



methylphenyl]ethyl]amine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 594$ .

5      EXAMPLE 560       $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-1,2,3,4-tetrahydro-1-naphthalenylamino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), (1S)-1,2,3,4-tetrahydro-1-  
10      naphthalenylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 592$ .

EXAMPLE 561       $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,5-dimethylbenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -  
15      dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), 2,5-dimethylbenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 580$ .

20      EXAMPLE 562       $N^1$ -[(1S,2R)-3-{[2-chloro-5-(trifluoromethyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), 2-chloro-5-trifluorobenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 654$ .

EXAMPLE 563       $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-5-methylbenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -  
30      dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-



oxiranyl]ethylcarbamate (V, EXAMPLE 3), 2-hydroxy-5-methylbenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 582$ .

EXAMPLE 564       $N^1-((1S,2R)-1-(3,5\text{-difluorobenzyl})-2\text{-hydroxy-3-}\{[(1S,2R)-2\text{-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}\text{propyl})-5\text{-methyl-}N^3,N^3\text{-dipropylisophthalamide (X)}$

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), [(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 594$ .

EXAMPLE 565       $N^1-\{(1S,2R)-1-(3,5\text{-difluorobenzyl})-3-[(1R)-2,3\text{-dihydro-1H-inden-1-ylamino}]-2\text{-hydroxypropyl}\}-5\text{-methyl-}N^3,N^3\text{-dipropylisophthalamide (X)}$

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), (1R)-2,3-dihydro-1H-inden-1-ylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 578$ .

EXAMPLE 566      5-chloro- $N^1-\{(1S,2R)-1-(3,5\text{-difluorobenzyl})-2\text{-hydroxy-3-}[(1\text{-methyl-1-phenylethyl})\text{amino}]\text{propyl}\}-N^3,N^3\text{-dipropylisophthalamide (X)}$

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), (1-methyl-1-phenylethyl)amine (VI) and "5-Cl-PHTH" (IX), the title compound is obtained,  $MH^+ = 601$ .

EXAMPLE 567       $N^1-[(1S,2R)-3-[(1\text{-benzofuran-2-ylmethyl})\text{amino}]-1-(3,5\text{-difluorobenzyl})-2\text{-hydroxypropyl}]-5\text{-methyl-}N^3,N^3\text{-dipropylisophthalamide (X)}$

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-

oxiranyl]ethylcarbamate (V, EXAMPLE 3), (1-benzofuran-2-ylmethyl)amine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 592$ .

EXAMPLE 568       $N^1$ -[(1S,2R)-3-{[(1R)-1-(3-bromophenyl)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3), (1R)-1-(3-bromophenyl)ethyl]amine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 645$ .

EXAMPLE 569       $N^1$ -{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(4-fluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-iodobenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 660$ .

EXAMPLE 570       $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[butyl(butyryl)amino]-5-methylbenzamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl 1-(2-oxiranyl)-2-phenylethylcarbamate (V), 3-methoxybenzylamine (VI) and 3-[butyl(butyryl)amino]-5-methylbenzoic acid (IX), the title compound is obtained,  $MH^+ = 560$ .

EXAMPLE 571       $N^1$ -{1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl 1-(2-oxiranyl)-2-phenylethylcarbamate (V), 3-methoxybenzylamine (VI) and 4-methyl- $N,N$ -dipropylisophthalic acid (IX), the title compound is obtained,  $MH^+ = 546$ .

EXAMPLE 572       $N^3$ -{1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^1,N^1$ -dipropylisophthalamide (X)

5            Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl 1-(2-oxiranyl)-2-phenylethylcarbamate (V), 3-methoxybenzylamine (VI) and 4-methyl-N,N-dipropylisophthalic acid (IX), the title compound is obtained,  $MH^+ = 546$ .

10    EXAMPLE 573       $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

          Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-methoxybenzylamine (VI) and 4-methyl-N,N-dipropylisophthalic acid (IX), the title compound is obtained,  $MH^+ = 582$ .

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EXAMPLE 574      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-butyl-1H-indole-6-carboxamide (X)

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          Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl 1-(2-oxiranyl)-2-phenylethylcarbamate (V), 3-methoxybenzylamine (VI) and 1-butyl-1H-indole-6-carboxylic acid (IX), the title compound is obtained,  $MH^+ = 500$ .

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EXAMPLE 575       $N^1$ -[(1S,2R)-3-anilino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

          Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), aniline (VI) and and "5-Me-PHTH" (IX), the title compound is obtained,  $MH^+ = 538$ .

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EXAMPLE 576      5-bromo-N<sup>1</sup>-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-bromobenzylamine (VI) and 5-bromo-N,N-dipropylisophthalic acid (IX), the title compound is obtained, MH<sup>+</sup> = 696.

EXAMPLE 577      N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-4-methylpentanamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-iodobenzylamine (VI) and 4-methylpentanoic acid (IX), the title compound is obtained, MH<sup>+</sup> = 531.

EXAMPLE 578      N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl]-3-methylpentanamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-iodobenzylamine (VI) and CH<sub>3</sub>-CH<sub>2</sub>-CH(CH<sub>3</sub>)-CH<sub>2</sub>-CO-OH (IX), the title compound is obtained, MH<sup>+</sup> = 531.

EXAMPLE 579      N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxybenzyl)amino]propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V), 3-hydroxybenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained, MH<sup>+</sup> = 568.

EXAMPLE 580      *tert*-butyl (1S)-1-(3,5-difluorobenzyl)-3-[(3-methoxybenzyl)amino]-2-oxopropylcarbamate (XI)

*tert*-butyl (1S)-3-bromo-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate (III, EXAMPLE 1, 1 equivalent) is dissolved in isopropanol and treated with 3-methoxybenzylamine (VI, 5 equivalents). The reaction is heated at reflux for 2 hours and monitored by TLC for disappearance of the ketone (III). Upon completion, the reaction is concentrated to dryness under reduced pressure and partitioned between equal parts water and ethyl acetate. The organic phase is extracted, washed two additional times with water, then saline, then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude material is purified by column chromatography on silica gel to give the title compound.

EXAMPLE 581      *tert*-butyl (1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (XIII)

*tert*-butyl-(1S, 2R)-3-azido-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (XII, EXAMPLE 165, 1 equivalent) is dissolved in methanol and treated with 10% palladium on carbon under hydrogen (50 psi). The reaction is shaken at 20-25 degrees C for 2 hours, filtered through a diatomaceous earthpad, and concentrated under reduced pressure to dryness. The crude material is purified by column chromatography on silica gel to give the title compound.

EXAMPLE 582      Benzyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII)

A mixture of benzyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V, 0.22 g, 0.74 mmol), 3-methoxybenzylamine (VI, 0.13 g, 0.92 mmol), and ethanol (2 mL) is stirred at reflux for 2.3 hours and then cooled and concentrated under reduced pressure. The residue is chromatographed (silica gel; methanol/dichloromethane/ammonium hydroxide, 4/96/trace) to give the title compound, MS  $m/z$  at  $(m + H)^+ = 435.2$ .

EXAMPLE 583      Benzyl (1S,2R)-1-benzyl-2-hydroxy-3-(*tert*-butylcarbamoyl)-3-[(3-methoxybenzyl)amino]propyl-carbamate (XXXIV)

A mixture of benzyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl-carbamate (VII, EXAMPLE 582, 9.00 g, 21.0 mmol), di-*tert*-butyl dicarbonate (5.00 g, 23 mmol), sodium carbonate monohydrate (3.12 g,

25 mmol), THF (200 mL), and water (100 mL) is stirred at 20-25 degrees C for 2 hours. THF is removed under reduced pressure and the residue is partitioned between ethyl acetate and water. The organic layer is then washed with saline, dried over anhydrous sodium sulfate, filtered, and concentrated. Column chromatography (silica gel; methanol/dichloromethane, 1/99) gives the title compound, NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.26, 6.79, 5.00, 4.42, 3.89, 3.78, 3.44, 3.28, 2.91, 1.49; MS (ESI+) for C<sub>31</sub>H<sub>38</sub>N<sub>2</sub>O<sub>6</sub>  $m/z$  (M+H)<sup>+</sup> = 535.3.

EXAMPLE 584      *tert*-Butyl (2R,3S)-3-amino-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate (XXXV)

A suspension of benzyl (1S,2R)-1-benzyl-2-hydroxy-3-(*tert*-butylcarbamoyl)-3-[(3-methoxybenzyl)amino]propyl-carbamate (XXXIV, EXAMPLE 583, 10.2 g, 18.6 mmol) and palladium on carbon (5%, 1.00 g) in ethanol (100 mL) is shaken in a hydrogenation apparatus under hydrogen (50 psi) for 2 hours. Then the mixture is filtered through diatomaceous earth and concentrated. The concentrate is chromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, NMR (CDCl<sub>3</sub>)  $\delta$  1.50, 2.46, 2.92, 3.04, 3.42, 3.52, 3.72, 3.82, 4.49, 6.83, 7.19 and 7.28; MS (ESI+) for C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>  $m/z$  (M+H)<sup>+</sup> = 401.3.

EXAMPLE 585      *tert*-butyl (2R,3S)-3-({3-cyano-5-[(dipropylamino)carbonyl]benzoyl}amino)-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate (XXXVI)

To a mixture of 3-cyano-5-[(dipropylamino)carbonyl]benzoic acid (IX/XXXII, PREPARATION 7, 0.086 g, 0.314 mmol) and *tert*-butyl (2R,3S)-3-amino-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate (XXXV, EXAMPLE 584, 0.126 g, 0.314 mmol) in dichloromethane (0.3 mL) is added diethylcyanophosphonate (0.062 g, 0.330 mmol) and triethylamine (0.032 g, 0.316 mmol). The mixture is stirred at 20-25 degrees for 65 hours and then partitioned between dichloromethane and saturated aqueous sodium bicarbonate. The organic phase is separated and dried over sodium sulfate and concentrated. The residue is chromatographed (silica gel, 20 mL; methanol/dichloromethane, 5/95) to give several mixed fractions, which are combined and rechromatographed (silica gel;

acetone/hexane, 20/80) to give the title compound, MS (ESI+) for  $C_{38}H_{48}N_4O_6$   $m/z$  657.6  $(M+H)^+ = 657.6$ ;  $(M+Na) = 679.5$  and  $(M-C_4H_9O_2) = 557.5$ .

5 EXAMPLE 586  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-cyano- $N^3,N^3$ -dipropylisophthalamide hydrochloride (X)

A mixture of *tert*-butyl (2R,3S)-3-({3-cyano-5-[(dipropylamino)carbonyl]benzoyl} amino)-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate (XXXVI, EXAMPLE 585, 0.080 g, 0.122 mmol),  
10 dichloromethane (1 mL), and methanol saturated with hydrochloric acid (1 mL) is stirred for 8 hours, after which time the solvents are removed under reduced pressure. A few drops of methanol, followed by ether, gives the title compound, MS (ESI+) for  $C_{33}H_{40}N_4O_4$   $m/z$   $(M+H)^+ = 557.5$

15 EXAMPLE 587  $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-1,3,5-benzenetricarboxamide (X)

To a mixture of 3-(aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoic acid (IX, PREPARATION 6, 0.18 g, 0.616 mmol) in dry DMF (16 mL) is added EDC  
20 (0.182 g, 0.9 mmol), HOBT (0.127 g, 0.9 mmol), triethylamine (0.062 g, 0.616 mol), and (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.185 g, 0.616 mmol). The mixture is stirred at 20-25 degrees C for 3 days. The mixture is partitioned between water and ethyl acetate. The phases are separated and the organic phase is washed three times with water. The organic  
25 phase is dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography (silica gel, 75 mL; methanol/methylene chloride, 10/90) gives the title compound, IR (diffuse reflectance) 3306, 3301, 3270, 2962, 1676, 1667, 1663, 1645, 1638, 1627, 1615, 1550, 1537, 1450 and 1439  $cm^{-1}$ ; NMR ( $CDCl_3$ )  $\delta$  0.645, 0.968, 1.20, 1.43, 1.67, 2.8, 2.97, 3.38, 3.47, 3.73, 3.87, 4.31, 6.78,  
30 6.91, 7.23, 7.72, 7.87, 8.22 and 8.43.

EXAMPLE 588 1- *tert*-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propylcarbamate (VII)

*tert*-Butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3, 1.75 g, 5.8 mmole) is mixed with isopropanol (30 ml). The reaction flask is charged with 3-iodobenzylamine (VI). The reaction mixture is heated to reflux for 45 minutes, HPLC analysis indicates complete disappearance of the epoxide (V). The reaction mixture is concentrated under reduced pressure and the residue is partitioned between ethyl acetate (150 ml) and aqueous hydrochloric acid (3%, 35 ml). The organic phase is separated and washed with aqueous hydrochloric acid (3%, 20 ml), bicarbonate, saline and dried over sodium sulfate. Concentration under reduced pressure gives the title compound, M + H = 535.

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EXAMPLE 589      1-9H-fluoren-9-ylmethyl (2R,3S)-3-(3-*t*-butyloxycarbonyl)amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3'-iodobenzyl)carbamate hydrochloride (XXXIV)

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1- *tert*-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propylcarbamate (VII, EXAMPLE 588, 2.5 g, 4.7 mmole) and triethylamine (0.72 ml, 5.1 mmole) in THF (10 ml) are mixed. The reaction is cooled to 0 degrees and treated with Fmoc-Cl (1.2 g, 4.7 mmole) in THF (2 ml) via addition funnel. After 15 minutes HPLC indicates complete disappearance of starting material. The reaction is diluted with ethyl acetate and washed with aqueous potassium bisulfate, saturated aqueous bicarbonate, saline and dried over sodium sulfate. Concentration under reduced pressure gives crude product which is purified by flash chromatography, eluting with ethyl acetate/hexane (20/80) followed by ethyl acetate to give the title compound, M + H = 757.

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EXAMPLE 590      1-9H-fluoren-9-ylmethyl (2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3-iodobenzyl)carbamate hydrochloride (XXXV)

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1-9H-fluoren-9-ylmethyl (2R,3S)-3-(3-*t*-butyloxycarbonyl)amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3'-iodobenzyl)carbamate hydrochloride (XXXIV, EXAMPLE 589, 2.9 g) in hydrochloric acid/dioxane (4N, 10 ml). The mixture is stirred 1 hour then slowly poured into rapidly stirring ether (200 ml). The product is filtered and dried to give the title compound, M + H = 657.

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EXAMPLE 591     1-9H-fluoren-9-ylmethyl (2R,3S)-4-(3,5-difluorophenyl)-2-hydroxy-3-{[5-oxo-5-(1-piperidinyl)pentanoyl]amino}butyl(3-iodobenzyl)carbamate (XXXVI)

5                     HOBt (81 mg, 0.6 mmole) and EDC (105 mg, 0.55 mmole) are added to 1-carboxy-5-piperdinyglutaramide (IX, 100 mg, 0.5 mmole) in DMF (2 ml). The acid is activated 60 minutes then treated with 1-9H-fluoren-9-ylmethyl (2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3-iodobenzyl)carbamate hydrochloride (XXXV, EXAMPLE 590, 300 mg, 0.43 mmole) and NMM (0.19 ml, 1.72 mmole).  
10                    The reaction is stirred 3 hours then concentrated under reduced pressure. The residue is partitioned between ethyl acetate and saturated aqueous bicarbonate. The organic phases are washed with aqueous potassium bisulfate, saline, dried over sodium sulfate and finally concentrated under reduced pressure to give crude  
15                    product. Purification via flash chromatography with ethyl acetate/hexane (50/50) then methanol/ethyl acetate (10/90) gives the title compound, M + H = 838.

EXAMPLE 592     1- N- {(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide trifluoroacetate (X)

20                    1- N- {(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide trifluoroacetate (XXXVI, EXAMPLE 591, 240 mg, 0.29 mmole is dissolved in diethylamine (10%, 9 ml) in methylene chloride. The reaction is stirred at 20-25 degrees overnight. The  
25                    next morning the reaction is concentrated under reduced pressure and the residue is redissolved in methylene chloride and purified by preparative reverse phase HPLC. The appropriate fractions are pooled and concentrated under reduced pressure and partitioned between ethyl acetate and saline. The organic phase is separated and dried over sodium sulfate and concentrated to give the title compound, M + H = 614.

30                    EXAMPLE 593     5-(Aminosulfonyl)-N<sup>1</sup>- {(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N-dipropylisophthalamide (X)

*O*-(7-Azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU, 0.0928 g, 0.244 mmol) is added to a mixture of, 3-(aminosulfonyl)-5-[(dipropylamino)-carbonyl]benzoic acid (XXXIX, PREPARATION 13, 0.0800 g, 0.244 mmol) and (2*R*,3*S*)-3-amino-1-[(3-methoxybenzyl)-amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.0732 g, 0.244 mmol) in dry DMF (3 mL). The mixture is stirred for 18 hours at 20-25 degrees, and then partitioned between ethyl acetate and water. The organic phase is separated and washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, MS (ESI+) for  $C_{32}H_{42}N_4O_6S$   $m/z$  (M+H)<sup>+</sup> = 611.5; HRMS (FAB) calculated for  $C_{32}H_{42}N_4O_6S + H_1$  = 611.2903, found = 611.2904.

EXAMPLE 594       $N^1$ -{(1*S*,2*R*)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-5-(1-pyrrolidinylsulfonyl)isophthalamide (X)

Following the general procedure of EXAMPLE 593 and making non-critical variations but using 3-[(dipropylamino)carbonyl]-5-(1-pyrrolidinylsulfonyl)benzoic acid (XXXIX, PREPARATION 15, the title compound is obtained, ES (ESI+) for  $C_{36}H_{48}N_4O_6S$   $m/z$  (M+H)<sup>+</sup> = 665.6; HRMS (FAB) calculated for  $C_{36}H_{48}N_4O_6S + H_1$  = 665.3372, found = 665.3393.

EXAMPLE 595       $N^1$ -{(1*S*,2*R*)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(methylamino)sulfonyl]- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 593 and making non-critical variations but using 3-[(dipropylamino)carbonyl]-5-[(methylamino)sulfonyl]benzoic acid (XXXIX, PREPARATION 17, the title compound is obtained, MS (ESI+) for  $C_{33}H_{44}N_4O_6S$   $m/z$  (M+H)<sup>+</sup> = 625.5.

EXAMPLE 596       $N^1$ -{(1*S*,2*R*)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(dimethylamino)sulfonyl]- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 593 and making non-critical variations but using 3-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl]-benzoic acid (XXXIX, PREPARATION 19), the title compound is obtained, MS (ESI<sup>+</sup>) for C<sub>34</sub>H<sub>46</sub>N<sub>4</sub>O<sub>6</sub>S *m/z* (M+H)<sup>+</sup> = 639.5

5

## EXAMPLES 597-619

Following the general procedure of EXAMPLEs 589 through 592 but starting with (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175) and using the amide forming agent (IX) of Column A, the

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Substituted Amine (X) of Column B is obtained.

| EX # | Column A<br>Amide Forming Agent (IX)                 | Column B<br>Substituted Amine (X)                                                                                    | MS Data<br>M + H |
|------|------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|------------------|
| 597  | 2-methyl-3-(methylsulfonyl)propanoic acid            | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methyl-3-(methylsulfonyl)propanamide hydrochloride | 449              |
| 598  | 3-(methylsulfonyl)propanoic acid                     | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(methylsulfonyl)propanamide hydrochloride          | 435              |
| 599  | 2-amino-1,3-thiazole-4-carboxylic acid hydrochloride | 2-amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1,3-thiazole-4-carboxamide dihydrochloride   | 427              |
| 600  | 5-(methylsulfonyl)pentanoic acid                     | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(methylsulfonyl)pentanamide hydrochloride          | 463              |

| EX # | Column A<br>Amide Forming Agent (IX)            | Column B<br>Substituted Amine (X)                                                                                                                  | MS Data<br>M + H |
|------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
| 601  | 4-anilino-4-oxobutanoic acid                    | N <sup>1</sup> -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>4</sup> -phenylsuccinamide hydrochloride                      | 476              |
| 602  | (2R)-4-amino-2,3,3-trimethyl-4-oxobutanoic acid | (3R)-N <sup>4</sup> -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2,2,3-trimethylbutanediamide hydrochloride                      | 442              |
| 603  | 3-[(dipropylamino)sulfonyl]propanoic acid       | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]-propanamide hydrochloride                              | 520              |
| 604  | 5-(dipropylamino)-5-oxopentanoic acid           | N <sup>1</sup> -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide hydrochloride | 498              |
| 605  | 4-oxo-4-(1-piperidinyl)butanoic acid            | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-oxo-4-(1-piperidinyl)butanamide hydrochloride                                    | 468              |
| 606  | 4-(dipropylamino)-4-oxobutanoic acid            | N-1-~{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>4</sup> ,N <sup>4</sup> -dipropylsuccinamide hydrochloride               | 484              |
| 607  | 5-oxo-5-(1-piperidinyl)                         | N-{(1S,2R)-1-benzyl-2-                                                                                                                             | 482              |

| EX # | Column A<br>Amide Forming Agent (IX)              | Column B<br>Substituted Amine (X)                                                                                                                            | MS Data<br>M + H |
|------|---------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|
|      | pentanoic acid                                    | hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide hydrochloride                                                                   |                  |
| 608  | 5-anilino-5-oxopentanoic acid                     | N <sup>1</sup> -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>5</sup> -phenylpentanediamide hydrochloride                             | 490              |
| 609  | 3,3-dimethyl-4-oxo-4-(1-piperidinyl)butanoic acid | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,3-dimethyl-4-oxo-4-(1-piperidinyl)butanamide hydrochloride                                 | 496              |
| 610  | 4-(isopentylsulfonyl)butanoic acid                | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(isopentylsulfonyl)butanamide hydrochloride                                                | 505              |
| 611  | 4-(dipropylamino)-2,2-dimethyl-4-oxobutanoic acid | N <sup>1</sup> -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2,2-dimethyl-N <sup>4</sup> ,N <sup>4</sup> -dipropylsuccinamide hydrochloride | 512              |
| 612  | 4-[(dipropylamino)sulfonyl]butanoic acid          | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-[(dipropylamino)sulfonyl]butanamide hydrochloride                                          | 534              |
| 613  | 4-[(methylanilino)sulfonyl]butanoic acid          | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)                                                                                                           | 540              |

| EX # | Column A<br>Amide Forming Agent (IX)      | Column B<br>Substituted Amine (X)                                                                                             | MS Data<br>M + H |
|------|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------|
|      |                                           | amino]propyl}-4-<br>[(methylanilino)sulfonyl]butanamide hydrochloride                                                         |                  |
| 614  | 3-[(methylanilino)sulfonyl]propanoic acid | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(methylanilino)sulfonyl]propanamide                        | 526              |
| 615  | Acetic acid                               | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl} acetamide hydrochloride                                       | 343              |
| 616  | 3-(isopentylsulfonyl)propanoic acid       | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(isopentylsulfonyl)propanamide hydrochloride                | 491              |
| 617  | 5-oxo-5-(1-piperidiny)pentanoic acid      | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidiny)pentanamide trifluoroacetate | 614              |
| 618  | 5-oxo-5-(1-piperidiny)pentanoic acid      | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidiny)pentanamide trifluoroacetate               | 578              |
| 619  | 3-[(dipropylamino)sulfonyl]propanoic acid | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]                        | 652              |

| EX # | Column A<br>Amide Forming Agent (IX) | Column B<br>Substituted Amine (X) | MS Data<br>M + H |
|------|--------------------------------------|-----------------------------------|------------------|
|      |                                      | propanamide                       |                  |

EXAMPLE 620       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-ethyl- $N^3,N^3$ -dipropylisophthalamide (X)

5                      Diethyl cyanophosphonate (0.132 mL, 0.870 mmol) is added to a mixture of 3-[(dipropylamino)carbonyl]-5-ethylbenzoic acid (IX, PREPARATION 21, 0.200 g, 0.720 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.216 mg, 0.720 mmol), and triethylamine (0.121 mL, 0.870  
10 mmol) in dichloromethane (3 mL). The mixture was stirred for 1 hour at 20-25 degrees C. Dichloromethane is then removed under reduced pressure. The residue is partitioned between ethyl acetate and water. The organic phase is separated and is washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chromatographed (silica gel;  
15 methanol/dichloromethane, 5/95) to give the title compound, MS (ESI+) for  $C_{34}H_{45}N_3O_4$   $m/z$   $(M+H)^+ = 560.4$ ; HOURMS (FAB) calculated for  $C_{34}H_{45}N_3O_4+H$  = 560.3488, found = 560.3487.

EXAMPLE 621       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-isobutyl- $N^3,N^3$ -dipropylisophthalamide

20                      Following the general procedure of PREPARATIONS 20 and 21 and making non-critical variations but using isobutylboronic acid, and following the general procedure of EXAMPLE 620 but using the 5-isobutylisophthalic acid (IX), the title  
25 compound is obtained, MS (ESI+) for  $C_{36}H_{49}N_3O_4$   $m/z$   $(M+H)^+ = 588.6$ ; HRMS (FAB) calculated for  $C_{36}H_{49}N_3O_4 + H_1$  = 588.3801, found = 588.3810.

EXAMPLE 622       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-tert-butyl- $N^3,N^3$ -dipropylisophthalamide

30

- Following the general procedure of PREPARATIONS 20 and 21 and making non-critical variations but using *tert*-butylboronic acid, and following the general procedure of EXAMPLE 620 but using the *tert*-butylphthalic acid (IX), the title compound is obtained, MS (ESI+) for  $C_{36}H_{49}N_3O_4$   $m/z$   $(M+H)^+ = 588.5$ ; HRMS (FAB) calculated for  $C_{36}H_{49}N_3O_4 + H_1 = 588.3801$ , found = 588.3791.

EXAMPLE 623  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-cyano- $N^3$ -propylisophthalamide (X)

- Following the general procedure of EXAMPLE 586 and making non-critical variations, but using *tert*-butyl (2R,3S)-3-({3-cyano-5-[(propylamino)carbonyl]benzoyl}amino)-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate (XXXVI) the title compound is obtained,  $M + H = 515.1$ .

#### EXAMPLES 624-628

Following the general procedure of EXAMPLE 587 and making non-critical variations, but using the appropriate amines (VIII) and amide forming agents (IX), for example PREPARATIONS 6 and 19, the titled compounds are obtained.

| EXAMPLE | Substituted Amine (X)                                                                                                                        | M + H = |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------|---------|
| 624     | $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3, N^3$ -dipropyl-1,3,5-benzenetricarboxamide         | 611.0   |
| 625     | $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3, N^3$ -dimethyl- $N^5, N^5$ -dipropyl-1,3,5-benzenetricarboxamide | 603.0   |
| 626     | $N^1$ -[(1S,2R)-3-amino-1-benzyl-2-hydroxypropyl]- $N^3, N^3$ -dipropyl-1,3,5-benzenetricarboxamide                                          | 455.1   |
| 627     | $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(isopentylamino)propyl]- $N^3, N^3$ -dipropyl-1,3,5-benzenetricarboxamide                               | 525.6   |
| 628     | $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3$ -propyl-1,3,5-benzenetricarboxamide                              | 533.1   |

EXAMPLE 629      *N*-{(1*S*,2*R*)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[butyryl(propyl)amino]-5-methylbenzamide (X)

Following the procedure of EXAMPLE 570 and making non-critical variations, diethyl cyanophosphonate (0.0760 mL, 0.550 mmol) is added to a mixture of 3-[butyryl(propyl)amino]-5-methylbenzoic acid (IX, 0.120 g, 0.460 mmol), (2*R*,3*S*)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, 0.137 g, 0.460 mmol), and triethylamine (0.0760 mL, 0.550 mmol) in dichloromethane (5 mL). The mixture is stirred for 1 hour at 20-25 degrees C. Dichloromethane is then removed under reduced pressure. The residue is partitioned between ethyl acetate and water. The organic is separated, is washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.09, 4.15, 3.80, 3.79, 3.60, 3.02, 2.84, 2.36, 1.94, 1.56, 1.49, 0.87 and 0.81; MS (ESI<sup>+</sup>) for C<sub>33</sub>H<sub>43</sub>N<sub>3</sub>O<sub>4</sub>  $m/z$  (M+H)<sup>+</sup> = 546.3; HRMS (FAB) calculated for C<sub>33</sub>H<sub>43</sub>N<sub>3</sub>O<sub>4</sub>+H = 546.3331, found = 546.3331.

EXAMPLE 630      *N*-{(1*S*,2*R*)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-propyl-1*H*-indole-6-carboxamide (X)

Following the general procedure of EXAMPLE 539 and making non-critical variations, the title compound is obtained, IR (diffuse reflectance) 3330, 3314, 2960, 2952, 2931, 2873, 1621, 1599, 1525, 1499, 1467, 1353, 1283, 1253 and 786 cm<sup>-1</sup>.

25

EXAMPLE 631      *N*-{(1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-propyl-1*H*-indole-6-carboxamide (X)

Following the general procedure of EXAMPLE 539 and making non-critical variations, the title compound is obtained, IR (diffuse reflectance) 3289, 1627, 1621, 1595, 1531, 1525, 1520, 1507, 1466, 1458, 1450, 1349, 1317, 1252 and 1117 cm<sup>-1</sup>.

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EXAMPLES 633-708

Following the general procedures of CHART A as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the substituted amines (X) of EXAMPLES 633-708 are obtained.

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| EXAMPLE | Substituted Amine (X)                                                                                                                                                                     | MH <sup>+</sup> = |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| 633     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                            | 580               |
| 634     | N <sup>1</sup> -[(1S,2R)-3-[(3-aminobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                 | 567               |
| 635     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}octanamide                                                                                                      | 559               |
| 636     | N <sup>3</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1-methyl-1-[3-(trifluoromethyl)phenyl]ethyl)amino)propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide | 635               |
| 637     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1-methyl-1-[3-(trifluoromethyl)phenyl]ethyl)amino)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    | 648               |
| 638     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[{(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  | 594               |
| 639     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1R)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                  | 578               |
| 640     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-methylbenzamide                                                                                              | 551               |
| 641     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1H-isoindol-3-ylamino)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                | 577               |
| 642     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[{(1R,2S,5R)-2-isopropyl-5-                                                                                                  | 600               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         | MH <sup>+</sup> = |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | methylcyclohexyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                                |                   |
| 643     | N <sup>1</sup> ,N <sup>1</sup> -diallyl-5-chloro-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}isophthalamide             | 597               |
| 644     | 5-chloro-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -bis(2-methoxyethyl)isophthalamide | 633               |
| 645     | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide            | 593               |
| 646     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     | 580               |
| 647     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-[[3-(dimethylamino)benzyl]amino]-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           | 595               |
| 648     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-[[4,5-dimethyl-2-furyl)methyl]amino]-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       | 570               |
| 649     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               | 606               |
| 650     | N <sup>1</sup> -[(1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                         | 502               |
| 651     | N <sup>1</sup> -[(1S,2R)-3-[(cyclopropylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 | 516               |
| 652     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide                               | 630               |
| 653     | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-furylmethyl)amino]-2-hydroxypropyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-                                       | 529               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                      | MH <sup>+</sup> = |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | pyridinedicarboxamide                                                                                                                                                      |                   |
| 654     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     | 546               |
| 655     | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide         | 565               |
| 656     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               | 573               |
| 657     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methyl-2-furyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        | 556               |
| 658     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2S)-tetrahydro-2-furanylmethyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 546               |
| 659     | 5-chloro-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -di(2-propynyl)isophthalamide   | 593               |
| 660     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropenylbenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            | 592               |
| 661     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-propoxyethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 | 548               |
| 662     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-(hexylamino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                            | 546               |
| 663     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide                                         | 633               |
| 664     | methyl 4-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-                                                                       | 610               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         | MH <sup>+</sup> = |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | hydroxybutyl]amino} methyl)benzoate                                                                                                                                           |                   |
| 665     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methoxyethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                    | 520               |
| 666     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-isoxazolylmethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                | 543               |
| 667     | (1R,2R)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide       | 628               |
| 668     | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2S)-tetrahydro-2-furanylmethyl]amino}propyl)-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide | 533               |
| 669     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                   | 582               |
| 670     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 | 594               |
| 671     | 4-(butyrylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}benzamide                                                                          | 622               |
| 672     | N <sup>1</sup> -[(1S,2R)-3-[(3-amino-3-oxopropyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               | 533               |
| 673     | N <sup>3</sup> -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide 1-oxide                   | 555               |
| 674     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-ethynyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     | 688               |
| 675     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-oxabicyclo[2.2.1]hept-2-ylmethyl)amino]propyl}-5-                                                             | 572               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         | MH <sup>+</sup> = |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                                                                 |                   |
| 676     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                   | 576               |
| 677     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-methyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 573               |
| 678     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethyl-1,3-thiazol-5-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  | 587               |
| 679     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3R)-2-oxoazepanyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                | 573               |
| 680     | N <sup>1</sup> -[(1S,2R)-3-(cyclobutylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                          | 516               |
| 681     | N <sup>1</sup> -[(1S,2R)-3-(butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-ethynyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                              | 528               |
| 682     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                    | 590               |
| 683     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-(5-hexynylamino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                           | 542               |
| 684     | N <sup>3</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(5-methyl-2-furyl)methyl]amino}propyl)-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide       | 543               |
| 685     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide                     | 532               |
| 686     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(2-furyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         | 570               |
| 687     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3-                                                                                                             | 599               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                           | MH <sup>+</sup> = |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | isobutyl-5-isoxazolyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                      |                   |
| 688     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 615               |
| 689     | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(dipropylamino)sulfonyl]propanamide                                                              | 554               |
| 690     | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-[(2-phenylethyl)amino]propyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                              | 516               |
| 691     | N <sup>1</sup> -((1S,2R)-1-benzyl-3-{{2-(2-chlorophenyl)ethyl]amino}-2-hydroxypropyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                    | 551               |
| 692     | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-{{3-(2-oxo-1-pyrrolidinyl)propyl]amino}propyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                             | 537               |
| 693     | N <sup>1</sup> -((1S,2R)-1-benzyl-3-[(cyclohexylmethyl)amino]-2-hydroxypropyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                           | 508               |
| 694     | N <sup>1</sup> -[(1S,2R)-1-benzyl-3-(cyclopropylamino)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                  | 452               |
| 695     | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                           | 523               |
| 696     | N-[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-(butylsulfonyl)benzamide                                                                                   | 531               |
| 697     | N <sup>1</sup> -[(1S,2R)-1-benzyl-3-{{2-[(2-ethylhexyl)oxy]ethyl}amino)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                 | 568               |
| 698     | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-{{[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               | 544               |
| 699     | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-{{1-(4-hydroxyphenyl)ethyl]amino}propyl)-N <sup>3</sup> ,N <sup>3</sup> -                                                         | 532               |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                            | MH <sup>+</sup> = |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
|         | dipropylisophthalamide                                                                                                                                                           |                   |
| 700     | N <sup>1</sup> -[(1S,2R)-1-benzyl-3-(cycloheptylamino)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                   | 508               |
| 701     | N <sup>1</sup> -{[(1S,2R)-1-benzyl-3-[[[1,1'-biphenyl]-2-ylmethyl)amino]-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                 | 578               |
| 702     | N <sup>1</sup> -{[(1S,2R)-1-benzyl-3-[(2-fluorobenzyl)amino]-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                             | 520               |
| 703     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-(dimethylamino)benzamide                                                                         | 484               |
| 704     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1-naphthamide                                                                                      | 491               |
| 705     | N <sup>1</sup> -[(1S,2R)-1-benzyl-3-({2-[(5-[(dimethylamino)methyl]-2-furyl)methyl)sulfanyl]ethyl}amino)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 609               |
| 706     | N <sup>1</sup> -[(1S,2R)-1-benzyl-3-({2-[(2-chloro-6-fluorobenzyl)sulfanyl]ethyl}amino)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                  | 615               |
| 707     | N <sup>1</sup> -[(1S,2R)-3-[[[1,1'-biphenyl]-4-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           | 628               |
| 708     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1-naphthylamino)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                             | 588               |

## EXAMPLES 709-737

Following the general procedure of CHART D and EXAMPLES 165-169 and making non-critical variations and using the appropriate reagents, the substituted amines (X) of EXAMPLES 709-737 are obtained.

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                                       | MH <sup>+</sup> |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| 709     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-imidazol-5-ylmethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                          | 542             |
| 710     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-phenyl-1H-imidazol-5-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                               | 618             |
| 711     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1-methyl-1H-imidazol-2-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                               | 556             |
| 712     | N <sup>1</sup> -[(1S,2R)-3-{[(2-butyl-4-chloro-1H-imidazol-5-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                       | 633             |
| 713     | N <sup>1</sup> -[(1S,2R)-3-{[(6-chloroimidazo[2,1-b][1,3]thiazol-5-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 | 633             |
| 714     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1-methyl-1H-benzimidazol-2-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                           | 606             |
| 715     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-hydroxy-1-naphthyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                    | 618             |
| 716     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-oxo-4H-chouromen-3-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                 | 620             |
| 717     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 662             |
| 718     | N <sup>1</sup> -[(1S,2R)-3-({[5-cyano-6-(methylsulfanyl)-2-pyridinyl]methyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                  | 624             |
| 719     | [5-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-                                                                                                              | 614             |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                           | MH <sup>+</sup> |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
|         | hydroxybutyl]amino} methyl)-2-furyl]methyl acetate                                                                                                                                              |                 |
| 720     | N <sup>1</sup> -[(1S,2R)-3-[(1-benzofuran-3-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                             | 592             |
| 721     | methyl 4-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl} amino)-2-hydroxybutyl]amino} methyl)-1-methyl-1H-pyrrole-2-carboxylate                              | 613             |
| 722     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({[1-(phenylsulfonyl)-1H-pyrrol-2-yl]methyl} amino)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          | 681             |
| 723     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{[1-methyl-1H-pyrrol-2-yl]methyl}amino} propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                    | 555             |
| 724     | N <sup>1</sup> -[(1S,2R)-3-{{[4-chloro-1-methyl-1H-pyrazol-3-yl]methyl}amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           | 591             |
| 725     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      | 646             |
| 726     | N <sup>1</sup> -[(1S,2R)-3-{{[(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 667             |
| 727     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{[(3-phenyl-1H-pyrazol-4-yl)methyl]amino} propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                  | 618             |
| 728     | N <sup>1</sup> -[(1S,2R)-3-{{[(5-chloro-2-thienyl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                         | 593             |
| 729     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{[(3-phenoxy-2-thienyl)methyl]amino} propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                       | 650             |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                         | MH <sup>+</sup> |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| 730     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-quinolinylmethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                | 603             |
| 731     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-quinolinylmethyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                | 603             |
| 732     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1H-indol-2-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     | 605             |
| 733     | N <sup>1</sup> -[(1S,2R)-3-[(1-benzyl-1H-indol-3-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     | 681             |
| 734     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1H-indol-3-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     | 605             |
| 735     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-[(4-methylphenyl)sulfonyl]-1H-indol-3-yl)methyl]amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 745             |
| 736     | N <sup>1</sup> -[(1S,2R)-3-[(2-butyl-1H-imidazol-5-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                   | 598             |
| 737     | methyl 3-([(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino)methyl)-1H-indole-6-carboxylate                                         | 649             |

EXAMPLE 738      3-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino)carbonyl]-5-[butyl(butyryl)amino]benzyl diethyl phosphate (X)

5      Following the general procedure of CHART L and EXAMPLE 620 and making non-critical variations, the title compound is obtained, HRMS (FAB) = 712.3749.

EXAMPLE 739       $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(cyanomethyl)- $N^3,N^3$ -dipropylisophthalamide (X)

5            Step 1. A mixture of diethyl 1,3,5-benzenetricarboxylate (5.2 g) and borane methylsulfide complex (6.1 g) is stirred in THF (150 mL) at 20-25 degrees C overnight. The mixture is then treated with methanol, concentrated to dryness, and chroumatographed (silica gel) to give diethyl 5-(hydroxymethyl)isophthalate. Diethyl 5-(hydroxymethyl)isophthalate (3.4 g) is hydrolyzed in ethanol and water  
10 with lithium hydroxide monohydrate (0.57 g) at 20-25 degrees C for 3.5 hours at which time the solvents are removed under reduced pressure. Water (100 mL) is added and the mixture is acidified to pH = 4 with concentrated hydrochloric acid. The mixture is extracted with ethyl acetate and dried over magnesium sulfate, filtered, and concentrated to give 3-(ethoxycarbonyl)-5-(hydroxymethyl)benzoic  
15 acid, high resolution MS  $MH^+ = 225.0769$ . 3-(Ethoxycarbonyl)-5-(hydroxymethyl)benzoic acid (2.3 g), EDC (3.0 g), 1-HOBT (2.1 g), diisopropylethylamine (2.7 mL), dipropyl amine (2.8 mL), and DMF (50 mL) are stirred at 20-25 degrees C overnight. The mixture is then partitioned between ethyl acetate, water, and saline. The organic phase is separated and dried over magnesium  
20 sulfate, filtered, and concentrated. Chromatography (silica gel) gives ethyl 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoate, NMR ( $CDCl_3$ )  $\delta$  0.77, 1.0, 1.4, 1.6, 1.7, 3.2, 3.5, 4.4, 4.8, 7.6, 8.0 and 8.1.

          Step 2. A mixture of ethyl 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoate (1.5 g) and phosphorous tribromide (0.95 mL) is stirred in  
25 dichloromethane (10 mL) and heated at 50 degrees C for 4 hours and then cooled and partitioned between dichloromethane and water. The organic phase is separated and washed with aqueous sodium bicarbonate and then dried over magnesium sulfate and taken to dryness to give ethyl 3-(bromomethyl)-5-  
[(dipropylamino)carbonyl]benzoate, high resolution MS  $MH^+ = 370.1020$ . Ethyl 3-(bromomethyl)-5-[(dipropylamino)carbonyl]benzoate (1.4 g) and sodium cyanide  
30 (0.2 g) are stirred in dry DMSO (25 mL) at 20-25 degrees C for 3.5 hours and the mixture is then partitioned between ethyl acetate, water and saline. The organic layer is separated and dried over magnesium sulfate and taken to dryness under

reduced pressure to give ethyl 3-(cyanomethyl)-5-  
[(dipropylamino)carbonyl]benzoate. Ethyl 3-(cyanomethyl)-5-  
[(dipropylamino)carbonyl]benzoate (0.6 g) is hydrolyzed with lithium hydroxide  
monohydrate (0.1 g) in ethanol and water at 20-25 degrees C overnight and then  
5 added to water (50 mL). The pH is adjusted to 4 using concentrated hydrochloric  
acid and the mixture is partitioned between ethyl acetate, water, and saline. The  
organic phase is separated and dried over magnesium sulfate and taken to dryness  
under reduced pressure to give 3-(cyanomethyl)-5-  
[(dipropylamino)carbonyl]benzoic acid, MS M+H = 287.2.

10 Step 3. A mixture of 3-(cyanomethyl)-5-[(dipropylamino)carbonyl]benzoic  
acid (IX, 0.13 g), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-  
butanol (VIII, 0.14 g), HATU (0.17 g), and dichloromethane (10 mL) is stirred at 40  
degrees C overnight. After cooling, the mixture is washed with water and the  
organic phase is separated and dried over magnesium sulfate and taken to dryness  
15 under reduced pressure. Chromatography (silica gel) gives the title compound, M +  
H = 571.2

EXAMPLE 740 N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-  
methoxybenzyl)amino]propyl}-5-(hydroxymethyl)-N<sup>3</sup>,N<sup>3</sup>-  
20 dipropylisophthalamide (X)

Following the procedure of CHART P and EXAMPLE 739 and making non-  
critical variations but using 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoic  
acid (IX) and (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol  
(VIII), the title compound is obtained, HRMS (FAB) = 615.3571.

25 EXAMPLE 741 N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-  
methoxybenzyl)amino]propyl}-5-ethynyl-N<sup>3</sup>,N<sup>3</sup>-  
dipropylisophthalamide (X)

Step 1: A mixture of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate  
30 (XXI, 200 mg, 0.58 mmol), PdCl<sub>2</sub>(Ph<sub>3</sub>P)<sub>2</sub> (16 mg, 0.03 mol %) and copper (I) iodide  
(6 mg, 0.05 mol %) in triethylamine (1.2 mL) is heated to reflux. (Trimethylsilyl)  
acetylene (100 microliter, 0.7 mmol) is added, and the mixture stirred for 3 hours,  
cooled to 20-25 degrees, diluted with water (20 mL), and extracted with chloroform  
(3 x 15 mL). The combined organic extracts are washed with saline (20 mL), dried

over sodium sulfate and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-ethynylbenzoate (XXXII, 185.5 mg), NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.95, 7.75, 7.43, 3.74, 3.25, 2.95, 1.49, 1.34, 0.79, 0.56 and 0.06.

Step 2: To a stirred mixture of the protected methyl 3-

- 5 [(dipropylamino)carbonyl]-5-ethynylbenzoate (XXXII, Step 1, 185.3 mg, 0.49 mmol) in methanol (2.5 mL) is added a mixture of potassium hydroxide (2.9 mL of a 1 M mixture in water, 2.9 mmol). The reaction mixture is stirred for 4 hours diluted with chloroform (40 mL), the phases are separated and the organic phase is concentrated under reduced pressure to give 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid, NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  8.22, 8.05, 7.71, 3.48, 3.17, 3.16, 1.71, 1.55, 1.00 and 0.78.

- Step 3: To a stirred mixture of 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid (70 mg, 0.24 mmol) in DMF (2.5 mL) is added (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 81 mg, 0.24 mmol), HOBt (36 mg, 0.26 mmol) and diisopropylethylamine (170 microliter, 0.96 mmol). To this reaction mixture is added EDC (51mg, 0.26 mmol) and the reaction mixture is stirred overnight. The reaction mixture is diluted with ethyl acetate (30 mL), washed with water (3 x 50 mL), hydrochloric acid (1 N, 30 mL), saturated sodium bicarbonate (30 mL), saline (30 mL), dried over sodium sulfate and concentrated under reduced pressure. Purification by flash chromatography (silica, ethyl acetate to methanol/chloroform, 1/10) gives the title compound, IR (KBr): 3276, 2956, 2921, 1610, 1450 and 1264 cm<sup>-1</sup>; ESI-MS (*m/z*) [M + H]<sup>+</sup> = 556.

- 25 EXAMPLE 742 N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropyl-5-prop-1-ynylisophthalamide (X)

- Following the general procedure of EXAMPLE 741 and making non-critical variations but using propyne in place of (trimethylsilyl) acetylene and using (2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII) in place of (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII), the title compound is obtained, IR (ATR): 3305, 2930, 2872, 1613 and 1537 cm<sup>-1</sup>; ESI-MS (*m/z*) [M+H]<sup>+</sup> = 666.

EXAMPLE 743       $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{{3-(trifluoromethyl)benzyl}amino}propyl)-5-ethynyl- $N^3,N^3$ -dipropylisophthalamide (X)

5            Step 1: A mixture of tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V, 2.3 g, 8.7 mmol) and 3-(trifluoromethyl)benzylamine (VI, 1.9 mL, 13.1 mmol) in 2-propanol (70 mL) is heated at reflux for 4 hours. The reaction mixture is cooled to 20-25 degrees and concentrated under reduced pressure to give tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{{3-(trifluoromethyl)benzyl}amino}propylcarbamate (VII, 3.1 g) as a solid, ESI-MS  
10            ( $m/z$ )  $[M + H]^+ = 439$ .

             Step 2: A mixture of tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{{3-(trifluoromethyl)benzyl}amino}propylcarbamate (VII, step 1, 2.5 g, 5.7 mmol) and hydrochloric acid (29 mL of a 4.0 M mixture in dioxane, 114 mmol) is stirred at 20-  
15            25 degrees. A precipitate forms and is collected by filtration, washed with ether, and dried under reduced pressure to give (2R,3S)-3-amino-4-phenyl-1-{{3-(trifluoromethyl)benzyl}amino}-2-butanol dihydrochloride (VIII, 2.13 g), ESI-MS  
             ( $m/z$ )  $[M +]^+ = 339$ .

             Step 3: A mixture of 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid  
20            (IX, 231 mg, 0.8 mmol), (2R,3S)-3-amino-4-phenyl-1-{{3-(trifluoromethyl)benzyl}amino}-2-butanol dihydrochloride (VIII, Step 2, 493.5 mg, 1.2 mmol) HOBt (162 mg, 1.2 mmol), and diisopropylethylamine (832 Micro Liter, 4.8 mmol) is stirred in methylene chloride (4 mL) for 15 minutes. EDC (206 mg, 1.2 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture  
25            is diluted with water, and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline dried over sodium sulfate and concentrated under reduced pressure. Purification by flash column chromatography (silica, 100% ethyl acetate to methanol/chloroform, 1/9) gives title compound, IR (ATR): 3302, 2963, 2932 and 1615  $cm^{-1}$ ; MS ( $m/z$ )  $[M + H]^+ = 549$ .  
30           

EXAMPLE 744       $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-ethynyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 744 and making non-critical variations but using 3-iodobenzylamine hydrochloride salt (VI), the title compound is obtained, IR (ATR) 3295, 2960, 2927 and 1616  $\text{cm}^{-1}$ , APCI-MS ( $m/z$ )  $[M + H]^+ = 652$ .

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EXAMPLE 745       $N^1$ -{(1S,2R)-1-benzyl-3-[(3-fluorobenzyl)amino]-2-hydroxypropyl}-5-ethynyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 744 and making non-critical variations but using 3-fluorobenzylamine (VI), the title compound is obtained, IR (ATR): 3217, 2961, 2918 and 1615  $\text{cm}^{-1}$ ; APCI-MS ( $m/z$ )  $[M + H]^+ = 544$ .

10

EXAMPLE 746       $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-5-(8-quinoliny)isophthalamide (X)

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Step 1: A mixture of methyl-3-bromo-5-[(dipropylamino)carbonyl]benzoate (XLVIII, 200 mg, 0.58 mmol), 8-quinolineboronic acid (200.6 mg, 1.2 mmol), sodium carbonate (870 Micro Liter of a 2 M mixture in water, 1.74 mmol) in toluene (6 mL) is degassed under reduced pressure for 15 minutes and purged with argon. Palladium tetrakis(triphenylphosphine) (139 mg, 0.12 mmol) is added and the reaction mixture is degassed under reduced pressure for 15 minutes and purged with argon. The reaction mixture is heated at reflux overnight, cooled to 20-25 degrees C and diluted with chloroform. The organic phase is separated and washed with water (3 x 50 mL), and saline, dried over sodium sulfate and concentrated under reduced pressure. Purification by flash column chromatography (silica, ethyl acetate/hexanes, 1.3/1) gives methyl 3-[(dipropylamino)carbonyl]-5-(8-quinoliny)benzoate (XLIX, 176 mg), NMR (300 MHz,  $\text{CDCl}_3$ ): delta 8.91, 8.42, 8.21, 8.09, 7.95, 7.86, 7.77, 7.64, 3.94, 3.49, 3.34, 1.64, 0.99 and 0.84.

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25

Step 2: To a mixture of methyl 3-[(dipropylamino)carbonyl]-5-(8-quinoliny)benzoate (XLIX, step 1, 175.5 mg, 0.45 mmol) in methanol (2 mL) is added lithium hydroxide (32.3 mg, 1.4 mmol) and water (500 microliter). After stirring overnight, the reaction mixture is partitioned between ethyl acetate (10 mL) and water (10 mL). The aqueous phase is separated and acidified with hydrochloric acid (1N), and extracted with chloroform (3 x 40 mL). The organic phase is washed with saline, dried (sodium sulfate) and concentrated under reduced pressure to give

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3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoic acid (IX – L, 130 mg), NMR (300 MHz, CD<sub>3</sub>OD)  $\delta$  8.84, 8.39, 8.35, 8.05, 7.96, 7.90, 7.87, 7.79, 7.68, 3.50, 3.37, 1.76-1.61, 0.99 and 0.84.

Step 3: A mixture of 3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoic acid (IX – L, Step 2, 130 mg, 0.35 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 117 mg, 0.35 mmol), HOBt (70 mg, 0.52 mmol) and diisopropylethylamine (241 microliter, 1.4 mmol) in methylene chloride (2 mL) is stirred for 15 minutes. EDC (89 mg, 0.52 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with water and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica; methanol/chloroform, 1/9) gives the title compound, IR (NaCl): 3301, 2916, 2365 and 1613 cm<sup>-1</sup>; APCI-MS (*m/z*) [M + H]<sup>+</sup> = 659.

EXAMPLE 747      N<sup>3</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4'-methoxy-N<sup>5</sup>,N<sup>5</sup>-dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Step 1: A mixture of 4-methoxyphenyl boronic acid (463 mg, 3.05 mmol), 3-bromo-5-[(dipropylamino)carbonyl]benzoic acid (XLVIII, 1.02 g, 3.05 mmol), and potassium phosphate (1.29 g, 6.10 mmol) in 1,2-dimethoxyethane (10 mL) and water (5 mL) is degassed with argon for 15 minutes. Bis(triphenylphosphine)palladium (II) chloride (21 mg, 0.03 mmol) is added, the reaction mixture is degassed again with argon, and heated at 85 degrees C overnight. The reaction mixture is cooled to 20-25 degrees C, and passed through a plug of diatomaceous earth.

The filtrate is acidified to pH = 4 with hydrochloric acid (1N) and extracted with ethyl acetate. The organic phase is washed with water and saline and dried (magnesium sulfate). The product is purified by flash column chromatography (silica gel; ethyl acetate/acetic acid, 99/1) to give 5-[(dipropylamino)carbonyl]-4'-methoxy[1,1'-biphenyl]-3-carboxylic acid (IX - L, 667 mg), ESI-MS (*m/z*) [M + H]<sup>+</sup> = 356.

Step 2: A mixture of 5-[(dipropylamino)carbonyl]-4'-methoxy[1,1'-biphenyl]-3-carboxylic acid (IX - L, step 1, 316 mg, 0.89 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 332 mg, 0.89 mmol), HOBt (181 mg, 1.34 mmol), and *N*-methylmorpholine (0.37 g, 3.56 mmol) in methylene chloride (8 mL) and dimethylformamide (2 mL) is stirred at 20-25 degrees for 15 minutes. EDC (257 mg, 1.34 mmol) is added and the reaction mixture is stirred for 4.5 hours. The reaction mixture is partitioned between methylene chloride and water. The organic phase is washed with hydrochloric acid (1N), water, and saline, dried (magnesium sulfate), and concentrated. The concentrate is dissolved in a minimum of methanol, treated with hydrochloric acid (3 mL of a 1.0 M mixture in ether, 3 mmol), and stirred for 10 minutes. More ether is added to precipitate the rest of the product. The precipitate is collected by filtration and dried in the vacuum oven at 50 degrees C to give the title compound, mp = 205-209 degrees C; IR (ATR): 2964 and 1649  $\text{cm}^{-1}$ ; APCI-MS ( $m/z$ )  $[\text{M} + \text{H}]^+$  = 638.

EXAMPLE 748  $\text{N}^3$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $\text{N}^5, \text{N}^5$ -dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Step 1: A mixture of tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, 500 mg, 1.67 mmol) and 3-methoxybenzylamine (VI, 0.34g, 2.51 mmol) in 2-propanol (3 mL) is heated at reflux overnight, allowed to cool to 20-25 degrees C, and concentrated under reduced pressure. The residue is crystallized from ethyl acetate/hexanes and collected by filtration to afford tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, 575 mg) as a solid: ESI-MS ( $m/z$ ): 437  $[\text{M} + \text{H}]^+$ .

Step 2: A mixture of tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, Step 1, 535 mg, 1.23 mmol) in methanol (2 mL) is treated with hydrochloric acid (3.2 mL of a 1.0 M mixture in ether, 3.2 mmol), and stirred at 20-25 degrees C for 30 minutes. Ether is added until a precipitate formed. The precipitate is collected by filtration is (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII).

Step 3: A mixture of 5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylic acid (IX, 188 mg, 0.56 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII, Step 2, 230 mg, 0.56 mmol), HOBt (114 mg, 0.84 mmol), and *N*-methylmorpholine (0.23 g, 2.24 mmol) in methylene chloride (6 mL) and dimethylformamide (1 mL) is stirred at 20-25 degrees C for 15 minutes. EDC (161 mg, 0.84 mmol) is added and the reaction mixture is stirred at 20-25 degrees C overnight. The reaction mixture is washed with water, 1 N hydrochloric acid, water, and saline, dried (sodium sulfate), and concentrated under reduced pressure to give the title compound, mp 230-233 degrees C; IR (ATR): 2965, 1651, 1596 and 1267  $\text{cm}^{-1}$ ; ESI-MS ( $m/z$ )  $[M + H]^+ = 644$ .

EXAMPLE 749       $N^3$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^5$ , $N^5$ -dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Following the general procedure of EXAMPLE 748 and making non-critical variations but using (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII) in place of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII), the title compound is obtained, mp = 214-219 degrees C; IR (KBr): 3227, 2961, 1632 and 1605  $\text{cm}^{-1}$ ; ESI-MS ( $m/z$ )  $[M + H]^+ = 608$ .

EXAMPLE 750       $N^3$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4'-[(dimethylamino)sulfonyl]- $N^5$ , $N^5$ -dipropyl-1,1'-biphenyl-3,5-dicarboxamide (X)

Step 1: A flask is charged with 1,1'-bis(diphenylphosphino)ferrocene-dichloropalladium 1:1 complex (37 mg, 0.05 mmol), potassium acetate (492 mg, 4.5 mmol) and bis(pinacolato)diboron (408 mg, 1.6 mmol) and is degassed under reduced pressure for 15 min and purged with argon. To this mixture is added a mixture of methyl-3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI, 500 mg, 1.5 mmol) in anhydrous dimethyl sulfoxide (9 mL) and the reaction mixture is stirred at 80 degrees C for 4 hours. The reaction mixture is cooled to 20-25 degrees C, diluted with toluene (50 mL), washed with water (3 x 150 mL), saline, dried (magnesium sulfate), and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate, ESI-MS ( $m/z$ )  $[M + H]^+ = 390$ .

Step 2: A mixture of methyl 3-[(dipropylamino)carbonyl]-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Step 1, 534 mg, 1.4 mmol), 4-bromobenzenedimethyl-sulfonamide (363 mg, 1.4 mmol), and sodium carbonate (2 mL of a 2 M mixture in water, 4.1 mmol) in toluene (10 mL) is degassed under reduced pressure for 15 minutes and then purged with argon. Palladium tetrakis(triphenylphosphine) (40 mg, 0.025 mmol) is added and the reaction mixture is degassed under reduced pressure for 15 minutes and then purged with argon. The reaction mixture is heated at reflux for 4 hours, cooled to 20-25 degrees C, filtered through a plug of diatomaceous earth and sodium sulfate, and the filtrate is concentrated under reduced pressure. Purification by flash column chromatography (silica; ethyl acetate/hexanes, 1/1) gives methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylate (XXXVIII), ESI-MS ( $m/z$ )  $[M + H]^+ = 447$ .

Step 3: A mixture of methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylate (XXXVIII, step 2, 555 mg, 1.24 mmol) in methanol (6 mL) and sodium hydroxide (2 mL of a 6.0 M mixture in water, 12 mmol) is stirred at 20-25 degrees C for 4 hours. The reaction mixture is partitioned between ethyl acetate (40 mL) and water (40 mL). The aqueous phase is acidified to pH = 4 with hydrochloric acid (1N), extracted with ether (3 x 100 mL), and the combined organic phases are concentrated under reduced pressure to give methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylic acid (IX - XXXIX), NMR (300 MHz,  $CDCl_3$ ):  $\delta$  8.37, 8.12, 7.89, 7.80, 3.51, 3.22, 2.76, 1.74, 1.59, 1.02 and 0.79.

Step 4: A mixture of the acid (IX - XXXIX, Step 3, 150 mg, 0.35 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 129 mg, 0.35 mmol) HOBt (47 mg, 0.35 mmol), and *N*-methylmorpholine (122  $\mu$ L, 1.1 mmol) is stirred in methylene chloride (4 mL) for 15 minutes EDC (107 mg, 0.62 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with water, and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica; 100% ethyl

acetate to methanol/chloroform, 1/9) gives the title compound, IR (ATR): 2932, 2837 and 1593  $\text{cm}^{-1}$ ; APCI-MS ( $m/z$ )  $[M + H]^+ = 715$ .

EXAMPLE 751  $N^3$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4'-[(dimethylamino)sulfonyl]- $N^5, N^5$ -dipropyl-1,1'-biphenyl-3,5-dicarboxamide (X)

Following the general procedure of EXAMPLE 750 and making non-critical variations but using 2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII), the title compound is obtained, IR (ATR): 3303, 2930, 2872 and 1614  $\text{cm}^{-1}$ ; APCI-MS ( $m/z$ )  $[M + H]^+ = 811$ .

EXAMPLE 752  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3, N^3$ -dipropyl-5-(3-thienyl)isophthalamide hydrochloride (X)

Step 1: To an ice-cold mixture of methyl 3-amino-5-[(dipropylamino)carbonyl]benzoate (XLVIII, 1.0 g, 3.60 mmol) in aqueous hydrogen tetrafluoroborate (48% wt. in  $\text{H}_2\text{O}$ , 12.9 mmol) is added a cold mixture of aqueous sodium nitrite (0.25 g, 3.60 mmol) dropwise. The mixture is stirred for 10 min and then extracted with ethyl acetate. The organic phase is washed with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give a diazonium salt which is used without further purification, NMR (500 MHz,  $\text{CD}_3\text{OD}$ ):  $\delta$  9.26, 8.86, 8.71, 4.03, 3.50, 3.22, 1.75, 1.60, 1.01 and 0.79.

Step 2: To a mixture of thiophene-3-boronic acid (1.0 g, 7.82 mmol) in methanol is added a concentrated aqueous mixture of potassium hydrogen difluoride (2.01 g, 25.8 mmol) dropwise. The reaction mixture is stirred for 10 minutes and concentrated under reduced pressure. The resulting solid is extracted with acetone and concentrated under reduced pressure gives crude material, which is recrystallized from acetone/ether to give potassium trifluoro(3-thienyl)borate salt, ESI-MS ( $m/z$ )  $[M + H]^+ = 151$ .

Step 3: A mixture of potassium trifluoro(3-thienyl)borate salt (step 2, 0.69 g, 1.82 mmol), diazonium salt from (XLVIII, step 1, 0.42 g, 2.19 mmol), and lead acetate (0.02 g, 0.09 mmol) in the dark is purged with argon for 15 minutes. Dioxane (8 mL) is added and the reaction mixture is degassed with argon and stirred

at 20-25 degrees C overnight. The reaction mixture is diluted with ether, washed with saline, dried over magnesium sulfate and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoate (XLIX) which is purified by flash chromatography (silica; ethyl acetate/hexanes, 1/1), ESI-MS ( $m/z$ )  $[M + H]^+ = 346$ .

Step 4: A mixture of methyl 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoate (XLIX, step 3, 0.31 g, 0.88 mmol) in THF/methanol/sodium hydroxide (3/1/1, 5 mL) is stirred at 40 degrees C for 2 hours. The reaction is cooled to 20-25 degrees C, diluted with water and extracted with ethyl acetate. The aqueous phase is acidified to pH = 4 and extracted with ethyl acetate. The organic phase is washed with water and saline, dried over magnesium sulfate and concentrated under reduced pressure to give 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoic acid (IX - L), ESI-MS ( $m/z$ )  $[M + H]^+ = 332$ .

Step 5: A mixture of 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoic acid (IX - L, step 4, 0.26 g, 0.79 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 0.26 g, 0.71 mmol), HOBt (0.16 g, 1.18 mmol), and triethylamine (0.44 mL, 3.15 mmol) in DMF (4 mL) is stirred at 20-25 degrees C for 10 minutes EDC (0.23 g, 1.18 mmol) is added and the reaction mixture is stirred for 4 hours. The reaction mixture is diluted with water and extracted with ethyl acetate. The organic phase is washed with hydrochloric acid (1 N), water, and saline, dried over magnesium sulfate and concentrated under reduced pressure. Recrystallization (methylene chloride/hexanes, 1/1) gives the title compound, mp = 199-201 degrees C; IR (KBr): 3278, 2961, 2874 and 2837  $\text{cm}^{-1}$ ; ESI-MS ( $m/z$ )  $[M + H]^+ = 614$ .

EXAMPLE 753      N-[(1R,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-methyl-5-pentanoylbenzamide (X)

Step 1: To an ice-cold, stirred mixture of oxalyl chloride (733 mg, 5.77 mmol) in methylene chloride (5 mL) is added 3 drops of dimethylformamide. After 10 minutes 3-(methoxycarbonyl)-5-methylbenzoic acid (LXXIII, 560 mg, 2.89 mmol) is added. The reaction mixture is stirred for 1 hour and concentrated under reduced pressure to provide an acid chloride (LXXIV), which is used without further purification.

- Step 2: To a -78 degrees C, stirred mixture of acid halide (LXXIV, step 1, 612 mg, 2.89 mmol) and copper (I) bromide (415 mg, 2.89 mmol) in tetrahydrofuran (5 mL) is added butyl magnesium chloride (1.44 mL of a 2.0 M mixture in tetrahydrofuran, 2.89 mmol). The reaction mixture is warmed to 20-25 degrees C, quenched by addition of saturated ammonium chloride, and diluted with ether. The organic phase is separated, washed with saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; hexanes/ethyl acetate, 6.5/1) gives methyl 3-methyl-5-pentanoylbenzoate (LXXVI), NMR (300 MHz, CD<sub>3</sub>OD):  $\delta$  8.43, 8.05, 3.96, 3.01, 1.77, 1.55 and 1.22.
- Step 3: A mixture of methyl 3-methyl-5-pentanoylbenzoate (LXXVI, step 2. 133 mg, 0.605 mmol) in methanol (1 mL) is stirred with tetrahydrofuran/methanol/sodium hydroxide (2 N) (3/1/1, 3 mL) for 3 days. The reaction mixture is diluted with ethyl acetate and washed with water. The aqueous phase is separated and acidified with hydrochloric acid (1 N) and extracted with methylene chloride. The organic phase is dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 3-methyl-5-pentanoylbenzoic acid (IX - LXXVII), NMR (300 MHz, CD<sub>3</sub>OD):  $\delta$  8.44, 8.03, 3.10, 2.33, 1.78, 1.64 and 1.34.
- Step 4: To a mixture of 3-methyl-5-pentanoylbenzoic acid (IX - LXXVII, 112 mg, 0.589 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII, 239 mg, 0.589 mmol), HOBt (80 mg, 0.589 mmol), and *N*-methylmorpholine (250 mg, 2.47 mmol) in methylene chloride (3 mL) is added EDC (203 mg, 1.06 mmol). The reaction mixture is stirred overnight and then partitioned between ethyl acetate and water. The organic phase is washed with hydrochloric acid (1 N), saturated sodium bicarbonate, saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol, 12/1) gives the title compound, IR (ATR): 3297, 2957, 1687 and 1628 cm<sup>-1</sup>; APCI-MS (*m/z*) [M + H]<sup>+</sup> = 539.

EXAMPLE 754      N<sup>1</sup>-(4-hydroxybutyl)-N<sup>3</sup>-{(1S)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N<sup>1</sup>-propylisophthalamide (X)

Step 1: To a mixture of methyl (2S)-3-[4-(benzyloxy)phenyl]-2-(tert-butoxycarbonyl)aminopropanoate (1.79 g, 4.65 mmol) in a THF/methanol/water (1/2/1, 16 ml) is added lithium hydroxide (340 mg, 13.9 mmol) and the mixture stirred at 20-25 degrees C for 12 hours. The mixture is quenched with citric acid (10%). The resulting mixture is extracted with ethyl acetate (3 x 15 ml). The combined organic extracts are washed three times with water, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give (2S)-3-[4-(benzyloxy)phenyl]-2-[(tert-butoxycarbonyl)amino]propanoic acid which is carried on without purification. To a -78 degrees C, stirred mixture of (2S)-3-[4-(benzyloxy)phenyl]-2-[(tert-butoxycarbonyl)amino]propanoic acid (10.0 g, 27.0 mmol) in THF (200 mL) is added NMM (3.20 mL, 29.0 mmol) and isobutyl chloroformate (3.8 mL, 29.0 mmol). The cold bath is removed, the reaction mixture is stirred for 1 hour, and then filtered. The filtrate is kept cold and used in the next step. To an ice-cold, stirred mixture of ether (110 mL) and potassium hydroxide (40%, 35 mL) is slowly added 1-methyl-3-nitro-1-nitrosoguanidine (8.40 g, 57.0 mmol). The reaction mixture is stirred until gas evolution ends. The organic phase is separated and slowly added to an ice-cold, stirred mixture of the mixed anhydride filtrate from step 2. After the reaction mixture is stirred for 1 hour, nitrogen is bubbled into the mixture for 10 minutes. The resulting mixture is concentrated under reduced pressure, diluted with ethyl acetate (200 mL), and washed with water (100 mL). The organic phase is washed with saturated sodium bicarbonate and saline, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the diazoketone, which is carried on without purification or characterization. To an ice-cold, stirred mixture of diazoketone in ether (100 mL) is added hydrobromous acid (48%, 4 mL, 73 mmol). The cold bath is removed, the reaction mixture stirred for 30 minutes, and partitioned between ether and water. The organic phase separated and washed with saturated sodium bicarbonate and saline, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give tert-butyl (1S)-1-[4-(benzyloxy)benzyl]-3-bromo-2-oxopropylcarbamate (IV) which is used without further purification or characterization. To a -78 degrees C, stirred mixture of tert-butyl (1S)-1-[4-(benzyloxy)benzyl]-3-bromo-2-oxopropylcarbamate (IV) in a isopropanol/THF (2/1, 150 mL) is slowly added sodium borohydride (1.15 g, 30.0 mmol). The reaction mixture is stirred for 30 minutes followed by the addition of water (30 mL). The resulting mixture is

warmed to 20-25 degrees C and concentrated under reduced pressure in a water bath not exceeding 30 degrees C. The crude residue is dissolved in ethyl acetate and washed with water and saline. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the bromohydrin as a solid.

- 5 To an ice-cold, stirred mixture of bromohydrin in ethanol (150 mL) and ethyl acetate (100 mL) is added a potassium hydroxide (1 N) ethanol mixture (36 mL, 36 mmol). The cold bath is removed and the reaction mixture is stirred for 30 minutes. The resulting mixture is partitioned between ethyl acetate and water. The organic phase is separated and washed with saline, dried over magnesium sulfate, filtered, and
- 10 concentrated under reduced pressure. Purification by flash chromatography (silica; hexanes/ethyl acetate, 5/1) gives tert-butyl (1S)-2-[4-(benzyloxy)phenyl]-1-[(2S)-oxiranyl]ethylcarbamate (V, as a 8/1 mixture of diastereomers), NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.44-7.32, 7.14, 6.93, 5.07, 4.45, 3.61, 3.00-2.60 and 1.39.

- Step 2: A mixture of 4-benzyloxybutyric acid (2.69 g, 13.8 mmol),
- 15 propylamine (0.82 g, 13.8 mmol), HOBt (2.05 g, 15.2 mmol), *N*-methylmorpholine (1.68 g, 16.6 mmol) and EDC (2.91 g, 15.2 mmol) in DMF (6 mL) is stirred at 20-25 degrees C for 18 hours. The mixture is diluted with ethyl acetate (40 mL) and washed with water (10 mL), hydrochloric acid (1 N, 10 mL), saturated sodium bicarbonate (10 mL), and saline (10 mL). The organic phase is separated, dried over
- 20 magnesium sulfate, filtered, and concentrated under reduced pressure to provide 4-(benzyloxy)-*N*-propylbutanamide (2.59 g), APCI-MS ( $m/z$ )  $[M + H]^+ = 236$ .

- Step 3: To an ice-cold, stirred mixture of 4-(benzyloxy)-*N*-propylbutanamide (2.59 g, 11.0 mmol) in THF (8 mL) is added lithium aluminum hydride (0.54 g, 14.3 mmol). The reaction mixture is heated to 40-50 degrees C for 5 hours. The cooled
- 25 reaction mixture is quenched with water (0.5 mL), sodium hydroxide (2 N, 1.0 mL), and saline (0.5 mL) then diluted with ether (30 mL). The precipitate that formed is filtered off, and the ether phase dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give *N*-[4-(benzyloxy)butyl]-*N*-propylamine (2.41 g), APCI-MS ( $m/z$ ): 222  $[M + H]^+$ .

- 30 Step 4: A mixture of *N*-[4-(benzyloxy)butyl]-*N*-propylamine (2.31 g, 10.44 mmol), 3-(ethoxycarbonyl)-5-methylbenzoic acid (2.18 g, 10.44 mmol), HOBt (1.56 g, 11.49 mmol), *N*-methylmorpholine (1.37 mL, 12.52 mmol), and EDC (2.20 g, 11.49 mmol) in DMF (12 mL) is stirred at 20-25 degrees C for 18 hours. The

reaction mixture is diluted with ethyl acetate (80 mL) and washed with water (2 x 20 mL), hydrochloric acid (1 N, 20 mL), saturated sodium bicarbonate (20 mL) and saline (20 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica; hexanes/ethyl acetate, 1/1) gives ethyl 3-[[[4-(benzyloxy)butyl](propyl)amino]carbonyl]-5-methylbenzoate (1.79 g), NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  7.80, 7.64, 7.40, 7.38-7.16, 4.50-4.43, 4.34-4.29, 3.53-3.30, 3.20-3.06, 2.41-2.36, 1.70-1.40, 1.36-1.29, 0.94-0.84 and 0.82-0.72; APCI-MS (*m/z*)  $[M + H]^+ = 412$ .

Step 5: To a mixture of ethyl 3-[[[4-(benzyloxy)butyl](propyl)amino]carbonyl]-5-methylbenzoate (1.75 g, 4.25 mmol) in THF/ethanol/water (1/2/1, 30 mL) is added lithium hydroxide (0.31 g, 12.76 mmol). The reaction mixture is stirred for 2 h and then acidified to pH = 3 with concentrated hydrochloric acid (0.5 mL). The reaction mixture is extracted with ethyl acetate (2 x 30 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give 3-[[[4-(benzyloxy)butyl](propyl)amino]carbonyl]-5-methylbenzoic acid (IX, 1.63 g), ESI-MS (*m/z*)  $[M + H]^+ = 384$ .

Step 6: A mixture of tert-butyl (1S)-2-[4-(benzyloxy)phenyl]-1-[(2S)-oxiranyl]ethylcarbamate (V, 1.58 g, 4.28 mmol) and 3-methoxybenzylamine (VI, 825 microliter, 6.42 mmol) in isopropanol (45 mL) is heated to 90 degrees C for 4 hours. Upon cooling to 20-25 degrees C, the reaction mixture is concentrated under reduced pressure. Purification by flash chromatography (silica; methylene chloride/methanol/ammonium hydroxide 98/1/1 to 95/4/1) gives tert-butyl (1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, 1.97 g), NMR (300 MHz, MeOH-*d*<sub>4</sub>):  $\delta$  7.41-6.79, 5.05, 4.33-3.33, 3.74, 3.54, 3.03-2.46 and 1.29; ESI-MS (*m/z*)  $[M + H]^+ = 507$ .

Step 7: tert-Butyl (1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, step 6, 2.34 g, 4.62 mmol) in dioxane (10 mL) is treated with hydrochloric acid (12 mL of a 4.0 M mixture in dioxane, 48 mmol) for 2 hours. The precipitate that forms is collected by filtration, washed with ether, and dried under reduced pressure overnight to give (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII), NMR (300 MHz, MeOH-*d*<sub>4</sub>):  $\delta$  7.44-6.96, 5.05, 4.21, 3.83, 3.65) and 3.21-2.77; ESI-MS (*m/z*)  $[M + H]^+ = 407$ .

Step 8: To an ice-cold, stirred mixture of 3-{[[4-(benzyloxy)butyl](propyl)amino]carbonyl}-5-methylbenzoic acid (IX, 310 mg, 0.809 mmol), (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII, 359 mg, 0.809 mmol), and  
 5 bromotripyrrolidinophosphonium hexafluorophosphate (415 mg, 0.890 mmol) in methylene chloride (10 mL) is added diisopropylethylamine (285 microL, 1.62 mmol) dropwise. The resulting mixture is stirred at 0 degrees C for 30 minutes and then warmed to 20-25 degrees C. After 4 hours, the reaction is concentrated under reduced pressure and is partitioned between ethyl acetate and water. The aqueous  
 10 phase is separated and extracted with ethyl acetate (3 x 15 mL), the combined organic phases are dried over magnesium sulfate, and concentrated under reduced pressure. The concentrate is purified by flash chromatography (silica; methylene chloride/methanol/ammonium hydroxide 96/3/0.5) to give N<sup>1</sup>-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>-[4-(benzyloxy)butyl]-5-methyl-N<sup>3</sup>-propylisophthalamide (X) NMR (300 MHz,  
 15 Acetone-*d*<sub>6</sub>): delta 7.99-6.74), 5.01 4.51-4.29, 4.36, 4.01, 3.80, 3.55-3.16, 2.98-2.82, 2.65-2.62, 2.36, 1.85-1.29, 1.01 and 0.68; ESI-MS (*m/z*) [M + H]<sup>+</sup> = 772.

Step 9. A mixture of N<sup>1</sup>-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>-[4-(benzyloxy)butyl]-5-methyl-N<sup>3</sup>-  
 20 propylisophthalamide (X, 100 mg, 0.130 mmol) and palladium on carbon (10%, 100 mg) in absolute glacial acetic acid (5 mL) is shaken under an atmosphere of hydrogen at 35 psi for 5 hours. The resulting mixture is filtered through diatomaceous earth and washed with methanol. The combined filtrates are concentrated under reduced pressure. The concentrate is purified by flash column  
 25 chromatography (silica; gradient of dichloromethane/methanol/ammonium hydroxide 97/3/0.05 to 93/7/0.05) to give the title compound: NMR (300 MHz, CD<sub>3</sub>OD): delta 7.55-6.64, 4.19, 3.99-3.72, 3.63-3.36, 3.21-3.09, 2.79-2.69, 2.39, 1.90-1.40, 1.29 and 1.02-0.6; ESI-MS (*m/z*) [M + H]<sup>+</sup> = 592.

EXAMPLE 755      N<sup>1</sup>-{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>-(3-hydroxypropyl)-5-methyl-N<sup>3</sup>-propylisophthalamide (X)  
 30

Following the general procedure of EXAMPLE 754 and making non-critical variations, but using 3-{[[3-(benzyloxy)propyl](propyl)amino]carbonyl}-5-

methylbenzoic acid (IX) in place of 3-[[[4-(benzyloxy)butyl](propyl)amino]-carbonyl]-5-methylbenzoic acid (IX), the title compound is obtained, ESI-MS ( $m/z$ )  $[M + H]^+ = 578$ .

5    EXAMPLE 756       $N^1$ -{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Step 1. To a stirred mixture of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (IX, 150 mg, 0.570 mmol), (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII, 274 mg, 0.571 mmol), *N,N*-diisopropylethylamine (400 microliter, 2.28 mmol), and HOBt (116 mg, 0.857 mmol) in dichloromethane (10 mL) is added EDC (165 mg, 0.857 mmol). The resulting mixture is stirred at 20-25 degrees C for 16 hours. The reaction mixture is partitioned between dichloromethane and water. The aqueous phase is separated and extracted with dichloromethane (3 x 15 mL). The combined organic phases are washed with water, dried (magnesium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica; dichloromethane/methanol/ammonium hydroxide, 97/3/0.05) gives  $N^1$ -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide, ESI-MS ( $m/z$ )  $[M + H]^+ = 652$ .

Step 2. A mixture of  $N^1$ -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (140 mg, 0.215 mmol) and palladium on carbon (10%, 140 mg) in absolute glacial acetic acid (5 mL) is shaken under an atmosphere of hydrogen at 35 psi for 5 hours. The resulting mixture is filtered through diatomaceous earth and washed with methanol. The combined filtrates are concentrated under reduced pressure. The concentrate is purified by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide gradient from 97/3/0.05 to 93/7/0.05) to give the title compound, IR (KBr) 2962, 2931, 1611, 1594 and 1263  $\text{cm}^{-1}$ ; ESI-MS ( $m/z$ )  $[M + H]^+ = 562$ .

EXAMPLE 757       $N^1$ -{(1S,2R)-1-benzyl-3-[[3-(2,4-dimethylphenyl)propyl]amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

- Step 1: A stirred mixture of tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V, 247 mg, 0.939 mmol), sodium carbonate (299 mg, 2.82 mmol), and 3-(2,4-dimethylphenyl)propylamine (VI, 628 mg, 2.82 mmol) is heated at reflux overnight. The reaction mixture is cooled to 20-25 degrees C and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide, 98/2/1) gives tert-butyl (1S,2R)-1-benzyl-3-{[3-(2,4-dimethylphenyl)propyl]amino}-2-hydroxypropylcarbamate (VII), NMR (300 MHz, CD<sub>3</sub>OD):  $\delta$  7.22-7.16, 3.81, 3.18, 2.77, 2.54, 2.15, 2.13, 1.89 and 1.23.
- Step 2: To a stirred mixture of tert-butyl (1S,2R)-1-benzyl-3-{[3-(2,4-dimethylphenyl)propyl]amino}-2-hydroxypropylcarbamate (VII, 180 mg, 0.423 mmol) in dioxane (2 mL) is added hydrochloric acid (0.32 mL of a 4 N mixture in dioxane, 1.27 mmol). The reaction mixture is stirred overnight and concentrated under reduced pressure to give (2R,3S)-3-amino-1-{[3-(2,4-dimethylphenyl)propyl]amino}-4-phenyl-2-butanol hydrochloride (VIII), NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  7.14, 3.73, 2.70, 2.32 and 1.86.
- Step 3: To a stirred mixture of (2R,3S)-3-amino-1-{[3-(2,4-dimethylphenyl)propyl]amino}-4-phenyl-2-butanol hydrochloride (VIII, 163 mg, 0.411 mmol), 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (IX, 108 mg, 0.411 mmol), HOBt (55 mg, 0.411 mmol), and *N*-methylmorpholine (133 mg, 1.32 mmol) in methylene chloride (5 mL) is added EDC (142 mg, 0.740 mmol). The reaction mixture is stirred overnight and then partitioned between ethyl acetate and water. The organic phase is washed with hydrochloric acid (1 N), saturated sodium bicarbonate, saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide, 95/5/1) gives the title compound, IR (ATR): 3299, 2930 and 1614 cm<sup>-1</sup>; APCI-MS (*m/z*) [M + H]<sup>+</sup> = 572.

- EXAMPLE 758      N<sup>1</sup>-((1S,2R)-1-benzyl-2-hydroxy-3-{[3-(4-methylphenyl)propyl]amino}propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide hydrochloride (X)

Following the general procedure of EXAMPLE 757 and making non-critical variations, but using 3-(4-methylphenyl)propylamine in place of 3-(2,4-

dimethylphenyl)propylamine, the title compound is obtained, IR (ATR): 3282, 2929 and 1594  $\text{cm}^{-1}$ ; APCI-MS ( $m/z$ )  $[M + H]^+ = 558$ .

EXAMPLE 759       $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5, and 6 and making non-critical variations but using tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and "5-Me-PHTH" (IX), the title compound is obtained, MS  $[M+H]^+ = 546.3$ .

EXAMPLE 760      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1,3-dioxo-2-propyl-5-isoindolinecarboxamide (X)

Following the general procedure of EXAMPLES 4, 5, and 6 and making non-critical variations but using tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and 1,3-dioxo-2-propylisoindoline-5-carboxylic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 516.2$ .

EXAMPLE 761      N-{(1R,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-bromo-5-methylbenzamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using benzyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-bromo-5-methylbenzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 497.1, 499.1$ .

EXAMPLE 762      3-bromo-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methylbenzamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]

ethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-bromo-5-methylbenzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 533.3, 535.3$ .

EXAMPLE 763       $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using benzyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-[(dipropylamino)carbonyl]-4-methylbenzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 546.4$ .

EXAMPLE 764       $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl-  $N^3,N^3$ -dipropylisophthalamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl] ethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-[(dipropylamino)carbonyl]-4-methylbenzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 582.3$ .

EXAMPLE 765       $N^3$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^1,N^1$ -dipropylisophthalamide (X)

3-Bromo-4-methylbenzoic acid (10.94 g, 43.25 mmol), copper(I)cyanide (7.75 g, 86.5 mmol) and 1-methyl-2-pyrrolidinone (75 ml) are heated to 160 degrees C overnight. The mixture is cooled and vacuum distilled to give a residue which is stirred in hydrochloric acid (6N, 60 ml) for 10 minutes. The resulting solid is collected by filtration, washed with water, ether, and dried. The solid is heated to 90 degrees C in sodium hydroxide (2N, 250 ml) for 3 hours and the mixture is then cooled and stirred overnight at 20-25 degrees C. The reaction is acidified to about pH 3 with concentrated hydrochloric acid which gives a precipitate. The solids are collected by filtration and washed with water, then triturated in boiling water,

filtered and dried in a vacuum oven at 60 degrees C. The solid is dissolved in methanol (75 ml) and concentrated hydrochloric acid (5 ml) is added and the mixture is refluxed overnight. The mixture then is cooled and concentrated under reduced pressure. Chromatography (silica gel; methanol/methylene chloride, 8/92) gives 5-(methoxycarbonyl)-2-methylbenzoic acid.

To 5-(methoxycarbonyl)-2-methylbenzoic acid (250 mg, 1.3 mmol) and triethylamine (0.72 ml, 5.2 mmol) in methylene chloride (14 ml) is added diethylcyanopyrocarbonate (90%, 0.24 ml, 1.4 mmol) with stirring. After 1 minute, (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 485 mg, 1.3 mmol) is added and the reaction is stirred overnight. The mixture is concentrated followed by chromatography (silica gel; methanol/methylene chloride 8/92) to afford 3-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino)carbonyl]-4-methylbenzoate.

3-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino) carbonyl]-4-methylbenzoate (200 mg, 0.42 mmol) is treated with lithium hydroxide (39 mg, 0.96 mmol) in tetrahydrofuran/methanol/water (2/1/1, 2 ml), and the mixture stirred overnight at 20-25 degrees C. The mixture is decanted and the supernatant concentrated to give 3-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino)carbonyl]-4-methylbenzoic acid.

3-[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino) carbonyl]-4-methylbenzoic acid (124 mg, 0.27 mmol) is dissolved in triethylamine (0.07 ml, 0.54 mmol) and methylene chloride (3 ml) and treated with diethylcyanopyrocarbonate (90%, 0.06 ml, 0.32 mmol) with stirring for 2 minutes. Dipropylamine (0.04 ml, 0.32 mmol) is added and stirring continued overnight. The organic phase is diluted with methylene chloride and washed with saturated sodium bicarbonate (2 X 50 ml) and saline (50 ml) then dried over anhydrous sodium sulfate, filtered and concentrated. Chromatography (silica gel; methanol/methylene chloride, 8/92) gives the title compound, MS  $[M+H]^+ = 546.3$ .

EXAMPLE 766      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(2-furyl)-5-methylbenzamide (X)

5      N-{(1R,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-bromo-5-methylbenzamide (X, EXAMPLE 761, 295 mg, 0.59 mmol), 2-furanylboronic acid (133 mg, 1.19 mmol) and sodium carbonate (366 mg, 2.95 mmol) are combined in dimethylformamide (5 ml) and sparged under a flow of nitrogen for 15 minutes. Tetrakis(triphenylphosphino)palladium (136 mg, 0.12 mmol) is added and the mixture heated to 100 degrees C overnight. The mixture is  
10      cooled to 20-25 degrees C, diluted with chloroform (50 ml) and extracted with water (3 x 100 ml). The organic phase is separated and washed with saturated sodium bicarbonate (2 x 100 ml) and saline (100 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is chromatographed (silica gel; methanol/methylene chloride, 8/92) to give the title compound, MS  
15       $[M+H]^+ = 485.3$ .

EXAMPLE 767      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3',5,5'-trimethyl-1,1'-biphenyl-3-carboxamide (X)

20      Following the general procedure of EXAMPLE 766 and making non-critical variations but using 3,5-dimethylphenylboronic acid, the title compound is obtained, MS  $[M+H]^+ = 523.3$ .

EXAMPLE 768      3'-Acetyl-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl[1,1'-biphenyl]-3-carboxamide (X)

25      Following the general procedure of EXAMPLE 766 and making non-critical variations but using 3-acetylphenylboronic acid, the title compound is obtained, MS  $[M+H]^+ = 537.3$ .

30

EXAMPLE 769      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3'-methoxy-5-methyl[1,1'-biphenyl]-3-carboxamide (X)

Following the general procedure of EXAMPLE 766 and making non-critical variations but using 3-methoxyphenylboronic acid, the title compound is obtained, MS  $[M+H]^+ = 525.3$ .

5    EXAMPLE 770    N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-5-methyl[1,1'-biphenyl]-3-carboxamide (X)

Following the general procedure of EXAMPLE 766 and making non-critical variations but using phenylboronic acid, the title compound is obtained, MS

10     $[M+H]^+ = 495.3$ .

EXAMPLE 771    3-Methyl-5-(3-thienyl)benzoic acid (IX)

Following the general procedure of EXAMPLE 766 and making non-critical variations but using 2-thiopheneboronic acid and methyl 3-bromo-5-

15    methylbenzoate, methyl 3-methyl-5-(3-thienyl)benzoate is obtained.

Methyl 3-methyl-5-(3-thienyl)benzoate (257 mg, 1.1 mmol) is treated with lithium hydroxide (186 mg, 4.4 mmol) in tetrahydrofuran/methanol/water (8 ml, 2:1:1) and the mixture is stirred for 2 hours at 20-25 degrees C. The mixture is acidified and concentrated to give the title compound, MS  $[M+H]^+ = 217.0$ .

20

EXAMPLE 772    N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-3-methyl-5-(3-thienyl)benzamide (X)

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using benzyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-methyl-5-(3-thienyl)benzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 501.2$ .

25

EXAMPLE 773    N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-3-methyl-5-(2-thienyl)benzamide (X)

30

Following the general procedure of EXAMPLES 4, 5 and 6 and making non-critical variations but using benzyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate

(V) and 3-methoxybenzylamine (VI) and 3-methyl-5-(2-thienyl)benzoic acid, the title compound is obtained, MS  $[M+H]^+ = 501.2$ .

EXAMPLE 774      N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-  
5 methoxybenzyl) amino]propyl}-3-methyl-5-(3-  
thienyl)benzamide (X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl] ethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-methyl-5-(3-  
10 thienyl)benzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 537.2$ .

EXAMPLE 775      N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-  
iodobenzyl)amino] propyl}-3-methyl-5-(3-thienyl)benzamide  
(X)

Following the general procedure of EXAMPLEs 4, 5 and 6 and making non-critical variations but using tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl] ethylcarbamate (V) and 3-iodobenzylamine (VI) and 3-methyl-5-(3-thienyl)benzoic acid (IX), the title compound is obtained, MS  $[M+H]^+ = 633.1$ .

EXAMPLE 776      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-  
20 methoxybenzyl)amino]propyl}-4-methyl-3-(3-  
thienyl)benzamide (X)

Following the general procedure of EXAMPLEs 4, 5, 6 and 766 and making non-critical variations but using benzyl (1S)-1-[(2S)-oxiranyl]-2-  
25 phenylethylcarbamate (V) and 3-methoxybenzylamine (VI) and 3-bromo-4-methylbenzoic acid (IX) and 3-thiopheneboronic acid, the title compound is obtained, MS  $[M+H]^+ = 501.2$ .

EXAMPLE 777      N<sup>1</sup>-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-  
30 methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>,N<sup>5</sup>,N<sup>5</sup>-  
tetrapropylbenzene-1,3,5-tricarboxamide hydrochloride (X)

Following the general procedures of CHART A as well as PREPARATIONS 1-13, EXAMPLEs 1-13, 321-48-579, 597-622 and 624-631 and making non-critical

variations and using the appropriate reagents, the title compound is obtained, HRMS (FAB) = 659.4155.

5      EXAMPLE 778      N<sup>1</sup>-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N<sup>3</sup>,N<sup>3</sup>-dipropylbenzene-1,3,5-tricarboxamide (X)

10      Following the general procedures of CHART A as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 609.2.

15      EXAMPLE 779      Ethyl 3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-5-[(dipropylamino)carbonyl]benzoate hydrochloride (X)

20      Following the general procedures of CHART A as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, HRMS (FAB) = 604.3392.

EXAMPLE 780      N<sup>1</sup>-{(1S,2R)-2-Hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropylbenzene-1,3,5-tricarboxamide (X)

25      Following the general procedures of CHART A as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 591.0.

30      EXAMPLE 781      N<sup>1</sup>-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropyl-5-[[{(trifluoromethyl)sulfonyl]amino}isophthalamide (X)

Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and

making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 679.2.

5      EXAMPLE 782      5-Amino-N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide (X)

Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound  
10 is obtained, MS (M+H)<sup>+</sup> = 547.3.

EXAMPLE 783      N<sup>1</sup>-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropyl-5-[(trifluoroacetyl)amino]isophthalamide (X)

15      Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 643.2

20      EXAMPLE 784      N<sup>1</sup>-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(methylsulfonyl)amino]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide hydrochloride (X)

Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and  
25 making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 625.0

EXAMPLE 785      N<sup>1</sup>-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropyl-5-[(thien-2-ylsulfonyl)amino]isophthalamide hydrochloride (X)

30

Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 693.1

EXAMPLE 786       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-5-[(thien-2-ylcarbonyl)amino]isophthalamide (X)

5            Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 657.2.

10    EXAMPLE 787       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(methacryloylamino)- $N^3,N^3$ -dipropylisophthalamide (X)

                 Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and  
15    making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 615.1.

EXAMPLE 788       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(2,2-dimethylpropanoyl)amino]- $N^3,N^3$ -dipropylisophthalamide (X)  
20

                 Following the general procedures of CHART A and CHART T as well as PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 631.3.

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EXAMPLE 789       $N^1$ -{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(phenylsulfonyl)amino]- $N^3,N^3$ -dipropylisophthalamide (X)

                 Following the general procedures of CHART A and CHART T as well as  
30    PREPARATIONS 1-13, EXAMPLES 1-13, 321-48-579, 597-622 and 624-631 and making non-critical variations and using the appropriate reagents, the title compound is obtained, MS (M+H)<sup>+</sup> = 687.2.

EXAMPLE 790      N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-5-(methylthio)pentanamide

Following the general procedure of EXAMPLES 588-592 and 597-619 and using the appropriate starting materials the title compound is obtained, HRMS m/z  
5      calculated for  $C_{24}H_{35}N_2O_3S$  (M+H) = 431.2363, found = 431.2397.

EXAMPLE 791      tert-butyl (2R,3S)-3-({3-[(dipropylamino)sulfonyl]propanoyl}amino)-2-hydroxy-4-phenylbutyl(3-methoxybenzyl)carbamate

10      Following the general procedure of EXAMPLES 588-592 and 597-619 and using the appropriate starting materials the title compound is obtained, HRMS  
calculated for M+H is 620.3369, observed = 620.3379.

EXAMPLE 792      2-Butylcyclopropylamine hydrochloride (VI)

15      A solution of triethylphosphonoacetate (22.4 g, 0.1 mol) in 13 mL of diglyme is added to a mixture of 13 mL of diglyme and sodium hydride (60%, 5.7 g, 0.12 mol) in mineral oil. When hydrogen evolution ceased, 1,2-epoxyhexane (12 g, 0.12 mol) in diglyme (12 mL) is added. The mixture is stirred for 1 day at 25 degrees C and 3 hours at 140 degrees C. A mixture of  
20      sodium hydroxide (15 g in 25 mL of water) is added in the cold. The mixture is refluxed 15 hours, diluted with cold water (100 mL), and washed with ether (3 x 50 mL). Acidification to pH = 2 with sulfuric acid (25%), extraction with ether (5 x 25 mL), drying the ether over anhydrous sodium sulfate, filtration and concentration gives 2-butylcyclopropanecarboxylic acid. The acid (5.0 g, 0.035  
25      mmol) in dichloromethane (15 mL) is heated with thionyl chloride (5.1 g, 3.1 mL) for 15 hours at 60 degrees C. The reaction mixture is distilled (76 degrees C- 80 degrees C) to give the acid chloride which is dissolved in acetone (15 mL), cooled to -10 degrees C and treated with sodium azide (2.2 g, 33.8 mmol) in water (5 mL). The reaction mixture is stirred at -10 degrees C for another 1 hour  
30      and then poured onto ice/water, extracted with ether (3x10 mL), dried, and cautiously evaporated to dryness at 20-25 degrees C under reduced pressure. The residue is dissolved in toluene (15 mL) and carefully warmed to 100 degrees C while vigorously stirring for 1 hour. Concentrated hydrochloric acid (7 mL) is

added and the reaction mixture is refluxed for 15 minutes. The acidic layer is evaporated to dryness to give the title compound,  $MH^+ = 114.2$ .

EXAMPLE 793      2-Aminomethyl-3-methylfuran (VI)

5            3-Methylfuroic acid (4.0 g, 32 mmol) is dissolved in DMF (10 mL) at 20-25 degrees C, and 1,1-carbonyldiimidazole (5.7 g, 35 mmol) is added. After 15 minutes, ammonia is bubbled into the mixture for approximately 2 minutes. This mixture is stirred at 20-25 degrees C for 2 hours then the mixture is concentrated under reduced pressure. The residue is partitioned between ethyl acetate and 10% aqueous citric acid. The layers are separated, and the aqueous layer extracted with additional ethyl acetate (2 x). The combined organic phases are washed with saturated sodium bicarbonate, then saline and dried over magnesium sulfate, filtered and concentrated. Crystals formed upon standing, which are isolated by filtration and washing with a small amount of ethyl acetate/hexanes (80/20), MS(ESI):  $MH^+$ : 126.1. 3-Methylfuroic amide (317 mg, 2.5 mmol) is dissolved in dry THF (5 mL). Lithium aluminum hydride (230 mg, 6.0 mmol) is added in one portion, and the mixture heated to reflux overnight. The mixture is cooled to 0 degrees C, and quenched by addition of THF/water (50/50). The mixture is then diluted with THF, and filtered through diatomaceous earth. The filtrate is concentrated to give the title compound, MS(ESI): (M-H) $^+$ : 109.1.

EXAMPLE 794      4-Aminomethyl-3,5-dimethylisoxazole (VI)

25            4-Chloromethyl-3,5-dimethylisoxazole (700 mg, 4.8 mmol) is suspended in concentrated aqueous ammonia at 20-25 degrees C, and vigorously stirred overnight. The reaction mixture is extracted with isopropyl alcohol/chloroform (10/90, 2 x). The combined organic phases are concentrated under nitrogen flow. The residue is purified by flash chromatography methanol/methylene chloride (5-20%, 1% triethylamine) to give the title compound, MR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  3.62, 2.37, 2.29, and 1.44.

EXAMPLE 795      5-Hydroxymethyl-2-(2-methylpropyl) thiazole (VI)

Isovalerothioamide is synthesized according to the procedure in *J. Med. Chem.* 41, 602-617 (1998). Isovaleramide (10 g, 9.9 mmol) is suspended in dry

ether (400 mL), then phosphorous(V) sulfide (4.4 g, 0.99 mmol) is added in portions. This is vigorously stirred at 20-25 degrees C for 2 hours, then filtered. The filtrate is concentrated under reduced pressure and the residue used without further purification: MS(ESI): MH<sup>+</sup>: 118.1.

5           Isovalerothioamide (6.0 g, 51 mmol) and ethyl formylchloroacetate (*Heterocycles* 32 (4), 693-701, (1991), 5.0 g, 33 mmol) are dissolved in dry DMF (20 mL), and heated to 95 degrees C for 4 hours. The reaction is subsequently cooled to 0 degrees C, and cold water (50 mL) is added. The mixture is basified to pH = 8 with solid sodium bicarbonate, then extracted with  
10 ether (3 x 35 mL). The combined organic extracts are washed with water, then saline and dried over magnesium sulfate, filtered, and concentrated. The residue is purified by flash chromatography (ethyl acetate/hexanes 4-10% elution) to give the desired product. NMR (CDCl<sub>3</sub>, 300 MHz) δ 8.27, 4.45-4.30, 3.70-3.50, 3.00-2.80, 2.30-2.10, 1.40-1.20, and 1.10-0.90.

15           A solution of ethyl 2-(2-methylpropyl)thiazole-5-carboxylate (2.05 g, 9.6 mmol) in THF (10 mL) is added dropwise with stirring to a suspension of lithium aluminum hydride (730 mg, 19 mmol) in dry THF (50 mL) at 0 degrees C. Upon complete addition, the reaction mixture is allowed to stir at 20-25 degrees C. The reaction mixture is cooled to 0 degrees C, and water (0.75 mL),  
20 aqueous sodium hydroxide (15%, 0.75 mL), and water (2.25 mL) is added in succession. This mixture is stirred at 0 degrees C for 1 hour, then filtered through diatomaceous earth, (THF and chloroform). The filtrate is concentrated to give 5-hydroxymethyl-2-(2-methylpropyl)thiazole, MS(ESI): MH<sup>+</sup>: 172.1.

25   EXAMPLE 796           3-(2-Methylpropyl)-5-aminomethylisoxazole (VI)

          Isovaleraldehyde (5.4 mL, 50 mmol) and hydroxylamine hydrochloride (3.5 g, 50.4 mmol) are vigorously stirred in water (6 mL). To this is added a solution of sodium carbonate (2.65 g, 25 mmol) in water (15 mL). This is vigorously stirred overnight. The mixture is extracted with ether. The organic layer is washed with  
30 water, then dried over sodium sulfate, filtered and concentrated. This is used in subsequent reactions without further purification: MS(ESI): MH<sup>+</sup>: 102.1.

          Propargylamine (8.0 mL, 117 mmol) is dissolved in methylene chloride (60 mL), and di-*tert*-butyl dicarbonate (25 g, 114 mmol) is added. This is stirred

overnight, and concentrated to provide the BOC-protected propargylamine, which is used without further purification: MS(ESI): MNa+: 178.0.

BOC-propargylamine (6.2 g, 39.7 mmol) and isovaleroxime (3.97 g, 39.3 mmol) is dissolved in methylene chloride (60 mL), and triethylamine (0.55 mL, 3.95 mmol) is added. This is cooled to 0 degrees C, and bleach (5% aqueous solution, 59.1 g) is added dropwise with vigorous stirring. After addition is complete, the mixture is allowed to warm to 20-25 degrees C over 22 hours. The layers are separated, and the aqueous layer is extracted with methylene chloride (2 x). The combined organic extracts are washed with saline, dried over magnesium sulfate, filtered and concentrated. The residue is purified by chromatography (silica gel, ethyl acetate/hexanes 5-10%) to give the BOC-protected title compound, MS(ESI): MH+: 255.3.

BOC-protected 3-(2-methylpropyl)-5-aminomethylisoxazole (2.4 g, 9.3 mmol) is dissolved in methylene chloride (10 mL) and treated with trifluoroacetic acid (10 mL) at 20-25 degrees C. This is stirred at 20-25 degrees C for 70 minutes, then concentrated. The product is dissolved in methylene chloride, and washed with aqueous potassium carbonate (1 M) until basic (pH = 11). The organic layer is isolated, dried over sodium sulfate, filtered and concentrated to give the title compound: MS(ESI): MH+: 155.2.

20

EXAMPLE 797      tert-butyl (3R)-2-oxo-1-propylazepanylcarbamate (VI)

To N-t-Boc-D-Lys-OH (10 g, 41.4mmole) in DMF (4 liters) is added benzotriazol-1-yloxytripyrrolidino-phosphonium hexafluorophosphate (BOP, 18.3 g, 41.4mmole) and sodium bicarbonate (17.4 g, 206.8mmole); the reaction is stirred at 20-25 degrees C for 12 hours. The reaction is then concentrated to 50 ml volume and diluted with ethyl acetate and washed with sodium bicarbonate 3x, water, 1M potassium bisulfate and brine, dried and concentrated. Purification by chromatography on silica gel afforded 5.05 g of the tert-butyl (3R)-2-oxoazepanylcarbamate as a solid; the procedure employed is similar to that described in *J.Med.Chem.* 1999, 4193. M+H-(t-Boc) (m/e=129.2), M+Na (m/e=251.1).

30

To the above lactam (2 g, 8.77mmole) in dry THF (20 ml) is added n-butyllithium /hexane (2.5 M, 5.3 ml, 13.2 mmole ) at -78 degrees C, the reaction is stirred for 1 hour and 1-bromopropane (3.2 ml, 35.1 mmole) is added. The reaction

is stirred for 1 hour and the cold bath removed and stirring continued for another 16 hours. Tetrabutylammonium iodide (0.49 g, 2.63mmole) is added and the reaction stirred for another 16 hours. The reaction is partitioned between ethyl acetate/hydrochloric acid + ice + water, the mixture is washed with water and saline and concentrated. Purification by chromatography on silica gel afforded the title compound, MS (M+Na+) 293.3.

EXAMPLE 798      N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide (X)

Following the procedure described in *J. Am. Chem. Soc.* 1986, 3150, the trifluoroacetic acid salt of N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide (92.9 mg, 0.117 mmol) is dissolved in triethylamine (0.2 M, 0.6 mL) before the addition of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (3.3 mg, 0.005 mmol), and copper (I) iodide (1.1 mg, 0.006 mmol). The reaction is heated to reflux. While the reaction is refluxing, trimethylsilylacetylene (0.02 ml, 0.14 mmol) is added via syringe. The reaction is refluxed for 3 hour under N<sub>2</sub> (g), and the reaction cooled to 20-25 degrees C before partitioning between aqueous sodium bicarbonate and ethyl acetate. The product is extracted with ethyl acetate (3 x), washed with saline, dried over sodium sulfate<sub>4</sub>, and filtered before the removal of solvent under reduced pressure.

The TMS protected acetylene (0.117 mmol) is dissolved in methanol (0.2 M, 0.5 mL) before the addition of potassium hydroxide (1M, 0.7 mL, 0.7 mmol). The reaction is stirred at 20-25 degrees C for 6 hours, at which point the mixture is partitioned between sodium bicarbonate and ethyl acetate. The product is extracted with ethyl acetate (3 x), washed with saline, dried over sodium sulfate, and filtered before the removal of solvent under reduced pressure. Column chromatography (silica gel; 1.5-2 % isopropanol/chloroform under basic conditions; a few drops of ammonium hydroxide per 100 mL of elution solvent) gives the title compound, MS  $m/z$  (M+H)<sup>+</sup> = 576.3.

EXAMPLE 799      1-phenylcyclopropylamine (VI)

Following the procedure described in N.W. Werner *et.al.*, *J. Org. Syn. Coll.* Vol. 5, 273-276, sodium azide (0.915g, 14.1 mmol) is slowly added to a solution of 1-phenyl-cyclopropanecarboxylic acid (1.0 g, 6.1 mmol) in concentrated sulfuric acid (5 ml) and dichloromethane (10 ml). The sodium sulfate precipitated out of solution.

5 The reaction mixture is heated to 50 degrees C for 17 hours and then cooled to 0 degrees C. The mixture is basified to pH = 11 with sodium hydroxide (1N) and extracted with dichloromethane (2 x). The organic layers are combined, dried over sodium sulfate, filtered and concentrated. The residue is purified by chromatography (silica gel; isopropyl alcohol/chloroform/ammonium hydroxide

10 4/95/1) to give the title compound, MS (ESI+) for  $C_9H_{11}N$   $m/z$  (M+H)<sup>+</sup> = 134.

EXAMPLE 800      7-methoxy-1,2,3,4-tetrahydro-1-naphthalenamine (VI)

7-Methoxy-1-tetralone (2.0 g, 11.3 mmol), hydroxylamine hydrochloride (1.56 g, 22.6 mmol) and sodium acetate (1.8g, 22.6 mmol) are suspended in

15 ethanol/water (3/1, 40 mL). The mixture is heated for 45 min. at 100 degrees C. The mixture is allowed to cool overnight and the precipitate obtained is filtered and washed with water to yield an intermediate oxime, MS (ES) (M+H): 192.1. The oxime is dissolved in glacial acetic acid (25 ml) and palladium/carbon (500 mg) is added and the mixture hydrogenated under 50 psi at 20-25 degrees C overnight. The

20 catalyst is filtered over diatomaceous earth and washed with methanol. The combined filtrates are concentrated. The concentrate is triturated with ether to give the title compound, MS (CI) (MH<sup>+</sup>): 178.2.

EXAMPLE 801      3-Amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methylbutanamide dihydrochloride

25

Following the general procedure of EXAMPLE 6 and making non-critical variations but starting with (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII) and reacting it with 3-[(tert-butoxycarbonyl)amino]-2-methylbutanoic acid (IX), and then treatment with HCl, the title compound is

30 obtained, HRMS calculated = 400.2600, observed = 400.2596.

EXAMPLE 802      N-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-ethylhexanamide hydrochloride

Following the general procedure of EXAMPLE 6 and making non-critical variations but starting with (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII) and reacting it with 2-ethylhexanoic acid (IX), the title compound is obtained, HRMS calculated = 427.2961, observed = 427.2961.

EXAMPLE 803      N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(isobutylsulfonyl)amino]propanamide trifluoroacetate

Following the general procedure of CHART I and making non-critical variations but starting with (2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol (VIII) and reacting it with N-(isobutylsulfonyl)-beta-alanine (IX), the title compound is obtained, HRMS calculated = 588.1393, observed = 588.1379.

EXAMPLE 804      N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N<sup>3</sup>-(isobutylsulfonyl)-beta-alaninamide trifluoroacetate

Following the general procedure of CHART I and making non-critical variations but starting with (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]-2-butanol (VIII) and reacting it with N-(isobutylsulfonyl)-beta-alanine (IX), the title compound is obtained, M + H = 624.

EXAMPLE 805      5-bromo-N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide hydrochloride

Following the general procedure of EXAMPLE 6 and making non-critical variations but starting with (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]-2-butanol (VIII) and reacting it with 3-bromo-5-[(dipropylamino)carbonyl]benzoic acid (IX), the title compound is obtained, M + H = 745.

EXAMPLE 806      N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide

Following the general procedure of EXAMPLE 6 and making non-critical variations but starting with (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1-phenylcyclopropyl)amino]-2-butanol (VIII) and reacting it with 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (IX), the substituted amine (X) is obtained. MH<sup>+</sup> = 578.

10    EXAMPLE 806.1      5-bromo-N<sup>1</sup>-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide

Following the general procedure of EXAMPLE 6 and making non-critical variations but starting with (2R,3S)-3-amino-1-[(3-bromobenzyl)amino]-4-(3,5-difluorophenyl)-2-butanol hydrochloride (VIII) and reacting it with 3-bromo-5-[(dipropylamino)carbonyl]benzoic acid (IX), the title compound is obtained, NMR (500 MHz, CD<sub>3</sub>OD): δ 7.85, 7.72, 7.69, 7.67, 7.52, 7.51, 6.88, 6.86, 6.74, 4.39-4.13, 3.95-3.88, 3.53-2.96, 2.82, 1.70, 1.50, 0.99 and 0.71.

20    EXAMPLES 807-1,064

Following the general procedure of CHART A and EXAMPLES 4-6, 321-327, 329-464, 466-527, 529-579, 597-619 and 633-708 and making non-critical variations, and using the appropriate amines (VIII) and amide forming agents (IX), the titled compounds are obtained.

| EXAMPLE | Substituted Amine (X)                                                                                              |
|---------|--------------------------------------------------------------------------------------------------------------------|
| 807     | N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl-5-(2-propylpentanoyl)benzamide            |
| 808     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethylpentanoyl)-5-methylbenzamide |
| 809     | N-{(1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(2-propylpentanoyl)benzamide              |
| 810     | N-{(1S,2R)-1-benzyl-3-[(3-ethynylbenzyl)amino]-2-                                                                  |

| EXAMPLE | Substituted Amine (X)                                                                                                                                              |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | hydroxypropyl}-3-methyl-5-(2-propylpentanoyl)benzamide                                                                                                             |
| 811     | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-(2-ethylbutanoyl)-5-methylbenzamide                                                  |
| 812     | N <sup>1</sup> -((1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-5-(2-propylpentanoyl)isophthalamide                                                    |
| 813     | N-((1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-(2-ethylpentanoyl)-5-methylbenzamide                                                               |
| 814     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-5-(2-propylpentanoyl)isophthalamide                                      |
| 815     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-5-(2-propylpentanoyl)isophthalamide                                    |
| 816     | N-[(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-(4-hydroxybenzyl)propyl]-3-methyl-5-(2-propylpentanoyl)benzamide                                                   |
| 817     | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-3-methyl-5-(2-propylpentanoyl)benzamide                                              |
| 818     | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-methyl-5-(2-propylpentanoyl)benzamide                                                |
| 819     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[3-(3-pyridinyl)benzyl]amino]propyl)-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 820     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[3-(4-pyridinyl)benzyl]amino]propyl)-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 821     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-(1-propynyl)isophthalamide |

| EXAMPLE | Substituted Amine (X)                                                                                                                                             |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 822     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-(1-propynyl)isophthalamide   |
| 823     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-(2-propynyl)isophthalamide   |
| 824     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-(2-propynyl)isophthalamide |
| 825     | N <sup>1</sup> -{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         |
| 826     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-thienylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     |
| 827     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-thienylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 828     | N <sup>1</sup> -{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-butyryl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                     |
| 829     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-thienylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 830     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(2-thienylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     |
| 831     | N <sup>1</sup> -{(1S,2R)-1-(3-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |

| EXAMPLE | Substituted Amine (X)                                                                                                                                    |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| 832     | N <sup>1</sup> -{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide   |
| 833     | N <sup>1</sup> -{(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide   |
| 834     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 835     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 836     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(1-naphthylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide      |
| 837     | 2,3,5-trideoxy-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-5-[(3-methoxybenzyl)amino]-1-S-phenyl-1-thio-D-erythouro-pentitol                  |
| 838     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(3-furylmethyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 839     | N <sup>1</sup> -((1S)-1-((1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl)-3-methylbutyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 840     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(4-fluorobenzyl)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide        |
| 841     | N <sup>1</sup> -{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 842     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(2-furylmethyl)-2-                                                                                            |

| EXAMPLE | Substituted Amine (X)                                                                                                                                              |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | hydroxypropyl]-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                                    |
| 843     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         |
| 844     | N <sup>1</sup> -{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-methylbutyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                 |
| 845     | N <sup>1</sup> -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 846     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-hydroxybenzyl)propyl]-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     |
| 847     | N <sup>1</sup> -{(1S)-1-[(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl]-3-butynyl}-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               |
| 848     | N <sup>1</sup> -{(1S)-1-[(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl]-3-butynyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide          |
| 849     | 5-(benzylamino)-2,3,5-trideoxy-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl} amino)-1-S-phenyl-1-thio-D-erythouro-pentitol                                      |
| 850     | N <sup>1</sup> -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 851     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-hydroxybenzyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                 |
| 852     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-                         |

| EXAMPLE | Substituted Amine (X)                                                                                                                                           |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | benzenetricarboxamide                                                                                                                                           |
| 853     | N <sup>1</sup> -{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-methylbutyl}-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                   |
| 854     | N <sup>1</sup> -{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide   |
| 855     | *N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(3-furylmethyl)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide               |
| 856     | N <sup>1</sup> -[(1S)-1-[(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl]-3-methylbutyl]- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide   |
| 857     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(4-fluorobenzyl)-2-hydroxypropyl]-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                   |
| 858     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-1-(2-furylmethyl)-2-hydroxypropyl]- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide               |
| 859     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 860     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(1-naphthylmethyl)propyl]-5-methyl- N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 |
| 861     | N <sup>1</sup> -{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 862     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(2-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide              |

| EXAMPLE | Substituted Amine (X)                                                                                                                                          |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 863     | N <sup>1</sup> -{(1S,2R)-1-(3-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide    |
| 864     | N <sup>1</sup> -{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 865     | N <sup>1</sup> -{(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide    |
| 866     | N <sup>1</sup> -[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide             |
| 867     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 868     | N <sup>1</sup> -{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-butynyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                       |
| 869     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 870     | N <sup>1</sup> -{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 871     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 872     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-thienylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 873     | N <sup>1</sup> -{(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-[(3-                                                                                                    |

| EXAMPLE | Substituted Amine (X)                                                                                                                                             |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                                                                 |
| 874     | N <sup>1</sup> -{(1S,2R)-1-(3-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide      |
| 875     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide    |
| 876     | N <sup>1</sup> -((1S)-1-((1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl)-3-methylbutyl)- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide     |
| 877     | N <sup>1</sup> -{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide     |
| 878     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]- N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide   |
| 879     | N <sup>1</sup> -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 880     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-[3-(hydroxymethyl)benzyl]-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 881     | N <sup>1</sup> -{(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-[3-(hydroxymethyl)benzyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 882     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-[3-(hydroxymethyl)benzyl]-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                 |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 883     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-[4-(hydroxymethyl)benzyl]-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         |
| 884     | N <sup>1</sup> -{(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-[4-(hydroxymethyl)benzyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        |
| 885     | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-[4-(hydroxymethyl)benzyl]-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 886     | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 887     | N <sup>1</sup> -[(1S,2R)-3-[(3-ethylbenzyl)amino]-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 888     | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        |
| 889     | N <sup>1</sup> -{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 890     | N <sup>1</sup> -{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 891     | N-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(dipropylamino)sulfonyl]propanamide                                                 |
| 892     | N <sup>1</sup> -{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -                                         |

| EXAMPLE | Substituted Amine (X)                                                                                                                            |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------|
|         | dipropylpentanediamide                                                                                                                           |
| 893     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]propanamide                               |
| 894     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide |
| 895     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]propanamide                                 |
| 896     | N <sup>1</sup> -[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide   |
| 897     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl]propanamide                                |
| 898     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide  |
| 899     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(3-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]propanamide                                  |
| 900     | N <sup>1</sup> -[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide    |
| 901     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]propanamide                                  |
| 902     | N <sup>1</sup> -[(1S,2R)-1-(3-furylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide    |
| 903     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-thienylmethyl)propyl]propanamide                                |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                            |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 904     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-thienylmethyl)propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide                                  |
| 905     | 3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-thienylmethyl)propyl]propanamide                                                                |
| 906     | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-thienylmethyl)propyl]-N <sup>5</sup> ,N <sup>5</sup> -dipropylpentanediamide                                  |
| 907     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(2R)-1-ethylpyrrolidinyl]carbonyl]-5-methylbenzamide                                            |
| 908     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(2S)-1-ethylpyrrolidinyl]carbonyl]-5-methylbenzamide                                            |
| 909     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(1-ethyl-1H-imidazol-2-yl)carbonyl]-5-methylbenzamide                                           |
| 910     | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-[(1-ethyl-4-methyl-1H-imidazol-5-yl)carbonyl]-5-methylbenzamide                                  |
| 911     | N <sup>1</sup> -[(1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-2-{1-[(3-methoxybenzyl)amino]cyclopropyl}ethyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        |
| 912     | N <sup>1</sup> -[(1S,2S)-1-(3,5-difluorobenzyl)-2-{1-[(3-ethylbenzyl)amino]cyclopropyl}-2-hydroxyethyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 913     | (1R,2R,3R)-N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2,3-cyclopropanetricarboxamide |
| 914     | (1R,2R,3R)-N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-3-phenyl-N <sup>2</sup> ,N <sup>2</sup> -                                 |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                                  |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | dipropyl-1,2-cyclopropanedicarboxamide                                                                                                                                                                 |
| 915     | (1R,2R,3R)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl- N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide                |
| 916     | (1R,2R,3S)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl- N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide                |
| 917     | (1R,2R,3S)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-phenyl- N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide                |
| 918     | (1R,2R,3S)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2,3-cyclopropanetricarboxamide                      |
| 919     | (1R,2R,3S)-3-(2-amino-2-oxoethyl)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl) amino]propyl}- N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide |
| 920     | (1R,2R,3R)-3-(2-amino-2-oxoethyl)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]-propyl}-N <sup>2</sup> ,N <sup>2</sup> -dipropyl-1,2-cyclopropanedicarboxamide  |
| 921     | (1R,2R,3S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[2-(dipropylamino)-2-oxoethyl]-3-methylcyclopropanecarboxamide                                              |
| 922     | (1R,2R,3R)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[2-(dipropylamino)-2-oxoethyl]-3-methylcyclopropanecarboxamide                                              |
| 923     | (1S,2R,3R)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[2-(dipropylamino)-2-oxoethyl]-3-phenylcyclopropanecarboxamide                                              |
| 924     | (1S,2R,3S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[2-(dipropylamino)-2-                                                                                       |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                         |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | oxoethyl]-3-phenylcyclopropanecarboxamide                                                                                                                                                     |
| 925     | (1S,2R,3R)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[2-(dipropylamino)-2-oxoethyl]-1,2-cyclopropanedicarboxamide                         |
| 926     | (1S,2R,3S)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[2-(dipropylamino)-2-oxoethyl]-1,2-cyclopropanedicarboxamide                         |
| 927     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[trifluoromethyl)sulfonyl]amino}isophthalamide        |
| 928     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[trifluoromethyl)sulfonyl]amino}isophthalamide          |
| 929     | N <sup>1</sup> -{(1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[trifluoromethyl)sulfonyl]amino}isophthalamide                        |
| 930     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{methyl[(trifluoromethyl)sulfonyl]amino}-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide   |
| 931     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-{methyl[(trifluoromethyl)sulfonyl]amino}-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 932     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-{propyl[(trifluoromethyl)sulfonyl]amino}isophthalamide |
| 933     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(methylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                  |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                        |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 934     | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(phenylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 935     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide                                                       |
| 936     | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide                                                         |
| 937     | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(dimethylamino)benzyl]amino}-2-hydroxypropyl)-3-[(dipropylamino)sulfonyl]propanamide                                                 |
| 938     | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethyl-1,3-thiazol-5-yl)methyl]amino}-2-hydroxypropyl)-3-[(dipropylamino)sulfonyl]propanamide                                        |
| 939     | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-3-[(dipropylamino)sulfonyl]propanamide                                     |
| 940     | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3-isobutyl-5-isoxazolyl)methyl]amino}propyl)-3-[(dipropylamino)sulfonyl]propanamide                                         |
| 941     | N-[(1S,2R)-3-[(3-cyclopropylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide                                                     |
| 942     | N <sup>1</sup> -[(1S,2R)-3-[(3-cyclopropylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 943     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1,3-thiazol-2-yl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 944     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1,3-                                                                                                        |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | oxazol-2-yl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                              |
| 945     | N <sup>1</sup> -[(1S,2R)-3-[(3-acetylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                    |
| 946     | N <sup>1</sup> -[(1S,2R)-3-[(3-acetylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide               |
| 947     | N <sup>1</sup> -[(1S,2R)-3-[(3-acetylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(aminosulfonyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 948     | N <sup>1</sup> -[(1S,2R)-3-[(3-acetylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(methylsulfonyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 949     | N <sup>1</sup> -[(1S,2R)-3-{[3-(diethylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |
| 950     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(4-morpholinyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 951     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1-piperazinyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 952     | N <sup>1</sup> -[(1S,2R)-3-{[3-(aminosulfonyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 953     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(dimethylamino)sulfonyl]benzyl}amino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 954     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1-piperidinylsulfonyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide   |
| 955     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(methylsulfonyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 956     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(isopropylsulfonyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 957     | N <sup>1</sup> -[(1S,2R)-3-{[3-(aminocarbonyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 958     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(dimethylamino)carbonyl]benzyl}amino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 959     | N <sup>1</sup> -[(1S,2R)-3-[(3-cyanobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                     |
| 960     | 3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenylcarbamate                                        |
| 961     | 3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl dimethylcarbamate                               |
| 962     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1-propynyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 963     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(3-methyl-1-butynyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                  |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 964     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(2-propynyl)benzyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                       |
| 965     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(5-isobutyl-1,3,4-oxadiazol-2-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 966     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{3-(5-ethyl-1,3,4-oxadiazol-2-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 967     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{3-(5-ethyl-1,3,4-thiadiazol-2-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 968     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(5-isobutyl-1,3,4-thiadiazol-2-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 969     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{3-(3-ethyl-1,2,4-thiadiazol-5-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 970     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(3-isobutyl-1,2,4-thiadiazol-5-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 971     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(3-isobutyl-1,2,4-oxadiazol-5-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 972     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{3-(3-ethyl-1,2,4-oxadiazol-5-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 973     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(2-ethyl-1,3-oxazol-5-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -                                  |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | dipropylisophthalamide                                                                                                                                                               |
| 974     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(2-isobutyl-1,3-oxazol-5-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 975     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(5-isobutyl-1,3,4-oxadiazol-2-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 976     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(5-isobutyl-1,3,4-thiadiazol-2-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 977     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(5-ethyl-1,3,4-thiadiazol-2-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 978     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(5-ethyl-1,3,4-oxadiazol-2-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 979     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(3-ethyl-1,2,4-oxadiazol-5-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 980     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(3-ethyl-1,2,4-thiadiazol-5-yl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 981     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(3-isobutyl-1,2,4-thiadiazol-5-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 982     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(3-isobutyl-1,2,4-oxadiazol-5-yl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |
| 983     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(2-ethyl-2H-                                                                                                                     |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                               |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | tetraazol-5-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                       |
| 984     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(2-isobutyl-2H-tetraazol-5-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide    |
| 985     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(2-ethyl-4-pyrimidinyl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 986     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(2-isopropyl-4-pyrimidinyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 987     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(2-ethynyl-4-pyrimidinyl)methyl]amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         |
| 988     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(6-isopropyl-4-pyrimidinyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 989     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[6-(dimethylamino)-4-pyrimidinyl]methyl}amino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 990     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[2-(dimethylamino)-4-pyrimidinyl]methyl}amino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 991     | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[4-(dimethylamino)-2-pyrimidinyl]methyl}amino)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 992     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(4-isopropyl-2-pyrimidinyl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                         |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 993     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(4-ethyl-2-pyrimidinyl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 994     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(5-ethyl-3-pyridazinyl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 995     | N <sup>3</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{3-(dimethylamino)benzyl}amino}-2-hydroxypropyl)-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide        |
| 996     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(5-isopropyl-3-pyridazinyl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 997     | N <sup>3</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(1-propynyl)benzyl}amino}propyl)-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide           |
| 998     | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(6-isopropyl-4-pyridazinyl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |
| 999     | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide                |
| 1000    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(6-ethyl-4-pyridazinyl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide     |
| 1001    | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide              |
| 1002    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(6-ethyl-2-pyrazinyl)methyl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -                             |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                                  |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | dipropylisophthalamide                                                                                                                                                                                 |
| 1003    | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropyl-3,5-pyridinedicarboxamide                                           |
| 1004    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(6-isopropyl-2-pyrazinyl)methyl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                            |
| 1005    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3,4,5-trifluorobenzyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                         |
| 1006    | N <sup>1</sup> -((1S,2R)-2-hydroxy-1-(3,4,5-trifluorobenzyl)-3-{{[3-(trifluoromethyl)benzyl]amino}propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                              |
| 1007    | N <sup>1</sup> -((1S,2R)-2-hydroxy-1-(2,3,5,6-tetrafluorobenzyl)-3-{{[3-(trifluoromethyl)benzyl]amino}propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                          |
| 1008    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2,3,5,6-tetrafluorobenzyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                     |
| 1009    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(1R,2S)-2-hydroxy-6-methoxy-2,3-dihydro-1H-inden-1-yl}amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1010    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(1R,2S)-2-hydroxy-6-methoxy-2,3-dihydro-1H-inden-1-yl}amino}propyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1011    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{(1R,2S)-6-ethyl-2-hydroxy-2,3-dihydro-1H-inden-1-yl}amino}-2-hydroxypropyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                                 |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1012    | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-[[ (1R,2S)-6-ethyl-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino]-2-hydroxypropyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1013    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(1H-indol-5-ylmethyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                          |
| 1014    | N <sup>1</sup> -[(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-(1H-indol-5-ylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                            |
| 1015    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-methylbenzyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                               |
| 1016    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-methylbenzyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                                          |
| 1017    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethyl)benzyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                    |
| 1018    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethyl)benzyl]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                               |
| 1019    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-pyridinylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                            |
| 1020    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-pyridinylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                                       |
| 1021    | N <sup>1</sup> -{(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-                                                                                                                                    |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                            |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                        |
| 1022    | N <sup>1</sup> -{(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1023    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethoxy)benzyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 1024    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethoxy)benzyl]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide         |
| 1025    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(3-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                         |
| 1026    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(3-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                    |
| 1027    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                          |
| 1028    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                     |
| 1029    | N <sup>1</sup> -{(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                 |
| 1030    | N <sup>1</sup> -{(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide            |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                 |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1031    | N <sup>1</sup> -{(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               |
| 1032    | N <sup>1</sup> -{(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide          |
| 1033    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(3-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 1034    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(3-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide         |
| 1035    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide              |
| 1036    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide         |
| 1037    | N <sup>1</sup> -{(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1038    | N <sup>1</sup> -{(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1039    | N <sup>1</sup> -{(1S,2R)-1-(4-chloro-3-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1040    | N <sup>1</sup> -{(1S,2R)-1-(4-chloro-3-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-                      |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                 |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | benzenetricarboxamide                                                                                                                                                 |
| 1041    | N <sup>1</sup> -{(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 1042    | N <sup>1</sup> -{(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide      |
| 1043    | N <sup>1</sup> -{(1S,2R)-1-[4-(dimethylamino)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1044    | N <sup>1</sup> -{(1S,2R)-1-[4-(dimethylamino)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1045    | N <sup>1</sup> -{(1S,2R)-1-(3-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               |
| 1046    | N <sup>1</sup> -{(1S,2R)-1-(3-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               |
| 1047    | N <sup>1</sup> -{(1S,2R)-1-(3-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide               |
| 1048    | N <sup>1</sup> -{(1S,2R)-1-(3-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide          |
| 1049    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-isopropylbenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |
| 1050    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-1-(4-isopropylbenzyl)-3-[(3-                                                                                                       |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                       |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide                                                                            |
| 1051    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(6-methoxy-2-pyridinyl)methyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1052    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(6-methoxy-2-pyridinyl)methyl]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |
| 1053    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(5-methyl-2-pyridinyl)methyl]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |
| 1054    | N <sup>1</sup> -{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(5-methyl-2-pyridinyl)methyl]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide  |
| 1055    | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |
| 1056    | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide       |
| 1057    | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |
| 1058    | N <sup>1</sup> -{(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide      |
| 1059    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-methoxy-5-methylbenzyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                    |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1060    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(2-methoxy-5-methylbenzyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide   |
| 1061    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1,3-thiazol-2-ylmethyl)propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |
| 1062    | N <sup>1</sup> -[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1,3-thiazol-2-ylmethyl)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide     |
| 1063    | N <sup>1</sup> -{(1S,2R)-1-[(5-chloro-2-thienyl)methyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      |
| 1064    | N <sup>1</sup> -{(1S,2R)-1-[(5-chloro-2-thienyl)methyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-1,3,5-benzenetricarboxamide |

## EXAMPLES 1,065-1,155

Following the general procedure of CHART A and EXAMPLES 4-6, 321-327, 329-464, 466-527, 529-579, 597-619 and 633-708 and making non-critical variations, and using the appropriate amines (VIII) and amide forming agents (IX), the titled compounds are obtained.

| EXAMPLE | Substituted Amine (X)                                                                                                                     |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------|
| 1,065   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-3-(1-pyrrolidinylcarbonyl)benzamide                 |
| 1,066   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide |
| 1,067   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide           |

| EXAMPLE | Substituted Amine (X)                                                                                                                                      |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1,068   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-2-[(propylsulfonyl)amino]-1,3-thiazole-4-carboxamide                           |
| 1,069   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-4-hydroxy-3-(1-pyrrolidinylcarbonyl)benzamide                                |
| 1,070   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-2-[(propylsulfonyl)amino]-1,3-thiazole-4-carboxamide                         |
| 1,071   | N-((1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                          |
| 1,072   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide             |
| 1,073   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-4-hydroxy-3-(1-pyrrolidinylcarbonyl)benzamide                |
| 1,074   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide          |
| 1,075   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                        |
| 1,076   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide |
| 1,077   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-hydroxy-3-(1-pyrrolidinylcarbonyl)benzamide                   |
| 1,078   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                          |

| EXAMPLE | Substituted Amine (X)                                                                                                                      |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------|
| 1,079   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide          |
| 1,080   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide |
| 1,081   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-4-hydroxy-3-(1-piperidinylcarbonyl)benzamide                 |
| 1,082   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-4-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide             |
| 1,083   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                           |
| 1,084   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-5-methyl-4-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide    |
| 1,085   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-hydroxy-3-(1-piperidinylcarbonyl)benzamide                   |
| 1,086   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide            |
| 1,087   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                  |
| 1,088   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-5-methyl-4-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide   |
| 1,089   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-hydroxy-3-(4-morpholinylcarbonyl)benzamide                   |
| 1,090   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-[(ethylsulfonyl)amino]-1,3-oxazole-2-carboxamide             |

| EXAMPLE | Substituted Amine (X)                                                                                                                      |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------|
| 1,091   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide    |
| 1,092   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-4-[(ethylsulfonyl)amino]-1,3-oxazole-2-carboxamide              |
| 1,093   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-hydroxy-3-(4-morpholinylcarbonyl)benzamide                   |
| 1,094   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-4-[(propylsulfonyl)amino]-1,3-oxazole-2-carboxamide             |
| 1,095   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide |
| 1,096   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-4-[(methylsulfonyl)amino]-1,3-thiazole-2-carboxamide            |
| 1,097   | N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-4-hydroxy-3-(1-piperazinylcarbonyl)benzamide                 |
| 1,098   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-[(methylsulfonyl)amino]-1,3-thiazole-2-carboxamide           |
| 1,099   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-5-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide   |
| 1,100   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-5-carboxamide            |
| 1,101   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-4-hydroxy-3-(1-piperazinylcarbonyl)benzamide                   |
| 1,102   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-                                                                              |

| EXAMPLE | Substituted Amine (X)                                                                                                                             |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------|
|         | hydroxypropyl}-4-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-5-carboxamide                                                                       |
| 1,103   | N <sup>4</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4,5-dicarboxamide |
| 1,104   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-5-carboxamide                    |
| 1,105   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> -methylisophthalamide          |
| 1,106   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-methyl-2-[(methylsulfonyl)amino]-1,3-oxazole-5-carboxamide           |
| 1,107   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(ethylsulfonyl)amino]-1,3-oxazole-4-carboxamide                    |
| 1,108   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide                    |
| 1,109   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-hydroxy-N <sup>3</sup> -methylisophthalamide        |
| 1,110   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-methyl-5-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide           |
| 1,111   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(ethylsulfonyl)amino]-1,3-oxazole-4-carboxamide                  |
| 1,112   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-5-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide          |
| 1,113   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-                                                                                  |

| EXAMPLE | Substituted Amine (X)                                                                                                                            |
|---------|--------------------------------------------------------------------------------------------------------------------------------------------------|
|         | methoxybenzyl)amino]propyl}-N <sup>3</sup> -ethyl-4-hydroxyisophthalamide                                                                        |
| 1,114   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)amino]-1,3-oxazole-2-carboxamide                  |
| 1,115   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(ethylsulfonyl)amino]-1,3-oxazole-4-carboxamide                    |
| 1,116   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)amino]-3-isoxazolecarboxamide                     |
| 1,117   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -ethyl-4-hydroxyisophthalamide          |
| 1,118   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-[(methylsulfonyl)amino]-3-isoxazolecarboxamide                      |
| 1,119   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(propylsulfonyl)amino]-1,3-oxazole-4-carboxamide                   |
| 1,120   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(methylsulfonyl)amino]-5-isoxazolecarboxamide                      |
| 1,121   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N <sup>3</sup> -ethyl-4-hydroxyisophthalamide           |
| 1,122   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)amino]-5-isoxazolecarboxamide                     |
| 1,123   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(propylsulfonyl)amino]-1,3-oxazole-4-carboxamide                |
| 1,124   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-(hydroxymethyl)-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide |
| 1,125   | N <sup>3</sup> -(cyclopropylmethyl)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-                                                           |

| EXAMPLE | Substituted Amine (X)                                                                                                                                             |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-hydroxyisophthalamide                                                                                                    |
| 1,126   | 5-cyclopropyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                      |
| 1,127   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(propylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                   |
| 1,128   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-isopropyl-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                        |
| 1,129   | N <sup>3</sup> -(cyclopropylmethyl)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxyisophthalamide             |
| 1,130   | N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                         |
| 1,131   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-[(propylsulfonyl)amino]-1,3-oxazole-4-carboxamide                          |
| 1,132   | N-[(1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                       |
| 1,133   | N-[(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-(4-hydroxybenzyl)propyl]-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                      |
| 1,134   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> -isobutylisophthalamide                        |
| 1,135   | 2-[[cyclopropylmethyl)sulfonyl]amino}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-oxazole-4-carboxamide                       |
| 1,136   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> -isobutyl-N <sup>3</sup> -methylisophthalamide |

| EXAMPLE | Substituted Amine (X)                                                                                                                                             |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1,137   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(isobutylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                 |
| 1,138   | N3-(cyclopropylmethyl)-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> -methylisophthalamide   |
| 1,139   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isobutylsulfonyl)amino]-1,3-oxazole-4-carboxamide                               |
| 1,140   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> -methyl-N <sup>3</sup> -propylisophthalamide   |
| 1,141   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(isobutylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                  |
| 1,142   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-hydroxy-N <sup>3</sup> -methyl-N <sup>3</sup> -propylisophthalamide |
| 1,143   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(phenylsulfonyl)amino]-1,3-oxazole-4-carboxamide                                    |
| 1,144   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N3-ethyl-4-hydroxy-N <sup>3</sup> -propylisophthalamide               |
| 1,145   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[[4-methylphenyl)sulfonyl]amino}-1,3-oxazole-4-carboxamide                           |
| 1,146   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N3-ethyl-4-hydroxy-N <sup>3</sup> -propylisophthalamide                 |
| 1,147   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[[4-methylphenyl)sulfonyl]amino}-1,3-oxazole-                                       |

| EXAMPLE | Substituted Amine (X)                                                                                                                                         |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
|         | 4-carboxamide                                                                                                                                                 |
| 1,148   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(phenylsulfonyl)amino]-1,3-oxazole-4-carboxamide                               |
| 1,149   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-N <sup>3</sup> , N <sup>3</sup> -dipropylisophthalamide   |
| 1,150   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                         |
| 1,151   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-hydroxy-N <sup>3</sup> , N <sup>3</sup> -dipropylisophthalamide |
| 1,152   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide                          |
| 1,153   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-hydroxy-N <sup>3</sup> , N <sup>3</sup> -dipropylisophthalamide    |
| 1,154   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide                               |
| 1,155   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide                              |

## EXAMPLES 1,156-1,214

Following the general procedure of CHART A and EXAMPLES 4-6, 321-327, 329-464, 466-527, 529-579, 597-619 and 633-708 and making non-critical variations, and using the appropriate amines (VIII) and amide forming agents (IX), the titled compounds are obtained.

| EXAMPLE | Substituted Amine (X) | MH <sup>+</sup> |
|---------|-----------------------|-----------------|
|---------|-----------------------|-----------------|

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                  | MH+                                                              |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| 1,156   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-3-methyl-5-[propionyl(propyl)amino]benzamide                                                                           | 532.5                                                            |
| 1,157   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-1-butyl-1H-indole-5-carboxamide                                                                                        | Anal.<br>Found:<br>C =<br>73.58;<br>H =<br>7.44;<br>N =<br>8.24. |
| 1,159   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-3-[butyl(propionyl)amino]-5-methylbenzamide                                                                            | 546.3                                                            |
| 1,160   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-4-methyl-1-propyl-1H-indole-6-carboxamide                                                                              | 500.3                                                            |
| 1,161   | N-((1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl)-1-(1-propylbutyl)-1H-indole-6-carboxamide                                                                              | 542.2                                                            |
| 1,162   | N <sup>1</sup> -((1S,2R)-1-benzyl-2-hydroxy-3-[[[(2-oxo-2,3-dihydro-1,3-benzoxazol-6-yl)methyl]amino]propyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           | 573.3                                                            |
| 1,163   | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[[(trifluoromethyl)sulfonyl]amino]isophthalamide | 713.0                                                            |
| 1,164   | 3-[[[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]amino]carbonyl]-5-[[[(dipropylamino)carbonyl]benzoic acid                                                             | 576.1                                                            |
| 1,165   | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-prop-1-ynylisophthalamide                         | 604.4                                                            |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                 | MH+                       |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| 1,166   | N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-(dipropylamino)isonicotinamide                                                                                     | HRMS<br>=<br>505.31<br>76 |
| 1,167   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           |                           |
| 1,168   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(ethylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |                           |
| 1,169   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[(propylsulfonyl)amino]isophthalamide           |                           |
| 1,170   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(isopropylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide        |                           |
| 1,171   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(isobutylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         |                           |
| 1,172   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[(thien-2-ylsulfonyl)amino]isophthalamide       |                           |
| 1,173   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(2-furylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide          |                           |
| 1,174   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[(1,3-thiazol-5-ylsulfonyl)amino]isophthalamide |                           |
| 1,175   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(1,3-oxazol-5-ylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide  |                           |
| 1,176   | N <sup>1</sup> -{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-                                                                                                                               |                           |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                                                 | MH+ |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
|         | ethylbenzyl)amino]-2-hydroxypropyl}-5-[(1,3-oxazol-4-ylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                                                                         |     |
| 1,177   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[(1,3-thiazol-4-ylsulfonyl)amino]isophthalamide                  |     |
| 1,178   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide       |     |
| 1,179   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(phenylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide                            |     |
| 1,180   | 5-{[(5-cyanopyridin-2-yl)sulfonyl]amino}-N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide             |     |
| 1,181   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-({[5-(trifluoromethyl)pyridin-2-yl]sulfonyl}amino)isophthalamide |     |
| 1,182   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}benzamide                                                                   |     |
| 1,183   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-({[5-(trifluoromethyl)pyridin-2-yl]sulfonyl}amino)benzamide                                                             |     |
| 1,184   | 3-{[(5-cyanopyridin-2-yl)sulfonyl]amino}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide                                                                         |     |
| 1,185   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(phenylsulfonyl)amino]benzamide                                                                                        |     |
| 1,186   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-                                                                                                                                                              |     |

| EXAMPLE | Substituted Amine (X)                                                                                                    | MH <sup>+</sup> |
|---------|--------------------------------------------------------------------------------------------------------------------------|-----------------|
|         | ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)amino]benzamide                                                   |                 |
| 1,187   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(ethylsulfonyl)amino]benzamide            |                 |
| 1,188   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(propylsulfonyl)amino]benzamide           |                 |
| 1,189   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(isobutylsulfonyl)amino]benzamide         |                 |
| 1,190   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(isopropylsulfonyl)amino]benzamide        |                 |
| 1,191   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-ethylpropyl)sulfonyl]amino} benzamide |                 |
| 1,192   | 3-[(cyclohexylsulfonyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide       |                 |
| 1,193   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-propylbutyl)sulfonyl]amino} benzamide |                 |
| 1,194   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(thien-2-ylsulfonyl)amino]benzamide       |                 |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                            | MH <sup>+</sup> |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| 1,195   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(2-furysulfonyl)amino]benzamide                                                                   |                 |
| 1,196   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(isoxazol-5-ylsulfonyl)amino]benzamide                                                            |                 |
| 1,197   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(isoxazol-3-ylsulfonyl)amino]benzamide                                                            |                 |
| 1,198   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(3-furysulfonyl)amino]benzamide                                                                   |                 |
| 1,199   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(thien-3-ylsulfonyl)amino]benzamide                                                               |                 |
| 1,200   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(1,3-thiazol-4-ylsulfonyl)amino]benzamide                                                         |                 |
| 1,201   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(1,3-thiazol-5-ylsulfonyl)amino]benzamide                                                         |                 |
| 1,202   | N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-3-[(1,3-thiazol-2-ylsulfonyl)amino]benzamide                                                         |                 |
| 1,203   | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[[(trifluoromethyl)sulfonyl]amino]isophthalamide |                 |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                | MH <sup>+</sup> |
|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| 1,204   | N <sup>1</sup> -[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-[[trifluoromethyl)sulfonyl]amino}isophthalamide  |                 |
| 1,205   | N <sup>1</sup> -[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-[(methylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide            |                 |
| 1,206   | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-[(methylsulfonyl)amino]-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide |                 |
| 1,207   | N <sup>1</sup> -(tert-butyl)-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isophthalamide                                 |                 |
| 1,208   | N <sup>1</sup> -(tert-butyl)-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide                        |                 |
| 1,209   | 5-bromo-N <sup>1</sup> -(tert-butyl)-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isophthalamide                         |                 |
| 1,210   | 3-tert-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide                                                                   |                 |
| 1,211   | 3-tert-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide                                                          |                 |
| 1,212   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[[trifluoromethyl)sulfonyl]amino}benzamide                                             |                 |

| EXAMPLE | Substituted Amine (X)                                                                                              | MH <sup>+</sup> |
|---------|--------------------------------------------------------------------------------------------------------------------|-----------------|
| 1,213   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoromethoxy)benzamide          |                 |
| 1,214   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(trifluoromethoxy)benzamide |                 |

## EXAMPLES 1,215-1,259

Following the general procedure of CHART A and EXAMPLES 4-6, 321-327, 329-464, 466-527, 529-579, 597-619 and 633-708 and making non-critical variations, and using the appropriate amines (VIII) and amide forming agents (IX), the titled compounds are obtained.

| EXAMPLE | Substituted Amine (X)                                                                                                          | [M+H] <sup>+</sup> |
|---------|--------------------------------------------------------------------------------------------------------------------------------|--------------------|
| 1,215   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-hydroxy-2-(4-methylphenyl)acetamide               | 581.4              |
| 1,216   | N1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-hydroxy-N3-methylisophthalamide                  | 610.4              |
| 1,217   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-hydroxy-2-(4-methoxy-3-nitrophenyl)acetamide      | 642.4              |
| 1,218   | 5-(aminosulfonyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-methoxybenzamide                | 646.5              |
| 1,219   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-hydroxy-3-(pyrrolidin-1-ylcarbonyl)benzamide      | 650.5              |
| 1,220   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide | 621.4              |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                              | [M+H] <sup>+</sup> |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| 1,221   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(3,5-dimethylisoxazol-4-yl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide   | 663.4              |
| 1,222   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N <sup>3</sup> ,N <sup>3</sup> -dipropyl-5-(1,3-thiazol-2-yl)isophthalamide            | 651.4              |
| 1,223   | 3-(cyclohexylcarbonyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methylbenzamide                                                             | 565.4              |
| 1,224   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N <sup>3</sup> -propylisophthalamide                                          | 540.4              |
| 1,225   | 3-[cyclohexyl(hydroxy)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methylbenzamide                                                      | 567.4              |
| 1,226   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide      | 647.5              |
| 1,227   | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpyridine-3,5-dicarboxamide                       | 567                |
| 1,228   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isobutyl-1,2,4-oxadiazol-5-yl)methyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 600                |
| 1,229   | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpyridine-3,5-dicarboxamide                     | 563                |
| 1,230   | N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N <sup>5</sup> ,N <sup>5</sup> -dipropylpyridine-3,5-dicarboxamide                   | 581                |
| 1,231   | N <sup>1</sup> -[(1S,2R)-3-[(1-acetylpiperidin-4-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -                                       | 587                |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                     | [M+H] <sup>+</sup> |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
|         | dipropylisophthalamide                                                                                                                                                    |                    |
| 1,232   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pent-1-ynylbenzyl)amino]propyl}-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide           | 618                |
| 1,233   | N <sup>1</sup> -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(4-hydroxybut-1-ynyl)benzyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide | 620                |
| 1,234   | 1-{3-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]amino}carbonyl-5-methylbenzoyl-L-prolinamide                                                | 593                |
| 1,235   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -isopropyl-5-methylisophthalamide                                | 538                |
| 1,236   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -ethyl-N <sup>3</sup> ,5-dimethylisophthalamide                  | 538                |
| 1,237   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,5-dimethyl-N <sup>3</sup> -prop-2-ynylisophthalamide            | 548                |
| 1,238   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -isobutyl-5-methylisophthalamide                                 | 552                |
| 1,239   | N <sup>1</sup> -(sec-butyl)-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide                              | 552                |
| 1,240   | N <sup>1</sup> -butyl-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide                                    | 552                |
| 1,241   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -diethyl-5-methylisophthalamide                  | 552                |
| 1,242   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-                                                                                                                    | 552                |

| EXAMPLE | Substituted Amine (X)                                                                                                                                            | [M+H] <sup>+</sup> |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
|         | ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,5-dimethyl-N <sup>3</sup> -propylisophthalamide                                                              |                    |
| 1,243   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -isopropyl-N <sup>3</sup> ,5-dimethylisophthalamide     | 552                |
| 1,244   | N <sup>1</sup> -butyl-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>1</sup> ,5-dimethylisophthalamide         | 566                |
| 1,245   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -isobutyl-N <sup>3</sup> ,5-dimethylisophthalamide      | 566                |
| 1,246   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -ethyl-5-methyl-N <sup>3</sup> -propylisophthalamide    | 566                |
| 1,247   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> -ethyl-N <sup>3</sup> -isopropyl-5-methylisophthalamide | 566                |
| 1,248   | N <sup>1</sup> ,N <sup>1</sup> -diallyl-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide         | 576                |
| 1,249   | 3-(azepan-1-ylcarbonyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide                                            | 578                |
| 1,250   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(4-hydroxypiperidin-1-yl)carbonyl]-5-methylbenzamide                              | 580                |
| 1,251   | N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-hydroxypiperidin-1-yl)carbonyl]-5-methylbenzamide                              | 580                |
| 1,252   | N <sup>1</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>3</sup> ,N <sup>3</sup> -diisopropyl-5-methylisophthalamide     | 580                |

| EXAMPLE | Substituted Amine (X)                                                                                                                                                             | [M+H] <sup>+</sup> |
|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|
| 1,253   | N <sup>1</sup> -butyl-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>1</sup> -ethyl-5-methylisophthalamide                      | 580                |
| 1,254   | N <sup>1</sup> -(cyclopropylmethyl)-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N <sup>1</sup> -propylisophthalamide       | 592                |
| 1,255   | 1-{3-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]amino)carbonyl]-5-methylbenzoyl}-D-prolinamide                                                      | 593                |
| 1,256   | N <sup>1</sup> -cyclohexyl-N <sup>3</sup> -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N <sup>1</sup> ,5-dimethylisophthalamide                     | 592                |
| 1,257   | N <sup>1</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-methylphenyl)cyclopropyl]amino}propyl)-5-methyl-N <sup>3</sup> ,N <sup>3</sup> -dipropylisophthalamide         | 592                |
| 1,258   | N <sup>3</sup> -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1,2,3,4-tetrahydronaphthalen-1-ylamino)propyl]-N <sup>5</sup> ,N <sup>5</sup> -diisopropylpyridine-3,5-dicarboxamide | 579                |
| 1,259   | N-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl]-3-[(trifluoromethyl)sulfonyl]amino}benzamide                                                          | 586.1              |

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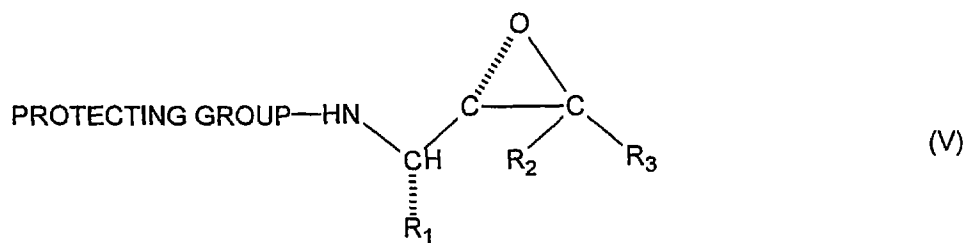
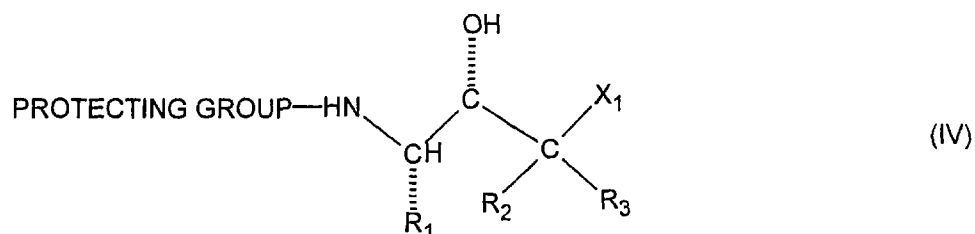
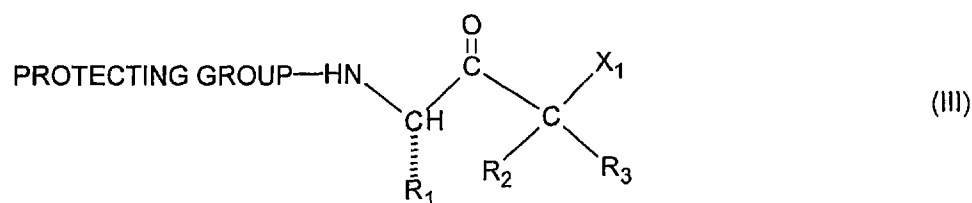
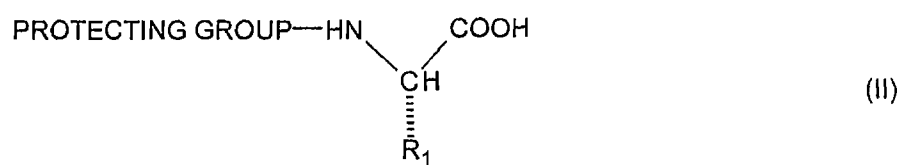
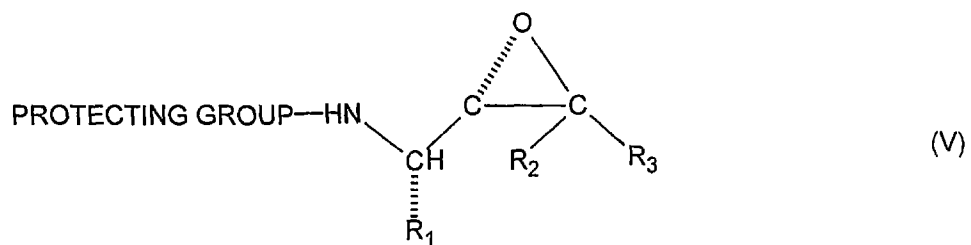
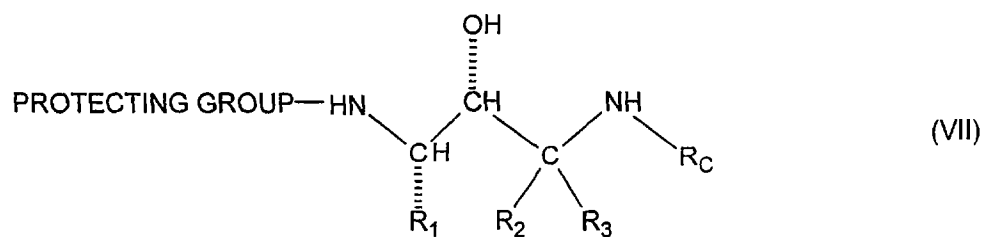
CHART A

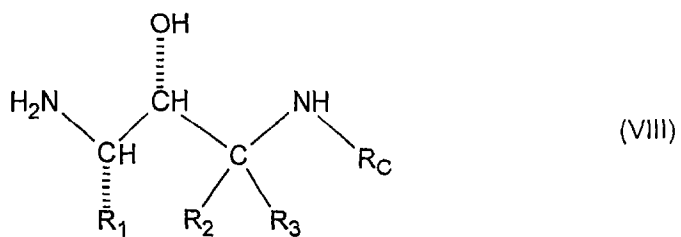
CHART A - Continued

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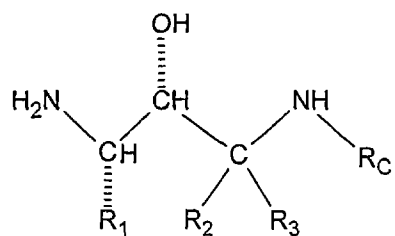
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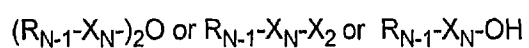
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CHART A - Continued

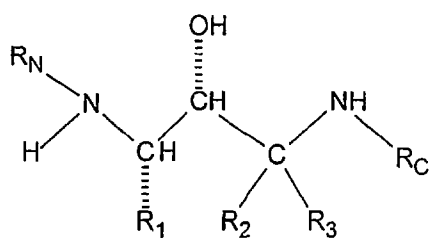
(VIII)

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(IX)

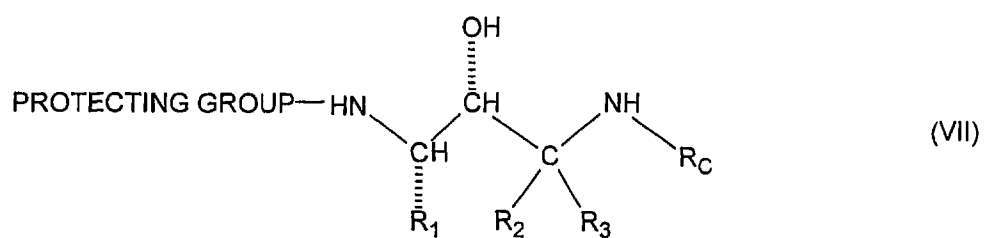
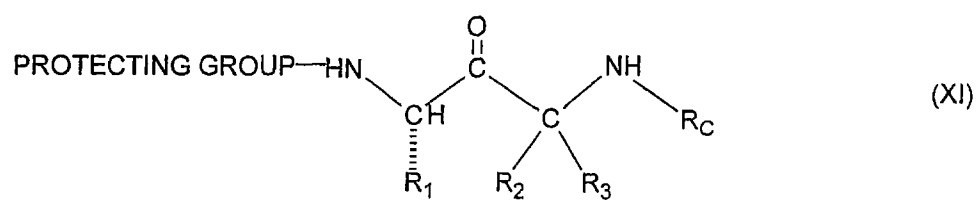
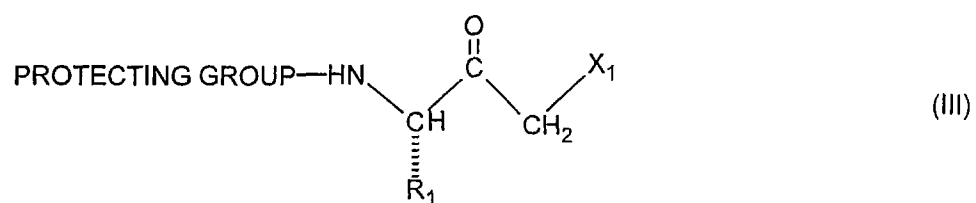


(X)

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CHART B

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313

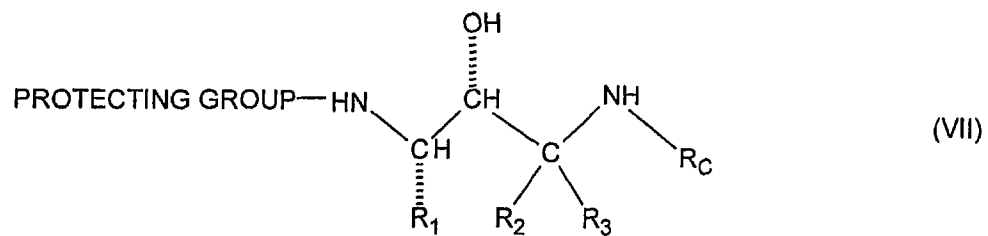
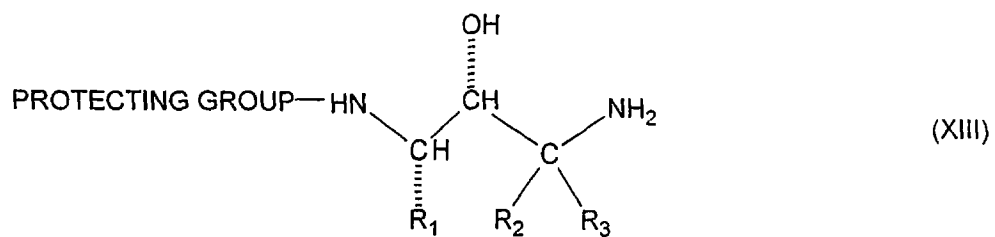
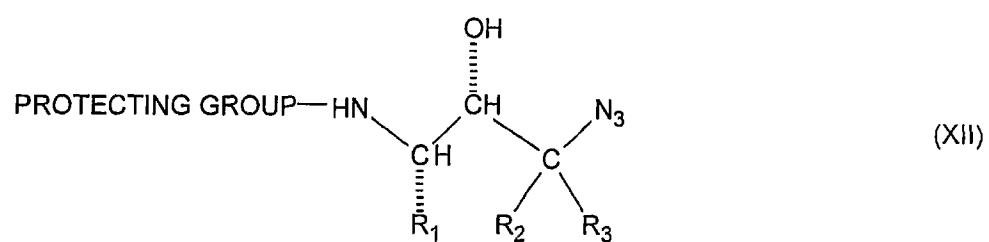
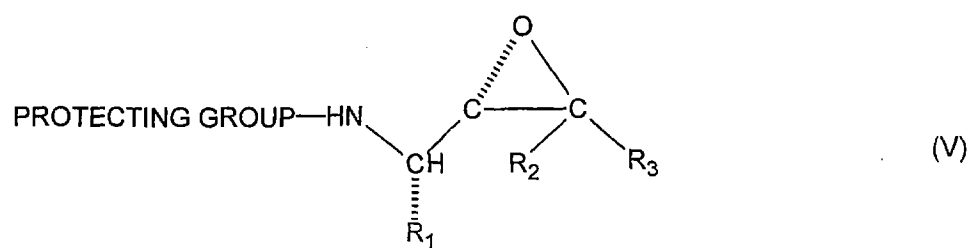
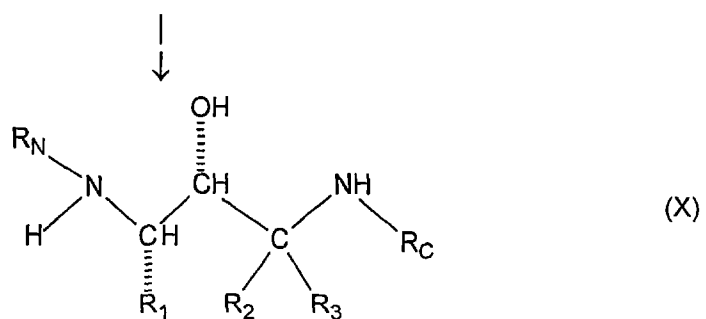
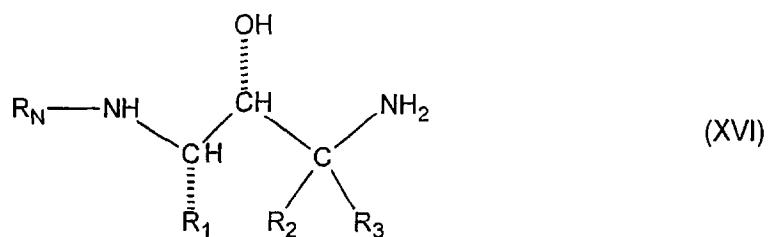
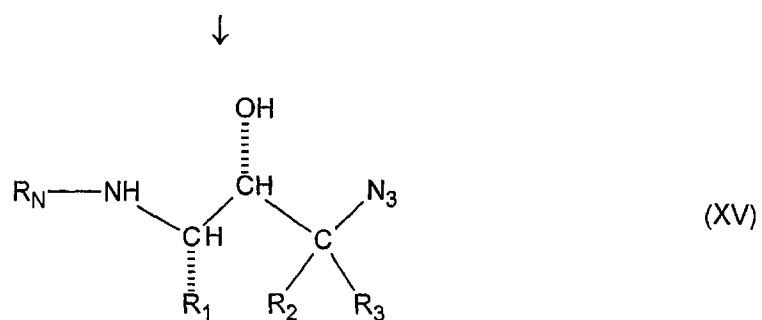
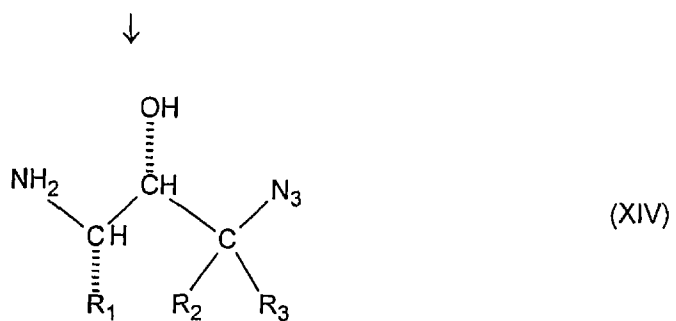
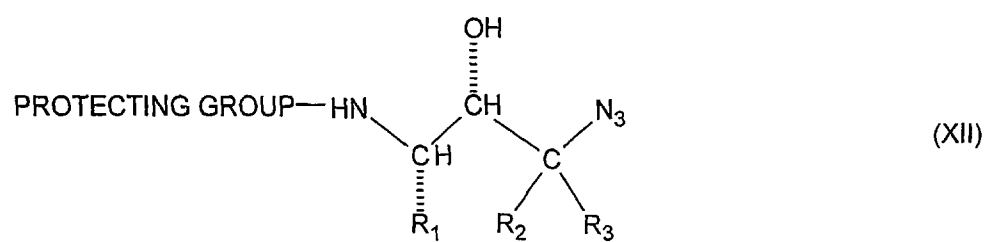
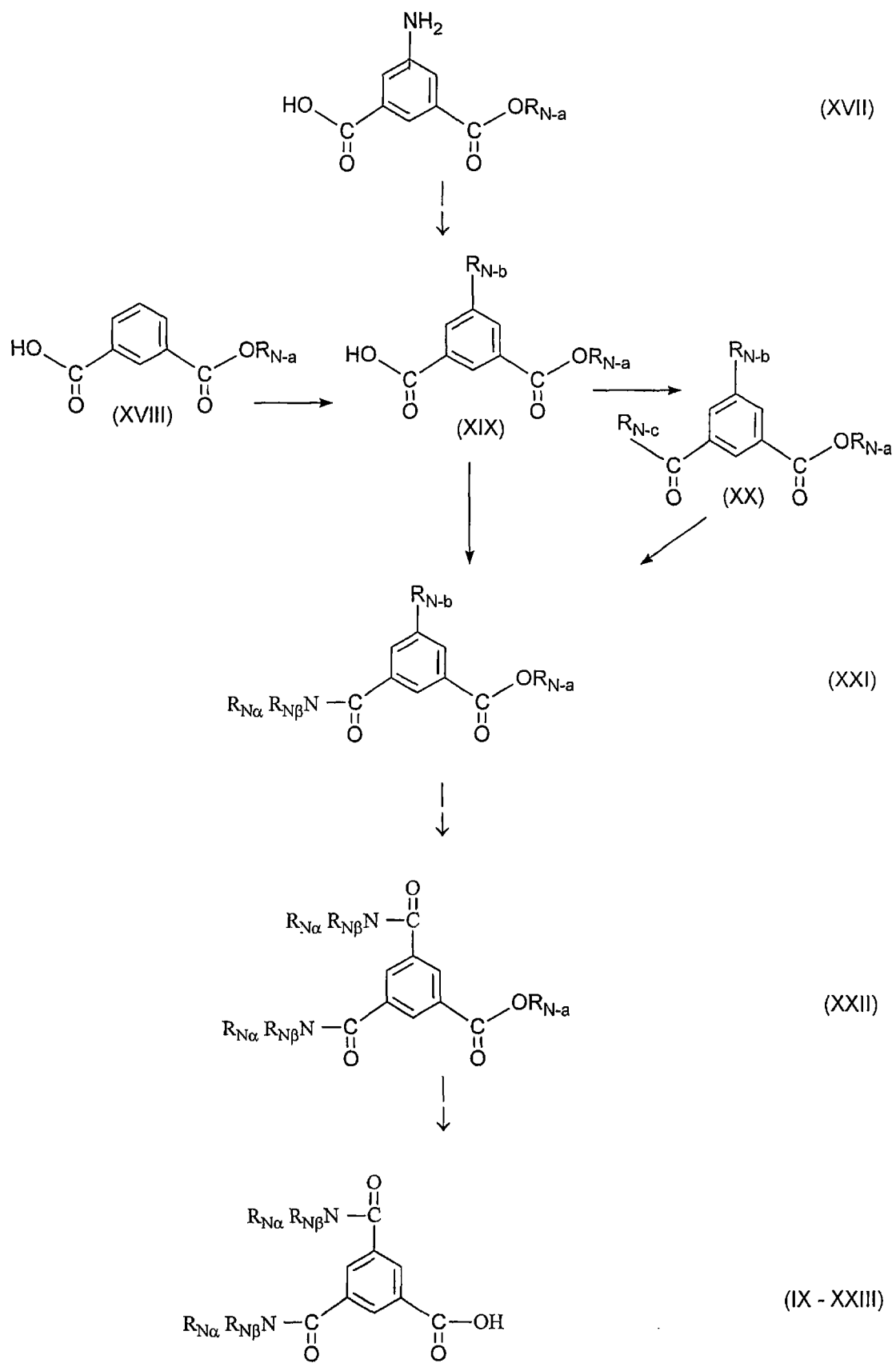
CHART C

CHART D

315

CHART E

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316

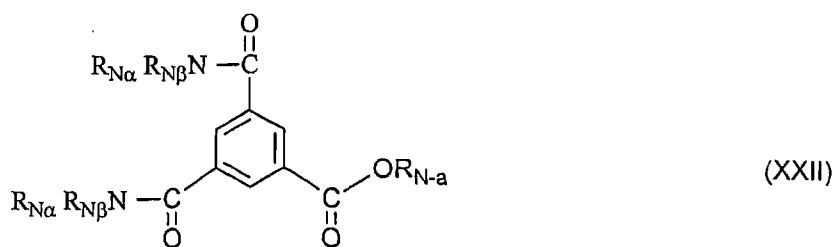
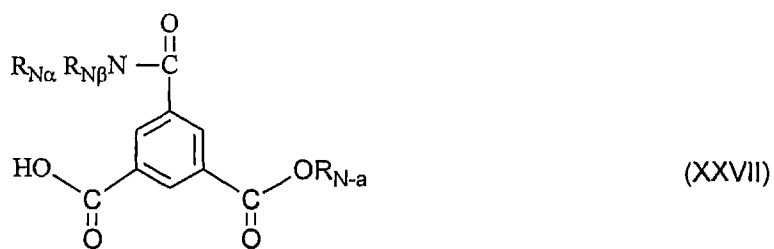
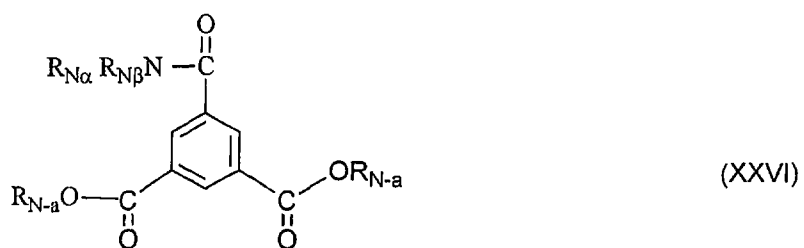
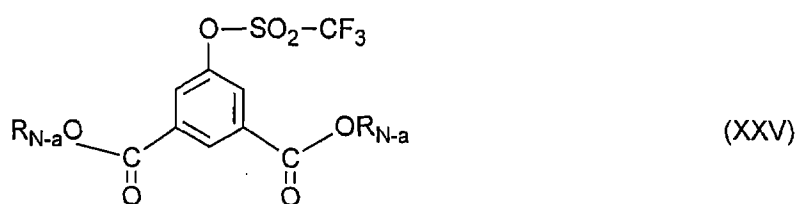
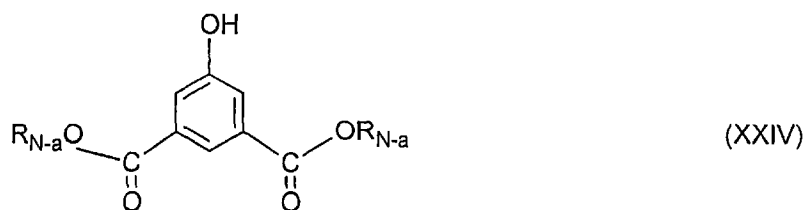
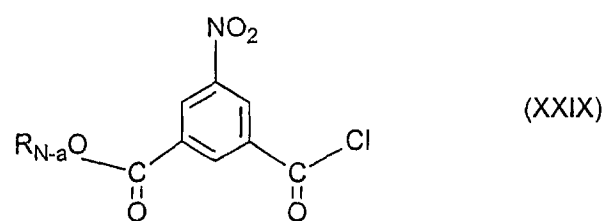
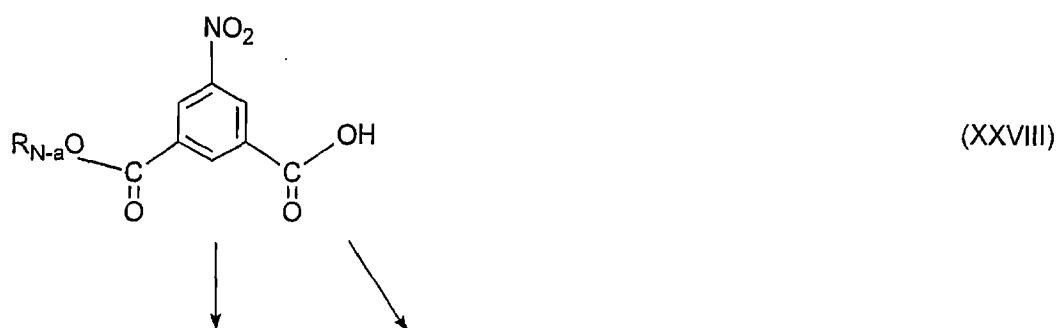
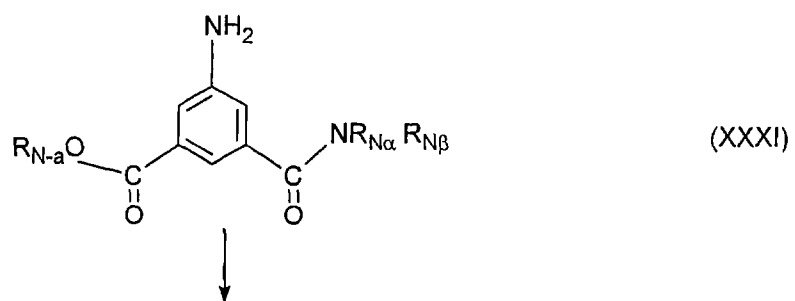
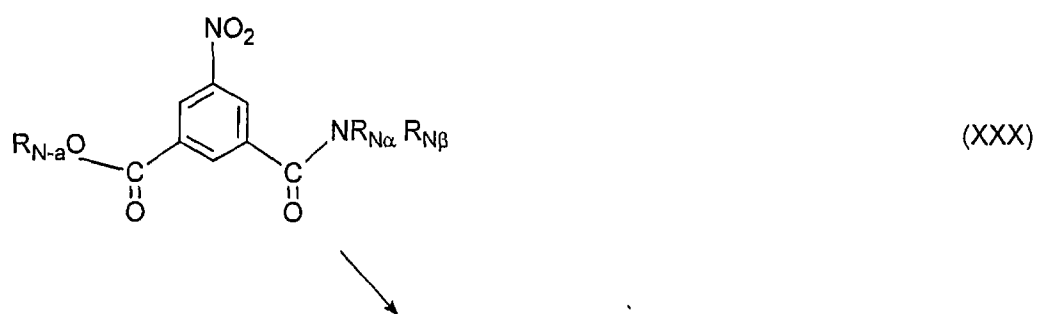
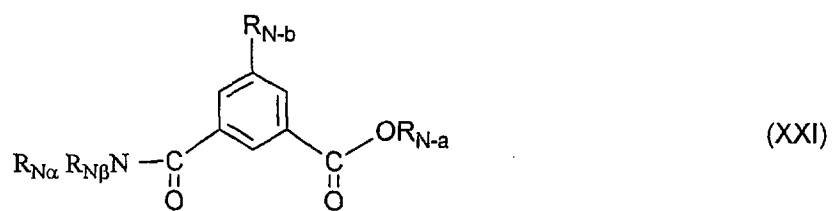
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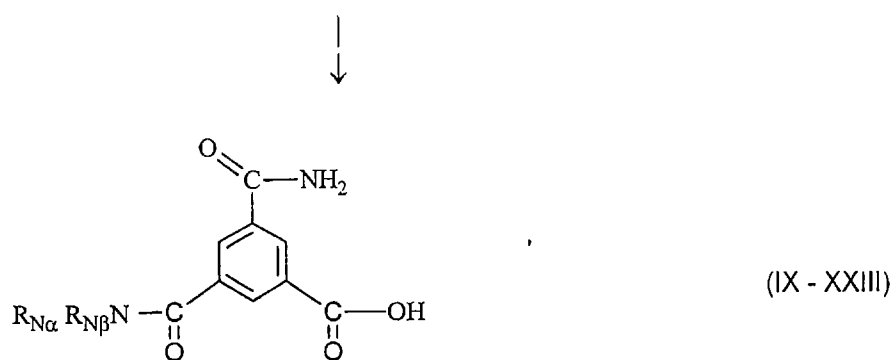
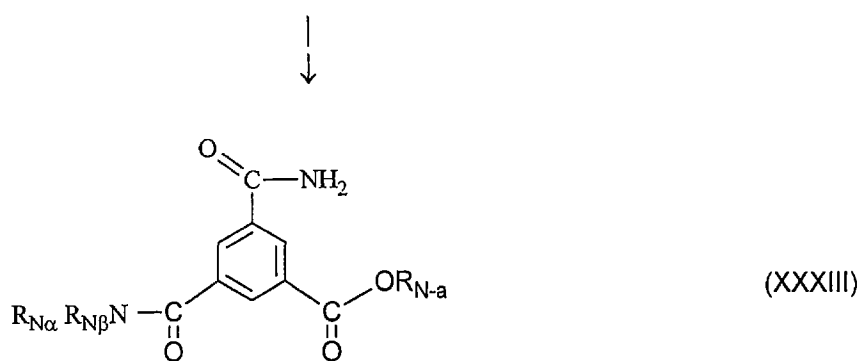
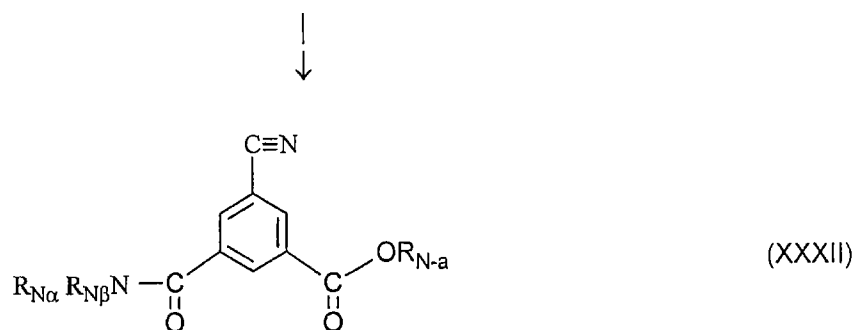
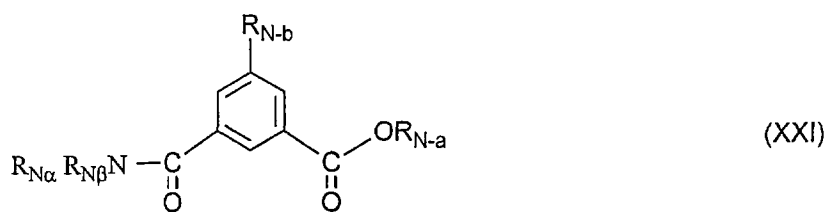
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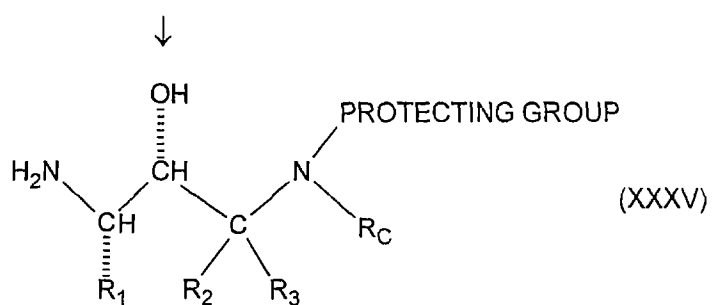
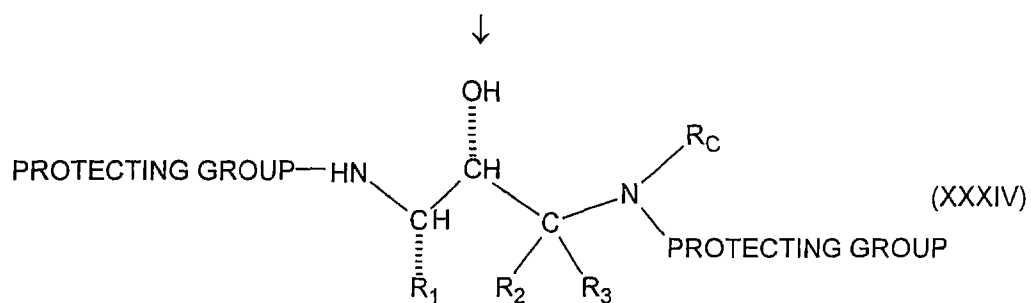
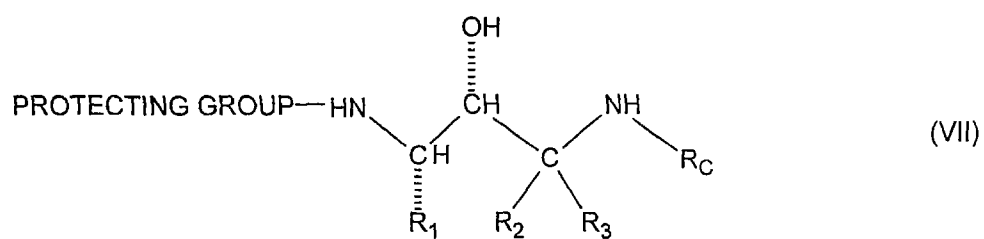
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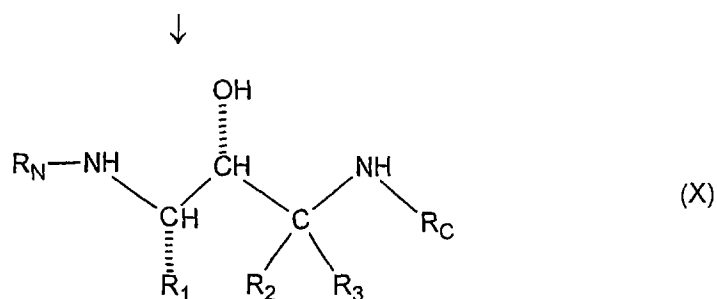
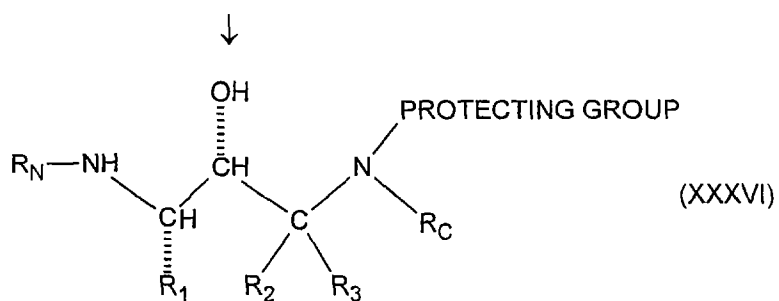
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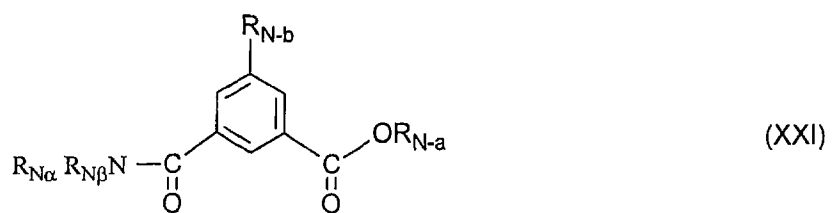
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CHART I

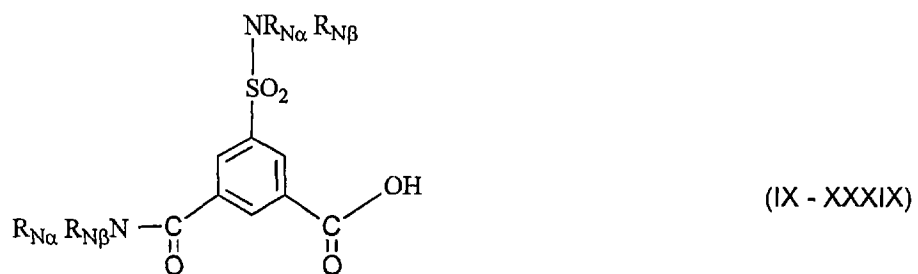
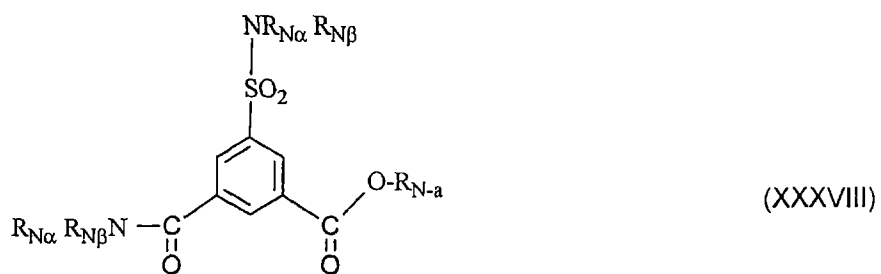
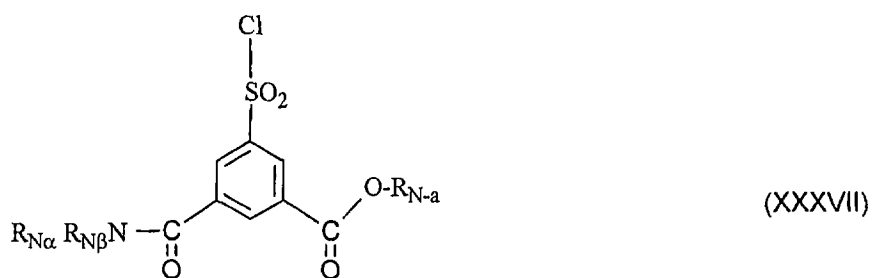
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320

CHART J

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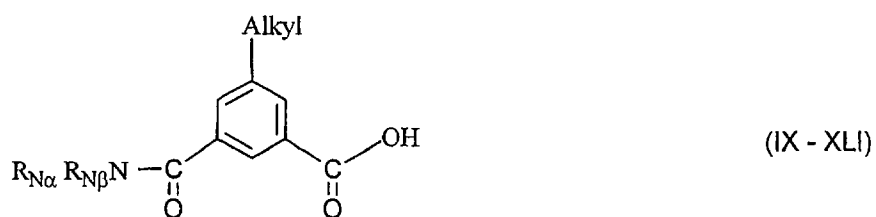
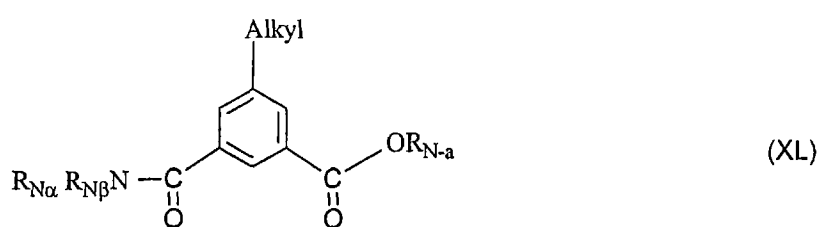
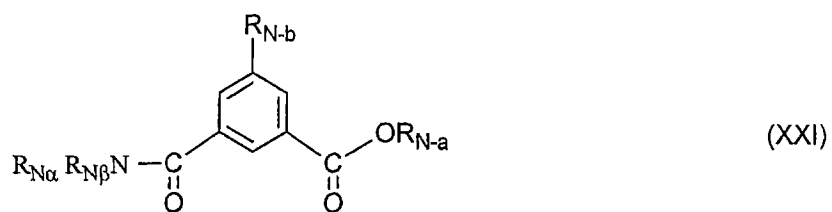
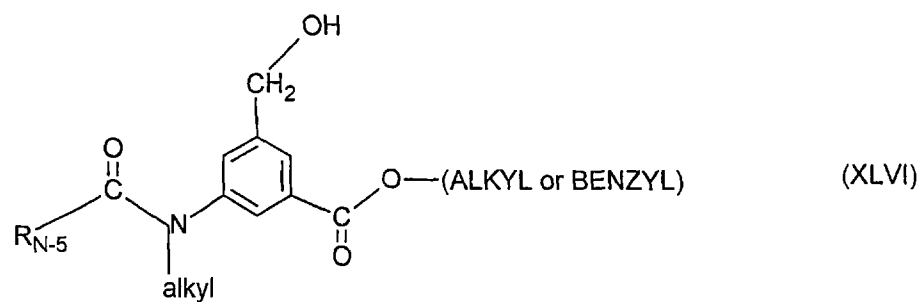
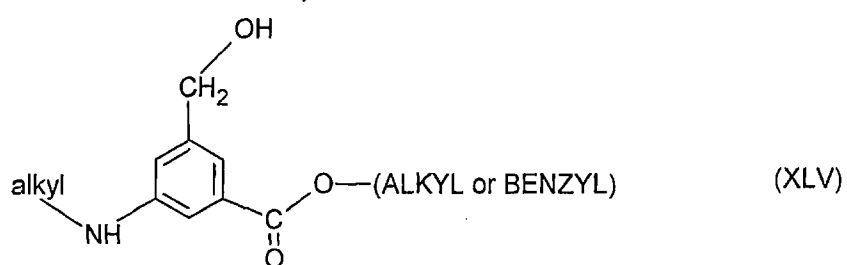
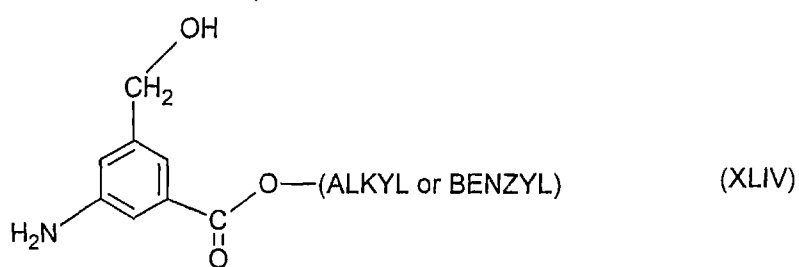
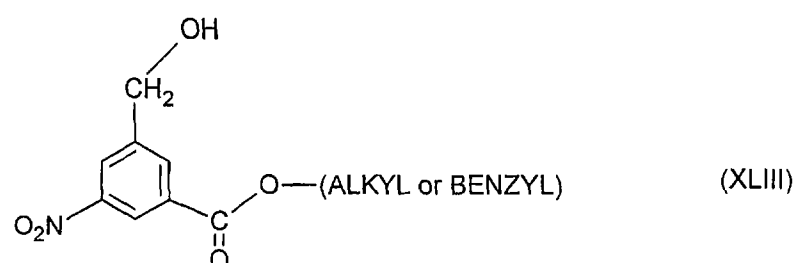
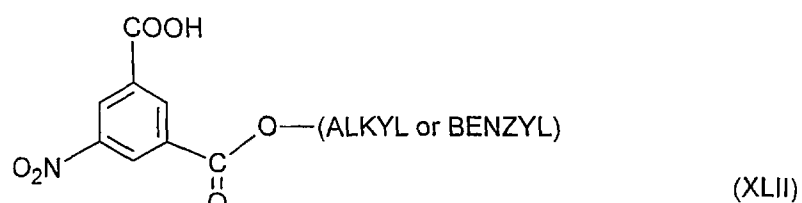
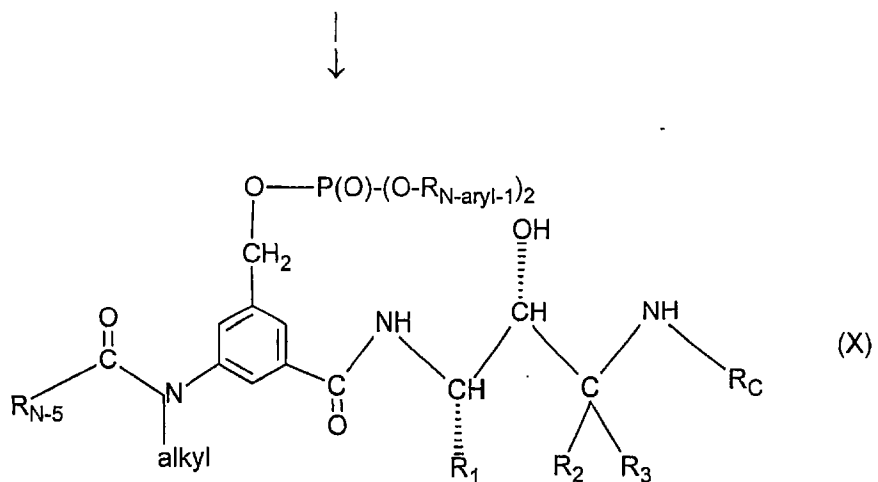
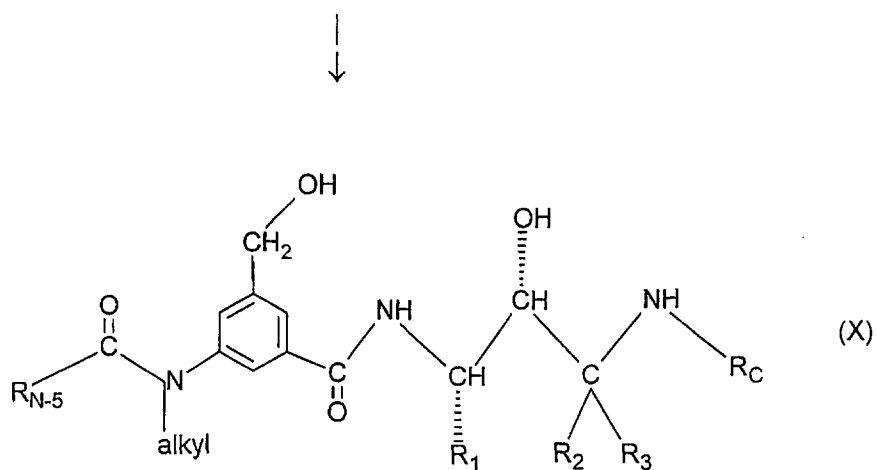
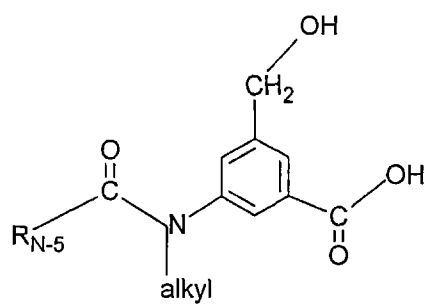
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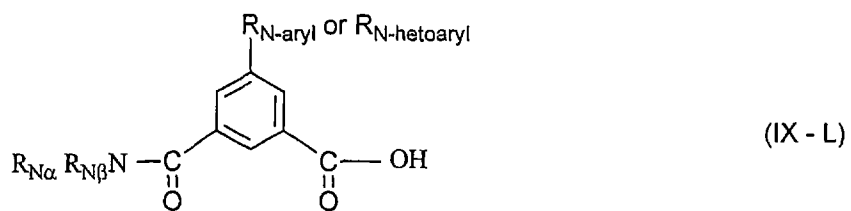
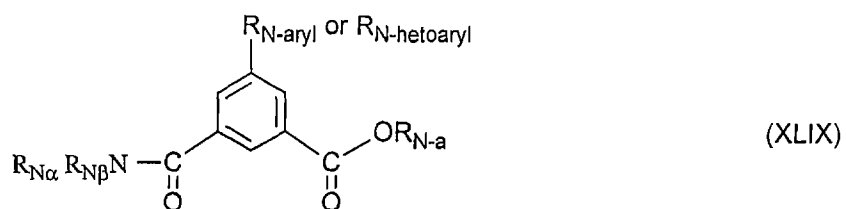
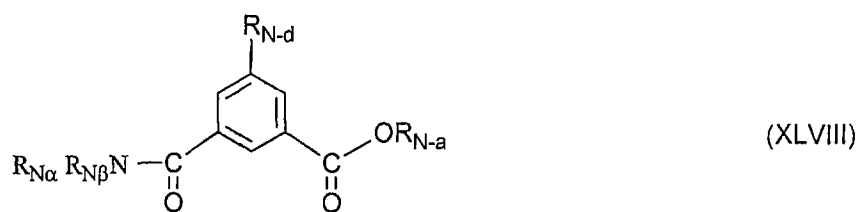
CHART L

323

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CHART L - Continued



324

CHART M

325

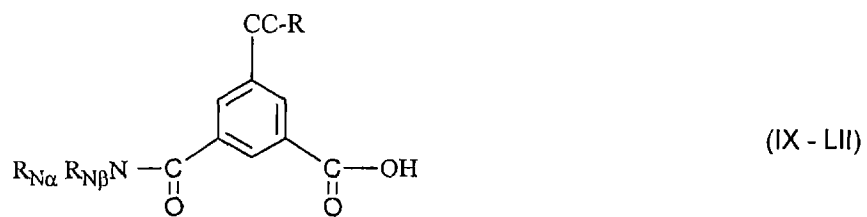
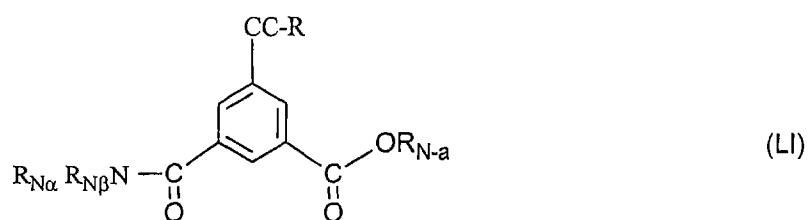
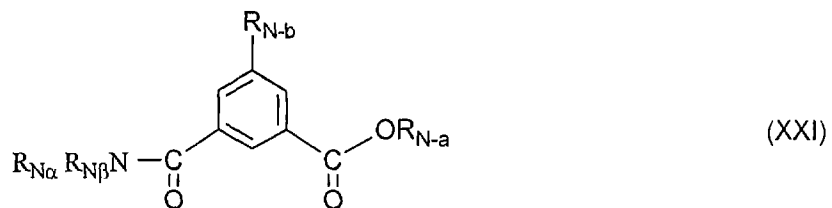
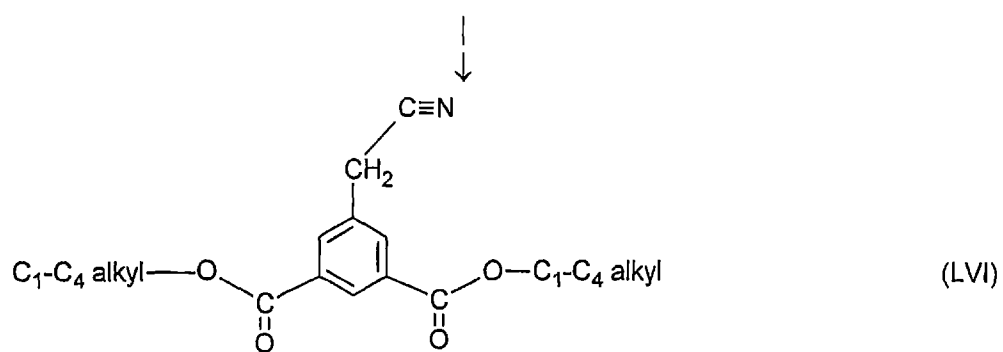
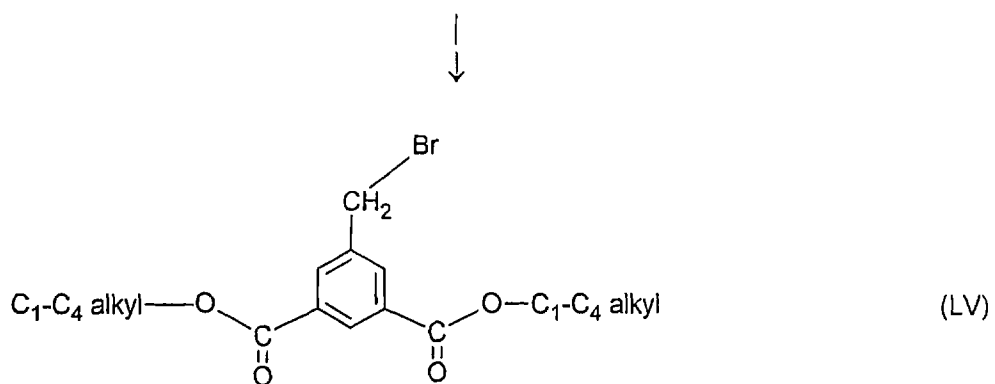
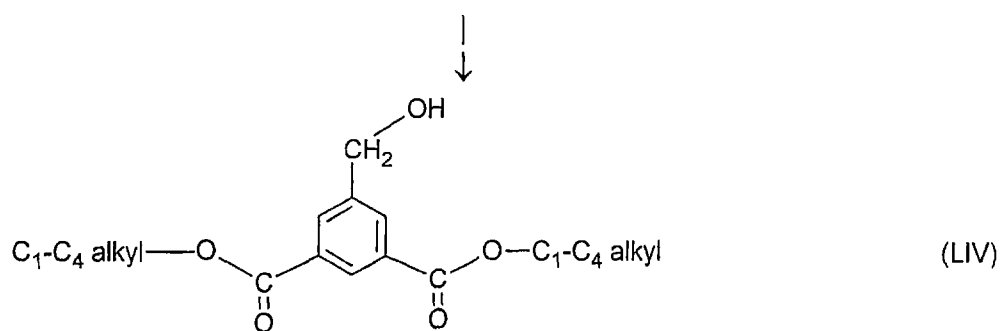
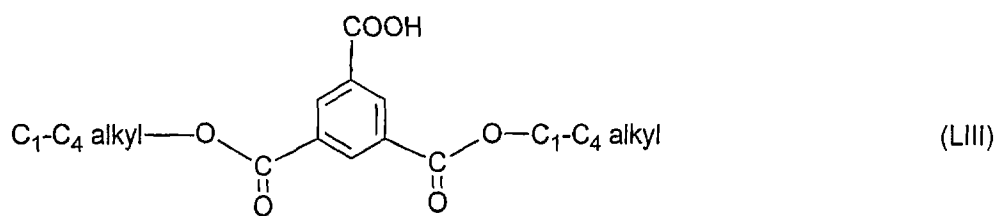
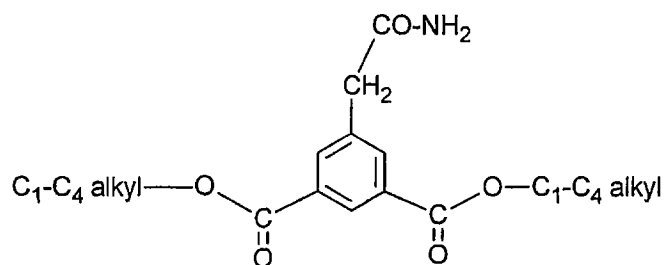
CHART N

CHART O

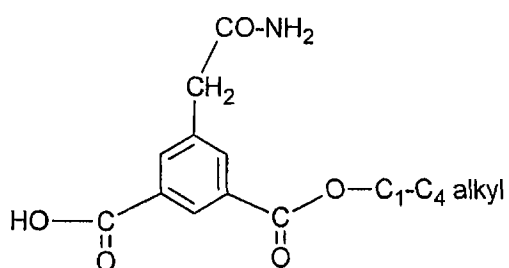
327



(LVII)

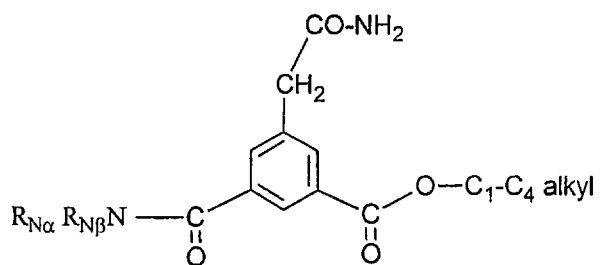
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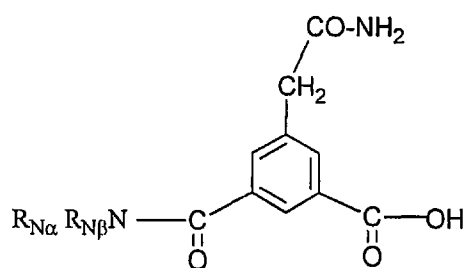
(LVIII)

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(LIX)

15



(IX - LX)

20

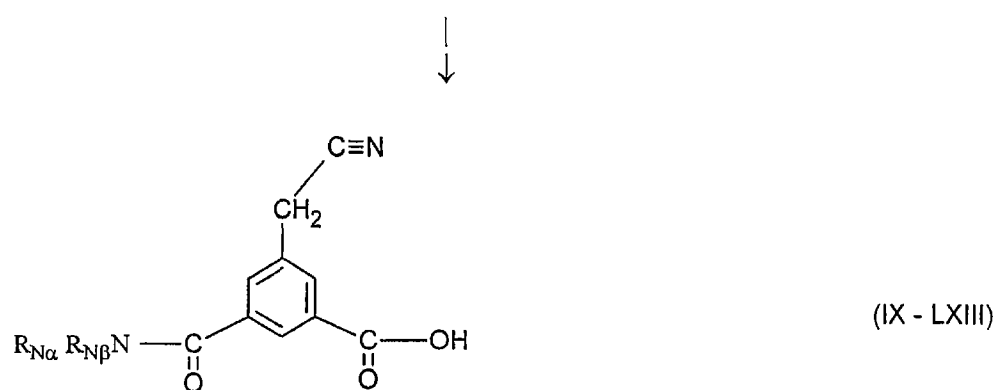
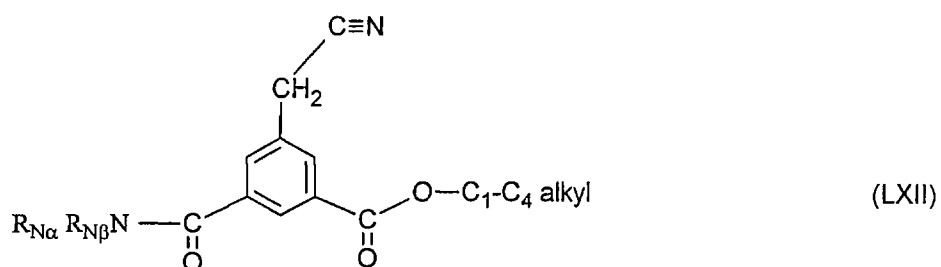
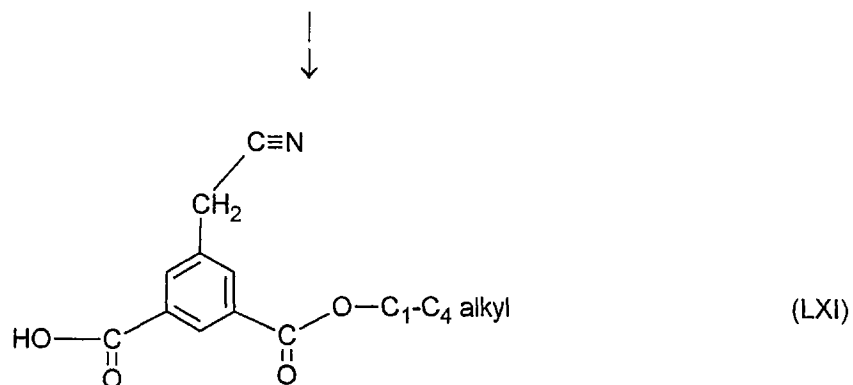
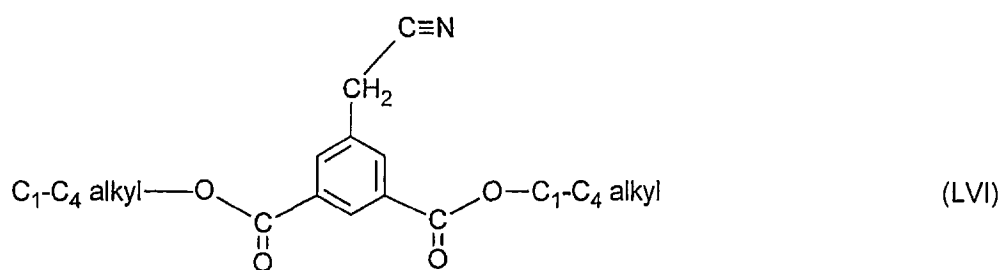
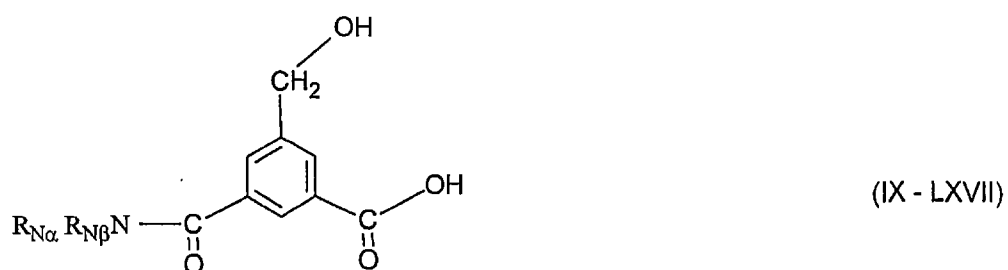
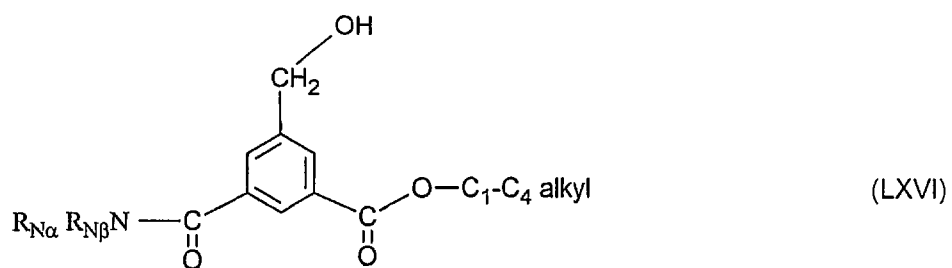
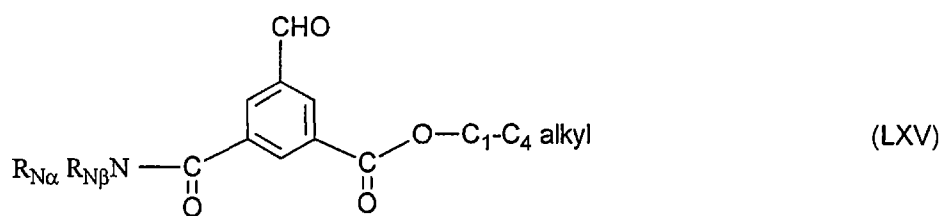
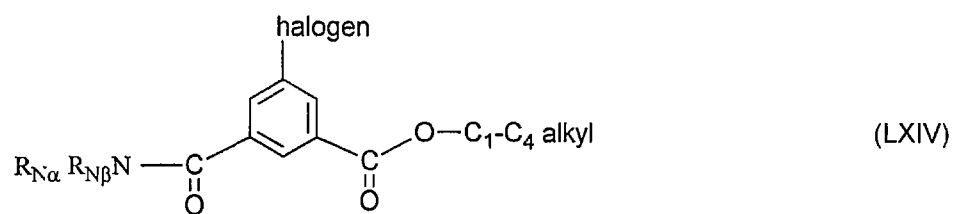
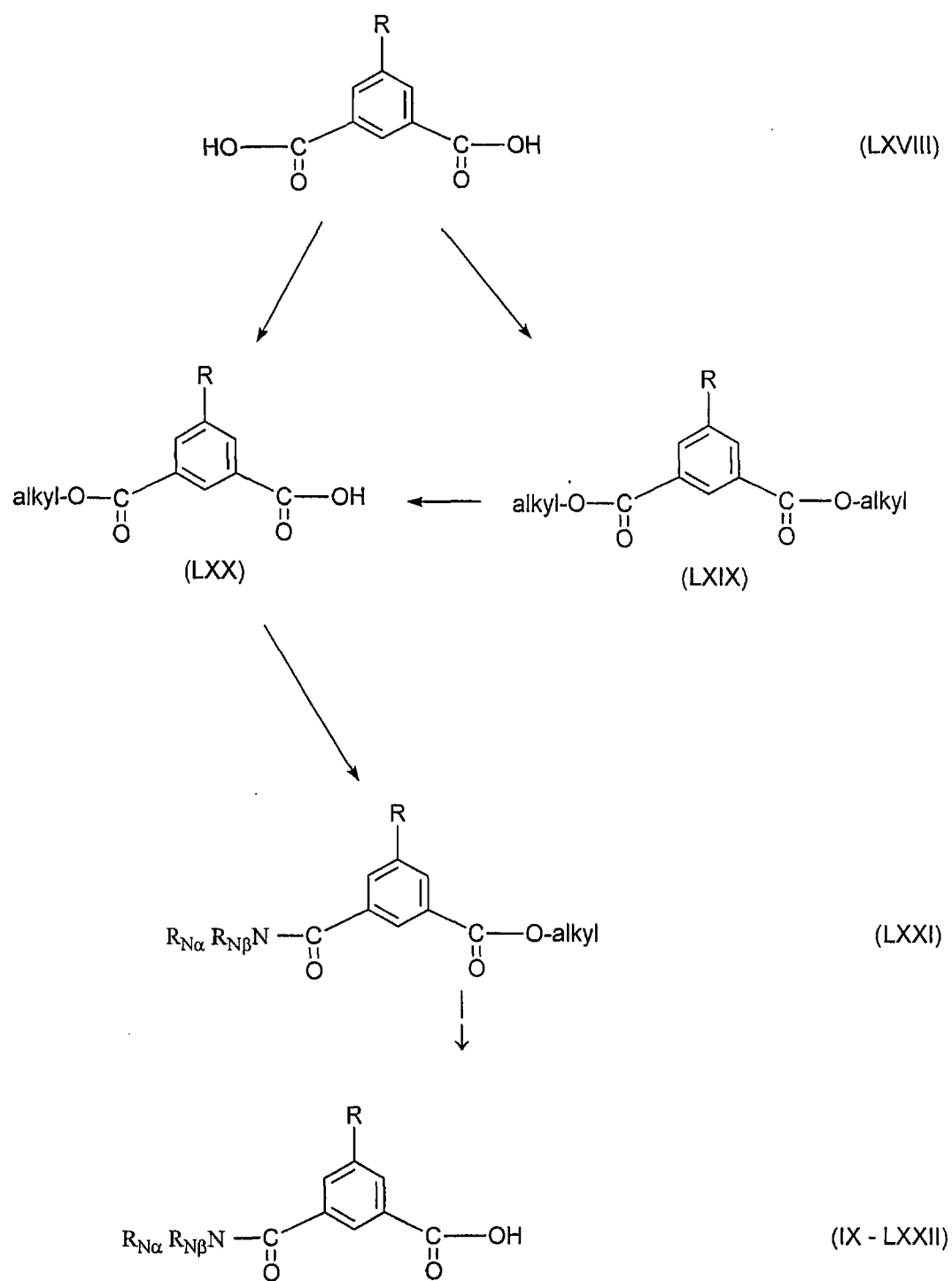
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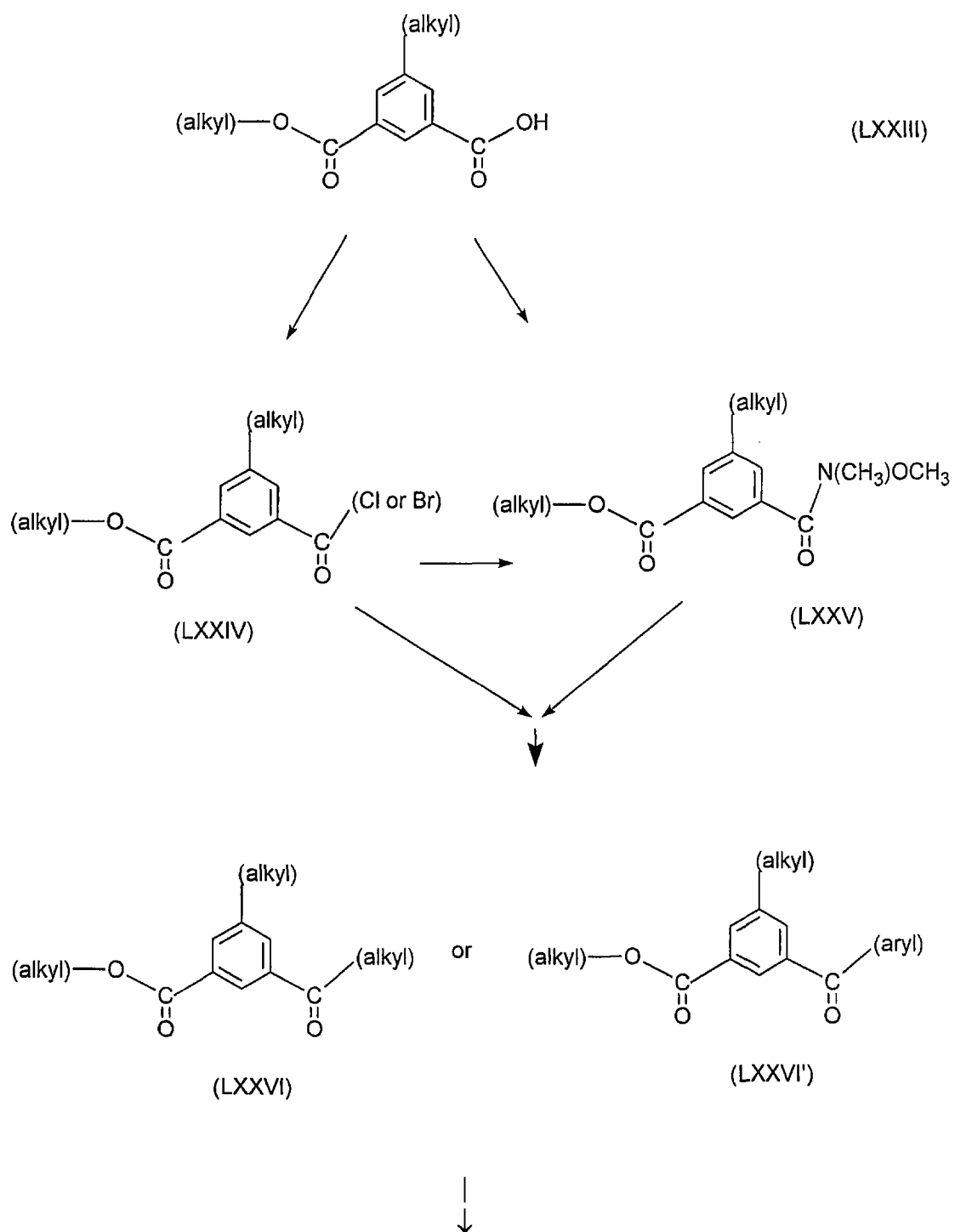
CHART P

330  
CHART Q

5

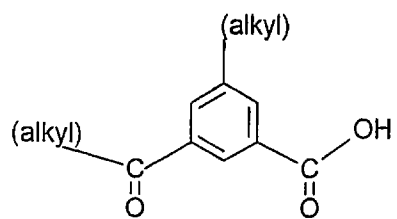
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331

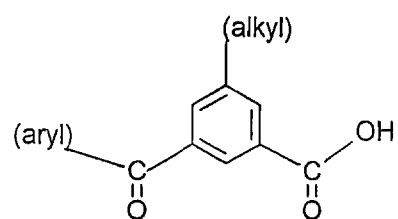
CHART R

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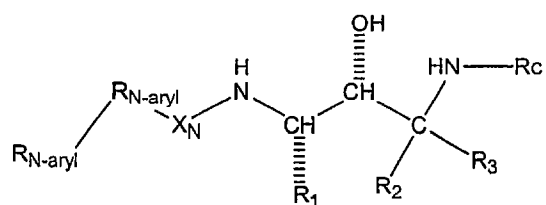
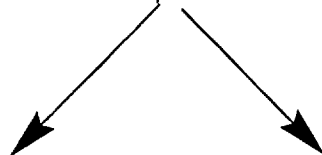
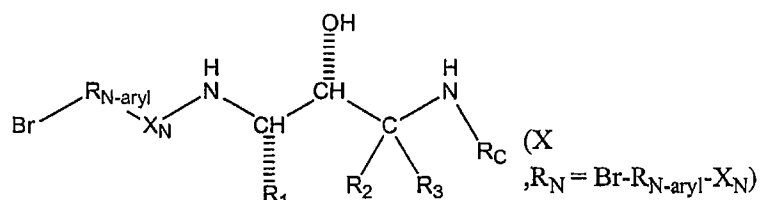
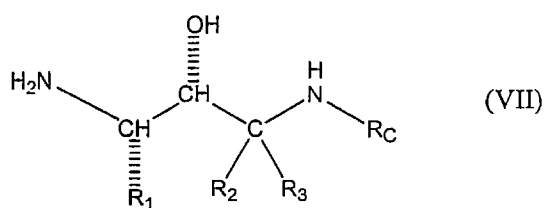


(IX - LXXVII)

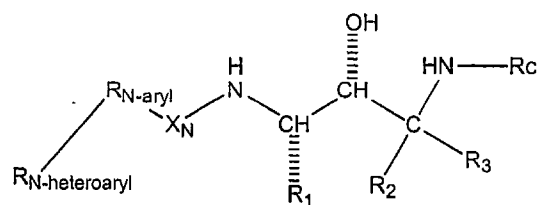


(IX - LXXVII')

333

CHART S

(X,  
 $R_N = R_{N\text{-aryl}}-R_{N\text{-aryl}}-X_N$ )



(X,  
 $R_N = R_{N\text{-heteroaryl}}-R_{N\text{-aryl}}-X_N$ )

334

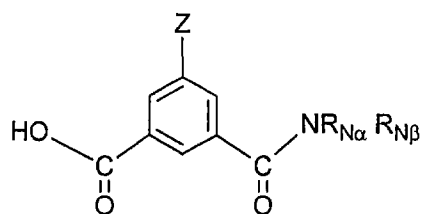
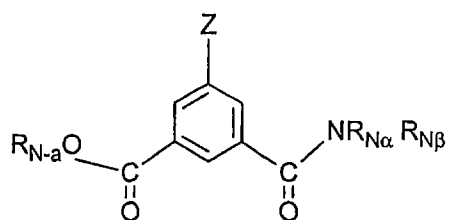
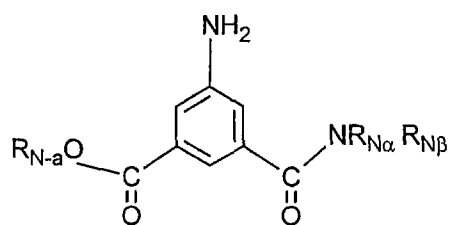
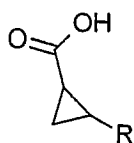
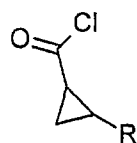
CHART T

CHART U

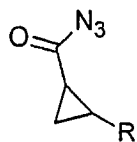
(LXXX)



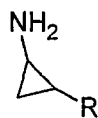
(LXXXI)



(LXXXII)



(LXXXIII)



(LXXXIV)

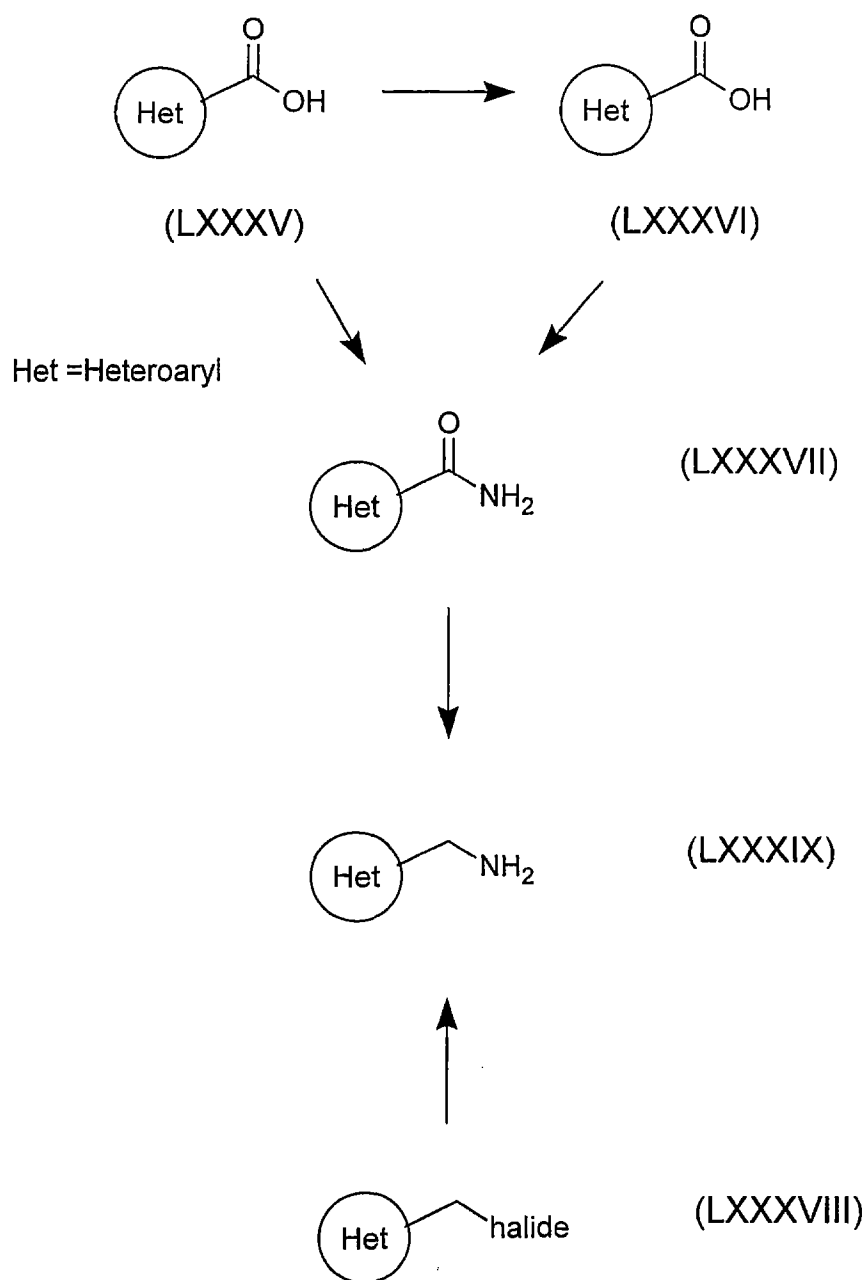
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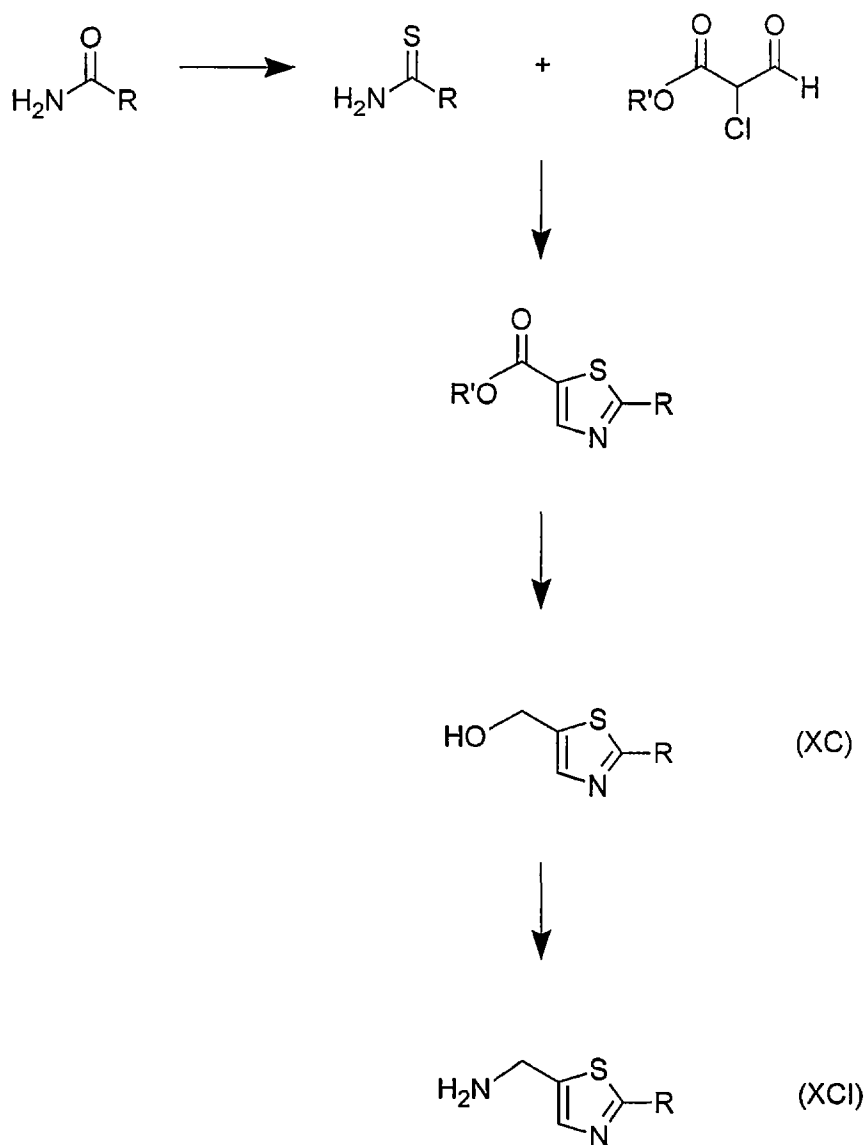
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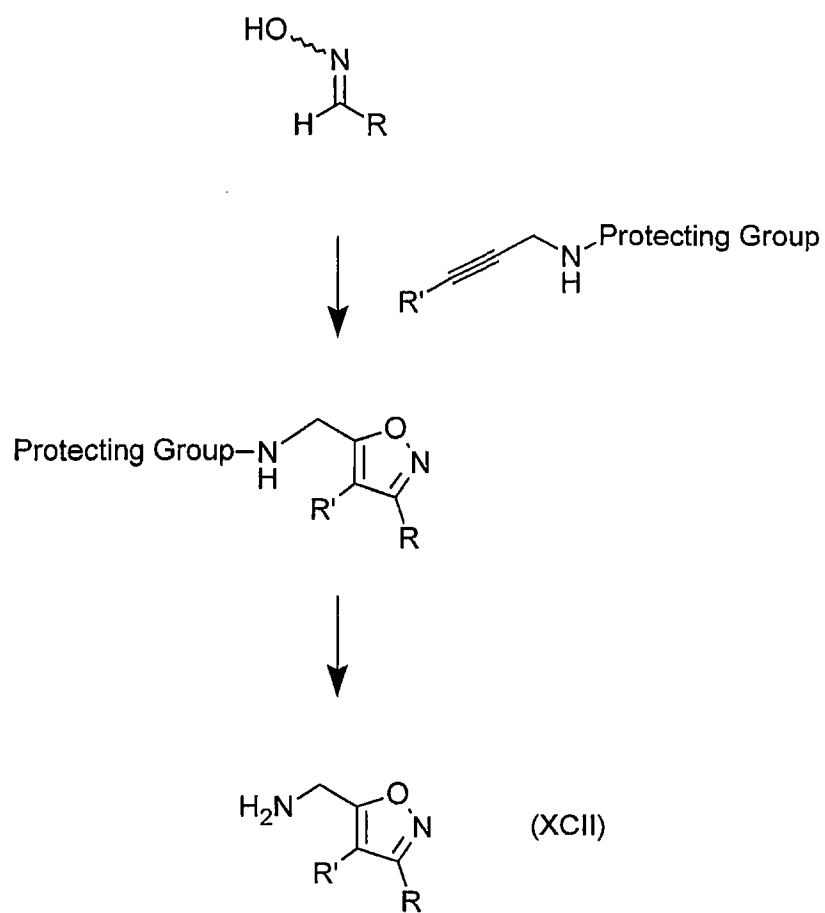
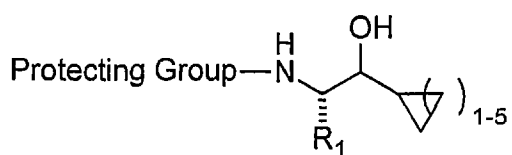
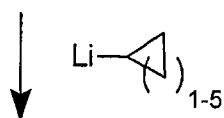
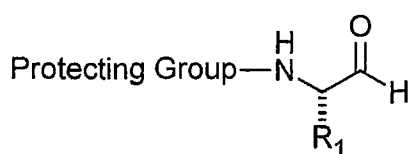
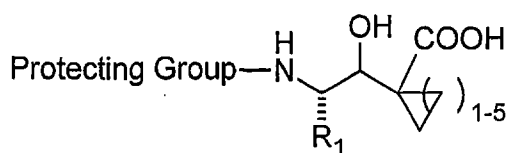
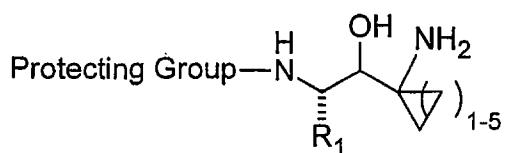
CHART X

CHART Y

(XCIII)



(XCIV)



(XCV)

BIOLOGICAL EXAMPLES

## Example A

## 5 Enzyme Inhibition Assay

The compounds of the invention are analyzed for inhibitory activity by use of the MBP-C125 assay. This assay determines the relative inhibition of beta-secretase cleavage of a model APP substrate, MBP-C125SW, by the compounds  
10 assayed as compared with an untreated control. A detailed description of the assay parameters can be found, for example, in U.S. Patent No. 5,942,400. Briefly, the substrate is a fusion peptide formed of maltose binding protein (MBP) and the carboxy terminal 125 amino acids of APP-SW, the Swedish mutation. The beta-secretase enzyme is derived from human brain tissue as described in Sinha et.al,  
15 1999, *Nature* 40:537-540) or recombinantly produced as the full-length enzyme (amino acids 1-501), and can be prepared, for example, from 293 cells expressing the recombinant cDNA, as described in WO00/47618.

Inhibition of the enzyme is analyzed, for example, by immunoassay of the enzyme's cleavage products. One exemplary ELISA uses an anti-MBP capture  
20 antibody that is deposited on precoated and blocked 96-well high binding plates, followed by incubation with diluted enzyme reaction supernatant, incubation with a specific reporter antibody, for example, biotinylated anti-SW192 reporter antibody, and further incubation with streptavidin/alkaline phosphatase. In the assay, cleavage of the intact MBP-C125SW fusion protein results in the generation of a  
25 truncated amino-terminal fragment, exposing a new SW-192 antibody-positive epitope at the carboxy terminus. Detection is effected by a fluorescent substrate signal on cleavage by the phosphatase. ELISA only detects cleavage following Leu 596 at the substrate's APP-SW 751 mutation site.

30 **Specific Assay Procedure:**

Compounds are diluted in a 1:1 dilution series to a six-point concentration curve (two wells per concentration) in one 96-plate row per compound tested. Each of the test compounds is prepared in DMSO to make up a 10 millimolar stock solution. The stock solution is serially diluted in DMSO to obtain a final compound

concentration of 200 micromolar at the high point of a 6-point dilution curve. Ten (10) microliters of each dilution is added to each of two wells on row C of a corresponding V-bottom plate to which 190 microliters of 52 millimolar NaOAc, 7.9% DMSO, pH 4.5 are pre-added. The NaOAc diluted compound plate is spun  
5 down to pellet precipitant and 20 microliters/well is transferred to a corresponding flat-bottom plate to which 30 microliters of ice-cold enzyme-substrate mixture (2.5 microliters MBP-C125SW substrate, 0.03 microliters enzyme and 24.5 microliters ice cold 0.09% TX100 per 30 microliters) is added. The final reaction mixture of 200 micromolar compound at the highest curve point is in 5% DMSO, 20 millimolar  
10 NaAc, 0.06% TX100, at pH 4.5.

Warming the plates to 37 degrees C starts the enzyme reaction. After 90 minutes at 37 degrees C, 200 microliters/well cold specimen diluent is added to stop the reaction and 20 microliters/well is transferred to a corresponding anti-MBP antibody coated ELISA plate for capture, containing 80 microliters/well specimen  
15 diluent. This reaction is incubated overnight at 4 degrees C and the ELISA is developed the next day after a 2 hours incubation with anti-192SW antibody, followed by Streptavidin-AP conjugate and fluorescent substrate. The signal is read on a fluorescent plate reader.

Relative compound inhibition potency is determined by calculating the  
20 concentration of compound that showed a fifty percent reduction in detected signal ( $IC_{50}$ ) compared to the enzyme reaction signal in the control wells with no added compound. In this assay, the compounds of the invention exhibited an  $IC_{50}$  of less than 50 micromolar.

## 25 **Example B**

### **Cell Free Inhibition Assay Utilizing a Synthetic APP Substrate**

A synthetic APP substrate that can be cleaved by beta-secretase and having N-terminal biotin and made fluorescent by the covalent attachment of oregon green  
30 at the Cys residue is used to assay beta-secretase activity in the presence or absence of the inhibitory compounds of the invention. Useful substrates include the following:

Biotin-SEVNL-DAEFR[oregon green]KK

[SEQ ID NO: 1]

Biotin-SEVKM-DAEFR[oregon green]KK [SEQ ID NO: 2]

Biotin-GLNIKTEEISEISY-EVEFRC[oregon green]KK [SEQ ID NO: 3]

Biotin-ADRGLTTRPGSGLTNIKTEEISEVNL-DAEF[oregon green]KK [SEQ ID NO:4]

- 5 Biotin-FVNQHLCoxGSHLVEALY-LVCoxGERGFFYTPKA[oregon green]KK  
[SEQ ID NO: 5]

The enzyme (0.1 nanomolar) and test compounds (0.001 - 100 micromolar) are incubated in pre-blocked, low affinity, black plates (384 well) at 37 degrees C for 30 minutes. The reaction is initiated by addition of 150 millimolar substrate to a  
10 final volume of 30 microliter per well. The final assay conditions are: 0.001 - 100 micromolar compound inhibitor; 0.1 molar sodium acetate (pH 4.5); 150 nanomolar substrate; 0.1 nanomolar soluble beta-secretase; 0.001% Tween 20, and 2% DMSO. The assay mixture is incubated for 3 hours at 37 degrees C, and the reaction is terminated by the addition of a saturating concentration of immunopure streptavidin.  
15 After incubation with streptavidin at room temperature for 15 minutes, fluorescence polarization is measured, for example, using a LJI Acquest (Ex485 nm/ Em530 nm). The activity of the beta-secretase enzyme is detected by changes in the fluorescence polarization that occur when the substrate is cleaved by the enzyme. Incubation in the presence or absence of compound inhibitor demonstrates specific  
20 inhibition of beta-secretase enzymatic cleavage of its synthetic APP substrate. In this assay, compounds of the invention exhibited an IC50 of less than 50 micromolar.

### Example C

#### Beta-secretase inhibition: P26-P4'SW assay

25

Synthetic substrates containing the beta-secretase cleavage site of APP are used to assay beta-secretase activity, using the methods described, for example, in published PCT application WO00/47618. The P26-P4'SW substrate is a peptide of the sequence: (biotin)CGGADRGLTTRPGSGLTNIKTEEISEVNLDAEF [SEQ ID  
30 NO: 6]

The P26-P1 standard has the sequence:

(biotin)CGGADRGLTTRPGSGLTNIKTEEISEVNL [SEQ ID NO: 7]

Briefly, the biotin-coupled synthetic substrates are incubated at a concentration of from about 0 to about 200 micromolar in this assay. When testing

inhibitory compounds, a substrate concentration of about 1.0 micromolar is preferred. Test compounds diluted in DMSO are added to the reaction mixture, with a final DMSO concentration of 5%. Controls also contain a final DMSO concentration of 5%. The concentration of beta secretase enzyme in the reaction is varied, to give product concentrations with the linear range of the ELISA assay, about 125 to 2000 picomolar, after dilution.

The reaction mixture also includes 20 millimolar sodium acetate, pH 4.5, 0.06% Triton X100, and is incubated at 37 degrees C for about 1 to 3 hours. Samples are then diluted in assay buffer (for example, 145.4 nanomolar sodium chloride, 9.51 millimolar sodium phosphate, 7.7 millimolar sodium azide, 0.05% Triton X405, 6g/liter bovine serum albumin, pH 7.4) to quench the reaction, then diluted further for immunoassay of the cleavage products.

Cleavage products can be assayed by ELISA. Diluted samples and standards are incubated in assay plates coated with capture antibody, for example, SW192, for about 24 hours at 4 degrees C. After washing in TTBS buffer (150 millimolar sodium chloride, 25 millimolar Tris, 0.05% Tween 20, pH 7.5), the samples are incubated with strepavidin-AP according to the manufacturer's instructions. After a one hour incubation at room temperature, the samples are washed in TTBS and incubated with fluorescent substrate solution A (31.2 g/liter 2-amino-2-methyl-1-propanol, 30 mg/liter, pH 9.5). Reaction with streptavidin-alkaline phosphate permits detection by fluorescence. Compounds that are effective inhibitors of beta-secretase activity demonstrate reduced cleavage of the substrate as compared to a control.

## 25 **Example D**

### **Assays using Synthetic Oligopeptide-Substrates**

Synthetic oligopeptides are prepared that incorporate the known cleavage site of beta-secretase, and optionally detectable tags, such as fluorescent or chromogenic moieties. Examples of such peptides, as well as their production and detection methods are described in U.S. Patent No: 5,942,400, herein incorporated by reference. Cleavage products can be detected using high performance liquid chromatography, or fluorescent or chromogenic detection

methods appropriate to the peptide to be detected, according to methods well known in the art.

By way of example, one such peptide has the sequence SEVNL-DAEF [SEQ ID NO: 8], and the cleavage site is between residues 5 and 6. Another preferred  
5 substrate has the sequence ADRGLTTRPGSGLTNIKTEEISEVNL-DAEF [SEQ ID NO: 9], and the cleavage site is between residues 26 and 27.

These synthetic APP substrates are incubated in the presence of beta-secretase under conditions sufficient to result in beta-secretase mediated cleavage of the substrate. Comparison of the cleavage results in the presence of the compound  
10 inhibitor to control results provides a measure of the compound's inhibitory activity.

### **Example E**

#### **Inhibition of beta-secretase activity - cellular assay**

15 An exemplary assay for the analysis of inhibition of beta-secretase activity utilizes the human embryonic kidney cell line HEKp293 (ATCC Accession No. CRL-1573) transfected with APP751 containing the naturally occurring double mutation Lys651Met52 to Asn651Leu652 (numbered for APP751), commonly called the Swedish mutation and shown to overproduce A beta (Citron et.al., 1992,  
20 *Nature* 360:672-674), as described in USPN 5,604,102.

The cells are incubated in the presence/absence of the inhibitory compound (diluted in DMSO) at the desired concentration, generally up to 10 micrograms/ml. At the end of the treatment period, conditioned media is analyzed for beta-secretase activity, for example, by analysis of cleavage fragments. A beta can be analyzed by  
25 immunoassay, using specific detection antibodies. The enzymatic activity is measured in the presence and absence of the compound inhibitors to demonstrate specific inhibition of beta-secretase mediated cleavage of APP substrate.

### **Example F**

#### **Inhibition of Beta-Secretase in Animal Models of AD**

Various animal models can be used to screen for inhibition of beta-secretase activity. Examples of animal models useful in the invention include, but are not limited to, mouse, guinea pig, dog, and the like. The animals used can be wild type,

transgenic, or knockout models. In addition, mammalian models can express mutations in APP, such as APP695-SW and the like described herein. Examples of transgenic non-human mammalian models are described in U.S. Patent Nos. 5,604,102, 5,912,410 and 5,811,633.

5 PDAPP mice, prepared as described in Games et.al., 1995, *Nature* 373:523-527 are useful to analyze *in vivo* suppression of A beta release in the presence of putative inhibitory compounds. As described in USPN 6,191,166, 4 month old PDAPP mice are administered compound formulated in vehicle, such as corn oil. The mice are dosed with compound (1-30 mg/ml; preferably 1-10 mg/ml). After  
10 time, e.g., 3-10 hours, the animals are sacrificed, and brains removed for analysis.

Transgenic animals are administered an amount of the compound inhibitor formulated in a carrier suitable for the chosen mode of administration. Control animals are untreated, treated with vehicle, or treated with an inactive compound. Administration can be acute, i.e., single dose or multiple doses in one day, or can be  
15 chronic, i.e., dosing is repeated daily for a period of days. Beginning at time 0, brain tissue or cerebral fluid is obtained from selected animals and analyzed for the presence of APP cleavage peptides, including A beta, for example, by immunoassay using specific antibodies for A beta detection. At the end of the test period, animals are sacrificed and brain tissue or cerebral fluid is analyzed for the presence of A beta  
20 and/or beta-amyloid plaques. The tissue is also analyzed for necrosis.

Animals administered the compound inhibitors of the invention are expected to demonstrate reduced A beta in brain tissues or cerebral fluids and reduced beta amyloid plaques in brain tissue, as compared with non-treated controls.

## 25 **Example G**

### **Inhibition of A beta production in human patients**

Patients suffering from Alzheimer's Disease (AD) demonstrate an increased amount of A beta in the brain. AD patients are administered an amount of the  
30 compound inhibitor formulated in a carrier suitable for the chosen mode of administration. Administration is repeated daily for the duration of the test period. Beginning on day 0, cognitive and memory tests are performed, for example, once per month.

Patients administered the compound inhibitors are expected to demonstrate slowing or stabilization of disease progression as analyzed by changes in one or more of the following disease parameters: A beta present in CSF or plasma; brain or hippocampal volume; A beta deposits in the brain; amyloid plaque in the brain; and scores for cognitive and memory function, as compared with control, non-treated patients.

### **Example H**

#### **Prevention of A beta production in patients at risk for AD**

10

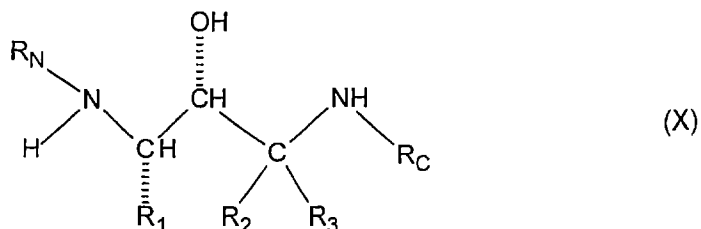
Patients predisposed or at risk for developing AD are identified either by recognition of a familial inheritance pattern, for example, presence of the Swedish Mutation, and/or by monitoring diagnostic parameters. Patients identified as predisposed or at risk for developing AD are administered an amount of the compound inhibitor formulated in a carrier suitable for the chosen mode of administration. Administration is repeated daily for the duration of the test period. Beginning on day 0, cognitive and memory tests are performed, for example, once per month.

Patients administered the compound inhibitors are expected to demonstrate slowing or stabilization of disease progression as analyzed by changes in one or more of the following disease parameters: A beta present in CSF or plasma; brain or hippocampal volume; amyloid plaque in the brain; and scores for cognitive and memory function, as compared with control, non-treated patients.

While this invention has been described with respect to various specific examples and embodiments, it is to be understood that the invention is not limited thereby and should only be construed by interpretation of the scope of the appended claims.

WE CLAIM:

1. A substituted amine of formula (X)



5

where  $\text{R}_1$  is:

- (I)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl,  $\text{C}_1\text{-C}_7$  alkyl (optionally substituted with  $\text{C}_1\text{-C}_3$  alkyl and  $\text{C}_1\text{-C}_3$  alkoxy), -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy,  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are -H or  $\text{C}_1\text{-C}_6$  alkyl, and  $\text{-OC=O NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,
- (II)  $\text{-CH}_2\text{-S(O)}_{0-2}\text{-(C}_1\text{-C}_6\text{ alkyl)}$ ,
- (III)  $\text{-CH}_2\text{-CH}_2\text{-S(O)}_{0-2}\text{-(C}_1\text{-C}_6\text{ alkyl)}$ ,
- (IV)  $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are -H or  $\text{C}_1\text{-C}_6$  alkyl,
- (V)  $\text{C}_2\text{-C}_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are -H or  $\text{C}_1\text{-C}_6$  alkyl,
- (VI)  $\text{-(CH}_2\text{)}_{n1}\text{-(R}_{1\text{-aryl}}\text{)}$  where  $n_1$  is zero or one and where  $\text{R}_{1\text{-aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl and indanyl, indenyl, dihydronaphthalyl, or tetralinyl optionally substituted with one, two, three, or four of the following substituents on the aryl ring:

- (A)  $\text{C}_1\text{-C}_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_3$  alkoxy,
- 30

(B) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

5 (C) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(D) -F, Cl, -Br or -I,

10 (F) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three of: -F,

(G) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

(H) -OH,

(I) -C≡N,

15 (J) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(K) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(L) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

20 (M) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

or

(N) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heteroaryl</sub>) where n<sub>1</sub> is as defined above and where R<sub>1-heteroaryl</sub> is selected from the group consisting of:

25 pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
30 indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoindolyl,

5                   isoquinolyl,  
                  quinazolinyI,  
                  quinoxalinyI,  
                  phthalazinyI,  
                  imidazolyl,  
                  isoxazolyl,  
                  pyrazolyl,  
                  oxazolyl,  
                  thiazolyl,  
10                  indolizinyI,  
                  indazolyl,  
                  benzothiazolyl,  
                  benzimidazolyl,  
                  benzofuranyl,  
15                  furanyl,  
                  thienyl,  
                  pyrrolyl,  
                  oxadiazolyl,  
                  thiadiazolyl,  
20                  triazolyl,  
                  tetrazolyl,  
                  oxazolopyridinyI,  
                  imidazopyridinyI,  
                  isothiazolyl,  
25                  naphthyridinyI,  
                  cinnolinyI,  
                  carbazolyl,  
                  beta-carbolinyI,  
                  isochromanyl,  
30                  chromanyl,  
                  tetrahydroisoquinolinyI,  
                  isoindolinyI,  
                  isobenzotetrahydrofuranyl,  
                  isobenzotetrahydrothienyl,

isobenzothienyl,  
benzoxazolyl,  
pyridopyridinyl,  
benzotetrahydrofuranyl,  
5 benzotetrahydrothienyl,  
purinyl,  
benzodioxolyl,  
triazinyl,  
phenoxazinyl,  
10 phenothiazinyl,  
pteridinyl,  
benzothiazolyl,  
imidazopyridinyl,  
imidazothiazolyl,  
15 dihydrobenzisoxazinyl,  
benzisoxazinyl,  
benzoxazinyl,  
dihydrobenzisoctiazinyl,  
benzopyranyl,  
20 benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromonyl,  
chromanonyl, and  
25 pyridinyl-N-oxide  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisoquinolinonyl  
30 dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl

- pyrrolyl N-oxide,  
 pyrimidinyll N-oxide,  
 pyridazinyll N-oxide,  
 pyrazinyll N-oxide,  
 5 quinolinyll N-oxide,  
 indolyll N-oxide,  
 indolinyll N-oxide,  
 isoquinolyll N-oxide,  
 quinazolinyl N-oxide,  
 10 quinoxalinyll N-oxide,  
 phthalazinyll N-oxide,  
 imidazolyl N-oxide,  
 isoxazolyl N-oxide,  
 oxazolyl N-oxide,  
 15 thiazolyl N-oxide,  
 indolizinyll N-oxide,  
 indazolyl N-oxide,  
 benzothiazolyl N-oxide,  
 benzimidazolyl N-oxide,  
 20 pyrrolyl N-oxide,  
 oxadiazolyl N-oxide,  
 thiadiazolyl N-oxide,  
 triazolyl N-oxide,  
 tetrazolyl N-oxide,  
 25 benzothiopyranyl S-oxide,  
 benzothiopyranyl S,S-dioxide,

where the  $R_{1\text{-heteroaryl}}$  group is bonded to  $-(CH_2)_{n1}-$  by any ring atom of the parent  $R_{1\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four:

(1)  $C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH,

-SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(2) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  
 5 -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(3) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  
 -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are  
 10 -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(4) -F, Cl, -Br or -I,

(6) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three of: -F,

(7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined below,

15 (8) -OH,

(9) -C≡N,

(10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

20 (11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

(13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,

or

(14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), with the proviso that when n<sub>1</sub> is zero  
 25 R<sub>1-heteroaryl</sub> is not bonded to the carbon chain by nitrogen, or

(VIII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1-heterocycle</sub>) where n<sub>1</sub> is as defined above and

R<sub>1-heterocycle</sub> is selected from the group consisting of:

morpholinyl,

thiomorpholinyl,

30 thiomorpholinyl S-oxide,

thiomorpholinyl S,S-dioxide,

piperazinyl,

homopiperazinyl,

- pyrrolidinyl,  
 pyrrolinyl,  
 tetrahydropyranyl,  
 piperidinyl,  
 5 tetrahydrofuranyl,  
 tetrahydrothienyl,  
 homopiperidinyl,  
 homomorpholinyl,  
 homothiomorpholinyl,  
 10 homothiomorpholinyl S,S-dioxide, and  
 oxazolidinonyl,  
 dihydropyrazolyl  
 dihydropyrrolyl  
 dihydropyrazinyl  
 15 dihydropyridinyl  
 dihydropyrimidinyl  
 dihydrofuryl  
 dihydropyranyl  
 tetrahydrothienyl S-oxide  
 20 tetrahydrothienyl S,S-dioxide  
 homothiomorpholinyl S-oxide

where the  $R_{1\text{-heterocycle}}$  group is bonded by any atom of the parent  $R_{1\text{-heterocycle}}$  group substituted by hydrogen such that the new bond to the  $R_{1\text{-heterocycle}}$  group replaces the hydrogen atom and its bond, where heterocycle is  
 25 optionally substituted with one, two, three, or four:

- (1)  $C_1\text{-}C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1\text{-}C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1\text{-}C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,  
 30 (2)  $C_2\text{-}C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1\text{-}C_3$  alkoxy, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are -H or  $C_1\text{-}C_6$  alkyl,

- (3) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,
- 5 (4) -F, Cl, -Br or -I,
- (5) C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (6) -C<sub>1</sub>-C<sub>6</sub> alkoxy optionally substituted with one, two, or three of -F,
- (7) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined
- 10 below,
- (8) -OH,
- (9) -C≡N,
- (10) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH,
- 15 -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,
- (11) -CO-(C<sub>1</sub>-C<sub>4</sub> alkyl),
- (12) -SO<sub>2</sub>-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,
- (13) -CO-NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined
- 20 above,
- (14) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub> alkyl), or
- (15) =O, with the proviso that when n<sub>1</sub> is zero
- R<sub>1-heterocycle</sub> is not bonded to the carbon chain by nitrogen;
- where R<sub>2</sub> is:
- 25 (I)-H,
- (II) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above,
- 30 (III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub> where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above;
- (IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of

-F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl,

(V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, optionally substituted  
 5 with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, or

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>- C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl;  
 10 where R<sub>3</sub> is:

(I)-H,

(II) C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined  
 15 above,

(III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is R<sub>1-aryl</sub> or R<sub>1-heteroaryl</sub> where R<sub>1-aryl</sub> and R<sub>1-heteroaryl</sub> are as defined above;

(IV) C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

20 (V) C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple bonds, or

(VI) -(CH<sub>2</sub>)<sub>0-4</sub>- C<sub>3</sub>-C<sub>7</sub> cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>3</sub> alkoxy, and -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are -H or C<sub>1</sub>-C<sub>6</sub> alkyl, and where R<sub>2</sub> and R<sub>3</sub> are taken together with the carbon to which they are attached to  
 25 form a carbocycle of three, four, five, six or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-,

-S-, -SO<sub>2</sub>-, and -NR<sub>N-2</sub>-, where R<sub>N-2</sub> is as defined below;

where R<sub>N</sub> is:

30 (I) R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is selected from the group consisting of:

(A) -CO-,

(B) -SO<sub>2</sub>-,

(C)  $-(CR'R'')_{1-6}$  where  $R'$  and  $R''$  are the same or different and are -H or  $C_1-C_4$  alkyl,

(D)  $-\text{CO}-(CR'R'')_{1-6}-X_{N-1}$  where  $X_{N-1}$  is selected from the group consisting of -O-, -S- and -NR'- and where  $R'$  and  $R''$  are as defined above,

5 and

(E) a single bond;

where  $R_{N-1}$  is selected from the group consisting of:

(A)  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl, 1-naphthyl, 2-naphthyl, tetralinyl, indanyl, dihydronaphthyl or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl, optionally substituted with one, two or three of the following substituents which can be the same or different and are:

(1)  $C_1-C_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_3$  alkoxy, and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(2) -OH,

(3)  $-\text{NO}_2$ ,

(4) -F, -Cl, -Br, or -I,

(5)  $-\text{CO}-\text{OH}$ ,

20

(6)  $-\text{C}\equiv\text{N}$ ,

(7)  $-(\text{CH}_2)_{0-4}-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are selected from the group consisting of:

(a) -H,

(b)  $-\text{C}_1-\text{C}_6$  alkyl optionally substituted with one

25 substituent selected from the group consisting of:

(i) -OH, and

(ii)  $-\text{NH}_2$ ,

(c)  $-\text{C}_1-\text{C}_6$  alkyl optionally substituted with one

to three -F, -Cl, -Br, or -I,

30

(d)  $-\text{C}_3-\text{C}_7$  cycloalkyl,

(e)  $-(\text{C}_1-\text{C}_2 \text{ alkyl})-(\text{C}_3-\text{C}_7 \text{ cycloalkyl})$ ,

(f)  $-(\text{C}_1-\text{C}_6 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_3 \text{ alkyl})$ ,

- bonds,  
 bonds,  
 5 and one triple bond,  
 above,  
 10 three double bonds),  
 three triple bonds),  
 15 above,  
 defined above,  
 20 defined above,  
 (15)  $-(CH_2)_{0-4}-CO-R_{N-4}$  where  $R_{N-4}$  is selected from the group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide,  
 25 homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is optionally substituted with one, two, three, or four of:  $C_1-C_6$  alkyl,  
 (16)  $-(CH_2)_{0-4}-CO-O-R_{N-5}$  where  $R_{N-5}$  is selected from the group consisting of:  
 (a)  $C_1-C_6$  alkyl,  
 30 (b)  $-(CH_2)_{0-2}-(R_{1-aryl})$  where  $R_{1-aryl}$  is as defined above,  
 (c)  $C_2-C_6$  alkenyl containing one or two double bonds,
- (g)  $-C_2-C_6$  alkenyl with one or two double bonds,  
 (h)  $-C_2-C_6$  alkynyl with one or two triple bonds,  
 (i)  $-C_1-C_6$  alkyl chain with one double bond and one triple bond,  
 (j)  $-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above, and  
 (k)  $-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,  
 (8)  $-(CH_2)_{0-4}-CO-(C_1-C_{12}$  alkyl),  
 (9)  $-(CH_2)_{0-4}-CO-(C_2-C_{12}$  alkenyl with one, two or three double bonds),  
 (10)  $-(CH_2)_{0-4}-CO-(C_2-C_{12}$  alkynyl with one, two or three triple bonds),  
 (11)  $-(CH_2)_{0-4}-CO-(C_3-C_7$  cycloalkyl),  
 (12)  $-(CH_2)_{0-4}-CO-R_{1-aryl}$  where  $R_{1-aryl}$  is as defined above,  
 (13)  $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$  where  $R_{1-heteroaryl}$  is as defined above,  
 (14)  $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$  where  $R_{1-heterocycle}$  is as defined above,

- (d) C<sub>2</sub>-C<sub>6</sub> alkynyl containing one or two triple bonds,
- (e) C<sub>3</sub>-C<sub>7</sub> cycloalkyl, and
- (f) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1</sub>-heteroaryl) where R<sub>1</sub>-heteroaryl is as defined above,
- (17) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined above,
- (18) -(CH<sub>2</sub>)<sub>0-4</sub>-SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (19) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>12</sub> alkyl),
- (20) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (21) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> can be the same or different and is as defined above,
- (22) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub> can be the same or different and is as defined above,
- (23) -(CH<sub>2</sub>)<sub>0-4</sub>-N-CS-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub> can be the same or different and is as defined above,
- (24) -(CH<sub>2</sub>)<sub>0-4</sub>-N(-H or R<sub>N-5</sub>)-CO-R<sub>N-2</sub> where R<sub>N-5</sub> and R<sub>N-2</sub> can be the same or different and are as defined above,
- (25) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or different and are as defined above,
- (26) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (27) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (28) -(CH<sub>2</sub>)<sub>0-4</sub>-O-P(O)-(OR<sub>N-aryl-1</sub>)<sub>2</sub> where R<sub>N-aryl-1</sub> is -H or C<sub>1</sub>-C<sub>4</sub> alkyl,
- (29) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-N(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined above,
- (30) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CS-N(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined above,
- (31) -(CH<sub>2</sub>)<sub>0-4</sub>-O-(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined above,
- (32) -(CH<sub>2</sub>)<sub>0-4</sub>-O-(R<sub>N-5</sub>)<sub>2</sub>-COOH where R<sub>N-5</sub> is as defined above,
- (33) -(CH<sub>2</sub>)<sub>0-4</sub>-S-(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined above,

(34)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl optionally substituted with one, two, three, four, or five -F}),$

(35)  $\text{C}_3-\text{C}_7 \text{ cycloalkyl},$

(36)  $\text{C}_2-\text{C}_6 \text{ alkenyl with one or two double bonds optionally substituted with } \text{C}_1-\text{C}_3 \text{ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C}\equiv\text{N, -CF}_3, \text{C}_1-\text{C}_3 \text{ alkoxy, or -NR}_{1-a}\text{R}_{1-b} \text{ where } \text{R}_{1-a} \text{ and } \text{R}_{1-b} \text{ are as defined above,}$

(37)  $\text{C}_2-\text{C}_6 \text{ alkynyl with one or two triple bonds optionally substituted with } \text{C}_1-\text{C}_3 \text{ alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C}\equiv\text{N, -CF}_3, \text{C}_1-\text{C}_3 \text{ alkoxy, or -NR}_{1-a}\text{R}_{1-b} \text{ where } \text{R}_{1-a} \text{ and } \text{R}_{1-b} \text{ are as defined above,}$

(38)  $-(\text{CH}_2)_{0-4}-\text{N}(-\text{H or R}_{N-5})-\text{SO}_2-\text{R}_{N-2} \text{ where } \text{R}_{N-5} \text{ and } \text{R}_{N-2} \text{ can be the same or different and are as described above, or}$

(39)  $-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7 \text{ cycloalkyl},$

(B)  $-\text{R}_{N-\text{heteroaryl}}$  where  $\text{R}_{N-\text{heteroaryl}}$  is selected from the group consisting of:

pyridinyl,  
pyrimidinyl,  
quinolinyl,  
benzothienyl,  
indolyl,  
indolinyl,  
pyridazinyl,  
pyrazinyl,  
isoindolyl,  
isoquinolyl,  
quinazolinyl,  
quinoxalinyl,  
phthalazinyl,  
imidazolyl,  
isoxazolyl,  
pyrazolyl,  
oxazolyl,  
thiazolyl,  
indolizinyl,

indazolyl,  
benzothiazolyl,  
benzimidazolyl,  
benzofuranyl,  
5 furanyl,  
thienyl,  
pyrrolyl,  
oxadiazolyl,  
thiadiazolyl,  
10 triazolyl,  
tetrazolyl,  
oxazolopyridinyl,  
imidazopyridinyl,  
isothiazolyl,  
15 naphthyridinyl,  
cinnolinyl,  
carbazolyl,  
beta-carbolinyl,  
isochromanlyl,  
20 chromanlyl,  
tetrahydroisoquinolinyl,  
isoindolinyl,  
isobenzotetrahydrofuranyl,  
isobenzotetrahydrothienyl,  
25 isobenzothieryl,  
benzoxazolyl,  
pyridopyridinyl,  
benzotetrahydrofuranyl,  
benzotetrahydrothienyl,  
30 purinyl,  
benzodioxolyl,  
triazinyl,  
phenoxazinyl,  
phenothiazinyl,

pteridinyl,  
benzothiazolyl,  
imidazopyridinyl,  
imidazothiazolyl,  
5 dihydrobenzisoxazinyl,  
benzisoxazinyl,  
benzoxazinyl,  
dihydrobenzisothiazinyl,  
benzopyranyl,  
10 benzothiopyranyl,  
coumarinyl,  
isocoumarinyl,  
chromonyl,  
chromanonyl, and  
15 pyridinyl-N-oxide,  
tetrahydroquinolinyl  
dihydroquinolinyl  
dihydroquinolinonyl  
dihydroisoquinolinonyl  
20 dihydrocoumarinyl  
dihydroisocoumarinyl  
isoindolinonyl  
benzodioxanyl  
benzoxazolinonyl  
25 pyrrolyl N-oxide,  
pyrimidinyl N-oxide,  
pyridazinyl N-oxide,  
pyrazinyl N-oxide,  
quinolinyl N-oxide,  
30 indolyl N-oxide,  
indolinyl N-oxide,  
isoquinolyl N-oxide,  
quinazolinyl N-oxide,  
quinoxalinyl N-oxide,

- phthalazinyll N-oxide,  
imidazolyl N-oxide,  
isoxazolyl N-oxide,  
oxazolyl N-oxide,  
5 thiazolyl N-oxide,  
indolizinyll N-oxide,  
indazolyl N-oxide,  
benzothiazolyl N-oxide,  
benzimidazolyl N-oxide,  
10 pyrrolyl N-oxide,  
oxadiazolyl N-oxide,  
thiadiazolyl N-oxide,  
triazolyl N-oxide,  
tetrazolyl N-oxide,  
15 benzothiopyranyl S-oxide,  
benzothiopyranyl S,S-dioxide,  
where the  $R_{N\text{-heteroaryl}}$  group is bonded by any atom of  
the parent  $R_{N\text{-heteroaryl}}$  group substituted by hydrogen such that the new bond to the  
 $R_{N\text{-heteroaryl}}$  group replaces the hydrogen atom and its bond, where heteroaryl is  
20 optionally substituted with one, two, three, or four of:
- (1)  $C_1\text{-}C_6$  alkyl, optionally substituted with one, two or  
three substituents selected from the group consisting of  $C_1\text{-}C_3$  alkyl, -F, -Cl, -Br, -I, -  
OH, -SH,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1\text{-}C_3$  alkoxy,  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined  
above,  
25 (2) -OH,  
(3)  $-NO_2$ ,  
(4) -F, -Cl, -Br, or -I  
(5)  $-CO-OH$ ,  
(6)  $-C\equiv N$ ,  
30 (7)  $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are  
the same or different and are selected from the group consisting of:
- (a) -H,

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(b) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH, and

(ii) -NH<sub>2</sub>,

5 (c) -C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one to three -F, -Cl, -Br, or -I,

(d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),

10 (g) -C<sub>2</sub>-C<sub>6</sub> alkenyl with one or two double bonds,

(h) -C<sub>2</sub>-C<sub>6</sub> alkynyl with one or two triple

bonds,

(i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond

15 and one triple bond,

(j) -R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and

(k) -R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as defined

above,

(8) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>1</sub>-C<sub>12</sub> alkyl),

20 (9) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkenyl with one, two or three double bonds),

(10) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>2</sub>-C<sub>12</sub> alkynyl with one, two or

three triple bonds),

(11) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

25 (12) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined

above,

(13) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heteroaryl</sub> where R<sub>1-heteroaryl</sub> is as

defined above,

(14) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>1-heterocycle</sub> where R<sub>1-heterocycle</sub> is as

30 defined above,

(15) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is selected from the

group consisting of morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl,

homomorpholinyl, homothiomorpholinyl, homomorpholinyl S-oxide,

homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl where each group is

optionally substituted with one, two, three, or four of: C<sub>1</sub>-C<sub>6</sub> alkyl,

(16) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is selected from

the group consisting of:

(a) C<sub>1</sub>-C<sub>6</sub> alkyl,

5 (b) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-aryl</sub>) where R<sub>1-aryl</sub> is as defined  
above,

(c) C<sub>2</sub>-C<sub>6</sub> alkenyl containing one or two double  
bonds,

(d) C<sub>2</sub>-C<sub>6</sub> alkynyl containing one or two triple  
10 bonds,

(e) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(f) -(CH<sub>2</sub>)<sub>0-2</sub>-(R<sub>1-heteroaryl</sub>) where R<sub>1-heteroaryl</sub> is as  
defined above,

(17) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are  
15 as defined above,

(18) -(CH<sub>2</sub>)<sub>0-4</sub>-SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(19) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>12</sub> alkyl),

(20) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),

(21) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub>  
20 can be the same or different and is as defined above,

(22) -(CH<sub>2</sub>)<sub>0-4</sub>-N(H or R<sub>N-5</sub>)-CO-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub>  
can be the same or different and is as defined above,

(23) -(CH<sub>2</sub>)<sub>0-4</sub>-N-CS-N(R<sub>N-5</sub>)<sub>2</sub>, where R<sub>N-5</sub> can be the  
same or different and is as defined above,

(24) -(CH<sub>2</sub>)<sub>0-4</sub>-N(-H or R<sub>N-5</sub>)-CO-R<sub>N-2</sub> where R<sub>N-5</sub> and  
R<sub>N-2</sub> can be the same or different and are as defined above,

(25) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be  
the same or different and are as defined above,

(26) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

30 (27) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(28) -(CH<sub>2</sub>)<sub>0-4</sub>-O-P(O)-(OR<sub>N-aryl-1</sub>)<sub>2</sub> where R<sub>N-aryl-1</sub> is -H  
or C<sub>1</sub>-C<sub>4</sub> alkyl,

(29) -(CH<sub>2</sub>)<sub>0-4</sub>-O-CO-N(R<sub>N-5</sub>)<sub>2</sub> where R<sub>N-5</sub> is as defined  
above,

- (30)  $-(\text{CH}_2)_{0-4}-\text{O}-\text{CS}-\text{N}(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,
- (31)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,
- 5 (32)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{R}_{\text{N}-5})_2-\text{COOH}$  where  $\text{R}_{\text{N}-5}$  is as defined above,
- (33)  $-(\text{CH}_2)_{0-4}-\text{S}-(\text{R}_{\text{N}-5})_2$  where  $\text{R}_{\text{N}-5}$  is as defined above,
- (34)  $-(\text{CH}_2)_{0-4}-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl optionally substituted}$   
 10  $\text{with one, two, three, four, or five of: } -\text{F}),$
- (35)  $\text{C}_3-\text{C}_7 \text{ cycloalkyl},$
- (36)  $\text{C}_2-\text{C}_6 \text{ alkenyl with one or two double bonds}$   
 $\text{optionally substituted with } \text{C}_1-\text{C}_3 \text{ alkyl, } -\text{F, } -\text{Cl, } -\text{Br, } -\text{I, } -\text{OH, } -\text{SH, } -\text{C}\equiv\text{N, } -\text{CF}_3, \text{ C}_1-$   
 $\text{C}_3 \text{ alkoxy, or } -\text{NR}_{1-\text{a}}\text{R}_{1-\text{b}} \text{ where } \text{R}_{1-\text{a}} \text{ and } \text{R}_{1-\text{b}} \text{ are as defined above,}$
- 15 (37)  $\text{C}_2-\text{C}_6 \text{ alkynyl with one or two triple bonds}$   
 $\text{optionally substituted with } \text{C}_1-\text{C}_3 \text{ alkyl, } -\text{F, } -\text{Cl, } -\text{Br, } -\text{I, } -\text{OH, } -\text{SH, } -\text{C}\equiv\text{N, } -\text{CF}_3, \text{ C}_1-$   
 $\text{C}_3 \text{ alkoxy, or } -\text{NR}_{1-\text{a}}\text{R}_{1-\text{b}} \text{ where } \text{R}_{1-\text{a}} \text{ and } \text{R}_{1-\text{b}} \text{ are as defined above, or}$
- (38)  $-(\text{CH}_2)_{0-4}-\text{N}(-\text{H or } \text{R}_{\text{N}-5})-\text{SO}_2-\text{R}_{\text{N}-2}$  where  $\text{R}_{\text{N}-5}$  and  $\text{R}_{\text{N}-2}$  can be the same or different and are as described above, or
- 20 (39)  $-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7 \text{ cycloalkyl},$
- (C)  $\text{R}_{\text{N-aryl}}-\text{W}-\text{R}_{\text{N-aryl}},$  where  $\text{R}_{\text{N-aryl}}$  is defined as above,
- (D)  $\text{R}_{\text{N-aryl}}-\text{W}-\text{R}_{\text{N-heteroaryl}},$  where  $\text{R}_{\text{N-aryl}}$  and  $\text{R}_{\text{N-heteroaryl}}$  are as defined above,
- (E)  $\text{R}_{\text{N-aryl}}-\text{W}-\text{R}_{\text{N-1-heterocycle}},$  where  $\text{R}_{\text{N-heterocycle}}$  is defined as
- 25  $\text{R}_{1-\text{heterocycle}},$  is defined above,
- (F)  $\text{R}_{\text{N-heteroaryl}}-\text{W}-\text{R}_{\text{N-aryl}},$  where  $\text{R}_{\text{N-aryl}}$  and  $\text{R}_{\text{N-heteroaryl}}$  are as defined above,
- (G)  $\text{R}_{\text{N-heteroaryl}}-\text{W}-\text{R}_{\text{N-heteroaryl}},$  where  $\text{R}_{\text{N-heteroaryl}}$  is as defined above,
- 30 (H)  $\text{R}_{\text{N-heteroaryl}}-\text{W}-\text{R}_{\text{N-1-heterocycle}},$  where  $\text{R}_{\text{N-1-heterocycle}}$  is as defined as  $\text{R}_{1-\text{heterocycle}}$  is as defined above, and where  $\text{R}_{\text{N-heteroaryl}}$  is as defined above,
- (I)  $\text{R}_{\text{N-heterocycle}}-\text{W}-\text{R}_{\text{N-aryl}},$  where  $\text{R}_{\text{N-heterocycle}}$  is as defined as  $\text{R}_{1-\text{heterocycle}}$  is defined and where  $\text{R}_{\text{N-aryl}}$  are as defined above,

(J)  $R_{N\text{-heterocycle}}\text{-W-}R_{N\text{-heteroaryl}}$ , where  $R_{N\text{-heterocycle}}$  is as defined as  $R_{1\text{-heterocycle}}$  as defined above and  $R_{N\text{-heteroaryl}}$  are as defined above, and

(K)  $R_{N\text{-heterocycle}}\text{-W-}R_{N\text{-1-heterocycle}}$ , where  $R_{N\text{-heterocycle}}$  and  $R_{N\text{-heteroaryl}}$  are as defined above,

5 where W is

(1)  $\text{-(CH}_2\text{)}_{0-4}\text{-}$ ,

(2)  $\text{-O-}$ ,

(3)  $\text{-S(O)}_{0-2}\text{-}$ ,

(4)  $\text{-N(R}_{N-5}\text{)-}$  where  $R_{N-5}$  is as defined above, or

10 (5)  $\text{-CO-}_1$

(II)  $\text{-CO-(C}_1\text{-C}_{10}\text{ alkyl)}$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A)  $\text{-OH}$ ,

(B)  $\text{-C}_1\text{-C}_6\text{ alkoxy}$ ,

15 (C)  $\text{-C}_1\text{-C}_6\text{ thioalkoxy}$ ,

(D)  $\text{-CO-O-}R_{N-8}$  where  $R_{N-8}$  is  $\text{-H}$ ,  $\text{C}_1\text{-C}_6\text{ alkyl}$  or  $\text{-phenyl}$ ,

(E)  $\text{-CO-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(F)  $\text{-CO-}R_{N-4}$  where  $R_{N-4}$  is as defined above,

20 (G)  $\text{-SO}_2\text{-(C}_1\text{-C}_8\text{ alkyl)}$ ,

(H)  $\text{-SO}_2\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(I)  $\text{-NH-CO-(C}_1\text{-C}_6\text{ alkyl)}$ ,

(J)  $\text{-NH-CO-O-}R_{N-8}$  where  $R_{N-8}$  is as defined above,

25 (K)  $\text{-NR}_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  are the same or different and are as defined above,

(L)  $\text{-}R_{N-4}$  where  $R_{N-4}$  is as defined above,

(M)  $\text{-O-CO-(C}_1\text{-C}_6\text{ alkyl)}$ ,

(N)  $\text{-O-CO-NR}_{N-8}R_{N-8}$  where  $R_{N-8}$  are the same or different

30 and are as defined above,

(O)  $\text{-O-(C}_1\text{-C}_5\text{ alkyl)-COOH}$ ,

(P)  $\text{-O-(C}_1\text{-C}_6\text{ alkyl)}$  optionally substituted with one, two, or three of:  $\text{-F}$ ,  $\text{-Cl}$ ,  $\text{-Br}$ , or  $\text{-I}$ ),

(Q)  $-\text{NH}-\text{SO}_2-(\text{C}_1-\text{C}_6 \text{ alkyl})$ , and

(R)  $-\text{F}$ , or  $-\text{Cl}$

(III)  $-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A)  $-\text{OH}$ ,

(B)  $-\text{C}_1-\text{C}_6 \text{ alkoxy}$ ,

(C)  $-\text{C}_1-\text{C}_6 \text{ thioalkoxy}$ ,

(D)  $-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is  $-\text{H}$ ,  $\text{C}_1-\text{C}_6 \text{ alkyl}$  or  $-\phi$ ,

(E)  $-\text{CO}-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(F)  $-\text{CO}-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,

(G)  $-\text{SO}_2-(\text{C}_1-\text{C}_8 \text{ alkyl})$ ,

(H)  $-\text{SO}_2-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(I)  $-\text{NH}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(J)  $-\text{NH}-\text{CO}-\text{O}-\text{R}_{\text{N-8}}$  where  $\text{R}_{\text{N-8}}$  is as defined above,

(K)  $-\text{NR}_{\text{N-2}}\text{R}_{\text{N-3}}$  where  $\text{R}_{\text{N-2}}$  and  $\text{R}_{\text{N-3}}$  are the same or different and are as defined above,

(L)  $-\text{R}_{\text{N-4}}$  where  $\text{R}_{\text{N-4}}$  is as defined above,

(M)  $-\text{O}-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(N)  $-\text{O}-\text{CO}-\text{NR}_{\text{N-8}}\text{R}_{\text{N-8}}$  where the  $\text{R}_{\text{N-8}}$ s are the same or different and are as defined above,

(O)  $-\text{O}-(\text{C}_1-\text{C}_5 \text{ alkyl})-\text{COOH}$ ,

(P)  $-\text{O}-(\text{C}_1-\text{C}_6 \text{ alkyl})$  optionally substituted with one, two, or three of:  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ , or  $-\text{I}$ ,

(Q)  $-\text{NH}-\text{SO}_2-(\text{C}_1-\text{C}_6 \text{ alkyl})$ ,

(R)  $-\text{F}$ ,  $-\text{Cl}$ ,

(IV)  $-\text{CO}-(\text{C}_1-\text{C}_6 \text{ alkyl})-\text{S}-(\text{C}_1-\text{C}_6 \text{ alkyl})$  where alkyl is optionally substituted with one, two, or three substituents selected from the group consisting of:

(A)  $-\text{OH}$ ,

- (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,  
 (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,  
 (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,  
 (E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or  
 5 different and are as defined above,  
 (F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,  
 (G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),  
 (H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or  
 different and are as defined above,  
 10 (I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
 (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,  
 (K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different  
 and are as defined above,  
 (L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,  
 15 (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
 (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where R<sub>N-8</sub> are the same or different  
 and are as defined above,  
 (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,  
 (P) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two, or  
 20 three of: -F, -Cl, -Br, -I),  
 (Q) -NH-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
 (R) -F, or -Cl,  
 (V) -CO-CH(-(CH<sub>2</sub>)<sub>0-2</sub>-O-R<sub>N-10</sub>)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>N-aryl</sub>/R<sub>N-heteroaryl</sub>) where  
 R<sub>N-aryl</sub> and R<sub>N-heteroaryl</sub> are as defined above, where R<sub>N-10</sub> is selected from the group  
 25 consisting of:  
 (A) -H,  
 (B) C<sub>1</sub>-C<sub>6</sub> alkyl,  
 (C) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,  
 (D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,  
 30 (E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,  
 (F) R<sub>1-aryl</sub> where R<sub>1-aryl</sub> is as defined above, and  
 (G) R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above, or

(VI) -CO-(C<sub>3</sub>-C<sub>8</sub> cycloalkyl) where alkyl is optionally substituted with one or two substituents selected from the group consisting of:

- (A) -(CH<sub>2</sub>)<sub>0-4</sub>-OH,  
 (B) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> alkoxy,  
 5 (C) -(CH<sub>2</sub>)<sub>0-4</sub>-C<sub>1</sub>-C<sub>6</sub> thioalkoxy,  
 (D) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -phenyl,  
 (E) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,  
 10 (F) -(CH<sub>2</sub>)<sub>0-4</sub>-CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,  
 (G) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),  
 (H) -(CH<sub>2</sub>)<sub>0-4</sub>-SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,  
 (I) -(CH<sub>2</sub>)<sub>0-4</sub>-NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
 15 (J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,  
 (K) -(CH<sub>2</sub>)<sub>0-4</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,  
 (L) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,  
 (M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),  
 20 (N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where R<sub>N-8</sub> are the same or different and are as defined above,  
 (O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,  
 (P) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted with one, two, or three of: -F, -Cl, -Br, or -I),  
 25 (Q) -NH-SO<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub> alkyl), and  
 (R) -F, or -Cl,

where R<sub>C</sub> is:

- (I)-C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with one, two or three substituents selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, -F, -Cl, -Br, -I, -OH,  
 30 -SH, -C≡N, -CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> alkoxy, -O-phenyl, -NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, -OC=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as defined above, -S(=O)<sub>0-2</sub> R<sub>1-a</sub> where R<sub>1-a</sub> is as defined above, -NR<sub>1-a</sub>C=O NR<sub>1-a</sub>R<sub>1-b</sub> where R<sub>1-a</sub> and R<sub>1-b</sub> are as

defined above,  $-\text{C}=\text{O NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above, and  $-\text{S}(=\text{O})_2 \text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(II)  $-(\text{CH}_2)_{0-3}-(\text{C}_3-\text{C}_8)$  cycloalkyl where cycloalkyl can be optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1-\text{C}_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $\text{C}_1-\text{C}_6$  alkoxy,  $-\text{O}$ -phenyl,  $-\text{CO}-\text{OH}$ ,  $-\text{CO}-\text{O}-(\text{C}_1-\text{C}_4 \text{ alkyl})$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(III)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are  $-\text{H}$ ,  $\text{C}_1-\text{C}_4$  alkyl optionally substituted with one or two  $-\text{OH}$ ,  $\text{C}_1-\text{C}_4$  alkoxy optionally substituted with one, two, or three of:  $-\text{F}$ ,

$-(\text{CH}_2)_{0-4}-\text{C}_3-\text{C}_7$  cycloalkyl,  $\text{C}_2-\text{C}_6$  alkenyl containing one or two double bonds,  $\text{C}_2-\text{C}_6$  alkynyl containing one or two triple bonds, phenyl-,

and where  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, or seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{SO}_2-$ , and  $-\text{NR}_{\text{N-2}}-$  and  $\text{R}_{\text{C-aryl}}$  is the same as  $\text{R}_{\text{N-aryl}}$ ;

(IV)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is the same as  $\text{R}_{\text{N-heteroaryl}}$  and  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(V)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VI)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(VIII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(IX)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-aryl}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above, and  $\text{R}_{\text{C-heterocycle}}$  is the same as  $\text{R}_{\text{N-heterocycle}}$ ,

(X)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heteroaryl}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XI)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-aryl}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-aryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-heteroaryl}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

5 (XIII)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XIV)  $-(\text{CR}_{\text{C-x}}\text{R}_{\text{C-y}})_{0-4}-\text{R}_{\text{C-heterocycle}}$  where  $\text{R}_{\text{C-heterocycle}}$ ,  $\text{R}_{\text{C-x}}$  and  $\text{R}_{\text{C-y}}$  are as defined above,

(XV)  $[\text{C}(\text{R}_{\text{C-1}})(\text{R}_{\text{C-2}})]_{1-3}-\text{CO}-\text{N}-(\text{R}_{\text{C-3}})_2$  where  $\text{R}_{\text{C-1}}$  and  $\text{R}_{\text{C-2}}$  are the  
10 same or different and are selected from the group consisting of:

(A) -H,

(B)  $\text{C}_1\text{-C}_6$  alkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are  
15 as defined above,

(C)  $\text{C}_2\text{-C}_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

20 (D)  $\text{C}_2\text{-C}_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl, and  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

(E)  $-(\text{CH}_2)_{1-2}-\text{S}(\text{O})_{0-2}-(\text{C}_1\text{-C}_6 \text{ alkyl})$ ,

25 (F)  $-(\text{CH}_2)_{0-4}-\text{C}_3\text{-C}_7$  cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of  $\text{C}_1\text{-C}_3$  alkyl, -F, -Cl, -Br, -I, -OH, -SH,  $\text{-C}\equiv\text{N}$ ,  $\text{-CF}_3$ ,  $\text{C}_1\text{-C}_6$  alkoxy, -O- phenyl,  $\text{-NR}_{1-a}\text{R}_{1-b}$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as defined above,

30 (G)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})-\text{R}_{\text{C'-aryl}}$  where  $\text{R}_{\text{C'-aryl}}$  is as defined for  $\text{R}_{1\text{-aryl}}$ ,

(H)  $-(\text{C}_1\text{-C}_4 \text{ alkyl})-\text{R}_{\text{C-heteroaryl}}$  where  $\text{R}_{\text{C-heteroaryl}}$  is as defined above,

(I)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(J)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(K)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

5 (M)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C'\text{-aryl}}$  where  $R_{C-4}$  is  $-O-$ ,  $-S-$  or  $-NR_{C-5}-$  where  $R_{C-5}$  is  $C_1-C_6$  alkyl, and where  $R_{C'\text{-aryl}}$  is as defined above,

(N)  $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C\text{-heteroaryl}}$  where  $R_{C-4}$  and  $R_{C\text{-heteroaryl}}$  are as defined above, and

(O)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

10 and where  $R_{C-3}$  is the same or different and is:

(A)  $-H$ ,

(B)  $-C_1-C_6$  alkyl optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are  
15 as defined above,

(C)  $C_2-C_6$  alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

20 (D)  $C_2-C_6$  alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(E)  $-(CH_2)_{0-4}-C_3-C_7$  cycloalkyl, optionally substituted with  
25 one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-SH$ ,  $-C\equiv N$ ,  $-CF_3$ ,  $C_1-C_6$  alkoxy,  $-O-$  phenyl, and  $-NR_{1-a}R_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(F)  $-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

30 (G)  $-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above,

(H)  $-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

(I)  $-(C_1-C_4 \text{ alkyl})-R_{C'\text{-aryl}}$  where  $R_{C'\text{-aryl}}$  is as defined above,

(J)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  is as defined above, or

(K)  $-(C_1-C_4 \text{ alkyl})-R_{C\text{-heterocycle}}$  where  $R_{C\text{-heterocycle}}$  is as defined above,

5 (XVI)  $-\text{CH}(R_{C\text{-aryl}})_2$  where  $R_{C\text{-aryl}}$  are the same or different and are as defined above,

(XVII)  $-\text{CH}(R_{C\text{-heteroaryl}})_2$  where  $R_{C\text{-heteroaryl}}$  are the same or different and are as defined above,

10 (XVIII)  $-\text{CH}(R_{C\text{-aryl}})(R_{C\text{-heteroaryl}})$  where  $R_{C\text{-aryl}}$  and  $R_{C\text{-heteroaryl}}$  are as defined above,

(XIX)  $-\text{cyclopentyl}$ ,  $-\text{cyclohexyl}$ , or  $-\text{cycloheptyl}$  ring fused to  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}$  where  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}$  are as defined above where one carbon of cyclopentyl, cyclohexyl, or  $-\text{cycloheptyl}$  is optionally replaced with  $\text{NH}$ ,  $\text{NR}_{N-5}$ ,  $\text{O}$ , or  $\text{S}(=\text{O})_{0-2}$ , and where cyclopentyl, cyclohexyl, or  $-\text{cycloheptyl}$  can be optionally substituted with one or two  $-C_1-C_3$  alkyl,  $-\text{F}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy,  $=\text{O}$ , or  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

20 (XX)  $C_2-C_{10}$  alkenyl containing one or two double bonds optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy,  $-\text{O}-\text{phenyl}$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $C_2-C_{10}$  alkynyl containing one or two triple bonds optionally substituted with one, two or three substituents selected from the group consisting of  $C_1-C_3$  alkyl,  $-\text{F}$ ,  $-\text{Cl}$ ,  $-\text{Br}$ ,  $-\text{I}$ ,  $-\text{OH}$ ,  $-\text{SH}$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{CF}_3$ ,  $C_1-C_6$  alkoxy,  $-\text{O}-\text{phenyl}$ , and  $-\text{NR}_{1-a}\text{R}_{1-b}$  where  $R_{1-a}$  and  $R_{1-b}$  are as defined above,

(XXI)  $-(\text{CH}_2)_{0-1}-\text{CHR}_{C-6}-(\text{CH}_2)_{0-1}-R_{C\text{-aryl}}$  where  $R_{C\text{-aryl}}$  is as defined above and  $R_{C-6}$  is  $-(\text{CH}_2)_{0-6}-\text{OH}$ ,

(XXII)  $-(\text{CH}_2)_{0-1}-\text{CHR}_{C-6}-(\text{CH}_2)_{0-1}-R_{C\text{-heteroaryl}}$  where  $R_{C\text{-heteroaryl}}$  and  $R_{C-6}$  is as defined above,

30 (XXIII)  $-\text{CH}(-R_{C\text{-aryl}} \text{ or } R_{C\text{-heteroaryl}})-\text{CO}-\text{O}(C_1-C_4 \text{ alkyl})$  where  $R_{C\text{-aryl}}$  and  $R_{C\text{-heteroaryl}}$  are as defined above,

(XXIV)  $-\text{CH}(-\text{CH}_2-\text{OH})-\text{CH}(-\text{OH})-\text{phenyl}-\text{NO}_2$ ,

(XXV)  $(C_1-C_6 \text{ alkyl})-\text{O}-(C_1-C_6 \text{ alkyl})-\text{OH}$ ,

(XXVII)  $-\text{CH}_2-\text{NH}-\text{CH}_2-\text{CH}(-\text{O}-\text{CH}_2-\text{CH}_3)_2$ ,

(XXVIII)  $-\text{H}$ , or

(XXIX)  $-(\text{CH}_2)_{0-6}-\text{C}(=\text{NR}_{1-a})(\text{NR}_{1-a}\text{R}_{1-b})$  where  $\text{R}_{1-a}$  and  $\text{R}_{1-b}$  are as

defined above;

5 or a pharmaceutically acceptable salt thereof.

2. A substituted amine of formula (X) according to claim 1

where  $\text{R}_1$  is:

$-(\text{CH}_2)_{0-1}-(\text{R}_{1-\text{aryl}})$

10  $-(\text{CH}_2)_{n1}-(\text{R}_{1-\text{heteroaryl}})$

where  $\text{R}_N$  is:

$\text{R}_{N-1}-\text{X}_N$  where  $\text{X}_N$  is selected from the group consisting of:

$-\text{CO}-$ , and

$-\text{SO}_2-$ ,

15 where  $\text{R}_{N-1}$  is selected from the group consisting of:

$-\text{R}_{N-\text{aryl}}$ , and

$-\text{R}_{N-\text{heteroaryl}}$ , or

$-\text{CO}-\text{CH}(-(\text{CH}_2)_{0-2}-\text{O}-\text{R}_{N-10})-(\text{CH}_2)_{0-2}-\text{R}_{N-\text{aryl}}/\text{R}_{N-\text{heteroaryl}};$

where  $\text{R}_C$  is:

20  $-\text{C}_1-\text{C}_8$  alkyl,

$-(\text{CH}_2)_{0-3}-(\text{C}_3-\text{C}_7)$  cycloalkyl,

$-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C-\text{aryl}}$ ,

$-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C-\text{heteroaryl}}$ ,

$-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C-\text{heterocycle}}$ , or

25  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to  $\text{R}_{C-\text{aryl}}$  or  $\text{R}_{C-\text{heteroaryl}}$  or  $\text{R}_{C-}$

heterocycle.

3. A substituted amine of formula (X) according to claim 2

where  $\text{R}_1$  is:

30  $-(\text{CH}_2)-(\text{R}_{1-\text{aryl}})$ , or

$-(\text{CH}_2)-(\text{R}_{1-\text{heteroaryl}});$

where  $\text{R}_2$  is  $-\text{H}$ ;

where  $\text{R}_3$  is  $-\text{H}$ ;

where  $\text{R}_N$  is:

$R_{N-1}-X_N$  where  $X_N$  is:

-CO-,

where  $R_{N-1}$  is selected from the group consisting of:

- $R_{N-aryl}$ ,

5

- $R_{N-heteroaryl}$ ,

where  $R_C$  is:

-(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>- $R_{C-aryl}$ ,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>- $R_{C-heteroaryl}$ ,

10

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>- $R_{C-heterocycle}$ , or

-cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or

$R_{C-heterocycle}$ .

4. A substituted amine of formula (X) according to claim 3 where  $R_C$  is:

15

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>- $R_{C-aryl}$ ,

-(CR<sub>C-x</sub>R<sub>C-y</sub>)<sub>0-4</sub>- $R_{C-heteroaryl}$ ,

-cyclopentyl or -cyclohexyl ring fused to a  $R_{C-aryl}$  or  $R_{C-heteroaryl}$  or

$R_{C-heterocycle}$ .

20 5. A substituted amine of formula (X) according to claim 1 where  $R_1$  is

-(CH<sub>2</sub>)-( $R_{1-aryl}$ ) where  $R_{1-aryl}$  is phenyl.

6. A substituted amine of formula (X) according to claim 1 where  $R_1$  is

-(CH<sub>2</sub>)-( $R_{1-aryl}$ ) where  $R_{1-aryl}$  is phenyl substituted with two -F.

25

7. A substituted amine of formula (X) according to claim 6 where the -F substitution is 3,5-difluorobenzyl.

8. A substituted amine of formula (X) according to claim 1 where  $R_2$  is -H.

30

9. A substituted amine of formula (X) according to claim 1 where  $R_3$  is -H.

10. A substituted amine of formula (X) according to claim 1 where  $R_N$  is

$R_{N-1}-X_N$ - where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl substituted with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where the substitution on phenyl is 1,3-.

11. A substituted amine of formula (X) according to claim 10 where  $R_{N-2}$  and  $R_{N-3}$   
5 are the same and are  $\text{C}_3$  alkyl.

12. A substituted amine of formula (X) according to claim 1 where  $R_N$  is  
 $R_{N-1}-X_N$ - where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N\text{-aryl}}$  where  $R_{N\text{-aryl}}$  is phenyl  
substituted with one  $\text{C}_1$  alkyl and with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$  where the substitution on  
10 the phenyl is 1,3,5-.

13. A substituted amine of formula (X) according to claim 12 where  $R_{N-2}$  and  $R_{N-3}$   
are the same and are  $\text{C}_3$  alkyl.

14. A substituted amine of formula (X) according to claim 1 where  $R_N$  is  
 $R_{N-1}-X_N$ - where  $X_N$  is  $-\text{CO}-$ , where  $R_{N-1}$  is  $R_{N\text{-heteroaryl}}$  where  $R_{N\text{-heteroaryl}}$  is  
substituted with one  $-\text{CO}-\text{NR}_{N-2}\text{R}_{N-3}$ .

15. A substituted amine of formula (X) according to claim 14 where  $R_{N-2}$  and  $R_{N-3}$   
20 are the same and are  $-\text{C}_3$  alkyl.

16. A substituted amine of formula (X) according to claim 1 where  $R_C$  is:  
 $-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C\text{-aryl}}$  where  $R_{C\text{-aryl}}$  is phenyl,  
 $-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C\text{-heteroaryl}}$ ,  
25  $-\text{cyclopentyl}$  or  $-\text{cyclohexyl}$  ring fused to a  $R_{C\text{-aryl}}$  or  $R_{C\text{-heteroaryl}}$  or  $R_{C\text{-heterocycle}}$ .

17. A substituted amine of formula (X) according to claim 16 where  $R_C$  is:  
 $-(\text{CR}_{C-x}\text{R}_{C-y})_{0-4}-\text{R}_{C\text{-aryl}}$  where  $R_{C\text{-aryl}}$  is phenyl.  
30

18. A substituted amine of formula (X) according to claim 17 where phenyl is  
substituted in the 3-position or 3,5-positions.

19. A substituted amine of formula (X) according to claim 16 where R<sub>C</sub> is:



20. A substituted amine of formula (X) according to claim 16 where R<sub>C</sub> is:



21. A substituted amine of formula (X) according to claim 16 where R<sub>C</sub> is:

-cyclohexyl ring fused to a phenyl ring.

10 22. A substituted amine of formula (X) according to claim 1 where the pharmaceutically acceptable salt is selected from the group consisting of salts of the following acids acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric, butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycollylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic.

15 20

23. A substituted amine of formula (X) according to claim 1 which is selected from the group consisting of:

25  $\text{N}^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 $\text{N}^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-furylmethyl)amino]-2-hydroxypropyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 $\text{N}^1$ -[(1S,2R)-1-benzyl-3-(ethylamino)-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
30  $\text{N}^1$ -[(1S,2R)-1-benzyl-3-(benzylamino)-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 $\text{N}^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(isopropylamino)propyl]-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

- $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(4-toluidino)propyl]- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-methoxyphenyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- 5  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,
- ethyl {[ (3S)-3-({3-[(dipropylamino)carbonyl]benzoyl} amino)-2-hydroxy-4-phenylbutyl]amino} (phenyl)acetate,
- $N^1$ -((1S)-1-benzyl-2-hydroxy-3-{[(1S)-2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- 10  $N^1$ -{(1S,2R)-1-benzyl-3-[(2-chlorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(4-chlorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- 15  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(2-hydroxyethoxy)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-benzyl-3-(2,3-dihydro-1H-inden-1-ylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-hydroxypropyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,
- 20  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(2,2-diethoxyethyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- 25  $N^1$ -[(1S,2R)-1-benzyl-3-(butylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-benzyl-3-(cyclohexylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-pyridinylmethyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,
- 30  $N^1$ -{(1S,2R)-3-[(2-aminobenzyl)amino]-1-benzyl-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-pyridinylmethyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{{2-(1-pyrrolidiny)ethyl}amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-hydroxy-2-phenylethyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- 5  $N^1$ -{{(1S,2R)-1-benzyl-3-[(3-butoxypropyl)amino]-2-hydroxypropyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-isopropoxypropyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(isopentylamino)propyl]- $N^3,N^3$ -dipropylisophthalamide,
- 10  $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-phenylpropyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-methoxyethyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- 15  $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-phenoxyethyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-propoxyethyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-3-[(3,3-dimethylbutyl)amino]-2-hydroxypropyl}}- $N^3,N^3$ -dipropylisophthalamide,
- 20  $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-phenylbutyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- 25  $N^1$ -{{(1S)-1-benzyl-2-hydroxy-3-[(4-nitrobenzyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-3-[(3-chlorobenzyl)amino]-2-hydroxypropyl}}- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-benzyl-3-{{2-(4-chlorophenyl)ethyl}amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,
- 30  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{{2-(2-pyridinyl)ethyl}amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-pyridinylmethyl)amino]propyl}}- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(2,3-dimethylbenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
5  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(trifluoromethoxy)benzyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(2-chloro-6-phenoxybenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[4-(trifluoromethyl)benzyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
10  $N^1$ -{(1S,2R)-1-benzyl-3-[(2,3-dichlorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(3,5-dichlorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -{(1S,2R)-1-benzyl-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[4-(trifluoromethoxy)benzyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-( {2-[4-(aminosulfonyl)phenyl]ethyl } amino)-1-benzyl-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-methylbenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3,4,5-trimethoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethoxy)benzyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -{(1S,2R)-1-benzyl-3-[(2,4-dimethoxybenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(1,1'-biphenyl]-3-ylmethyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-benzyl-3-[(3,4-dichlorobenzyl)amino]-2-hydroxypropyl}-  
 $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(2-fluorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -  
dipropylisophthalamide,
- 5  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[[3-(trifluoromethyl)benzyl]amino}  
propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-methylbenzyl)amino]propyl)- $N^3,N^3$ -  
dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1R)-1-phenylethyl]amino}propyl)-  
10  $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1S)-1-phenylethyl]amino}propyl)-  
 $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[[3,5-bis(trifluoromethyl)benzyl]amino]-2-  
hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,
- 15  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[[2-(trifluoromethyl)benzyl]amino}  
propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1S)-1-(1-  
naphthyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1R)-1-(1-  
20 naphthyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-hydroxy-3-  
methoxybenzyl)amino]propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(3,4-dihydroxybenzyl)amino]-2-hydroxypropyl)-  
 $N^3,N^3$ -dipropylisophthalamide,
- 25  $N^1$ -{(1S)-1-benzyl-2-hydroxy-3-[(3-methoxypropyl)amino]propyl)- $N^3,N^3$ -  
dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1S)-2-hydroxy-1-  
methylethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1R)-2-hydroxy-1-  
30 methylethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(2-propynylamino)propyl)- $N^3,N^3$ -  
dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[[2-(2-fluorophenyl)ethyl]amino]-2-  
hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-benzyl-3-{[2-(3-fluorophenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-{[2-(4-fluorophenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
5  $N^1$ -((1S,2R)-1-benzyl-3-{[2-(4-bromophenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S)-1-benzyl-2-hydroxy-3-{[2-(3-methoxyphenyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-{[2-(2,4-dichlorophenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
10  $N^1$ -((1S,2R)-1-benzyl-3-{[2-(3-chlorophenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S)-1-benzyl-3-{[2-(2,5-dimethoxyphenyl)ethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-methylphenyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-{[(1R)-1-benzyl-2-hydroxyethyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[3-(4-morpholinyl)propyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(isobutylamino)propyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-morpholinyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-hydroxybutyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[2-(2-thienyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(4-hydroxybutyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-2-hydroxy-1-phenylethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(2,4-dichlorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[(1R)-2-hydroxy-1-phenylethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(4-tert-butylbenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- 5  $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(1-phenylethyl)amino]propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-benzyl-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,
- 10  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,
- 15  $N^3$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propyl)- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,
- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-1,1-dimethyl-2-oxoethyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 20  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-2-oxoethyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1S)-1-[(isobutylamino)carbonyl]propyl}amino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 25  $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1R)-1-[(isobutylamino)carbonyl]propyl}amino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 30  $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-3-(ethylamino)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isobutylamino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{3-(isobutylamino)-2-methyl-3-oxopropyl}amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{4-(dimethylamino)benzyl}amino}-2-hydroxypropyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 5  $N^1$ -[(1S,2R)-3-{{(1S)-1-benzyl-2-(isobutylamino)-2-oxoethyl}amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-((1S)-1-[(isobutylamino)carbonyl]-2-methylpropyl)amino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 10  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-3-{{2-(dimethylamino)ethyl}amino}-2-hydroxypropyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridinylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-3-{{(1S)-1-[(benzyloxy)methyl]-2-(isobutylamino)-2-oxoethyl}amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 15  $N^1$ -{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-((1R)-1-[(isobutylamino)carbonyl]-2-methylpropyl)amino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 20  $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-((1S)-1-[(isobutylamino)carbonyl]butyl)amino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(1S)-1-(hydroxymethyl)-2-(isobutylamino)-2-oxoethyl}amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 25  $N^1$ -{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenylethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 30  $N^1$ -[(1S,2R)-3-{{(1S)-2-(benzylamino)-1-methyl-2-oxoethyl}amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{{(1S)-1-phenylpropyl}amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-3-[[ (1S)-2-(ethylamino)-1-methyl-2-oxoethyl]amino]-2-hydroxypropyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[ (1S)-2-(isobutylamino)-2-oxo-1-phenylethyl]amino]propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 5  $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(cyclohexylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-  
 10 methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxypropyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-2-phenylethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 15  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-3-[[ (3R,5S)-3,5-dimethoxycyclohexyl]amino]-2-hydroxypropyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 dimethyl (1R,3S)-5-[[ (2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino]-1,3-  
 20 cyclohexanedicarboxylate,  
 (1R,3S)-5-[[ (2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino]-1,3-cyclohexanedicarboxylic acid,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[ (1R)-1-phenylpropyl]amino]propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 25  $N^1$ -[(1S,2R)-3-[(3-chlorobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(2-propylpentyl)sulfonyl]benzamide,  
 30  $N^1$ -[(1S,2R)-3-[[ (1,1'-biphenyl)-3-ylmethyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methylbenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenylpropyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
5  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1,3-thiazol-5-ylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-thienylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
10  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-pyrazinylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -{(1S,2R)-3-[(1,3-benzodioxol-5-ylmethyl)amino]-1-benzyl-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[3-(trifluoromethyl)benzyl]amino]propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[3-(trifluoromethoxy)benzyl]amino]propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-fluorobenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[5-methyl-2-furyl)methyl]amino]propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1,2,3,4-tetrahydro-1-naphthalenylamino)propyl]- $N^3,N^3$ -dipropylisophthalamide,  
5  $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methoxy- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-chloro- $N^3,N^3$ -dipropylisophthalamide,  
10  $N^3$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-fluoro- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^2$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^5,N^5$ -dipropyl-2,5-thiophenedicarboxamide,  
 $N^4$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^2,N^2$ -dipropyl-2,4-pyridinedicarboxamide,  
 $N^4$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-  
20  $N^6,N^6$ -dipropyl-4,6-pyrimidinedicarboxamide,  
 $N$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-(4-morpholinylcarbonyl)benzamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methylbenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^5,N^5$ -dipropylpentanediamide,  
 $N^1$ -[(1S,2R)-3-{[(1R)-1-[(benzyloxy)methyl]-2-(isobutylamino)-2-oxoethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-(hydroxymethyl)-2-(isobutylamino)-2-oxoethyl]amino}propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-benzyl-2-hydroxy-3-(pentylamino)propyl]- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -[(1S)-3-({2-[4-(aminosulfonyl)phenyl]ethyl} amino)-1-benzyl-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^3$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1,3-thiazol-5-ylmethyl)amino]propyl}- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
5      3-benzoyl-N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl} benzamide,  
N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}[1,1'-biphenyl]-3-carboxamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^3$ -  
10 (2-methoxyethyl)- $N^3$ -propylisophthalamide,  
N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-ethoxybenzamide,  
N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-naphthamide,  
15  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1R)-1,2,3,4-tetrahydro-1-naphthalenylamino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1R)-3-[[3,5-bis(trifluoromethyl)benzyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-[[2-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -[(1S,2R)-1-benzyl-3-[(2,3-difluorobenzyl)amino]-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-[[3-fluoro-4-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -[(1S,2R)-1-benzyl-3-[(2,5-difluorobenzyl)amino]-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-[[3-fluoro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -[(1S,2R)-1-benzyl-3-[(3,4-difluorobenzyl)amino]-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-[[4-fluoro-3-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-[[2-chloro-5-(trifluoromethyl)benzyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -((1S,2R)-1-benzyl-3-{[4-chloro-3-(trifluoromethyl)benzyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-benzyl-3-(2,3-dihydro-1H-inden-2-ylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
5  $N^1$ -{(1S)-1-benzyl-2-hydroxy-3-[(3-nitrobenzyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-3-{[3-(difluoromethoxy)benzyl]amino}-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
10  $N^1$ -{(1S,2R)-1-benzyl-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-{[(5-methyl-2-pyrazinyl)methyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(3-bromo-4-fluorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,5-dimethylbenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethoxybenzyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenoxyethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isobutoxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
25  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-methyl-1,3-thiazol-2-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^3$ -methyl- $N^3$ -propylisophthalamide,  
 $N^2$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^5,N^5$ -dipropyl-2,5-furandicarboxamide,  
30  $N^3$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
 $N^3$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,

- $N^1$ -[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1,2-diphenylethyl)amino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 5  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide, isomer A,
- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,
- 10 isomer B,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(dimethylamino)benzamide,
- $N$ -[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-2-methyl-1H-benzimidazole-5-carboxamide,
- 15 3-(aminosulfonyl)- $N$ -{(1S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-chlorobenzamide,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-cyanobenzamide,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-
- 20 chloro-3-nitrobenzamide,
- methyl 3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl} amino)carbonyl]-5-nitrobenzoate,
- tert-butyl 3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl} amino)carbonyl]phenylcarbamate,
- 25  $N$ -[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-9,10-dioxo-9,10-dihydro-2-anthracenylcarboxamide,
- $N$ -[(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl]-1H-1,2,3-benzotriazole-6-carboxamide,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(3-
- 30 methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1H-indole-5-carboxamide,
- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-fluoro-5-(trifluoromethyl)benzamide,

- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(trifluoromethyl)benzamide,
- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(butylamino)benzamide,
- 5 N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(trifluoromethoxy)benzamide,
- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,5-dimethoxybenzamide,
- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,5-dimethylbenzamide,
- 10 N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,5-difluorobenzamide,
- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,5-dichlorobenzamide,
- 15 N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(benzyloxy)benzamide,
- N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1,3-benzodioxole-5-carboxamide,
- 3-(acetylamino)-N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide,
- 20 4-(acetylamino)-N-{{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide,
- N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[{(3,5-dimethyl-4-isoxazolyl)methyl}amino]-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- 25 N<sup>1</sup>-{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-phenylpropyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-{{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-furylmethyl)amino]-2-hydroxypropyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- 30 N<sup>1</sup>-{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(tetrahydro-3-furanylmethyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-{{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-propoxybenzyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-pyridinylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-hydroxy- $N^3,N^3$ -dipropylisophthalamide,  
5      $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-methyl-1-(3-methylphenyl)ethyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-1,2,3,4-tetrahydro-1-naphthalenylamino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,5-dimethylbenzyl)amino]-2-  
10    hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-{[2-chloro-5-(trifluoromethyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-5-methylbenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
15      $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1R)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
5-chloro- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-  
20    phenylethyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-[(1-benzofuran-2-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-{[(1R)-1-(3-bromophenyl)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
25      $N^1$ -{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[butyl(butyryl)amino]-5-methylbenzamide,  
30      $N^1$ -{1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^3$ -{1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^1,N^1$ -dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-butyl-1H-indole-6-carboxamide,  
5      $N^1$ -[(1S,2R)-3-anilino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
5-bromo- $N^1$ -[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-methylpentanamide,  
10      $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-methylpentanamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxybenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
15      $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-cyano- $N^3,N^3$ -dipropylisophthalamide hydrochloride,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-1,3,5-benzenetricarboxamide,  
1-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide trifluoroacetate,  
20     5-(aminosulfonyl)- $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}- $N^3,N^3$ -dipropyl-5-(1-pyrrolidinylsulfonyl)isophthalamide,  
25      $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(methylamino)sulfonyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-[(dimethylamino)sulfonyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methyl-3-(methylsulfonyl)propanamide,  
30      $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(methylsulfonyl)propanamide,  
2-amino- $N$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1,3-thiazole-4-carboxamide,

- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(methylsulfonyl)pentanamide,
- N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>4</sup>-phenylsuccinamide,
- 5 (3R)-N<sup>4</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2,2,3-trimethylbutanediamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide,
- N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-
- 10 N<sup>5</sup>,N<sup>5</sup>-dipropylpentanediamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-oxo-4-(1-piperidinyl)butanamide,
- N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>4</sup>,N<sup>4</sup>-dipropylsuccinamide,
- 15 N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide,
- N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>5</sup>-phenylpentanediamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3,3-
- 20 dimethyl-4-oxo-4-(1-piperidinyl)butanamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(isopentylsulfonyl)butanamide,
- N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2,2-dimethyl-N<sup>4</sup>,N<sup>4</sup>-dipropylsuccinamide,
- 25 N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-[(dipropylamino)sulfonyl]butanamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-[(methylanilino)sulfonyl]butanamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-
- 30 [(methylanilino)sulfonyl]propanamide,
- N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}acetamide, N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(isopentylsulfonyl)propanamide,

- N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidiny)pentanamide,  
N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidiny)pentanamide and
- 5 N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide,  
N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-ethyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-isobutyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- 10 N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-tert-butyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-cyano-N<sup>3</sup>-propylisophthalamide,
- 15 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dipropyl-1,3,5-benzenetricarboxamide,  
N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>,N<sup>3</sup>-dimethyl-N<sup>5</sup>,N<sup>5</sup>-dipropyl-1,3,5-benzenetricarboxamide,  
N<sup>1</sup>-[(1S,2R)-3-amino-1-benzyl-2-hydroxypropyl]-N<sup>3</sup>,N<sup>3</sup>-dipropyl-1,3,5-benzenetricarboxamide,
- 20 N<sup>1</sup>-[(1S,2R)-1-benzyl-2-hydroxy-3-(isopentylamino)propyl]-N<sup>3</sup>,N<sup>3</sup>-dipropyl-1,3,5-benzenetricarboxamide,  
N<sup>1</sup>-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N<sup>3</sup>-propyl-1,3,5-benzenetricarboxamide,
- 25 N-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[butyryl(propyl)amino]-5-methylbenzamide,  
N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-propyl-1H-indole-6-carboxamide,
- N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-propyl-1H-indole-6-carboxamide,
- 30 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
N<sup>1</sup>-[(1S,2R)-3-[(3-aminobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

- N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)octanamide,
- N<sup>3</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({1-methyl-1-[3-(trifluoromethyl)phenyl]ethyl} amino)propyl]-N<sup>5</sup>,N<sup>5</sup>-dipropyl-3,5-pyridinedicarboxamide,
- 5 N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({1-methyl-1-[3-(trifluoromethyl)phenyl]ethyl} amino)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino)propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- 10 N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(1R)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl)-3-methylbenzamide,
- 15 N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1H-isoindol-3-ylamino)propyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]amino)propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>,N<sup>1</sup>-diallyl-5-chloro-N<sup>3</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl)isophthalamide,
- 20 N<sup>1</sup>,N<sup>1</sup>-diallyl-5-chloro-N<sup>3</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl)isophthalamide,
- N<sup>3</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl)-N<sup>5</sup>,N<sup>5</sup>-dipropyl-3,5-pyridinedicarboxamide,
- 25 N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[3-(dimethylamino)benzyl]amino]-2-hydroxypropyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(4,5-dimethyl-2-furyl)methyl]amino)-2-hydroxypropyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- 30 N<sup>1</sup>-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopentyl)amino]propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,
- N<sup>1</sup>-[(1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

- $N^1$ -[(1S,2R)-3-[(cyclopropylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}- $N^5,N^5$ -dipropylpentanediamide,  
5  $N^3$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-furylmethyl)amino]-2-hydroxypropyl}- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^3$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
10  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methyl-2-furyl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2S)-tetrahydro-2-furanylmethyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
5-chloro- $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}- $N^3,N^3$ -di(2-propynyl)isophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropenylbenzyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-propoxyethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-3-(hexylamino)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
25  $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide,  
methyl 4-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)benzoate,  
30  $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methoxyethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-isoxazolylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,

- (1R,2R)-N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N<sup>2</sup>,N<sup>2</sup>-dipropyl-1,2-cyclopropanedicarboxamide,  
 N<sup>3</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2S)-tetrahydro-2-furanylmethyl]amino}propyl)-N<sup>5</sup>,N<sup>5</sup>-dipropyl-3,5-pyridinedicarboxamide,  
 5 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methoxybenzyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 4-(butyrylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}benzamide,  
 10 N<sup>1</sup>-[(1S,2R)-3-[(3-amino-3-oxopropyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>3</sup>-[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N<sup>5</sup>,N<sup>5</sup>-dipropyl-3,5-pyridinedicarboxamide 1-oxide,  
 15 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-ethynyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-oxabicyclo[2.2.1]hept-2-ylmethyl)amino]propyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 20 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-ethyl-1,3-thiazol-5-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 25 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3R)-2-oxoazepanyl]amino}propyl)-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2R)-3-(cyclobutylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2R)-3-(butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-ethynyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 30 N<sup>1</sup>-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,  
 N<sup>1</sup>-[(1S,2R)-1-(3,5-difluorobenzyl)-3-(5-hexynylamino)-2-hydroxypropyl]-5-methyl-N<sup>3</sup>,N<sup>3</sup>-dipropylisophthalamide,

- $N^3$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methyl-2-furyl)methyl]amino}propyl)- $N^5,N^5$ -dipropyl-3,5-pyridinedicarboxamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}- $N^5,N^5$ -dipropylpentanediamide,  
5  $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-3-[[1-(2-furyl)-1-methylethyl]amino]-2-hydroxypropyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isobutyl-5-isoxazolyl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
10  $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-phenylethyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
15  $N^1$ -((1S,2R)-1-benzyl-3-[[2-(2-chlorophenyl)ethyl]amino]-2-hydroxypropyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-[[3-(2-oxo-1-pyrrolidinyl)propyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(cyclohexylmethyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
20  $N^1$ -[(1S,2R)-1-benzyl-3-(cyclopropylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-oxo-3-azepanyl)amino]propyl}- $N^3,N^3$ -dipropylisophthalamide,  
25  $N$ -[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-(butylsulfonyl)benzamide,  
 $N^1$ -[(1S,2R)-1-benzyl-3-(2-[(2-ethylhexyl)oxy]ethyl)amino]-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
30  $N^1$ -((1S,2R)-1-benzyl-2-hydroxy-3-[[1-(4-hydroxyphenyl)ethyl]amino}propyl)- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-benzyl-3-(cycloheptylamino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,

- $N^1$ -{(1S,2R)-1-benzyl-3-[(1,1'-biphenyl]-2-ylmethyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-benzyl-3-[(2-fluorobenzyl)amino]-2-hydroxypropyl}- $N^3,N^3$ -dipropylisophthalamide,  
5       $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(dimethylamino)benzamide,  
 $N$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-naphthamide,  
 $N^1$ -[(1S,2R)-1-benzyl-3-({2-[(5-[(dimethylamino)methyl]-2-furyl)methyl]sulfanyl}ethyl)amino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
10       $N^1$ -[(1S,2R)-1-benzyl-3-({2-[(2-chloro-6-fluorobenzyl)sulfanyl]ethyl)amino)-2-hydroxypropyl]- $N^3,N^3$ -dipropylisophthalamide,  
15       $N^1$ -[(1S,2R)-3-[(1,1'-biphenyl]-4-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(1-naphthylamino)propyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-imidazol-5-ylmethyl)amino]propyl}-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
20       $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenyl-1H-imidazol-5-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1H-imidazol-2-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
25       $N^1$ -[(1S,2R)-3-[(2-butyl-4-chloro-1H-imidazol-5-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -[(1S,2R)-3-[(6-chloroimidazo[2,1-b][1,3]thiazol-5-yl)methyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1H-benzimidazol-2-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
30       $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-1-naphthyl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,  
 $N^1$ -((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(4-oxo-4H-chromen-3-yl)methyl]amino}propyl)-5-methyl- $N^3,N^3$ -dipropylisophthalamide,