, 1H) 7.76 (dd, *J*=1.6, 8.4Hz, 1H) 7.97 (d, *J*=1.6Hz, 1H) 9.86 (s, 1H)

Production example 230b)

Dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate

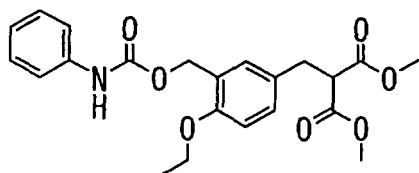


Using 3-([1-(*t*-butyl)-1,1-dimethylsilyl]oxy)methyl)-4-ethoxybenzaldehyde and dimethyl malonate, the title compound was obtained in the same manner as described in Production example 192a).

¹H-NMR (CDCl₃)

δ : 1.42 (d, J=6.8Hz, 3H) 3.15 (d, J=8.0Hz, 2H) 3.63 (t, J=8.0Hz, 1H) 3.70 (s, 6H) 4.05 (q, J=6.8Hz, 2H) 4.65 (d, J=6.4Hz, 2H) 6.77 (d, J=8.4Hz, 1H) 7.06-7.09 (m, 2H)

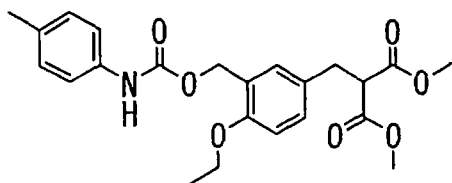
Example 230c) Dimethyl 2-(3-([(anilinocarbonyl)oxy]methyl)-4-ethoxybenzyl)malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]-malonate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 416 (MH⁺)

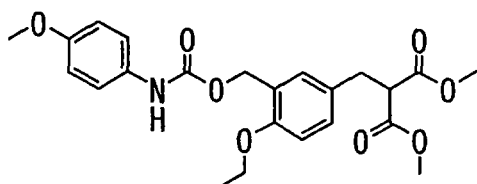
Example 231. Dimethyl 2-(4-ethoxy-3-([(4-toluidinocarbonyl)oxy]methyl)benzyl)malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 430 (MH⁺)

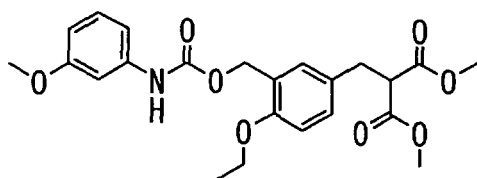
Example 232. Dimethyl 2-[4-ethoxy-3-(((4-methoxyanilino)-carbonyl)oxy)methyl]benzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 446 (MH⁺)

Example 233. Dimethyl 2-[4-ethoxy-3-(((3-methoxyanilino)-carbonyl)oxy)methyl]benzyl]malonate

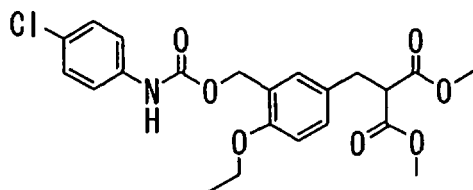


Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]-

malonate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 446 (MH⁺)

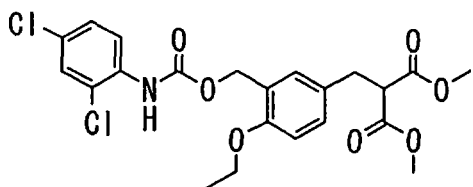
Example 234. Dimethyl 2-[3-(((4-chloroanilino)carbonyl)-oxy)methyl)-4-ethoxybenzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 450 (MH⁺)

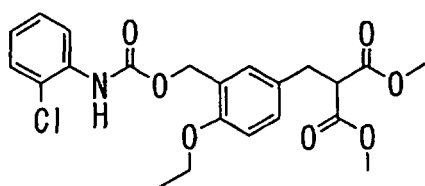
Example 235. Dimethyl 2-[3-(((2,4-dichloroanilino)carbonyl)-oxy)methyl)-4-ethoxybenzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 484 (MH⁺)

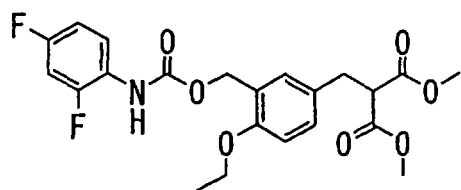
Example 236. Dimethyl 2-[3-(((2-chloroanilino)carbonyl)oxy)methyl)-4-ethoxybenzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]-malonate and 2-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 450 (MH^+)

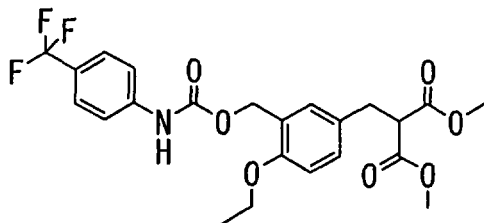
Example 237. Dimethyl 2-[3-(((2,4-difluoroanilino)carbonyl)oxy)methyl]-4-ethoxybenzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]-malonate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS m/e (ESI) 452 (MH^+)

Example 238. Dimethyl 2-[4-ethoxy-3-(((4-(trifluoromethyl)anilino)carbonyl)oxy)methyl]benzyl]malonate

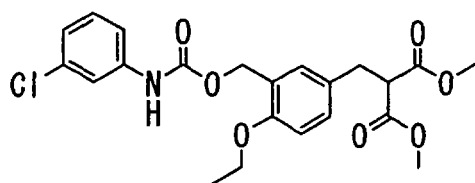


Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]-

malonate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 484 (MH⁺)

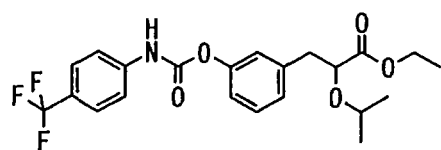
Example 239. Dimethyl 2-[3-([(3-chloroanilino)carbonyl]oxy)-methyl)-4-ethoxybenzyl]malonate



Using dimethyl 2-[4-ethoxy-3-(hydroxymethyl)benzyl]malonate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 450 (MH⁺)

Example 240. Ethyl 2-isopropoxy-3-[3-([(4-(trifluoromethyl)anilino)carbonyl]oxy)phenyl]propanoate



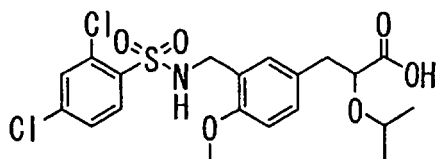
Using ethyl 3-(3-hydroxyphenyl)-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 192b).

MS *m/e* (ESI) 484 (MH⁺)

Example 241.

3-[3-([(2,4-Dichlorophenyl)sulfonyl]amino)methyl)-

4-methoxyphenyl]-2-isopropoxypropanoic acid

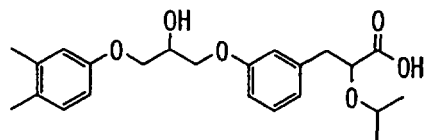


To a solution of 33 mg of ethyl 3-[3-(aminomethyl)-4-methoxyphenyl]-2-isopropoxypropanoate and 25 mg of 2,4-dichlorobenzenesulfonyl chloride in 0.8 ml of dichloromethane was added 40 μ l of pyridine under ice-cooling, and stirring was continued at room temperature for 4 hours. After removing the solvent, to the residue were added 1.0 ml of ethanol and 0.3 ml of 2N aqueous sodium hydroxide, and the mixture was stirred at room temperature for 2 hours. The reaction solution was diluted with water, and neutralized with 2N hydrochloric acid. The mixture was extracted with ethyl acetate and concentrated. Then, the residue was purified by HPLC using a reverse-phase column by using an elution solvent of water-acetonitrile-trifluoroacetic acid system, to give 2.0 mg of the title compound.

MS m/e (ESI) 476 (MH^+)

Example 242.

3-{3-[3-(3,4-Dimethylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



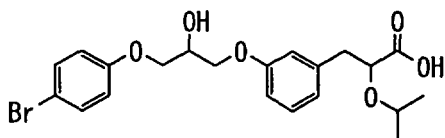
Using 3,4-dimethylphenol, the title compound was obtained

in the same manner as described in Example 1c).

MS m/e (ESI) 425 (MNa^+)

Example 243.

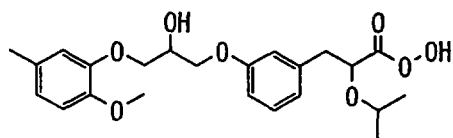
3-{3-[3-(4-Bromophenoxy)-2-hydroxypropoxy]phenyl}-
2-isopropoxypropanoic acid



Using 4-bromophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 475 (MNa^+)

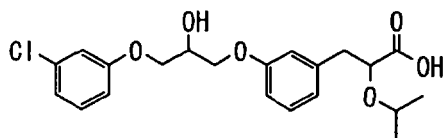
Example 244. 3-{3-[2-Hydroxy-3-(2-methoxy-
5-methylphenoxy)propoxy]phenyl}-2-isopropoxypropanoic acid



Using 2-methoxy-5-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 441 (MNa^+)

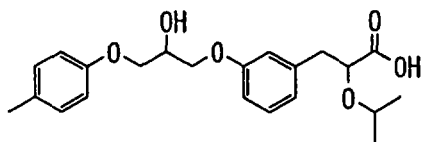
Example 245. 3-{3-[3-(3-Chlorophenoxy)-
2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 431 (MNa⁺)

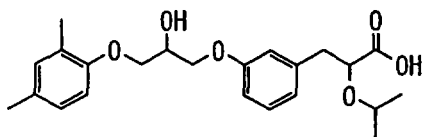
Example 246. 3-[3-(2-Hydroxy-3-p-tolyloxypropoxy)phenyl]-
2-isopropoxypropanoic acid



Using 4-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 411 (MNa⁺)

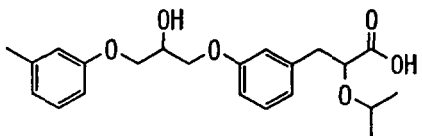
Example 247. 3-{3-[3-(2,4-Dimethylphenoxy)-
2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 425 (MNa⁺)

Example 248. 3-[3-(2-Hydroxy-3-m-tolyloxypropoxy)phenyl]-
2-isopropoxypropanoic acid

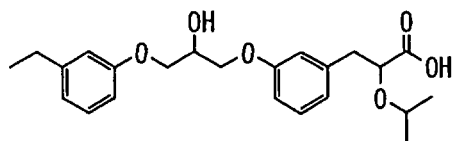


Using 3-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 411 (MNa⁺)

Example 249. 3-{3-[3-(3-Ethylphenoxy)-

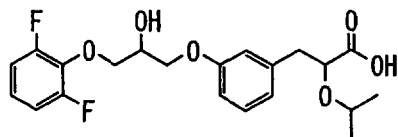
2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-ethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 425 (MNa⁺)

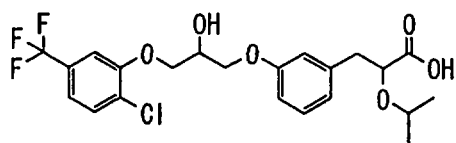
Example 250. 3-{3-[3-(2,6-Difluorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 2,6-difluorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 433 (MNa⁺)

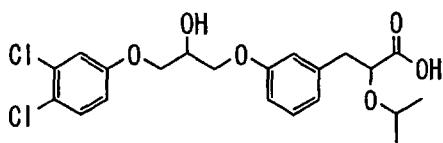
Example 251. 3-{3-[3-(2-Chloro-5-trifluoromethylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 2-chloro-5-trifluoromethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 499 (MNa⁺)

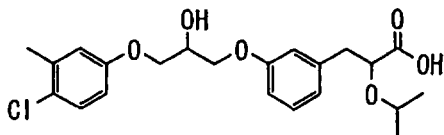
Example 252. 3-{3-[3-(3,4-Dichlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 465 (MNa^+)

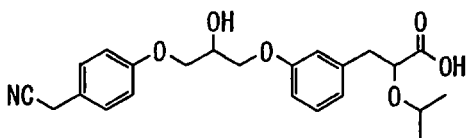
Example 253. 3-{3-[3-(4-Chloro-3-methylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chloro-3-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 445 (MNa^+)

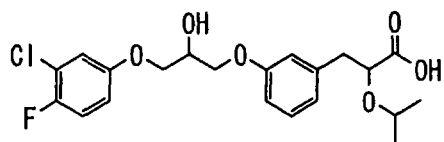
Example 254. 3-{3-[3-(4-Cyanomethylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-cyanomethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 435 (MNa^+)

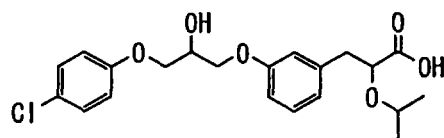
Example 255. 3-{3-[3-(3-Chloro-4-fluorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-chloro-4-fluorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 449 (MNa^+)

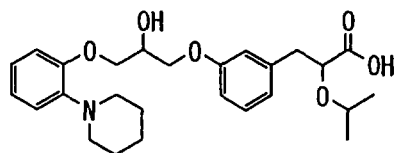
Example 256. 3-{3-[3-(4-Chlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 431 (MNa^+)

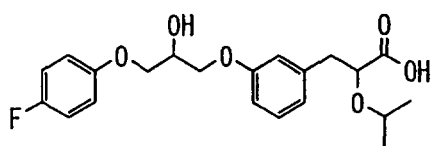
Example 257. 3-{3-[2-Hydroxy-3-(2-piperidino-1-yl-phenoxy)propoxy]phenyl}-2-isopropoxypropanoic acid



Using 2-piperidinophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 480 (MNa^+)

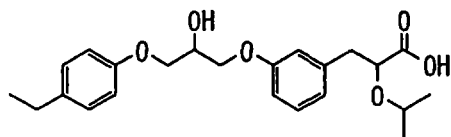
Example 258. 3-{3-[3-(4-Fluorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-fluorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 415 (MNa^+)

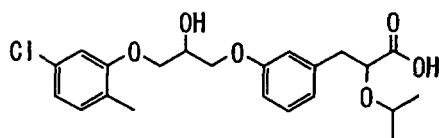
Example 259. 3-{3-[3-(4-Ethylphenoxy)-2-hydroxy]propoxy}phenyl}-2-isopropoxypropanoic acid



Using 4-ethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 425 (MNa^+)

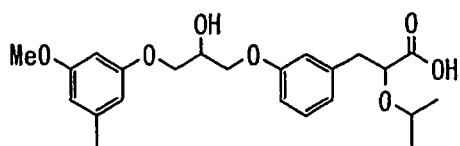
Example 260. 3-{3-[3-(5-Chloro-2-methylphenoxy)-2-hydroxy]propoxy}phenyl}-2-isopropoxypropanoic acid



Using 2-methyl-3-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 445 (MNa^+)

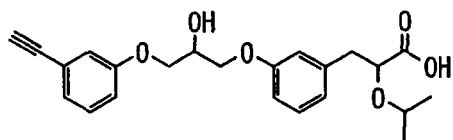
Example 261. 3-{3-[2-Hydroxy-3-(3-methoxy-5-methylphenoxy)propoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-methyl-5-methoxyphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 441 (MNa^+)

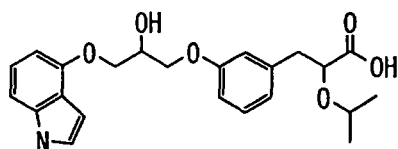
Example 262. 3-{3-[3-(3-Ethynylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-ethynylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 421 (MNa^+)

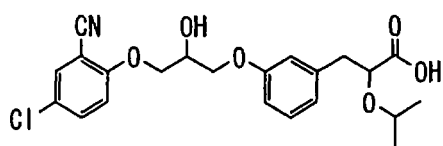
Example 263. 3-{3-[2-Hydroxy-3-(1H-indol-4-yloxy)propoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-hydroxyindole, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 435 (MNa^+)

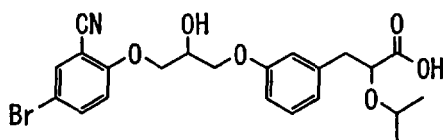
Example 264. 3-{3-[3-(4-Chloro-2-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 456(MNa⁺)

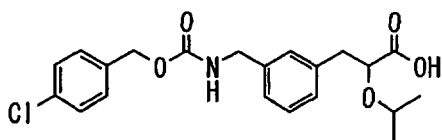
Example 265. 3-{3-[3-(4-Bromo-2-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-bromo-2-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 500(MNa⁺)

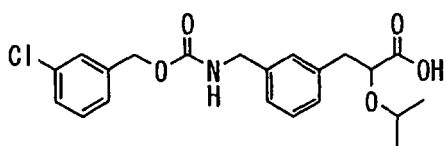
Example 266. 2-Isopropoxy-3-(3-{[4-chlorobenzyl]oxy}-carbonyl)amino]methyl}phenyl)propanoic acid



Using 4-chlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 428(MH⁺)

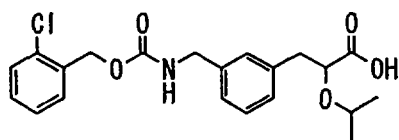
Example 267. 2-Isopropoxy-3-(3-{[3-chlorobenzyl]oxy}-carbonyl)amino]methyl}phenyl)propanoic acid



Using 3-chlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 428(MH⁺)

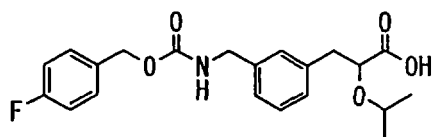
Example 268. 2-Isopropoxy-3-(3-(((2-chlorobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 2-chlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 428(MH⁺)

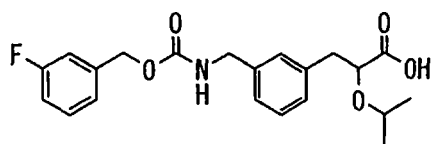
Example 269. 2-Isopropoxy-3-(3-(((4-fluorobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 4-fluorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 412(MH⁺)

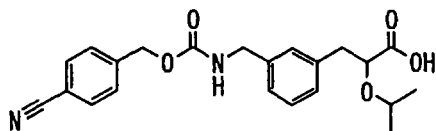
Example 270. 2-Isopropoxy-3-(3-(((3-fluorobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 3-fluorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 412(MH^+)

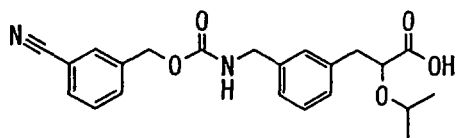
Example 271. 2-Isopropoxy-3-(3-(((4-cyanobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 4-cyanobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 419(MH^+)

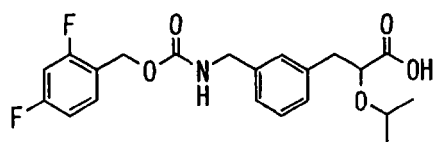
Example 272. 2-Isopropoxy-3-(3-(((3-cyanobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 3-cyanobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 419(MH^+)

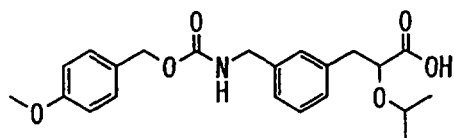
Example 273. 2-Isopropoxy-3-(3-(((2,4-difluorobenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 2,4-difluorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 430 (MH^+)

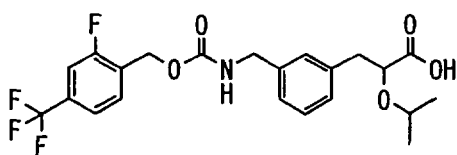
Example 274. 2-Isopropoxy-3-(3-(((4-methoxybenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 4-methoxybenzyl chloride, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 424 (MH^+)

Example 275. 2-Isopropoxy-3-(3-(((2-fluoro-4-trifluoromethylbenzyl)oxy)carbonyl)amino)methyl)phenyl)propanoic acid



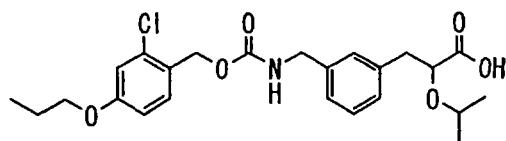
Using 2-fluoro-4-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 480 (MH^+)

Example 276.

2-Isopropoxy-3-(3-(((2-chloro-4-propoxybenzyl)oxy)-

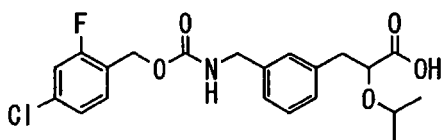
carbonyl)amino]methyl)phenyl)propanoic acid



Using 2-chloro-4-propoxybenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 486 (MH⁺)

Example 277. 2-Isopropoxy-3-(3-(((2-fluoro-4-chlorobenzyl)oxy)carbonyl)amino)methyl)phenyl)propanoic acid

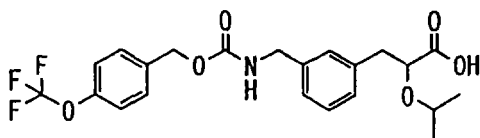


Using 2-fluoro-4-chlorobenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

MS m/e (ESI) 446 (MH⁺)

Example 278.

2-Isopropoxy-3-(3-(((4-trifluoromethoxybenzyl)oxy)-carbonyl)amino)methyl)phenyl)propanoic acid



Using 4-trifluoromethoxybenzyl bromide, the title compound was obtained in the same manner as described in Example 138f).

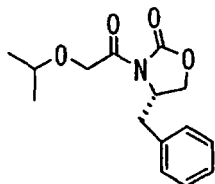
MS m/e (ESI) 478 (MH⁺)

Example 279. 3-{3-[3-(2,4-Dichlorophenoxy)-

2(S)-hydroxypropoxy]phenyl)-2(S)-isopropoxypropanoic acid

Production example 279a)

4(S)-Benzyl-3-(2-isopropoxyacetyl)oxazolidin-2-one



A solution containing 98 g of 2-isopropoxyacetic acid and 360 ml of triethylamine in tetrahydrofuran (4L) was cooled to -25°C. After 92 ml of 2,2-dimethylpropanoyl chloride was dropwise added, the reaction solution was stirred at -20°C for 5 hours. Then, 50 g of anhydrous lithium chloride and 120 g of (4S)-4-benzyl-1,3-oxazolon-2-one were successively added, and stirring was continued at room temperature overnight. Then, the reaction solution was filtered and evaporated. The residue was dissolved in 2L of ethyl acetate, washed with saturated aqueous sodium hydrogen carbonate, and then dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was purified by silica gel column chromatography (elution solvent: hexane-ethyl acetate), to give 106.6 g of (4S)-4-benzyl-3-(2-isopropoxyacetyl)-1,3-oxazolon-2-one as a colorless oil.

¹H NMR (CDCl₃)

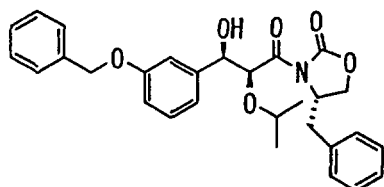
δ : 1.17 (d, J=6.0Hz, 6H) 2.81 (dd, J=9.5, 13.4Hz, 1H) 3.35 (dd, J=3.2, 13.4Hz, 1H) 3.74 (sept, J=6.0Hz, 1H) 4.24 (dd, J=3.5, 9.3Hz) 4.29 (t, J=9.3Hz, 1H) 4.65 (d, J=19.5Hz, 1H) 4.69 (m, 1H) 4.70 (d, J=19.5Hz, 1H) 7.22 (d, J=7.2Hz,

2H) 7.30-7.45 (m, 3H)

Production example 279b)

4(S)-Benzyl-3-[3-(3-benzyloxyphenyl)-

3-hydroxy-2(S)-isopropoxypropionyl]oxazolidin-2-one



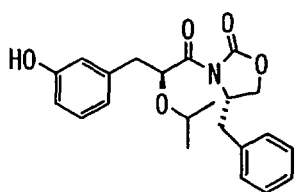
After cooling a solution containing 8.1 g of (4S)-4-benzyl-3-(2-isopropoxyacetyl)-1,3-oxazolon-2-one in toluene (120 ml) was cooled to -75°C , 5.0 ml of triethylamine was added. 30.5 ml of dibutylboron triflate (1M solution in dichloromethane) was added dropwise at such a rate that the inside temperature did not exceed -70°C . After the dropwise addition, the mixture was stirred for 50 minutes. Then, the inside temperature was raised to 0°C and the mixture was stirred for another 50 minutes, and again cooled to -75°C . To the reaction solution was added a solution containing 5.2 g of 3-benzyloxybenzaldehyde in dichloromethane (25 ml) by means of cannula, and stirring was continued at -75°C for 30 minutes. Then, the inside temperature was raised to 0°C over about 1 hour by 10°C per 10 minutes. Again after cooling to -75°C , a solution containing 2.0 g of 3-benzyloxybenzaldehyde in dichloromethane (10 ml) was added. The temperature was gradually raised to room temperature and stirred for 3 days at room temperature. The reaction solution was poured into a mixed solution of 150 ml

of methanol, 100 ml of pH 7 buffer (disodium hydrogen phosphate-citric acid) and 30 ml of hydrogen peroxide (30% aqueous solution), and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 13.1 g of 4(S)-benzyl-3-[3-(3-benzyloxyphenyl)-3-hydroxy-2(S)-isopropoxypropionyl]oxazolidin-2-one as a colorless oil in the 2:1 → 3:2 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 1.11 (d, J=6.0Hz, 3H) 1.19 (d, J=6.0Hz, 3H) 2.75 (dd, J=9.6, 13.2Hz, 1H) 3.08 (d, J=5.6Hz, 1H) 3.26 (dd, J=3.2, 13.2Hz, 1H) 3.60-3.69 (m, 2H) 3.99 (dd, J=1.6, 8.8Hz, 1H) 4.27-4.33 (m, 1H) 4.84 (t, J=5.6Hz, 1H) 5.07 (s, 2H) 5.44 (d, J=5.2Hz, 1H) 6.88-6.90 (m, 1H) 7.00 (d, J=7.6Hz, 1H) 7.09 (t, J=2.0Hz, 1H) 7.16-7.24 (m, 3H) 7.28-7.35 (m, 6H) 7.39-7.43 (m, 2H)

Production example 279c) 4(S)-Benzyl-3-[3-(3-hydroxyphenyl)-2(S)-isopropoxypropionyl]oxazolidin-2-one



12.9 g of

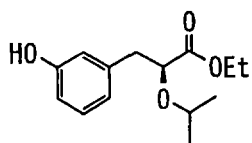
4-Benzyl-3-[3-(3-benzyloxyphenyl)-3-hydroxy-2-isopropoxy propionyl]oxazolidin-2-one was dissolved in 30 ml of pyridine, and 3.06 ml of methanesulfonyl chloride was dropwise added thereto under ice-cooling. After stirring was continued at room

temperature for 2 hours, the reaction solution was diluted with ethyl acetate and washed successively with 1N hydrochloric acid and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was concentrated, to give 3-(4(S)-benzyl-2-oxooxazolidin-3-yl)-1-(3-benzyloxyphenyl)-2(S)-isopropoxy-3-oxopropyl methanesulfonate. This product was then dissolved in 300 ml of ethanol, and 2 g of 10% palladium carbon was added, and the mixture was stirred overnight under hydrogen atmosphere at room temperature. The reaction solution was filtered, and the filtrate was concentrated. The residue was diluted with ethyl acetate, and washed with saturated aqueous sodium hydrogen carbonate, The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 5.87 g of the title compound as a colorless oil in the 2:1 → 3:2 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 1.04 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.78 (dd, J=9.6, 13.2Hz, 1H) 2.86-2.96 (m, 2H) 3.31 (dd, J=2.4, 13.6Hz, 1H) 3.53 (Sept, J=6.0Hz, 1H) 4.01 (t, J=8.0Hz, 1H) 4.13 (dd, J=2.4, 9.2Hz, 1H) 4.50-4.55 (m, 1H) 5.22 (s, 1H) 5.39 (dd, J=5.2, 8.4Hz, 1H) 6.71 (dd, 2.4, 8.0Hz, 1H) 6.82 (t, J=2.0Hz, 1H) 6.87 (d, J=7.6Hz, 1H) 7.14 (t, J=8.0Hz, 1H) 7.18-7.23 (m, 2H) 7.27-7.35 (m, 3H)

Production example 279d) 3-(3-Hydroxyphenyl)-2(S)-isopropoxypropanoic acid ethyl ester



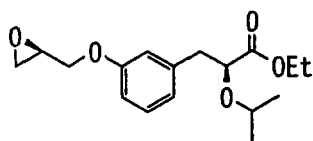
1.535 g of 4(S)-Benzyl-3-[3-(3-hydroxyphenyl)-2(S)-isopropoxypropionyl]oxazolidin-2-one was dissolved in 40 ml of tetrahydrofuran, and 3.3 ml of 30% aqueous hydrogen peroxide and 12 ml of 1N aqueous lithium hydroxide were successively added under ice-cooling, and stirring was continued at room temperature overnight. After adding water to the reaction solution, the mixture was extracted with dichloromethane and the aqueous layer was acidified by 1N hydrochloric acid. Following extraction (x3) was conducted with ethyl acetate, the organic layer was dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressures, to give 847 mg of 3-(3-hydroxyphenyl)-2(S)-isopropoxypropanoic acid. This product was then dissolved in 10 ml of N,N-dimethylformamide, and 400 mg of potassium hydrogencarbonate and 0.32 ml of ethane iodide were successively added thereto, and stirring was continued at room temperature for 3 days. The reaction solution was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 567 mg of the title compound as a colorless oil in the 3:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 0.98 (d, $J=6.4\text{Hz}$, 3H) 1.16 (d, $J=6.4\text{Hz}$, 3H) 1.24 (t, $J=7.2\text{Hz}$, 3H) 2.89 (dd, $J=8.8$, 14.0Hz , 1H) 2.97 (dd, $J=4.8$, 13.6Hz , 1H) 3.52 (Sept, $J=6.0\text{Hz}$, 1H) 4.05 (dd, $J=4.8$, 8.8Hz , 1H) 4.12-4.19 (m, 2H) 5.01 (br, 1H) 6.09-6.72 (m, 1H) 6.81-6.83 (m, 1H) 6.75 (t, $J=1.6\text{Hz}$, 1H) 7.15 (t, $J=7.6\text{Hz}$, 1H)

Production example 279e) 2(S)-Isopropoxy-

3-(3(R)-oxilanylmethoxyphenyl)propanoic acid ethyl ester



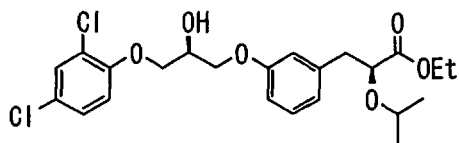
127 mg of 3-(3-hydroxyphenyl)-2(S)-isopropoxypropanoic acid ethyl ester was dissolved in 1.7 ml of N,N-dimethylformamide, and 83 mg of potassium carbonate, 15 mg of cesium fluoride and 156 mg of (R)-glycidyl nosylate were added, and stirring was continued at room temperature overnight. The reaction solution was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 100 mg of the title compound as a colorless oil in the 4:1 hexane-ethyl acetate fraction.

^1H NMR (CDCl_3)

δ : 0.96 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 1.24 (t, $J=7.2\text{Hz}$, 3H) 2.76 (dd, $J=2.8$, 4.8Hz , 1H) 2.87-2.93 (m, 2H) 2.98 (dd, $J=4.8$, 14.0Hz , 1H) 3.33-3.37 (m, 1H) 3.50 (Sept, $J=6.0\text{Hz}$, 1H) 3.95 (dd, $J=6.0$, 11.2Hz , 1H) 4.04 (dd, $J=4.8$, 9.2Hz , 1H) 4.14-4.22 (m, 3H) 6.78 (dd, $J=2.8$, 8.4Hz , 1H) 6.83 (d, $J=2.0\text{Hz}$, 1H) 6.86 (d, $J=7.6\text{Hz}$, 1H) 7.19 (t, $J=8.4\text{Hz}$, 1H)

Production example 279f)

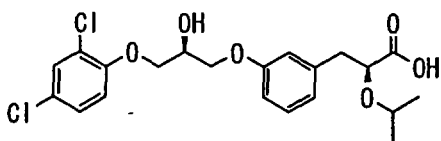
3-{3-[3-(2,4-Dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-
2(S)-isopropoxypropanoic acid ethyl ester



126 mg of

2-Isopropoxy-3-(3-oxilanylmethoxyphenyl)propanoic acid ethyl ester was dissolved in ethanol, and 130 mg of 2,4-dichlorophenol and 17 mg of potassium carbonate were added, and the mixture was stirred at 50°C for 1.5 days. The reaction solution was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 177 mg of the title compound as a colorless oil in the 3:1 hexane-ethyl acetate fraction.

Example 279g) 3-{3-[3-(2,4-Dichlorophenoxy)-2(S)-
hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid

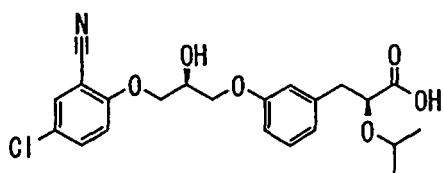


220 mg of 3-{3-[3-(2,4-Dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester was dissolved in 4 ml of ethanol, followed by adding 1 ml of 1N sodium hydroxide. After standing as it was at room temperature for 4 hours, the solution was neutralized with 1N hydrochloric acid and extracted with ethyl acetate. The organic

layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 200 mg of the title compound as a colorless oil in the 3:2 → 2:3 hexane-ethyl acetate fraction.

MS m/e (ESI) 465 (MNa^+)

Example 280. 3-{3-[3-(4-Chloro-2-cyanophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid

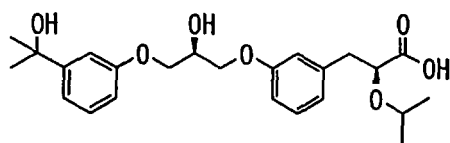


Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 456 (MNa^+)

Example 281.

3-(3-{2(S)-Hydroxy-3-[3-(1-hydroxy-1-methylethyl)phenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 3-(1-hydroxy-1-methylethyl)phenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

^1H NMR ($CDCl_3$)

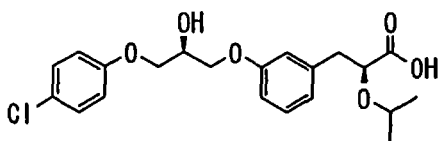
δ : 1.04 (d, $J=6.0$ Hz, 3H) 1.16 (d, $J=6.0$ Hz, 3H) 1.57 (s, 6H) 2.92 (dd, $J=7.6, 14.0$ Hz, 1H) 3.10 (dd, $J=3.2, 13.6$ Hz, 1H) 3.55 (Sept, $J=6.0$ Hz, 1H) 4.11-4.12

(m, 5H) 4.38 (Sept, J=5.2Hz, 1H) 6.80-6.88 (m, 4H) 7.06 (d, J=7.2Hz, 1H)
7.12 (t, J=2.4Hz, 1H) 7.21 (dd, J=7.6, 8.0Hz, 1H) 7.24 (m, 1H)

MS m/e (ESI) 453 (MNa⁺)

Example 282.

3-(3-(2(R)-Hydroxy-3-[4-chlorophenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chlorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

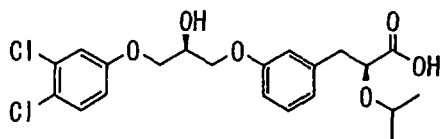
¹H NMR (CDCl₃)

δ : 1.03 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.92 (dd, J=7.2, 13.6Hz, 1H) 3.11 (dd, J=3.6, 13.6Hz, 1H) 3.53 (Sept, J=6.0Hz, 1H) 4.09-4.17 (m, 5H) 4.38 (Sept, J=5.6Hz, 1H) 6.80-6.89 (m, 4H) 7.20-7.26 (m, 4H)

MS m/e (ESI) 431 (MNa⁺)

Example 283.

3-(3-(2(S)-Hydroxy-3-[3,4-dichlorophenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



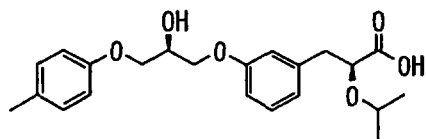
Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

¹H NMR (CDCl₃)

δ : 1.04 (d, J=6.4Hz, 3H) 1.17 (d, J=6.0Hz, 3H) 2.93 (dd, J=7.6, 14.0Hz, 1H) 3.11 (dd, J=4.0, 13.6Hz, 1H) 3.56 (Sept, J=6.0Hz, 1H) 4.09-4.16 (m, 5H) 4.38 (Sept, J=6.4Hz, 1H) 6.80 (dd, J=2.8, 8.8Hz, 1H) 6.83 (brs, 2H) 6.87 (d, J=7.6Hz, 1H) 7.05 (d, J=2.8Hz, 1H) 7.22 (dd, J=7.6, 8.8Hz, 1H) 7.34 (d, 8.8Hz, 1H)

MS *m/e*(ESI) 465 (MNa⁺)

Example 284. 3-(3-{2(R)-Hydroxy-3-[4-methylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid



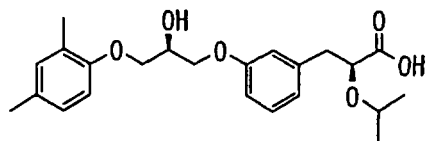
Using 4-methylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

¹H NMR (CDCl₃)

δ : 1.03 (d, J=6.4Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.29 (s, 3H) 2.91 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=3.6, 13.6Hz, 1H) 3.54 (Sept, J=6.4Hz, 1H) 4.09-4.17 (m, 5H) 4.37 (Sept, J=6.4Hz, 1H) 6.80-6.87 (m, 5H) 7.09 (d, J=8.4Hz, 2H) 7.21 (dd, J=7.6, 9.2Hz, 1H)

MS *m/e*(ESI) 411 (MNa⁺)

Example 285. 3-(3-{2(S)-Hydroxy-3-[2,4-dimethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid



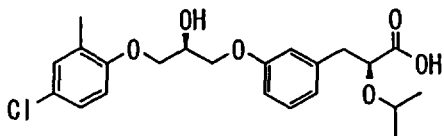
Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.4\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 2.20 (s, 3H) 2.26 (s, 3H) 2.91 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=4.0$, 14.0Hz , 1H) 3.54 (Sept, $J=6.0\text{Hz}$, 1H) 4.10-4.20 (m, 5H) 4.39 (Sept, $J=5.2\text{Hz}$, 1H) 6.75 (d, $J=7.6\text{Hz}$, 1H) 6.81-6.87 (m, 3H) 6.93-6.97 (m, 2H) 7.22 (dd, $J=8.0$, 8.8Hz , 1H)

MS m/e (ESI) 425 (MNa^+)

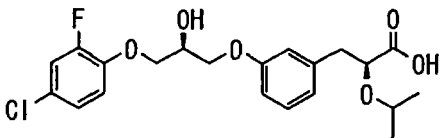
Example 286. 3-(3-{2(S)-Hydroxy-3-[4-chloro-2-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-methylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 445 (MNa^+)

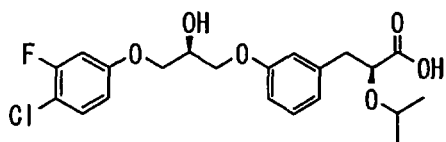
Example 287. 3-(3-{2(S)-Hydroxy-3-[4-chloro-2-fluorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-fluorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 449 (MNa⁺)

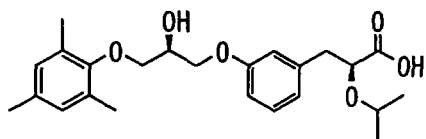
Example 288. 3-(3-(2(S)-Hydroxy-3-[4-chloro-3-fluorophenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-3-fluorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 449 (MNa⁺)

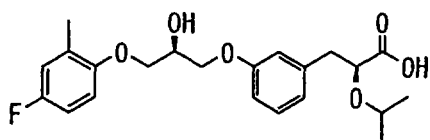
Example 289. 3-(3-(2(S)-Hydroxy-3-[2,4,6-trimethylphenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 2,4,6-trimethylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 439 (MNa⁺)

Example 290. 3-(3-(2(S)-Hydroxy-3-[4-fluoro-2-methylphenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid

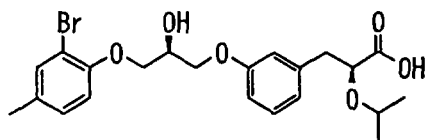


Using 4-fluoro-2-methylphenol, the title compound was obtained in the same manner as described in Production example

279f) and Example 279g).

MS m/e (ESI) 429 (MNa⁺)

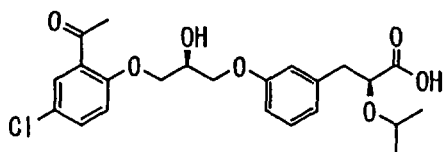
Example 291. 3-(3-{2(S)-Hydroxy-3-[2-bromo-4-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 2-bromo-4-methylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 489 (MNa⁺)

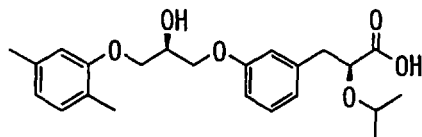
Example 292. 3-(3-{2(S)-Hydroxy-3-[2-acetyl-4-chlorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 2-acetyl-4-chlorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 473 (MNa⁺)

Example 293. 3-(3-{2(S)-Hydroxy-3-[2,5-dimethylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid

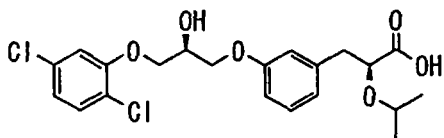


Using 2,5-dimethylphenol, the title compound was obtained

in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 425 (MNa⁺)

Example 294. 3-(3-{2(S)-Hydroxy-3-[2,5-dichlorophenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid

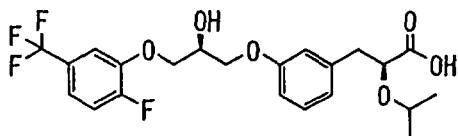


Using 2,5-dichlorophenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 465 (MNa⁺)

Example 295.

3-(3-{2(S)-Hydroxy-3-[2-fluoro-5-trifluoromethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid

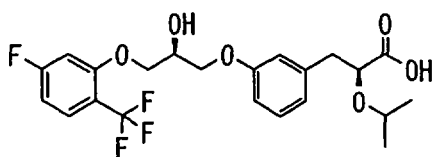


Using 2-fluoro-5-trifluoromethylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 483 (MNa⁺)

Example 296.

3-(3-{2(S)-Hydroxy-3-[5-fluoro-2-trifluoromethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid

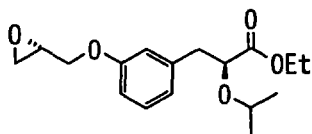


Using 5-fluoro-2-trifluoromethylphenol, the title compound was obtained in the same manner as described in Production example 279f) and Example 279g).

MS m/e (ESI) 483(MNa⁺)

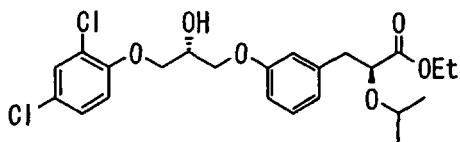
Example 297. 3-(3-{2(R)-Hydroxy-3-[2,4-dichlorophenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid

Production example 297a) 2(S)-Isopropoxy-3-(3-(S)-oxilanylmethoxyphenyl)propanoic acid ethyl ester



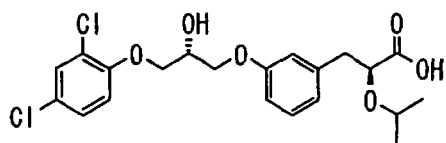
Using (S)-glycidyl nosylate, the title compound was obtained as a colorless oil in the same manner as described in Production example 279e).

Production example 297b) 3-{3-[3-(2,4-Dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl)-2(S)-isopropoxypropanoic acid ethyl ester



Using 2(S)-isopropoxy-3-(3-(S)-oxilanylmethoxyphenyl)-propanoic acid ethyl ester, the title compound was obtained in the same manner as described in 279f).

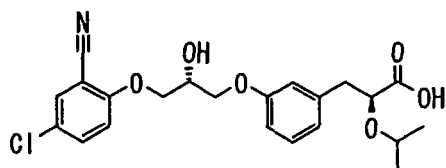
Example 297c) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester, the title compound was obtained in the same manner as described in Example 279g).

MS m/e (ESI) 465(MNa^+)

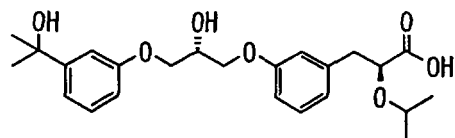
Example 298. 3-{3-[3-(4-Chloro-2-cyanophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 458(MNa^+)

Example 299. 3-(3-{2(R)-Hydroxy-3-[3-(1-hydroxy-1-methylethyl)phenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 3-dimethylhydroxyphenol, the title compound was

obtained in the same manner as described in Production example 297b) and Example 297c).

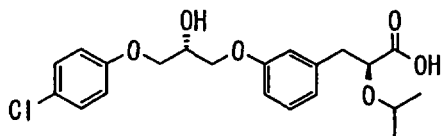
^1H NMR (CDCl_3)

δ : 1.04 (d, $J=6.0\text{Hz}$, 3H) 1.16 (d, $J=6.0\text{Hz}$, 3H) 1.57 (s, 6H) 2.92 (dd, $J=8.0$, 14.0Hz, 1H) 3.10 (dd, $J=3.6$, 13.6Hz, 1H) 3.55 (Sept, $J=6.0\text{Hz}$, 1H) 4.09-4.21 (m, 5H) 4.39 (Sept, $J=5.2\text{Hz}$, 1H) 6.80-6.88 (m, 4H) 7.05-7.07 (m, 1H) 7.12 (t, $J=2.4\text{Hz}$, 1H) 7.21 (dd, $J=7.6$, 8.0Hz, 1H) 7.24-7.28 (m, 1H)

MS m/e (ESI) 453 (MNa^+)

Example 300.

3-(3-{2(S)-Hydroxy-3-[4-chlorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



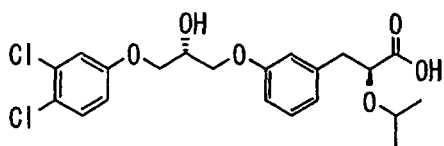
Using 4-chlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.0\text{Hz}$, 3H) 1.16 (d, $J=6.0\text{Hz}$, 3H) 2.92 (dd, $J=8.0$, 13.6Hz, 1H) 3.11 (dd, $J=4.0$, 13.6Hz, 1H) 3.55 (Sept, $J=6.0\text{Hz}$, 1H) 4.08-4.17 (m, 5H) 4.38 (Sept, $J=4.8\text{Hz}$, 1H) 6.80-6.89 (m, 4H) 7.20-7.26 (m, 4H)

MS m/e (ESI) 431 (MNa^+)

Example 301. 3-(3-{2(R)-Hydroxy-3-[3,4-dichlorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

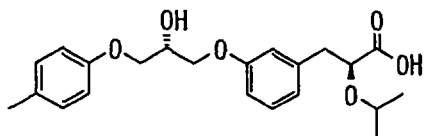
^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.4\text{Hz}$, 3H) 1.16 (d, $J=6.0\text{Hz}$, 3H) 2.93 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=6.0$, 14.0Hz , 1H) 3.56 (Sept, $J=6.4\text{Hz}$, 1H) 4.09–4.16 (m, 5H) 4.37 (Sept, $J=6.4\text{Hz}$, 1H) 6.78–6.84 (m, 3H) 6.87 (d, $J=7.6\text{Hz}$, 1H) 7.04 (d, $J=2.8\text{Hz}$, 1H) 7.22 (t, $J=7.6\text{Hz}$, 1H) 7.33 (d, $J=8.8\text{Hz}$, 1H)

MS m/e (ESI) 465 (MNa^+)

Example 302.

3-(3-{2(S)-Hydroxy-3-[4-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



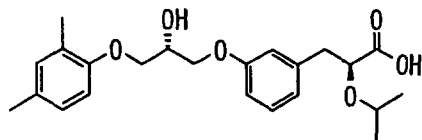
Using 4-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.4\text{Hz}$, 3H) 1.16 (d, $J=6.0\text{Hz}$, 3H) 2.29 (s, 3H) 2.91 (dd, $J=8.0$, 13.6Hz , 1H) 3.11 (dd, $J=4.0$, 14.0Hz , 1H) 3.54 (Sept, $J=6.4\text{Hz}$, 1H) 4.09–4.17 (m, 5H) 4.37 (Sept, $J=5.2\text{Hz}$, 1H) 6.80–6.88 (m, 5H) 7.09 (d, $J=8.4\text{Hz}$, 2H) 7.21 (dd, $J=7.6$, 9.2Hz , 1H)

MS m/e (ESI) 411(MNa⁺)

Example 303. 3-(3-{2(R)-Hydroxy-3-[2,4-dimethylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



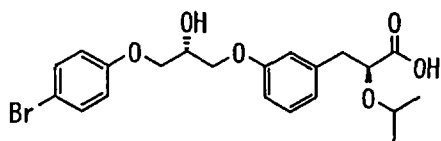
Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.20 (s, 3H) 2.26 (s, 3H) 2.91 (dd, J=8.0, 13.6Hz, 1H) 3.11 (dd, J=3.6, 13.6Hz, 1H) 3.54 (Sept, J=6.0Hz, 1H) 4.09-4.20 (m, 5H) 4.39 (Sept, J=5.2Hz, 1H) 6.75 (d, J=8.0Hz, 1H) 6.80-6.87 (m, 3H) 6.93-6.97 (m, 2H) 7.22 (dd, J=8.0, 8.8Hz, 1H)

MS m/e (ESI) 425(MNa⁺)

Example 304. 3-(3-{2(S)-Hydroxy-3-[4-bromophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 4-bromophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

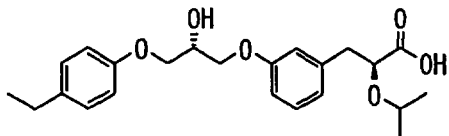
¹H NMR (CDCl₃)

δ : 1.04 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.92 (dd, J=7.6, 14.0Hz, 1H) 3.11 (dd, J=4.0, 13.6Hz, 1H) 3.55 (Sept, J=6.0Hz, 1H) 4.08-4.17 (m,

5H) 4.38 (Sept, J=4.8Hz, 1H) 6.80-6.84 (m, 4H) 6.87 (d, J=7.6Hz, 1H) 7.22 (dd, J=7.6, 8.8Hz, 1H) 7.39 (d, J=8.8Hz, 1H)

MS m/e (ESI) 475 (MNa⁺)

Example 305. 3-(3-{2(S)-Hydroxy-3-[4-ethylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



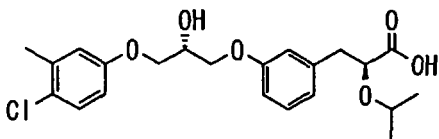
Using 4-ethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

¹H NMR (CDCl₃)

δ : 1.03 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 1.20 (t, J=7.2Hz, 3H) 2.59 (q, J=7.6Hz, 2H) 2.91 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=3.6, 13.6Hz, 1H) 3.54 (Sept, J=6.0Hz, 1H) 4.10-4.17 (m, 5H) 4.38 (Sept, J=5.2Hz, 1H) 6.83 (t, J=6.8Hz, 2H) 6.86 (d, J=8.4Hz, 3H) 7.12 (d, J=8.4Hz, 2H) 7.21 (dd, J=7.2, 9.2Hz, 1H)

MS m/e (ESI) 425 (MNa⁺)

Example 306. 3-(3-{2(S)-Hydroxy-3-[4-chloro-3-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



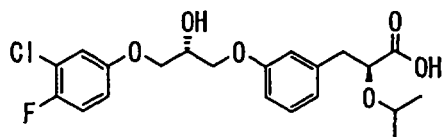
Using 4-chloro-3-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.0\text{Hz}$, 3H) 1.16 (d, $J=6.4\text{Hz}$, 3H) 2.92 (dd, $J=7.6$, 13.6Hz, 1H) 3.11 (dd, $J=3.6$, 13.6Hz, 1H) 3.55 (Sept, $J=6.0\text{Hz}$, 1H) 4.08-4.16 (m, 5H) 4.37 (Sept, $J=5.2\text{Hz}$, 1H) 6.71 (dd, $J=2.8$, 8.8Hz, 1H) 6.80-6.84 (m, 3H) 6.87 (d, $J=7.2\text{Hz}$, 1H) 7.19-7.24 (m, 2H)

MS m/e (ESI) 445 (MNa^+)

Example 307. 3-(3-{2(R)-Hydroxy-3-[3-chloro-4-fluorophenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



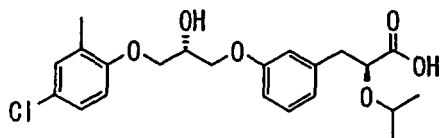
Using 3-chloro-4-fluorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

^1H NMR (CDCl_3)

δ : 1.04 (d, $J=6.0\text{Hz}$, 3H) 1.17 (d, $J=6.0\text{Hz}$, 3H) 2.93 (dd, $J=8.0$, 14.0Hz, 1H) 3.11 (dd, $J=4.0$, 14.0Hz, 1H) 3.56 (Sept, $J=6.4\text{Hz}$, 1H) 4.07-4.16 (m, 5H) 4.37 (Sept, $J=4.8\text{Hz}$, 1H) 6.77-6.84 (m, 3H) 6.87 (d, $J=7.6\text{Hz}$, 1H) 6.98 (dd, $J=3.2$, 6.0Hz, 1H) 7.06 (t, $J=8.8\text{Hz}$, 1H) 7.22 (dd, $J=7.6$, 9.2Hz, 1H)

MS m/e (ESI) 449 (MNa^+)

Example 308. 3-(3-{2(R)-Hydroxy-3-[4-chloro-2-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid

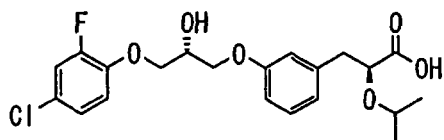


Using 4-chloro-2-methylphenol, the title compound was

obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 445 (MNa^+)

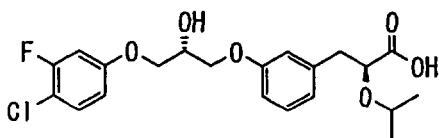
Example 309. 3-(3-(2(R)-Hydroxy-3-[4-chloro-2-fluorophenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-fluorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 449 (MNa^+)

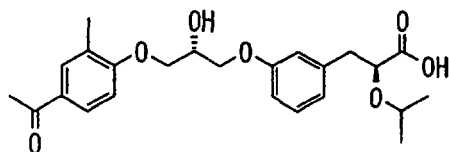
Example 310. 3-(3-(2(R)-Hydroxy-3-[4-chloro-3-fluorophenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-3-fluorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 449 (MNa^+)

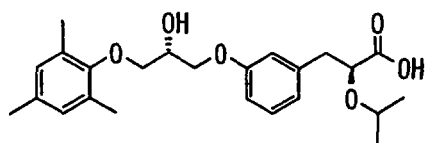
Example 311. 3-(3-(2(R)-Hydroxy-3-[4-acetyl-2-methylphenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 4-acetyl-2-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 453 (MNa⁺)

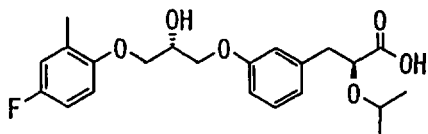
Example 312. 3-(3-{2(R)-Hydroxy-3-[2,4,6-trimethylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 2,4,6-trimethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 439 (MNa⁺)

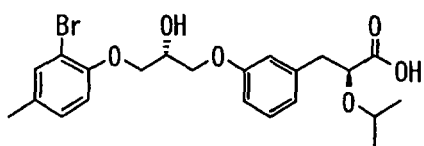
Example 313. 3-(3-{2(R)-Hydroxy-3-[4-fluoro-2-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 4-fluoro-2-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 429 (MNa⁺)

Example 314. 3-(3-{2(R)-Hydroxy-3-[2-bromo-4-methylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid

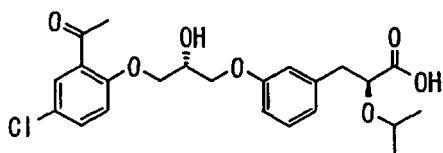


Using 2-bromo-4-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 489 (MNa^+)

Example 315.

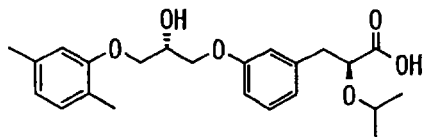
3-(3-(2(R)-Hydroxy-3-[2-acetyl-4-chlorophenoxy]propoxy)-phenyl)-2(S)-isopropoxypropanoic acid



Using 2-acetyl-4-chlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 473 (MNa^+)

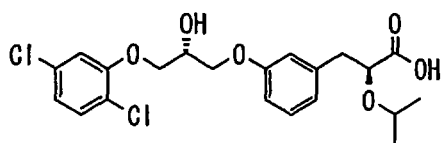
Example 316. 3-(3-(2(R)-Hydroxy-3-[2,5-dimethylphenoxy]propoxy)phenyl)-2(S)-isopropoxypropanoic acid



Using 2,5-dimethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 425 (MNa^+)

Example 317. 3-(3-{2(R)-Hydroxy-3-[2,5-dichlorophenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid

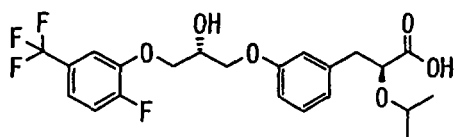


Using 2,5-dichlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 465 (MNa^+)

Example 318.

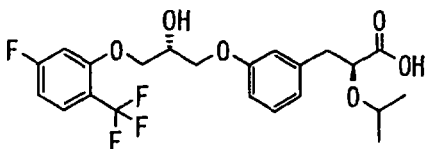
3-(3-{2(R)-Hydroxy-3-[2-fluoro-5-trifluoromethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid



Using 2-fluoro-5-trifluoromethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 483 (MNa^+)

Example 319. 3-(3-{2(R)-Hydroxy-3-[5-fluoro-2-trifluoromethylphenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid

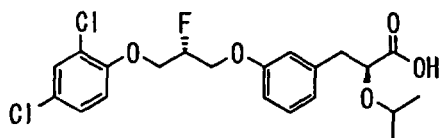


Using 5-fluoro-2-trifluoromethylphenol, the title

compound was obtained in the same manner as described in Production example 297b) and Example 297c).

MS m/e (ESI) 483(MNa⁺)

Example 320. 3-{3-[3-(2,4-Dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 174 mg of

3-{3-[3-(2,4-dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester (Production example 279e) was dissolved in 5 ml of dichloromethane, and the mixture was cooled to -78°C. To the solution was added 0.15 ml (diethylamino)sulfur trifluoride, and stirring was continued at room temperature for 2 days. Water was added thereto, and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, filtered and the solvent was removed. The residue was purified by silica gel column chromatography, to give 79 mg of 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester in the 7:1 → 5:1 hexane-ethyl acetate fraction. This product was dissolved in 4 ml of ethanol and 0.5 ml of tetrahydrofuran and 0.5 ml of 1N lithium hydroxide were added, and stirring was continued overnight at room temperature. The solution was acidified with 1N hydrochloric acid, and extracted with ethyl acetate. The

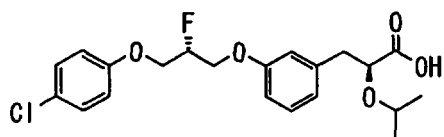
organic layer was dried over anhydrous magnesium sulfate, filtered and the solvent was removed. The residue was purified by silica gel column chromatography, to give 61 mg of the title compound in the 3:1 → 1:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 1.03 (d, J=6.4Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.92 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=3.6, 14.0Hz, 1H) 3.54 (Sept, J=6.4Hz, 1H) 4.13 (q, J=4.0Hz, 1H) 4.28-4.39 (m, 4H) 5.18 (dt, J=4.0, 46.8Hz, 1H) 6.82-6.92 (m, 4H) 7.19-7.29 (m, 3H)

MS *m/e*(ESI) 467 (MNa⁺)

Example 321. 3-{3-[3-(4-Chlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



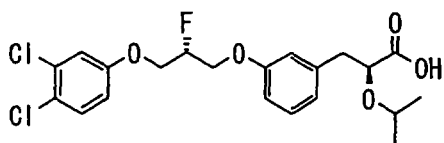
Using 4-chlorophenol, the title compound was obtained in the same manner as described in Production example 279e) and Example 319.

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.92 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=3.6, 14.0Hz, 1H) 3.55 (Sept, J=6.0Hz, 1H) 4.13 (q, J=3.6Hz, 1H) 4.26 (d, J=4.4Hz, 2H) 4.31 (d, J=4.8Hz, 2H) 5.14 (dsept, J=4.8, 47.2Hz, 1H) 6.80-6.90 (m, 5H) 7.20-7.26 (m, 3H)

MS *m/e*(ESI) 433 (MNa⁺)

Example 322. 3-{3-[3-(3,4-Dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



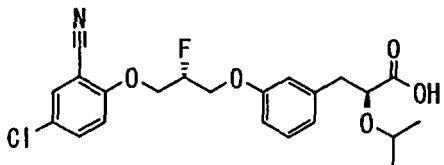
Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Production example 279e) and Example 320.

¹H NMR (CDCl₃)

δ : 1.03 (d, J=6.4Hz, 3H) 1.17 (d, J=6.4Hz, 3H) 2.93 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=4.0, 14.0Hz, 1H) 3.55 (Sept, J=6.4Hz, 1H) 4.14 (q, J=3.6Hz, 1H) 4.26 (d, J=4.4Hz, 2H) 4.31 (t, J=4.8Hz, 2H) 5.13 (dsept, J=4.8, 46.8Hz, 1H) 6.79-6.84 (m, 3H) 6.88 (d, J=7.6Hz, 1H) 7.05 (d, J=2.8Hz, 1H) 7.23 (dt, J=1.2, 7.6Hz, 1H) 7.34 (d, J=8.8Hz, 1H)

MS *m/e*(ESI) 467 (MNa⁺)

Example 323. 3-{3-[3-(4-Chloro-2-cyanophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Production example 279e) and Example 320.

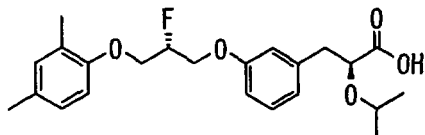
¹H NMR (CDCl₃)

δ : 1.04 (d, J=6.0Hz, 3H) 1.17 (d, J=6.0Hz, 3H) 2.94 (dd, J=7.6, 13.6Hz, 1H) 3.10 (dd, J=4.0, 13.6Hz, 1H) 3.57 (Sept, J=6.0Hz, 1H) 4.14 (q, J=4.0Hz, 1H) 4.28-4.50 (m, 4H) 5.20 (dsept, J=4.4, 46.4Hz, 1H) 6.80-6.85 (m, 2H) 6.88 (d, J=7.6Hz, 1H) 6.98 (d, J=8.8Hz, 1H) 7.22 (dt, J=0.8, 7.6Hz, 1H)

7.49-7.64 (m, 2H)

MS m/e (ESI) 458(MNa⁺)

Example 324. 3-{3-[3-(2,4-Dimethylphenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



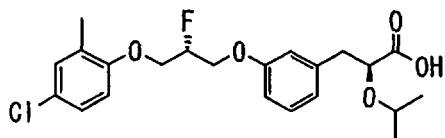
Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Production example 279e) and Example 320.

¹H NMR (CDCl₃)

δ : 1.01 (d, J=6.4Hz, 3H) 1.16 (d, J=6.4Hz, 3H) 2.20 (s, 3H) 2.26 (s, 3H) 2.91 (dd, J=8.4, 14.0Hz, 1H) 3.11 (dd, J=4.0, 13.6Hz, 1H) 3.53 (Sept, J=6.0Hz, 1H) 4.13 (q, J=4.0Hz, 1H) 4.21-4.35 (m, 4H) 5.16 (dsept, J=4.4, 47.6Hz, 1H) 6.74 (d, J=8.0Hz, 1H) 6.80-6.84 (m, 2H) 6.87 (d, J=7.6Hz, 1H) 6.93-6.97 (m, 2H) 7.22 (dt, J=0.6, 7.6Hz, 1H)

MS m/e (ESI) 458(MNa⁺)

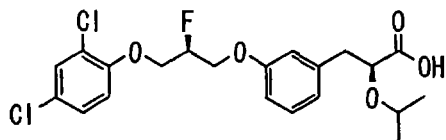
Example 325. 3-{3-[3-(4-Chloro-2-methylphenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-methylphenol, the title compound was obtained in the same manner as described in Production example 279e) and Example 320.

MS m/e (ESI) 447(MNa⁺)

Example 326. 3-{3-[3-(2,4-Dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



174 mg of 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester (Production example 297b) was dissolved in 5 ml of dichloromethane, and the mixture was cooled to -78°C . 0.15 ml of (diethylamino)sulfur trifluoride was added thereto, and stirring was continued at room temperature for 2 days. Water was added and the mixture was extracted with dichloromethane. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed. The residue was purified by silica gel column chromatography, to give 87 mg of 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid ethyl ester in the 7:1 $\rightarrow$ 5:1 hexane-ethyl acetate fraction. This product was dissolved in 4 ml of ethanol and 0.5 ml of tetrahydrofuran, 0.5 ml of 1N lithium hydroxide was added, and the mixture was stirred overnight at room temperature. The solution was acidified with 1N hydrochloric acid, and extracted with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed. The residue was purified by silica gel column chromatography, to give 83 mg of the title compound in the 3:1 $\rightarrow$ 1:1 hexane-ethyl acetate fraction.

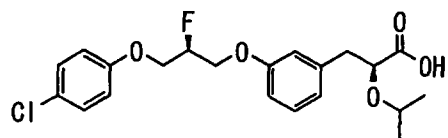
^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.4\text{Hz}$, 3H) 1.16 (d, $J=6.4\text{Hz}$, 3H) 2.92 (dd, $J=7.6$, 13.6Hz , 1H) 3.11 (dd, $J=3.6$, 13.6Hz , 1H) 3.55 (Sept, $J=6.0\text{Hz}$, 1H) 4.13 (q, $J=4.0\text{Hz}$, 1H) 4.29–4.39 (m, 4H) 5.18 (dt, $J=4.4$, 46.8Hz , 1H) 6.82–6.92 (m, 4H) 7.18–7.26 (m, 3H)

MS m/e (ESI) 467 (MNa^+)

Example 327.

3-{3-[3-(4-Chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



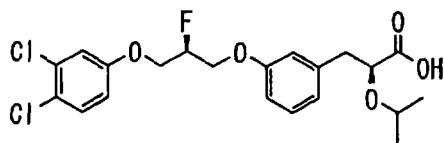
Using 4-chlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 326.

^1H NMR (CDCl_3)

δ : 1.02 (d, $J=6.0\text{Hz}$, 3H) 1.16 (d, $J=6.4\text{Hz}$, 3H) 2.93 (dd, $J=8.4$, 14.0Hz , 1H) 3.10 (dd, $J=4.0$, 14.0Hz , 1H) 3.55 (Sept, $J=6.0\text{Hz}$, 1H) 4.13 (q, $J=4.0\text{Hz}$, 1H) 4.26 (d, $J=4.4\text{Hz}$, 2H) 4.31 (d, $J=4.8\text{Hz}$, 2H) 5.11 (dsept, $J=4.8$, 47.4Hz , 1H) 6.80–6.90 (m, 5H) 7.20–7.26 (m, 3H)

MS m/e (ESI) 433 (MNa^+)

Example 328. 3-{3-[3-(3,4-Dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



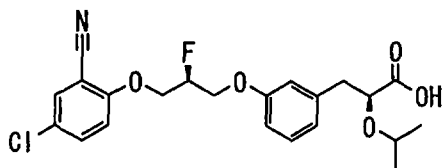
Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 326.

^1H NMR (CDCl_3)

δ : 1.03 (d, $J=6.0\text{Hz}$, 3H) 1.17 (d, $J=6.4\text{Hz}$, 3H) 2.93 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=3.6$, 14.0Hz , 1H) 3.56 (Sept, $J=6.0\text{Hz}$, 1H) 4.14 (q, $J=4.0\text{Hz}$, 1H) 4.26 (d, $J=4.4\text{Hz}$, 2H) 4.31 (t, $J=4.4\text{Hz}$, 2H) 5.13 (dsept, $J=4.8$, 47.2Hz , 1H) 6.79–6.85 (m, 3H) 6.88 (d, $J=7.6\text{Hz}$, 1H) 7.05 (d, $J=2.8\text{Hz}$, 1H) 7.23 (dt, $J=7.6$, 8.8Hz , 1H) 7.34 (d, $J=8.8\text{Hz}$, 1H)

MS m/e (ESI) 467 (MNa^+)

Example 329. 3-{3-[3-(4-Chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 326.

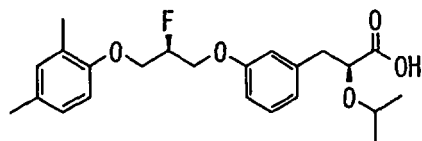
^1H NMR (CDCl_3)

δ : 1.04 (d, $J=6.4\text{Hz}$, 3H) 1.17 (d, $J=6.0\text{Hz}$, 3H) 2.94 (dd, $J=8.0$, 13.6Hz , 1H) 3.10 (dd, $J=3.6$, 13.2Hz , 1H) 3.57 (Sept, $J=4.0\text{Hz}$, 1H) 4.15 (br, 1H) 4.29–4.50 (m, 4H) 5.20 (dsept, $J=4.4$, 46.4Hz , 1H) 6.81–6.85 (m, 2H) 6.88 (d, $J=7.6\text{Hz}$, 1H) 6.98 (d, $J=8.8\text{Hz}$, 1H) 7.22 (dt, $J=8.0$, 9.2Hz , 1H) 7.50–7.54 (m, 2H)

MS m/e (ESI) 458 (MNa^+)

Example 330. 3-{3-[3-(2,4-Dimethylphenoxy)-2(S)-

fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



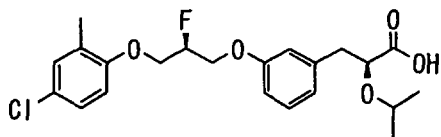
Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 326.

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.4Hz, 3H) 1.16 (d, J=6.4Hz, 3H) 2.20 (s, 3H) 2.26 (s, 3H) 2.91 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=4.0, 14.0Hz, 1H) 3.54 (Sept, J=6.0Hz, 1H) 4.13 (q, J=4.0Hz, 1H) 4.24-4.35 (m, 4H) 5.16 (dsept, J=4.8, 47.6Hz, 1H) 6.74 (d, J=8.0Hz, 1H) 6.81-6.89 (m, 3H) 6.93-6.97 (m, 2H) 7.22 (dt, J=7.6, 8.8Hz, 1H)

MS *m/e*(ESI) 458 (MNa⁺)

Example 331. 3-{3-[3-(4-Chloro-2-methylphenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid



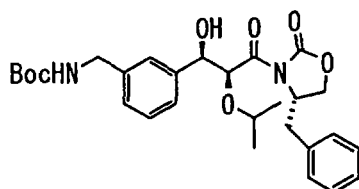
Using 4-chloro-2-methylphenol, the title compound was obtained in the same manner as described in Production example 297b) and Example 326.

MS *m/e*(ESI) 447 (MNa⁺)

Example 332. 2(S)-Isopropoxy-3-{3-[(4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid

Production example 332a)

{3-[3-(4(S)-benzyl-2-oxooxazolidin-3-yl)-1(R)-hydroxy-2(S)-isopropoxy-3-oxopropyl]benzyl}carbamic acid t-butyl ester



A solution of 15.3 g of (4S)-4-benzyl-3-(2-isopropoxyacetyl)-1,3-oxazolon-2-one in toluene (250 ml) was cooled to -75°C , and 9.0 ml of triethylamine was added thereto. 55 ml of dibutylboron triflate (1M solution in dichloromethane) was added dropwise at such a rate that the inside temperature did not exceed -70°C . After the dropwise addition, the mixture was stirred for 50 minutes and then the inside temperature was raised to 0°C . The mixture was stirred for another 50 minutes, and again cooled to -75°C . To this reaction solution was added a solution containing 9.6 g of t-butyl N-(3-formylbenzyl) carbamate in dichloromethane (40 ml) by means of cannula and the mixture was stirred at -75°C for 30 minutes. Then the temperature was raised to 0°C over about 1 hour by 10°C per 10 minutes. The temperature was gradually raised to room temperature and stirring was continued overnight at room temperature. The reaction solution was poured into a mixed solution of 200 ml of methanol, 200 ml of pH 7 buffer (disodium hydrogen phosphate-citric acid) and 60 ml of hydrogen peroxide (30% aqueous solution), and extracted with ethyl acetate. The

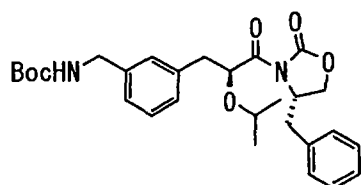
organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 19.2 g of the title compound as a colorless oil in the 1:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 1.12 (d, J=6.0Hz, 3H) 1.19 (d, J=6.0Hz, 3H) 1.44 (s, 9H) 2.75 (dd, J=10.0, 13.6Hz, 1H) 3.25 (dd, J=2.4, 13.6Hz, 1H) 3.65 (Sept, J=6.0Hz, 1H) 3.72 (t, J=8.0Hz, 1H) 4.02 (d, J=8.4Hz, 1H) 4.29 (d, J=6.0Hz, 1H) 4.37-4.43 (m, 1H) 4.85 (t, J=4.8Hz, 1H) 4.91 (m, 1H) 5.43 (d, J=5.6Hz, 1H) 7.12-7.73 (m, 8H) 7.63 (s, 1H)

Production example 332b)

{3-[3-(4(S)-Benzyl-2-oxooxazolidin-3-yl)-2(S)-isopropoxy-3-oxopropyl]benzyl}carbamic acid t-butyl ester



19.2 g of {3-[3-(4(S)-Benzyl-2-oxooxazolidin-3-yl)-1-(R)-hydroxy-2(S)-isopropoxy-3-oxopropyl]benzyl}-carbamic acid t-butyl ester was dissolved in 100 ml of pyridine, and 4.35 ml of methanesulfonyl chloride was added dropwise under ice-cooling. After stirring was continued for 2 hours under ice-cooling and for 3 hours at room temperature, the reaction solution was diluted with ethyl acetate and washed successively with 1N hydrochloric acid and saturated brine. The organic layer

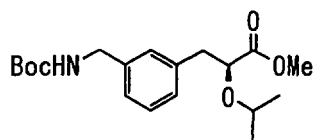
was dried over anhydrous magnesium sulfate, filtered, and the solvent was concentrated, to give methanesulfonic acid 1(R)-(3-aminomethylphenyl)-3-(4(S)-benzyl-2-oxooxazolidin-3-yl)-2(S)-isopropoxy-3-oxopropyl ester. This product was dissolved in 500 ml of ethanol, and 10 g of 10% palladium carbon and 5g of potassium acetate were added, and the mixture was stirred overnight at room temperature under hydrogen atmosphere. The reaction solution was filtered and the filtrate was concentrated. The residue was diluted with ethyl acetate and washed with saturated aqueous sodium hydrogen carbonate. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 15.3g of the title compound as a white solid in the 2:1 → 3:2 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.16 (d, J=6.4Hz, 3H) 1.45 (s, 9H) 2.78 (dd, J=9.6, 13.6Hz, 1H) 2.93-2.98 (m, 2H) 3.30 (dd, J=2.4, 13.2Hz, 1H) 3.51 (Sept, J=6.0Hz, 1H) 3.87-4.01 (m, 1H) 4.08-4.12 (m, 1H) 4.28 (d, J=6.0Hz, 2H) 4.52-4.59 (m, 1H) 4.80-4.88 (m, 1H) 5.34-5.40 (m, 1H) 7.12-7.35 (m, 9H)

Production example 332c)

3-[3-(t-Butoxycarbonylaminoethyl)phenyl]-2(S)-isopropoxypropionic acid methyl ester



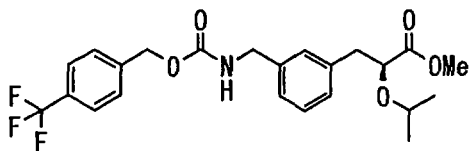
15.3g of {3-[3-(4(S)-Benzyl-2-oxooxazolidin-3-yl)-2(S)-

isopropoxy-3-oxopropyl]benzyl)carbamic acid t-butyl ester was dissolved in 300 ml of tetrahydrofuran, and 15 ml of 30% aqueous hydrogen peroxide and 75 ml of 1N aqueous lithium hydroxide were successively added under ice-cooling, and stirring was continued overnight at room temperature. The reaction solution was treated with water, extracted with dichloromethane, and the aqueous layer was acidified with 1N hydrochloric acid. The mixture was extracted (x3) with ethyl acetate, and the organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated, to give 16.68 g of 3-[3-(t-butoxycarbonylaminoethyl)phenyl]-2(S)-isopropoxypropionic acid. The product was then dissolved in 100 ml of N,N-dimethylformamide, and 7 g of potassium hydrogen carbonate and 3.5 ml of iodomethane were successively added, and the mixture was stirred overnight at room temperature. The reaction solution was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 8.58 g of the title compound as a white solid in the 4:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

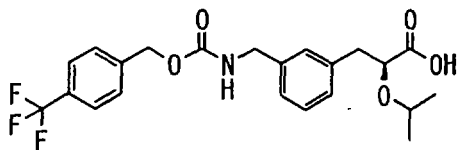
δ : 0.94 (d, J=6.0Hz, 3H) 1.14 (d, J=6.4Hz, 3H) 1.46 (s, 9H) 2.92 (dd, J=9.2, 14.0Hz, 1H) 2.99 (dd, J=5.2, 14.0Hz, 1H) 3.48 (Sept, J=6.0Hz, 1H) 4.06 (dd, J=4.8, 8.8Hz, 1H) 4.29 (brd, J=6.0Hz, 2H) 4.80 (br, 1H) 7.13-7.15 (m, 3H) 7.24 (t, J=7.6Hz, 1H)

Production example 332d) 2(S)-Isopropoxy-3-{3-[(4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid methyl ester



234 mg of 3-[3-(t-Butoxycarbonylaminomethyl)phenyl]-2(S)-isopropoxypropionic acid methyl ester was dissolved in 10 ml of 1,4-dioxane, and the mixture was stirred at room temperature for 1 hour. The reaction solution was concentrated, and the residue was treated with 320 mg of 4-trifluoromethylbenzyl bromide, 500 mg of tetrabutylammonium iodide and 650 mg cesium carbonate, and dissolved in 7 ml of N,N-dimethylformamide. While adding dry ice small by small, the solution was stirred overnight at room temperature. The reaction solution was dissolved in ethyl acetate, and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 173 mg of the title compound in the 3:1 hexane-ethyl acetate fraction.

Example 332e) 2(S)-Isopropoxy-3-{3-[(4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid



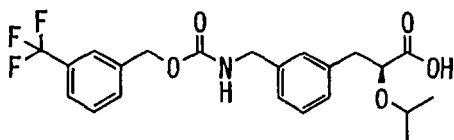
173 mg of 2(S)-Isopropoxy-3-{3-[(4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid methyl ester was dissolved in 4 ml of ethanol, 1 ml of 1N lithium hydroxide was added, and the mixture was stirred at room temperature for 3 hours. The reaction solution was acidified with 1N hydrochloric acid, extracted with ethyl acetate, and washed with water. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 168 mg of the title compound in the 3:2 hexane-ethyl acetate fraction.

^1H NMR (CDCl_3)

δ : 1.00 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 2.95 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=2.4$, 13.6Hz , 1H) 3.54 (Sept, $J=6.4\text{Hz}$, 1H) 4.13 (q, $J=4.0\text{Hz}$, 1H) 4.37 (d, $J=6.0\text{Hz}$, 2H) 5.12 (br, 1H) 5.19 (s, 2H) 7.15–7.19 (m, 3H) 7.25–7.27 (m, 1H) 7.48 (d, $J=8.0\text{Hz}$, 1H) 7.62 (t, $J=8.0\text{Hz}$, 1H)

MS m/e (ESI) 462 (MNa^+)

Example 333. 2(S)-Isopropoxy-3-{3-[(3-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid



Using 3-trifluoromethylbenzyl bromide, the title compound was obtained in the same manner as described in Example 332e).

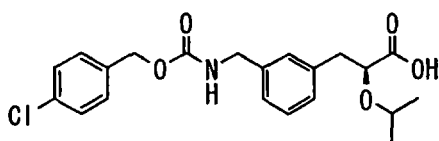
^1H NMR (CDCl_3)

δ : 0.99 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 2.94 (dd, $J=8.4$, 14.0Hz ,

1H) 3.11 (dd, J=4.0, 14.0Hz, 1H) 3.53 (Sept, J=6.4Hz, 1H) 4.12 (q, J=4.0Hz, 1H) 4.38 (d, J=6.4Hz, 2H) 5.13 (br, 1H) 5.19 (s, 2H) 7.11-7.18 (m, 3H) 7.24-7.29 (m, 1H) 7.48 (t, J=7.2Hz, 1H) 7.53-7.64 (m, 2H)

MS m/e (ESI) 462(MNa⁺)

Example 334. 2(S)-Isopropoxy-3-{3-[(4-chlorobenzoyloxy)carbonylamino)methyl]phenyl}propanoic acid



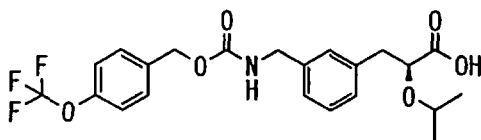
Using 4-chlorobenzyl chloride, the title compound was obtained in the same manner as described in Example 332e).

¹H NMR (CDCl₃)

δ : 1.00 (d, J=6.4Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.94 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=4.0, 14.0Hz, 1H) 3.53 (Sept, J=6.0Hz, 1H) 4.12 (q, J=4.0Hz, 1H) 4.36 (d, J=6.0Hz, 2H) 5.07 (br, 1H) 5.09 (s, 2H) 7.11-7.18 (m, 3H) 7.24-7.34 (m, 5H)

MS m/e (ESI) 428(MNa⁺)

Example 335. 2(S)-Isopropoxy-3-{3-[(4-trifluoromethoxybenzyloxy)carbonylamino)methyl]phenyl}-propanoic acid



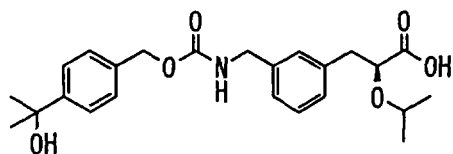
Using 4-trifluoromethoxybenzyl bromide, the title compound was obtained in the same manner as described in Example 332e).

¹H NMR (CDCl₃)

δ : 0.99 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 2.94 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=3.6$, 14.0Hz , 1H) 3.53 (Sept, $J=6.0\text{Hz}$, 1H) 4.12 (q, $J=4.0\text{Hz}$, 1H) 4.37 (d, $J=6.0\text{Hz}$, 2H) 5.09 (br, 1H) 5.13 (s, 2H) 7.12–7.18 (m, 3H) 7.24–7.28 (m, 1H) 7.40 (d, $J=8.0\text{Hz}$, 2H)

MS m/e (ESI) 478(MNa^+)

Example 336. 3-(3-([4-(1-Hydroxy-1-methylethyl)-benzyloxycarbonylamino]methyl)phenyl)-2(S)-isopropoxypropanoic acid



Using 1-hydroxy-1-methylethylbenzyl chloride, the title compound was obtained in the same manner as described in Example 332e).

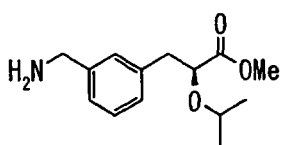
^1H NMR (CDCl_3)

δ : 1.00 (d, $J=6.4\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 1.58 (s, 6H) 2.93 (dd, $J=7.2$, 12.8Hz , 1H) 3.06–3.12 (m, 1H) 3.52 (Sept, $J=6.0\text{Hz}$, 1H) 4.11 (t, $J=7.2\text{Hz}$, 1H) 4.37 (d, $J=5.6\text{Hz}$, 2H) 5.07 (br, 1H) 5.13 (s, 2H) 7.14–7.17 (m, 3H) 7.24–7.27 (m, 1H) 7.35 (d, $J=8.4\text{Hz}$, 2H) 7.49 (d, $J=8.0\text{Hz}$, 2H)

MS m/e (ESI) 452(MNa^+)

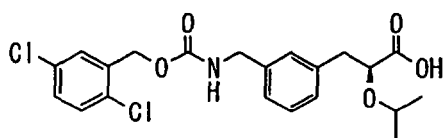
Example 337. 3-{3-[(2,5-Dichlorobenzyloxycarbonylamino)-methyl]}phenyl)-2(S)-isopropoxypropanoic acid

Production example 337a) 3-(3-Aminomethylphenyl)-2(S)-isopropoxypropanoic acid methyl ester



1.034g of 3-[3-(t-Butoxycarbonylaminomethyl)phenyl]-2(S)-isopropoxypropionic acid methyl ester was dissolved in 20 ml of hydrogen chloride 1,4-dioxane, and the mixture was stirred at room temperature for 1 hour. The reaction solution was concentrated, the residue was dissolved in ethyl acetate, and washed with saturated aqueous sodium hydrogen carbonate. The organic layer was dried over anhydrous magnesium sulfate and the solvent was evaporated, to give 653 mg of the title compound as a colorless oil.

Example 337b) 3-{3-[(2,5-Dichlorobenzoyloxycarbonylamino)-methyl]}phenyl}-2(S)-isopropoxypropanoic acid

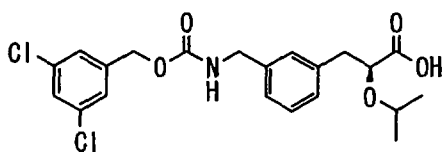


305 mg of 3-(3-Aminomethylphenyl)-2(S)-isopropoxypropanoic acid methyl ester was dissolved in 3 ml of dichloromethane, and a solution of 0.05 ml of pyridine and 180 mg triphosgen in dichloromethane (4 ml) were added under ice-cooling. 0.5 ml of triethylamine was added, and the mixture was stirred at room temperature for 30 minutes. The solution was filtered, and diluted so that the total amount was 5 ml. To the resultant 0.5 ml of solution (containing about 13 mg of isocyanate of 3-(3-aminomethylphenyl)-2(S)-

isopropoxypropanoic acid methyl ester) was added 20 mg of 2,5-dichlorobenzyl alcohol. The reaction solution was concentrated and 0.4 ml of tetrahydrofuran was added, and the mixture was stirred at room temperature for 30 minutes. 0.5 ml of ethanol and 0.1 ml of 1N sodium hydroxide were added thereto, and stirring was continued overnight. The reaction solution was acidified with 1N hydrochloric acid, and extracted with ethyl acetate. The solvent was concentrated, and the residue was purified by reverse-phase high performance liquid chromatography, to give 10.27 mg of the title compound.

MS m/e (ESI) 462 (MNa^+)

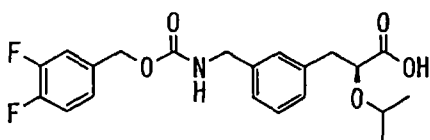
Example 338. 3-(3-([2,5-Dichlorobenzoyloxycarbonylamino]-methyl)phenyl)-2(S)-isopropoxypropanoic acid



Using 2,5-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 462 (MNa^+)

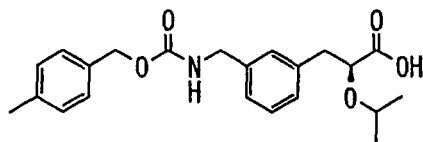
Example 339. 3-(3-([3,4-Difluorobenzoyloxycarbonylamino]-methyl)phenyl)-2(S)-isopropoxypropanoic acid



Using 3,4-difluorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 432 (MNa⁺)

Example 340. 3-(3-([4-Methylbenzyloxycarbonylamino]methyl)-phenyl)-2(S)-isopropoxypropanoic acid



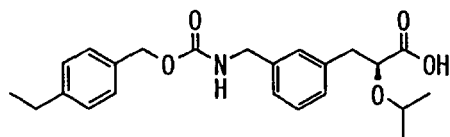
Using 4-methylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

¹H NMR (CDCl₃)

δ : 0.99 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.35 (s, 3H) 2.93 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=3.6, 14.0Hz, 1H) 3.52 (Sept, J=6.4Hz, 1H) 4.11 (q, J=4.0Hz, 1H) 4.36 (d, J=5.6Hz, 2H) 5.05 (br, 1H) 5.09 (s, 2H) 7.14-7.18 (m, 5H) 7.23-7.28 (m, 3H)

MS m/e (ESI) 408 (MNa⁺)

Example 341. 3-(3-([4-Ethylbenzyloxycarbonylamino]methyl)-phenyl)-2(S)-isopropoxypropanoic acid



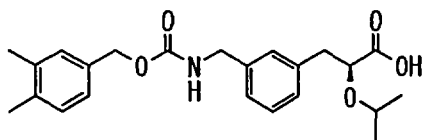
Using 4-ethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

¹H NMR (CDCl₃)

δ : 0.99 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.23 (t, J=7.2Hz, 3H) 2.65 (q, J=7.6Hz, 2H) 2.93 (dd, J=8.0, 14.0Hz, 1H) 3.11 (dd, J=4.0, 14.0Hz, 1H) 3.52 (Sept, J=6.4Hz, 1H) 4.11 (q, J=4.0Hz, 1H) 4.36 (d, J=6.0Hz, 2H) 5.05 (br, 1H) 5.10 (s, 2H) 7.14-7.21 (m, 5H) 7.23-7.31 (m, 3H)

MS m/e (ESI) 422(MNa⁺)

Example 342. 3-(3-([3,4-Dimethylbenzyloxycarbonylamino]-methyl)phenyl)-2(S)-isopropoxypropanoic acid



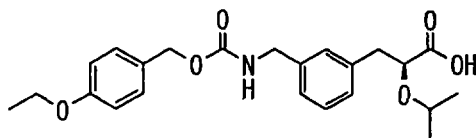
Using 3,4-dimethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

¹H NMR (CDCl₃)

δ : 0.99 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.26 (s, 6H) 2.93 (dd, J=8.0, 13.6Hz, 1H) 3.10 (dd, J=3.6, 14.0Hz, 1H) 3.52 (Sept, J=6.0Hz, 1H) 4.11 (q, J=4.0Hz, 1H) 4.36 (d, J=5.6Hz, 2H) 5.07 (brs, 3H) 7.09-7.18 (m, 6H) 7.26-7.28 (m, 1H)

MS m/e (ESI) 422(MNa⁺)

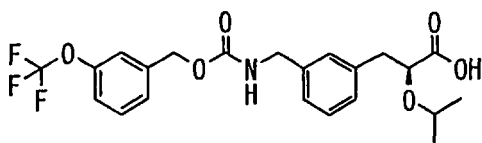
Example 343. 3-(3-([4-Ethoxybenzyloxycarbonylamino]methyl)-phenyl)-2(S)-isopropoxypropanoic acid



Using 4-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 438(MNa⁺)

Example 344. 3-(3-([3-Trifluoromethoxybenzyloxycarbonylamino]methyl)phenyl)-2(S)-isopropoxypropanoic acid



Using 3-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

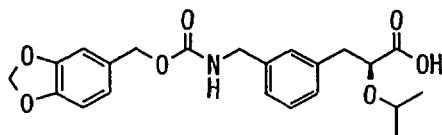
^1H NMR (CDCl_3)

δ : 0.99 (d, $J=6.4\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 2.94 (dd, $J=8.0$, 14.0Hz , 1H) 3.11 (dd, $J=4.0$, 14.0Hz , 1H) 3.53 (Sept, $J=6.0\text{Hz}$, 1H) 4.12 (q, $J=4.0\text{Hz}$, 1H) 4.38 (d, $J=6.0\text{Hz}$, 2H) 5.13 (brs, 1H) 5.15 (s, 2H) 7.14–7.20 (m, 4H) 7.21–7.30 (m, 3H) 7.38 (t, $J=8.0\text{Hz}$, 1H)

MS m/e (ESI) 478 (MNa^+)

Example 345.

3-{3-[(Benzo[1,3]dioxol-5-ylmethoxycarbonylamino)methyl]-phenyl}-2(S)-isopropoxypropanoic acid



Using piperonyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

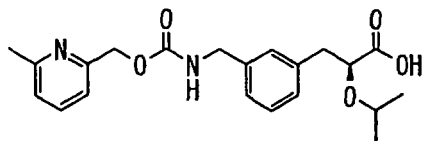
^1H NMR (CDCl_3)

δ : 0.99 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 2.93 (dd, $J=8.4$, 14.0Hz , 1H) 3.11 (dd, $J=3.6$, 14.0Hz , 1H) 3.52 (Sept, $J=6.0\text{Hz}$, 1H) 4.11 (q, $J=3.6\text{Hz}$, 1H) 4.36 (d, $J=5.6\text{Hz}$, 2H) 5.03 (s, 3H) 5.96 (s, 2H) 6.76–6.89 (m, 3H) 7.12–7.18 (m, 3H) 7.23–7.28 (m, 1H)

MS m/e (ESI) 438 (MNa^+)

Example 346. 2(S)-Isopropoxy-3-{3-[(6-methylpyridin-2-

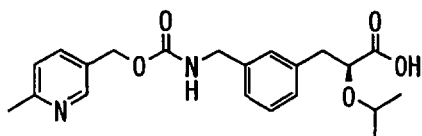
ylmethoxycarbonylamino)methyl]phenyl}propanoic acid



Using (6-methylpyridin-2-yl)methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 409 (MNa^+)

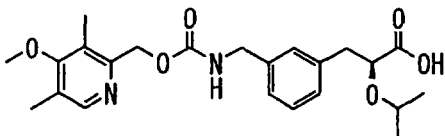
Example 347. 2(S)-Isopropoxy-3-{3-[(6-methylpyridin-3-ylmethoxycarbonylamino)methyl]phenyl}propanoic acid



Using (6-methylpyridin-3-yl)methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 409 (MNa^+)

Example 348. 2(S)-Isopropoxy-3-{3-[(4-methoxy-3,5-dimethylpyridin-2-yl)methoxycarbonylamino)methyl]phenyl}propanoic acid

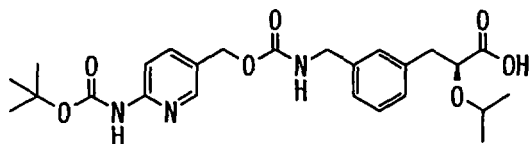


Using (4-methoxy-3,5-dimethylpyridin-2-yl)methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 453 (MNa^+)

Example 349. 3-{3-[(6-t-Butoxycarbonylamino)pyridin-3-

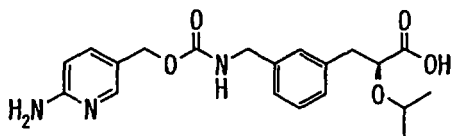
ylmethoxycarbonylamino)methyl]phenyl)-2(S)-
isopropoxypropanoic acid



Using (5-hydroxymethylpyridin-2-yl) carbamic acid t-butyl ester, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 510 (MNa^+)

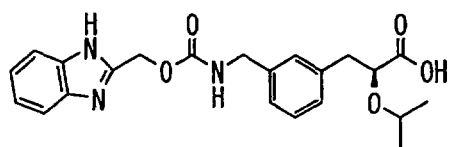
Example 350. 3-{3-[(6-Aminopyridin-3-
ylmethoxycarbonylamino)methyl]phenyl)-2(S)-
isopropoxypropanoic acid



3-{3-[(6-t-Butoxycarbonylamino)pyridin-3-ylmethoxycarbonylamino)methyl]phenyl)-2(S)-isopropoxypropanoic acid was dissolved in trifluoroacetic acid, and the mixture was concentrated. The residue was purified by reverse-phase high performance liquid chromatography, to give the title compound.

MS m/e (ESI) 510 (MNa^+)

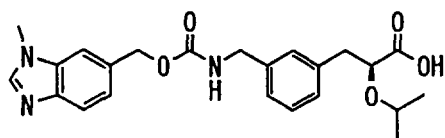
Example 351. 3-{3-[(1H-Benzoimidazol-2-
ylmethoxycarbonylamino)methyl]phenyl)-2(S)-
isopropoxypropanoic acid



Using (1H-benzotriazol-2-yl)methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 434 (MNa^+)

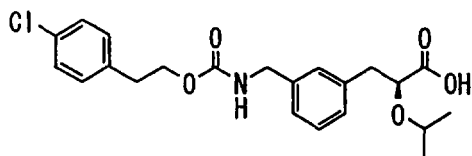
Example 352. 2(S)-Isopropoxy-3-{3-[(3-methyl-3H-benzotriazol-5-yl)methoxycarbonylamino)methyl]phenyl}-propanoic acid



Using (3-methyl-3H-benzotriazol-5-yl)methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 449 (MNa^+)

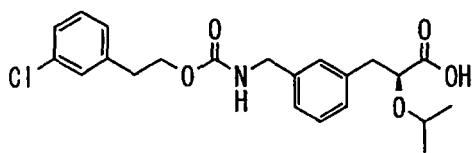
Example 353. 3-(3-{[2-(4-Chlorophenyl)ethoxycarbonylamino]-methyl}phenyl)-2(S)-isopropoxypropanoic acid



Using 4-chloro-2-phenethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 442 (MNa^+)

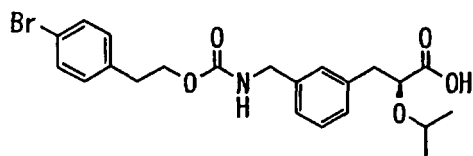
Example 354. 3-(3-{[2-(3-Chlorophenyl)ethoxycarbonylamino]-methyl}phenyl)-2(S)-isopropoxypropanoic acid



Using 3-chloro-2-phenethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 442 (MNa^+)

Example 355. 3-(3-([2-(4-Bromophenyl)ethoxycarbonylamino]methyl)phenyl)-2(S)-isopropoxypropanoic acid

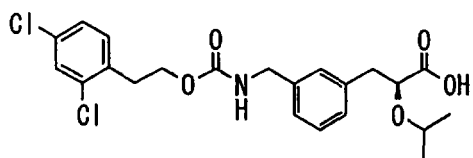


Using 4-bromo-2-phenethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 486 (MNa^+)

Example 356.

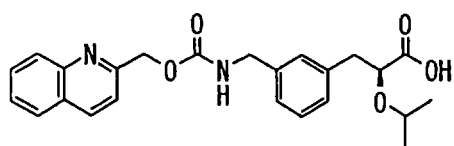
3-(3-([2-(2,4-Dichlorophenyl)ethoxycarbonylamino]methyl)phenyl)-2(S)-isopropoxypropanoic acid



Using 2,4-dichloro-2-phenethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 476 (MNa^+)

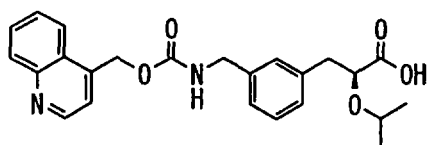
Example 357. 2(S)-Isopropoxy-3-{3-[(quinolin-2-ylmethoxycarbonylamino)methyl]phenyl}propanoic acid



Using quinolin-2-yl-methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 445 (MNa^+)

Example 358. 2(S)-Isopropoxy-3-{3-[(quinolin-4-ylmethoxycarbonylamino)methyl]phenyl}propanoic acid

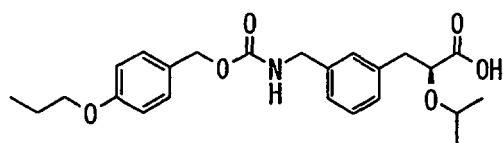


Using quinolin-4-yl-methanol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 445 (MNa^+)

Example 359.

2(S)-Isopropoxy-3-{3-[(4-propoxybenzyloxycarbonylamino)-methyl]phenyl}propanoic acid

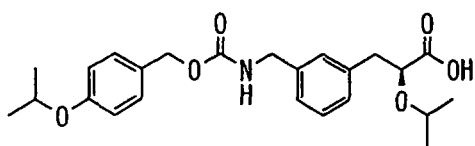


Using 4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 452 (MNa^+)

Example 360.

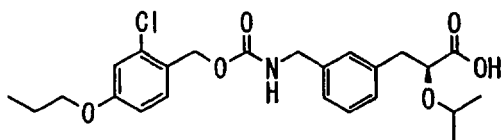
2(S)-Isopropoxy-3-{3-[(4-isopropoxybenzyloxycarbonylamino)-methyl]phenyl}propanoic acid



Using 4-isopropoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 452 (MNa^+)

Example 361. 2(S)-Isopropoxy-3-{3-[(2-chloro-4-propoxybenzyloxy)carbonylamino]methyl}phenyl}propanoic acid

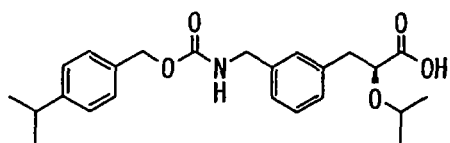


Using 2-chloro-4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 486 (MNa^+)

Example 362.

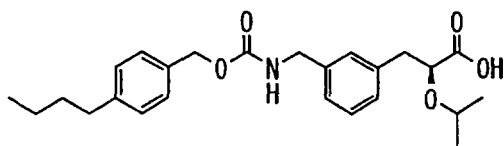
2(S)-Isopropoxy-3-{3-[(4-isopropylbenzyloxy)carbonylamino]methyl}phenyl}propanoic acid



Using 4-isopropylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 436 (MNa^+)

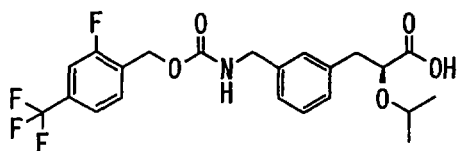
Example 363. 2(S)-Isopropoxy-3-{3-[(4-butylbenzyloxy)carbonylamino]methyl}phenyl}propanoic acid



Using 4-butylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 450 (MNa^+)

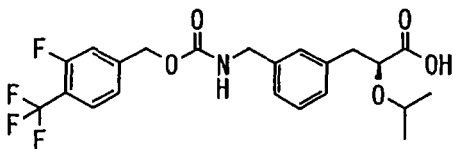
Example 364. 2(S)-Isopropoxy-3-{3-[(2-fluoro-4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid



Using 2-fluoro-4-trifluoromethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 480 (MNa^+)

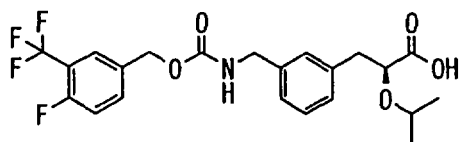
Example 365. 2(S)-Isopropoxy-3-{3-[(3-fluoro-4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid



Using 3-fluoro-4-trifluoromethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 480 (MNa^+)

Example 366. 2(S)-Isopropoxy-3-{3-[(4-fluoro-3-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid



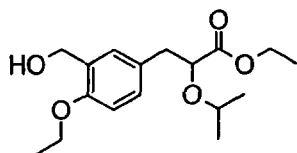
Using 4-fluoro-3-trifluoromethyl alcohol, the title compound was obtained in the same manner as described in Example 337b).

MS m/e (ESI) 480 (MNa^+)

MS m/e (ESI) 440 (MH^+)

Example 367. 3-[(4-Ethoxy-3-phenylcarbamoyloxymethyl)-phenyl]-2-isopropoxypropanoic acid

Production example 367a) Ethyl 3-[4-ethoxy-3-(hydroxymethyl)-phenyl]-2-isopropoxypropanoate



400 mg of sodium hydride was suspended in 10 ml of tetrahydrofuran, and 15 ml of a solution of 2.8 g of diethyl 2-isopropoxyphosphonoacetate in tetrahydrofuran was added under ice-cooling. The solution was stirred at room temperature for 30 minutes, and 25 ml of a solution of 2.4 g of 3-([1-(*t*-butyl)-1,1-dimethylsilyl]oxy)methyl)-4-ethoxybenzaldehyde in tetrahydrofuran was added. After stirring was continued overnight at room temperature, the

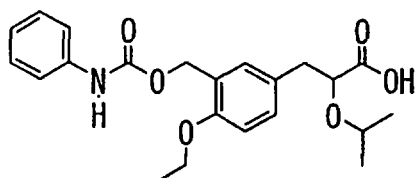
reaction solution was treated with 1N hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give ethyl (E,Z)-3-[3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)-4-ethoxyphenyl]-2-isopropoxy-2-propenoate in the 4:1 hexane-ethyl acetate fraction. Then, the obtained ethyl (E,Z)-3-[3-([1-(t-butyl)-1,1-dimethylsilyl]oxy)methyl)-4-ethoxyphenyl]-2-isopropoxy-2-propenoate was dissolved in 25 ml of tetrahydrofuran, and 10 ml of tetrabutyl ammonium fluoride (1M solution in tetrahydrofuran) was added thereto. After stirring was continued at room temperature for 7 hours, the reaction mixture was diluted with ethyl acetate. The organic layer was washed with water and saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. Then, the resulting crude product was dissolved in 25 ml of ethanol, and the mixture was treated with 0.40g of rhodium-alumina, and stirred overnight under hydrogen atmosphere. The catalyst was filtered off, the solvent was evaporated, and then the residue was purified by silica gel column chromatography, to give 0.96 g of the title compound in the 3:1 hexane-ethyl acetate fraction.

¹H-NMR (CDCl₃)

δ : 0.97 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.24 (t, J=7.2Hz, 3H) 1.43 (t, J=6.8Hz, 3H) 2.87 (dd, J=8.4, 14.0Hz, 1H) 2.94 (dd, J=5.2, 14.0Hz, 1H) 3.50 (sept, J=6.0Hz, 1H) 4.00 (dd, J=5.2, 8.4Hz, 1H) 4.07 (q, J=6.8Hz, 2H)

4.14-4.20 (m, 2H) 4.66 (s, 2H) 6.78 (d, J=8.0Hz, 1H) 7.13 (d, J=8.0Hz, 1H)
7.14 (s, 1H)

Production example 367b) 3-[(4-Ethoxy-3-phenylcarbomyloxymethyl)phenyl]-2-isopropoxypropanoic acid

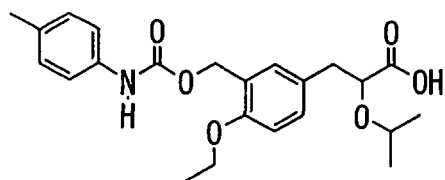


Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 402 (MH⁺)

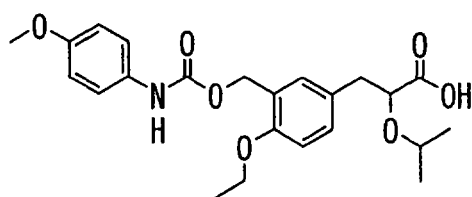
Example 368. 3-[(4-Ethoxy-3-*p*-tolylcarbomyloxymethyl)phenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 416 (MH⁺)

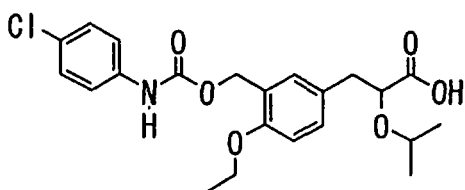
Example 369. 3-([4-Ethoxy-3-(4-methoxyphenyl)-carbamyloxymethyl]phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 432 (MH^+)

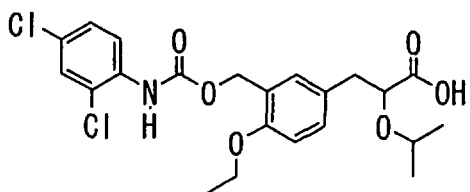
Example 370. 3-([3-(4-Chlorophenyl)carbamoyloxymethyl]-4-ethoxyphenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 436 (MH^+)

Example 371. 3-([3-(2,4-Dichlorophenyl)carbamoyloxymethyl]-4-ethoxyphenyl)-2-isopropoxypropanoic acid

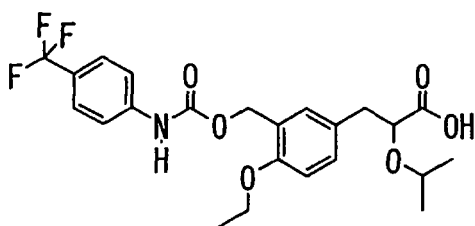


Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 470 (MH⁺)

Example 372. 3-([4-Ethoxy-3-[4-(trifluoromethyl)phenyl]-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid

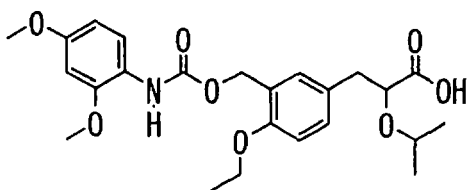


Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 470 (MH⁺)

Example 373. 3-([3-(2,4-Dimethoxyphenyl)carbamoyloxymethyl]-4-ethoxy]phenyl)-2-isopropoxypropanoic acid



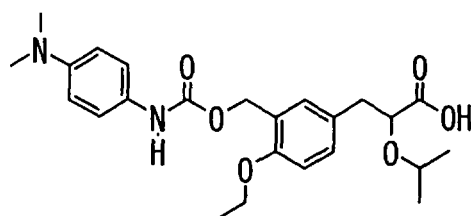
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dimethoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 462 (MH⁺)

Example 374.

3-{[3-(4-Dimethylaminophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid



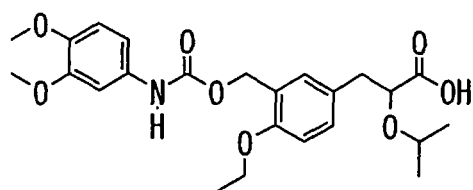
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-dimethylaminophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 445 (MH⁺)

Example 375.

3-{[3-(3,4-Dimethoxyphenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid

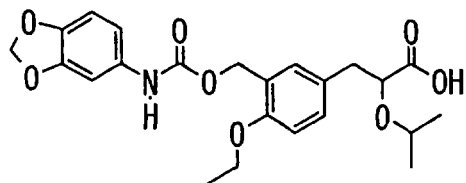


Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dimethoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 462 (MH⁺)

Example 376.

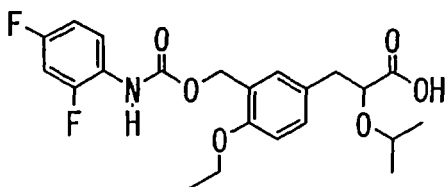
3-({3-[5-(Benzo[1,3]dioxolyl)]carbamoyloxymethyl-4-ethoxy}phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3,4-(methylenedioxy)phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 446 (MH⁺)

Example 377. 3-{{3-(2,4-Difluorophenyl)carbamoyloxymethyl-4-ethoxy}phenyl)-2-isopropoxypropanoic acid



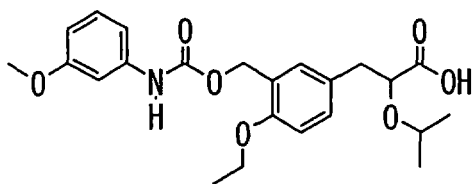
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 438 (MH⁺)

Example 378.

3-{{4-Ethoxy-3-(3-methoxyphenyl)carbamoyloxymethyl}phenyl)-2-isopropoxypropanoic acid

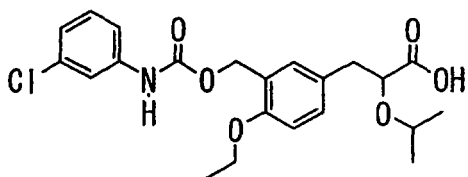


Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 432 (MH^+)

Example 379. 3-([3-(3-Chlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl)-2-isopropoxypropanoic acid



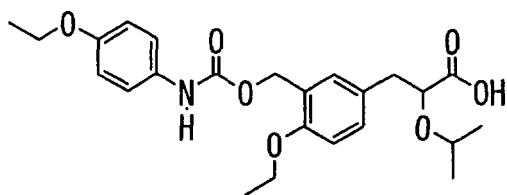
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 436 (MH^+)

Example 380.

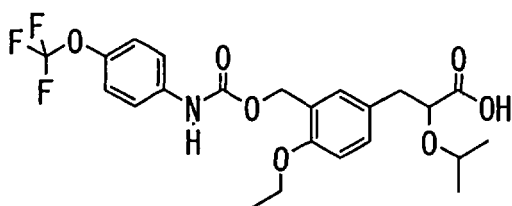
3-([4-Ethoxy-3-(4-ethoxyphenyl)carbamoyloxymethyl]-phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-ethoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 446 (MH^+)

Example 381. 3-([4-Ethoxy-3-[4-(trifluoromethoxy)phenyl]-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid

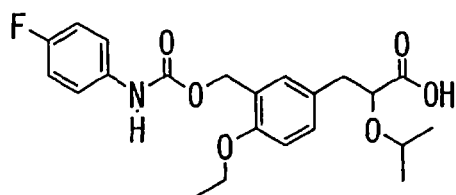


Using ethyl 3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-(trifluoromethoxy)phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 486 (MH^+)

Example 382.

3-([4-Ethoxy-3-(4-fluorophenyl)carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid



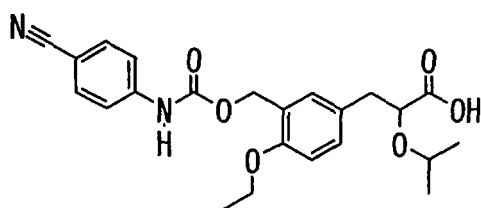
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-fluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 420 (MH^+)

Example 383.

3-([3-(4-Cyanophenyl) carbamoyloxymethyl-4-ethoxy]phenyl)-2-isopropoxypropanoic acid

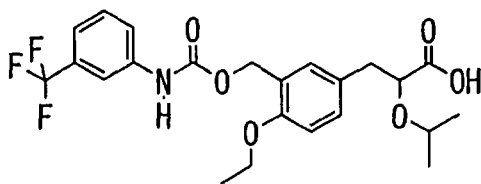


Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-cyanophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 427 (MH^+)

Example 384. 3-([4-Ethoxy-3-[3-(trifluoromethyl)phenyl]-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid



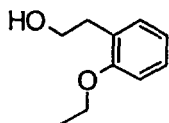
Using ethyl

3-[4-ethoxy-3-(hydroxymethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 470 (MH^+)

Example 385. 3-{4-Ethoxy-3-[2-(phenylcarbamoyloxy)-ethyl]phenyl}-2-isopropoxypropanoic acid

Production example 385a) 2-(2-Ethoxyphenyl)ethanol



4.4 g of 2-hydroxyphenethyl alcohol was dissolved in 80 ml of N,N-dimethylformamide, and 15.3 g of ethyl iodide and 4.7 g of potassium carbonate were added. After stirring was continued at 70°C overnight, the solution was diluted with ethyl acetate, and washed successively with water and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 3.2 g of the title compound in the 4:1 hexane-ethyl acetate fraction.

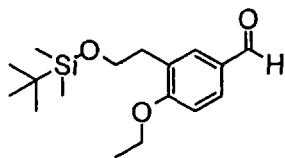
^1H -NMR ($CDCl_3$)

δ : 1.43 (t, $J=6.8$ Hz, 3H) 2.92 (t, $J=6.0$ Hz, 2H) 3.85 (br, 2H) 4.05 (q,

J=6.8Hz, 2H) 6.85-6.91 (m, 2H) 7.15-7.22 (m, 1H)

Production example 385b)

3-[2-(t-Butyldimethylsilyloxy)ethyl]-4-ethoxybenzaldehyde

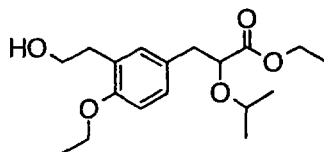


Using 2-(2-ethoxyphenyl)ethanol, the title compound was obtained in the same manner as described in Production example 117a) followed by Production example 117b).

¹H-NMR(CDCl₃)

δ : 0.00 (s, 6H) 0.88 (s, 9H) 1.48 (t, J=6.8Hz, 3H) 2.92 (t, J=7.2Hz, 2H) 3.83 (t, J=7.2Hz, 2H) 4.15 (q, J=6.8Hz, 2H) 6.94 (d, J=8.4Hz, 1H) 7.72 (s, 1H) 7.75 (d, J=8.4Hz, 1H) 9.87 (s, 1H)

Production example 385c) Ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate



Using 3-[2-(t-butyldimethylsilyloxy)ethyl]-4-ethoxybenzaldehyde and triethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 147b).

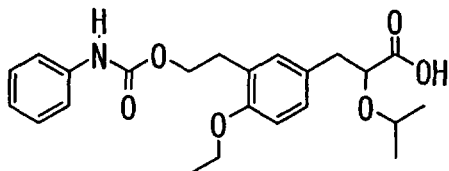
¹H-NMR(CDCl₃)

δ : 0.97 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.24 (t, J=7.2Hz, 3H) 1.41 (t, J=6.8Hz, 3H) 2.86 (dd, J=8.4, 14.0Hz, 1H) 2.88 (t, J=6.4Hz, 2H) 2.92 (dd, J=5.2, 14.0Hz, 1H) 3.50 (sept, J=6.0Hz, 1H) 3.82 (t, J=6.4Hz, 2H)

3.99-4.05 (m, 3H) 4.14-4.20 (m, 2H) 6.76 (d, J=8.4Hz, 1H) 7.04-7.07 (m, 2H)

Production example 385d)

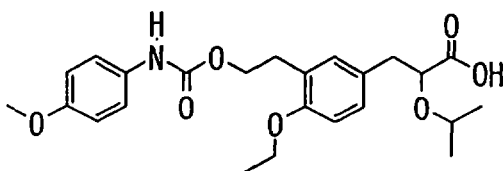
3-{4-Ethoxy-3-[2-(phenylcarbamoyloxy)ethyl]phenyl}-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 416 (MH⁺)

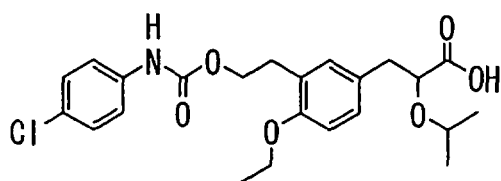
Example 386. 3-(4-Ethoxy-3-{2-[(4-methoxyphenyl)-carbamoyloxy]ethyl}phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 446 (MH⁺)

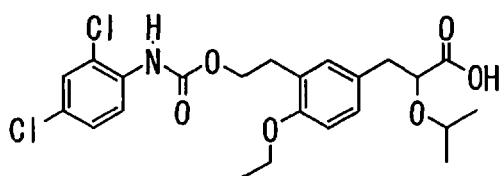
Example 387. 3-(3-{2-[(4-Chlorophenyl)carbamoyloxy]ethyl}-4-ethoxyphenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 450 (MH^+)

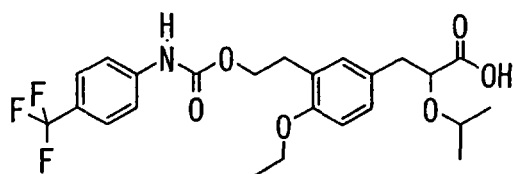
Example 388. 3-(3-{2-[(2,4-Dichlorophenyl)carbamoyloxy]-ethyl}-4-ethoxyphenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxy propanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 484 (MH^+)

Example 389. 3-[4-Ethoxy-3-(2-{[4-(trifluoromethyl)phenyl]-carbamoyloxy}ethyl)phenyl]-2-isopropoxypropanoic acid

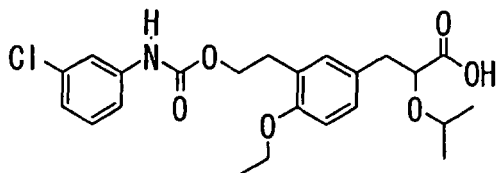


Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxy propanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described

in Example 148.

MS m/e (ESI) 484 (MH^+)

Example 390. 3-(3-{2-[(3-Chlorophenyl)carbamoyloxy]ethyl}-4-ethoxyphenyl)-2-isopropoxypropanoic acid



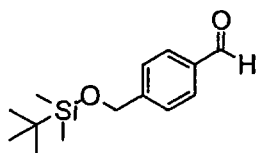
Using ethyl 3-[4-ethoxy-3-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 450 (MH^+)

Example 391. 2-Isopropoxy-3-[(4-phenylcarbamoyloxymethyl)-phenyl]propanoic acid

Production example 391a)

4-(t-Butyldimethylsilyloxymethyl)benzaldehyde



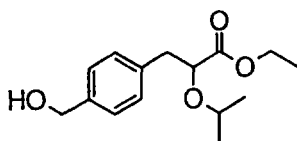
Using 4-bromobenzyl alcohol, the title compound was obtained in the same manner as described in Production example 147a).

^1H -NMR ($CDCl_3$)

δ : 0.12 (s, 6H) 0.96 (s, 9H) 4.82 (s, 2H) 7.49 (d, $J=8.0$ Hz, 2H) 7.85 (d, $J=8.0$ Hz, 2H) 9.88 (s, 1H)

Production example 391b) Ethyl 3-[(4-hydroxymethyl)phenyl]-2-

isopropoxypropanoate

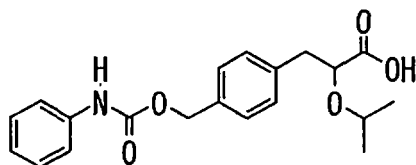


Using 4-(t-butyltrimethylsilyloxymethyl)benzaldehyde and triethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 147b).

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

δ : 0.95 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 1.24 (t, $J=7.2\text{Hz}$, 3H) 2.94 (dd, $J=8.4$, 14.0Hz , 1H) 3.01 (dd, $J=4.8$, 14.0Hz , 1H) 3.50 (sept, $J=6.0\text{Hz}$, 1H) 4.05 (dd, $J=4.8$, 8.4Hz , 1H) 4.15-4.23 (m, 2H) 4.67 (s, 2H) 7.25 (d, $J=8.0\text{Hz}$, 2H) 7.28 (d, $J=8.0\text{Hz}$, 2H)

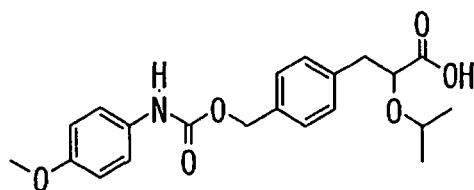
Production example 391c) 2-Isopropoxy-3-[(4-phenylcarbamoyloxymethyl)phenyl]propanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 358 (MH^+)

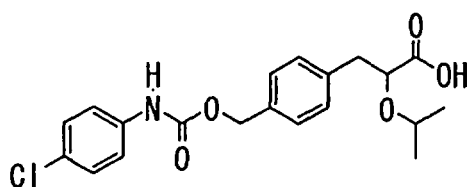
Example 392. 2-Isopropoxy-3-[[4-(4-methoxyphenyl)carbamoyloxymethyl]phenyl]propanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 388 (MH^+)

Example 393. 3-[[4-(4-Chlorophenyl)carbamoyloxymethyl]-phenyl]-2-isopropoxypropanoic acid

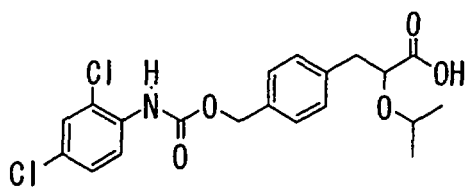


Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 392 (MH^+)

Example 394.

3-[[4-(2,4-Dichlorophenyl)carbamoyloxymethyl]phenyl]-2-isopropoxypropanoic acid

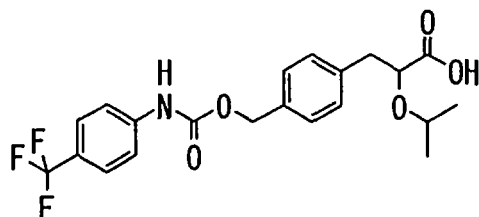


Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dichlorophenylisocyanate, the

stitle compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 426 (MH⁺)

Example 395. 2-Isopropoxy-3-({4-[4-(trifluoromethyl)-phenyl]carbamoyloxymethyl}phenyl)propanoic acid

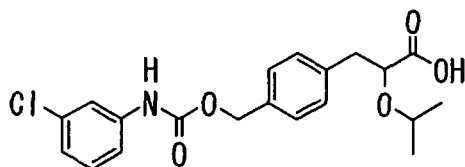


Using ethyl

3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 426 (MH⁺)

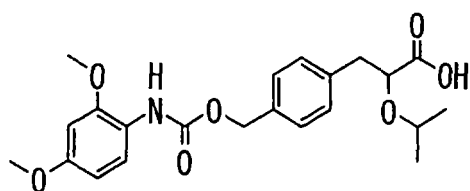
Example 396. 3-([4-(3-Chlorophenyl)carbamoyloxymethyl]-phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 392 (MH⁺)

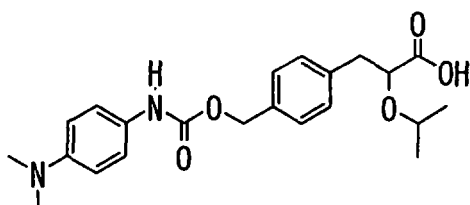
Example 397. 3-([4-(2,4-Dimethoxyphenyl)-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-dimethoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 418 (MH⁺)

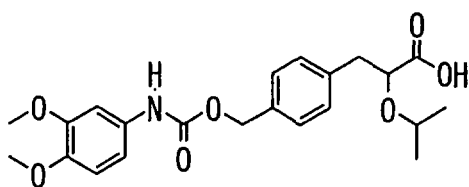
Example 398. 3-[[4-(4-Dimethylaminophenyl)-carbamoyloxymethyl]phenyl]-2-isopropoxypropanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-dimethylaminophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 401 (MH⁺)

Example 399. 3-[[4-(3,4-Dimethoxyphenyl)-carbamoyloxymethyl]phenyl]-2-isopropoxypropanoic acid

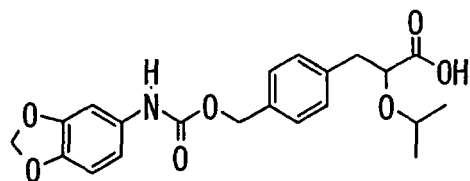


Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3,4-dimethoxyphenylisocyanate, the

title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 418 (MH^+)

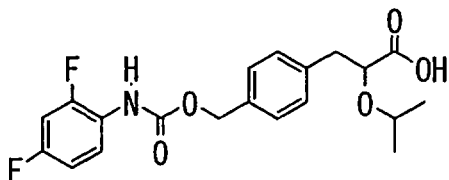
Example 400. 3-([4-[5-(Benzo[1,3]dioxolyl)]-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-([4-(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3,4-(methylenedioxy)phenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 402 (MH^+)

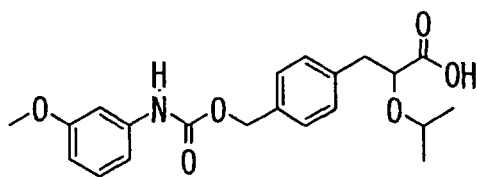
Example 401. 3-([4-(2,4-Difluorophenyl)carbamoyloxymethyl]-phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-([4-(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 394 (MH^+)

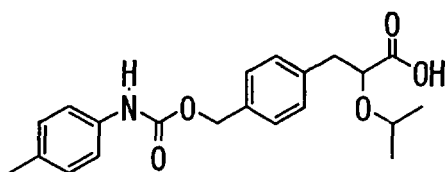
Example 402. 2-Isopropoxy-3-([4-(3-methoxyphenyl)-carbamoyloxymethyl]phenyl)propanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 3-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 388 (MH⁺)

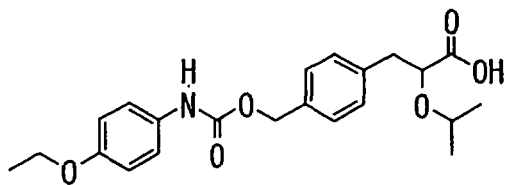
Example 403. 2-Isopropoxy-3-[(4-*p*-tolylcarbamoyloxymethyl)phenyl]propanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and *p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

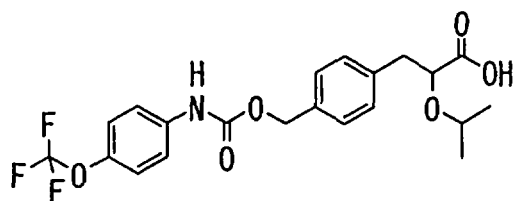
MS *m/e* (ESI) 372 (MH⁺)

Example 404. 3-[[4-(4-Ethoxyphenyl)carbamoyloxymethyl]-phenyl]-2-isopropoxypropanoic acid

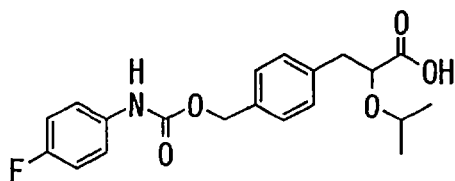


Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-ethoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

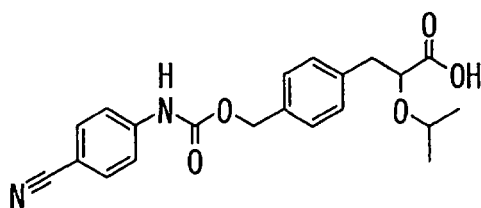
Example 405. 2-Isopropoxy-3-({4-[4-(trifluoromethoxy)-
phenyl]carbamoyloxymethyl}phenyl)propanoic acid

MS m/e (ESI) 442 (MH^+)

Example 406. 3-([4-(4-Fluorophenyl)carbamoyloxymethyl]-
phenyl)-2-isopropoxypropanoic acid

MS m/e (ESI) 376 (MH^+)

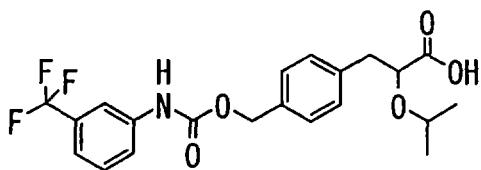
Example 407. 3-{[4-(4-Cyanophenyl)carbamoyloxymethyl]-
phenyl}-2-isopropoxypropanoic acid



Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and 4-cyanophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 383 (MH⁺)

Example 408. 2-Isopropoxy-3-({4-[3-(trifluoromethyl)-phenyl]carbamoyloxymethyl}phenyl)propanoic acid



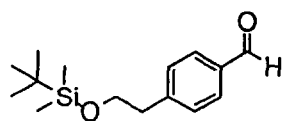
Using ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*m*-tolyl isocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 426 (MH⁺)

Example 409. 2-Isopropoxy-3-{4-[2-(phenylcarbamoyloxy)-ethyl]phenyl}propanoic acid

Production example 409a)

4-[2-(*t*-Butyldimethylsilyloxy)ethyl]benzaldehyde



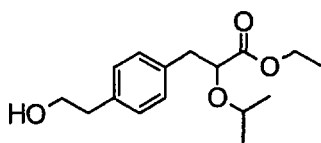
Using 4-bromophenethyl alcohol, the title compound was

obtained in the same manner as described in Production example 147a).

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 0.00 (s, 6H) 0.89 (s, 9H) 2.94 (t, $J=6.8\text{Hz}$, 2H) 3.89 (t, $J=6.8\text{Hz}$, 2H) 7.42 (d, $J=8.0\text{Hz}$, 2H) 7.85 (d, $J=8.0\text{Hz}$, 2H) 9.88 (s, 1H)

Production example 409b) Ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate

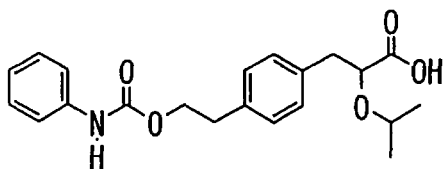


Using 4-[2-(*t*-butyldimethylsilyloxy)ethyl]benzaldehyde and triethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 147b).

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 0.96 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.0\text{Hz}$, 3H) 1.23 (t, $J=7.2\text{Hz}$, 3H) 2.84 (t, $J=6.4\text{Hz}$, 2H) 2.92 (dd, $J=8.4, 14.0\text{Hz}$, 1H) 2.98 (dd, $J=5.2, 14.0\text{Hz}$, 1H) 3.51 (sept, $J=6.0\text{Hz}$, 1H) 3.84 (t, $J=6.4\text{Hz}$, 2H) 4.04 (dd, $J=5.2, 8.4\text{Hz}$, 1H) 4.12-4.20 (m, 2H) 7.14 (d, $J=8.0\text{Hz}$, 2H) 7.20 (d, $J=8.0\text{Hz}$, 2H)

Production example 409c) 2-Isopropoxy-3-{4-[2-(phenylcarbamoyloxy)ethyl]phenyl}propanoic acid

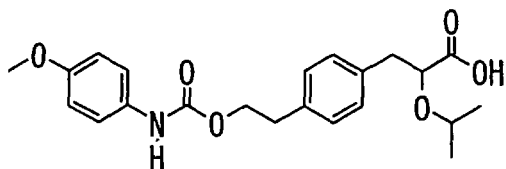


Using ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and phenylisocyanate, the title compound

was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 372 (MH⁺)

Example 410. 2-Isopropoxy-3-(4-{2-[(4-methoxyphenyl)carbamoyloxy]ethyl}phenyl)propanoic acid

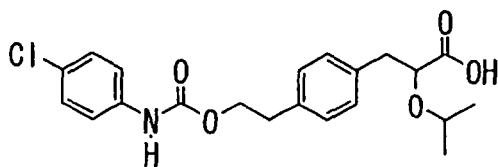


Using ethyl

3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 402 (MH⁺)

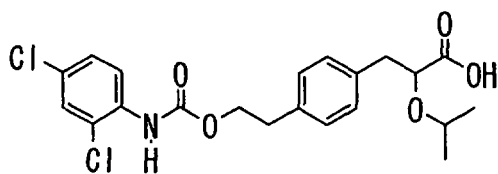
Example 411. 3-(4-{2-[(4-Chlorophenyl)carbamoyloxy]-ethyl}phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS *m/e* (ESI) 406 (MH⁺)

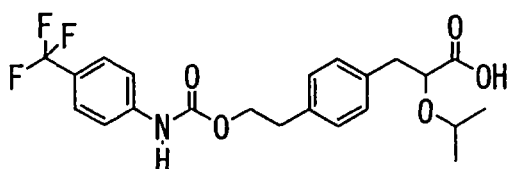
Example 412. 3-(4-{2-[(2,4-Dichlorophenyl)carbamoyloxy]-ethyl}phenyl)-2-isopropoxypropanoic acid



Using ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 440 (MH^+)

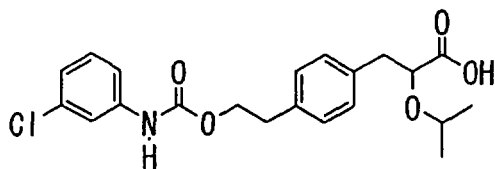
Example 413. 2-Isopropoxy-3-[4-(2-([4-(trifluoromethyl)phenyl]carbamoyloxy)ethyl)phenyl]propanoic acid



Using ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and α,α,α -trifluoro-*p*-tolylisocyanate, the title compound was obtained in the same manner as described in Example 148.

MS m/e (ESI) 440 (MH^+)

Example 414. 3-(4-{2-[(3-Chlorophenyl)carbamoyloxy]ethyl}phenyl)-2-isopropoxypropanoic acid



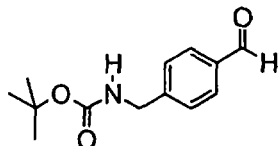
Using ethyl 3-[4-(2-hydroxyethyl)phenyl]-2-isopropoxypropanoate and 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example

148.

MS m/e (ESI) 406 (MH^+)

Example 415. 3-{4-[[[(4-Chlorobenzyl)oxy]carbonyl]amino]-methyl}phenyl}-2-isopropoxypropanoic acid

Production example 415a) t-Butyl N-(4-formylbenzyl)carbamate

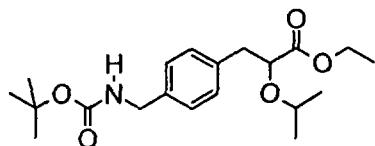


Using 4-bromobenzylaminehydrochloride, the title compound was obtained in the same manner as described in Production example 138a) followed by Production example 138b).

^1H -NMR ($CDCl_3$)

δ : 1.47 (s, 9H) 4.40 (d, $J=6.0$ Hz, 2H) 4.95 (br, 1H) 7.45 (d, $J=8.0$ Hz, 2H) 7.85 (d, $J=8.0$ Hz, 2H) 10.00 (s, 1H)

Production example 415b) Ethyl 3-(4-[(t-butoxycarbonyl)-amino]methyl}phenyl)-2-isopropoxypropanoate



Using t-butyl N-(4-formylbenzyl)carbamate and triethyl 2-isopropoxyphosphonoacetate, the title compound was obtained in the same manner as described in Production example 46a) followed by Production example 46b).

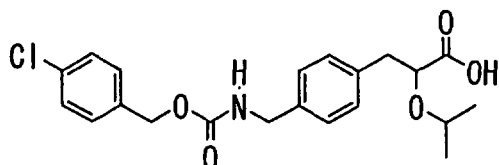
^1H -NMR ($CDCl_3$)

δ : 0.95 (d, $J=6.0$ Hz, 3H) 1.15 (d, $J=6.0$ Hz, 3H) 1.24 (t, $J=7.2$ Hz, 3H) 1.46 (s, 9H) 2.92 (dd, $J=8.4, 14.0$ Hz, 1H) 2.99 (dd, $J=4.8, 14.0$ Hz, 1H) 3.50

(sept, J=6.0Hz, 1H) 4.03 (dd, J=4.8, 8.4Hz, 1H) 4.15-4.20 (m, 2H) 4.28 (d, J=6.0Hz, 2H) 4.80 (br, 1H) 7.17-7.18 (m, 4H)

Example 415c)

3-{4-[[[(4-Chlorobenzyl)oxy]carbonyl]amino)methyl]phenyl}-
2-isopropoxypropanoic acid

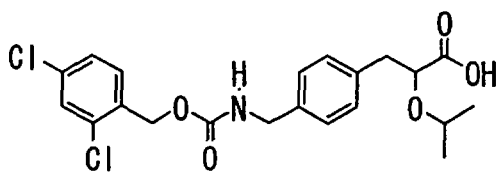


1.6 g of Ethyl 3-(4-[(t-butoxycarbonyl)amino]methyl)-phenyl)-2-isopropoxypropanoate was dissolved in 10 ml of 4N hydrogen chloride-dioxane solution. After stirring was continued at room temperature for 1 hour, the solution was concentrated, to give 1.4 g of ethyl 3-[4-(ammoniomethyl)-phenyl]-2-isopropoxypropanoate chloride. Next, 25 mg of the obtained ethyl 3-[4-(ammoniomethyl)phenyl]-2-isopropoxypropanoate chloride was dissolved in 0.8 ml of N,N-dimethylformamide which was saturated with carbon dioxide by adding dry ice, and 65 mg of cesium carbonate and 74 mg tetrabutylammoniumiodidewereadded, andthemixturewas stirred at room temperature for 30 minutes. Then 41 mg of 4-chlorobenzyl bromide was added thereto, and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with ethyl acetate and washed with water. The solvent was concentrated, and the residue was treated with 1.0 ml of ethanol and 0.2 ml of 5N sodium hydroxide, and the mixture was stirred at room temperature for 3 hours. Then the solution was neutralized with

2N hydrochloric acid, extracted with ethyl acetate, and the solvent was removed. The residue was purified by reverse-phase high performance liquid chromatography, to give 9.27 mg of the title compound.

MS m/e (ESI) 406 (MH^+)

Example 416. 3-[4-[[[(2,4-Dichlorobenzyl)oxy]carbonyl]-amino)methyl]phenyl]-2-isopropoxypropanoic acid

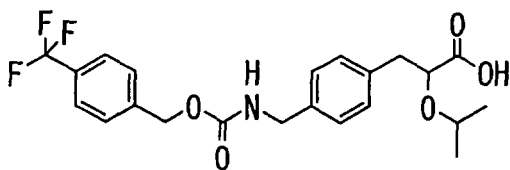


Using ethyl

3-[4-(ammoniomethyl)phenyl]-2-isopropoxypropanoate chloride and 2,4-dichlorobenzyl bromide, the title compound was obtained in the same manner as described in Production example 415c).

MS m/e (ESI) 440 (MH^+)

Example 417. 2-Isopropoxy-3-(4-[[[(4-trifluoromethyl)-benzyl]oxy]carbonyl]amino)methyl]phenyl)propanoic acid

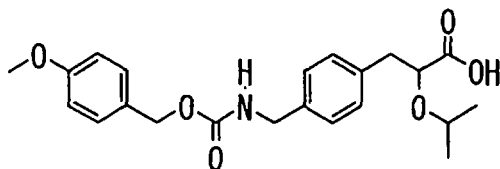


Using ethyl

3-[4-(ammoniomethyl)phenyl]-2-isopropoxypropanoate chloride and 4-(trifluoromethyl)benzyl bromide, the title compound was obtained in the same manner as described in Production example 415c).

MS m/e (ESI) 440 (MH^+)

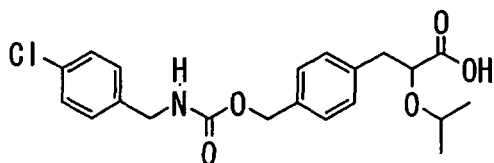
Example 418. 2-Isopropoxy-3-{4-[[[(4-methoxybenzyl)-oxy]carbonyl]amino)methyl]phenyl}propanoic acid



Using ethyl 3-[4-(ammoniomethyl)phenyl]-2-isopropoxypropanoate chloride and 4-methoxybenzyl chloride, the title compound was obtained in the same manner as described in Production example 415c).

MS *m/e* (ESI) 402 (MH⁺)

Example 419. 3-{4-[[[(4-Chlorobenzyl) carbamoyloxy]-carbonyl]amino)methyl]phenyl}-2-isopropoxypropanoic acid



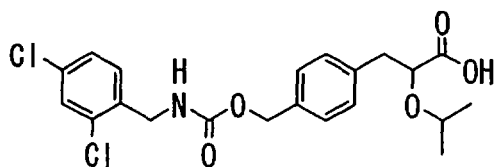
0.60g of Ethyl 3-[(4-hydroxymethyl)phenyl]-2-isopropoxypropanoate was dissolved in 5 ml of dimethoxyethane, and 0.17 ml of phosphorous tribromide was added under ice-cooling. The solution was stirred at 0°C for 1 hour, was diluted with ether, and successively washed with water and saturated brine. After drying the organic layer over anhydrous magnesium sulfate, the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 0.51 g of ethyl 3-[(4-bromomethyl)phenyl]-2-isopropoxypropanoate from the 4:1 hexane-ethyl acetate fraction. Next 11 mg of 4-chlorobenzylamine was dissolved in 0.5 ml of

N,N-dimethylformamide pre-saturated with carbon dioxide by adding dry ice, 33 mg of cesium carbonate and 37 mg of tetrabutylammonium iodide were added, and the mixture was stirred at room temperature for 30 minutes. 25 mg of the previously obtained ethyl 3-[(4-bromomethyl)phenyl]-2-isopropoxypropanoate was added and the mixture was stirred at room temperature for 4 hours. The reaction mixture was diluted with ethyl acetate and washed with water. The solvent was concentrated, and the residue was treated with 1.0 ml of ethanol and 0.2 ml of 5N-sodium hydroxide, and the mixture was stirred at room temperature for 3 hours. The solution was neutralized with 2N hydrochloric acid, then extracted with ethyl acetate. The solvent was removed, and the residue was purified by reverse-phase high performance liquid chromatography, to give 4.08 mg of the title compound.

MS m/e (ESI) 406 (MH^+)

Example 420.

3-{4-[(2,4-Dichlorobenzyl) carbamoyloxy] carbonyl}-amino)methyl]phenyl}-2-isopropoxypropanoic acid

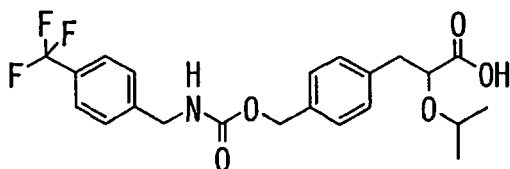


Using ethyl 3-[(4-bromomethyl)phenyl]-2-isopropoxypropanoate and 2,4-dichlorobenzylamine, the title compound was obtained in the same manner as described in Example 419.

MS m/e (ESI) 440 (MH^+)

Example 421.

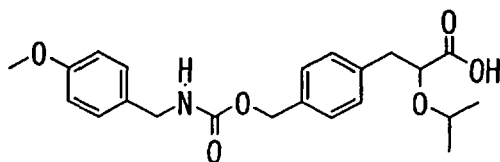
2-Isopropoxy-3-(4-([[(4-trifluoromethyl)benzyl]-
carbamoyloxy]carbonyl)amino)methyl]phenyl)propanoic acid



Using ethyl 3-[(4-bromomethyl)phenyl]-2-isopropoxypropanoate and 4-trifluoromethyl)benzylamine, the title compound was obtained in the same manner as described in Example 419.

MS m/e (ESI) 440 (MH^+)

Example 422. 2-Isopropoxy-3-{4-([[(4-methoxybenzyl)-
carbamoyloxy]carbonyl)amino)methyl]phenyl)propanoic acid

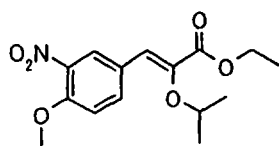


Using ethyl 3-[(4-bromomethyl)phenyl]-2-isopropoxypropanoate and 4-methoxybenzylamine, the title compound was obtained in the same manner as described in Example 419.

MS m/e (ESI) 402 (MH^+)

Example 423.

a) Ethyl 2-isopropoxy-3-(4-methoxy-3-nitrophenyl)-2-
propanoate

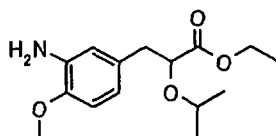


1.5 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 10 ml of tetrahydrofuran, and 0.22 g of 60% sodium hydride was added under ice-cooling. After stirring the reaction solution under ice-cooling for 20 minutes, 0.88 g of 4-methoxy-3-nitrobenzaldehyde was added and the mixture was stirred at room temperature for 2 hours. The reaction mixture was added with aqueous ammonium chloride, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was subjected to silica gel column chromatography, to give 0.85 g of the title compound from the 9:1 hexane-ethyl acetate fraction.

¹H-NMR (CDCl₃)

δ : 1.17+1.37 (t, J=6.0Hz, 3H) 1.27+1.31 (d, J=6.0Hz, 6H) 3.94+3.98 (s, 3H)
4.17+4.28 (q, J=6.0Hz, 2H) 6.10+6.88 (s, 1H) 7.00+7.06 (d, J=8.0Hz, 1H)
7.40+7.91 (dd, J=8.0, 2.0Hz, 1H) 7.75+8.37 (d, J=2.0Hz, 1H)

b) Ethyl 3-(3-amino-4-methoxyphenyl)-2-isopropoxypropanoate



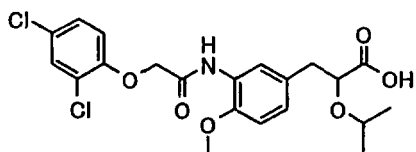
0.85 g of Ethyl 2-isopropoxy-3-(4-methoxy-3-nitrophenyl)-2-propanoate was dissolved in 15 ml of ethanol, 0.3 g of 10% palladium carbon was added, and the mixture was stirred for 4

hours under hydrogen atmosphere. The catalyst was filtered off, the solvent was evaporated, and then the residue was subjected to silica gel column chromatography, to give 0.72 g of the title compound from the 6:1 hexane-ethyl acetate fraction.

¹H-NMR (CDCl₃)

δ : 1.00 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.24 (t, J=6.0Hz, 3H)
2.83 (m, 2H) 3.50 (dq, J=6.4, 6.4Hz, 1H) 3.81 (s, 3H) 4.00 (dd, J=8.4, 4.8Hz, 1H) 4.17 (q, J=6.0Hz, 2H) 6.60 (dd, J=8.0, 2.0Hz, 1H) 6.67 (d, J=2.0Hz, 1H) 6.70 (d, J=8.0Hz, 1H)

c) 3-{3-[2-(2,4-Dichlorophenoxy)acetyl amino]-4-methoxyphenyl}-2-isopropoxypropanoic acid



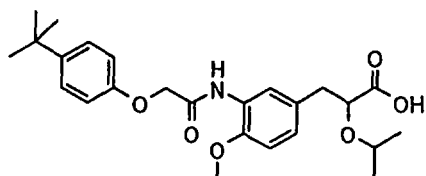
30 mg of Ethyl 3-(3-amino-4-methoxyphenyl)-2-isopropoxypropanoate and 20 mg of 2,4-dichlorophenoxyacetic acid were dissolved in 0.5 ml of tetrahydrofuran, and 30 mg of carbonyldiimidazole and 0.05 ml of triethylamine were added, and the mixture was stirred at 50°C for 4 hours. The reaction mixture was then partitioned between water and ethyl acetate, and the organic layer was concentrated. The residue was dissolved in 0.6 ml of ethanol, and 0.12 ml of 5N sodium hydroxide was added, and the mixture was stirred at room temperature for 1 hour. The reaction solution was neutralized with dilute hydrochloric acid, and extracted with ethyl acetate. The organic layer was concentrated, and the residue was purified

by HPLC using a reverse-phase column and a water-acetonitrile-trifluoroacetic acid elution solvent, to give 3.4 mg of the title compound.

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

δ : 1.02(d, $J=6.0\text{Hz}$, 3H) 1.11(d, $J=6.0\text{Hz}$, 3H) 2.86(dd, $J=14.0$, 6.0Hz, 1H) 3.05(dd, $J=14.0$, 4.4Hz, 1H) 3.53(dq, $J=6.0$, 6.0Hz, 1H) 3.81(s, 3H) 4.09(dd, $J=7.6$, 4.4Hz, 1H) 4.55(s, 2H) 6.75(d, $J=8.0\text{Hz}$, 1H) 6.81(d, $J=8.0\text{Hz}$, 1H) 6.90(dd, $J=8.0$, 2.0Hz, 1H) 7.18(m, 1H) 7.38(d, $J=2.0\text{Hz}$, 2H) 8.24(d, $J=2.0\text{Hz}$, 1H) 9.19(s, 1H)

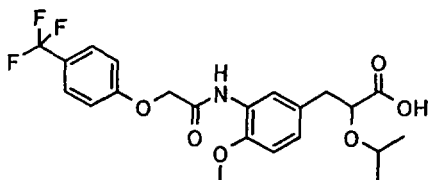
Example 424. 3-{3-[2-(4-t-Butylphenoxy)acetylamino]-4-methoxyphenyl}-2-isopropoxypropanoic acid



Using 4-t-butylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 444 (MH^+)

Example 425. 2-Isopropoxy-3-{4-methoxy-3-[2-(4-trifluoromethylphenoxy)acetylamino]phenyl}propanoic acid



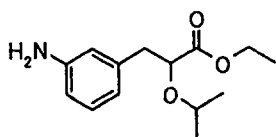
Using 4-trifluoromethylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example

423c).

MS m/e (ESI) 478 (MNa⁺)

Example 426.

a) Ethyl-3-(3-aminophenyl)-2-isopropoxypropanoate

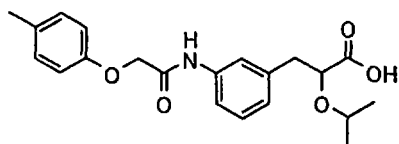


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

¹H-NMR(CDCl₃)

δ : 0.97(d, J=6.0Hz, 3H) 1.15(d, J=6.0Hz, 3H) 1.24(t, J=6.0Hz, 3H)
2.86(m, 2H) 3.50(dq, J=6.4, 6.4Hz, 1H) 4.03(dd, J=8.4, 4.8Hz, 1H)
4.17(q, J=6.0Hz, 2H) 6.55(dd, J=8.0, 2.0Hz, 1H) 6.59(d, J=2.0Hz, 1H)
6.65(d, J=8.0Hz, 1H) 7.06(t, J=8.0Hz, 1H)

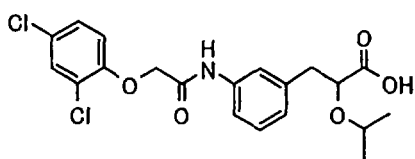
b) 2-Isopropoxy-3-[3-(2-p-tolyloxyacetylamino)phenyl]-propanoic acid



Using 4-methylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 372 (MH⁺)

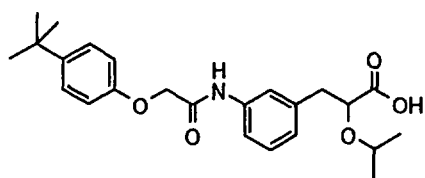
Example 427. 3-{3-[2-(2,4-Dichlorophenoxy)acetylamino]-phenyl}-2-isopropoxypropanoic acid



Using 2,4-dichlorophenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 426 (MH^+)

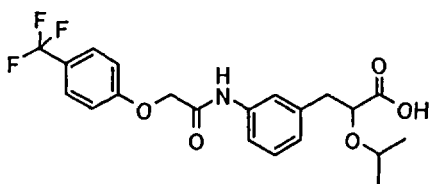
Example 428. 3-{3-[2-(4-t-Butylphenoxy)acetylamino]-phenyl}-2-isopropoxypropanoic acid



Using 4-*t*-butylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 436 (MNa^+)

Example 429. 2-Isopropoxy-3-{3-[2-(4-trifluoromethylphenoxy)acetylamino]phenyl}propanoic acid

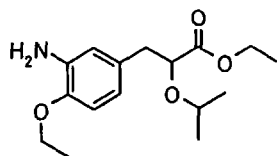


Using 4-trifluoromethylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 448 (MNa^+)

Example 430.

a) Ethyl-3-(3-amino-4-ethoxyphenyl)-2-isopropoxypropanoate

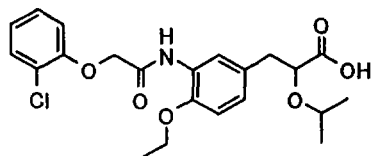


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

¹H-NMR(CDCl₃)

δ : 0.98(d, J=6.0Hz, 3H) 1.14(d, J=6.0Hz, 3H) 1.24(t, J=6.0Hz, 3H)
1.40(t, J=6.0Hz, 3H) 2.83(m, 2H) 3.50(dq, J=6.4, 6.4Hz, 1H) 4.00(m, 3H)
4.17(q, J=6.0Hz, 2H) 6.55(dd, J=8.0, 2.0Hz, 1H) 6.62(d, J=2.0Hz, 1H)
6.67(d, J=8.0Hz, 1H)

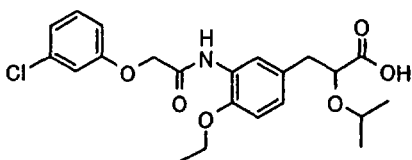
b) 3-{3-[2-(2-Chlorophenoxy)acetylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid



Using 2-chlorophenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS *m/e*(ESI) 436 (MH⁺)

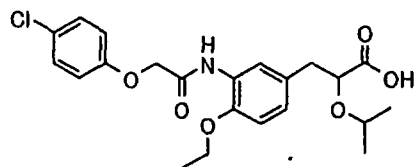
Example 431. 3-{3-[2-(3-Chlorophenoxy)acetylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid



Using 3-chlorophenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 436 (MH^+)

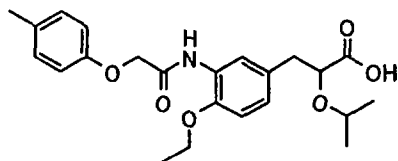
Example 432. 3-{3-[2-(4-Chlorophenoxy)acetylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid



Using 4-chlorophenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 436 (MH^+)

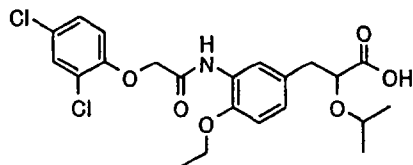
Example 433. 3-[4-Ethoxy-3-(2-p-tolyloxyacetylamino)-phenyl]-2-isopropoxypropanoic acid



Using 4-methylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 416 (MH^+)

Example 434. 3-{3-[2-(2,4-Dichlorophenoxy)acetylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

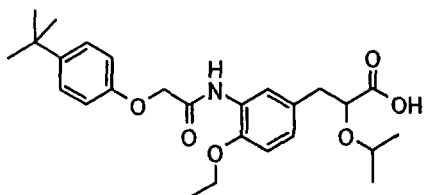


Using 2,4-dichlorophenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 470 (MH^+)

Example 435. 3-{3-[2-(4-t-Butylphenoxy)acetylamino]-4-

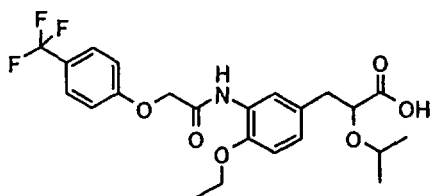
ethoxyphenyl}-2-isopropoxypropanoic acid



Using 4-*t*-butylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS *m/e*(ESI) 458 (MH⁺)

Example 436. 3-{4-Ethoxy-3-[2-(4-trifluoromethylphenoxy)]-acetamino]phenyl}-2-isopropoxypropanoic acid

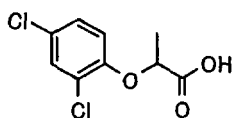


Using 4-trifluoromethylphenoxyacetic acid, the title compound was obtained in the same manner as described in Example 423c).

MS *m/e*(ESI) 492 (MNa⁺)

Example 437.

a) 2-(2,4-Dichlorophenoxy)propanoic acid



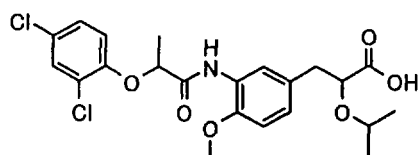
1 g of 2,4-Dichlorophenol was dissolved in 15 ml of N,N-dimethylformamide, and 0.27 g of 60% sodium hydride was added thereto under ice-cooling, and the mixture was stirred at room temperature for 30 minutes. 1.1 ml of Ethyl α -bromopropionate

was added to the mixture, and stirring was continued at room temperature for another 1 hour. To the reaction solution was added aqueous ammonium chloride, and the mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and then the solvent was evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluted with 50:1 n-hexane:ethyl acetate was evaporated and the residue was dissolved in ethanol. To this solution was added 6.5 ml of 5N sodium hydroxide. It was then refluxed for 1 hour. The reaction solution was cooled, and water was added thereto. Then, the mixture was acidified with dilute hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated, to give 1.5 g of the title compound.

¹H-NMR (CDCl₃)

δ : 1.70 (d, J=6.0Hz, 3H) 4.77 (q, J=6.0Hz, 1H) 6.83 (d, J=8.0Hz, 1H)
7.17 (dd, J=2.0, 8.0Hz, 1H) 7.41 (d, J=2.0Hz, 1H)

b) 3-{3-[2-(2,4-Dichlorophenoxy)propionylamino]-4-methoxyphenyl}-2-isopropoxypropanoic acid

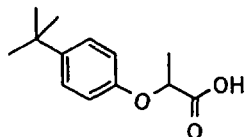


The title compound was obtained in the same manner as described in Example 423c).

MS *m/e*(ESI) 492 (MNa⁺)

Example 438.

a) 2-(4-t-Butylphenoxy)propionic acid

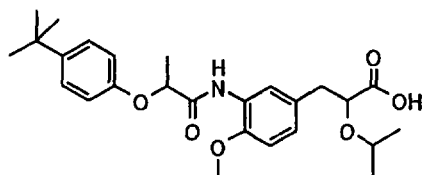


Using 4-t-butylphenol, the title compound was obtained in the same manner as described in Example 435a).

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

δ : 1.19(s, 9H) 1.64(d, $J=6.0\text{Hz}$, 3H) 4.77(q, $J=6.0\text{Hz}$, 1H) 6.83(d, $J=8.0\text{Hz}$, 2H) 7.30(d, $J=8.0\text{Hz}$, 2H)

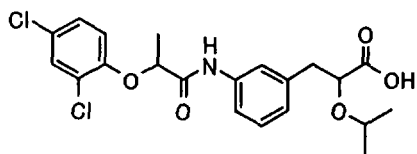
b) 3-{3-[2-(4-t-Butylphenoxy)propionylamino]-4-methoxyphenyl}-2-isopropoxypropanoic acid



The title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 458 (MH^+)

Example 439. 3-{3-[2-(2,4-Dichlorophenoxy)propionylamino]-phenyl}-2-isopropoxypropanoic acid



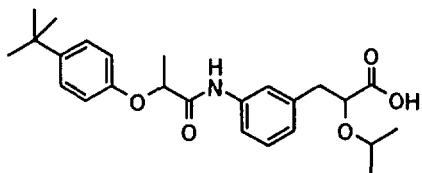
The title compound was obtained in the same manner as described in Example 423c).

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

δ : 0.97(d, $J=6.0\text{Hz}$, 3H) 1.09(d, $J=6.0\text{Hz}$, 3H) 1.64(d, $J=6.0\text{Hz}$, 3H)
2.88(dd, $J=14.0$, 6.0Hz, 1H) 3.07(dd, $J=14.0$, 4.4Hz, 1H) 3.49(dq, $J=6.0$,
6.0Hz, 1H) 4.08(dd, $J=7.6$, 4.4Hz, 1H) 4.74(q, $J=6.0\text{Hz}$, 1H) 6.86(d,
 $J=8.0\text{Hz}$, 1H) 6.97(d, $J=8.0\text{Hz}$, 2H) 7.16(dd, $J=8.0$, 2.0Hz, 1H)
7.20(m, 1H) 7.38-7.43(m, 2H) 8.48(s, 1H)

MS m/e (ESI) 462 (MNa^+)

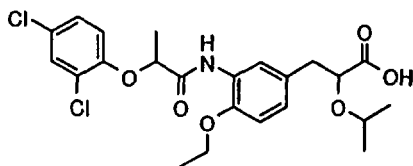
Example 440. 3-{3-[2-(4-*t*-Butylphenoxy)propionylamino]-phenyl}-2-isopropoxypropanoic acid



The title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 450 (MNa^+)

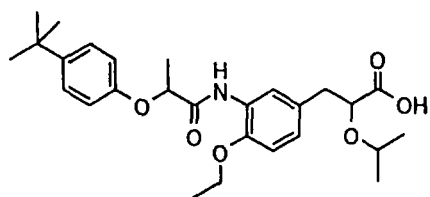
Example 441. 3-{3-[2-(2,4-dichlorophenoxy)propionylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid



The title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 506 (MNa^+)

Example 442. 3-{3-[2-(4-*t*-Butylphenoxy)propionylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

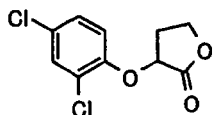


The title compound was obtained in the same manner as described in Example 423c).

MS m/e (ESI) 472 (MH^+)

Example 443.

a) 3-(2,4-Dichlorophenoxy)-dihydrofuran-2-one



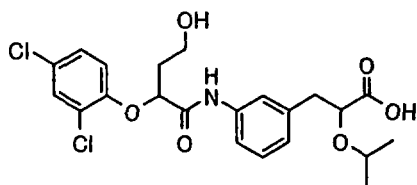
1 g of 2,4-Dichlorophenol was dissolved in 10 ml of N,N-dimethylformamide, and 0.27 g of 60% sodium hydride was added thereto under ice-cooling, and the mixture was stirred at room temperature for 30 minutes. 0.7 ml of Ethyl α -bromo- β -butyrolactone was added to the mixture which was then stirred at room temperature for another 1 hour. The reaction solution was diluted with aqueous ammonium chloride, and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was subjected to silica gel column chromatography, to give 1 g of the title compound.

^1H -NMR($CDCl_3$)

δ : 2.61(m, 1H) 2.72(m, 1H) 4.34(m, 1H) 4.56(m, 1H) 4.86(t, $J=6.0$ Hz, 1H) 7.20(m, 2H) 7.38(m, 1H)

b) 3-{3-[2-(2,4-Dichlorophenoxy)-4-

hydroxybutyrylamino]phenyl)-2-isopropoxypropanoic acid



20 mg of 3-(2,4-Dichlorophenoxy) dihydrofuran-2-one and 30 mg of ethyl 3-(3-aminophenyl)-2-isopropoxypropanoate were dissolved in 1 ml of toluene, and the solution was heated under reflux for 8 hours. After removing the solvent under a stream of nitrogen, the residue was dissolved in 0.6 ml of ethanol, and 0.12 ml of 5N sodium hydroxide was added thereto, and the mixture was stirred at room temperature for 1 hour. The reaction solution was diluted with 2 ml of water and 0.14 ml of 5N hydrochloric acid, and extracted with ethyl acetate. The organic layer was collected, and the solvent was removed under a stream of nitrogen. The residue was purified by HPLC using a reverse-phase column and a water-acetonitrile-trifluoroacetic acid elution solvent, to give 6.8 mg of the title compound.

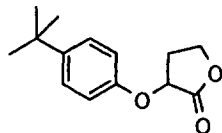
¹H-NMR (CDCl₃)

δ : 1.05 (d, J=6.0Hz, 3H) 1.16 (d, J=6.0Hz, 3H) 2.30 (d, J=6.0Hz, 2H)
2.95 (m, 2H) 3.11 (dd, J=14.0, 4.4Hz, 1H) 3.58 (dq, J=6.0, 6.0Hz, 1H)
3.87-3.95 (m, 2H) 4.16 (dd, J=7.6, 4.4Hz, 1H) 4.93 (d, J=6.0Hz, 1H) 7.05 (m, 2H)
7.21-7.27 (m, 2H) 7.38 (m, 1H) 7.44 (dd, J=8.0, 2.0Hz, 1H) 7.50 (d, J=2.0Hz, 2H) 8.61 (s, 1H)

MS *m/e* (ESI) 470 (MH⁺)

Example 444.

a) 3-(4-t-Butylphenoxy)dihydrofuran-2-one



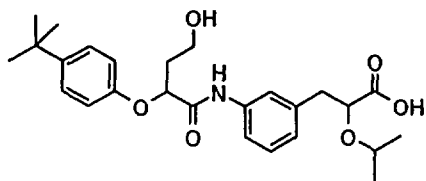
Using 4-t-butylphenol, the title compound was obtained in the same manner as described in Example 443a).

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

δ : 2.46 (m, 1H) 2.70 (m, 1H) 4.36 (m, 1H) 4.51 (m, 1H) 4.92 (t, $J=6.0\text{Hz}$, 1H) 6.96 (d, $J=8.0\text{Hz}$, 2H) 7.32 (d, $J=8.0\text{Hz}$, 2H)

b) 3-{3-[2-(4-t-Butylphenoxy)-4-

hydroxybutyrylamino]phenyl}-2-isopropoxypropanoic acid

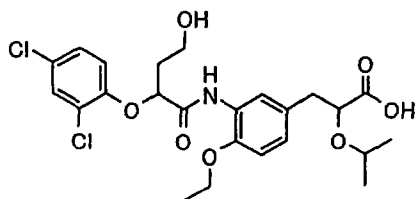


The title compound was obtained in the same manner as described in Example 443b).

MS m/e (ESI) 458 (MH^+)

Example 445.

3-{3-[2-(2,4-Dichlorophenoxy)-4-hydroxybutyrylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

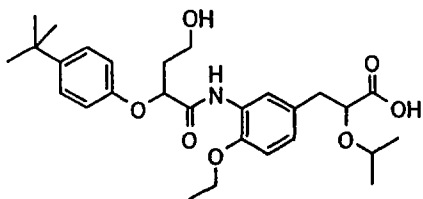


The title compound was obtained in the same manner as described in Example 443.

MS m/e (ESI) 514 (MH^+)

Example 446.

3-{3-[2-(4-*t*-Butylphenoxy)-4-hydroxybutyrylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

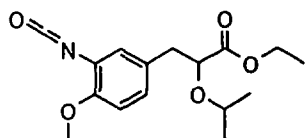


The title compound was obtained in the same manner as described in Example 443.

MS m/e (ESI) 502 (MH^+)

Example 447.

a) Ethyl 3-(3-isocyanato-4-methoxyphenyl)-2-isopropoxypropanoate



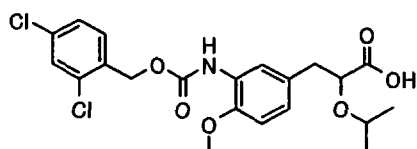
0.13 g of di-*t*-Butyl dicarbonate was dissolved in 2.5 ml of acetonitrile, and a solution containing 60 mg of 4-dimethylaminopyridine and 0.12 g of ethyl 3-(3-amino-4-methoxy-phenyl)-2-isopropoxypropanoate in acetonitrile were added thereto, and the mixture was stirred at room temperature for 10 minutes. The reaction solution was cooled in ice, and 0.73 ml of 40% sulfuric acid-acetonitrile

solution was added and stirring was continued at room temperature for 2 minutes, then the mixture was extracted with hexane. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated, to give 28 mg of the title compound.

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

δ : 0.98(d, $J=6.0\text{Hz}$, 3H) 1.15(d, $J=6.0\text{Hz}$, 3H) 1.24(t, $J=6.0\text{Hz}$, 3H)
2.83(m, 2H) 3.50(dq, $J=6.4$, 6.4Hz, 1H) 3.89(s, 3H) 3.97(dd, $J=8.4$,
4.8Hz, 1H) 4.17(q, $J=6.0\text{Hz}$, 2H) 6.77(d, $J=8.0\text{Hz}$, 1H) 6.89(d, $J=2.0\text{Hz}$,
1H) 7.02(dd, $J=8.0$, 2.0Hz, 1H)

b) 3-[3-(2,4-Dichlorobenzoyloxycarbonylamino)-4-methoxyphenyl]-2-isopropoxypropanoic acid



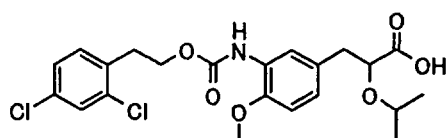
14 mg of Ethyl 3-(3-isocyanato-4-methoxyphenyl)-2-isopropoxypropanoate was dissolved in 1 ml of tetrahydrofuran, and 10 mg of 2,4-dichlorobenzyl alcohol and 5 μl of pyridine were added thereto, and the mixture was stirred at room temperature for 16 hours. The solvent was removed under a stream of nitrogen, and the residue was dissolved in 0.6 ml of ethanol, and 0.12 ml of 5N sodium hydroxide was added and stirred at room temperature for 1 hour. The reaction solution was diluted with 1 ml of water and 0.14 ml of 5N hydrochloric acid, and extracted with ethyl acetate. The organic layer was collected, and the solvent was removed under a stream of nitrogen. The residue

was purified by HPLC using a reverse-phase column and a water-acetonitrile-trifluoroacetic acid elution solvent, to give 3.1 mg of the title compound.

MS m/e (ESI) 478 (MNa^+)

Example 448.

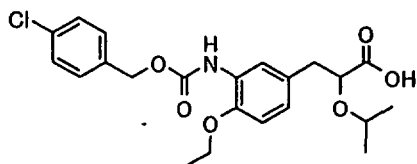
3-{3-[2-(2,4-dichlorophenyl)ethoxycarbonylamino]-4-methoxyphenyl}-2-isopropoxypropanoic acid



Using 2,4-dichlorophenethyl alcohol, the title compound was obtained in the same manner as described in Example 449b).

MS m/e (ESI) 492 (MNa^+)

Example 449. 3-[3-(4-Chlorobenzylloxycarbonylamino)-4-ethoxyphenyl]-2-isopropoxypropanoic acid



25 mg of di-*t*-Butyl dicarbonate was dissolved in 0.5 ml of acetonitrile, and a solution of 10 mg of 4-dimethylaminopyridine and 25 mg of ethyl 3-(3-amino-4-ethoxyphenyl)-2-isopropoxypropanoate in acetonitrile was added, and the mixture was stirred for 2 minutes. The reaction solution was treated with 20 mg of 4-chlorobenzyl alcohol, then stirred at 80°C for 2 hours. The solvent was removed under a stream of nitrogen, and the residue was dissolved

in 0.6 ml of ethanol, and 0.12 ml of 5N sodium hydroxide was added. The mixture was stirred at room temperature for 1 hour, and 1 ml of water and 0.14 ml of 5N hydrochloric acid were added, and the mixture was extracted with ethyl acetate. The organic layer was collected, and the solvent was removed under a stream of nitrogen. The residue was purified by HPLC on a reverse-phase column using a water-acetonitrile-trifluoroacetic acid solvent system, to give 19 mg of the title compound.

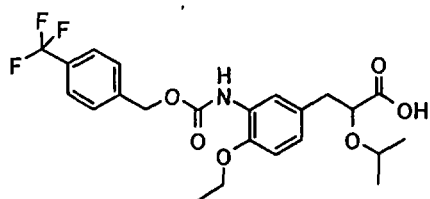
¹H-NMR(CDCl₃)

δ : 1.06(d, J=6.0Hz, 3H) 1.16(d, J=6.0Hz, 3H) 1.42(t, J=6.0Hz, 3H)
2.89(dd, J=14.0, 6.0Hz, 1H) 3.08(dd, J=14.0, 4.4Hz, 1H) 3.56(dq, J=6.0,
6.0Hz, 1H) 4.11(m, 3H) 5.17(s, 2H) 6.75(d, J=8.0Hz, 1H) 6.84(dd,
J=8.0, 2.0Hz, 1H) 7.25-7.38(m, 5H)

MS *m/e*(ESI) 436 (MH⁺)

Example 450.

3-[4-Ethoxy-3-(4-trifluoromethylbenzyloxycarbonylamino)-
phenyl]-2-isopropoxypropanoic acid



Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

¹H-NMR(CDCl₃)

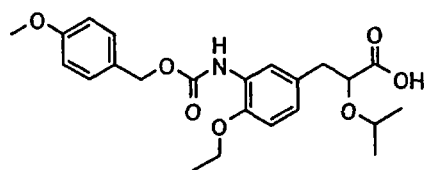
δ : 1.06(d, J=6.0Hz, 3H) 1.15(d, J=6.0Hz, 3H) 1.43(t, J=6.0Hz, 3H)
2.90(dd, J=14.0, 6.0Hz, 1H) 3.08(dd, J=14.0, 4.4Hz, 1H) 3.57(dq, J=6.0,

6.0Hz, 1H) 4.08(q, J=6.0Hz, 2H) 4.14(dd, J=7.6, 4.4Hz, 1H) 5.26(s, 2H)
6.76(d, J=8.0Hz, 1H) 6.85(dd, J=8.0, 2.0Hz, 1H) 7.31(s, 1H) 7.54(d,
J=8.0Hz, 2H) 7.64(d, J=8.0Hz, 2H) 8.01(s, 1H)

MS m/e (ESI) 470 (MH^+)

Example 451.

3-[4-Ethoxy-3-(4-methoxybenzyloxycarbonylamino)phenyl]-2-
isopropoxypropanoic acid

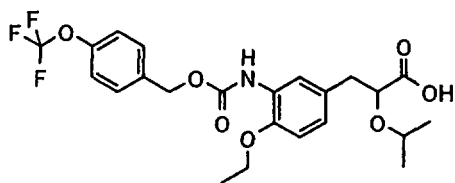


Using 4-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 454 (MNa^+)

Example 452.

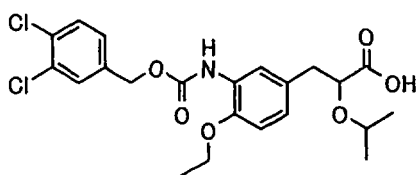
3-[4-Ethoxy-3-(4-trifluoromethoxybenzyloxycarbonylamino)-
phenyl]-2-isopropoxypropanoic acid



Using 4-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 508 (MNa^+)

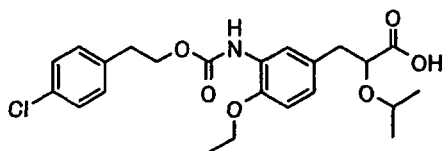
Example 453. 3-[3-(3,4-Dichlorobenzoyloxycarbonylamino)-4-
ethoxyphenyl]-2-isopropoxypropanoic acid



Using 3,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 492 (MNa^+)

Example 454. 3-{3-[2-(4-Chlorophenyl)ethoxycarbonylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

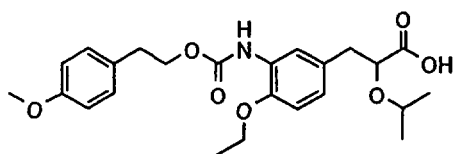


Using 4-chlorophenethyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 472 (MNa^+)

Example 455.

3-{4-Ethoxy-3-[2-(4-methoxyphenyl)ethoxycarbonylamino]-phenyl}-2-isopropoxypropanoic acid

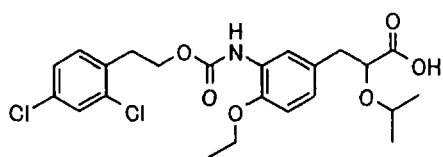


Using 4-methoxyphenethyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 468 (MNa^+)

Example 456.

3-{3-[2-(2,4-Dichlorophenyl)ethoxycarbonylamino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid

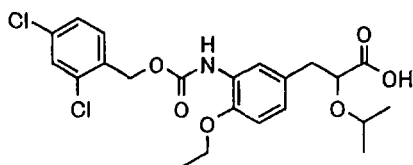


Using 2,4-dichlorophenethyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 484 (MH^+)

Example 457.

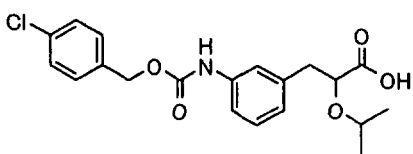
3-[3-(2,4-Dichlorobenzoyloxycarbonylamino)-4-ethoxyphenyl]-2-isopropoxypropanoic acid



Using 2,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 470 (MH^+)

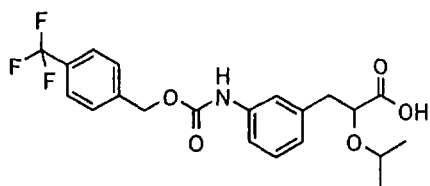
Example 458. 3-[3-(4-Chlorobenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using 4-chlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 414 (MNa^+)

Example 459. 2-Isopropoxy-3-[3-(4-trifluoromethylbenzyloxycarbonylamino)phenyl]propanoic acid



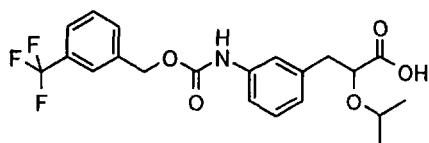
Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 1.03(d, $J=6.0\text{Hz}$, 3H) 1.16(d, $J=6.0\text{Hz}$, 3H) 2.93(dd, $J=14.0$, 6.0Hz, 1H) 3.12(dd, $J=14.0$, 4.4Hz, 1H) 3.56(dq, $J=6.0$, 6.0Hz, 1H) 4.15(dd, $J=7.6$, 4.4Hz, 1H) 5.25(s, 2H) 6.69(s, 1H) 6.97(d, $J=8.0\text{Hz}$, 1H) 7.23(d, $J=8.0\text{Hz}$, 1H) 7.28(m, 2H) 7.52(d, $J=8.0\text{Hz}$, 2H) 7.64(d, $J=8.0\text{Hz}$, 2H)

MS m/e (ESI) 448 (MNa^+)

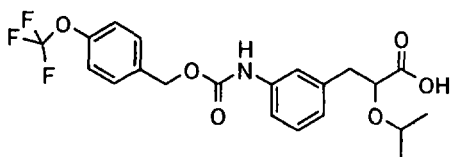
Example 460. 2-Isopropoxy-3-[3-(3-trifluoromethylbenzyloxycarbonylamino)phenyl]propanoic acid



Using 3-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 448 (MNa^+)

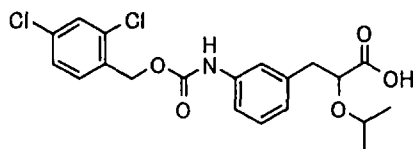
Example 461. 2-Isopropoxy-3-[3-(4-trifluoromethoxybenzyloxycarbonylamino)phenyl]propanoic acid



Using 4-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 464 (MNa^+)

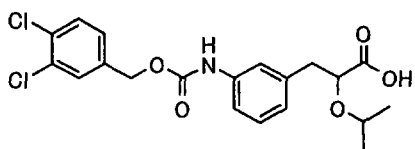
Example 462. 3-[3-(2,4-Dichlorobenzoyloxycarbonylamino)-phenyl]-2-isopropoxypropanoic acid



Using 2,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 448 (MNa^+)

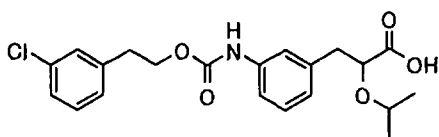
Example 463. 3-[3-(3,4-Dichlorobenzoyloxycarbonylamino)-phenyl]-2-isopropoxypropanoic acid



Using 3,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 448 (MNa^+)

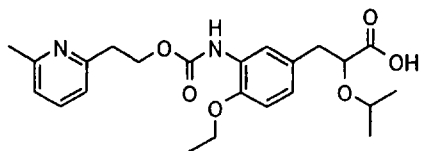
Example 464. 3-[3-[2-(3-Chlorophenyl)ethoxycarbonylamino]-phenyl]-2-isopropoxypropanoic acid



Using 3-chlorophenethyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 428 (MNa^+)

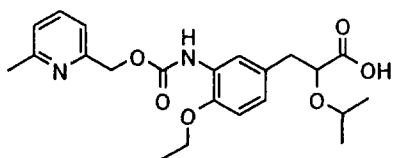
Example 465. 3-[4-Ethoxy-[2-(6-methylpyridin-2-yl)ethoxycarbonylamino]phenyl]-2-isopropoxypropanoic acid



Using 2-(6-methylpyridin-2-yl)ethanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 431 (MH^+)

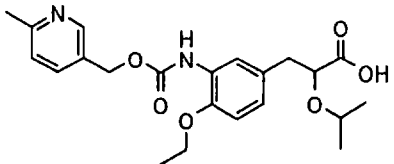
Example 466. 3-[4-Ethoxy-3-(6-methylpyridin-2-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using (6-methylpyridin-2-yl)methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 417 (MH^+)

Example 467. 3-[4-Ethoxy-3-(6-methylpyridin-3-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

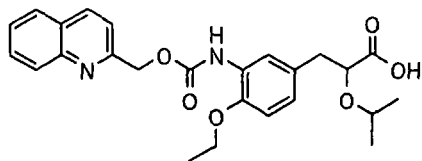


Using (6-methylpyridin-3-yl)methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 417 (MH^+)

Example 468. 3-[4-Ethoxy-3-(quinolin-2-

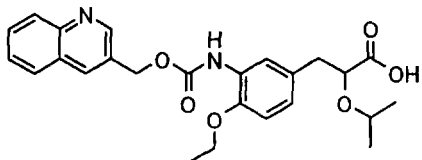
ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using quinolin-2-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 453 (MH^+)

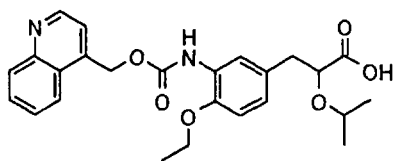
Example 469. 3-[4-Ethoxy-3-(quinolin-3-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using quinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 453 (MH^+)

Example 470. 3-[4-Ethoxy-3-(quinolin-4-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

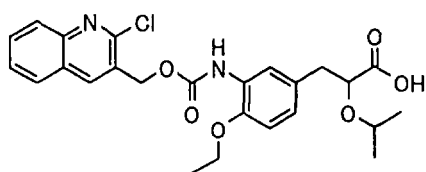


Using quinolin-4-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 453 (MH^+)

Example 471.

3-[3-(2-Chloroquinolin-3-ylmethoxycarbonylamino)-4-ethoxyphenyl]-2-isopropoxypropanoic acid

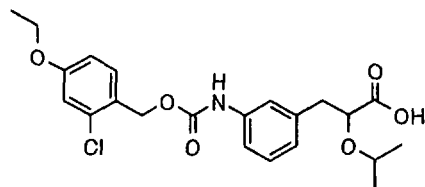


Using 2-chloroquinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 487 (MH^+)

Example 472.

3-[3-(2-Chloro-4-ethoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

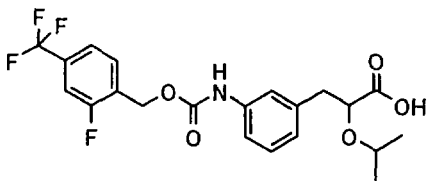


Using 2-chloro-3-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 472 (MNa^+)

Example 473.

3-[3-(2-Fluoro-4-trifluoromethylbenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

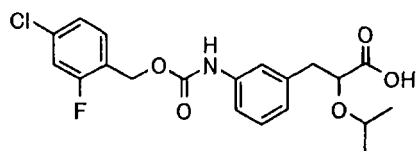


Using 2-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 466 (MNa^+)

Example 474.

3-[3-(4-Chloro-2-fluorobenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

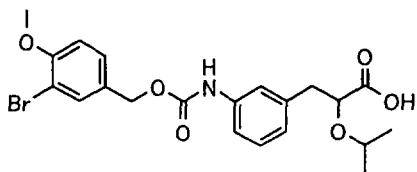


Using 4-chloro-2-fluorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 432 (MNa^+)

Example 475.

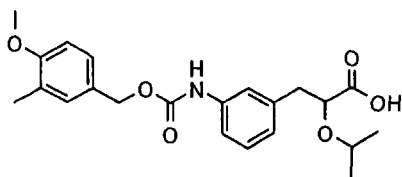
3-[3-(3-Bromo-4-methoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using 3-bromo-4-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 488 (MNa^+)

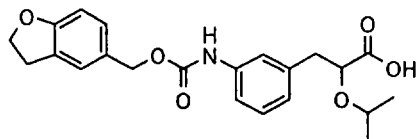
Example 476. 2-Isopropoxy-3-[3-(4-methoxy-3-methylbenzyloxycarbonylamino)phenyl]propanoic acid



Using 4-methoxy-3-methylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 424 (MNa^+)

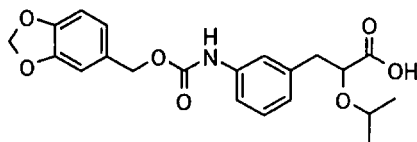
Example 477. 3-[3-(2,3-Dihydrobenzofuran-5-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using (2,3-dihydrobenzofuran-5-yl)methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 422 (MNa^+)

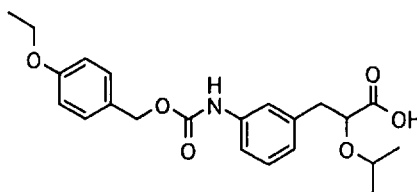
Example 478. 3-[3-(Benzo[1,3]dioxol-5-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using benzo[1,3]dioxol-5-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 402 (MH^+)

Example 479. 3-[3-(4-Ethoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

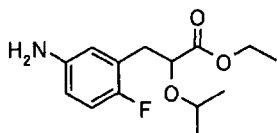


Using 4-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 424 (MNa^+)

Example 480.

a) Ethyl 3-(5-amino-2-fluorophenyl)-2-isopropoxypropanoate

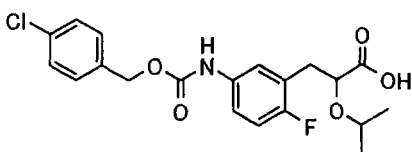


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

^1H -NMR($CDCl_3$)

δ : 0.98(d, $J=6.0$ Hz, 3H) 1.14(d, $J=6.0$ Hz, 3H) 1.24(t, $J=6.0$ Hz, 3H)
2.83(m, 1H) 3.05(m, 1H) 3.55(dq, $J=6.0$ Hz, 1H) 4.08(dd, $J=8.4$, 4.8Hz, 1H)
4.17(q, $J=6.0$ Hz, 2H) 6.49(m, 1H) 6.53(d, $J=8.0$ Hz, 1H) 6.80(d, $J=8.0$ Hz, 1H)

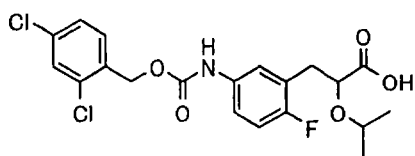
b) 3-[5-(4-Chlorobenzoyloxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid



Using 4-chlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 432 (MNa^+)

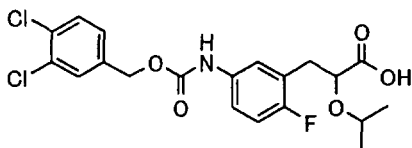
Example 481. 3-[5-(2,4-Dichlorobenzoyloxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid



Using 2,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 466 (MNa^+)

Example 482. 3-[5-(3,4-Dichlorobenzoyloxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid

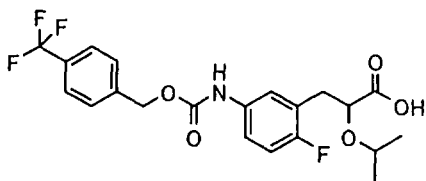


Using 3,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 466 (MNa^+)

Example 483.

3-[2-Fluoro-5-(4-trifluoromethylbenzyloxycarbonylamino)-phenyl]-2-isopropoxypropanoic acid



Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

^1H -NMR($CDCl_3$)

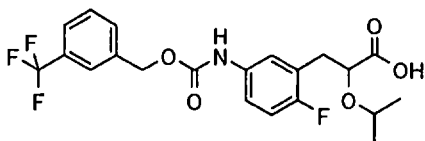
δ : 1.01(d, $J=6.0$ Hz, 3H) 1.16(d, $J=6.0$ Hz, 3H) 2.97(dd, $J=14.0$, 6.0Hz, 1H)
3.20(dd, $J=14.0$, 4.4Hz, 1H) 3.60(dq, $J=6.0$, 6.0Hz, 1H) 4.20(dd, $J=7.6$,

4.4Hz, 1H) 5.24(s, 2H) 6.70(bs, 1H) 6.99(t, J=9.2Hz, 1H) 7.23(m, 2H)
7.28(m, 1H) 7.50(d, J=8.0Hz, 2H) 7.64(d, J=8.0Hz, 2H)

MS m/e (ESI) 466 (MNa^+)

Example 484.

3-[2-Fluoro-5-(3-trifluoromethylbenzyloxycarbonylamino)-
phenyl]-2-isopropoxypropanoic acid

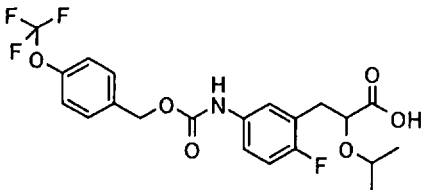


Using 3-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 466 (MNa^+)

Example 485.

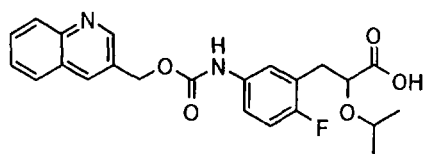
3-[2-Fluoro-5-(4-trifluoromethoxybenzyloxycarbonylamino)-
phenyl]-2-isopropoxypropanoic acid



Using 4-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 483 (MNa^+)

Example 486. 3-[2-Fluoro-5-(quinolin-3-
ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

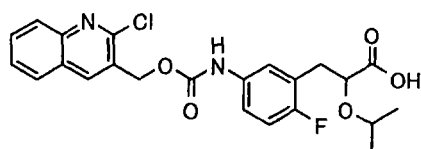


Using quinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 427 (MH^+)

Example 487.

3-[5-(2-Chloroquinolin-3-ylmethoxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid

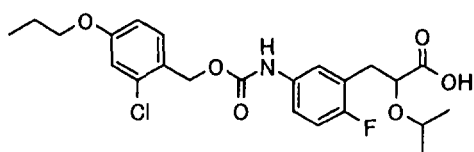


Using 2-chloroquinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 461 (MH^+)

Example 488.

3-[5-(2-Chloro-4-propoxybenzyloxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid

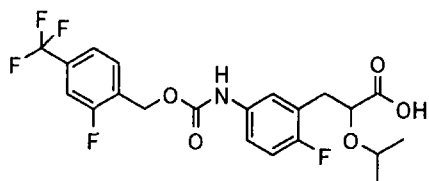


Using 2-chloro-4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 490 (MNa^+)

Example 489. 3-[2-Fluoro-5-(2-fluoro-4-trifluoromethylbenzyloxycarbonylamino)phenyl]-2-

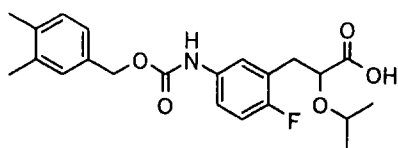
isopropoxypropanoic acid



Using 2-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 484 (MNa^+)

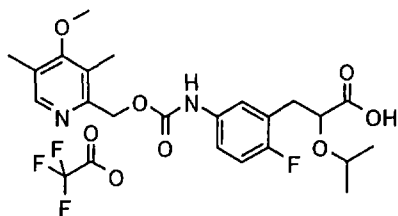
Example 490. 3-[5-(3,4-Dimethylbenzyloxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid



Using 3,4-dimethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 426 (MNa^+)

Example 491. 3-[2-Fluoro-5-(4-methoxy-3,5-dimethylpyridin-2-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid trifluoroacetate



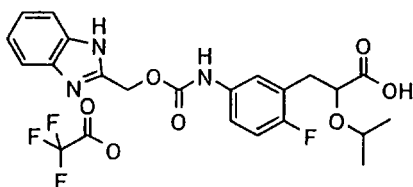
Using (4-methoxy-3,5-dimethylpyridin-2-yl)methanol, the title compound was obtained in the same manner as described in

Example 449.

MS m/e (ESI) 435 (MH^+)

Example 492.

3-[5-(1H-Benzimidazol-2-ylmethoxycarbonylamino)-2-fluorophenyl]-2-isopropoxypropanoic acid trifluoroacetate

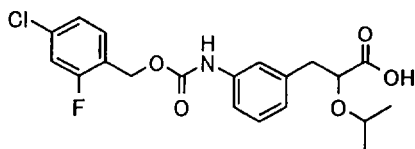


Using 1H-benzimidazol-2-yl methanol, the title compound was obtained in the same manner as described in Example 449.

MS m/e (ESI) 416 (MH^+)

Example 493.

3-[3-(4-Chloro-2-fluorobenzylloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

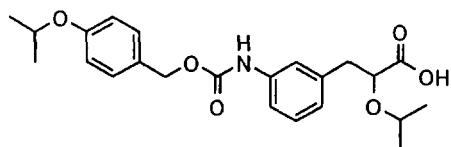


25 mg of Triphosgene was dissolved in 0.5 ml of dichloromethane, 5 μ l of pyridine was added, and a solution of 20 mg of ethyl-3-(3-aminophenyl)-2-isopropoxypropanoate in dichloromethane and 50 μ l of triethylamine were added under ice-cooling. After the insoluble substances had been removed by cotton plug filtration, 15 mg of 2-fluoro-4-chlorobenzyl alcohol was added. The solvent was removed under a stream of nitrogen, and the residue was dissolved in 0.6 ml of ethanol.

0.12 ml of 5N sodium hydroxide was added, followed by stirring at room temperature for 1 hour. The reaction solution was treated with 1 ml of water and 0.14 ml of 5N hydrochloric acid, then extracted with ethyl acetate. The organic layers were collected, and the solvent was removed under a stream of nitrogen. The residue was purified by reverse-phase HPLC using a water-acetonitrile-trifluoroacetic acid solvent system, to give 1.4 mg of the title compound.

MS m/e (ESI) 438 (MNa^+)

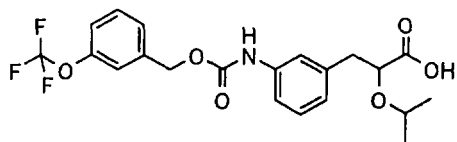
Example 494. 2-Isopropoxy-3-[3-(4-isopropoxybenzyloxycarbonylamino)phenyl]propanoic acid



Using 4-isopropoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 464 (MNa^+)

Example 495. 2-Isopropoxy-3-[3-(3-trifluoromethoxybenzyloxycarbonylamino)phenyl]propanoic acid

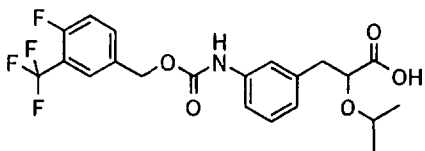


Using 3-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 463 (MNa^+)

Example 496.

3-[3-(4-Fluoro-3-trifluoromethylbenzyloxycarbonylamino)-
phenyl]-2-isopropoxypropanoic acid

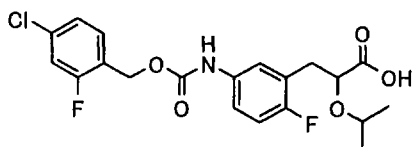


Using 4-fluoro-3-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 466 (MNa^+)

Example 497.

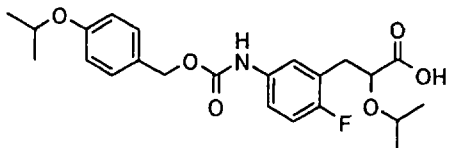
3-[5-(4-Chloro-2-fluorobenzyloxycarbonylamino)-2-
fluorophenyl]-2-isopropoxypropanoic acid



Using 4-chloro-2-fluorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 450 (MNa^+)

Example 498. 3-[2-Fluoro-5-(4-
isopropoxybenzyloxycarbonylamino)phenyl]-2-
isopropoxypropanoic acid



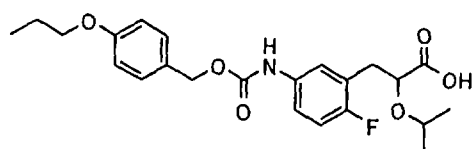
Using 4-isopropoxybenzyl alcohol, the title compound was

obtained in the same manner as described in Example 493.

MS m/e (ESI) 456 (MNa^+)

Example 499.

3-[2-Fluoro-5-(4-propoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

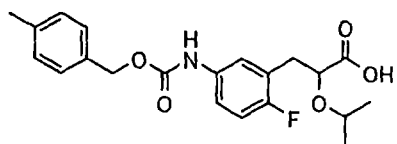


Using 4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 456 (MNa^+)

Example 500.

3-[2-Fluoro-5-(4-methylbenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

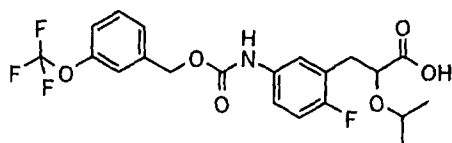


Using 4-methylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 412 (MNa^+)

Example 501.

3-[2-Fluoro-5-(3-trifluoromethoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

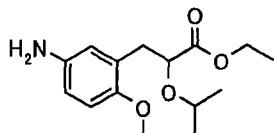


Using 3-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 482 (MNa^+)

Example 502.

a) Ethyl 3-(5-amino-2-methoxyphenyl)-2-isopropoxypropionate

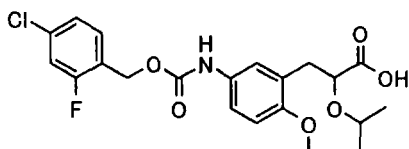


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

^1H -NMR($CDCl_3$)

δ : 0.98(d, $J=6.0$ Hz, 3H) 1.14(d, $J=6.0$ Hz, 3H) 1.20(t, $J=6.0$ Hz, 3H)
2.84(dd, $J=14.0, 6.0$ Hz, 1H) 3.00(dd, $J=14.0, 4.4$ Hz, 1H) 3.52(dq, $J=6.0, 6.0$ Hz, 1H) 3.76(s, 3H) 4.15(m, 3H) 6.54(m, 2H) 6.67(d, $J=8.0$ Hz, 1H)

b) 3-[5-(4-Chloro-2-fluorobenzoyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid

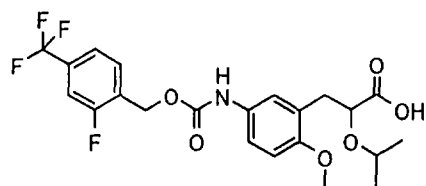


Using 4-chloro-2-fluorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 440 (MH^+)

Example 503.

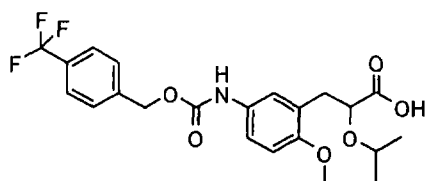
3-[5-(2-Fluoro-4-trifluoromethylbenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 2-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 496 (MNa^+)

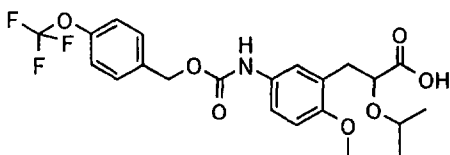
Example 504. 2-Isopropoxy-3-[2-methoxy-5-(4-trifluoromethylbenzyloxycarbonylamino)phenyl]propanoic acid



Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 478 (MNa^+)

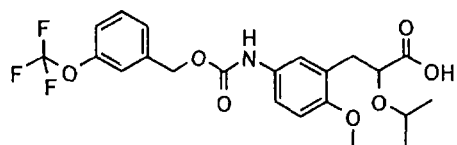
Example 505. 2-Isopropoxy-3-[2-methoxy-5-(4-trifluoromethoxybenzyloxycarbonylamino)phenyl]propanoic acid



Using 4-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 494 (MNa^+)

Example 506. 2-Isopropoxy-3-[2-methoxy-5-(3-trifluoromethoxybenzyloxycarbonylamino)phenyl]propanoic acid

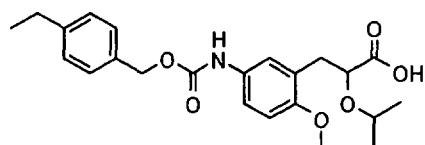


Using 3-trifluoromethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 472 (MH^+)

Example 507.

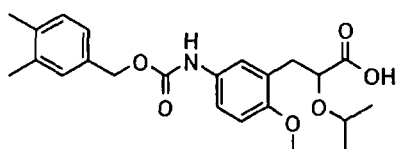
3-[5-(4-Ethylbenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 4-ethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 438 (MNa^+)

Example 508. 3-[5-(3,5-Dimethylbenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid

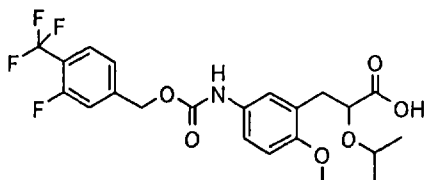


Using 3,4-dimethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 438 (MNa^+)

Example 509.

3-[5-(3-Fluoro-4-trifluoromethylbenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid

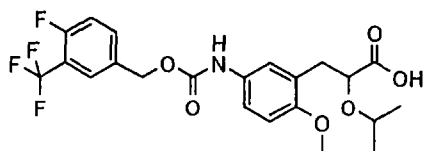


Using 3-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS *m/e*(ESI) 474 (MH⁺)

Example 510.

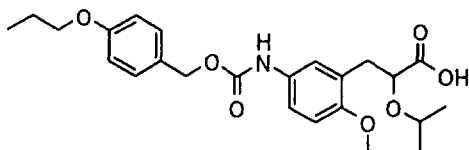
3-[5-(4-Fluoro-3-trifluoromethylbenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 4-fluoro-3-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS *m/e*(ESI) 474 (MH⁺)

Example 511. 2-Isopropoxy-3-[2-methoxy-5-(4-propoxybenzyloxycarbonylamino)phenyl]propanoic acid

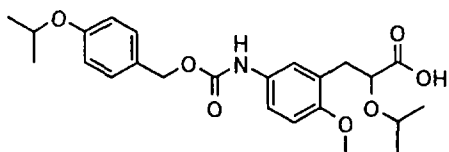


Using 4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 468 (MNa^+)

Example 512.

2-Isopropoxy-3-[5-(4-propoxybenzyloxycarbonylamino)-2-methoxyphenyl]propanoic acid

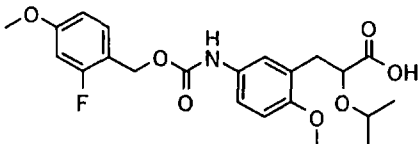


Using 4-isopropoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 468 (MNa^+)

Example 513.

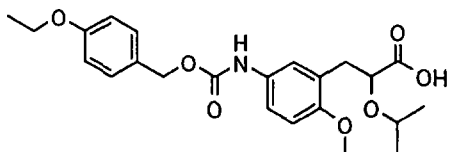
3-[5-(2-Fluoro-4-methoxybenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 2-fluoro-4-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 458 (MNa^+)

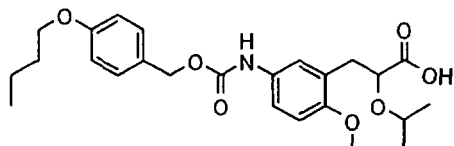
Example 514. 3-[5-(4-Ethoxybenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 4-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 454 (MNa^+)

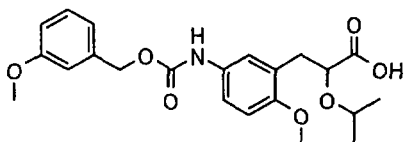
Example 515. 3-[5-(4-Butoxybenzyloxycarbonylamino)-2-methoxyphenyl]-2-isopropoxypropanoic acid



Using 4-butoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 482 (MNa^+)

Example 516. 2-Isopropoxy-3-[2-methoxy-5-(3-methoxybenzyloxycarbonylamino)phenyl]propanoic acid

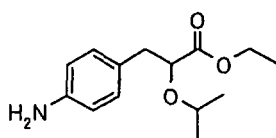


Using 3-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 440 (MNa^+)

Example 517.

a) Ethyl 3-(4-aminophenyl)-2-isopropoxypropionate

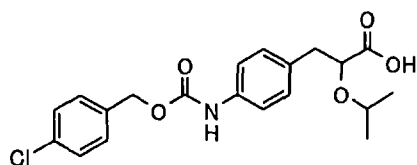


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

¹H-NMR (CDCl₃)

δ : 0.98(d, J=6.0Hz, 3H) 1.14(d, J=6.0Hz, 3H) 1.22(t, J=6.0Hz, 3H)
2.84(m, 2H) 3.48(dq, J=6.0, 6.0Hz, 1H) 3.98(dd, J=7.6, 4.4Hz, 1H)
4.15(q, J=6.0Hz, 2H) 6.60(d, J=8.0Hz, 2H) 7.02(d, J=8.0Hz, 2H)

b) 3-[4-(4-Chlorobenzylloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

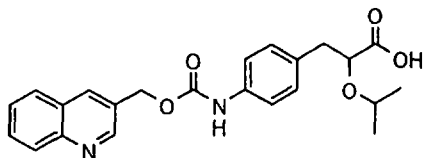


Using 4-chlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS *m/e*(ESI) 414 (MNa⁺)

Example 518.

2-Isopropoxy-3-[4-(quinolin-3-ylmethoxycarbonylamino)-phenyl]propanoic acid

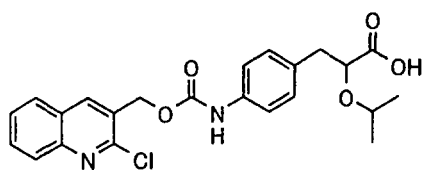


Using quinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 493.

MS *m/e*(ESI) 409 (MH⁺)

Example 519.

3-[4-(2-Chloroquinolin-3-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

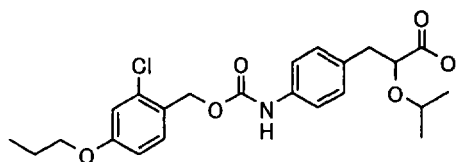


Using 2-chloroquinolin-3-yl methanol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 443 (MH^+)

Example 520.

3-[4-(2-Chloro-4-propoxybenzyloxy)carbonylamino]phenyl]-2-isopropoxypropanoic acid

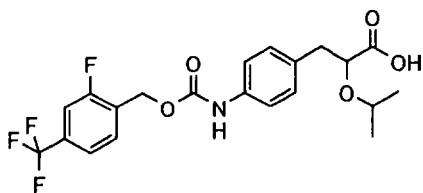


Using 2-chloro-4-propoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 472 (MNa^+)

Example 521.

3-[4-(2-Fluoro-4-trifluoromethylbenzyloxy)carbonylamino]phenyl]-2-isopropoxypropanoic acid

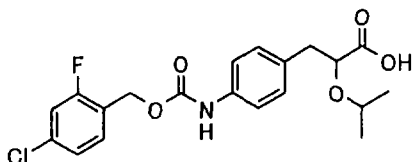


Using 2-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 466 (MNa^+)

Example 522.

3-[4-(2-Chloro-4-fluorobenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

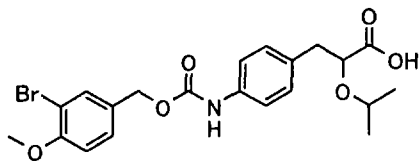


Using 4-chloro-2-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 432 (MNa^+)

Example 523.

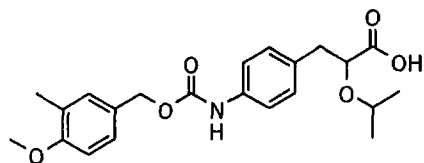
3-[4-(3-Bromo-4-methoxybenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using 3-bromo-4-methoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 488 (MNa^+)

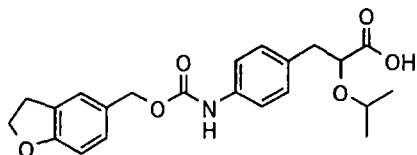
Example 524. 2-Isopropoxy-3-[4-(4-methoxy-3-methylbenzoyloxycarbonylamino)phenyl]propanoic acid



Using 4-methoxy-3-methylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 424 (MNa^+)

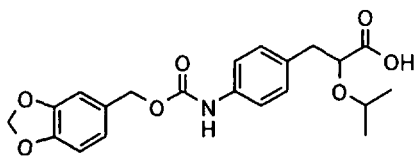
Example 525. 3-[4-(2,3-Dihydrobenzofuran-5-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using (2,3-dihydrobenzofuran-5-yl)methanol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 422 (MNa^+)

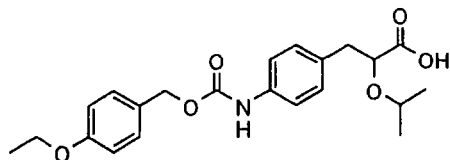
Example 526. 3-[4-(Benzo[1,3]dioxol-5-ylmethoxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using benzo[1,3]dioxol-5-yl methanol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 424 (MNa^+)

Example 527. 3-[4-(4-Ethoxybenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

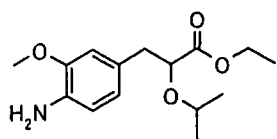


Using 4-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 424 (MNa^+)

Example 528.

a) Ethyl 3-(4-amino-3-methoxyphenyl)-2-isopropoxypropionate

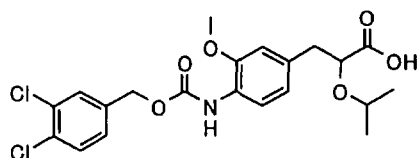


The title compound was obtained in the same manner as described in Examples 423a) and 423b).

¹H-NMR (CDCl₃)

δ : 0.98(d, J=6.0Hz, 3H) 1.14(d, J=6.0Hz, 3H) 1.25(t, J=6.0Hz, 3H)
2.86(m, 2H) 3.48(dq, J=6.0, 6.0Hz, 1H) 3.82(s, 3H) 3.98(dd, J=7.6,
4.4Hz, 1H) 4.16(q, J=6.0Hz, 2H) 6.65(m, 2H) 6.71(bs, 1H)

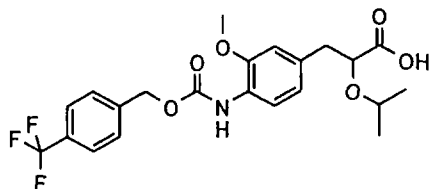
b) 3-[4-(3,4-Dichlorobenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



Using 3,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS *m/e*(ESI) 456 (MH⁺)

Example 529. 2-Isopropoxy-3-[3-methoxy-4-(4-trifluoromethylbenzyloxycarbonylamino)phenyl]propanoic acid

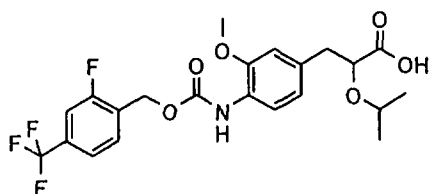


Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 456 (MH^+)

Example 530.

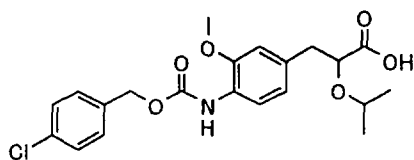
3-[4-(2-Fluoro-4-trifluoromethylbenzyloxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid



Using 2-fluoro-4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 496 (MNa^+)

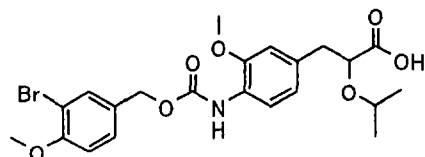
Example 531. 3-[4-(4-Chlorobenzylloxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid



Using 4-chlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 462 (MNa^+)

Example 532. 3-[4-(3-Bromo-4-methoxybenzyloxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid

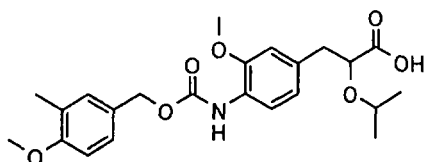


Using 3-bromo-4-methoxybenzyl alcohol, the title compound

was obtained in the same manner as described in Example 493.

MS m/e (ESI) 518 (MNa^+)

Example 533. 2-Isopropoxy-3-[3-methoxy-4-(4-methoxy-3-methylbenzyloxycarbonylamino)phenyl]propanoic acid

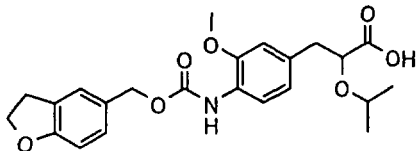


Using 4-methoxy-3-methylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 5 454 (MNa^+)

Example 534.

3-[4-(2,3-Dihydrobenzofuran-5-ylmethoxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid

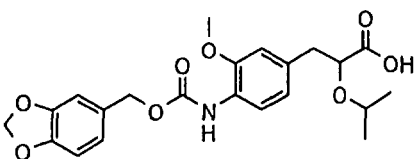


Using (2,3-dihydrobenzofuran-5-yl)methanol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 5 452 (MNa^+)

Example 535.

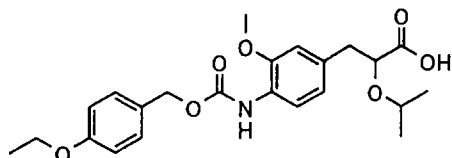
3-[4-(Benzo[1,3]-dioxol-5-ylmethoxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid



Using benzo[1,3]dioxol-5-yl methanol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 5 454 (MNa⁺)

Example 536. 3-[4-(4-Ethoxybenzyloxycarbonylamino)-3-methoxyphenyl]-2-isopropoxypropanoic acid

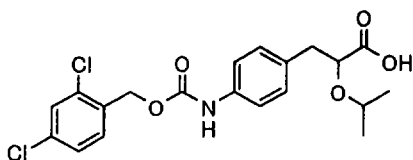


Using 4-ethoxybenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 5 454 (MNa⁺)

Example 537.

3-[4-(2,4-Dichlorobenzoyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid

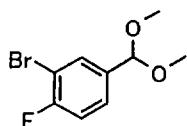


Using 2,4-dichlorobenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

MS m/e (ESI) 5 426 (MH⁺)

Example 538.

a) 2-Bromo-4-fluorobenzaldehyde



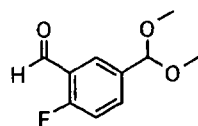
5 g of 3-Bromo-4-fluorobenzaldehyde was dissolved in 40

ml of methanol, and 7.8 g trimethyl o-formate and 0.42 g of p-toluene sulfonic acid were added thereto, and the mixture was stirred at room temperature for 4 hours. The reaction solution was diluted with water and sodium hydrogencarbonate, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated, to give 6.2 g of the title compound.

$^1\text{H-NMR}$ (DMSO-d_6)

δ 3.20(s, 3H) 3.31(s, 3H) 5.48(s, 1H) 7.40(m, 2H) 7.65(m, 1H)

b) 5-Dimethoxymethyl-2-fluorobenzaldehyde

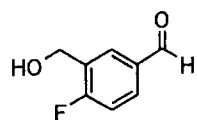


6.2 g of 2-Bromo-4-dimethoxymethyl-1-fluorobenzene was dissolved in 65 ml of tetrahydrofuran, and the solution was cooled to -60°C under a nitrogen gas flow. 18 ml of 1.6M n-Butyl lithium in hexane was added dropwise and the mixture was stirred at -60°C for 1 hour. 3.3 ml of N-Formylmorpholine was added thereto, and the reaction mixture was allowed to warm to room temperature. The mixture was stirred for 1 hour, then ice-cooled, and treated with water and ammonium chloride solution, then extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, to give 2.8 g of the title compound (8% ethyl acetate-hexane).

$^1\text{H-NMR}$ (DMSO-d_6)

δ 3.24(s, 3H) 3.32(s, 3H) 5.45(s, 1H) 7.41(t, J=10.0Hz, 1H) 7.71(t, J=8.0Hz, 1H) 7.82(d, J=8.0Hz, 1H) 10.20(s, 1H)

c) 4-Fluoro-3-hydroxymethylbenzaldehyde

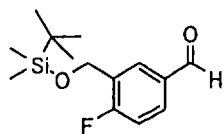


2.8 g of 5-Dimethoxymethyl-2-fluorobenzaldehyde was dissolved in 40 ml of diethyl ether, and 0.38 g of lithium aluminum hydride was added under ice-cooling. After being stirred at room temperature for 5 minutes, the reaction solution was ice-cooled and diethyl ether-water was added. When the insoluble precipitate adhered to the wall of the flask, the reaction solution was dried over anhydrous magnesium sulfate, then evaporated. The residue was dissolved in 25 ml of dichloromethane, and 8 ml of trifluoroacetic acid was added. The reaction mixture was stirred at room temperature for 2.5 hours, the reaction solution was diluted with water and the mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and then evaporated. The residue was subjected to silica gel column chromatography (30% ethyl acetate-hexane), to give 1.6 g of the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 4.85(s, 2H) 7.20(t, J=10.0Hz, 1H) 7.85(t, J=8.0Hz, 1H) 8.04(d, J=8.0Hz, 1H) 9.98(s, 1H)

d) 3-(t-Butyldimethylsilanyloxymethyl)-4-fluorobenzaldehyde

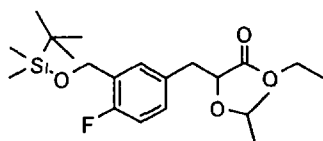


1.6 g of 4-Fluoro-3-hydroxymethylbenzaldehyde was dissolved in 20 ml of dichloromethane, and 1.4 g of imidazole and 1.75 g of t-butyldimethylchlorosilane were added under ice-cooling, then the mixture was stirred at room temperature for 16 hours. The reaction solution was diluted with water and the reaction mixture was extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography (18% ethyl acetate-hexane), to give 2.6 g of the title compound.

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

δ : 0.00 (s, 6H) 0.82 (s, 9H) 4.70 (s, 2H) 7.01 (t, $J=10.0\text{Hz}$, 1H) 7.64 (t, $J=8.0\text{Hz}$, 1H) 7.92 (d, $J=8.0\text{Hz}$, 1H) 9.82 (s, 1H)

e) Ethyl 3-[3-(t-butyldimethylsilyloxymethyl)-4-fluorophenyl]-2-isopropoxypropionate



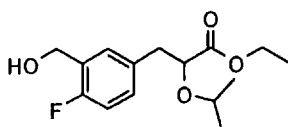
1.36 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 15 ml of tetrahydrofuran, and 0.19 g of 60% sodium hydride was added under ice-cooling, and the mixture was stirred for 20 minutes under ice-cooling. The reaction solution was treated with 1g of 3-(t-butyldimethylsilyloxymethyl)-

4-fluorobenzaldehyde dissolved in 5 ml of tetrahydrofuran, and was stirred at room temperature for 16 hours. The reaction solution was treated with water and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluting with 14% ethyl acetate-hexane was concentrated. The residue was dissolved in 10 ml of ethanol and 10 ml of ethyl acetate, and 0.4 g of 10% palladium-barium sulfate was added, and the atmosphere was replaced with hydrogen, and the mixture was stirred at room temperature for 5 hours. Thereafter, the atmosphere was replaced with nitrogen and the catalyst was filtered off. The solvent was evaporated, and the residue was subjected to silica gel column chromatography (20% ethyl acetate-hexane), to give 1.2 g of the title compound.

¹H-NMR(CDCl₃)

δ : 0.00(s, 6H) 0.82(m, 12H) 1.04(d, J=6.0Hz, 3H) 1.13(t, J=6.0Hz, 1H)
 2.84(m, 2H) 3.49(dq, J=6.0, 6.0Hz, 1H) 3.91(dd, J=7.6, 4.4Hz, 1H)
 4.06(q, J=6.0Hz, 2H) 4.65(s, 2H) 6.80(t, J=10.0Hz, 1H) 6.98(m, 1H)
 7.28(d, J=8.0Hz, 1H)

f) Ethyl 3-(4-fluoro-3-hydroxymethylphenyl)-2-isopropoxypropionate



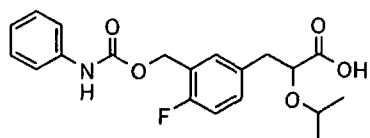
1.2 g of Ethyl 3-[3-(t-butyltrimethylsilyloxymethyl)-4-

fluorophenyl]-2-isopropoxypropionate was dissolved in 15 ml of tetrahydrofuran, and 3.3 ml of 1.0M tetrabutyl ammonium fluoride in tetrahydrofuran was added. The mixture was stirred at room temperature for 2 hours. The reaction solution was diluted with water and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography (30% ethyl acetate-hexane), to give 1.0 g of the title compound.

¹H-NMR(CDCl₃)

δ : 0.95(d, J=6.0Hz, 12H) 1.15(d, J=6.0Hz, 3H) 1.25(t, J=6.0Hz, 1H)
 2.94(m, 2H) 3.49(dq, J=6.0, 6.0Hz, 1H) 4.02(dd, J=7.6, 4.4Hz, 1H)
 4.15(q, J=6.0Hz, 2H) 4.72(s, 2H) 6.95(t, J=10.0Hz, 1H) 7.06(m, 1H)
 7.28(d, J=8.0Hz, 1H)

g) 3-(4-Fluoro-3-phenylcarbamoyloxymethylphenyl)-2-isopropoxypropionic acid



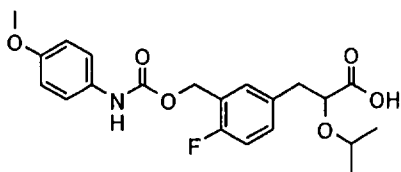
20 mg of Ethyl 3-(4-fluoro-3-hydroxymethylphenyl)-2-isopropoxypropionate and 15 mg of phenylisocyanate were dissolved in 0.6 ml of tetrahydrofuran, and 5 µl of pyridine was added thereto. The mixture was stirred at room temperature for 16 hours. The solvent was removed under a stream of nitrogen, and the residue was dissolved in 0.6 ml of ethanol, then 0.12 ml of 5N sodium hydroxide was added, and the mixture was stirred

at room temperature for 1 hour. The reaction solution was diluted with 1 ml of water and 0.14 ml of 5N hydrochloric acid, and extracted with ethyl acetate. The organic layer was collected, and the solvent was removed under a stream of nitrogen. The residue was purified by HPLC using a reverse phase system column and a water-acetonitrile-trifluoroacetic acid eluent, to give 3.1 mg of the title compound.

MS m/e (ESI) 398 (MNa^+)

Example 539.

3-[4-Fluoro-3-(4-methoxyphenylcarbamoylmethyl)phenyl]-2-isopropoxypropanoic acid

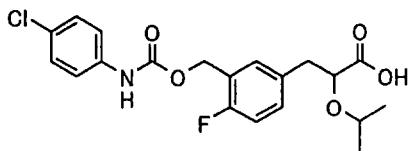


Using 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 428 (MNa^+)

Example 540.

3-[3-(4-Chlorophenylcarbamoylmethyl)-4-fluorophenyl]-2-isopropoxypropanoic acid

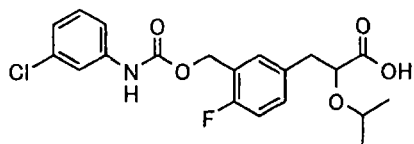


Using 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 432 (MNa^+)

Example 541.

3-[3-(3-Chlorophenylcarbamoylmethyl)-4-fluorophenyl]-2-isopropoxypropanoic acid

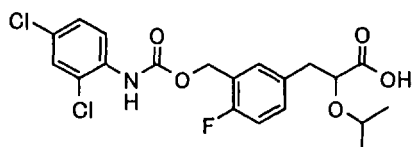


Using 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 432 (MNa^+)

Example 542.

3-[3-(2,4-Dichlorophenylcarbamoylmethyl)-4-fluorophenyl]-2-isopropoxypropanoic acid

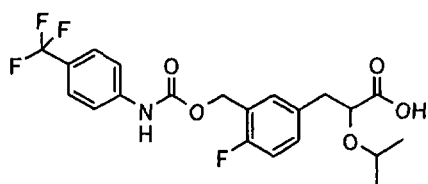


Using 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 466 (MNa^+)

Example 543.

3-[4-Fluoro-3-(4-trifluoromethylphenylcarbamoylmethyl)-phenyl]-2-isopropoxypropanoic acid

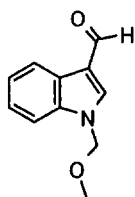


Using 4-trifluoromethylphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 466 (MNa^+)

Example 544.

a) 1-Methoxymethyl-1H-indol-3-aldehyde

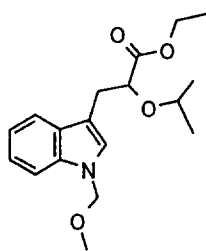


5 g of Indol-3-aldehyde was dissolved in 40 ml of N,N-dimethylformamide, and 1.38 g of 60% sodium hydride was added under ice-cooling. The reaction solution was stirred for 20 minutes with ice-cooling, then 3.2 ml of chloromethyl methyl ether was added, and stirring was continued at room temperature for 16 hours. The reaction solution was cooled in ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, to give 6.1 g of the title compound (20-44% ethyl acetate-hexane).

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

δ : 3.30(s, 3H) 5.51(s, 2H) 7.36(m, 2H) 7.53(d, $J=8.0\text{Hz}$, 1H) 7.80(s, 1H) 8.31(d, $J=8.0\text{Hz}$, 1H) 10.10(s, 1H)

b) Ethyl 2-isopropoxy-3-(1-methoxymethyl-1H-indol-3-yl)propionate



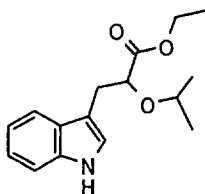
3.9 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 35 ml of tetrahydrofuran, and 0.51 g of 60% sodium hydride was added under ice-cooling, and the mixture was stirred for 20 minutes under ice-cooling. The reaction solution was treated with a solution of 2 g of 1-methoxymethyl-1H-indol-3-aldehyde in 10 ml of tetrahydrofuran, and then stirred at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluting with 22% ethyl acetate-hexane was evaporated, and the residue was dissolved in 30 ml of ethanol. To this solution was added 0.5 g of 10% palladium carbon, the atmosphere was replaced with hydrogen, and the mixture was stirred at room temperature for 3 days. The atmosphere was replaced with nitrogen, the catalyst was filtered off, and the solvent was evaporated, to give 2.3 g of the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$

δ : 1.00(d, $J=6.0\text{Hz}$, 3H) 1.20(m, 6H) 3.10(dd, $J=14.0, 6.0\text{Hz}$, 1H) 3.20(m, 4H) 3.55(dq, $J=6.0, 6.0\text{Hz}$, 1H) 4.15(m, 3H) 5.40(dd, $J=6.0, 10.0\text{Hz}$, 2H)

7.18(s, 1H) 7.15(t, J=8.0Hz, 1H) 7.20(d, J=8.0Hz, 1H) 7.44(d, J=8.0Hz, 1H) 7.63(dd, J=2.0, 8.0Hz, 1H)

c) Ethyl 3-(1H-indol-3-yl)-2-isopropoxypropionate



2.3 g of Ethyl

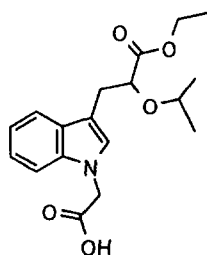
2-isopropoxy-3-(1-methoxymethyl-1H-indol-3-yl)propionate was dissolved in 25 ml of acetone, and 15 ml of 5N hydrochloric acid was added, and the mixture was stirred for 2 hours. The reaction solution was cooled with ice, treated with water and sodium hydrogencarbonate, and extracted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was dissolved in 20 ml of ethanol, and an aqueous solution containing 2g of potassium carbonate was added, and the mixture was stirred at 50°C for 3 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and then evaporated. The residue was subjected to silica gel column chromatography (50% ethyl acetate-hexane), to give 0.75 g of the title compound.

¹H-NMR (CDCl₃)

δ : 1.00(d, J=6.0Hz, 3H) 1.18(m, 6H) 3.10(dd, J=14.0, 6.0Hz, 1H)

3.20(dd, J=14.0, 4.4Hz, 1H) 3.55(dq, J=6.0, 6.0Hz, 1H) 4.15(m, 3H)
7.05-7.20(m, 3H) 7.35(d, J=8.0Hz, 1H) 7.63(d, J=8.0Hz, 1H)

d) Ethyl 3-(1-carboxymethyl-1H-indol-3-yl)-2-
isopropoxypropionate



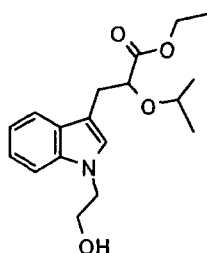
0.75 g of Ethyl 3-(1H-indol-3-yl)-2-isopropoxypropionate was dissolved in 10 ml of N,N-dimethylformamide, and 0.12 g of 60% sodium hydride was added under ice-cooling. The reaction mixture was stirred at room temperature for 30 minutes, 0.53 ml of t-butyl bromoacetate was added, and stirring was continued at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluted with 10% ethyl acetate-hexane was evaporated, and the residue was dissolved in 15 ml of dichloromethane. 3 ml of Trifluoroacetic acid was added under ice-cooling, and the mixture was stirred at 0°C for 7 hours. The reaction solution was diluted with toluene, and the solvent was evaporated. The residue was subjected to silica gel column chromatography (33% ethyl acetate-hexane), to give

0.3 g of the title compound.

¹H-NMR(CDCl₃)

δ : 1.00(d, J=6.0Hz, 3H) 1.18(m, 6H) 3.10(dd, J=14.0, 6.0Hz, 1H)
3.20(dd, J=14.0, 4.4Hz, 1H) 3.54(dq, J=6.0, 6.0Hz, 1H) 4.13(m, 3H)
4.83(s, 2H) 6.97(s, 1H) 7.05-7.20(m, 3H) 7.65(d, J=8.0Hz, 1H)

e) Ethyl 3-[1-(2-hydroxyethyl)-1H-indol-3-yl]-2-
isopropoxypropionate

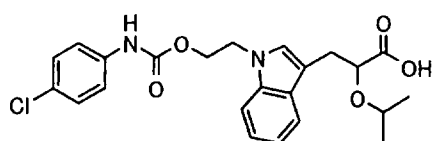


0.3 g of Ethyl 3-(1-carboxymethyl-1H-indol-3-yl)-2-isopropoxypropionate was dissolved in 10 ml of tetrahydrofuran, and 0.2 ml of triethylamine was added under ice-cooling, followed by 0.1 ml of ethyl chloroformate, then the mixture was stirred at 0°C for 15 minutes. After filtering off the precipitated insoluble substances, the reaction solution was again cooled with ice, and 60 mg of sodium borohydride and water were added, and stirring was continued at room temperature for 1 hour. The reaction solution was cooled with ice, acidified with diluted hydrochloric acid, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography (33% ethyl acetate-hexane), to give 143 mg of the title compound.

¹H-NMR (CDCl₃)

δ : 0.98 (d, J=6.0Hz, 3H) 1.15 (m, 6H) 3.00-3.15 (m, 2H) 3.50 (dq, J=6.0, 6.0Hz, 1H) 3.85 (t, J=6.0Hz, 2H) 4.06 (m, 3H) 4.17 (t, J=6.0Hz, 2H) 7.00 (s, 1H) 7.05 (d, J=8.0Hz, 1H) 7.13 (t, J=8.0Hz, 1H) 7.28 (d, J=8.0Hz, 1H) 7.57 (d, J=8.0Hz, 1H)

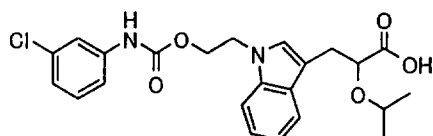
f) 3-{1-[2-(4-Chlorophenylcarbamoyloxy)ethyl]-1H-indol-3-yl}-2-isopropoxypropanoic acid



Using 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 536g).

MS *m/e*(ESI) 445 (MH⁺)

Example 545. 3-{1-[2-(3-Chlorophenylcarbamoyloxy)ethyl]-1H-indol-3-yl}-2-isopropoxypropanoic acid

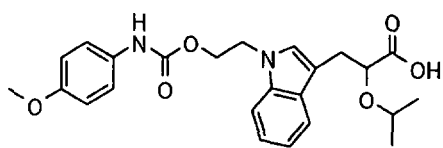


Using 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS *m/e*(ESI) 445 (MH⁺)

Example 546.

2-Isopropoxy-3-{1-[2-(4-methoxyphenylcarbamoyloxy)ethyl]-1H-indol-3-yl}propanoic acid

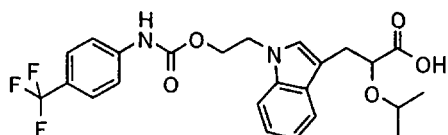


Using 4-methoxyphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 441 (MH^+)

Example 547.

2-Isopropoxy-3-(1-[2-(4-trifluoromethylphenyl)carbamoyloxy]-ethyl)-1H-indol-3-yl)propanoic acid

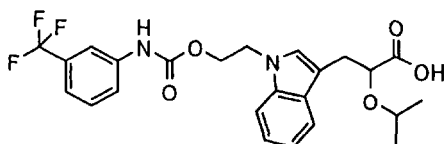


Using 4-trifluoromethylphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 479 (MH^+)

Example 548.

2-Isopropoxy-3-(1-[2-(3-trifluoromethylphenyl)carbamoyloxy]-ethyl)-1H-indol-3-yl)propanoic acid

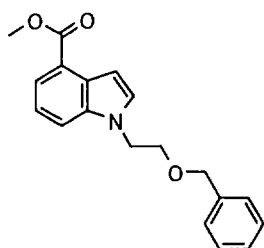


Using 3-trifluoromethylphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 479 (MH^+)

Example 549.

a) Methyl 1-(2-benzyloxyethyl)-1H-indol-4-carboxylate

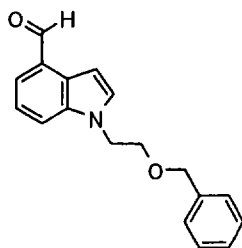


2.75 g of Methyl 1H-indol-4-carboxylate was dissolved in 10 ml of N,N-dimethylformamide, and 0.7 g of 60% sodium hydride was added under ice-cooling. The reaction solution was stirred at room temperature for 30 minutes, treated with 2.5 ml of benzyl 2-bromoethyl ether, and stirred at room temperature for a further 2 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography (8% ethyl acetate-hexane), to give 3.6 g of the title compound.

¹H-NMR (CDCl₃)

δ : 3.78 (t, J=6.0Hz, 2H) 3.99 (s, 3H) 4.37 (t, J=6.0Hz, 2H) 4.43 (s, 2H)
7.12-7.27 (m, 7H) 7.32 (s, 1H) 7.55 (d, J=8.0Hz, 1H) 7.91 (d, J=8.0Hz, 1H)

b) 1-(2-Benzyloxyethyl)-1H-indol-4-aldehyde



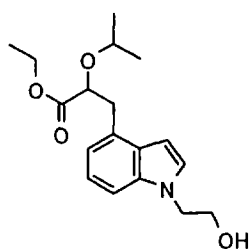
3.6 g of Methyl 1-(2-benzyloxyethyl)-1H-indol-4-

carboxylate was dissolved in 40 ml of diethyl ether, and 0.44 g of lithium aluminum hydride was added under ice-cooling. After stirring at room temperature for 10 minutes, the reaction solution was cooled with ice, and diethyl ether and water were added. When the insoluble substances adhered to and solidified on the wall of the flask, the reaction solution was dried over anhydrous magnesium sulfate, then the solvent was evaporated. The residue was dissolved in 40 ml of dichloromethane, 20 g of manganese dioxide was added, and the mixture was stirred at room temperature for 2 hours. After filtering off the manganese dioxide through Celite, and washing through with ethyl acetate, the solvent was evaporated, to give 1.5 g of the title compound.

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

δ : 3.80 (t, $J=6.0\text{Hz}$, 2H) 4.37 (t, $J=6.0\text{Hz}$, 2H) 4.43 (s, 2H) 7.16 (m, 2H)
7.20-7.27 (m, 5H) 7.38 (s, 1H) 7.63 (m, 2H) 10.25 (s, 1H)

c) Ethyl 3-[1-(2-hydroxyethyl)-1H-indol-4-yl]-2-isopropoxypropionate



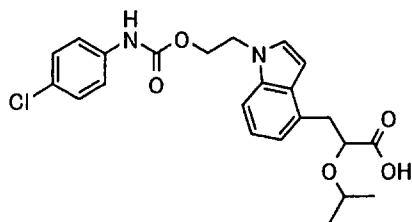
1.3 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 15 ml of tetrahydrofuran, and 0.18 g of 60% sodium hydride was added under ice-cooling, and the mixture was stirred for 20 minutes under ice-cooling. The reaction solution was treated with a solution of 1g of 1-(2-benzyloxyethyl)-1H-

indol-4-aldehyde in 5 ml of tetrahydrofuran, and stirred at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluted with 20% ethyl acetate-hexane was evaporated and the residue was dissolved in 10 ml of ethanol and 10 ml of acetic acid. The solution was treated with 0.5 g of 10% palladium carbon, the atmosphere was replaced with hydrogen, and the mixture was stirred at room temperature for 24 hours. The atmosphere was replaced with nitrogen, the catalyst filtered off, and the solvent was evaporated, to give 0.2 g of the title compound.

¹H-NMR(CDCl₃)

δ : 0.92(d, J=6.0Hz, 12H) 1.13(d, J=6.0Hz, 3H) 1.17(t, J=6.0Hz, 1H)
 3.23(dd, J=14.0, 6.0Hz, 1H) 3.32(dd, J=14.0, 4.4Hz, 1H) 3.47(dq, J=6.0,
 6.0Hz, 1H) 3.96(t, J=6.0Hz, 2H) 4.14(q, J=6.0Hz, 2H) 4.22(dd, J=7.6,
 4.4Hz, 1H) 4.29(t, J=6.0Hz, 2H) 6.60(d, J=4.5Hz, 1H) 7.00(d, J=8.0Hz,
 1H) 7.10(d, J=8.0Hz, 1H) 7.15(s, 1H) 7.25(m, 1H)

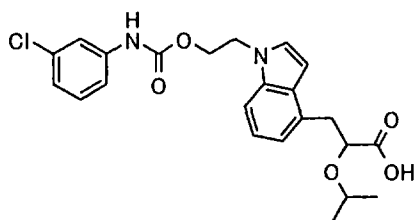
d) 3-{1-[2-(4-Chlorophenylcarbamoyloxy)ethyl]-1H-indol-4-yl}-2-isopropoxypropanoic acid



Using 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 536g).

MS m/e (ESI) 445 (MH^+)

Example 550. 3-{1-[2-(3-Chlorophenylcarbamoyloxy)ethyl]-1H-indol-4-yl}-2-isopropoxypropanoic acid

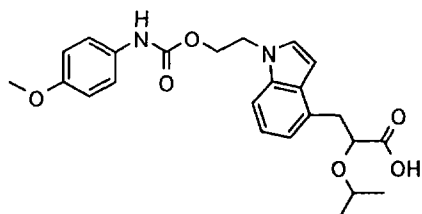


Using 3-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 445 (MH^+)

Example 551.

2-Isopropoxy-3-{1-[2-(4-methoxyphenylcarbamoyloxy)ethyl]-1H-indol-4-yl}propanoic acid

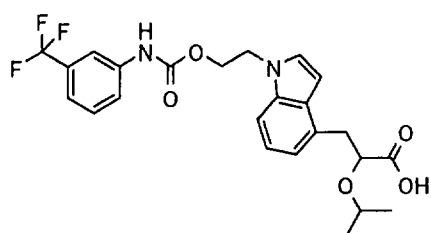


Using 4-chlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 441 (MH^+)

Example 552.

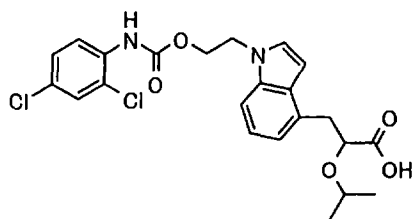
2-Isopropoxy-3-{1-[2-(3-trifluoromethylphenylcarbamoyloxy)ethyl]-1H-indol-4-yl}propanoic acid



Using 3-trifluoromethylphenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 479 (MH^+)

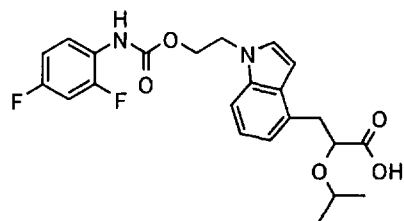
Example 553. 3-((1-((2-(2,4-Dichlorophenyl)carbamoyloxy)ethyl)-1H-indol-4-yl)-2-isopropoxypropanoic acid



Using 2,4-dichlorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 479 (MH^+)

Example 554. 3-((1-((2-(2,4-Difluorophenyl)carbamoyloxy)ethyl)-1H-indol-4-yl)-2-isopropoxypropanoic acid

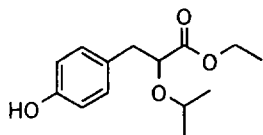


Using 2,4-difluorophenylisocyanate, the title compound was obtained in the same manner as described in Example 538g).

MS m/e (ESI) 447 (MH^+)

Example 555.

a) Ethyl 3-(4-hydroxyphenyl)-2-isopropoxypropanoate



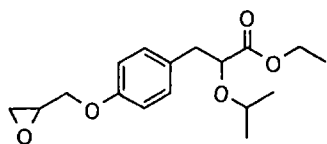
5.2 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 40 ml of tetrahydrofuran, and 0.53 g of 60% sodium hydride was added under ice-cooling, and the mixture was stirred for 20 minutes under ice-cooling. The reaction solution was treated with a solution of 3.0 g of 4-benzyloxybenzaldehyde in 15 ml of tetrahydrofuran and 10 ml of N,N-dimethylformamide, and stirred at room temperature for 16 hours. The reaction solution was diluted with water, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluting with 5% ethyl acetate-hexane was concentrated. The residue was dissolved in 40 ml of ethanol, and 0.4 g of 10% palladium carbon was added, the atmosphere was replaced with hydrogen, and the mixture was stirred at room temperature for 5 hours. Then, the atmosphere was replaced with nitrogen, the catalyst was filtered off, and the solvent was evaporated. The residue was subjected to silica gel column chromatography (20% ethyl acetate-hexane), to give 2.7 g of the title compound.

^1H NMR (CDCl_3)

δ : 0.98 (d, $J=6.4\text{Hz}$, 3H) 1.16 (d, $J=6.4\text{Hz}$, 3H) 1.24 (t, $J=7.2\text{Hz}$, 3H)

2.85-2.95 (m, 2H) 3.52 (Sept, J=6.0Hz, 1H) 4.05 (dd, J=4.8, 8.8Hz, 1H)
4.12-4.19 (m, 2H) 4.86 (br, 1H) 6.73(d, J=8.0Hz, 2H) 7.10(d, J=8.0Hz, 2H)

b) Ethyl 2-isopropoxy-3-[4-(2-oxiranymethoxy)phenyl]-propanoate

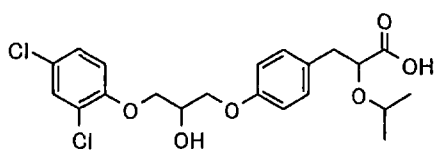


Using ethyl 3-(4-hydroxyphenyl)-2-isopropoxypropanoate, the title compound was obtained in the same manner as described in Production example 1b).

¹H NMR (CDCl₃)

δ : 0.96 (d, J=6.4Hz, 3H) 1.15 (d, J=6.4Hz, 3H) 1.24 (t, J=7.2Hz, 3H) 2.75 (dd, J=2.8, 4.8Hz, 1H) 2.83-2.93 (m, 3H) 3.34 (dt, J=2.8, 9.6Hz, 1H) 3.50 (Sept, J=6.0Hz, 1H) 3.94 (dd, J=5.6, 11.2Hz, 1H) 4.00 (dd, J=4.8, 8.8Hz, 1H) 4.15-4.22 (m, 2H) 6.82(d, J=8.0Hz, 2H) 7.15(d, J=8.0Hz, 2H)

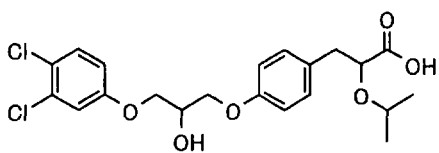
c) 3-{4-[3-(2,4-Dichlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 2,4-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 443 (MH⁺)

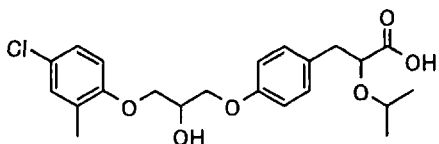
Example 556. 3-{4-[3-(3,4-Dichlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 465 (MNa^+)

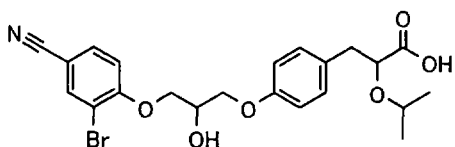
Example 557. 3-{4-[3-(4-Chloro-2-methylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chloro-2-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 445 (MNa^+)

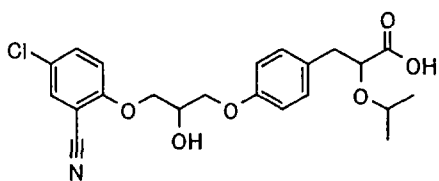
Example 558. 3-{4-[3-(2-Bromo-4-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 2-bromo-4-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 478 (MH^+)

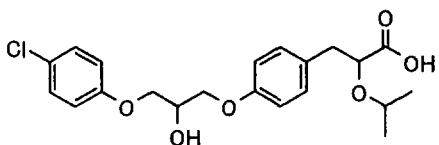
Example 559. 3-{4-[3-(4-Chloro-2-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 456 (MNa^+)

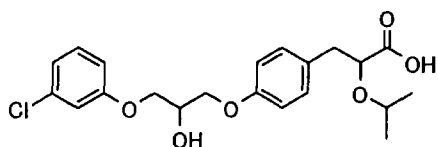
Example 560. 3-{4-[3-(4-Chlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 431 (MNa^+)

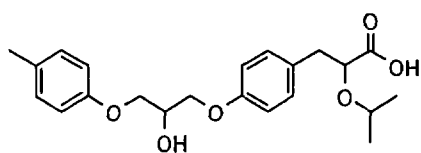
Example 561. 3-{4-[3-(3-Chlorophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 431 (MNa^+)

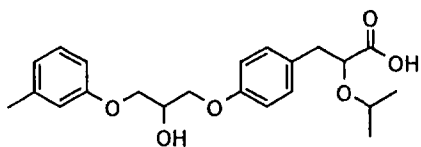
Example 562. 3-[4-(2-Hydroxy-3-p-tolyloxypropoxy)phenyl]-2-isopropoxypropanoic acid



Using 4-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 411 (MNa^+)

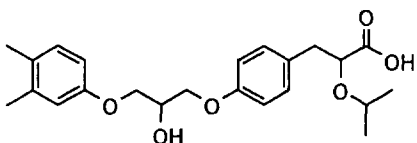
Example 563. 3-[4-(2-Hydroxy-3-m-tolyloxypropoxy)phenyl]-2-isopropoxypropanoic acid



Using 3-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 389 (MH^+)

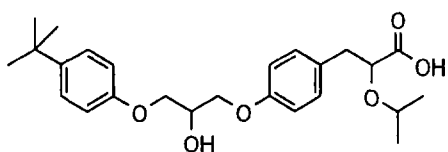
Example 564. 3-{4-[3-(3,4-Dimethylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3,4-dimethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 425 (MNa^+)

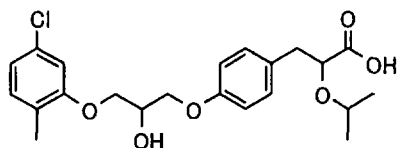
Example 565. 3-{4-[3-(4-t-Butylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 4-*t*-butyl phenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 453 (MNa⁺)

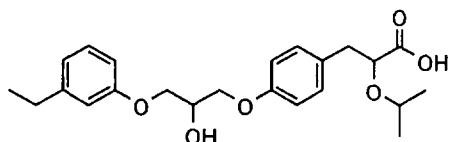
Example 566. 3-{4-[3-(5-Chloro-2-methylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid



Using 3-chloro-6-methylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 445 (MNa⁺)

Example 567. 3-{4-[3-(3-Ethylphenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid

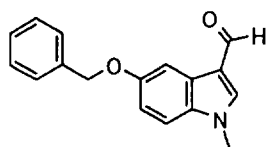


Using 3-ethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS *m/e*(ESI) 425 (MNa⁺)

Example 568.

a) 5-Benzoyloxy-1-methyl-1H-indol-3-aldehyde

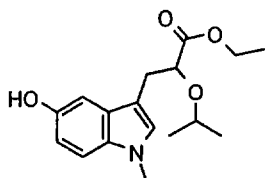


5 g of 5-Benzyloxyindol-3-aldehyde was dissolved in 50 ml of N,N-dimethylformamide, and 0.84 g of 60% sodium hydride was added under ice-cooling. The reaction solution was stirred at room temperature for 30 minutes, 2.5 ml of methyl iodide was added and stirring was continued at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride, and extracted with ethyl acetate and tetrahydrofuran. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was treated with diethyl ether and filtered, to give 4.6 g of the title compound.

¹H-NMR (CDCl₃)

δ : 3.83 (s, 3H) 5.15 (s, 2H) 7.06 (dd, J=2.0, 8.0 Hz, 1H) 7.26 (m, 2H) 7.33 (m, 1H) 7.40 (m, 2H) 7.50 (m, 2H) 7.62 (s, 1H) 7.91 (d, J=2.0 Hz, 1H) 9.92 (s, 1H)

b) Ethyl 3-(5-hydroxy-1-methyl-1H-indol-3-yl)-2-isopropoxypropionate



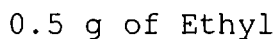
3.2 g of Ethyl 2-(diethylphosphoryl)-2-isopropylacetate was dissolved in 25 ml of tetrahydrofuran, and 0.44 g of 60% sodium hydride was added under ice-cooling, and stirring was

continued for 20 minutes under ice-cooling. The reaction solution was treated with a solution of 2 g of 5-benzyloxy-1-methyl-1H-indol-3-aldehyde in 5 ml of tetrahydrofuran and 5 ml of N,N-dimethylformamide, and stirred at 50°C for one hour and then at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography, and the fraction eluting with 20% ethyl acetate-hexane was evaporated and the residue was dissolved in 10 ml of ethanol. 0.6 g of 10% Palladium carbon was added to this solution, the atmosphere was replaced with hydrogen, and the mixture was stirred at room temperature for 24 hours. The reaction atmosphere was replaced with nitrogen, the catalyst was filtered off, and the solvent was evaporated. The residue was subjected to silica gel column chromatography (30% ethyl acetate hexane), to give 2 g of the title compound.

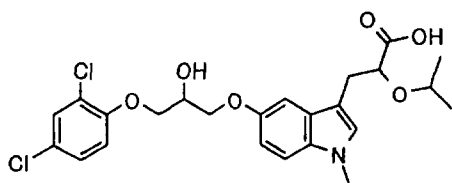
¹H-NMR(CDCl₃)

δ : 1.00(d, J=6.0Hz, 3H) 1.18(m, 6H) 3.05(dd, J=14.0, 6.0Hz, 1H)
3.12(dd, J=14.0, 4.4Hz, 1H) 3.55(dq, J=6.0, 6.0Hz, 1H) 3.70(s, 3H)
4.15(m, 3H) 6.77(dd, J=2.0, 8.0Hz, 1H) 6.91(s, 1H) 7.02(s, 1H) 7.11(d, J=2.0Hz, 1H)

c) Ethyl 2-isopropoxy-3-(1-methyl-5-oxilanylmethoxy-1H-indol-3-yl)propionate

¹H-NMR (CDCl₃)

d) 3-(5-[3-(2,4-Dichlorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl)-2-isopropoxypropanoic acid

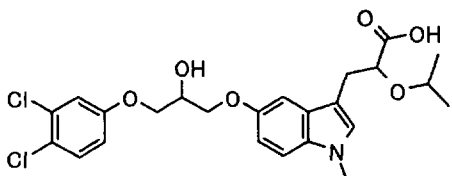


Using 2,4-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 496 (MH^+)

Example 569.

3-{5-[3-(3,4-Dichlorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

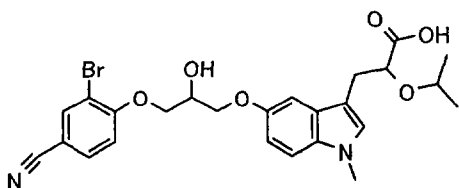


Using 3,4-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 496 (MH^+)

Example 570.

3-{5-[3-(2-Bromo-4-cyanophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

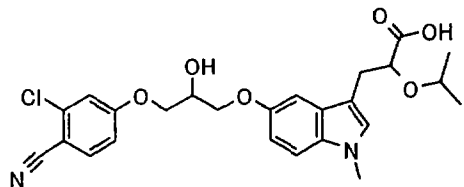


Using 2-bromo-4-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 531 (MH^+)

Example 571.

3-{5-[3-(3-Chloro-4-cyanophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

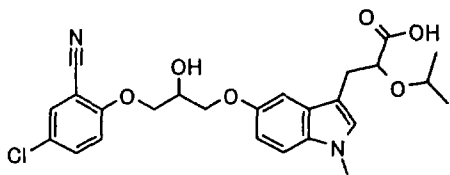


Using 3-chloro-4-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 487 (MH^+)

Example 572.

3-{5-[3-(4-Chloro-2-cyanophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

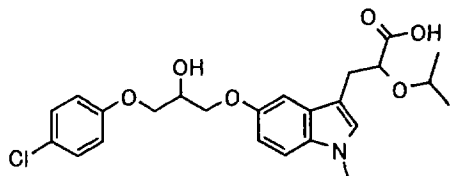


Using 4-chloro-2-cyanophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 487 (MH^+)

Example 573.

3-{5-[3-(4-Chlorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

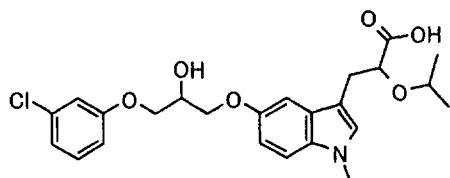


Using 4-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 462 (MH^+)

Example 574.

3-{5-[3-(3-Chlorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

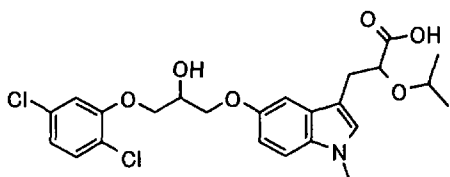


Using 3-chlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 462 (MH^+)

Example 575.

3-{5-[3-(2,5-Dichlorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid

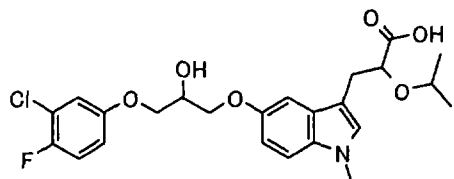


Using 2,5-dichlorophenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 496 (MH^+)

Example 576.

3-{5-[3-(3-Chloro-4-fluorophenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid



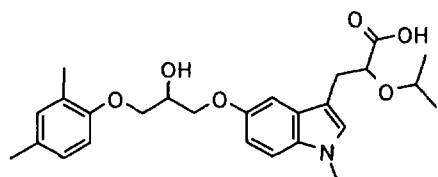
Using 3-chloro-4-fluorophenol, the title compound was

obtained in the same manner as described in Example 1c).

MS m/e (ESI) 480 (MH^+)

Example 577.

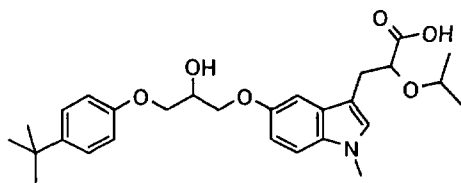
3-{5-[3-(2,4-Dimethylphenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid



Using 2,4-dimethylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 456 (MH^+)

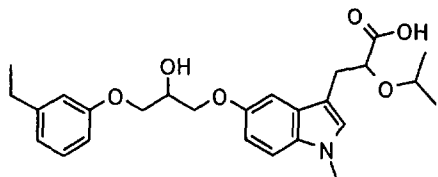
Example 578. 3-{5-[3-(4-t-Butylphenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid



Using 4-t-butylphenol, the title compound was obtained in the same manner as described in Example 1c).

MS m/e (ESI) 484 (MH^+)

Example 579. 3-{5-[3-(3-Ethylphenoxy)-2-hydroxypropoxy]-1-methyl-1H-indol-3-yl}-2-isopropoxypropanoic acid



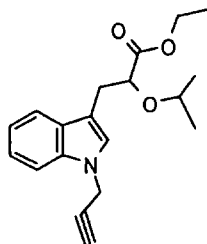
Using 3-ethylphenol, the title compound was obtained in

the same manner as described in Example 1c).

MS m/e (ESI) 456 (MH⁺)

Example 580.

a) Ethyl 2-isopropoxy-3-(1-prop-2-ynyl-1H-indol-3-yl)propionate

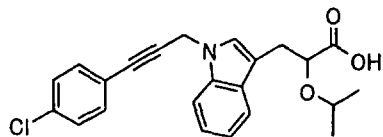


0.23 g of Ethyl 3-(1H-indol-3-yl)-2-isopropoxypropionate was dissolved in 5 ml of N,N-dimethylformamide, and 34 mg of 60% sodium hydride was added under ice-cooling. The reaction solution was stirred for 30 minutes under ice-cooling, then 0.09 ml of propargyl bromide was added, and stirring was continued at room temperature for 16 hours. The reaction solution was cooled with ice, treated with water and ammonium chloride solution, and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous magnesium sulfate, and evaporated. The residue was subjected to silica gel column chromatography (9% ethyl acetate-hexane), to give 0.18 g of the title compound.

¹H-NMR(CDCl₃)

δ : 1.00(d, J=6.0Hz, 3H) 1.18(m, 6H) 3.10(dd, J=14.0, 6.0Hz, 1H)
3.20(dd, J=14.0, 4.4Hz, 1H) 3.55(dq, J=6.0, 6.0Hz, 1H) 4.13(m, 3H)
4.83(s, 2H) 7.13(m, 3H) 7.22(d, J=8.0Hz, 1H) 7.35(d, J=8.0Hz, 1H)
7.64(d, J=8.0Hz, 1H)

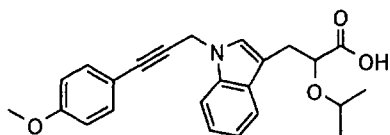
b) 3-(1-[3-(4-Chlorophenyl)prop-2-ynyl]-1H-indol-3-yl)-2-isopropoxypropanoic acid



Using 1-chloro-4-iodobenzene, the title compound was obtained in the same manner as described in Example 77b).

MS m/e (ESI) 396 (MH^+)

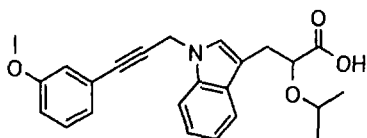
Example 581. 2-Isopropoxy-3-(1-[3-(4-methoxyphenyl)prop-2-ynyl]-1H-indol-3-yl)propanoic acid



Using 4-iodoanisole, the title compound was obtained in the same manner as described in Example 77b).

MS m/e (ESI) 392 (MH^+)

Example 582. 2-Isopropoxy-3-(1-[3-(3-methoxyphenyl)prop-2-ynyl]-1H-indol-3-yl)propanoic acid



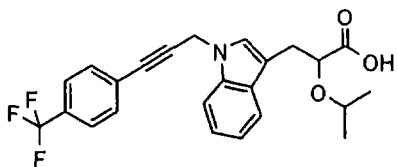
Using 3-iodoanisole, the title compound was obtained in the same manner as described in Example 77b).

MS m/e (ESI) 392 (MH^+)

Example 583.

2-Isopropoxy-3-(1-[3-(4-trifluoromethylphenyl)prop-2-ynyl]-

1H-indol-3-yl}propanoic acid

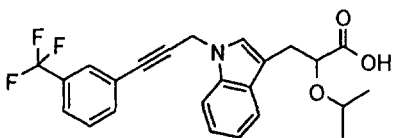


Using 4-iodobenzotrifluoride, the title compound was obtained in the same manner as described in Example 77b).

MS m/e (ESI) 430 (MH^+)

Example 584.

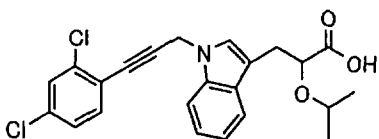
2-Isopropoxy-3-{1-[3-(3-trifluoromethylphenyl)prop-2-ynyl]-1H-indol-3-yl}propanoic acid



Using 3-iodobenzotrifluoride, the title compound was obtained in the same manner as described in Example 77b).

MS m/e (ESI) 430 (MH^+)

Example 585. 3-{1-[3-(2,4-Dichlorophenyl)prop-2-ynyl]-1H-indol-3-yl}-2-isopropoxypropanoic acid



Using 2,4-dichloroiodobenzene, the title compound was obtained in the same manner as described in Example 77b).

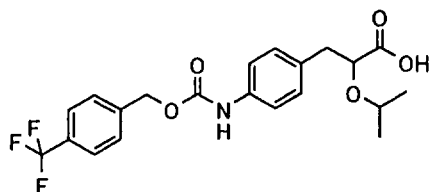
^1H -NMR ($CDCl_3$)

δ : 1.04(d, J =6.0Hz, 3H) 1.15(d, J =6.0Hz, 3H) 3.15(dd, J =14.0, 6.0Hz, 1H)
3.31(dd, J =14.0, 4.4Hz, 1H) 3.61(dq, J =6.0, 6.0Hz, 1H) 4.23(dd, J =7.6,

4.4Hz, 1H) 5.11(s, 2H) 7.15-7.20(m, 3H) 7.25(m, 1H) 7.34(d, J=8.0Hz, 1H) 7.40(d, J=2.0Hz, 2H) 7.44(d, J=8.0Hz, 1H) 7.67(d, J=8.0Hz, 1H)
MS m/e (ESI) 480 (MH⁺)

Example 586.

3-[4-(4-Trifluoromethylbenzyloxycarbonylamino)phenyl]-2-isopropoxypropanoic acid



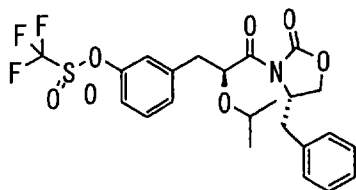
Using 4-trifluoromethylbenzyl alcohol, the title compound was obtained in the same manner as described in Example 493.

¹H-NMR(CDCl₃)

δ :1.03(d, J=6.0Hz, 3H) 1.16(d, J=6.0Hz, 3H) 2.91(dd, J=14.0, 6.0Hz, 1H) 3.09(dd, J=14.0, 4.4Hz, 1H) 3.55(dq, J=6.0, 6.0Hz, 1H) 4.12(dd, J=7.6, 4.4Hz, 1H) 5.25(s, 2H) 6.71(s, 1H) 7.19(d, J=8.0Hz, 2H) 7.32(d, J=8.0Hz, 2H) 7.51(d, J=8.0Hz, 2H) 7.63(d, J=8.0Hz, 2H)

Example 587. 3-{3-[3-(2,4-Dichlorophenoxy)-1-propynyl]-phenyl}-2(S)-isopropoxypropanoic acid

Production example 587a) 3-[3-(4-Benzyl-2-(oxo)-oxazolidin-3-yl)-2-isopropoxy-3-oxo-propyl]-phenyl trifluoromethanesulfonate

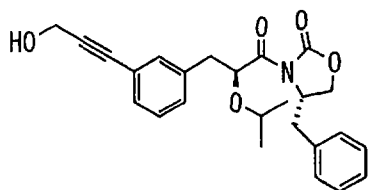


1.002 g of 4(S)-Benzyl-3-[3-(3-hydroxyphenyl)-2(S)-isopropoxypropionyl]-oxazolidin-2-one was dissolved in 15 ml of dichloromethane, and 0.4 ml of triethylamine, 16 ml of N,N-dimethylaminopyridine and 950 mg of N-phenyltrifluoromethanesulfonylimide were added under ice-cooling. After being stirred overnight at room temperature, the reaction solution was diluted with ethyl acetate and the organic layer was successively washed with 1N hydrochloric acid and saturated brine, then dried over anhydrous magnesium sulfate. The solvent was evaporated and the residue was purified by silica gel column chromatography, to give 1.492 g of the title compound as a colorless oil in the 2:1 hexane-ethyl acetate fraction.

^1H NMR (CDCl_3)

δ : 0.91 (d, $J=6.4\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 2.78-2.90 (m, 2H) 3.02-3.09 (m, 1H) 3.36 (dd, $J=2.4, 13.2\text{Hz}$, 1H) 3.45 (Sept, $J=6.4\text{Hz}$, 1H) 4.18-4.24 (m, 2H) 4.64-4.69 (m, 1H) 5.23 (dd, $J=2.4, 9.2\text{Hz}$, 1H) 7.14-7.41 (m, 9H)

Production example 587b) 4-Benzyl-3-{3-[3-(3-hydroxy-1-propynyl)phenyl]-2-isopropoxypropionyl}-oxazolidin-2-one



390 mg of 3-[3-(4-Benzyl-2-(oxo)-oxazolidin-3-yl)-2-isopropoxy-3-oxo-propyl]-phenyl trifluoromethanesulfonate was dissolved in 2 ml of N,N-dimethylformamide, 85 mg of propargyl alcohol, 8 mg of copper iodide, 45 mg of tetrakis

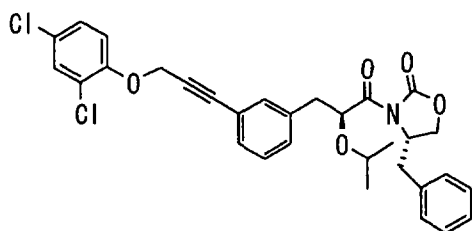
(triphenylphosphine)palladium and 0.3 ml of triethylamine were added in succession, and the mixture was stirred overnight at 50°C under a nitrogen atmosphere. The reaction solution was filtered through silica gel, and the filtrate was dissolved in ethyl acetate, washed with water, 1N hydrochloric acid and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 207 mg of the title compound as a colorless oil in the 3:2 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 0.98 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.76-2.88 (m, 2H) 2.96 (dd, J=4.4, 13.2Hz, 1H) 3.33 (dd, J=2.8, 10.4Hz, 1H) 3.47 (Sept, J=6.0Hz, 1H) 4.13-4.19 (m, 2H) 4.48 (d, J=6.0Hz, 1H) 4.56-4.62 (m, 1H) 5.30 (dd, J=4.4, 9.2Hz, 1H) 7.16-7.18 (m, 1H) 7.21-7.36 (m, 8H)

Production example 587c)

4-Benzyl-3-(3-{3-[3-(2,4-dichloro-phenoxy)-1-propynyl]-phenyl}-2-isopropoxypropionyl)-oxazolidin-2-one

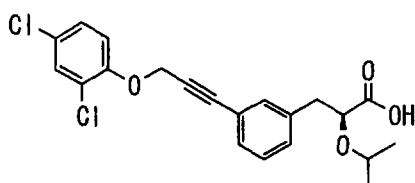


Using 4-benzyl-3-{3-[3-(3-hydroxy-1-propynyl)phenyl]-2-isopropoxypropionyl}oxazolidin-2-one, the title compound was obtained in the same manner as described in Production examples 102c) and Example 102d).

¹H NMR (CDCl₃)

δ : 0.98 (d, J=6.0Hz, 3H) 1.15 (d, J=6.4Hz, 3H) 2.77-2.93 (m, 2H) 2.96 (dd, J=4.4, 13.6Hz, 1H) 3.32 (dd, J=3.6, 13.2Hz, 1H) 3.45 (Sept, J=6.0Hz, 1H) 4.13-4.19 (m, 2H) 4.57-4.61 (m, 1H) 4.97 (s, 2H) 5.27 (dd, J=4.0, 9.2Hz, 1H) 7.10 (d, J=8.8Hz, 1H) 7.17-7.39 (m, 11H)

Example 587d) 3-{3-[3-(2,4-Dichlorophenoxy)-1-propynyl]-phenyl}-2(S)-isopropoxypropanoic acid



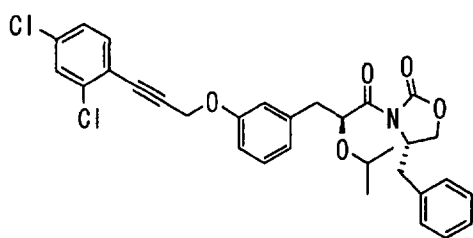
Using 4-benzyl-3-(3-{3-[3-(2,4-dichlorophenoxy)-1-propynyl]phenyl}-2-isopropoxypropionyl)oxazolidin-2-one, an hydrolysis reaction was conducted in the same manner as described in Production example 279d), and after purification by reverse-phase high performance liquid chromatography, the title compound was obtained.

MS *m/e*(ESI) 429(MNa⁺)

Example 588. 3-{3-[3-(2,4-Dichlorophenyl)-2-propynyloxy]-phenyl}-2(S)-isopropoxypropanoic acid

Production example 588a)

4-Benzyl-3-(3-{3-[3-(2,4-dichlorophenyl)-2-propynyloxy]-phenyl}-2-isopropoxypropanoyl)oxazolidin-2-one

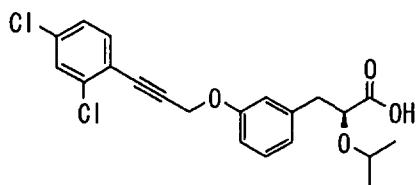


Using 4(S)-benzyl-3-[3-(3-hydroxyphenyl)-2(S)-isopropoxypropynyl]oxazolidin-2-one and 1-(3-bromo-1-propynyl)-2,4-dichlorobenzene, the title compound was obtained in the same manner as described in Production example 77a).

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 2.77 (dd, J=8.8, 13.2Hz, 1H) 2.89-3.00 (m, 1H) 2.77-3.32 (m, 2H) 3.52 (Sept, J=6.0Hz, 1H) 3.99 (t, J=8.4Hz, 1H) 4.08-4.13 (m, 1H) 4.49-4.54 (m, 1H) 4.93 (s, 2H) 5.40 (dd, J=5.2, 8.4Hz, 1H) 6.89-6.92 (m, 1H) 6.96 (d, J=5.6Hz, 1H) 7.00 (br, 1H) 7.16-7.34 (m, 7H) 7.37-7.40 (m, 2H)

Example 588b) 3-{3-[3-(2,4-Dichlorophenyl)-2-propynyloxy]phenyl}-2(S)-isopropoxypropanoic acid



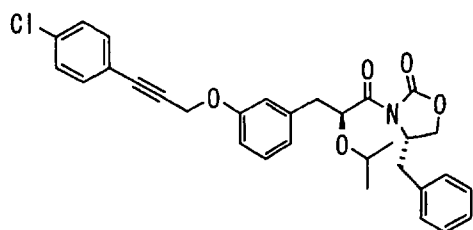
Using 4-benzyl-3-(3-{3-[3-(2,4-dichlorophenyl)-2-propynyloxy]phenyl}-2-isopropoxypropanoyl)oxazolidin-2-one, an hydrolysis reaction was conducted in the same manner as described in Production example 279d), and after purification by reverse-phase high performance liquid chromatography, the title compound was obtained.

MS m/e (ESI) 429(MNa⁺)

Example 589. 3-{3-[3-(4-Chlorophenyl)-2-propynyloxy]-
phenyl}-2(S)-isopropoxypropanoic acid

Production example 589a)

4-Benzyl-3-(3-{3-[3-(4-chlorophenyl)-2-propynyloxy]-
phenyl}-2-isopropoxypropanoyl)-oxazolidin-2-one

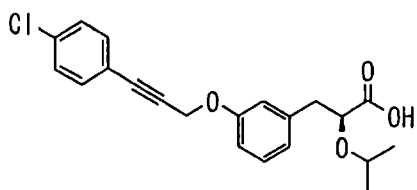


Using 4(S)-benzyl-3-[3-(3-hydroxyphenyl)-2(S)-isopropoxypropynyl]oxazolidin-2-one and 1-(3-bromo-1-propynyl)-4-chlorobenzene, the title compound was obtained in the same manner as described in Production example 77a).

¹H NMR (CDCl₃)

δ : 1.02 (d, J=6.0Hz, 3H) 1.15 (d, J=6.4Hz, 3H) 2.77 (dd, J=9.6, 13.2Hz, 1H) 2.93-2.98 (m, 1H) 3.29 (dd, J=4.0, 13.2Hz, 1H) 3.52 (Sept, J=6.0Hz, 1H) 3.99 (t, J=9.6Hz, 1H) 4.08-4.15 (m, 1H) 4.50-4.54 (m, 1H) 4.88 (s, 2H) 5.40 (dd, J=5.6, 8.4Hz, 1H) 6.87 (dd, J=2.4, 8.4Hz, 1H) 6.96 (d, J=7.6Hz, 1H) 7.00 (br, 1H) 7.18-7.21 (m, 2H) 7.27-7.37 (m, 8H)

Example 589b) 3-{3-[3-(4-Chlorophenyl)-2-propynyloxy]-
phenyl}-2(S)-isopropoxypropanoic acid



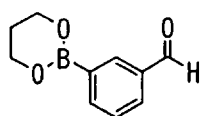
Using 4-benzyl-3-(3-(3-(3-(4-chlorophenyl)-2-propynyloxy)phenyl)-2-isopropoxypropanoyl)-oxazolidin-2-one, an hydrolysis reaction was conducted in the same manner as described in Production example 279d), and after purification by reverse-phase high performance liquid chromatography, the title compound was obtained.

MS m/e (ESI) 395 (MNa^+)

Example 590. 3-[3-(2,4-Dichlorobenzoylaminoxy)phenyl]-2-isopropoxypropanoic acid

Production example 590a)

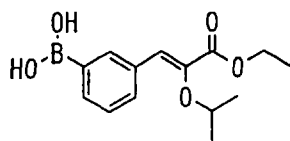
3-[1,3,2]Dioxaborinan-2-yl-benzaldehyde



5.0 g of 3-Formylbenzene boronate was suspended in diethyl ether, and 3.7 ml of ethylene glycol was added, and the mixture was stirred at room temperature for 15 minutes. The solvent was concentrated, to give 10.36 g of the title compound as a colorless oil.

Production example 590b)

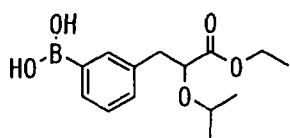
Ethyl 3-(3-boronyl-phenyl)-2-isopropoxyacrylate



2.38 g of Ethyl (diethoxyphosphoryl)isopropoxyacrylate was dissolved in anhydrous tetrahydrofuran, and 316 mg of sodium hydride was added. This mixture was stirred at room temperature for 15 minutes, then a solution of 1.0 g of 3-[1,3,2]dioxaborinan-2-yl-benzaldehyde in N,N-dimethylformamide was added, and stirring was continued at room temperature for 1 hour. The reaction solution was diluted with ethyl acetate, washed with 1N hydrochloric acid and saturated brine. The organic layer was dried over anhydrous magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography, to give 511 mg of the title compound as a colorless oil in the 3:2 hexane-ethyl acetate fraction.

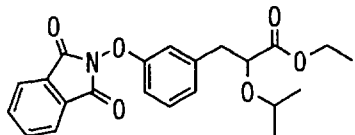
Production example 590c)

Ethyl 3-(3-boronyl-phenyl)-2-isopropoxypropanoate



511 mg of Ethyl 3-(3-boronylphenyl)-2-isopropoxyacrylate was dissolved in anhydrous ethanol, and 10% palladium carbon was added, and the mixture was stirred overnight at room temperature under an hydrogen atmosphere. The reaction solution was filtered, and the filtrate was concentrated, to give 539 mg of the title compound.

Production example 590d) Ethyl 3-[3-(1,3-dioxo-1,3-dihydroisoindol-2-yloxy)phenyl]-2-isopropoxypropanoate



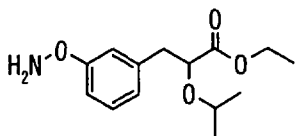
539 mg of Ethyl 3-(3-boronylphenyl)-2-isopropoxypropanoate, 389 mg of N-hydroxyphthalimide and 380 mg of copper (II) acetate were suspended in 10 ml of 1,2-dichloroethane, and 0.2 ml of pyridine was added, and the mixture was stirred at room temperature for 3 days. The reaction solution was filtered through a silica gel column, and the filtrate was concentrated. The residue was purified by silica gel column chromatography, to give 275 mg of the title compound as a colorless oil in the 4:1 hexane-ethyl acetate fraction.

¹H NMR (CDCl₃)

δ : 0.99 (d, J=6.0Hz, 3H) 1.10 (d, J=6.4Hz, 3H) 1.23 (t, J=4.8Hz, 3H) 2.89 (dd, J=9.6, 14.0Hz, 1H) 2.97 (dd, J=4.4, 13.6Hz, 1H) 3.46 (Sept, J=6.0Hz, 1H) 4.00 (dd, J=4.4, 9.2Hz, 1H) 4.13-4.21 (m, 2H) 7.01-7.06 (m, 3H) 7.25-7.28 (m, 1H) 7.81-7.84 (m, 2H) 7.89-7.93 (m, 2H)

Production example 590e)

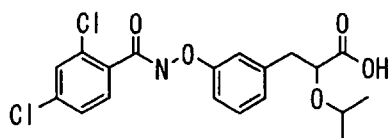
Ethyl 3-(3-aminooxyphenyl)-2-isopropoxypropanoate



275 mg of Ethyl 3-[3-(1,3-dioxo-1,3-dihydroisoindol-2-yloxy)phenyl]-2-isopropoxypropanoate was dissolved in ethanol,

and 50 mg of hydrazine monohydrate was added. The mixture was stirred at 70°C for 30 minutes, then the insoluble substances were filtered off. The filtrate was concentrated. The residue was purified by silica gel column chromatography, to give 163 mg of the title compound as a colorless oil in the 3:1 hexane-ethyl acetate fraction.

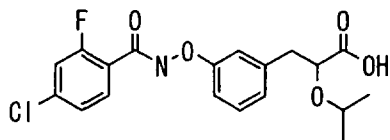
Example 590f). 3-[3-(2,4-Dichlorobenzoylaminoxy)phenyl]-2-isopropoxypropanoic acid



10 mg of Ethyl 3-(3-aminooxyphenyl-2-isopropoxypropionate and 7 mg of 2,4-dichlorobenzoic acid were dissolved in 0.3 ml of N,N-dimethylformamide, 0.006 ml of diethyl phosphonate cyanide and 0.05 ml of triethylamine were added, and the mixture was stirred overnight at room temperature. The reaction solution was diluted with ethyl acetate and washed with water. The organic layer was concentrated, to give ethyl 3-[3-(2,4-dichlorobenzoylaminoxy)phenyl]-2-isopropoxypropionate. This product was then dissolved in 0.4 ml of ethanol, 0.1 ml of 5N sodium hydroxide was added, and the mixture was stirred overnight at room temperature. The reaction solution was treated with 1N hydrochloric acid, extracted with ethyl acetate, and the organic layer was concentrated. The residue was purified by reverse-phase high performance liquid chromatography, to give the title compound.

MS m/e (ESI) 434 (MNa^+)

Example 591. 3-[3-(4-chloro-2-fluorobenzoylaminoxy)phenyl]-2-isopropoxypropanoic acid

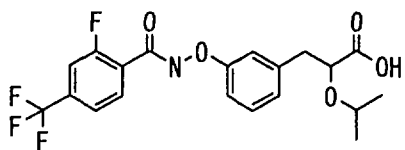


Using 4-chloro-2-fluorobenzoic acid, the title compound was obtained in the same manner as described in Example 590f).

MS m/e (ESI) 418 (MNa^+)

Example 592.

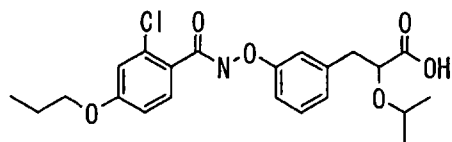
3-[3-(4-Trifluoromethyl-2-fluorobenzoylaminoxy)phenyl]-2-isopropoxypropanoic acid



Using 4-trifluoromethyl-2-fluorobenzoic acid, the title compound was obtained in the same manner as described in Example 590f).

MS m/e (ESI) 452 (MNa^+)

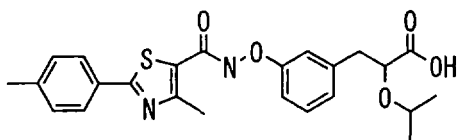
Example 593. 3-[3-(4-Propoxy-2-chlorobenzoylaminoxy)-phenyl]-2-isopropoxypropanoic acid



Using 4-propoxy-2-chlorobenzoic acid, the title compound was obtained in the same manner as described in Example 590f).

MS m/e (ESI) 458 (MNa⁺)

Example 594. 2-Isopropoxy-3-{3-[(4-methyl-2-p-tolyl-thiazol-5-carbonyl)aminoxy]phenyl}propanoic acid



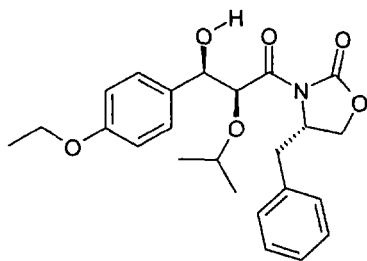
Using 4-methyl-2-p-tolylthiazol-5-carboxylic acid, the title compound was obtained in the same manner as described in Example 590f).

MS m/e (ESI) 477 (MNa⁺)

Example 595).

2(S)-3-{[3-(2,4-Dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid

Production example 595a)

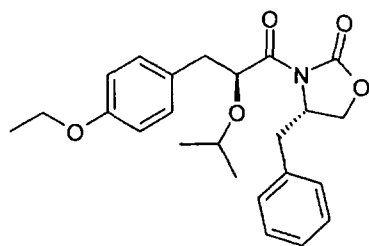


Under the similar conditions to those described in Production example 332a), 2.4 g of 4-ethoxybenzaldehyde and 5.6g of (4S)-4-benzyl-3-(2-isopropoxyacetyl)-1,3-oxazolon-2-one were reacted, to give 7.2g of (4S)-3-[(3R,2S)-3-(4-ethoxyphenyl)-3-hydroxy-2-isopropoxypropanoyl]-4-benzyl-1,3-oxazolan-2-one as a colorless solid.

¹H-NMR (CDCl₃)

δ : 1.15 (d, J=6.0Hz, 3H) 1.20 (d, J=6.0Hz, 3H) 1.38 (d, J=7.0Hz, 3H)
 2.73 (dd, J=13.5, 10.0Hz, 1H) 3.05 (d, J=5.4Hz, 1H) 3.16 (dd, J=13.5, 3.6Hz, 1H)
 3.69 (sept, J=6.0Hz, 1H) 3.70 (m, 1H) 3.99 (q, J=7.0Hz, 2H) 4.05 (m, 1H)
 4.43 (m, 1H) 4.79 (t, J=5.4Hz, 1H) 5.41 (d, J=5.4Hz, 1H) 6.82 (d, J=8.0Hz, 2H)
 7.19 (d, J=8.0Hz, 2H) 7.24-7.35 (m, 5H)

Production example 595b)

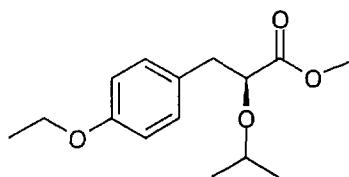


7.2 g of (4S)-3-[(3R,2S)-3-(4-Ethoxyphenyl)-3-hydroxy-2-isopropoxypropanoyl]-4-benzyl-1,3-oxazolan-2-one was dissolved in 200 ml of trifluoroacetic acid, 40 ml of triethylsilane was added, and the mixture was stirred for 24 hours. The solvent was evaporated, and the residue was purified by silica gel column chromatography (elution solvent: hexane-ethyl acetate), to give 7.0g of (4S)-3-[(2S)-3-(4-ethoxyphenyl)-2-isopropoxypropanoyl]-4-benzyl-1,3-oxazolan-2-one as a colorless solid.

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

δ : 1.03 (d, J=6.0Hz, 3H) 1.15 (d, J=6.0Hz, 3H) 1.39 (t, J=7.2Hz, 3H)
 2.77 (dd, J=13.5, 9.9Hz, 1H) 2.88 (dd, J=13.8, 8.4Hz, 1H)
 2.92 (dd, J=13.8, 6.0Hz, 1H) 3.31 (dd, J=13.5, 3.6Hz, 1H) 3.52 (sept, J=6.0Hz, 1H)
 3.97 (dd, J=9.0, 3.6Hz, 1H) 3.98 (q, J=7.2Hz, 2H) 4.13 (dd, J=9.0, 2.4Hz, 1H)
 4.51 (dtd, J=9.6, 3.6, 2.4Hz, 1H) 5.35 (dd, J=8.4, 6.0Hz, 1H) 6.79 (d, J=8.0Hz, 2H)
 7.20 (d, J=8.0Hz, 2H) 7.20-7.34 (m, 5H)

Production example 595c)

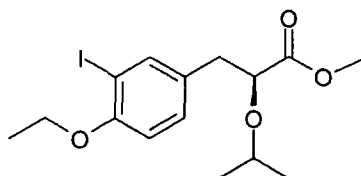


7.0 g of (4*S*)-3-[(2*S*)-3-(4-Ethoxyphenyl)-2-isopropoxypropanoyl]-4-benzyl-1,3-oxazolan-2-one was hydrolyzed and methylated in the same manner as described in Production example 332c), to give 3.9 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxyphenyl)-propanoate as a colorless oil.

¹H-NMR (CDCl₃)

δ : 0.95(d, J=6.2Hz, 3H) 1.13(d, J=6.0Hz, 3H) 1.39(t, J=7.2Hz, 3H)
2.87(dd, J=13.7, 8.6Hz, 1H) 2.94(dd, J=13.7, 5.2Hz, 1H) 3.48(sept, J=6.2Hz, 1H)
3.71(s, 3H) 4.01(q, J=7.2Hz, 2H) 4.02(dd, J=8.6, 6.2Hz, 1H) 6.80(d, J=8.0Hz, 2H)
7.13(d, J=8.0Hz, 2H)

Production example 595d)



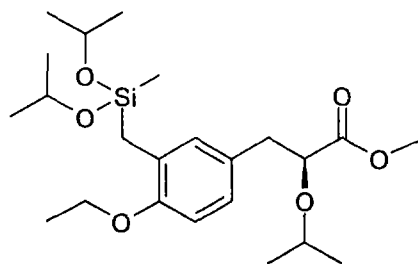
To a solution of 3.9 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxyphenyl)propanoate in dichloromethane (180 ml) were added 4.58 g of silver sulfate and 3.72g of iodine, and the mixture was stirred for 18 hours. The reaction solution was poured into ethyl acetate (500 ml):water (200 ml), and excess iodine was decomposed with sodium thiosulfate. The organic layer was dried over magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography (elution

solvent: hexane-ethyl acetate), to give 3.9 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxy-3-iodophenyl)propanoate as a yellow oil.

¹H-NMR(CDCl₃)

δ : 0.97(d, J=6.1Hz, 3H) 1.15(d, J=6.1Hz, 3H) 1.46(t, J=6.9Hz, 3H)
2.83(dd, J=13.6, 9.0Hz, 1H) 2.99(dd, J=13.6, 6.9Hz, 1H) 3.48(sept, J=6.1Hz, 1H)
3.72(s, 3H) 3.99(dd, J=9.0Hz, 1H) 4.06(q, J=6.9Hz, 2H) 6.71(d, J=8.5Hz, 1H)
7.15(dd, J=8.5, 2.0Hz, 1H) 7.67(d, J=2.0Hz, 1H)

Production example 595e)



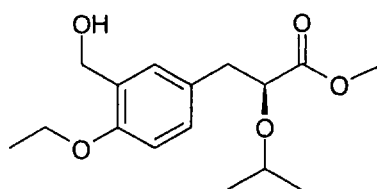
0.43 g of Magnesium, 1 ml of tetrahydrofuran and 1,2-dibromomethane were heated, and several drops of chloromethyl-diisopropoxy methylsilane were added. The solution was cooled to 0°C, and a solution of 3.7 g of silane in tetrahydrofuran (30 ml) was added dropwise. After 30 minutes, this solution was added to a 0.5M zinc chloride solution in tetrahydrofuran (35.5 ml), and after stirring this mixture for 30 minutes, a solution of 3.9 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxy-3-iodophenyl)propanoate in tetrahydrofuran (50 ml) and 0.33 g of dichlorophosphinoferrocene palladium were added, and the mixture was heated under reflux for 40 hours. After adding an equivalent amount of zinc reagent, the solution was

heated under reflux for another 16 hours. The reaction solution was poured into ethyl acetate (500 ml) and a saturated solution of ammonium chloride (300 ml). The organic layer was dried over magnesium sulfate. The solvent was evaporated and the residue was purified by silica gel column chromatography (elution solvent: hexane-ethyl acetate), to give 5.6 g of methyl 2(*S*)-isopropoxy-3-{3-[(diisopropoxymethyl)methylsilanyl)-methyl]-4-ethoxyphenyl}propanoate as a yellow oil.

¹H-NMR (CDCl₃)

δ : 0.01 (s, 3H) 0.97 (d, J=6.2 Hz, 3H) 1.13 (d, J=6.2 Hz, 3H) 1.14 (d, J=6.2 Hz, 6H) 1.17 (d, J=6.2 Hz, 6H) 1.41 (t, J=7.0 Hz, 3H) 2.15 (d, J=14.0 Hz, 1H) 2.19 (d, J=14.0 Hz, 1H) 2.82 (dd, J=13.6, 8.3 Hz, 1H) 2.89 (dd, J=13.6, 5.5 Hz, 1H) 3.48 (sept, J=6.2 Hz, 1H) 3.70 (s, 3H) 3.98 (q, J=7.0 Hz, 2H) 4.01 (dd, J=8.3, 5.5 Hz, 1H) 4.13 (sept, J=6.2 Hz, 1H) 6.67 (d, J=8.3 Hz, 1H) 6.90 (dd, J=8.3, 2.2 Hz, 1H) 6.98 (d, J=2.2 Hz, 1H)

Production example 595f)



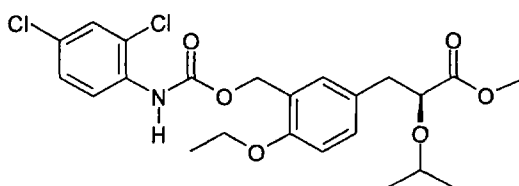
To a solution of 5.6 g of methyl 2(*S*)-isopropoxy-3-{3-[(diisopropoxymethyl)methylsilanyl)methyl]-4-ethoxyphenyl}propanoate in tetrahydrofuran (13 ml) and methanol (13 ml) were added 0.75 g of potassium fluoride, 1.30 g of potassium hydrogencarbonate and 2.5 ml of 30% aqueous hydrogen peroxide solution. The mixture was stirred for 24 hours. 3.0 g of sodium thiosulfate was added, and the mixture was poured into ethyl

acetate (200 ml) : water (100 ml). The organic layer was dried over magnesium sulfate, and the solvent was evaporated. The residue was purified by silica gel column chromatography (elution solvent: hexane-ethyl acetate), to give 1.4 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxy-3-hydroxymethylphenyl)-propanoate as a colorless oil.

¹H-NMR(CDCl₃)

δ: 0.97(d, J=6.2Hz, 3H) 1.14(d, J=6.2Hz, 3H) 1.43(t, J=7.0Hz, 3H)
 2.43(t, J=5.9Hz, 1H) 2.88(dd, J=14.6, 9.0Hz, 1H) 2.95(dd, J=14.6, 5.2Hz, 1H)
 3.49(sept, J=6.2Hz, 1H) 3.72(s, 3H) 4.03(dd, J=9.0, 5.2Hz, 1H)
 4.07(q, J=7.0Hz, 2H) 4.66(d, J=5.9Hz, 1H) 6.78(d, J=8.2Hz, 1H)
 7.11(dd, J=8.2, 2.3Hz, 1H) 7.13(d, J=2.3Hz, 1H)

Production example 595g)



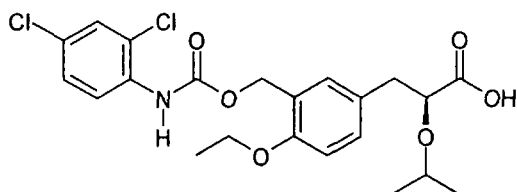
Under similar conditions to those described in Production example 147c), 2.5 g of methyl 2(*S*)-isopropoxy-3-(4-ethoxy-3-hydroxymethylphenyl)propanoate and 1.9 g of 2,4-dichlorophenylisocyanate were reacted, to give 3.0 g of methyl 2(*S*)-3-{[3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoate as a colorless solid.

¹H-NMR(CDCl₃)

δ: 0.96(d, J=6.0Hz, 3H) 1.13(d, J=6.0Hz, 3H) 1.41(t, J=6.9Hz, 3H)
 2.89(dd, J=13.8, 9.0Hz, 1H) 2.95(dd, J=13.8, 5.1Hz, 1H) 3.49(sept, J=6.0Hz, 1H)
 3.71(s, 3H) 4.04(d, J=9.0, 5.1Hz, 1H) 4.05(q, J=6.9Hz, 2H) 5.26(s, 2H)

6. 81 (d, J=8. 4Hz, 1H) 7. 15 (br. s, 1H) 7. 17 (dd, J=8. 4, 2. 3Hz, 1H) 7. 21-7. 23 (m, 2H)
 7. 35 (d, J=2. 3Hz, 1H) 8. 18 (d, J=8. 8Hz, 1H)

Example 595h)



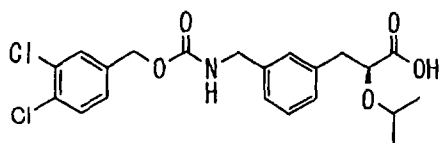
3.0 g of Methyl 2(S)-3-([3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl)-2-isopropoxypropanoate was hydrolyzed in the same manner as described in Production example 147d, to give 1.6 g of 2(S)-3-([3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl)-2-isopropoxypropanoic acid as a colorless solid.

¹H-NMR (CDCl₃)

δ: 1. 04 (d, J=6. 1Hz, 3H) 1. 15 (d, J=6. 1Hz, 3H) 1. 41 (t, J=7. 0Hz, 3H)
 2. 91 (dd, J=14. 0, 7. 9Hz, 1H) 3. 08 (dd, J=14. 0, 3. 5Hz, 1H) 3. 55 (sept, J=6. 1Hz, 1H)
 4. 06z (q, J=7. 0Hz, 2H) 4. 09 (dd, J=6. 1, 3. 5Hz, 1H) 5. 27 (s, 2H)
 6. 82 (d, J=8. 3Hz, 1H) 7. 16 (br. s, 1H) 7. 17 (dd, J=8. 3, 2. 2Hz, 1H)
 7. 24 (dd, J=9. 0, 2. 2Hz, 1H) 7. 25 (d, J=2. 2Hz, 1H) 7. 36 (d, J=2. 2Hz, 1H)
 8. 17 (d, J=9. 0Hz, 1H)

Example 596.

3-{3-[(2,5-Dichlorobenzoyloxycarbonylamino)methyl]}-phenyl}-2(S)-isopropoxypropanoic acid



Using 3,4-dichlorobenzylchloride, the title compound was obtained in the same manner as described in Example 332e).

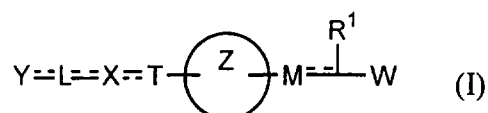
^1H NMR (CDCl_3)

δ : 1.00 (d, $J=6.0\text{Hz}$, 3H) 1.15 (d, $J=6.4\text{Hz}$, 3H) 2.95 (dd, $J=8.0$, 14.0Hz , 1H) 3.12 (dd, $J=4.0$, 14.0Hz , 1H) 3.54 (Sept, $J=6.0\text{Hz}$, 1H) 4.12 (q, $J=4.0\text{Hz}$, 1H) 4.37 (d, $J=6.0\text{Hz}$, 2H) 5.08 (s, 2H) 5.10 (br, 1H) 7.12–7.22 (m, 4H) 7.25–7.29 (m, 1H) 7.41–7.47 (m, 2H)

MS m/e (ESI) 462(MNa^+)

Claims

1. A carboxylic acid compound represented by the following formula, a salt thereof, an ester thereof or a hydrate of them.

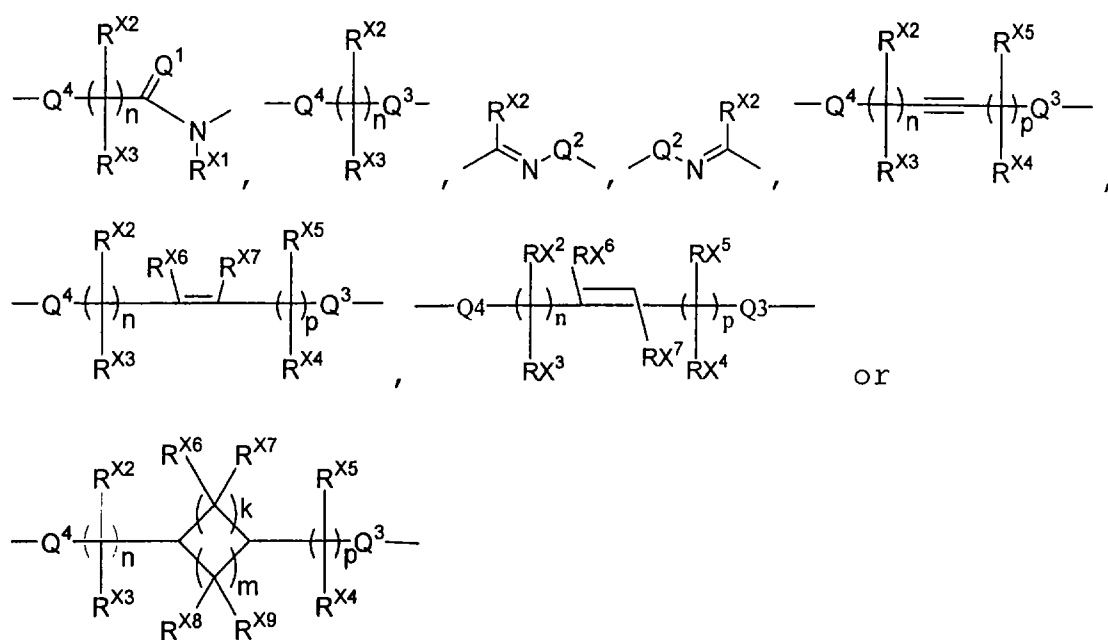


Wherein R^1 represents a hydrogen atom, hydroxyl group, halogen, carboxyl group, or a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a C_{1-6} hydroxyalkyl group, a C_{1-6} hydroxyalkoxy group, a C_{1-6} hydroxyalkylthio group, a C_{1-6} aminoalkyl group, an amino C_{1-6} alkoxy group, an amino C_{1-6} alkylthio group, a halogeno C_{1-6} alkyl group, a halogeno C_{1-6} alkoxy group, a halogeno- C_{1-6} alkylthio group, a C_{2-12} alkoxyalkyl group, a C_{2-12} alkoxyalkoxy group, a C_{2-12} alkoxyalkylthio group, a C_{3-7} cycloalkyl group, a C_{3-7} cycloalkyloxy group, a C_{4-13} cycloalkylalkyloxy group, a C_{3-7} cycloalkylthio group, a C_{2-6} alkenyl group, a C_{2-6} alkenyloxy group, C_{2-6} alkenylthio group, a C_{2-6} alkynyl group, a C_{2-6} alkynyloxy group, a C_{2-6} alkynylthio group, a C_{6-12} aryl group, a C_{6-12} aryloxy group, a C_{6-12} arylthio group, a C_{7-18} alkylaryl group, a C_{7-18} alkylaryloxy group, a C_{7-18} alkylarylthio group, a C_{7-18} aralkyl group, a C_{7-18} aralkyloxy group or a C_{7-18} aralkylthio group, each of which may have one or more substituents; L represents a single bond, or a C_{1-6} alkylene group, a C_{2-6} alkenylene group or a C_{2-6} alkynylene group, each of which may have one or more substituents; M represents a single bond, or a C_{1-6} alkylene group, a C_{2-6} alkenylene group or a C_{2-6} alkynylene group, each

of which may have one or more substituents; T represents a single bond, or a C₁₋₃ alkylene group, a C₂₋₃ alkenylene group or a C₂₋₃ alkynylene group, each of which may have one or more substituents; W represents a carboxyl group;

--

represents a single bond or a double bond; X represents a single bond, oxygen atom, a group represented by -NR^{X1}CQ¹O- (wherein Q¹ represents an oxygen atom or sulfur atom; and R^{X1} represents a hydrogen atom, formyl group, or a C₁₋₆ alkyl group, a C₁₋₆ hydroxyalkyl group, a C₁₋₆ aminoalkyl group, a halogeno C₁₋₆ alkyl group, a C₂₋₁₂ alkoxyalkyl group, a C₃₋₇ cycloalkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₆₋₁₂ aryl group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ aralkyl group, a C₂₋₇ aliphatic acyl group or a C₇₋₁₉ aromatic acyl group, each of which may have one or more substituents), -OCQ¹NR^{X1}- (wherein Q¹ and R^{X1} are as defined above), -CQ¹NR^{X1}O- (wherein Q¹ and R^{X1} are as defined above), ONR^{X1}CQ¹- (wherein Q¹ and R^{X1} are as defined above), -Q²SO₂- (wherein Q² is an oxygen atom or -NR^{X10}- (wherein R^{X10} represents a hydrogen atom, formyl group, or a C₁₋₆ alkyl group, a C₁₋₆ hydroxyalkyl group, a C₁₋₆ aminoalkyl group, a halogeno-C₁₋₆ alkyl group, a C₂₋₁₂ alkoxyalkyl group, a C₃₋₇ cycloalkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₆₋₁₂ aryl group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ aralkyl group, a C₂₋₇ aliphatic acyl group or a C₇₋₁₉ aromatic acyl group, each of which may have one or more substituents)) or -SO₂Q²- (wherein Q² is as defined above), or a group represented by the formula:



(wherein Q^1 , Q^2 and R^{X1} are as defined above; k represents 0 to 5; m represents 1 to 5; n and p are the same as or different from each other and each represents 1 to 5; R^{X2} , R^{X3} , R^{X4} , R^{X5} , R^{X6} , R^{X7} , R^{X8} and R^{X9} are the same as or different from each other and each represents a hydrogen atom, hydroxy group, halogen, $-N(R^{X11})R^{X12}-$ (wherein R^{X11} and R^{X12} are the same as or different from each other and each represents a hydrogen atom, formyl group, or a C_{1-6} alkyl group, a C_{1-6} hydroxyalkyl group, a C_{1-6} aminoalkyl group, a halogeno- C_{1-6} alkyl group, a C_{2-12} alkoxyalkyl group, a C_{3-7} cycloalkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group, a C_{6-12} aryl group, a C_{7-18} alkylaryl group, a C_{7-18} aralkyl group, a C_{2-7} aliphatic acyl group or a C_{7-19} aromatic acyl group, each of which may have one or more substituents), or a C_{1-6} alkyl group, C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a C_{1-6} hydroxyalkyl group, a C_{1-6} hydroxyalkoxy group, a C_{1-6} hydroxyalkylthio group, a C_{1-6} aminoalkyl group, a C_{1-6} aminoalkoxy group, a C_{1-6} aminoalkylthio

group, a halogeno-C₁₋₆ alkyl group, a halogeno-C₁₋₆ alkoxy group, a halogeno-C₁₋₆ alkylthio group, a C₂₋₁₂ alkoxyalkyl group, a C₂₋₁₂ alkoxyalkoxy group, a C₂₋₁₂ alkoxyalkylthio group, a C₃₋₇ cycloalkyl group, a C₃₋₇ cycloalkyloxy group, a C₄₋₁₃ cycloalkylalkyloxy group, a C₃₋₇ cycloalkylthio group, a C₂₋₆ alkenyl group, a C₂₋₆ alkenyloxy group, a C₂₋₆ alkenylthio group, a C₂₋₆ alkynyl group, a C₂₋₆ alkynyloxy group, a C₂₋₆ alkynylthio group, a C₆₋₁₂ aryl group, a C₆₋₁₂ aryloxy group, a C₆₋₁₂ arylthio group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ alkylaryloxy group, a C₇₋₁₈ alkylarylthio group, a C₇₋₁₈ aralkyl group, a C₇₋₁₈ aralkyloxy group or a C₇₋₁₈ aralkylthio group, each of which may have one or more substituents, provided that R^{X2} and R^{X3}, and/or R^{X4} and R^{X5} may together form a ring; and Q³ and Q⁴ are the same as or different from each other and each represents an oxygen atom, (O)S(O) or NR^{X10} (wherein NR^{X10} is as defined above); Y represents a 5- to 14-membered aromatic group or a C₃₋₇ alicyclic hydrocarbon group, each of which may have one or more substituents and one or more hetero atoms; and the ring Z represents a 5- to 14-membered aromatic group which may have 1 to 4 substituents and one or more hetero atoms, and wherein part of the ring may be saturated.

2. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), Y is a 5- to 14-membered aromatic group which may have 1 to 4 substituents and one or more hetero atoms.

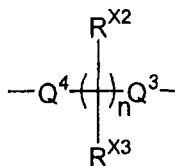
3. The carboxylic acid compound according to claim 1 or 2, a salt thereof, an ester thereof or a hydrate of them, wherein

$$\begin{array}{c}
 \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_n\begin{array}{c} \diagup Q^1 \\ \diagdown N^{X1} \end{array}, \quad \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_nQ^3\text{---}, \quad \begin{array}{c} R^{X2} \\ \diagdown \\ N^{X2}-Q^2 \end{array}, \quad \begin{array}{c} R^{X2} \\ \diagup \\ Q^2-N^{X2} \end{array}, \quad \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_n\equiv\left(\begin{array}{c} R^{X5} \\ | \\ \text{---} \\ | \\ R^{X4} \end{array}\right)_pQ^3\text{---}, \\
 \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_n\begin{array}{c} R^{X6} \\ \diagdown \\ \text{---} \\ \diagup R^{X7} \end{array}\begin{array}{c} R^{X5} \\ | \\ \text{---} \\ | \\ R^{X4} \end{array}\right)_pQ^3\text{---}, \quad \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_n\begin{array}{c} R^{X6} \\ \diagdown \\ \text{---} \\ \diagup R^{X7} \end{array}\begin{array}{c} R^{X5} \\ | \\ \text{---} \\ | \\ R^{X4} \end{array}\right)_pQ^3\text{---} \quad \text{or} \\
 \text{---}Q^4\left(\begin{array}{c} R^{X2} \\ | \\ \text{---} \\ | \\ R^{X3} \end{array}\right)_n\begin{array}{c} R^{X6} \\ \diagdown \\ \text{---} \\ \diagup R^{X7} \end{array}\begin{array}{c} R^{X5} \\ | \\ \text{---} \\ | \\ R^{X4} \end{array}\right)_pQ^3\text{---}
 \end{array}$$

4. The carboxylic acid compound according to any one of claims 1 to 3, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is $-NR^{X1}CQ^1O-$ (wherein Q^1 and R^{X1} are as defined above) or $-OCQ^1NR^{X1}-$ (Q^1 and R^{X1} are as defined above).

490

by the formula:

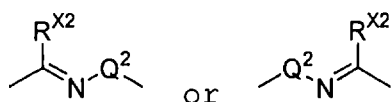


wherein n, Q³, Q⁴, R^{X2} and R^{X3} are as defined above.

6. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), L is a single bond or a C₁₋₆ alkylene group which may have one or more substituents; X is a single bond or oxygen atom; and T is a C₂₋₆ alkynylene group which may have one or more substituents.

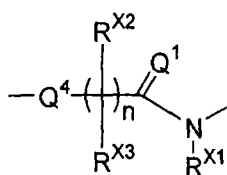
7. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), L is a C₂₋₆ alkynylene which may have one or more substituents; X is a single bond or oxygen atom; and T is a single bond or a C₁₋₆ alkylene group which may have one or more substituents.

8. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:



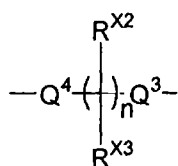
wherein Q² and R^{X2} are as defined above.

9. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:



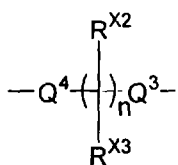
wherein n , Q^1 , Q^4 , R^{X1} , R^{X2} and R^{X3} are as defined above.

10. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:



wherein Q^3 and Q^4 represent an oxygen atom; and n , R^{X2} and R^{X3} are as defined above.

11. The carboxylic acid according to claim 10, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:

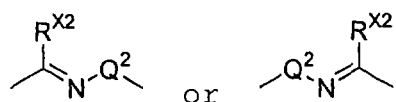


(wherein Q^3 and Q^4 represent an oxygen atom; n represents 2 to 5; and R^{X2} and R^{X3} are as defined above, provided that either one of R^{X2} and R^{X3} should be a group other than a hydrogen atom); L is a single bond or a C_{1-3} alkylene group which may have one or more substituents; and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

12. The carboxylic acid compound according to claim 4, a salt thereof, an ester thereof or a hydrate of them, wherein

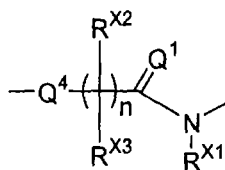
in the formula (I), X is a group represented by the formula $-NR^{X1}CQ^1O-$ (wherein Q^1 represents an oxygen atom, R^{X1} is as defined above) or $-OCQ^1NR^{X1}-$ (wherein Q^1 represents an oxygen atom, R^{X1} is as defined above), L is a single bond or a C_{1-3} alkylene group which may have one or more substituents, and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

13. The carboxylic acid compound according to claim 8, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:



(wherein, Q^2 represents an oxygen atom and R^{X2} is as defined above); L is a single bond or a C_{1-3} alkylene group which may have one or more substituents; and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

14. The carboxylic acid compound according to claim 9, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:



(wherein, Q^1 and Q^4 represent an oxygen atom; R^{X1} , R^{X2} and R^{X3} are as defined above; and n represents 1 to 5); L is a single bond or a C_{1-3} alkylene group which may have one or more substituents; and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

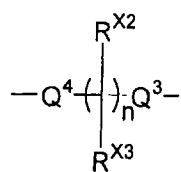
15. The carboxylic acid compound according to claim 3, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is $-Q^2SO_2-$ or $-SO_2Q^2-$ (wherein Q^2 represents an oxygen atom); L is a single bond or a C_{1-3} alkylene group which may have one or more substituents; and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

16. The carboxylic acid compound according to claim 3, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is $-CQ^1NR^{X1}O-$ or $-ONR^{X1}CQ^1-$ (wherein Q^1 represents an oxygen atom; and R^{X1} is as defined above); L is a single bond or a C_{1-3} alkylene group which may have one or more substituents; and T is a single bond or a C_{1-3} alkylene group which may have one or more substituents.

17. The carboxylic acid compound according to claim 11, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), wherein M is a C_{1-6} alkylene group; R^1 is a carboxyl group, or a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a C_{6-12} aryloxy group or a C_{7-18} aralkyloxy group, each of which may have one or more substituents.

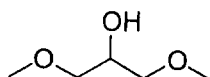
18. The carboxylic acid compound according to claim 17, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), the ring Z is a 1,3-phenylene group which may have 1 to 4 substituents.

19. The carboxylic acid compound according to claim 11 or 18, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is a group represented by the formula:

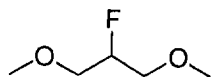


wherein Q^3 and Q^4 represent an oxygen atom; n represents 3 to 5; and R^{X2} and R^{X3} represent a hydrogen atom, hydroxyl group or fluorine atom, provided that either one of R^{X2} and R^{X3} should be a group other than hydrogen atom.

20. The carboxylic acid compound according to claim 19, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is represented by the formula:



21. The carboxylic acid compound according to claim 19, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), X is represented by the formula:



22. The carboxylic acid compound according to any one of claims 19 to 21, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), M is a methylene group; and R^1 is a C_{1-6} alkoxy group which may have one or more substituents.

23. The carboxylic acid compound according to claim 12, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), M is a C_{1-6} alkylene group; and R^1 is a carboxyl group, or a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a C_{6-12} aryloxy group or a C_{7-18} aralkyloxy group, each

of which may have one or more substituents.

24. The carboxylic acid compound according to claim 23, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), L is a C₁₋₃ alkylene group which may have one or more substituents; and T is a C₁₋₃ alkylene group which may have one or more substituents.

25. The carboxylic acid compound according to claim 24, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), the ring Z is a 1,3-phenylene group which may have 1 to 4 substituents.

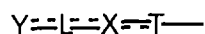
26. The carboxylic acid compound according to claim 25, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), M is a methylene group; and R¹ is a C₁₋₆ alkoxy group which may have one or more substituents.

27. The carboxylic acid compound according to any one of claims 6, 7, 13, 14, 15 and 16, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), M is a C₁₋₆ alkylene group; R¹ is a carboxyl group, or a C₁₋₆ alkyl group, a C₁₋₆ alkoxy group, a C₁₋₆ alkylthio group, a C₆₋₁₂ aryloxy group or a C₇₋₁₈ aralkyloxy group, each of which may have one or more substituents.

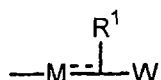
28. The carboxylic acid compound according to any one of claims 11 to 27, a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), Y is a phenyl group which may have 1 or 2 substituents.

29. The carboxylic acid compound according to claim 1,

a salt thereof, an ester thereof or a hydrate of them, wherein in the formula (I), a group represented by the formula:



(wherein each symbol represents a group as defined above) and a group represented by the formula:



(wherein each symbol represents a group as defined above) are bound with each other on the ring Z via from 2 to 8 atoms.

30. The carboxylic acid compound according to claim 1, a salt thereof, an ester thereof or a hydrate of them, wherein the compound represented by the formula (I) is one selected from:

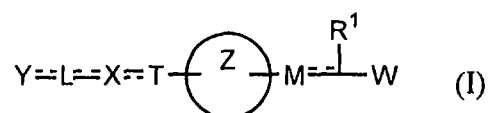
- (1) 2-isopropoxy-3-(3-[3-(2,4-dichlorophenyl)-2-propynyl]oxyphenyl)propanoic acid;
- (2) 3-3-[3-(4-trifluoromethylphenyl)-1-hydroxy-1-methyl-2-propynyl]phenyl-2-isopropoxypropanoic acid;
- (3) 2-isopropoxy-3-[3-([4-(trifluoromethyl)benzyl]-oxyethaneimido)]phenyl]propanoic acid;
- (4) 2-ethoxy-3-{3-[2-([4-(trifluoromethyl)anilino]-carbonyl)oxy]ethyl]phenyl}propanoic acid;
- (5) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid;
- (6) 2-isopropoxy-3-(3-{[4-trifluoromethoxybenzyl]-oxy}carbonyl)amino)methyl]phenyl)propanoic acid;
- (7) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid;

- (8) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(S)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (9) 3-(3-{2(S)-hydroxy-3-[3-(1-hydroxy-1-methylethyl)-phenoxy]propoxy}phenyl)-2(S)-isopropoxypropanoic acid;
- (10) 3-(3-{2(R)-hydroxy-3-[4-chlorophenoxy]propoxy}-phenyl)-2(S)-isopropoxypropanoic acid;
- (11) 3-(3-{2(S)-hydroxy-3-[2,4-dimethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid;
- (12) 3-(3-{2(S)-hydroxy-3-[4-chloro-2-fluorophenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid;
- (13) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (14) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(R)-hydroxypropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (15) 3-(3-{2(R)-hydroxy-3-[2,4-dimethylphenoxy]-propoxy}phenyl)-2(S)-isopropoxypropanoic acid;
- (16) 3-{3-[3-(2,4-dichlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (17) 3-{3-[3-(4-chlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (18) 3-{3-[3-(4-chloro-2-cyanophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (19) 3-{3-[3-(2,4-dichlorophenoxy)-2(S)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (20) 3-{3-[3-(4-chlorophenoxy)-2(R)-fluoropropoxy]phenyl}-2(S)-isopropoxypropanoic acid;

- (21) 3-(3-[3-(4-chloro-2-cyanophenoxy)-2(S)-fluoropropoxy]phenyl)-2(S)-isopropoxypropanoic acid;
- (22) 3-(3-[3-(2,4-dimethylphenoxy)-2(S)-fluoropropoxy]phenyl)-2(S)-isopropoxypropanoic acid;
- (23) 2(S)-isopropoxy-3-{3-[(4-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid;
- (24) 2(S)-isopropoxy-3-{3-[(3-trifluoromethylbenzyloxycarbonylamino)methyl]phenyl}-propanoic acid;
- (25) 2(S)-isopropoxy-3-{3-[(4-trifluoromethoxybenzyloxycarbonylamino)methyl]phenyl}-propanoic acid;
- (26) 3-(3-{[4-(1-hydroxy-1-methylethyl)-benzyloxycarbonylamino]methyl}phenyl)-2(S)-isopropoxypropanoic acid;
- (27) 3-(3-{[2,5-dichlorobenzyloxycarbonylamino]methyl}phenyl)-2(S)-isopropoxypropanoic acid;
- (28) 3-(3-{[4-ethoxybenzyloxycarbonylamino]methyl}phenyl)-2(S)-isopropoxypropanoic acid;
- (29) 3-(3-{[3-trifluoromethoxybenzyloxycarbonylamino]methyl}phenyl)-2(S)-isopropoxypropanoic acid;
- (30) 3-(3-{[2-(4-chlorophenyl)ethoxycarbonylamino]methyl}phenyl)-2(S)-isopropoxypropanoic acid;
- (31) 2(S)-isopropoxy-3-{3-[(quinolin-2-ylmethoxycarbonylamino)methyl]phenyl}propanoic acid;

- (32) 3-([3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl)-2-isopropoxypropanoic acid;
- (33) 3-([4-[5-(benzo[1,3]dioxolyl)]-carbamoyloxymethyl]phenyl)-2-isopropoxypropanoic acid;
- (34) 3-{3-[3-(2,4-dichlorophenoxy)-1-propynyl]phenyl}-2(S)-isopropoxypropanoic acid;
- (35) 3-{3-[3-(2,4-dichlorophenyl)-2-propynyloxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (36) 3-{3-[3-(4-chlorophenyl)-2-propynyloxy]phenyl}-2(S)-isopropoxypropanoic acid;
- (37) 2(S)-3-{[3-(2,4-dichlorophenyl)carbamoyloxymethyl-4-ethoxy]phenyl}-2-isopropoxypropanoic acid;
- (38) 3-{3-[2-(4-chlorophenoxy)acetyl amino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid;
- (39) 3-{3-[2-(2,4-dichlorophenoxy)acetyl amino]-4-ethoxyphenyl}-2-isopropoxypropanoic acid; and
- (40) 3-{4-[3-(4-chloro-2-cyanophenoxy)-2-hydroxypropoxy]phenyl}-2-isopropoxypropanoic acid.

31. A medicament comprising a carboxylic acid compound represented by the following formula, a salt thereof, an ester thereof or a hydrate of them.

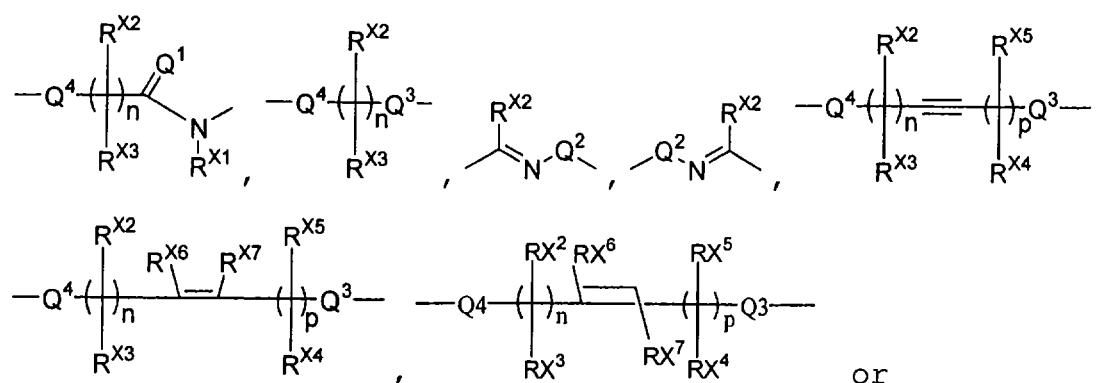


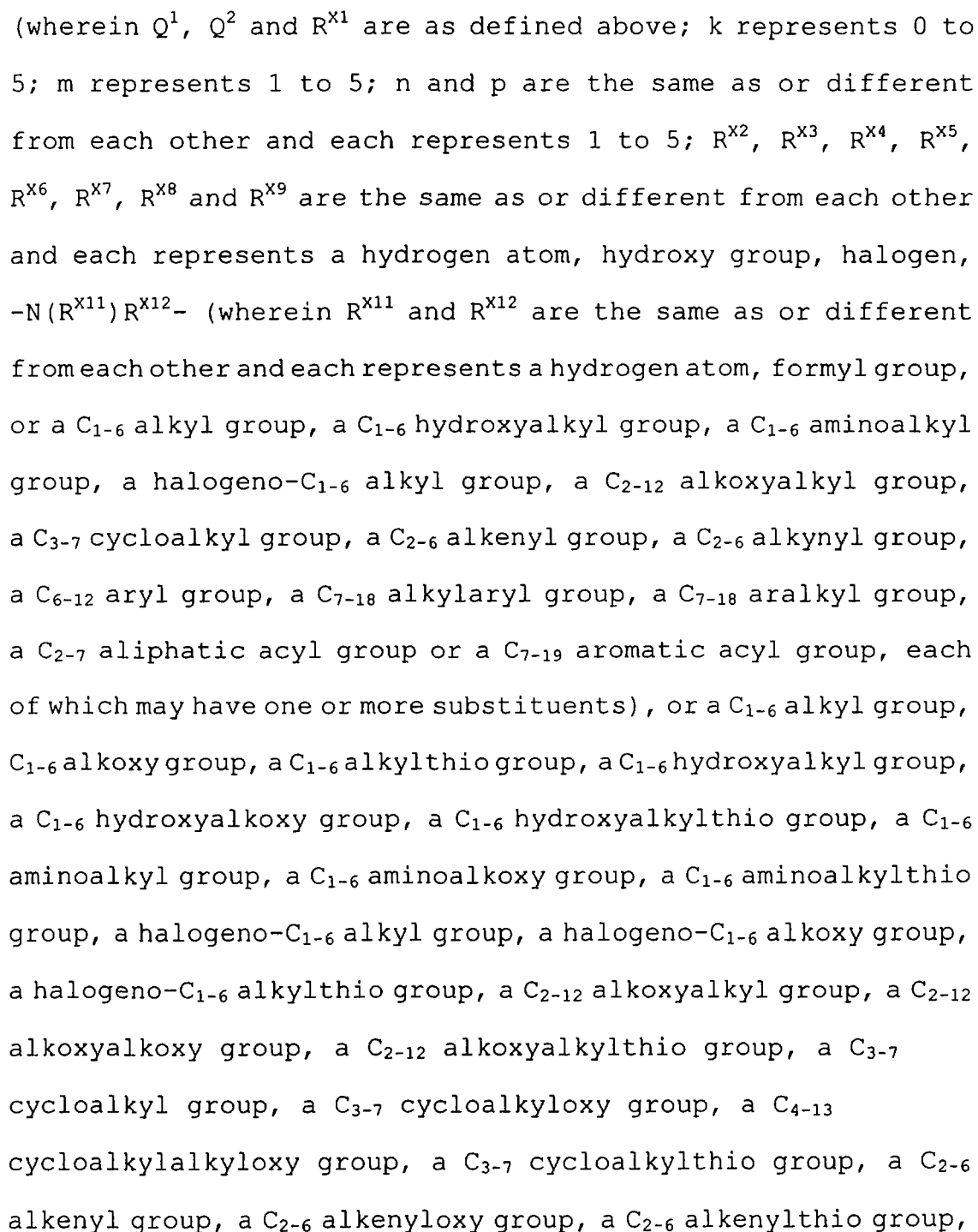
Wherein R^1 represents a hydrogen atom, hydroxyl group, halogen, carboxyl group, or a C_{1-6} alkyl group, a C_{1-6} alkoxy group, a C_{1-6} alkylthio group, a C_{1-6} hydroxyalkyl group, a C_{1-6} hydroxyalkoxy

group, a C₁₋₆ hydroxyalkylthio group, a C₁₋₆ aminoalkyl group, anaminoC₁₋₆alkoxygroup, anaminoC₁₋₆alkylthiogroup, ahalogeno C₁₋₆ alkyl group, a halogeno C₁₋₆ alkoxy group, a halogeno-C₁₋₆ alkylthio group, a C₂₋₁₂ alkoxyalkyl group, a C₂₋₁₂ alkoxyalkoxy group, a C₂₋₁₂ alkoxyalkylthio group, a C₃₋₇ cycloalkyl group, a C₃₋₇ cycloalkyloxy group, a C₄₋₁₃ cycloalkylalkyloxy group, a C₃₋₇ cycloalkylthio group, a C₂₋₆ alkenyl group, a C₂₋₆ alkenyloxy group, C₂₋₆ alkenylthio group, a C₂₋₆ alkynyl group, a C₂₋₆ alkynyloxy group, a C₂₋₆ alkynylthio group, a C₆₋₁₂ aryl group, a C₆₋₁₂ aryloxy group, a C₆₋₁₂ arylthio group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ alkylaryloxy group, a C₇₋₁₈ alkylarylthio group, a C₇₋₁₈ aralkyl group, a C₇₋₁₈ aralkyloxy group or a C₇₋₁₈ aralkylthio group, each of which may have one or more substituents; L represents a single bond, or a C₁₋₆ alkylene group, a C₂₋₆ alkenylene group or a C₂₋₆ alkynylene group, each of which may have one or more substituents; M represents a single bond, or a C₁₋₆ alkylene group, a C₂₋₆ alkenylene group or a C₂₋₆ alkynylene group, each of which may have one or more substituents; T represents a single bond, or a C₁₋₃ alkylene group, a C₂₋₃ alkenylene group or a C₂₋₃ alkynylene group, each of which may have one or more substituents; W represents a carboxyl group;

represents a single bond or a double bond; X represents a single bond, oxygen atom, a group represented by -NR^{X1}CQ¹O- (wherein Q¹ represents an oxygen atom or sulfur atom; and R^{X1} represents a hydrogen atom, formyl group, or a C₁₋₆ alkyl group, a C₁₋₆

hydroxyalkyl group, a C₁₋₆ aminoalkyl group, a halogeno C₁₋₆ alkyl group, a C₂₋₁₂ alkoxyalkyl group, a C₃₋₇ cycloalkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₆₋₁₂ aryl group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ aralkyl group, a C₂₋₇ aliphatic acyl group or a C₇₋₁₉ aromatic acyl group, each of which may have one or more substituents), -OCQ¹NR^{X1}- (wherein Q¹ and R^{X1} are as defined above), -CQ¹NR^{X1}O- (wherein Q¹ and R^{X1} are as defined above), ONR^{X1}CQ¹- (wherein Q¹ and R^{X1} are as defined above), -Q²SO₂- (wherein Q² is an oxygen atom or -NR^{X10}- (wherein R^{X10} represents a hydrogen atom, formyl group, or a C₁₋₆ alkyl group, a C₁₋₆ hydroxyalkyl group, a C₁₋₆ aminoalkyl group, a halogeno-C₁₋₆ alkyl group, a C₂₋₁₂ alkoxyalkyl group, a C₃₋₇ cycloalkyl group, a C₂₋₆ alkenyl group, a C₂₋₆ alkynyl group, a C₆₋₁₂ aryl group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ aralkyl group, a C₂₋₇ aliphatic acyl group or a C₇₋₁₉ aromatic acyl group, each of which may have one or more substituents)) or -SO₂Q²- (wherein Q² is as defined above), or a group represented by the formula:





a C₂₋₆ alkynyl group, a C₂₋₆ alkynyloxy group, a C₂₋₆ alkynylthio group, a C₆₋₁₂ aryl group, a C₆₋₁₂ aryloxy group, a C₆₋₁₂ arylthio group, a C₇₋₁₈ alkylaryl group, a C₇₋₁₈ alkylaryloxy group, a C₇₋₁₈ alkylarylthio group, a C₇₋₁₈ aralkyl group, a C₇₋₁₈ aralkyloxy group or a C₇₋₁₈ aralkylthio group, each of which may have one or more substituents, provided that R^{X2} and R^{X3}, and/or R^{X4} and R^{X5} may together form a ring; and Q³ and Q⁴ are the same as or different from each other and each represents an oxygen atom, (O)S(O) or NR^{X10} (wherein NR^{X10} is as defined above); Y represents a 5- to 14-membered aromatic group or a C₃₋₇ alicyclic hydrocarbon group, each of which may have one or more substituents and one or more hetero atoms; and the ring Z represents a 5- to 14-membered aromatic group which may have 1 to 4 substituents and one or more hetero atoms, and wherein part of the ring may be saturated.

32. The medicament according to claim 31, which is based on PPAR α and γ dual agonism.

33. The medicament according to claim 31, which is based on PPAR α , $\beta(\delta)$ and γ triple agonism.

34. The medicament according to any one of claims 31 to 33, which is an insulin sensitizer.

35. The medicament according to any one of claims 31 to 33, which is an agent for preventing or treating diabetes mellitus.

36. The medicament according to any one of claims 31 to 33, which is an agent for preventing or treating syndrome X.

37. The medicament according to any one of claims 31 to

33, which is an agent for preventing or treating diabetic complications.

38. The medicament according to any one of claims 31 to 33, which is an agent for preventing or treating hyperlipemia.

39. The medicament according to any one of claims 31 to 33, which is a lipid-lowering agent.

40. The medicament according to any one of claims 31 to 33, which is an agent for preventing or treating obesity.

41. The medicament according to any one of claims 31 to 33, which is an agent for treating osteoporosis.

42. The medicament according to any one of claims 31 to 33, which is an anti-inflammatory agent.

43. The medicament according to any one of claims 31 to 33, which is an agent for preventing or treating digestive disease.

44. The medicament according to claim 43, wherein the digestive disease is a disease selected from the group consisting of 1) inflammatory diseases of the digestive organs; 2) proliferative diseases of the digestive organs; and 3) ulcerative diseases of the digestive organs.

45. The medicament according to claim 44, wherein the inflammatory disease of the digestive organs is a disease selected from the group consisting of 1) ulcerative colitis; 2) Crohn's disease; 3) pancreatitis; and (4) gastritis.

46. The medicament according to claim 44, wherein the inflammatory disease of the digestive organs is ulcerative

colitis.

47. An agent for preventing or treating a disease against which an insulin sensitizing action is efficacious, which comprises the compound according to any one of claims 1 to 30 as the active ingredient.

48. The agent for preventing or treating digestive disease according to claim 44, wherein the proliferative diseases of the digestive organs is a disease selected from the group consisting of 1) benign tumor of the digestive organs; 2) digestive polyp; 3) hereditary polyposis syndrome; 4) colon cancer; 5) rectum cancer and 6) stomach cancer.

49. The medicament according to any one of claims 31 to 33 whose action is improving energy metabolism, which is an agent for preventing or treating 1) stenocardia and myocardial infarction, and sequelae thereof; 2) senile dementia; or 3) cerebrovascular dementia.

50. The medicament according to any one of claims 31 to 33 which is an immunomodulatory agent.

51. The medicament according to any one of claims 31 to 33 which is an agent for preventing or treating cancer.

52. A method of preventing or treating a disease against which an insulin sensitizing action is efficacious, which comprises administering to a patient a pharmaceutically effective amount of the carboxylic acid compound according to any one of claims 1 to 30, a salt thereof, an ester thereof or a hydrate of them.

53. Use of the carboxylic acid compound according to any one of claims 1 to 30, a salt thereof, an ester thereof or a hydrate of them, for producing an agent for preventing or treating a disease against which an insulin sensitizing action is efficacious.

54. A pharmaceutical composition comprising a carboxylic acid compound represented by the formula (I), a salt thereof, an ester thereof or a hydrate of them, and a pharmaceutically acceptable carrier.

55. A method of preventing or treating a disease against which PPAR α and γ dual agonism or PPAR α , $\beta(\delta)$ and γ triple agonism is efficacious, which comprises administering to a patient a pharmaceutically effective amount of the carboxylic acid compound according to any one of claims 1 to 30, a salt thereof, an ester thereof or a hydrate of them.

56. Use of the carboxylic acid compound according to any one of claims 1 to 30, a salt thereof, an ester thereof or a hydrate of them, for producing an agent for preventing or treating a disease against which PPAR α and γ dual agonism or PPAR α , $\beta(\delta)$ and γ triple agonism is efficacious.

57. The method according to claim 55, wherein the disease is diabetes mellitus; syndrome X; diabetic complications; hyperlipemia; a disease against which a lipid-lowering action is efficacious; obesity; osteoporosis; a disease against which an anti-inflammatory action is efficacious, digestive diseases including 1) inflammatory diseases of digestive organs including

ulcerative colitis, Crohn's disease, pancreatitis and gastritis; 2) the proliferative diseases of digestive organs including benign tumor of digestive organs, digestive polyp, hereditary polyposis syndrome, colon cancer, rectum cancer and stomach cancer; and 3) ulcerative diseases of digestive organs; 1) stenocardia and myocardial infarction, and sequelae thereof; 2) senile dementia; or 3) cerebrovascular dementia based on energy metabolism improving effect, respectively, a disease against which an immunomodulatory action is efficacious, or tumor disease.

58. The use according to claim 56, wherein the disease is diabetes mellitus, syndrome X, diabetic complications, hyperlipemia, a disease against which a lipid-lowering action is efficacious, obesity, osteoporosis, a disease against which an anti-inflammatory action is efficacious, digestive diseases including 1) inflammatory diseases of digestive organs including ulcerative colitis, Crohn's disease, pancreatitis and gastritis; 2) the proliferative diseases of digestive organs including benign tumor of digestive organs, digestive polyp, hereditary polyposis syndrome, colon cancer, rectum cancer and stomach cancer; and 3) ulcerative diseases of digestive organs; 1) stenocardia and myocardial infarction, and sequelae thereof; 2) senile dementia; or 3) cerebrovascular dementia based on energy metabolism improving effect, respectively, a disease against which an immunomodulatory action is efficacious, or tumor disease.