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Fisher et al.

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[54] **SUBSTITUTED SULFONAMIDES AS SELECTIVE β_3 AGONISTS FOR THE TREATMENT OF DIABETES AND OBESITY**

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[21] Appl. No.: **445,630**

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Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 404,565, Mar. 21, 1995, abandoned, which is a continuation-in-part of Ser. No. 233,166, Apr. 26, 1994, abandoned.

[51] **Int. Cl.**[6] **C07D 413/12**; C07D 213/30; A61K 31/44; A61K 31/47

[52] **U.S. Cl.** **514/312**; 546/153; 546/194; 546/269; 546/271; 546/275; 546/276; 546/277; 546/286; 546/338; 514/318; 514/337; 514/338; 514/340; 514/342

[58] **Field of Search** 546/153, 194, 546/269, 271, 275, 276, 277, 280, 338; 514/312, 318, 337, 338, 340, 342

[56] **References Cited**

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3,816,516	6/1974	Cox et al.	514/653
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4,396,627	8/1983	Ainsworth et al.	424/309
4,478,849	10/1984	Ainsworth et al.	424/285
4,999,377	3/1991	Ainsworth et al.	424/285
5,017,619	5/1991	Alig et al.	514/653
5,153,210	10/1992	Ainsworth et al.	546/344
5,321,036	6/1994	Sher	514/366

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Attorney, Agent, or Firm—Mollie M. Yang; David L. Rose

[57] **ABSTRACT**

Substituted sulfonamides are selective β_3 adrenergic receptor agonists with very little β_1 and β_2 adrenergic receptor activity and as such the compounds are capable of increasing lipolysis and energy expenditure in cells. The compounds thus have potent activity in the treatment of Type II diabetes and obesity. The compounds can also be used to lower triglyceride levels and cholesterol levels or raise high density lipoprotein levels or to decrease gut motility. In addition, the compounds can be used to reduced neurogenic inflammation or as antidepressant agents. The compounds are prepared by coupling an aminoalkylphenyl-sulfonamide with an appropriately substituted epoxide. Compositions and methods for the use of the compounds in the treatment of diabetes and obesity and for lowering triglyceride levels and cholesterol levels or raising high density lipoprotein levels or for increasing gut motility are also disclosed.

18 Claims, No Drawings

SUBSTITUTED SULFONAMIDES AS SELECTIVE β_3 AGONISTS FOR THE TREATMENT OF DIABETES AND OBESITY

CROSS-REFERENCE

This is a continuation-in-part of co-pending application U.S. patent application Ser. No. 08/404,565 filed Mar. 21, 1995, now abandoned, which is a continuation-in-part of U.S. patent application Ser. No. 08/233,166 filed Apr. 26, 1994, now abandoned these applications are hereby incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

β-Adrenoceptors have been subclassified as β_1 and β_2 since 1967. Increased heart rate is the primary consequence of β_1-receptor stimulation, while bronchodilation and smooth muscle relaxation typically result from β_2 stimulation. Adipocyte lipolysis was initially thought to be solely a β_1-mediated process. However, more recent results indicate that the receptor-mediating lipolysis is atypical in nature. These atypical receptors, later called β_3-adrenoceptors, are found on the cell surface of both white and brown adipocytes where their stimulation promotes both lipolysis (breakdown of fat) and energy expenditure.

Early developments in this area produced compounds with greater agonist activity for the stimulation of lipolysis (β_3 activity) than for stimulation of atrial rate (β_1) and tracheal relaxation (β_2). These early developments disclosed in Ainsworth et al., U.S. Pat. Nos. 4,478,849 and 4,396,627, were derivatives of phenylethanolamines.

Such selectivity for β_3-adrenoceptors could make compounds of this type potentially useful as antiobesity agents. In addition, these compounds have been reported to show antihyperglycemic effects in animal models of non-insulin-dependent diabetes mellitus.

A major drawback in treatment of chronic diseases with β_3 agonists is the potential for stimulation of other β-receptors and subsequent side effects. The most likely of these include muscle tremor (β_2) and increased heart rate (β_1). Although these phenylethanolamine derivatives do possess some β_3 selectivity, side effects of this type have been observed in human volunteers. It is reasonable to expect that these side effects resulted from partial β_1 and/or β_2 agonism.

More recent developments in this area are disclosed in Ainsworth et al., U.S. Pat. No. 5,153,210, Caulkett et al., U.S. Pat. No. 4,999,377, Alig et al., U.S. Pat. No. 5,017,619, Lecount et al., European Patent 427480 and Bloom et al., European Patent 455006.

Even though these more recent developments purport to describe compounds with greater β_3 selectivity over the β_1 and β_2 activities, this selectivity was determined using rodents, in particular, rats as the test animal. Because even the most highly selective compounds, as determined by these assays, still show signs of side effects due to residual β_1 and β_2 agonist activity when the compounds are tested in humans, it has become apparent that the rodent is not a good model for predicting human β_3 selectivity.

Recently, assays have been developed which more accurately predict the effects that can be expected in humans. These assays utilize cloned human β_3 receptors which have been expressed in Chinese hamster ovary cells. See Emorine et al, *Science,* 1989, 245:1118–1121; and Liggett, *Mol. Pharmacol.,* 1992, 42:634–637. The agonist and antagonist effects of the various compounds on the cultivated cells provide an indication of the antiobesity and antidiabetic effects of the compounds in humans.

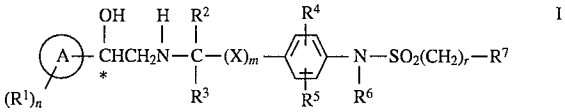
SUMMARY OF THE INVENTION

The instant invention is concerned with substituted sulfonamides which are useful as antiobesity and antidiabetic compounds. Thus, it is an object of this invention to describe such compounds. It is a further object to describe the specific preferred stereoisomers of the substituted sulfonamides. A still further object is to describe processes for the preparation of such compounds. Another object is to describe methods and compositions which use the compounds as the active ingredient thereof.

Further objects will become apparent from reading the following description.

DESCRIPTION OF THE INVENTION

The present invention provides compounds having the formula I:



I

where

n is

m is 0to 5;

0or 1;

r is 0to 3;

A is (1) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, 2) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, 3) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (4) phenyl, or (5) a benzene ring fused to a C_3–C_8 cycloalkyl ring;

R^1 is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR^8R^8, (6) SRS, (7) trifluoromethyl, (8) C_1–C_{10} alkyl, (9) ORS, (10) SO_2R^9, (11) $OCOR^9$, (12) NR^8COR^9, (13) COR^9, (14) $NR^8SO_2R^9$, (15) $NR^8CO_2R^8$, or (16) C_1–C_{10} alkyl substituted by hydroxy, halogen, cyano, NR^8R^8, SR^8, trifluoromethyl, OR^8, C_3–C_8 cycloalkyl, phenyl, NR^8COR^9, COR^9, SO_2R^9, $OCOR^9$, $NR^8SO_2R^9$ or $NR^8CO_2R^8$;

R^2 and R^3 are independently (1) hydrogen, (2) C_1–C_{10} alkyl or (3) C_1–C_{10} alkyl with 1 to 4 substituents selected from hydroxy, C_1–C_{10} alkoxy, and halogen;

X is (1) —CH_2—, (2) —CH_2—CH_2—, (3) —CH=CH— or (4) —CH_2O—;

R^4 and R^5 are independently (1)hydrogen, (2) C_1–C_{10} alkyl, (3) halogen, (4) NHR^8, (5) OR^8, (6) SO_2R^9 or (7) $NHSO_2R^9$;

R6 is (1) hydrogen or (2) C_1–C_{10} alkyl;

R^7 is Z-$(R^{1a})_n$;

R^{1a} is (1) R^1, with the proviso that when A is phenyl, R^{1a} is not C_1–C_{10} alkyl, (2) C_3–C_8 cycloalkyl, 3) phenyl optionally substituted with up to 4 groups independently selected from R^8, NR^8R^8, OR^8, SR^8 and halogen, or (4) 5 or 6-membered heterocycle with from 1 to

4 heteroatoms selected from oxygen, sulfur and nitrogen, optionally substituted with up to four groups independently selected from oxo, R^8, NR^8R^8, OR^8, SR^8, and halogen;

Z is (1) phenyl, (2) naphthyl, (3) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (4) a benzene ring fused to a C_3–C_8 cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a C_3–C_8 cycloalkyl ring;

R^8 is (1) hydrogen, (2) C_1–C_{10} alkyl, (3) C_3–C_8 cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, $NR^{10}R^{10}$, C_1–C_{10} alkyl, C_1–C_{10} alkoxy, C_1–C_{10} alkylthio, and C_1"C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO_2H, CO_2–C_1–C_{10} alkyl, SO_2–C_1–C_{10} alkyl, C_3–C_8 cycloalkyl, C_1–C_{10} alkoxy, and Z optionally substituted by from 1 to 3 of halogen, C_1–C_{10} alkyl or C_1–C_{10} alkoxy, or (5) C_1–C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO_2H, CO_2—C_1—C_{10} alkyl, SO_2—C_1—C_{10} alkyl, C_3–C_8 cycloalkyl, C_1–C_{10} alkoxy, C_1–C_{10} alkyl, and Z optionally substituted by from 1 to 4 of halogen, C_1–C_{10} alkyl or C_1–C_{10} alkoxy;

R^9 is (1) R^8 or (2) NR^8R^8;

R^{10} is (1) C_1–C_{10} alkyl, or (2) two R^{10} groups together with the N to which they are attached formed a 5 or 6-membered ring optionally substituted with C_1–C_{10} alkyl; or

a pharmaceutically acceptable salt thereof.

In one embodiment of the instant invention A is a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen.

In another embodiment of the instant invention A is phenyl or benzene fused to a C_3–C_8 cycloalkyl ring.

Preferred compounds of the instant invention are realized when in the above structural formula I:

R^2 and R^3 are hydrogen or methyl;

X is —CH_2—;

n is 0 to 3;

m is 1;

r is 0 to 2; and

R^4, R^5 and R^6 are hydrogen.

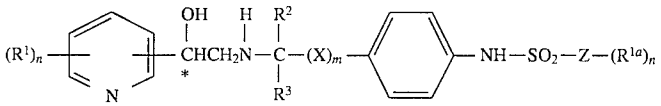
Other preferred compounds of the instant invention are realized when in the above structural formula I:

A is phenyl or a 6-membered heterocyclic ring with 1 or 2 heteroatoms selected from nitrogen and sulfur;

R^1 is hydroxy, halogen, cyano, trifluoromethyl, NR^8R^8, $NR^8SO_2R^9$, NR^8COR^9, $NRSCO_2R^8$, C_1–C_6 alkyl optionally substituted by hydroxy; and

r is 0 or 2.

More preferred compounds are represented by the formula Ia:



Ia

wherein

n is 0to 3;

m is 1

R^1 is (1) halogen or (2) NR^8R^8;

R^2, R^3 are independently hydrogen or methyl;

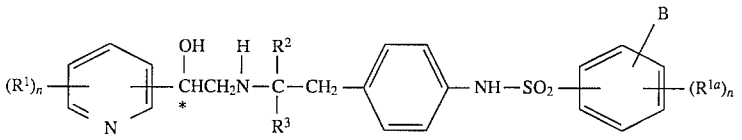
R^{1a} is (1) halogen, (2) C_1–C_{10} alkyl, (3) NR^8R^8, (4) NR^8COR^9, (5) $NR^8CO_2R^8$, (6) COR^9, (7) $OCOR^9$, or (8) a 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, optionally substituted with up to four groups independently selected from oxo, halogen, R^8, NR^8R^8, OR^8, and SR^8;

Z is (1) phenyl, (2) naphthyl, (3) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (4) benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 3 heteroatoms selected from oxygen, sulfur and nitrogen, or (5) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a C_3–C_8 cycloalkyl ting;

X is —CH_2—; and

R^8 and R^9 are as defined in claim **1**.

Even more preferred compounds are those represented by formula Id:



Id

n is 0 or 1;

R^1 is NR^8R^8;

R^2 and R^3 are independently (1) hydrogen, or (2) methyl;

B is (1) hydrogen, (2) benzene fused to the benzene ring to form naphthyl, or (3) a 5 or 6-membered heterocycle with 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen atom fused to the benzene ring;

R^{1a} is (1) halogen, (2) C_1–C_{10} alkyl, (3) NR^8R^8, (4) NR^8COR^9, (5) $NR^8CO_2R^8$, (6) COR^9, or (7) a 5 or

6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, optionally substituted with up to four groups independently selected from oxo, R^8, SR^8, OR^8, and NR^8R^8; when B and the benzene ring form a fused ring system, R^{1a} is attached to either ring;

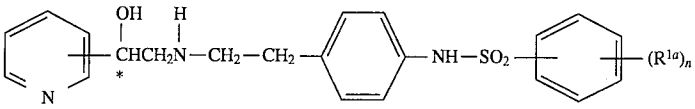
R^8 is (1) hydrogen, (2) C_1–C_{10} alkyl, (3) Z optionally having 1 to 4 substituents selected from nitro, oxo, and $NR^{10}R^{10}$, or (5) C_1–C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, C_1–C_{10} alkyl, C_3–C_8 cycloalkyl, and Z optionally substituted by from 1 to 4 of halogen, C_1–C_{10} alkyl or C_1–C_{10} alkoxy;

R^9 is (1) R^8 or (2) NR^8R^8;

R^{10} is (1) C_1–C_{10} alkyl, or

(2) two R^{10} groups together with the N to which they are attached formed a 5 or 6-membered ring optionally substituted with C_1–C_{10} alkyl; and

Z is (1) phenyl, (2) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, (3) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, or (4) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen fused to a C_3–C_8 cycloalkyl ring. Most preferred compounds are those having the formula Ie



Ie

n is 0or 1;

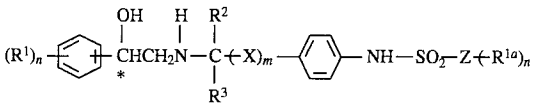
R^{1a} is (1) halogen, (2) NR^8COR^9, or (3) a 5-membered heterocycle substituted with 0 or 1 oxo selected from imidazolidinone, imidazolone, oxadiazole, oxazole, triazole and tetrazolone, optionally substituted with up to three groups independently selected from R^8;

R^8 is (1) hydrogen, (2) C_1–C_{10} alkyl, or (3) C_1–C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, C_1–C_{10} alkyl, C_3–C_8 cycloalkyl, and Z optionally substituted by from 1 to 4 of halogen, C_1–C_{10} alkyl or C_1–C_{10} alkoxy;

R^9 is NR^8R^8;

Z is phenyl.

Other more preferred compounds are represented by formula Ib:



Ib

wherein

n is

0to 3;

m is

R^{1a} is (1) hydroxy, (2) cyano, (3) NR^8R^8 or (4) halogen;

R^{1a} is (1) halogen, (2) NR^8R^8, (3) NR^8COR^9, (4) $NR^8CO_2R^8$, (5) $OCOR^9$, or (6) a 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen, optionally substituted with up to three groups independently selected from oxo, halogen, R^8, NR^8R^8, OR^8 and SR^8;

Z is (1) phenyl, (2) naphthyl or (3) benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur and nitrogen;

X is —CH_2—; and

R^2 and R^3 are independently hydrogen or methyl.

Representative antiobesity and antidiabetic compounds of the present invention include the following:

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]- 4-(hexylaminocarbonylamino)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]- 4-iodobenzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]-benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyllamino] ethyl]phenyl]- 2-naphthalenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]- 3-quinolinesulfonamide N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino]ethyllphenyl]- 5-benzisoxazolesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyllamino] ethyl]phenyl]- 4-[(hexylmethylaminocarbonyl)amino] benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]- 4-[(dimethylaminocarbonyl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] ethyl]phenyl]- 4-(3-hexyl-2-imidazolidon- 1-yl)benzenesulfonamide

N-[4-[3-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] propyl]-phenyl]- 4-(hexylaminocarbonylamino)benzenesulfonamide

N-[4-[3-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] propyl]-phenyl]- 4-iodobenzenesulfonamide

N-[4-[3-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] propyl]-phenyl]benzenesulfonamide

N-[4-[3-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] propyl]-phenyl]- 2-naphthalenesulfonamide

N-[4-[3-[[2-hydroxy-2-(6-aminopyridin-3-yl)ethyl]amino] propyl]-phenyl]- 3-quinolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-(hexylaminocarbonylamino)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-isopropylbenzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 2-naphthalenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 3-quinolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl] phenyl]- 4-[(hexylmethylaminocarbonyl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-hexyl-2-imidazolidinon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-iodobenzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[5-(3-cyclopentylpropyl)-[1,2,4]-oxadiazol-3-yl] benzensulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[(1-oxoheptyl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[(1-oxo- 4-phenylbutyl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-[(propoxycarbonyl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[[(fur- 2-ylmethyl)amino]carbonyl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[[(2-phenylethyl)amino]carbonyl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[[(2-indol-3-ylethyl)amino]carbonyl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-[[(octylamino)carbonyl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 1-[(hexylamino)carbonyl]-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 1-[(octylamino)carbonyl]-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 1-[(N-methyl-N-octylamino)carbonyl]-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-1-(1-oxononyl)-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 1-(4-methylthiazo-1-2-yl)-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 1-(4-octylthiazol-2-yl)-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-1-(4-ethyl-5-methylthiazol-2-yl)-5-indolinesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-octyl-2imidazolidinon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(4,4,4-trifluorobutyl)-2-imidazolidinon-1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(3-phenylpropyl)-2-imidazolidinon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(4,4,5,5,5-pentafluoropentyl)-2-imidazolidinon-1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(2-cyclohexylethyl)-2-imidazolidinon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-[3-(4-chlorophenyl)propyl]-2-imidazolidinon-1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-pentyl-2-imidazolidinon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(3-cyclopentylpropyl)-2-imidazolidinon-1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]- 4-[cyclopentylethyl)-2-imidazolidinon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(3-cyclohexylpropyl)-2-imidazolidinon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(2,2-dimethylhexyl)-2-imidazolidinon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-hexyl-2-imidazolon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(4,4,4-trifluorobutyl)-2-imidazolon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(3-octyl- 2-imidazolon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[3-(3-cyclopentylpropyl)-2-imidazolon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(2-octyl- 3-oxo-[1,2,4]-triazol-4-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(4-hexyl-5-tetrazolon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(4-octyl- 5-tetrazolon-1-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[4-(3-cyclopentylpropyl)-5-tetrazolon- 1-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(2-pentyloxazol-5-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(2-octyloxazol-5-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[2-(2-cyclopentylethyl)oxazol-5-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[(4-ethyl-5-methylthiazol-2-yl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[(4,5,6,7-tetrahydrobenzothiazol-2-yl)amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(2-hexylimidazol-4-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(1-methyl-2-octylimidazol-5-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[1-methyl-2-(2-cyclopentylethyl)imidazol-5-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[1-methyl-2-[2-(4-fluorophenyl)ethyl]imidazol-5-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(5-pentyl-[1,2,4]-oxadiazol-3-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[5-(2-cyclopentylethyl)-[1,2,4]-oxadiazol-3-yl]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(5-heptyl-[1,2,4]-oxadiazol-3-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(5-octyl-[1,2,4]-oxadiazol-3-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(5-hexylthio-[1,2,4]-triazol-3-yl)benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[4-(4-propylpiperidin-1-yl)-1,1-dioxo-[1,2,5]-thiadiazol- 3-yl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[4-(hexylmethylamino)-1,1-dioxo-[1,2,5]-thiadiazol- 3-yl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-[[4-(heptylmethylamino)-1,1-dioxo-[1,2,5]-thiadiazol- 3-yl]amino]benzenesulfonamide

N-[4-[2-[[2-hydroxy-2-(3-pyridinyl)ethyl]amino]ethyl]phenyl]-4-(1-octyl-2,4-imidazolidinedion-3-yl)benzenesulfonamide

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