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(54) Titre : INHIBITEURS 1,3-OXAZEPAN-2-ONE ET 1,3-DIAZEPAN-2-ONE DE LA 11β-HYDROXYSTEROIDE DESHYDROGENASE (TYPE1)

(54) Title: 1,3-OXAZEPAN-2-ONE AND 1,3-DIAZEPAN-2-ONE INHIBITORS OF 11β-HYDROXYSTEROID DEHYDROGENASE 1

(57) Abrégé/Abstract:
This invention relates to novel compounds of the Formula (I)1 (I*), (I**), (Ia), (Ib), (Ic), (Id), (Ie)1 (If), (Ig), pharmaceutically acceptable salts thereof, and pharmaceutical compositions thereof, which are useful for the therapeutic treatment of diseases associated with the modulation or inhibition of 11 β-HSD1 in mammals. The invention further relates to pharmaceutical compositions of the novel compounds and methods for their use in the reduction or control of the production of Cortisol in a cell or the inhibition of the conversion of cortisone to Cortisol in a cell.

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(54) Title: 1,3-OXAZEPAN-2-ONE AND 1,3-DIAZEPAN-2-ONE INHIBITORS OF 11β -HYDROXYSTEROID DEHYDROGENASE 1

(57) Abstract: This invention relates to novel compounds of the Formula (I)1 (I*), (I**), (Ia), (Ib), (Ic), (Id), (Ie)1 (If), (Ig), pharmaceutically acceptable salts thereof, and pharmaceutical compositions thereof, which are useful for the therapeutic treatment of diseases associated with the modulation or inhibition of 11 β-HSD1 in mammals. The invention further relates to pharmaceutical compositions of the novel compounds and methods for their use in the reduction or control of the production of Cortisol in a cell or the inhibition of the conversion of cortisone to Cortisol in a cell.

1,3-OXAZEPAN-2-ONE AND 1,3-DIAZEPAN-2-ONE INHIBITORS OF 11β-HYDROXYSTEROID DEHYDROGENASE 1

RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 61/065,301, filed on February 11, 2008. The entire teachings of the application are incorproated herein by referenced.

FIELD OF THE INVENTION

The present invention relates to inhibitors of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1), pharmaceutical compositions thereof and methods of using the same.

BACKGROUND OF THE INVENTION

Glucocorticoids, such as cortisol (hydrocortisone), are steroid hormones that regulate fat metabolism, function and distribution, and play a role in carbohydrate, protein and fat metabolism. Glucocorticoids are also known to have physiological effects on development, neurobiology, inflammation, blood pressure, metabolism, and programmed cell death. Cortisol and other corticosteroids bind both the glucocorticoid receptor (GR) and the mineralocorticoid receptor (MR), which are members of the nuclear hormone receptor superfamily and have been shown to mediate cortisol function in vivo. These receptors directly modulate transcription via DNA-binding zinc finger domains and transcriptional activation domains.

Until recently, the major determinants of glucocorticoid action were attributed to three primary factors: (1) circulating levels of glucocorticoid (driven primarily by the hypothalamic-pituitary-adrenal (HPA) axis); (2) protein binding of glucocorticoids in circulation; and (3) intracellular receptor density inside target tissues. Recently, a fourth determinant of glucocorticoid function has been identified: tissue-specific pre-receptor metabolism by glucocorticoid-activating and -inactivating enzymes. These 11β-hydroxysteroid dehydrogenase (11β-HSD) pre-receptor control enzymes modulate activation of GR and MR by regulation of glucocorticoid hormones. To date, two distinct isozymes of 11-beta-HSD have been cloned and characterized: 11β-HSD1 (also known as 11-beta-HSD type 1, 11betaHSD1, HSD11B1, HDL, and

HSD11L) and 11β-HSD2. 11β-HSD1 is a bi-directional oxidoreductase that regenerates active cortisol from inactive 11-keto forms, whereas 11β-HSD2 is a unidirectional dehydrogenase that inactivates biologically active cortisol by converting it into cortisone.

The two isoforms are expressed in a distinct tissue-specific fashion, consistent with the differences in their physiological roles. 11β-HSD1 is widely distributed in rat and human tissues; expression of the enzyme and corresponding mRNA have been detected in human liver, adipose tissue, lung, testis, bone and ciliary epithelium. In adipose tissue, increased cortisol concentrations stimulate adipocyte differentiation and may play a role in promoting visceral obesity. In the eye, 11β-HSD1 may regulate intraocular pressure and may contribute to glaucoma; some data suggest that inhibition of 11β-HSD1 may cause a drop in intraocular pressure in patients with intraocular hypertension (Kotelevstev et al. (1997), Proc. Natl. Acad. Sci. USA 94(26):14924-9). Although 11β-HSD1 catalyzes both 11-beta-dehydrogenation and the reverse 11-oxoreduction reaction, 11β-HSD1 acts predominantly as a NADPH-dependent oxoreductase in intact cells and tissues, catalyzing the formation of active cortisol from inert cortisone (Low et al. (1994) J. Mol. Endocrin. 13: 167-174). In contradistinction, 11β-HSD2 expression is found mainly in mineralocorticoid target tissues such as kidney (cortex and medulla), placenta, sigmoid and rectal colon, salivary gland and colonic epithelial cell lines. 11β-HSD2 acts as an NAD-dependent dehydrogenase catalyzing the inactivation of cortisol to cortisone (Albiston et al. (1994) Mol. Cell. Endocrin. 105: R11-R17), and has been shown to protect the MR from glucocorticoid excess (e.g., high levels of receptor-active cortisol) (Blum, et al. (2003) Prog. Nucl. Acid Res. Mol. Biol. 75:173-216).

Mutations in either the 11β-HSD1 or the 11β-HSD2 genes result in human pathology. For example, individuals with mutations in 11β-HSD2 are deficient in this cortisol-inactivation activity and, as a result, present with a syndrome of apparent mineralocorticoid excess (also referred to as `SAME`) characterized by hypertension, hypokalemia, and sodium retention (Edwards et al. (1988) Lancet 2: 986-989; Wilson et al. (1998) Proc. Natl. Acad. Sci. 95: 10200-10205). Similarly, mutations in 11β-HSD1 and in the gene encoding a co-localized NADPH-generating enzyme, hexose 6-phosphate dehydrogenase (H6PD), can result in cortisone reductase deficiency (CRD); these individuals present with ACTH-mediated androgen excess (hirsutism,

menstrual irregularity, hyperandrogenism), a phenotype resembling polycystic ovary syndrome (PCOS) (Draper et al. (2003) Nat. Genet. 34: 434-439).

Notably, disruption of homeostasis in the HPA axis by either deficient or excess secretion or action results in Cushing's syndrome or Addison's disease, respectively (Miller and Chrousos (2001) Endocrinology and Metabolism, eds. Felig and Frohman (McGraw-Hill, New York), 4th Ed.: 387-524). Patients with Cushing's syndrome or receiving glucocorticoid therapy develop reversible visceral fat obesity. The phenotype of Cushing's syndrome patients closely resembles that of Reaven's metabolic syndrome (also known as Syndrome X or insulin resistance syndrome), the symptoms of which include visceral obesity, glucose intolerance, insulin resistance, hypertension, type 2 diabetes and hyperlipidemia (Reaven (1993) Ann. Rev. Med. 44: 121-131). Although the role of glucocorticoids in human obesity is not fully characterized, there is mounting evidence that 11β-HSD1 activity plays an important role in obesity and metabolic syndrome (Bujalska et al. (1997) Lancet 349: 1210-1213); (Livingstone et al. (2000) Endocrinology 131: 560-563; Rask et al. (2001) J. Clin. Endocrinol. Metab. 86: 1418-1421; Lindsay et al. (2003) J. Clin. Endocrinol. Metab. 88: 2738-2744; Wake et al. (2003) J. Clin. Endocrinol. Metab. 88: 3983-3988).

Data from studies in mouse transgenic models supports the hypothesis that adipocyte 11β-HSD1 activity plays a central role in visceral obesity and metabolic syndrome (Alberts et al. (2002) Diabetologia. 45(11): 1526-32). Over-expression in adipose tissue of 11β-HSD1 under the control of the aP2 promoter in transgenic mice produced a phenotype remarkably similar to human metabolic syndrome (Masuzaki et al. (2001) Science 294: 2166-2170; Masuzaki et al. (2003) J. Clinical Invest. 112: 83-90). Moreover, the increased activity of 11β-HSD1 in these mice is very similar to that observed in human obesity (Rask et al. (2001) J. Clin. Endocrinol. Metab. 86: 1418-1421). In addition, data from studies with 11β-HSD1-deficient mice produced by homologous recombination demonstrate that the loss of 11β-HSD1 leads to an increase in insulin sensitivity and glucose tolerance due to a tissue-specific deficiency in active glucocorticoid levels (Kotelevstev et al. (1997) Proc. Natl. Acad. Sci. 94: 14924-14929; Morton et al. (2001) J. Biol. Chem. 276: 41293-41300; Morton et al. (2004) Diabetes 53: 931-938).

The published data supports the hypothesis that increased expression of 11β-HSD1 contributes to increased local conversion of cortisone to cortisol in adipose tissue and hence that 11β-HSD1 plays a role in the pathogenesis of central obesity

and the appearance of the metabolic syndrome in humans (Engeli, et al., (2004) Obes. Res. 12: 9-17). Therefore, 11β-HSD1 is a promising pharmaceutical target for the treatment of the metabolic syndrome (Masuzaki, et al., (2003) Curr. Drug Targets Immune Endocr. Metabol. Disord. 3: 255-62). Furthermore, inhibition of 11β-HSD1 activity may prove beneficial in treating numerous glucocorticoid-related disorders. For example, 11β-HSD1 inhibitors could be effective in combating obesity and/or aspects of the metabolic syndrome cluster, including glucose intolerance, insulin resistance, hyperglycemia, hypertension, and/or hyperlipidemia (Kotelevstev et al. (1997) Proc. Natl. Acad. Sci. 94: 14924-14929; Morton et al. (2001) J. Biol. Chem. 276: 41293-41300; Morton et al. (2004) Diabetes 53: 931-938). In addition, inhibition of 11β-HSD1 activity may have beneficial effects on the pancreas, including the enhancement of glucose-stimulated insulin release (Billaudel and Sutter (1979) Horm. Metab. Res. 11: 555-560; Ogawa et al. (1992) J. Clin. Invest. 90: 497-504; Davani et al. (2000) J. Biol. Chem. 275: 34841-34844).

Furthermore, given that inter-individual differences in general cognitive function have been linked to variability in the long-term exposure to glucocorticoids (Lupien et al. (1998) Nat. Neurosci. 1: 69-73) and dysregulation of the HPA axis resulting in chronic exposure to glucocorticoid excess in certain brain subregions has been theorized to contribute to the decline of cognitive function (McEwen and Sapolsky (1995) Curr. Opin. Neurobiol. 5: 205-216), one might predict that inhibition of 11β-HSD1 could reduce exposure to glucocorticoids in the brain and thereby protect against deleterious glucocorticoid effects on neuronal function, including cognitive impairment, dementia, and/or depression. Notably, it is known that stress and glucocorticoids influence cognitive function (de Quervain et al. (1998) Nature 394: 787-790); and it has been shown that 11β-HSD1, through its control of glucocorticoid action in the brain, may have effects on neurotoxicity (Rajan et al. (1996) Neuroscience 16: 65-70; Seckl (2000) Neuroendocrinol. 18:49-99).

There is also evidence that glucocorticoids and 11β-HSD1 play a role in regulation of in intra-ocular pressure (IOP) (Stokes et al. (2000) Invest. Ophthalmol. Vis. Sci. 41: 1629-1683; Rauz et al. (2001) Invest. Ophthalmol. Vis. Sci. 42: 2037-2042); if left untreated, elevated IOP can lead to partial visual field loss and eventually blindness. Thus, inhibition of 11β-HSD1 in the eye could reduce local glucocorticoid concentrations and IOP, and 11β-HSD1 hence could potentially be used to treat glaucoma and other visual disorders.

Transgenic aP2-11βHSD1 mice exhibit high arterial blood pressure and have increased sensitivity to dietary salt. Moreover, plasma angiotensinogen levels are elevated in the transgenic mice, as are angiotensin II and aldosterone; and treatment of the mice with an angiotensin II antagonist alleviates the hypertension (Masuzaki et al. (2003) J. Clinical Invest. 112: 83-90). This suggests that hypertension may be caused or exacerbated by 11β-HSD1 activity. Thus, 11β-HSD1 inhibitors may be useful for treatment of hypertension and hypertension-related cardiovascular disorders. Inhibition of 11β-HSD1 in mature adipocytes is also expected to attenuate secretion of plasminogen activator inhibitor 1 (PAI-1), which is an independent cardiovascular risk factor (Halleux et al. (1999) J. Clin. Endocrinol. Metabl. 84: 4097-4105).

Glucocorticoids can have adverse effects on skeletal tissues; and prolonged exposure to even moderate glucocorticoid doses can result in osteoporosis (Cannalis (1996) J. Clin. Endocrinol. Metab. 81: 3441-3447). In addition, 11β-HSD1 has been shown to be present in cultures of human primary osteoblasts as well as cells from adult bone (Cooper et al. (2000) Bone 27: 375-381), and the 11β-HSD1 inhibitor carbenoxolone has been shown to attenuate the negative effects of glucocorticoids on bone nodule formation (Bellows et al. (1998) Bone 23: 119-125). Thus, inhibition of 11β-HSD1 is predicted to decrease the local glucocorticoid concentration within osteoblasts and osteoclasts, thereby producing beneficial effects in various forms of bone disease, including osteoporosis.

11β-HSD1 inhibitors may also be useful for immunomodulation. Although glucocorticoids are perceived to suppress the immune system, in actuality, there is a complex, dynamic interaction between the HPA axis and the immune system (Rook (1999) Baillier's Clin. Endocrinol. Metabl. 13: 576-581). Glucocorticoids play a role in modulating the balance between cell-mediated and humoral immune response, with high glucocorticoid activity normally associated with a humoral response. Inhibition of 11β-HSD1 therefore can be used a means of shifting the immune response towards a cell-mediated response. Certain disease states, such as tuberculosis, leprosy (Hansen's disease) and psoriasis, trigger immune responses that are biased towards a humoral response whereas the more effective immune response may be a cell-mediated response. Hence, 11β-HSD1 inhibitors may be useful for treating such diseases.

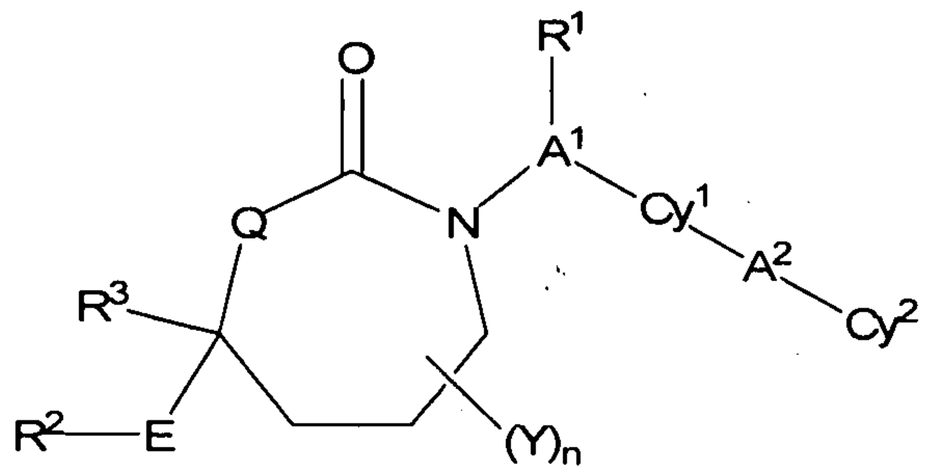
It has been reported that glucocorticoids inhibit wound healing, especially in diabetic patients with ulcers (Bitar et al. (1999) J. Surg. Res. 82: 234-243; Bitar et al.

(1999) Surgery 125: 594-601; Bitar (2000) Surgery 127: 687-695; Bitar (1998) Am. J. Pathol. 152: 547-554). Patients that exhibit impaired glucose tolerance and/or type 2 diabetes often also have impaired wound healing. Glucocorticoids have been shown to increase the risk of infection and delay wound healing (Anstead (1998) Adv. Wound Care 11:277-285). Moreover, there is a correlation between elevated levels of cortisol in wound fluid and non-healing wounds (EP Patent App. No. 0 902 288). Recent published patent applications have suggested that certain 11β-HSD1 inhibitors may be useful for promoting wound healing (PCT/US2006/043,951).

As evidenced herein, there is a continuing need for new and improved drugs that inhibit 11β-HSD1. The novel compounds of the instant invention are effective inhibitors of 11β-HSD1.

SUMMARY OF THE INVENTION

It has now been found that compounds of Formula I or pharmaceutically acceptable salts or prodrugs thereof, are effective inhibitors of 11β-HSD1. Formula I and its constituent members are defined herein as follows:



I

R^1 is (a) absent or (b) is selected from $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl or $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-,

$(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

A^1 is (a) a bond, or (b) $(C_1$-$C_3)$alkylene, CH_2CH_2O, wherein the oxygen is attached to Cy^1, or $CH_2C(=O)$, wherein the carbonyl carbon is attached to Cy^1;

Cy^1 is aryl, heteroaryl, monocyclic cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, oxo, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl amino$(C_2$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxy, di$(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxyl and $(C_1$-$C_6)$alkylcarbonyl;

A^2 is (a) a bond, O, S or NR^4; or (b) $(C_1$-$C_3)$alkylene or $(C_1$-$C_2)$alkyleneoxy, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo;

Cy^2 is (a) hydrogen or (b) aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkyl-alkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, oxo, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl amino$(C_2$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxy, di$(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxyl and $(C_1$-$C_6)$alkylcarbonyl;

Y is $(C_1$-$C_6)$alkyl or halo$(C_1$-$C_6)$alkyl;

n is 0, 1 or 2;

E is (a) a bond or (b) $(C_1$-$C_3)$alkylene or $(C_1$-$C_2)$alkylenyloxy, wherein the O is attached to R^2, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo;

R^2 is $(C_1\text{-}C_6)$alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}C_7)$cycloalkylalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, $(C_4\text{-}C_7)$cycloalkylalkoxy, halo$(C_1\text{-}C_6)$alkoxy, halo$(C_3\text{-}C_6)$cycloalkoxy, halo$(C_4\text{-}C_7)$cycloalkylalkoxy, $(C_1\text{-}C_6)$alkylthio, $(C_3\text{-}C_6)$cycloalkythio, $(C_4\text{-}C_7)$cycloalkyl-alkylthio, halo$(C_1\text{-}C_6)$alkylthio, halo$(C_3\text{-}C_6)$cycloalkythio, halo$(C_4\text{-}C_7)$cycloalkylalkylthio, $(C_1\text{-}C_6)$alkanesulfinyl, $(C_3\text{-}C_6)$cycloalkanesulfinyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, halo$(C_1\text{-}C_6)$alkane-sulfinyl, halo$(C_3\text{-}C_6)$cycloalkanesulfinyl, halo$(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, $(C_1\text{-}C_6)$alkanesulfonyl, $(C_3\text{-}C_6)$cycloalkanesulfonyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfonyl, halo$(C_1\text{-}C_6)$alkanesulfonyl, halo$(C_3\text{-}C_6)$cycloalkanesulfonyl, halo$(C_4\text{-}C_7)$cyclo-alkylalkanesulfonyl, $(C_1\text{-}C_6)$alkylamino, di$(C_1\text{-}C_6)$alkylamino, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1\text{-}C_6)$alkylaminocarbonyl, di$(C_1\text{-}C_6)$alkylaminocarbonyl, $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1\text{-}C_6)$alkylaminosulfonyl, di$(C_1\text{-}C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1\text{-}C_6)$alkylcarbonylamino, $(C_1\text{-}C_6)$alkylcarbonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylsulfonylamino, $(C_1\text{-}C_6)$alkylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkoxy, heteroaryl, oxo, amino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl, di$(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl amino$(C_2\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylamino$(C_2\text{-}C_6)$alkoxy, di$(C_1\text{-}C_6)$alkylamino$(C_2\text{-}C_6)$alkoxyl and $(C_1\text{-}C_6)$alkylcarbonyl;

R^3 is selected from $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl and $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$,

$R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), aryl-amino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

Q is O or NR^5;

R^4 is independently selected from H, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl and $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl; and

R^5 is H, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, or hydroxy$(C_1$-$C_6)$alkyl;
or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a pharmaceutical composition comprising: i) a pharmaceutically acceptable carrier or diluent; and ii) compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig; or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof

Another embodiment of the invention is a method of inhibiting 11β-HSD1 activity comprising the step of administering to a mammal in need of such treatment an effective amount of a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig, or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of the invention is a method of treating a subject with a disease associated with the activity or expression of 11β-HSD1, comprising the step of administering to the subject an effective amount of a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig, or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment of the invention is the use of a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig, or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof for the manufacture of a medicament for inhibiting 11β-HSD1 activity in a mammal in need of such treatment.

Another embodiment of the invention is the use of a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig, or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof for the manufacture of a medicament for treating a subject with a disease associated with the activity or expression of 11β-HSD1.

Another embodiment of the invention is a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof for use in inhibiting 11β-HSD1 activity in a mammal in need of such treatment.

Another embodiment of the invention is a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig, or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof for use in for treating a subject with a disease associated with the activity or expression of 11β-HSD1.

The present invention further provides methods of inhibiting 11β-HSD1 by contacting 11β-HSD1 with a compound of Formula I, I*, I**, Ia, Ib, Ic, Id, Ie, If or Ig of the invention.

The present invention further provides methods of inhibiting or reducing the conversion of cortisone to cortisol in a cell using a compound of Formula I, I*, I**, Ia, Ib, Ic, Id, Ie, If or Ig of the invention.

The present invention further provides methods of inhibiting or reducing production of cortisol in a cell using a compound of Formula I, I*, I**, Ia, Ib, Ic, Id, Ie, or If of the invention.

The present invention further provides methods of increasing insulin sensitivity in a subject in need thereof using a compound of Formula I, I*, I**, Ia, Ib, Ic, Id, Ie, If or Ig of the invention.

DETAILED DESCRIPTION OF THE INVENTION

Another embodiment is a compound of Structural Formula I, wherein

R^3 is selected from substituted $(C_1\text{-}C_6)$alkyl, or optionally substituted $(C_2\text{-}C_6)$alkenyl, optionally substituted $(C_2\text{-}C_6)$alkynyl and optionally substituted $(C_1\text{-}C_3)$alkoxy$(C_2\text{-}C_3)$alkyl, wherein each substituted group represented by R^3 has up to four groups

independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), aryl-amino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

and the remaining values are as defined for Formula I above or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Structural Formula I, wherein
R^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkyl-alkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-

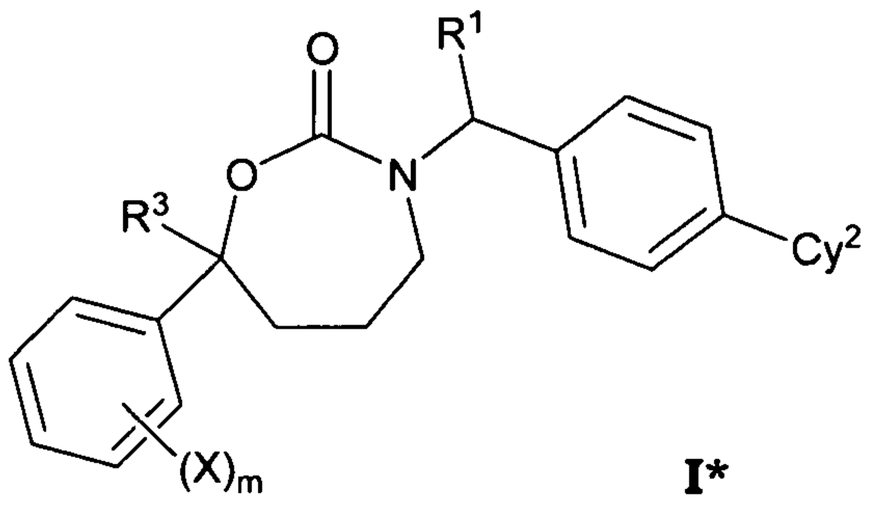
C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

R^3 is selected from substituted (C_1-C_6)alkyl, or optionally substituted (C_2-C_6)alkenyl, optionally substituted (C_2-C_6)alkynyl and optionally substituted (C_1-C_3)alkoxy(C_2-C_3)alkylwherein each substituted group represented by R^3 has up to four groups independently selected from cyano, R^4, $(R^4)_2N$-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen,

trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

and the remaining values are as defined for Formula I above or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Structural Formula I*:



I*

wherein

R^1 is $(C_1\text{-}C_6)$alkyl, optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

Cy^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}$

C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkyl-alkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkyl-alkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

Substituents X are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-

C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

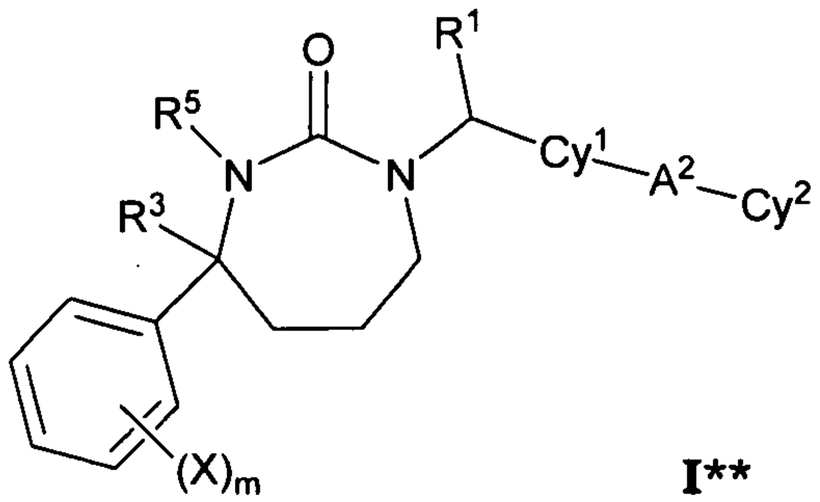
m is 0, 1, 2, 3, 4;

R^3 is (C_1-C_6)alkyl substituted by up to four groups independently selected from cyano, oxo, HO-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment, m is 1, 2, or 3 in Structural Formula I* and the remaining values are as described above.

Another embodiment is a compound of Structural Formula I**:



I**, wherein

R^1 is $(C_1\text{-}C_6)$alkyl, optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

Cy^1 is aryl, heteroaryl, monocyclic cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}C_7)$cycloalkylalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, $(C_4\text{-}C_7)$cycloalkylalkoxy, halo$(C_1\text{-}C_6)$alkoxy, halo$(C_3\text{-}C_6)$cycloalkoxy, halo$(C_4\text{-}C_7)$cycloalkylalkoxy, $(C_1\text{-}C_6)$alkylthio, $(C_3\text{-}C_6)$cycloalkythio, $(C_4\text{-}C_7)$cycloalkylalkylthio, halo$(C_1\text{-}C_6)$alkylthio, halo$(C_3\text{-}C_6)$cycloalkythio, halo$(C_4\text{-}C_7)$cycloalkylalkylthio, $(C_1\text{-}C_6)$alkanesulfinyl, $(C_3\text{-}C_6)$cycloalkanesulfinyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, halo$(C_1\text{-}C_6)$alkane-sulfinyl, halo$(C_3\text{-}C_6)$cycloalkanesulfinyl, halo$(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, $(C_1\text{-}C_6)$alkanesulfonyl, $(C_3\text{-}C_6)$cycloalkanesulfonyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfonyl, halo$(C_1\text{-}$

C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

A^2 is a bond;

Cy^2 is (a) hydrogen or (b) aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkyl-alkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-

C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

Substituents X are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

m is 0, 1, 2, 3, 4;

R^3 is selected from (C_1-C_6)alkyl substituted with up to four groups independently selected from cyano, oxo, R^4, HO-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-,

$(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In another embodiment, m is 1, 2, or 3 in Structural Formula I* and the remaining values are as described above.

Another embodiment is a compound of Formula I, I*, I** or any one of Formulas Ia-g wherein:

R^1 (for Formulas I, I*, I** and Id) is absent or is methyl or ethyl;

A^1 (for Formulas I, I*, I** and Id) is a bond or CH_2 or if R^1 is present, then A^1 is CH;

Cy^1 (for Formulas I, I*, I** and Ia-e) is phenyl, cyclopropyl, cyclohexyl, pyrrolidinyl, pyridyl, N-oxo-pyridyl, thiazolyl or pyrimidinyl optionally substituted with 1 to 4 groups independently selected from halo, methyl, trifluoromethyl, hydroxy, methoxy, methoxycarbonyl, carboxy, ethoxycarbonylmethoxy, 2-hydroxy-2-methylpropoxy, cyano, difluoromethoxy, t-butoxycarbonyl, hydroxy, hydroxymethyl, 2-hydroxyethyl, 2-hydroxy-2-propyl, methoxymethyl, methylsulfonyl and methylsulfonylamino;

A^2 (for Formulas I, I*, I** and Ia-e) is a bond, O, OCH_2CO or C=O;

Cy^2 (for Formulas I, I*, I** and Ia-e) is (a) hydrogen or (b) phenyl, thienyl, pyridyl, N-oxo-pyridyl, cyclopropyl, piperidinyl, piperazinyl, morpholinyl, thiazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, S,S-dioxothiazinyl, 2-oxo-1,2-dihydropyridyl optionally substituted by 1 to 4 groups independently selected from halo, hydroxy, methoxy, hydroxymethyl, methoxycarbonyl, amino, carbamoyl, methylcarbamoyl, dimethylcarbamoyl, (2-methoxyethyl)aminocarbonyl, acetylaminomethyl, methylsulfonyl, methylsulfonylamino, methylaminosulfonyl, isopropylaminosulfonyl, dimethylaminosulfonyl, pyrrolidine-1-sulfonyl, methylsulfonylaminomethyl, tetrazolyl, methyl, trifluoromethyl, acetyl, 2-hydroxyethyl and 1-aminoethyl;

n (for Formula I) is 0;

E (for Formulas I, Ia-c and Ie-g) is a bond or CH_2;

R^2 (for Formuals I, Ia-c and Ie-g) is isopropyl, thienyl, phenyl, or pyridyl, each optionally substituted with halo, methyl, methylthio or (4-morpholino)methyl;

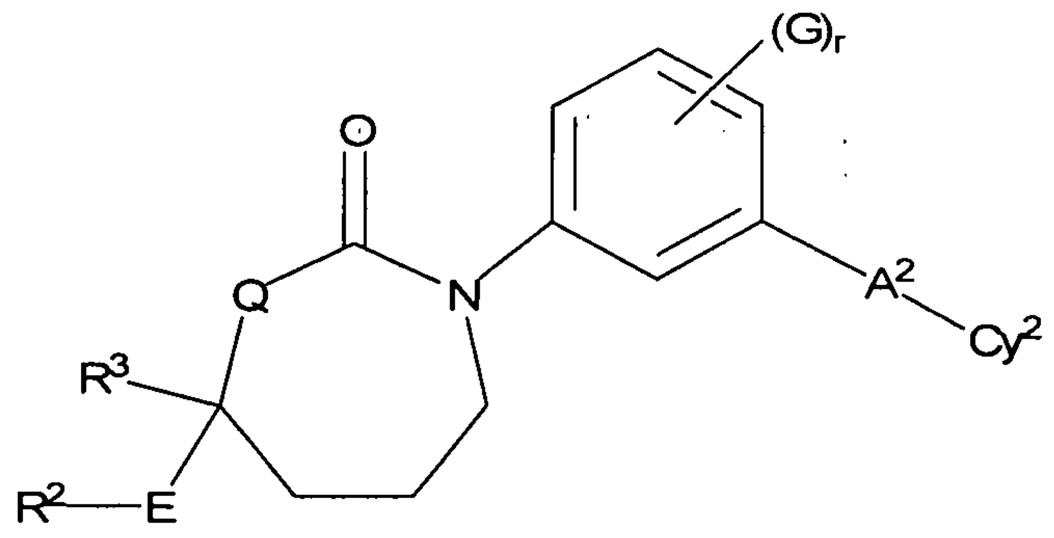
R^3 (for Formulas I, I*, I**, and Ia-g) is methyl, ethyl, propyl, butyl, vinyl, allyl or ethoxyethyl, each optionally substituted with up to two groups independently selected from HO-, MeO-, H_2N-, $MeC(=O)NH$-, $MeS(=O)_2NH$-, $H_2NC(=O)$-, $MeNHC(=O)$-, HO_2C-, $(HO)_2P(=O)O$-, $H_2NS(=O)_2O$-, $H_2NS(=O)_2NH$-, $MeNHC(=O)NH$-, $MeNHC(=O)O$- oxo, cyano, HO_2C-, $HOCH_2CH_2NH$-, 4-morpholino, $HOCH_2C(=O)NH$-, $H_2NCH_2C(=O)NH$-, EtNHC(=O)NH, $MeOC(=O)NH$-, $MeNHC(=NC{\equiv}N)NH$-, Me-, MeS-, $MeSO_2$- $MeSO_2N(Me)$-, $MeS(=O)_2NHC(=O)$-, imidazolylamino-, imidazolyl, tetrazolyl, H_2NCONH-, H_2NCO_2-, $HOCH_2CH_2O$-, MeNH-, Me_2N- and MeCONMe;

Q (Formulas I and Ia-g) is O or NR^5;

R^5 (Formulas I, I*, I**, and Ia-g) is hydrogen or methyl. ;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula Ia:



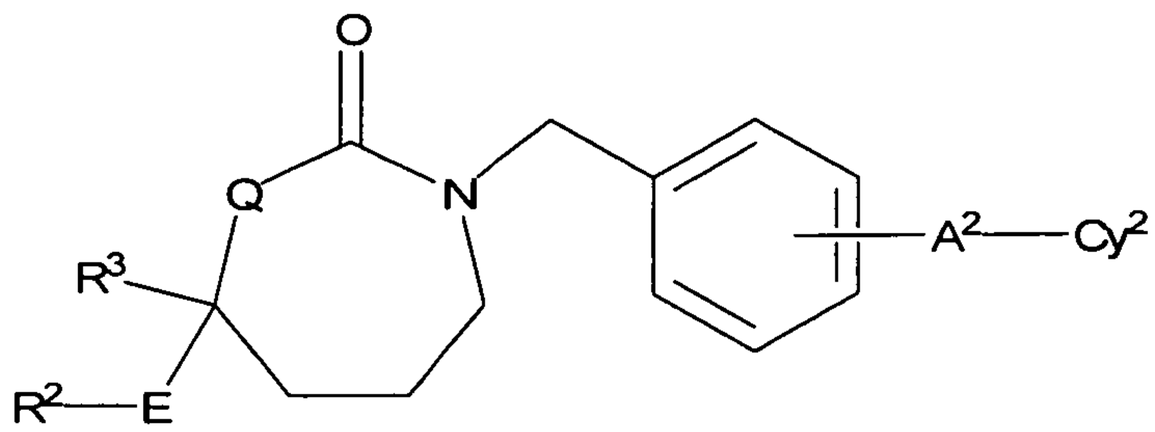
Ia

wherein A^2, Cy^2, E, Q, R^2, R^3, and R^5 are as defined for Formula I above; r is 0, 1, 2, 3 or 4; and substituents G are independently selected from fluorine, chlorine,

bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkane-sulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl or (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula Ib:

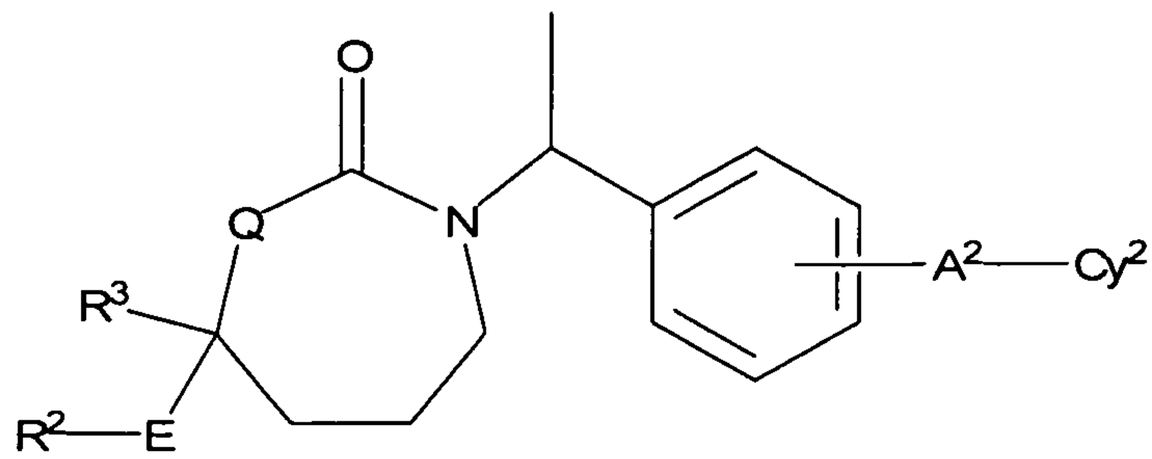


Ib

wherein A^2, Cy^2, Q, E, R^2, R^3 and R^5 are as defined for Formula I above;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula Ic:

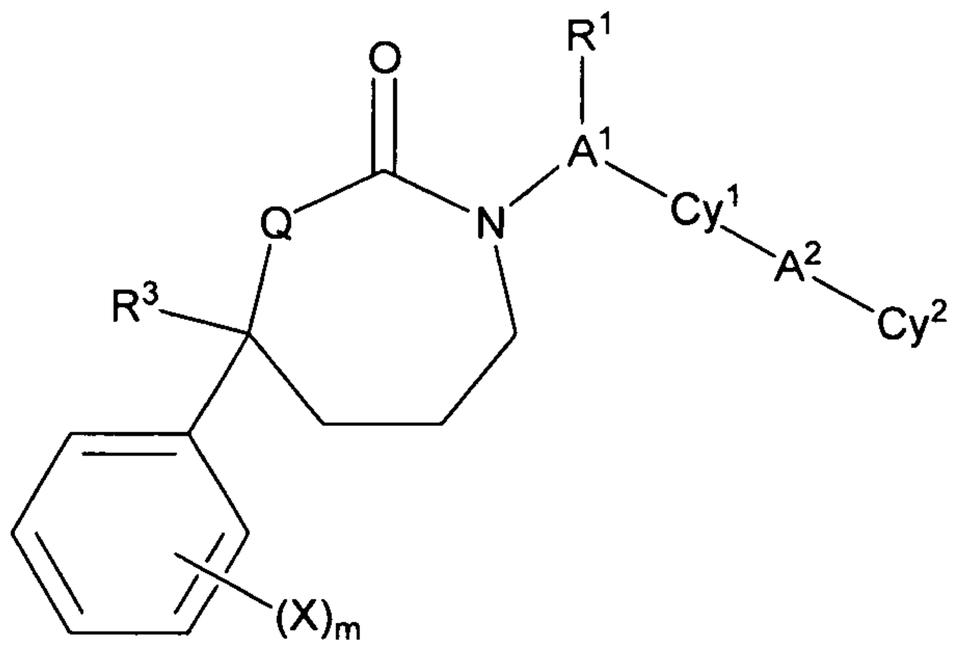


Ic

wherein A^2, Cy^2, E, Q, R^2, R^3 and R^5 are as defined for Formula I above;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula Id:



Id

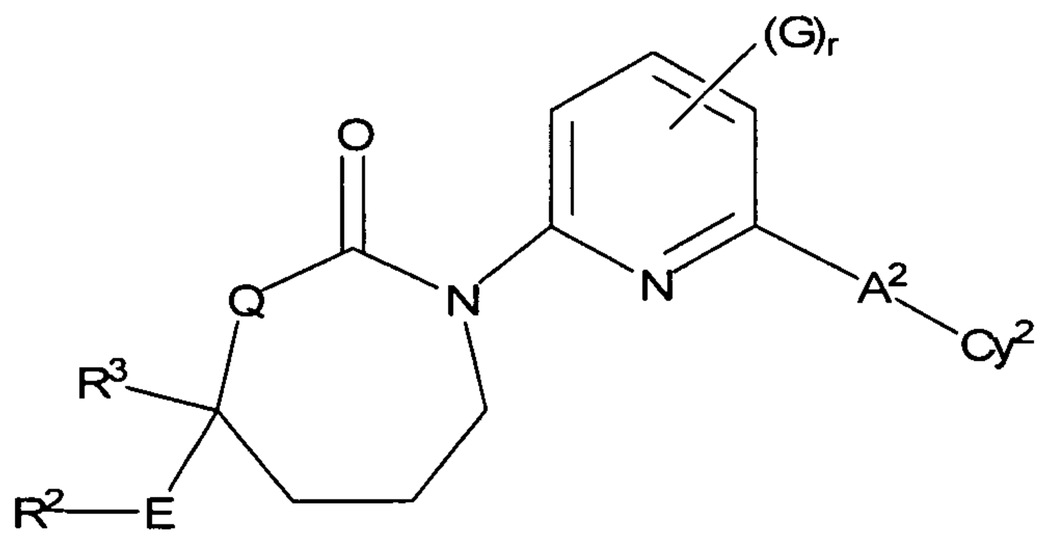
wherein A^1, R^1, Cy^1, A^2, Cy^2, Q, R^3, and R^5 are as defined for Formula I above; m is 0, 1, 2, 3 or 4; and substituents X are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkyl-alkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkyl-alkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-

C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In a specific embodiment, A^2-Cy^2 is meta or para to the carbon atom bonded to $-A_1$.

Another embodiment is a compound of Formula Ie:



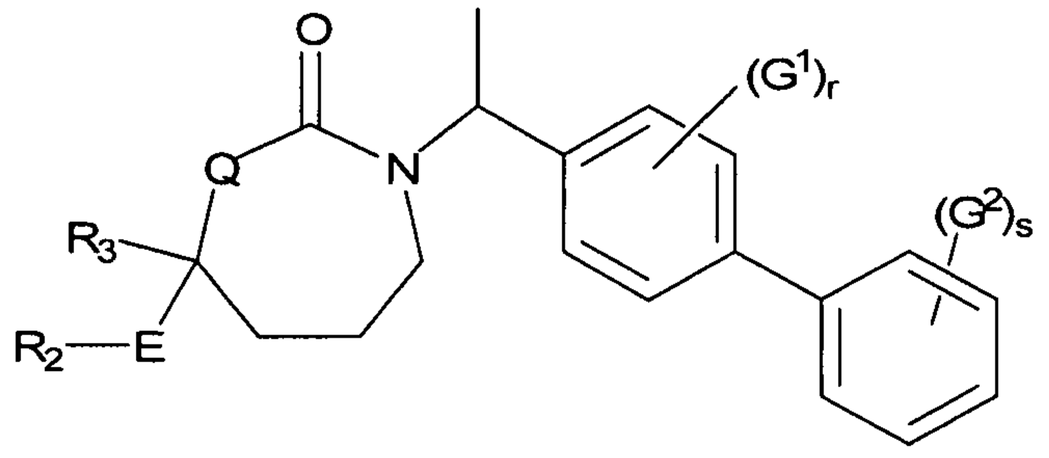
Ie

wherein A^2, Cy^2, E, Q, R^2, R^3, and R^5 are as defined for Formula I above, r is 0, 1, 2, 3 or 4; and substituents G are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkyl-alkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkyl-alkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-

C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula If:



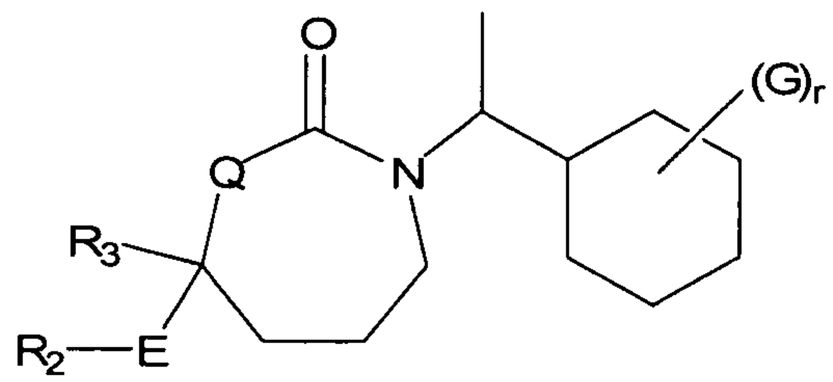
If

wherein E, Q, R^2, R^3, and R^5 are as defined for Formula I above, r and s are independently 0, 1, 2, 3 or 4; and G^1 and G^2 are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkyl-alkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkyl-alkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl,

di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

Another embodiment is a compound of Formula Ig:



Ig

wherein E, Q, R^2, R^3 and R^5 are as defined for Formula I above, r is 0, 1, 2, 3 or 4; and substituents G are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-

C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;
or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

In certain specific embodiments of the invention, the variables in the above-described structural formulas have the following values:

A^1 is (a) a bond, or (b) (C_1-C_3)alkylene, CH_2CH_2O, wherein the oxygen is attached to Cy^1, or $CH_2C(=O)$, wherein the carbonyl carbon is attached to Cy^1.

Alternatively, A^1 is a bond. Alternatively, A^1 is (C_1-C_3)alkylene. In another specific embodiment, A^1 is methylene. In another specific embodiment, if R^1 is present, A^1 is CH. In another specific embodiment, if R^1 is ethyl or methyl and A^1 is CH.

R^1 is (a) absent or (b) is selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl or (C_1-C_3)alkoxy(C_1-C_3)alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino. In another alternative, R^1 is (C_1-C_6)alkyl. Alternatively, R^1 is absent, or is methyl or ethyl.

Alternatively, R^1 is (C_1-C_6)alkyl, optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-,

$R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino.

Cy^1 is aryl, heteroaryl, monocyclic cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, oxo, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl amino$(C_2$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxy, di$(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxyl or $(C_1$-$C_6)$alkylcarbonyl.

Alternatively, Cy^1 is optionally substituted aryl or optionally substituted heteroaryl. Alternatively, Cy^1 is optionally substituted phenyl or optionally substituted pyridyl. In another alternative, Cy^1 is optionally substituted monocyclic cycloalkyl. In another alternative, Cy^1 is optionally substituted cyclohexyl. In another alternative, Cy^1 is optionally substituted phenyl. In another alternative, Cy^1 is phenyl optionally substituted with fluorine, bromine, trifluoromethyl, fluorine, methoxy, methyl,

fluorocarboxy, hydroxy alkyl, methoxycarbonyl, or methyoxymethyl. In yet another specific embodiment, Cy^1 is substituted with fluorine chlorine, bromine, methoxy, methoxycarbonyl, carboxy, or methyl. Alternatively, Cy^1 is pyridyl optionally substituted with chlorine. In yet another specific embodiment, Cy^1 is substituted with fluorine or bromine. In another embodiment A^2 is a bond, Cy^2 is H and Cy^1 is optionally substituted monocyclic cycloalkyl. In another embodiment A^2 is a bond, Cy^2 is H and Cy^1 is optionally substituted cyclohexyl. In another embodiment A^2 is a bond, Cy^2 is H and Cy^1 is phenyl substituted with fluorine, chlorine, bromine, methyl, methoxy, methoxycarbony, trifluoromethyl, hydroxymethyl or 2-hydroxy-2-propyl. In another embodiment, Cy^1 is 1-(*t*-BuOC(=O))pyrrolidin-3-yl).

Cy^1 is phenyl, cyclopropyl, cyclohexyl, pyrrolidinyl, pyridyl, N-oxo-pyridyl, thiazolyl or pyrimidinyl optionally substituted with 1 to 4 groups independently selected from halo, methyl, trifluoromethyl, hydroxy, methoxy, methoxycarbonyl, carboxy, ethoxycarbonylmethoxy, 2-hydroxy-2-methylpropoxy, cyano, difluoromethoxy, t-butoxycarbonyl, hydroxy, hydroxymethyl, 2-hydroxyethyl, 2-hydroxy-2-propyl, methoxymethyl, methylsulfonyl and methylsulfonylamino.

A^2 is (a) a bond, O, S or NR^4; or (b) $(C_1\text{-}C_3)$alkylene or $(C_1\text{-}C_2)$alkyleneoxy, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo.

Alternatively, A^2 is a bond. Alternatively, A^2 is a bond and Cy^2 is hydrogen. Alternatively, A^2 is a bond and Cy^2 is cyclopropyl. Alternatively, A^2 is a bond and Cy^2 is optionally substituted aryl or optionally substituted heteroaryl. In another specific embodiment, A^2 is a bond and Cy^2 is optionally substituted phenyl or optionally substituted pyridyl. In yet another specific embodiment, A^2 is a bond and Cy^2 is optionally substituted phenyl. In yet another specific embodiment, A^2 is a bond and Cy^2 is substituted with 1 to 4 groups independently selected from chlorine or fluorine. In yet another specific embodiment, A^2 is a bond and Cy^2 is difluorophenyl. In yet another specific embodiment, A^2 is a bond and Cy^2 is fluorophenyl. In yet another specific embodiment A^2 is a bond and Cy^2 is optionally substituted 2-thienyl, 1-pyrazolyl, 3-pyrazolyl,1,2,4-thiadiazol-3-yl, thiazolyl or 2-oxo-1,2-dihydro-5-pyridyl. In yet another specific embodiment, A^2 is a bond and Cy^2 is phenyl or thienyl substituted with amino$(C_1\text{-}C_6)$alkyl.

Alternatively, A^2 is a bond, O, OCH_2CO or C=O.

Cy^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine,

bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkyl-alkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkyl-alkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl.

Alternatively, Cy^2 is optionally substituted pyridyl. In one embodiment, Cy^2 is pyridyl optionally substituted with oxo, alkyl, methoxy, fluorine, chlorine, or trifluoromethyl. Alternatively, Cy^2 is optionally substituted thienyl. In one embodiment, Cy^2 is thienyl optionally substituted with MeCO, H_2NCHMe or HOCHMe. Alternatively, Cy^2 is optionally substituted phenyl. In one embodiment, Cy^2 is phenyl optionally substituted with fluorine, chlorine, methoxy, methyl or cyano. Alternatively, Cy^2 is optionally substituted phenyl. In one embodiment, Cy^2 is thiazolyl or thiaziazol, each optionally substituted with methyl. Alternatively, Cy^2 is pyrazolyl optionally substituted with trifluoromethyl. Alternatively, Cy^2 is optionaly substituted pyrazolyl, morpholinyl, or cyclopropyl.

Cy^2 is (a) hydrogen or (b) aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl,

hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkyl-alkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl or (C_1-C_6)alkylcarbonyl.

Cy^2 is (a) hydrogen or (b) phenyl, thienyl, pyridyl, N-oxo-pyridyl, cyclopropyl, piperidinyl, piperazinyl, morpholinyl, thiazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, S,S-dioxothiazinyl, 2-oxo-1,2-dihydropyridyl optionally substituted by 1 to 4 groups independently selected from halo, hydroxy, methoxy, hydroxymethyl, methoxycarbonyl, amino, carbamoyl, methylcarbamoyl, dimethylcarbamoyl, (2-methoxyethyl)aminocarbonyl, acetylaminomethyl, methylsulfonyl, methylsulfonylamino, methylaminosulfonyl, isopropylaminosulfonyl, dimethylaminosulfonyl, pyrrolidine-1-sulfonyl, methylsulfonylaminomethyl, tetrazolyl, methyl, trifluoromethyl, acetyl, 2-hydroxyethyl and 1-aminoethyl.

Y is (C_1-C_6)alkyl or halo(C_1-C_6)alkyl.

n is 0, 1 or 2. In another embodiment, n is 0.

X is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-

C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl.

m is 0, 1, 2, 3, 4. Alternatively, m is 1, 2, 3, or 4. In another embodiment, m is 1, 2 or 3.

E is (a) a bond or (b) (C_1-C_3)alkylene or (C_1-C_2)alkylenyloxy, wherein the O is attached to R^2, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo.

E is a bond or CH_2.

In a specific embodiment E is a bond. In another specific embodiment, E is a bond when R^2 is optionally substituted aryl, optionally substituted heteroaryl or optionally substituted cycloalkyl. In another specific embodiment, E is a bond when R^2 is optionally substituted phenyl, optionally substituted thienyl or optionally substituted pyridyl. In yet another specific embodiment, E is a bond when R^2 is optionally substituted phenyl.

R^2 is (C_1-C_6)alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with up to 4 groups independently selected from fluorine,

chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkyl-alkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, oxo, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl amino$(C_2$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxy, di$(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxyl or $(C_1$-$C_6)$alkylcarbonyl.

R^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl,

(C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl and E is a bond.

R^2 is optionally substituted aryl, optionally substituted heteroaryl or cycloalkyl or alkyl. In one specific embodiment, R^2 is optionally substituted phenyl, optionally substituted pyridyl or optionally substituted thienyl. In another embodiment, R^2 is optionally substituted alkyl. In one specific embodiment, R^2 is optionally substituted isopropyl. In one specific embodiment, R^2 is phenyl optionally substitueted with methyl, chlorine, flourine, or methylthio.. In another specific embodiment, R^2 is optionally substituted phenyl. In yet another specific embodiment, R^2 is fluorophenyl.

R^2 is isopropyl, thienyl, phenyl, or pyridyl, each optionally substituted with halo, methyl, methylthio or (4-morpholino)methyl.

R^3 is selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl and (C_1-C_3)alkoxy(C_1-C_3)alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy,

alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), aryl-amino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo).

R^3 is selected from substituted $(C_1\text{-}C_6)$alkyl, or optionally substituted $(C_2\text{-}C_6)$alkenyl, optionally substituted $(C_2\text{-}C_6)$alkynyl and optionally substituted $(C_1\text{-}C_3)$alkoxy$(C_2\text{-}C_3)$alkyl, wherein each substituted group represented by R^3 has up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), aryl-amino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

In another embodiment, R^3 is selected from substituted $(C_1\text{-}C_6)$alkyl, or optionally substituted $(C_2\text{-}C_6)$alkenyl, optionally substituted $(C_2\text{-}C_6)$alkynyl and optionally substituted $(C_1\text{-}C_3)$alkoxy$(C_2\text{-}C_3)$alkylwherein each substituted group represented by R^3 has up to four groups independently selected from cyano, R^4, $(R^4)_2N$-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-,

$(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), aryl-amino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo).

R^3 is $(HO)_2P(=)O(C_1$-$C_4)$alkyl. R^3 is hydroxy$(C_2$-$C_5)$alkyl. In yet another specific embodiment R^3 is 3-hydroxybutyl, 3-hydroxy-3-methylbutyl, 3-hydroxypropyl, 2-hydroxypropyl, 2-hydroxy-2-methylpropyl, or 2-hydroxyethyl. Alternatively, R^3 is dihydroxy$(C_3$-$C_4)$alkyl. In yet another specific embodiment R^3 is 2,3-dihydroxypropyl. R^3 is amino$(C_2$-$C_5)$alkyl or methylamino$(C_2$-$C_5)$alkyl, each optionally substituted with hydroxy. In another specific embodiment, R^3 is ω-$H_2NCO(C_1$-$C_3)$alkyl. In another specific embodiment, R^3 is $H_2NCONH(C_1$-$C_3)$alkyl, optionally substituted with hydroxy. In another specific embodiment, R^3 is $H_2NCH_2CONH(C_1$-$C_3)$alkyl, optionally substituted with hydroxy. In another specific embodiment, R^3 is $(C_1$-$C_3)$alkylHNCONH$(C_1$-$C_3)$alkyl. In yet another specific embodiment, R^3 is $H_2NC(=O)C_1$-C_4 alkyl. In yet another specific embodiment, R^3 is $MeC(=O)NHC_1$-C_4 alkyl. In yet another specific embodiment, R^3 is $MeOC(=O)NHC_1$-C_4 alkyl. In yet another specific embodiment, R^3 is $MeNHC(=O)C_1$-C_4 alkyl. In yet another specific embodiment R^3 is $H_2NC(=O)OC_1$-C_4 alkyl. In yet another specific embodiment, R^3 is $MeHNC(=O)OC_1$-C_4 alkyl. In yet another specific embodiment, R^3 is $(C_1$-$C_2)$alkoxy$(C_1$-$C_3)$alkyl, optionally substituted with hydroxy. In yet another specific embodiment, R^3 is $(C_1$-$C_2)$alkylthio$(C_1$-$C_3)$alkyl, optionally substituted with hydroxy. In yet another specific embodiment, R^3 is $H_2NSO_2O(C_2$-$C_4)$alkyl. In yet another specific

embodiment, R^3 is $H_2NSO_2NH(C_2\text{-}C_4)$alkyl. In yet another specific embodiment, R^3 is oxo$(C_2\text{-}C_4)$alkyl. In yet another specific embodiment, R^3 is $MeCO(C_1\text{-}C_2$alkyl). In yet another specific embodiment, R^3 is $HOCO(C_1\text{-}C_2$alkyl). In yet another specific embodiment, R^3 is alkenyl. In yet another specific embodiment, R^3 is alkyl. In yet another specific embodiment, R^3 is allyl. In yet another specific embodiment, R^3 is $MeC(=O)NH(C_2\text{-}C_4)$alkyl. In yet another specific embodiment, R^3 is $MeOC(=O)NH(C_2\text{-}C_4)$alkyl. In yet another specific embodiment, R^3 is cyanoalkyl. In yet another specific embodiment, R^3 is alkylsulfonylaminoalkyl. In yet another specific embodiment, R^3 is alkylsulfonylalkyl. In yet another specific embodiment R^3 is $MeSO_2NH(C_2\text{-}C_4)$alky, optionally substituted with hydroxy. In yet another specific embodiment, R^3 is aminocarbonylaminoalkyl. In yet another specific embodiment, R^3 is aminocarboxyalkyl. In yet another specific embodiment R^3 is 2-(4-morpholino)ethyl. In yet another specific embodiment R^3 is 2-(1-imidazolyl)ethyl. In yet another specific embodiment R^3 is 2-(1-aminoimidazolyl)ethyl.

Alternatively, R^3 is $(C_1\text{-}C_6)$alkyl substituted by up to four groups independently selected from cyano, oxo, HO-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo).

R^3 is methyl, ethyl, propyl, butyl, vinyl, allyl or ethoxyethyl, each optionally substituted with up to two groups independently selected from HO-, MeO-, H_2N-, MeC(=O)NH-, $MeS(=O)_2NH$-, $H_2NC(=O)$-, MeNHC(=O), HO_2C-, $(HO)_2P(=O)O$-, $H_2NS(=O)_2O$-, $H_2NS(=O)_2NH$-, MeNHC(=O)NH-, MeNHC(=O)O oxo, cyano, HO_2C-, $HOCH_2CH_2NH$-, 4-morpholino, $HOCH_2C(=O)NH$-, $H_2NCH_2C(=O)NH$, EtNHC(=O)NH, MeOC(=O)NH-, MeNHC(=NC≡N)NH-, Me-, MeS-, $MeSO_2$- $MeSO_2N(Me)$-, $MeS(=O)_2NHC(=O)$-, imidazolylamino-, imidazolyl, tetrazolyl, H_2NCONH-, H_2NCO_2-, $HOCH_2CH_2O$-, MeNH-, Me_2N- or MeCONMe.

R^4 is independently selected from H, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl and $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl.

R^5 is H, $(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, or hydroxy$(C_1$-$C_6)$alkyl. R^5 is hydrogen or methyl. In one specific embodiment, R^5 is hydrogen.

r is 0, 1, 2, 3 or 4.

s is 0, 1, 2, 3 or 4.

G is fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkane-sulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkane-sulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxycarbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl,, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-

C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl or (C_1-C_6)alkylcarbonyl.

G^1 and G^2 are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl.

In another embodiment of the invention, the provisos applied to pharmaceutical compositions comprising compounds of Formula I, I*, I** also apply to methods of treatment utilizing any one of the compounds of Formula I, I*, I** or Formulas Ia-Ig.

Another embodiment of the invention is a compound of Formulas I, I*, I**, Ia, Ib, Ic, Id, Ie, If, or Ig or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof wherein any of the following provisos apply

Proviso 1: If (a) Q is O; (b) A^1-Cy^1 is alkyl substituted with aryl; or cycloalkyl or aryl; each optionally substituted by aryl, alkyl , alkenyl, alkynyl, alkoxy, formyl, carbonyl, carboxyl, alkoxycarbonyl, hydroxyl, mercapto, halogen, sulfonyl or amino; (c) R^3 is an alkyl, alkenyl, alkynyl optionally substituted with alkyl, alkoxy, oxo, carboxy, alkoxycarbonyl, hydroxy, mercapto, fluorine, sulfonyl, and amino; (d) then E-R^2 is not alkyl, aryl, cycloalkyl each optionally substituted with alkyl, alkenyl, alkynyl, aryl, alkoxy, oxo, carboxy, alkoxycarbonyl, hydroxy, mercapto, halogen, sulfonyl, or amino.

Proviso 2: If (a) A^1-Cy^1 is cycloalkyl; and (b) R^3 is alkyl optionally substituted with hydroxy or alkoxy; or alkoxyalkyl substituted with oxo; (c) then (i) E-R^2 is not alkyl optionally substituted with aryl, hydroxy or alkoxy; or (ii) E-R^2 is not unsubstituted cycloalkyl or unsubstituted aryl or (iii) E is not alkoxy and R^2 is not alkyl substituted with oxo.

Proviso 3: If (a) A^1 and A^2 are both bonds, (b) R^3 is an alkyl optionally substituted with amino, alkyl, alkoxy, oxo, carboxy, hydroxy, fluorine, or sulfonyl, or an unsubstituted alkynyl (c) E-R^2 is (i) a optionally substituted alkyl or an optionally substituted carbocyclic aromatic group wherein the substituent is an amino, alkyl, alkenyl, alkynyl, alkoxy, carboxy, hydroxy, halogen or sulfonyl, or (ii) an unsubstituted cycloalkyl, and (d) Cy^2 is H, then Cy_1 is not (i) an unsubstituted monocyclic cycloalkyl or (ii) a substituted or unsubstituted carbocyclic aromatic group.

Proviso 4: If (a) A^1 and A^2 are both bonds, (b) R^3 is an alkyl optionally substituted with amino, alkyl, alkoxy, oxo, carboxy, hydroxy, fluorine, or sulfonyl, or an unsubstituted alkynyl (c) E-R^2 is (i) a optionally substituted alkyl or an optionally substituted carbocyclic aromatic group wherein the substituent is an amino, alkyl, alkenyl, alkynyl, alkoxy, carboxy, hydroxy, halogen or sulfonyl, or (ii) an unsubstituted cycloalkyl, and (d) Cy^1 is an optionally substituted carbocyclic aromatic group, then Cy^2 is not an unsubstituted carbocyclic aromatic group.

Proviso 5: If (a) A^1 is alkyl optionally substituted with amino, alkyl, alkoxy, oxo, carboxy, hydroxy, fluorine, or sulfonyl, (b) R^3 is an alkyl substituted with amino, alkyl, alkoxy, oxo, carboxy, hydroxy, fluorine, or sulfonyl, or an unsubstituted alkynyl (c) E-R^2 is (i) a optionally substituted alkyl or an optionally substituted carbocyclic aromatic group wherein the substituent is an amino, alkyl, alkenyl, alkynyl, alkoxy, carboxy,

hydroxy, halogen or sulfonyl, or (ii) an unsubstituted cycloalkyl, then Cy^1 is a carbocyclic aromatic group optionally substituted with C_1C_4 alkoxy or halogen.

DEFINITIONS

The term "alkyl" means a straight or branched hydrocarbon radical having 1-10 carbon atoms and includes, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl and the like.

The term "cycloalkyl" means a monocyclic, bicyclic or tricyclic, saturated hydrocarbon ring having 3-10 carbon atoms and includes, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicyclo[2.2.2]octyl, bicyclo[2.2.1]heptyl, spiro [4.4]nonane, adamantyl and the like.

The term "aryl" means an aromatic radical which is a phenyl group, a naphthyl group, an indanyl group or a tetrahydronaphthalene group. An aryl group is optionally substituted with 1-4 substituents. Exemplary substituents include alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido.

The term "heteroaryl" means a 5- and 6-membered heteroaromatic radical which may optionally be fused to a saturated or unsaturated ring containing 0-4 heteroatoms selected from N, O, and S and includes, for example, a heteroaromatic radical which is 2- or 3-thienyl, 2- or 3-furanyl, 2- or 3- pyrrolyl, 2-,3-, or 4-pyridyl, 2-pyrazinyl, 2-, 4-, or 5-pyrimidinyl, 3- or 4-pyridazinyl, 1H-indol-6-yl, 1H-indol-5-yl, 1H-benzimidazol-6-yl, 1H-benzimidazol-5-yl, 2-, 4-, 5-, 6-, 7- or 8-quinazolinyl, 2-, 3-, 5-, 6-, 7- or 8-quinoxalinyl, 2-, 3-, 4-, 5-, 6-, 7- or 8-quinolinyl, 1-, 3-, 4-, 5-, 6-, 7- or 8-isoquinolinyl, 2-, 4-, or 5-thiazolyl, 2-, 3-, 4-, or 5-pyrazolyl, 2-, 3-, 4-, or 5-imidazolyl. A heteroaryl is optionally substituted. Exemplary substituents include alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido, or by oxo to form an N-oxide.

The term "heterocyclyl" means a 4-, 5-, 6- and 7-membered saturated or partially unsaturated heterocyclic ring containing 1 to 4 heteroatoms independently selected from N, O, and S. Exemplary heterocyclyls include pyrrolidine, pyrrolidin-2-one, 1-methylpyrrolidin-2-one, piperidine, piperidin-2-one, 2-pyridone, 4-pyridone, piperazine, 1-(2,2,2-trifluoroethyl)piperazine, piperazin-2-one, 5,6-dihydropyrimidin-4-one, pyrimidin-4-one, tetrahydrofuran, tetrahydropyran, tetrahydrothiophene, tetrahydrothiopyran, isoxazolidine, 1,3-dioxolane, 1,3-dithiolane, 1,3-dioxane, 1,4-

dioxane, 1,3-dithiane, 1,4-dithiane, oxazolidin-2-one, imidazolidin-2-one, imidazolidine-2,4-dione, tetrahydropyrimidin-2(1H)-one, morpholine, N-methylmorpholine, morpholin-3-one, 1,3-oxazinan-2-one, thiomorpholine, thiomorpholine 1,1-dioxide, tetrahydro-1,2,5-thiaoxazole 1,1-dioxide, tetrahydro-2H-1,2-thiazine 1,1-dioxide, hexahydro-1,2,6-thiadiazine 1,1-dioxide, tetrahydro-1,2,5-thiadiazole 1,1-dioxide and isothiazolidine 1,1-dioxide. A heterocyclyl can be optionally substituted with 1-4 susbtituents. Exemplary substituents include alkyl, haloalkyl and oxo.

As used herein the terms "subject" and "patient" may be used interchangeably, and means a mammal in need of treatment, e.g., companion animals (e.g., dogs, cats, and the like), farm animals (e.g., cows, pigs, horses, sheep, goats and the like) and laboratory animals (e.g., rats, mice, guinea pigs and the like). Typically, the subject is a human in need of treatment.

When a disclosed compound or its pharmaceutically acceptable salt is named or depicted by structure, it is to be understood that solvates or hydrates of the compound or its pharmaceutically acceptable salts are also included. "Solvates" refer to crystalline forms wherein solvent molecules are incorporated into the crystal lattice during crystallization. Solvate may include water or nonaqueous solvents such as ethanol, isopropanol, DMSO, acetic acid, ethanolamine, and EtOAc. Solvates, wherein water is the solvent molecule incorporated into the crystal lattice, are typically referred to as "hydrates." Hydrates include stoichiometric hydrates as well as compositions containing variable amounts of water.

Certain of the disclosed comopounds may exist in various stereoisomeric forms. Stereoisomers are compounds that differ only in their spatial arrangement. Enantiomers are pairs of stereoisomers whose mirror images are not superimposable, most commonly because they contain an asymmetrically substituted carbon atom that acts as a chiral center. "Enantiomer" means one of a pair of molecules that are mirror images of each other and are not superimposable. Diastereomers are stereoisomers that are not related as mirror images, most commonly because they contain two or more asymmetrically substituted carbon atoms. The symbol "*" in a structural formula represents the presence of a chiral carbon center. "*R*" and "*S*" represent the configuration of substituents around one or more chiral carbon atoms. Thus, "*R**" and "*S**" denote the relative configurations of substituents around one or more chiral carbon atoms.

"Racemate" or "racemic mixture" means a compound of equimolar quantities of two enantiomers, wherein such mixtures exhibit no optical activity; i.e., they do not rotate the plane of polarized light.

"Geometric isomer" means isomers that differ in the orientation of substituent atoms in relationship to a carbon-carbon double bond, to a cycloalkyl ring, or to a bridged bicyclic system. Atoms (other than H) on each side of a carbon-carbon double bond may be in an E (substituents are on opposite sides of the carbon-carbon double bond) or Z (substituents are oriented on the same side) configuration.

"R," "S," "S*," "R*," "E," "Z," "cis," and "trans," indicate configurations relative to the core molecule.

The compounds of the invention may be prepared as individual isomers by either isomer-specific synthesis or resolved from an isomeric mixture. Conventional resolution techniques include forming the salt of a free base of each isomer of an isomeric pair using an optically active acid (followed by fractional crystallization and regeneration of the free base), forming the salt of the acid form of each isomer of an isomeric pair using an optically active amine (followed by fractional crystallization and regeneration of the free acid), forming an ester or amide of each of the isomers of an isomeric pair using an optically pure acid, amine or alcohol (followed by chromatographic separation and removal of the chiral auxiliary), or resolving an isomeric mixture of either a starting material or a final product using various well known chromatographic methods.

When the stereochemistry of a disclosed compound is named or depicted by structure, the named or depicted stereoisomer is at least 60%, 70%, 80%, 90%, 99% or 99.9% by weight pure relative to the other stereoisomers. When a single enantiomer is named or depicted by structure, the depicted or named enantiomer is at least 60%, 70%, 80%, 90%, 99% or 99.9% by weight optically pure. Percent optical purity by weight is the ratio of the weight of the enatiomer over the weight of the enantiomer plus the weight of its optical isomer.

When a disclosed compound is named or depicted by structure without indicating the stereochemistry, and the compound has at least one chiral center, it is to be understood that the name or structure encompasses one enantiomer of compound free from the corresponding optical isomer, a racemic mixture of the compound and mixtures enriched in one enantiomer relative to its corresponding optical isomer.

When a disclosed compound is named or depicted by structure without indicating the stereochemistry and has at least two chiral centers, it is to be understood that the name or structure encompasses a diastereomer free of other diastereomers, a pair of diastereomers free from other diastereomeric pairs, mixtures of diastereomers, mixtures of diastereomeric pairs, mixtures of diastereomers in which one diastereomer is enriched relative to the other diastereomer(s) and mixtures of diastereomeric pairs in which one diastereomeric pair is enriched relative to the other diastereomeric pair(s).

The compounds of the invention may be present in the form of pharmaceutically acceptable salts. For use in medicines, the salts of the compounds of the invention refer to non-toxic "pharmaceutically acceptable salts." Pharmaceutically acceptable salt forms include pharmaceutically acceptable acidic/anionic or basic/cationic salts.

Pharmaceutically acceptable acidic/anionic salts include, the acetate, benzenesulfonate, benzoate, bicarbonate, bitartrate, bromide, calcium edetate, camsylate, carbonate, chloride, citrate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, glyceptate, gluconate, glutamate, glycollylarsanilate, hexylresorcinate, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isethionate, lactate, lactobionate, malate, maleate, malonate, mandelate, mesylate, methylsulfate, mucate, napsylate, nitrate, pamoate, pantothenate, phosphate/diphospate, polygalacturonate, salicylate, stearate, subacetate, succinate, sulfate, hydrogensulfate, tannate, tartrate, teoclate, tosylate, and triethiodide salts.

Pharmaceutically acceptable basic/cationic salts include, the sodium, potassium, calcium, magnesium, diethanolamine, n-methyl-D-glucamine, L-lysine, L-arginine, ammonium, ethanolamine, piperazine and triethanolamine salts.

The following abbreviations have the indicated meanings:

Abbreviation	Meaning
Boc	*tert*-butoxy carbonyl or *t*-butoxy carbonyl
$(Boc)_2O$	di-*tert*-butyl dicarbonate
Cbz	Benzyloxycarbonyl
CbzCl	Benzyl chloroformate

DAST	diethylaminosulfur trifluoride
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	N,N'-dicyclohexylcarbodiimide
DCU	N,N'-dicyclohexylurea
DIAD	diisopropyl azodicarboxylate
DIEA	N,N-diisopropylethylamine
DMAP	4-(dimethylamino)pyridine
DMF	N,N-dimethylformamide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone
2,4-DNP	2,4-dinitrophenylhydrazine
DPTBS	Diphenyl-t-butylsilyl
EDC.HCl, EDCI	1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride
Equiv	equivalents
Fmoc	1-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-
Fmoc-OSu	1-[[(9H-fluoren-9-ylmethoxy)carbonyl]oxy]-2,5-pyrrolidinedione
h, hr	hour(s)
HOBt	1-hydroxybenzotriazole
HATU	2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
HBTU	2-(1H-Benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate
KHMDS	potassium hexamethyldisilazane
LAH or $LiAlH_4$	lithium aluminum hydride
LC-MS	liquid chromatography-mass spectroscopy
LHMDS	lithium hexamethyldisilazane
Me	methyl
MsCl	methanesulfonyl chloride

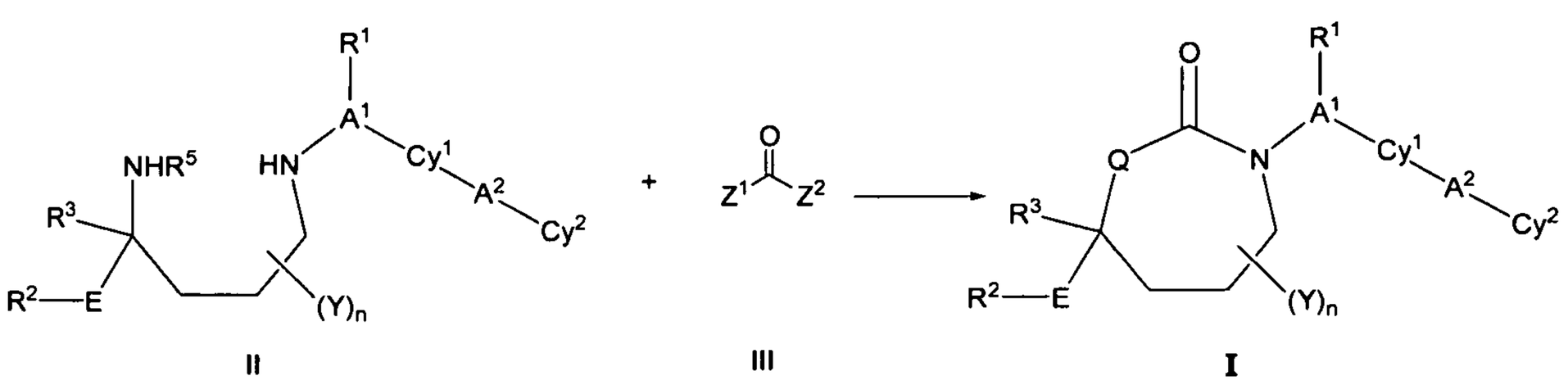
Min	minute
MS	mass spectrum
NaH	sodium hydride
$NaHCO_3$	sodium bicarbonate
NaN_3	sodium azide
NaOH	sodium hydroxide
Na_2SO_4	sodium sulfate
NMM	N-methylmorpholine
NMP	N-methylpyrrolidinone
$Pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium(0)
PE	petroleum ether
Quant	quantitative yield
Satd	saturated
$SOCl_2$	thionyl chloride
SFC	supercritical fluid chromatography
SPA	scintillation proximity assay
SPE	solid phase extraction
TBAF	tetrabutylammonium fluoride
TBS	t-butyldimethylsilyl
TBDPS	t-butyldiphenylsilyl
TBSCl	t-butyldimethylsilyl chloride
TBDPSCl	t-butyldiphenylsilyl chloride
TEA	triethylamine or Et_3N
TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy free radical
Teoc	1-[2-(trimethylsilyl)ethoxycarbonyloxy]-
Teoc-OSu	1-[2-(trimethylsilyl)ethoxycarbonyloxy]pyrrolidin-2,5-dione
TFA	trifluoroacetic acid
Tlc, TLC	thin layer chromatography

TMS	trimethylsilyl
TMSCl	chlorotrimethylsilane or trimethylsilyl chloride
t_R	retention time
TsOH	p-toluenesulfonic acid

GENERAL DESCRIPTION OF SYNTHETIC METHODS

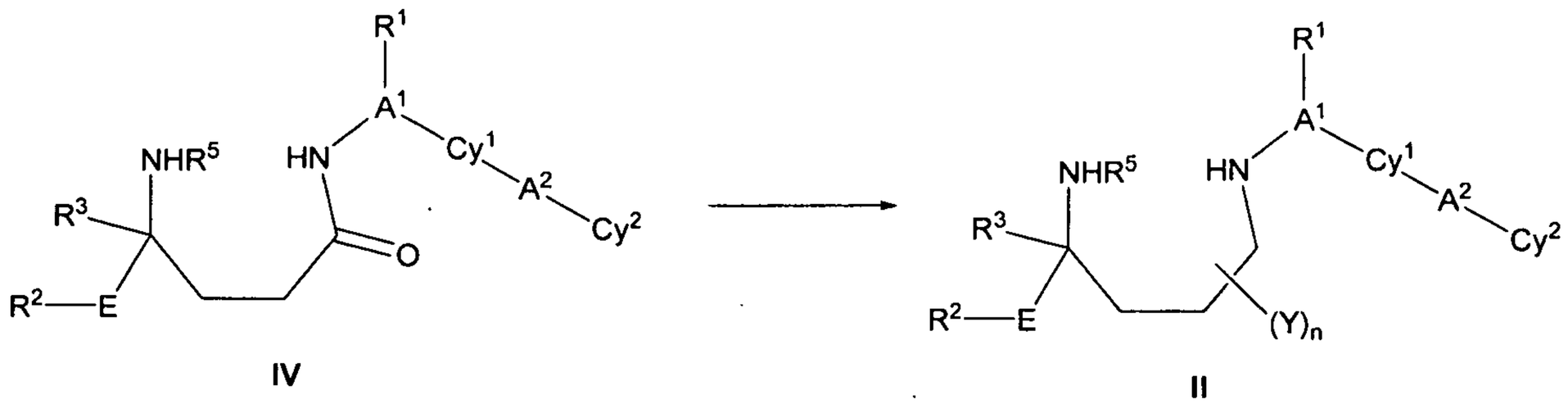
Compounds of Formula I can be prepared by several processes. In the discussion below, A^1, A^2, Cy^1, Cy^2, E, Q, R^1, R^2, R^3, R^5, Y and n have the meanings indicated above unless otherwise noted. In cases where the synthetic intermediates and final products of Formulas I described below contain potentially reactive functional groups, for example amino, hydroxyl, thiol and carboxylic acid groups, that may interfere with the desired reaction, it may be advantageous to employ protected forms of the intermediate. Methods for the selection, introduction and subsequent removal of protecting groups are well known to those skilled in the art. (T.W. Greene and P. G. M. Wuts "Protective Groups in Organic Synthesis" John Wiley & Sons, Inc., New York 1999). Such protecting group manipulations are assumed in the discussion below and not described explicitly. Generally, reagents in the reaction schemes are used in equimolar amounts; however, in certain cases it may be desirable to use an excess of one reagent to drive a reaction to completion. This is especially the case when the excess reagent can be readily removed by evaporation or extraction. Bases employed to neutralize HCl in reaction mixtures are generally used in slight to substantial excess (1.05 – 5 equivalents).

In a first process a compound of Formula I, wherein Q is NR^5 can be prepared by reaction of diamine intermediate of Formula II with a reagent of Formula III, wherein Z^1 and Z^2 are leaving groups such as chloride, 1-imidazolyl or aryloxide in an inert solvent such as THF, CH_2Cl_2, toluene or MeCN, usually in the presence of an organic or inorganic base such as triethylamine or $NaHCO_3$ respectively, at -10 °C to 120 °C:



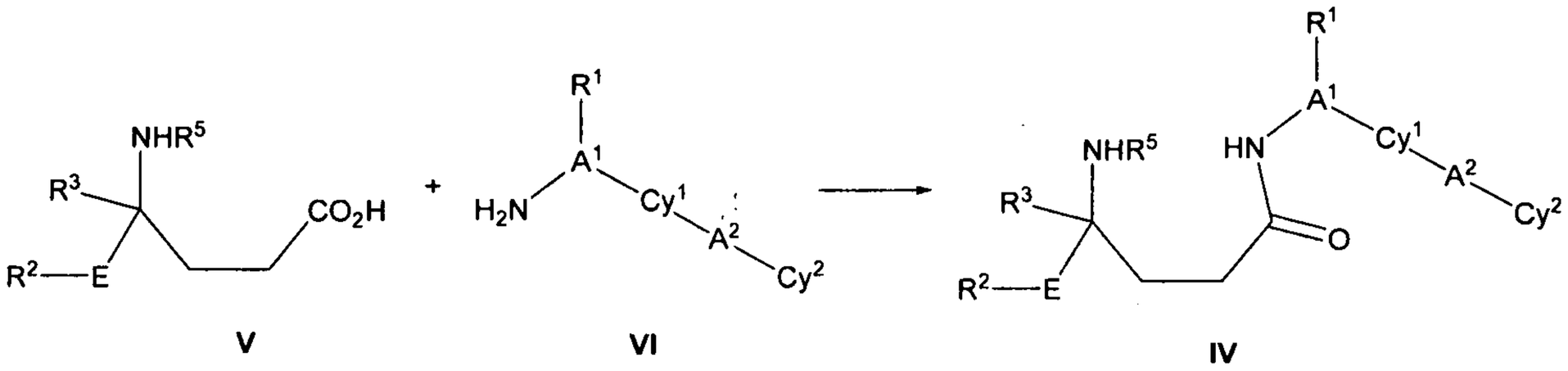
Certain instances of reagent III are especially convenient because they are commercially available. For example when Z^1 and Z^2 are both chloride, III is phosgene. When Z^1 and Z^2 are both 1-imidazolyl, III is carbonyl diimidazole. When Z^1 is chloride and Z^2 is p-nitrophenoxide, III is p-nitrophenyl chloroformate. When Z^1 and Z^2 are both $OCCl_3$, III is triphosgene and as little as one third of molar equivalent can be used.

Diamine intermediates of Formula II, wherein n = 0, can be prepared by reduction of amides of Formula IV using a hydride reagent such as BH_3.THF solution, $BH_3.Me_2S$ or $LiAlH_4$ in an inert solvent ethereal such as THF or DME at 20 °C to 100 °C for between 1 h and 48 h:



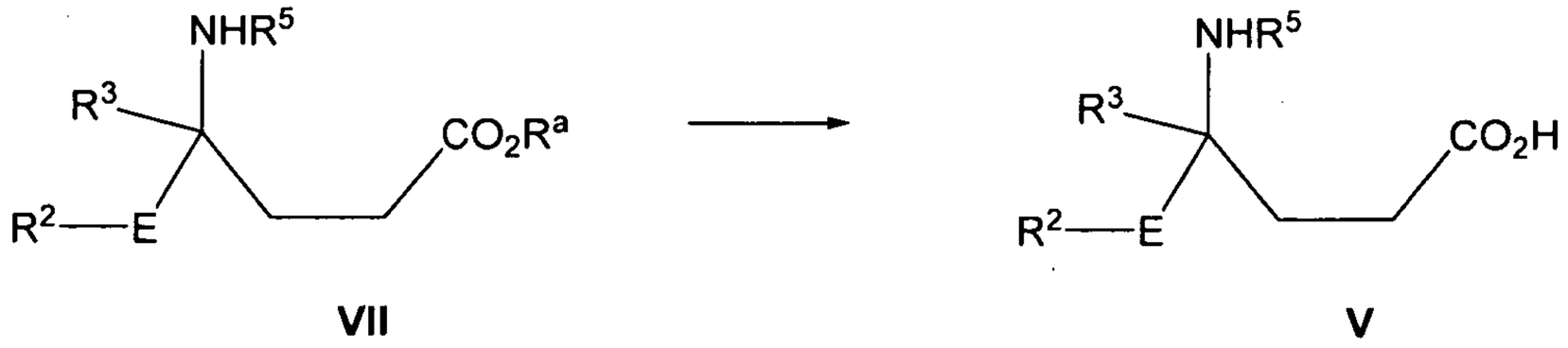
IV II

Aminoamide intermediates of Formula IV can be prepared by coupling of a γ-aminoacid of Formula V with an amine of Formula VI using standard peptide coupling reagents such as EDC in the presence of HOBt and N,N-diisopropylethylamine in an inert solvent such as CH_2Cl_2 at 0 – 30 °C for between 1 h and 24 h:



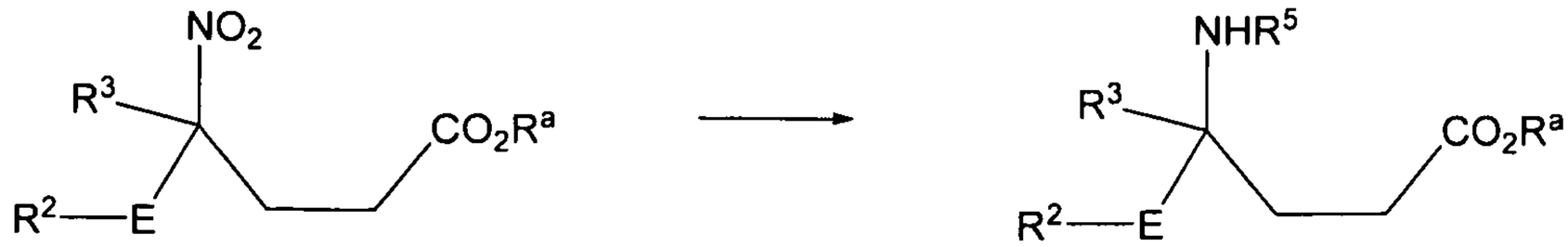
V VI IV

γ-Amino acids of Formula V can be prepared hydrolysis of γ-aminoesters of Formula VII, wherein R^a is lower alkyl, with LiOH, NaOH or KOH.



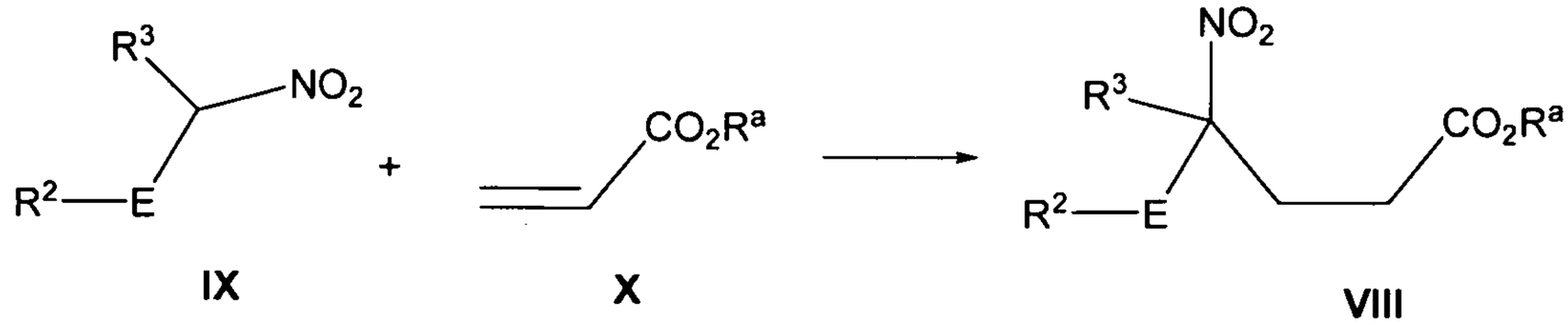
VII V

γ-Aminoesters of Formula VII, wherein R^5 is H, can be prepared by reduction of γ-nitroesters of Formula VIII.



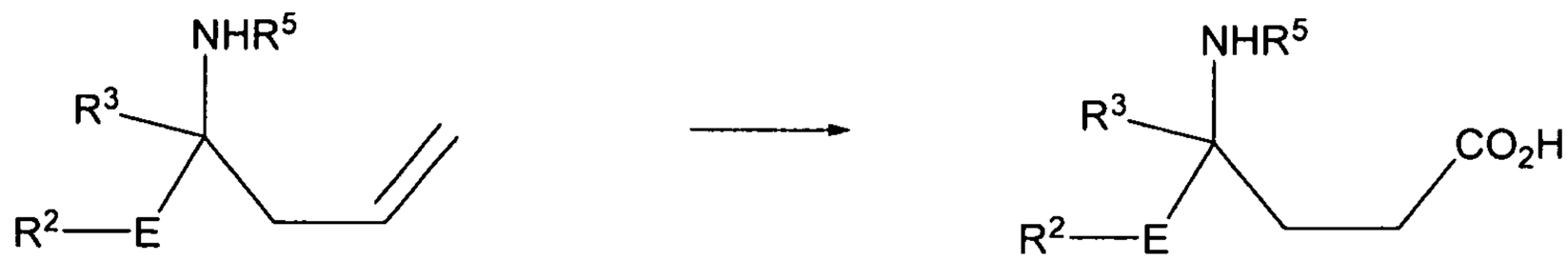
VIII VII

γ-Nitroesters of Formula VIII can be prepared by Michael addition of nitro compounds of Formula IX to acrylate esters of Formula X.



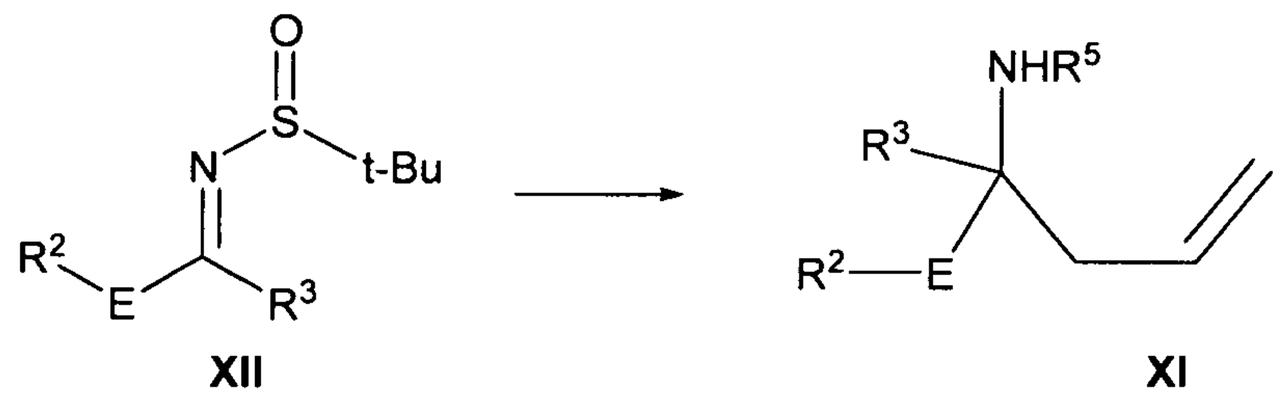
IX X VIII

γ-Aminoacids of Formula V can also be prepared from homoallyl amines of Formula XI by hydroboration using a borane such as disiamylborane, followed by oxidation with, for example, Jones reagent.



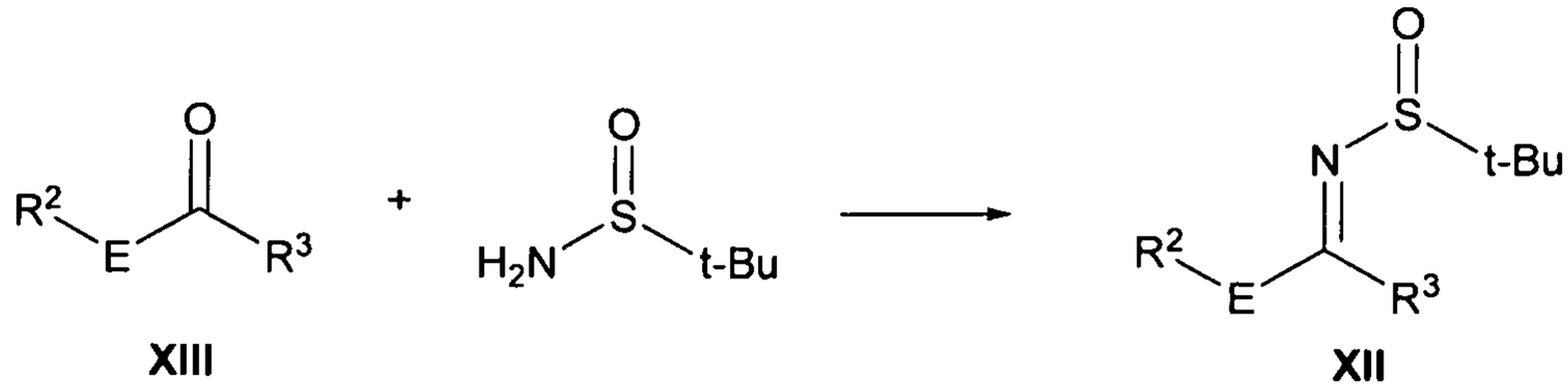
XI V

Homoallyl amines of Formula XI can be prepared by addition of allylmagnesium halides to sulfinylimines of Formula XII, followed by acid treatment to remove the t-butylsulfinyl group.



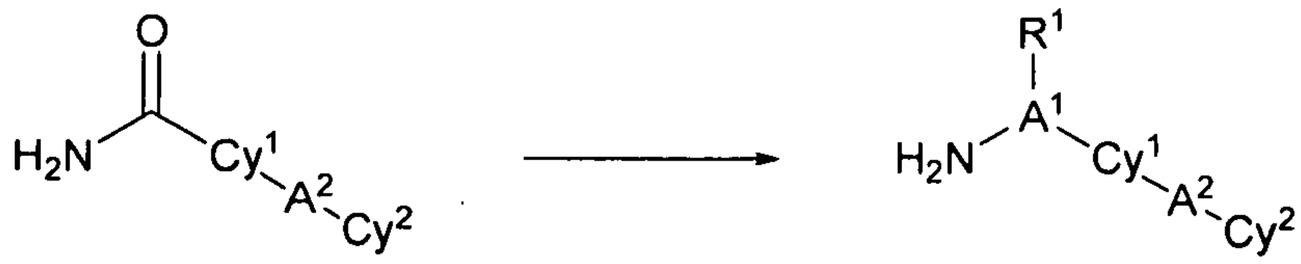
XII XI

Sulfinylimines of Formula XII can be prepared by reaction of ketones of Formula XIII with 2-methylpropane-2-sulfinamide.



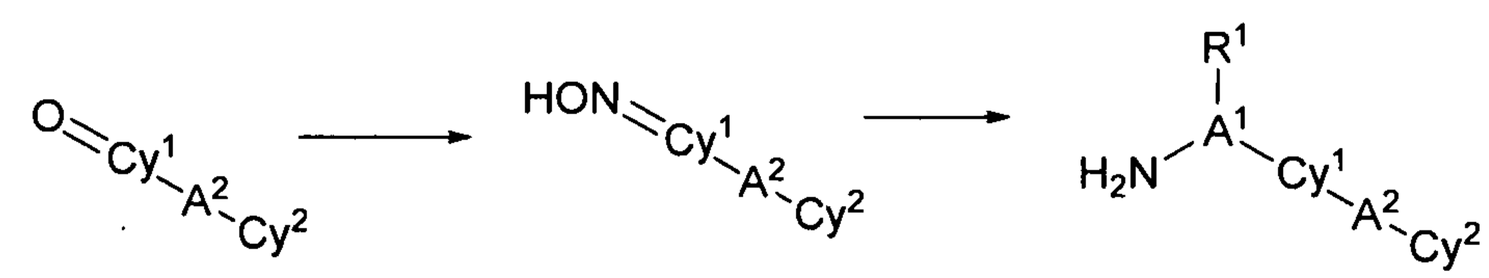
XIII XII

Amine intermediates of Formula VI, wherein A^1 = CH_2 and R^1 is absent, can be prepared by reduction of amides of Formula XIV using a hydride reagent such as BH_3.THF solution, $BH_3.Me_2S$ or $LiAlH_4$ in an inert solvent ethereal such as THF or DME at 20 °C to 100 °C for between 1 h and 48 h:



XIV VI

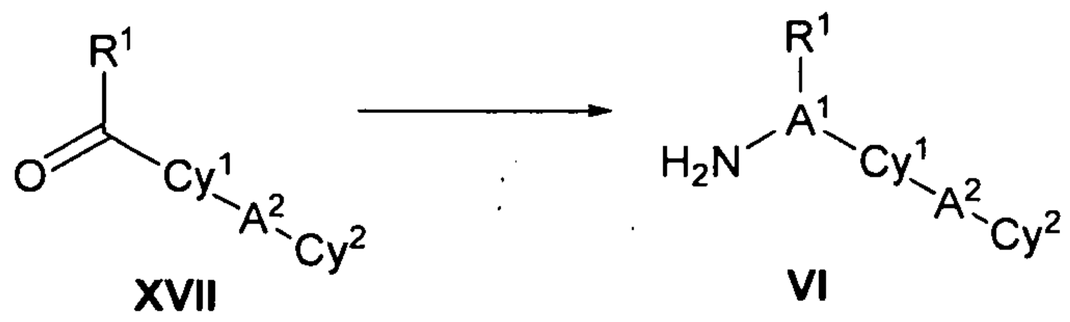
Amine intermediates of Formula VI, wherein A^1 is a bond, R^1 is absent and Cy^1 is not an aromatic or heteroaromatic ring, can be prepared from ketones of formula XV via oximes of Formula XVI or by reductive amination of ketones of Formula XV with ammonia:



XV XVI VI

Methods for the conversion of ketones to oximes are described in Smith, M. B. and March, J. "March's Advanced Organic Chemistry" pp 1194-1195, 5th Edition, Wiley, New York, NY, 2001. Methods for the reduction of oximes to primary amines are described in Smith, M. B. and March, J. "March's Advanced Organic Chemistry" p 1555, 5th Edition, Wiley, New York, NY, 2001. Methods for the reductive amination of ketones are described in Baxter, E. W. and Reitz, A. B. "Organic Reactions" Volume 59, Ed. Overman, L. E., Wiley Interscience, 2002.

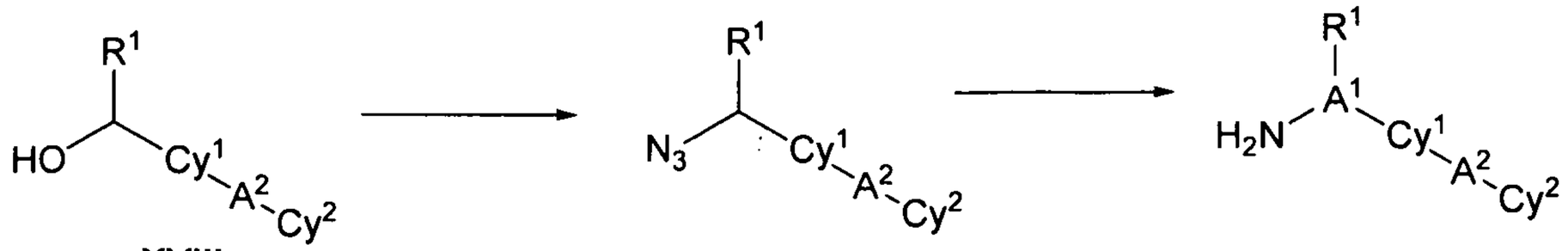
Amine intermediates of Formula VI, wherein A^1 is CH, can be prepared from ketones of Formula XVII by reductive amination with ammonia.



XVII VI

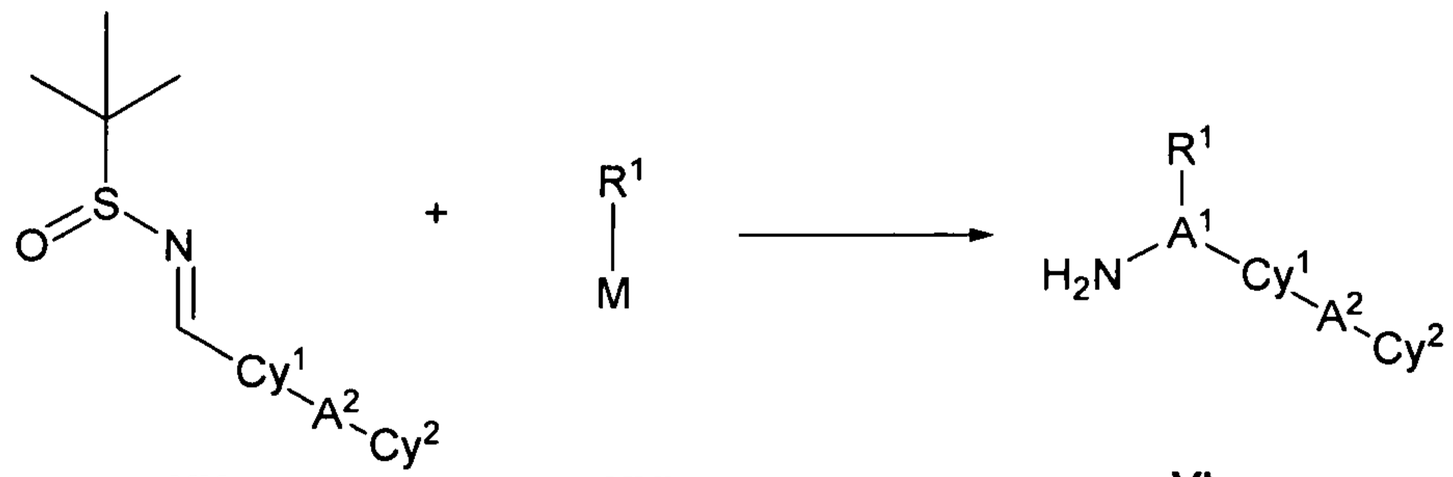
Amine intermediates of Formula VI, wherein A^1 is CH, can be prepared from alcohols of Formula XVIII via azides of Formula XIX. The conversion of alcohols of

Formula XVIII to azides of Formula XIX can be accomplished with, for example, diphenylphosphoryl azide. Reduction of azides of Formula XIX to amines of Formula VI can be effected, for example, by hydrogenation in the presence of a palladium catalyst or by reaction with triphenylphosphine in wet THF.



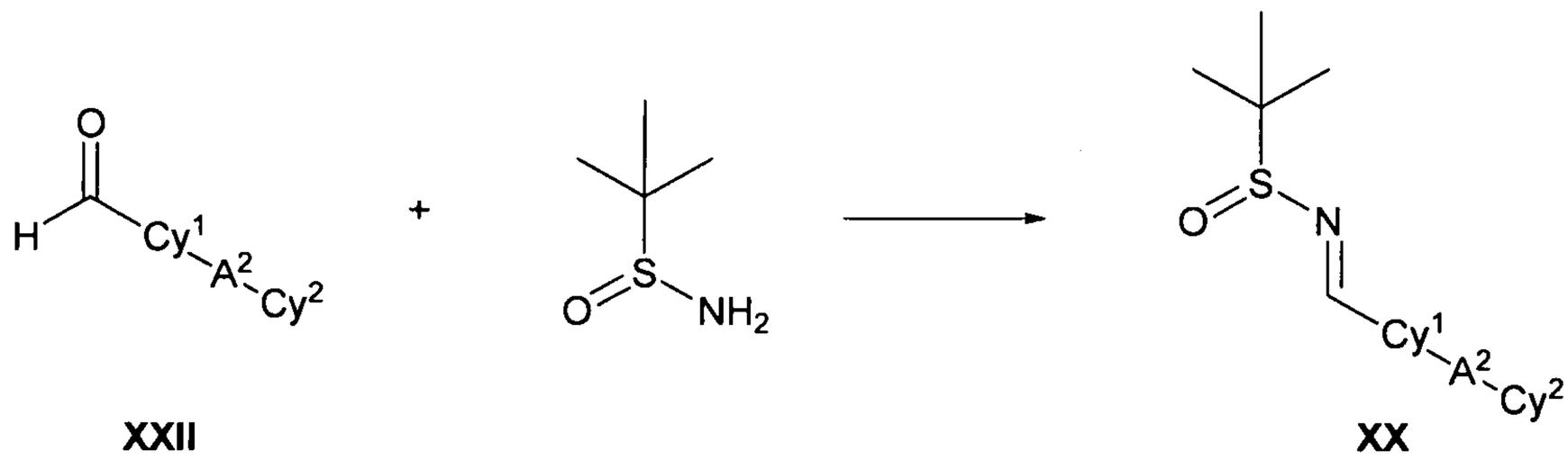
XVIII XIX VI

Amine intermediates of Formula VI, wherein A^1 is CH, can be prepared by reaction of sulfinyl imine intermediates of Formula XX with organometallic reagents of Formula XXI, wherein M is Li, MgCl, MgBr or MgI, followed by treatment with acid to remove the t-butylsulfinyl group.



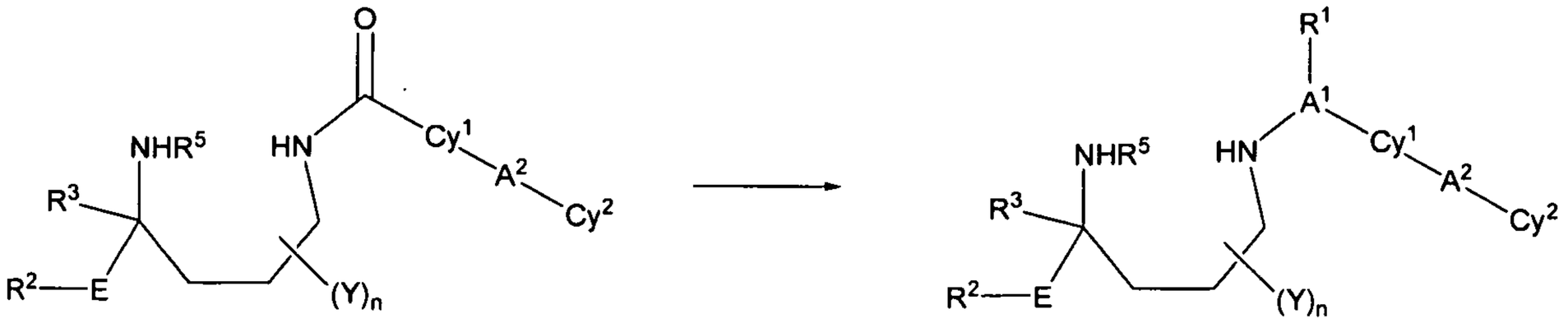
XX XXI VI

Sulfinyl imines of Formula XX can be prepared by treatment of aldehyde intermediates of Formula XXII with 2-methylpropane-2-sulfinamide.



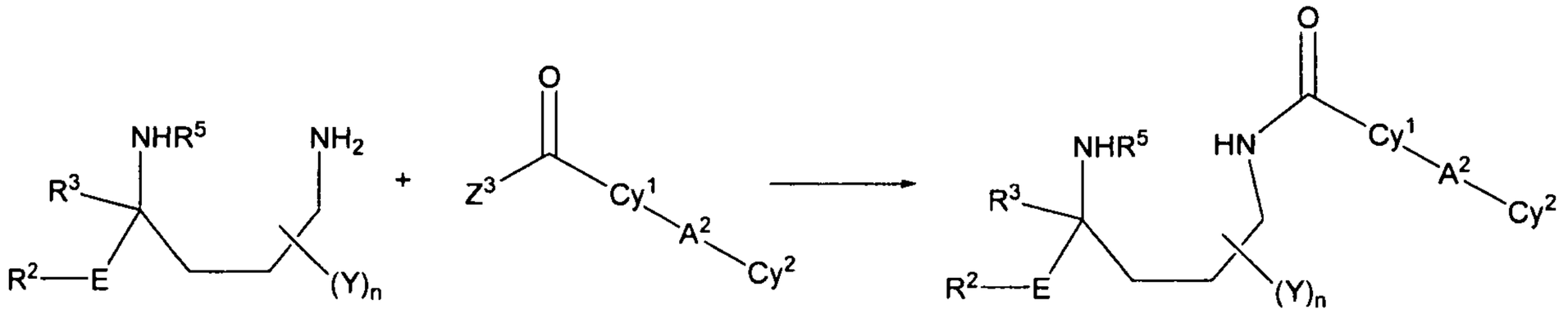
XXII XX

Intermediates of Formula II, wherein A^1 is CH_2 and R^1 is absent, can be prepared by reduction of amide intermediates of formula XXIII using hydride reagents such as BH_3.THF solution, $BH_3.Me_2S$ or $LiAlH_4$ in an inert solvent ethereal such as THF or DME at 20 °C to 100 °C for between 1 h and 48 h:



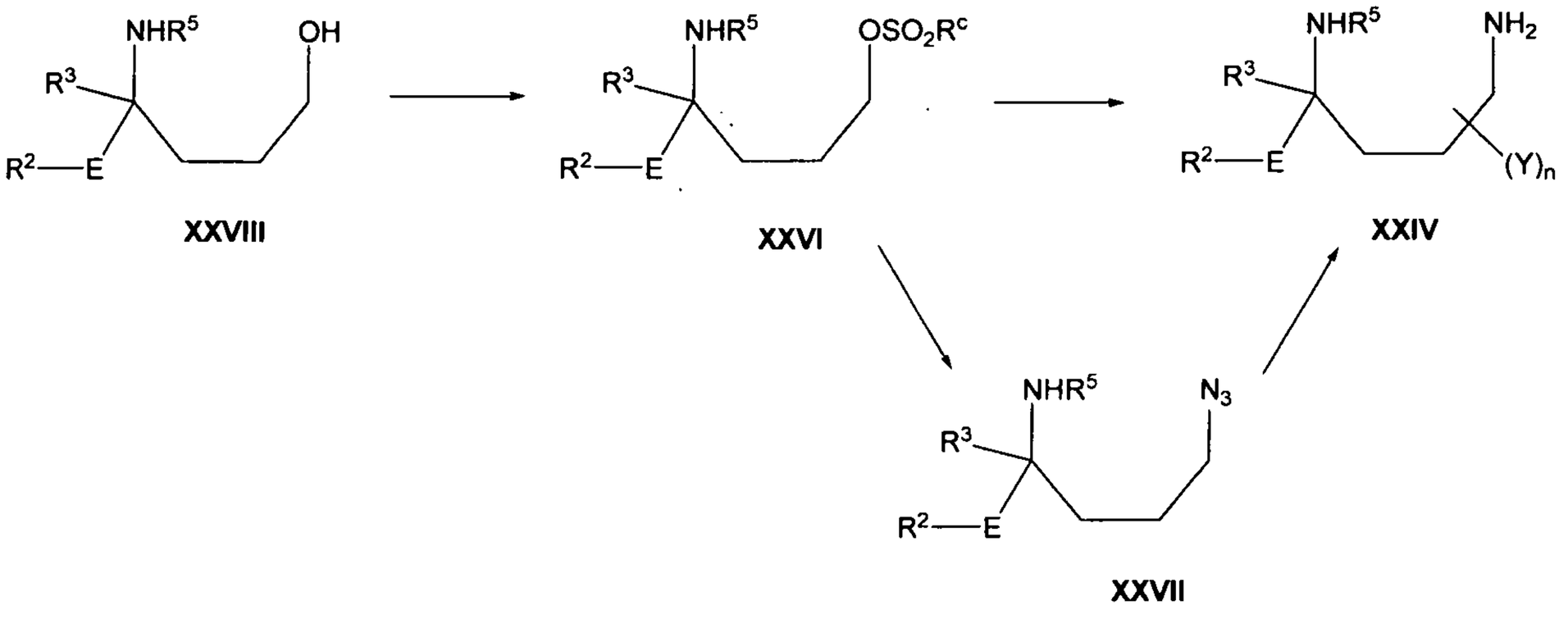
XXIII II

Amide intermediates of Formula XXIII can be prepared by reaction of diamine intermediates of Formula XXIV with activated carboxylic acids of Formula XXV wherein Z^3 is chloride or an activated ester, such as an N-hydroxysuccinimide ester:



XXIV XXV XXIII

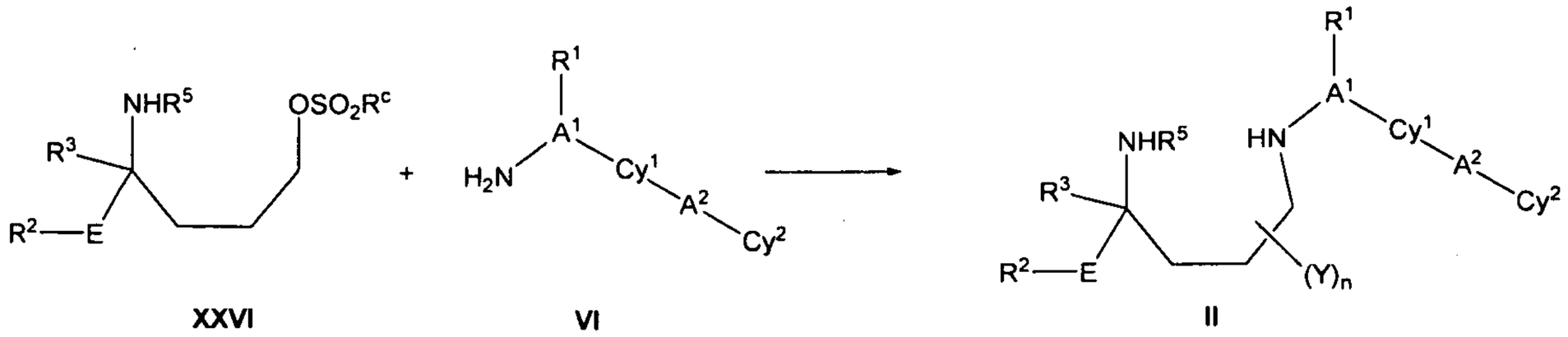
Diamine intermediates of Formula XXIV, wherein n is 0, can be prepared directly by treatment of sulfonate intermediates of Formula XXVI, wherein R^c is for example methyl, trifluoromethyl or p-methylphenyl, with ammonia. Alternatively, sulfonate intermediates of Formula XXVI can be treated with NaN_3 to give azides XXVII, followed by reduction using PPh_3 in wet THF or H_2 gas and a palladium catalyst to give diamines of Formula XXIV.



XXVIII XXVI XXIV

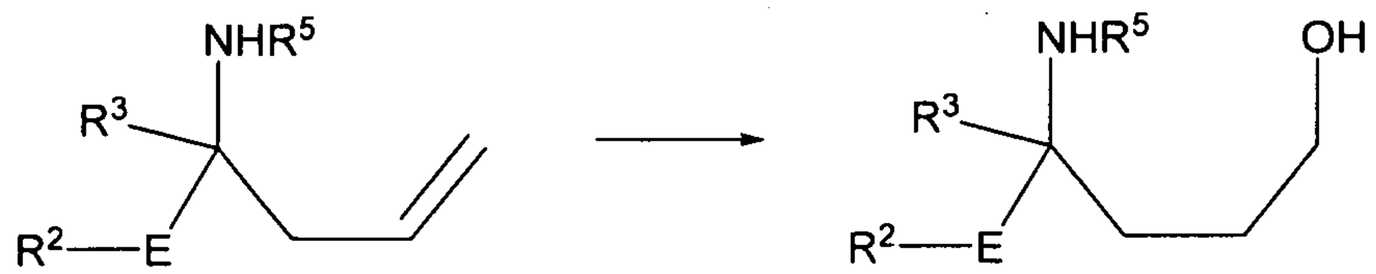
XXVII

Sulfonate intermediates of Formula XXVI are prepared by reaction of, preferably N-protected, aminoalcohol intermediates Formula XXVIII with R^cSO_2Cl or $(R^cSO_2)_2O$. In addition sulfonate intermediates of Formula XXVI can be reacted with amines of Formula VI to afford diamine intermediates of Formula II:



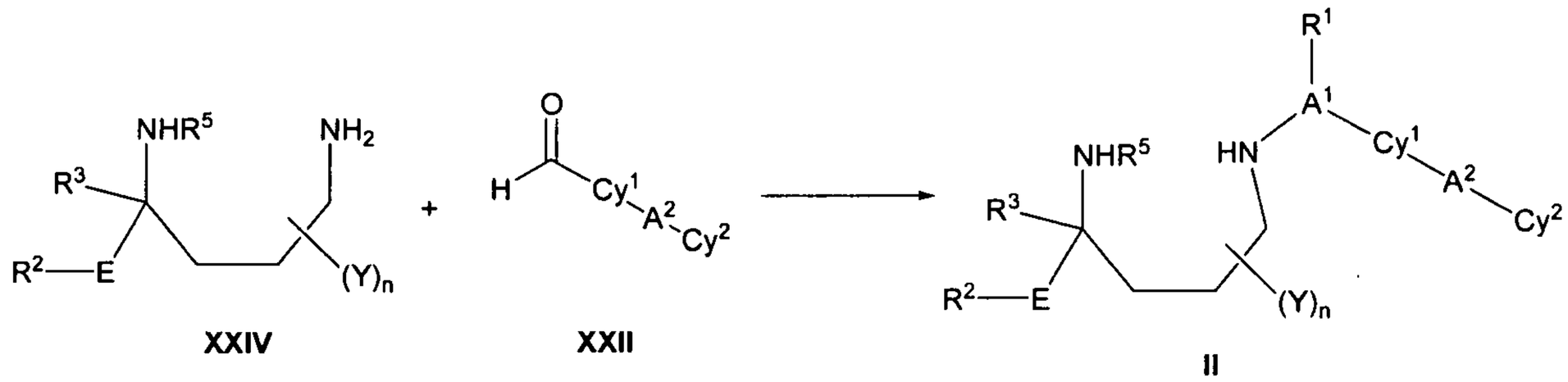
XXVI VI II

Aminoalcohol intermediates of Formula XXVIII can be prepared by hydroboration of homoallylic amines of Formula XI:



XI XXVIII

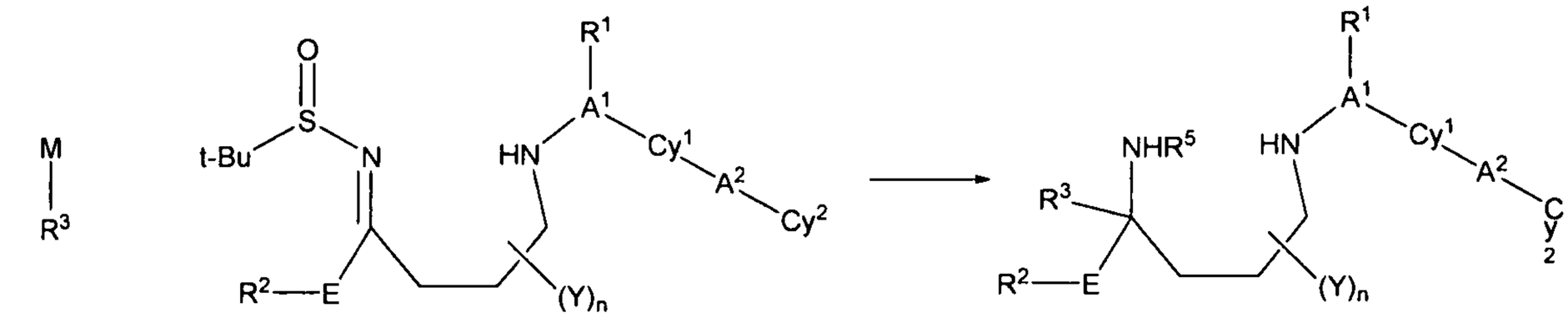
Diamine intermediates of Formula II, wherein A^1 is CH_2 and R^1 is absent, can be prepared by reaction of, preferably protected, diamines of Formula XXIV with aldehydes of Formula XXII in the presence of a reducing agent such as $NaCNBH_3$ or $Na(OAc)_3BH$:



XXIV XXII II

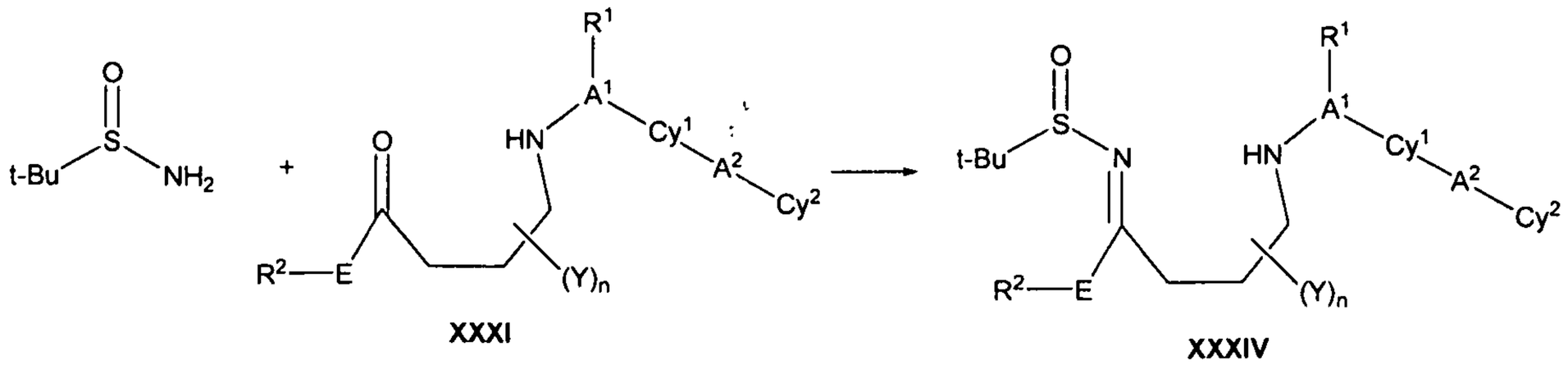
Methods for the reductive amination of aldehydes and ketones are described in Baxter, E. W. and Reitz, A. B. "Organic Reactions" Volume 59, Ed. Overman, L. E., Wiley Interscience, 2002.

Diamines of Formula II can also be prepared by addition of organometallic reagents of Formula XXXIII to sulfinylimines of Formula XXXIV.



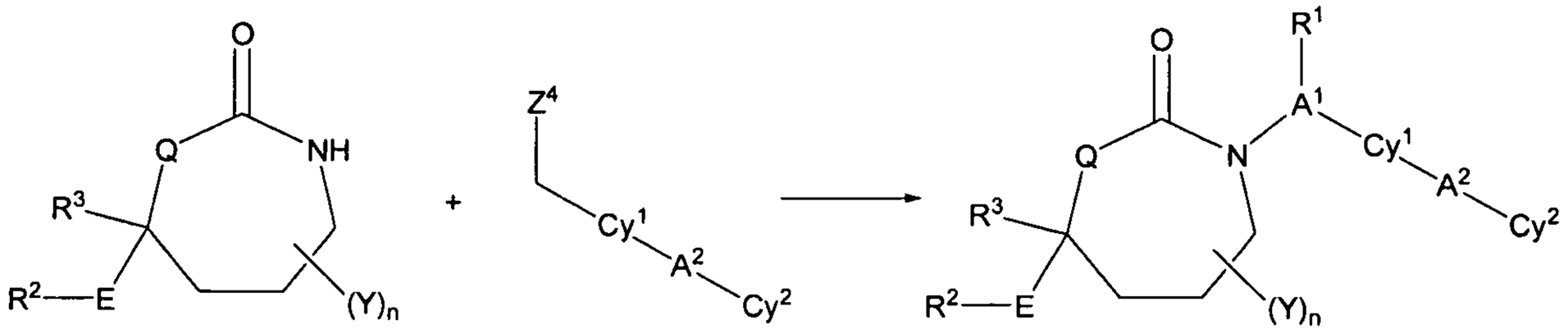
XXXIII XXXIV II

Sulfinylimines of Formula XXXIV can be prepared by condensation of ketoamides of Formula XXXI with 2-methylpropane-2-sulfinamide.



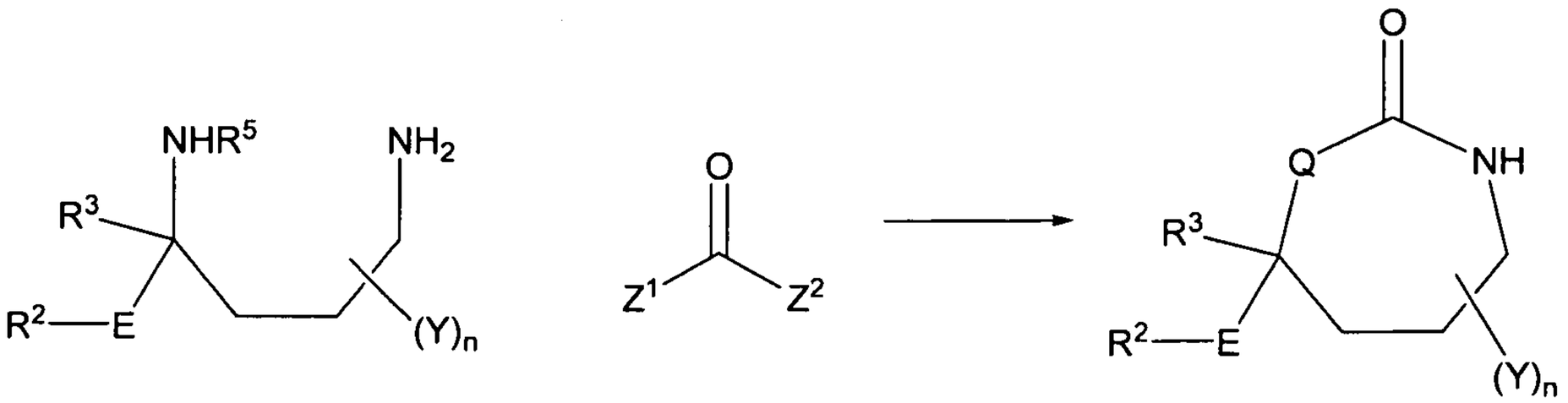
XXXI XXXIV

In a second process compounds of Formula I, wherein R^1 is absent and A^1 is CH_2, can be prepared by reaction of compounds of Formula XXXV, with alkylating agents of Formula XXXVI, wherein Z^4 is a leaving group such as Br, I, OSO_2Me, OSO_2CF_3 or OSO_2Ph, in the presence of a base such as NaH or K_2CO_3:



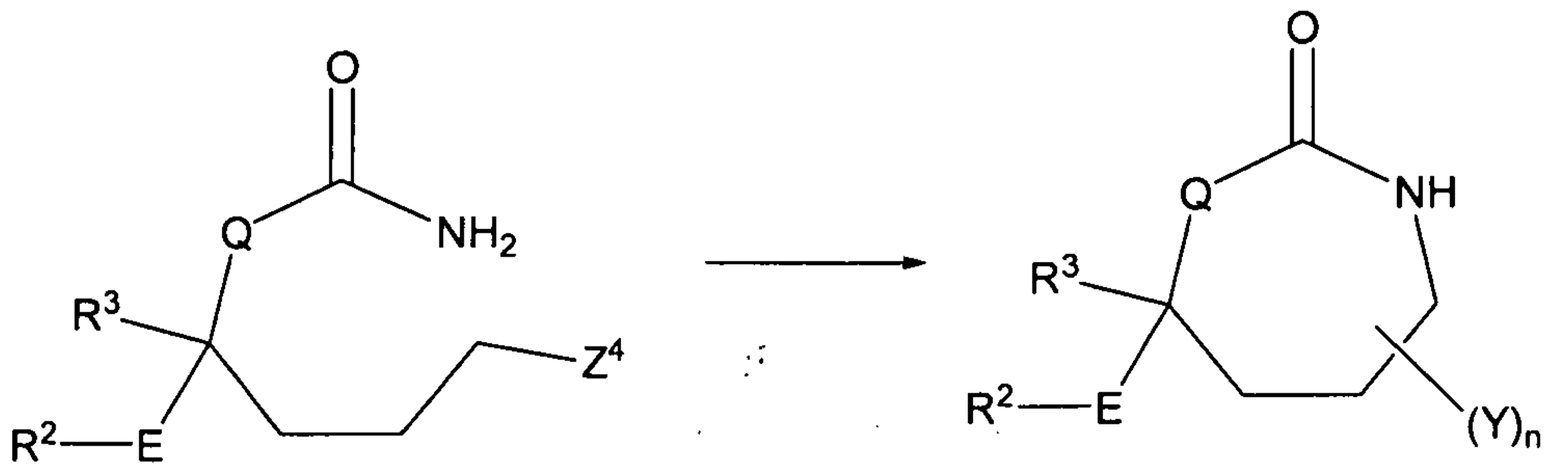
XXXV XXXVI I

Compounds of Formula XXXV, wherein Q is NR^5, can be prepared by treatment of compounds of Formula XXIV with various reagents of Formula III, wherein Z^1 and Z^2 are leaving groups such as chloride, 1-imidazolyl or aryloxide in an inert solvent such as THF, CH_2Cl_2, toluene or MeCN, usually in the presence of an organic or inorganic base such as triethylamine or $NaHCO_3$ respectively, at -10 °C to 120 °C:



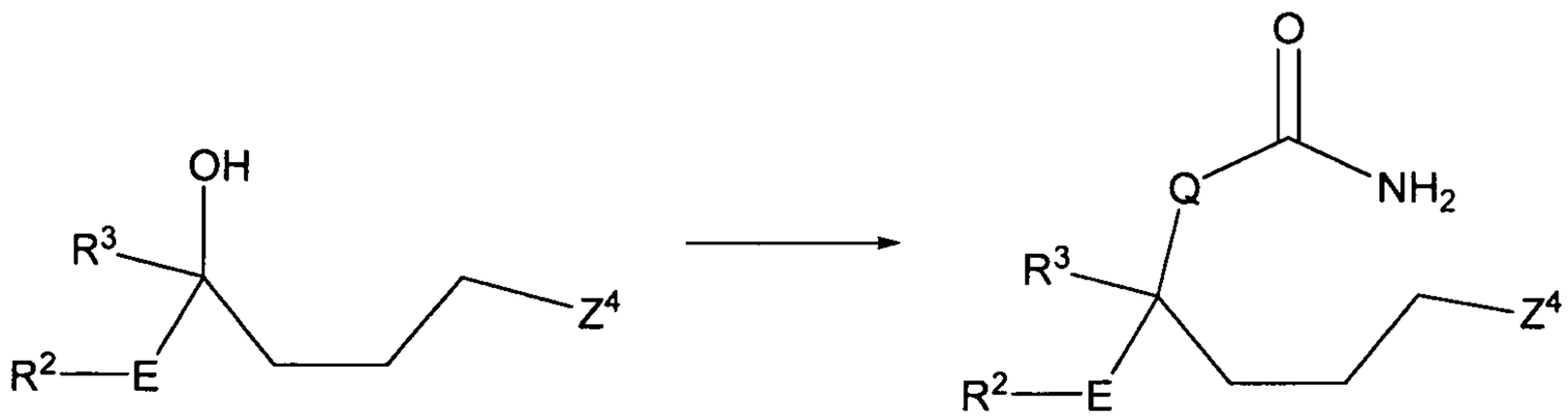
XXIV III XXXV

Compounds of Formula XXXV, wherein n is 0, Q is O or NR^5 and R^5 is (C_1-C_6)alkyl, can be prepared by treatment of intermediates of Formula XXXVII with strong bases, such as sodium hydride, in inert solvents, such as DMF.



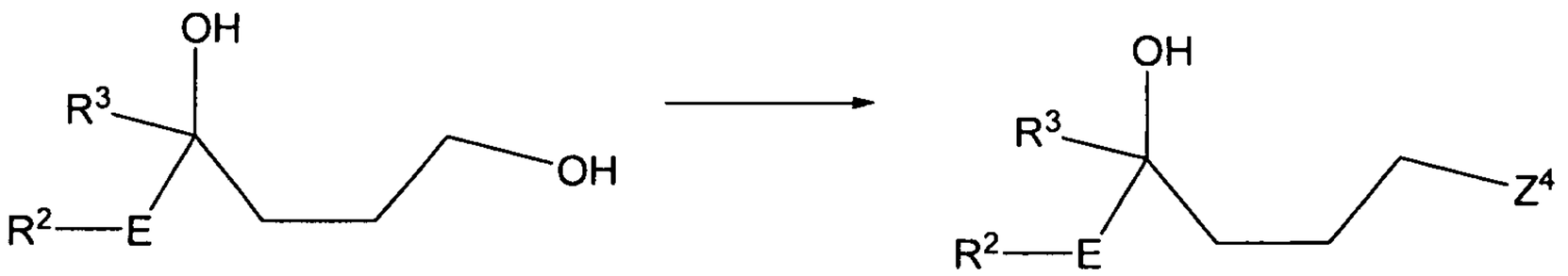
XXXVII XXXV

Intermediates of Formula XXXVII, wherein Q is O, can be prepared from alcohols of Formula XXXVIII by treatment with HNCO, prepared from *in situ* from KNCO and CF_3CO_2H, with Me_3SiNCO or with $Cl_3CC(=O)NCO$.



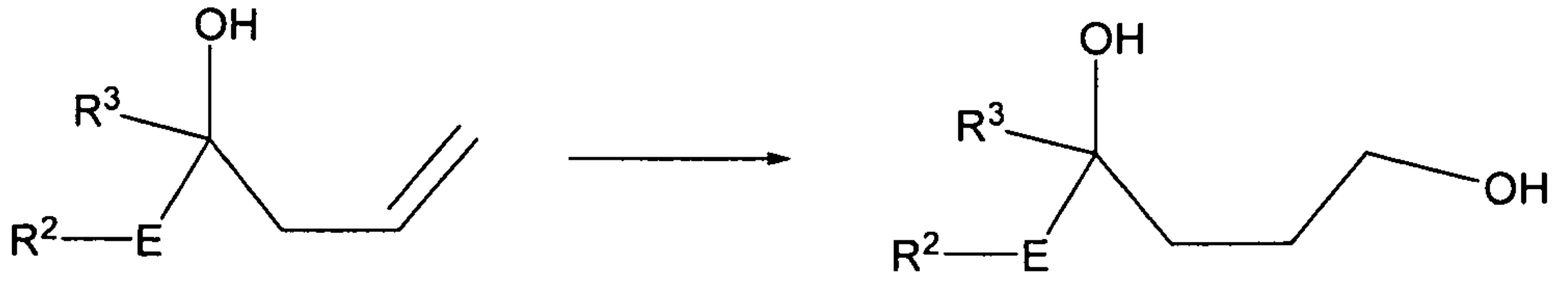
XXXVIII XXXVII

Alcohols of Formula XXXVIII, wherein Z^4 is a sulfonate, such as OSO_2Me, OSO_2CF_3 or OSO_2Ph, can be prepared diols of Formula XXXIX by treatment with a sulfonyl chlorides, such as $MeSO_2Cl$ or $PhSO_2Cl$, or sulfonic anhydrides, such as methanesulfonic anhydride or triflic anhydride.



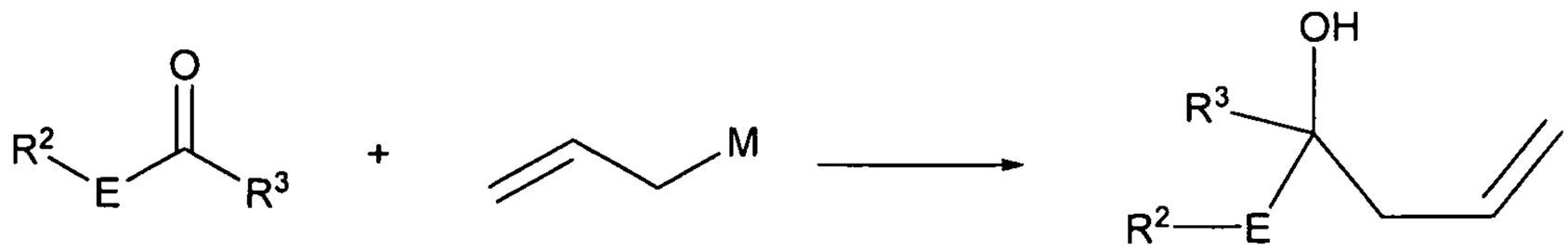
XXXIX XXXVIII

Diols of Formula XXXIX can be prepared by hydroboration of homoallylic alcohols of Formula XL, using, for example diasiamylborane.



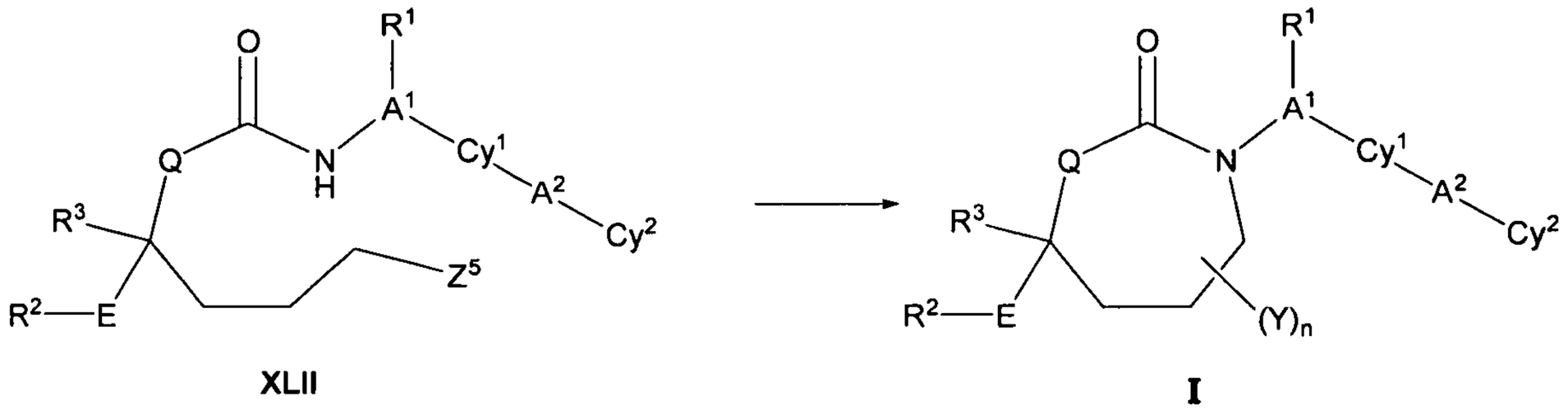
XL XXXIX

Homoallylic alcohols of Formula XL can be prepared from aldehydes or ketones of Formula XIII and allyl organometallic reagents of Formula XLI, wherein M is MgBr, MgCl or $SiMe_3$.



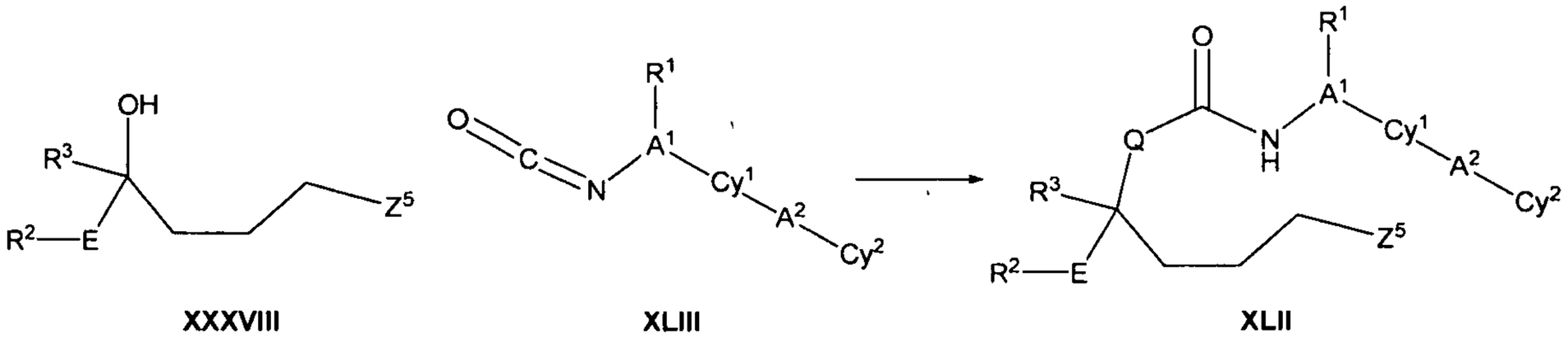
XIII XLI XL

In a third process, compounds of Formula I wherein n is 0, Q is O or NR^5 and R^5 is $(C_1\text{-}C_6)$alkyl, can be prepared by treatment of compounds of Formula XLII, wherein wherein Z^5 is a leaving group such as Cl, Br, I, OSO_2Me, OSO_2CF_3 or OSO_2Ph, with strong bases, such as NaH, in inert solvents, such as DMF.



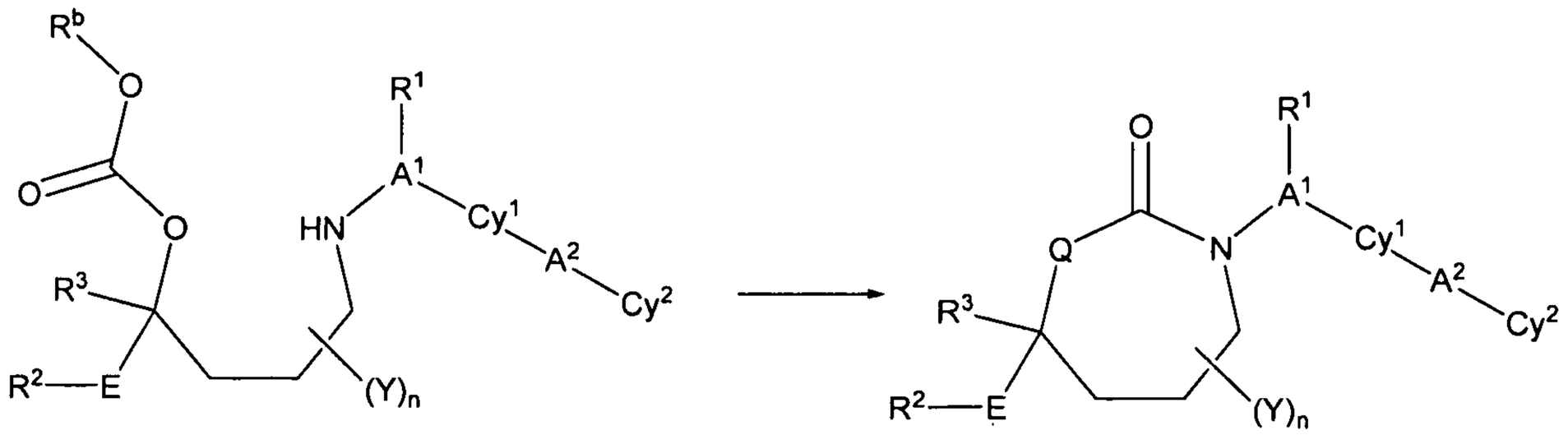
XLII I

Compounds of Formula XLII, wherein Q is O and Z^5 is a sulfonate such as OSO_2Me, OSO_2CF_3 or OSO_2Ph, can be prepared by reaction of intermediates of Formula XXXVIII by treatment with isocyanates of Formula XLIII, in the presence of base, such as NaH or DBU.



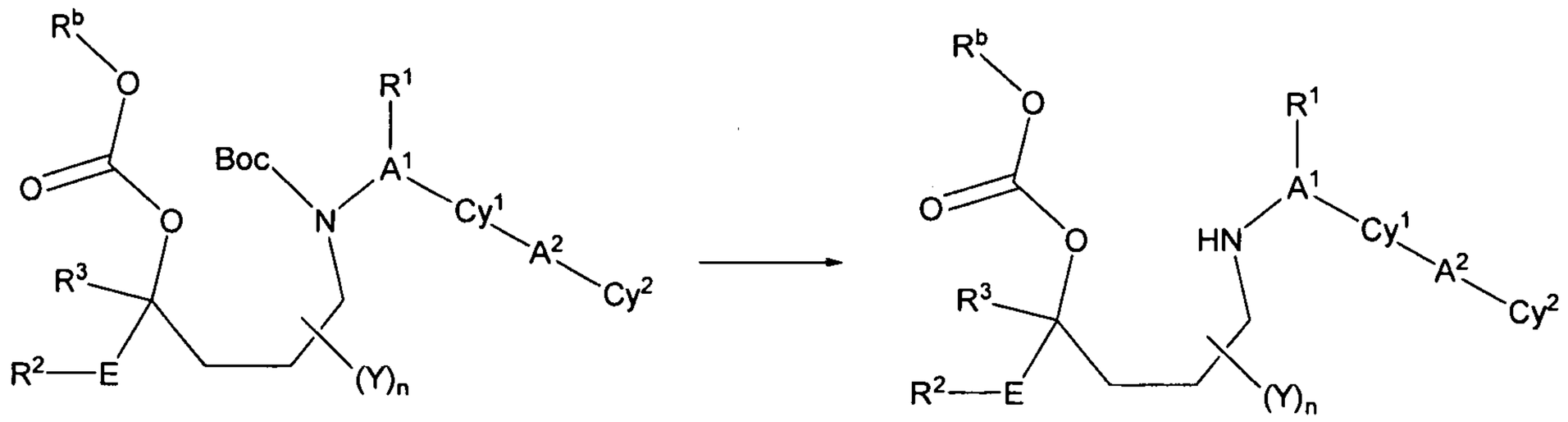
XXXVIII XLIII XLII

In a fourth process, compounds of Formula I, wherein Q is O, can be prepared by subjecting carbonates of Formula XLIV, wherein R^b is lower alkyl or phenyl, to base in an inert solvent at from about 20 °C to about 175 °C.



XLIV I

Carbonates of Formula XLIV can be prepared by deprotection of precursors such as XLV.



XLV XLIV

In a fifth process a compound of Formula I can be prepared from another compound of Formula I. For example:

(1) a compound of Formula I wherein Cy^1 is substituted with bromine or iodine, A^2 is a bond and Cy^2 is hydrogen can be reacted with an optionally substituted aryl or heteroarylboronic acid or ester in the presence of a palladium catalyst to give a compound of Formula I wherein A^2 is a bond and Cy^2 is optionally substituted aryl or heteroaryl.

(2) a compound of Formula I wherein R^1 or R^3 is ω-hydroxy(C_2-C_6)alkyl can be oxidized to a compound of Formula I wherein R^1 or R^3 is ω-carboxy(C_1-C_5)alkyl using Jones reagent.

(3) a compound of Formula I wherein R^1 or R^3 is ω-carboxy(C_1-C_6)alkyl can be coupled with ammonia or a (C_1-C_6)alkylamine using a standard peptide coupling reagent such as EDC to afford a compound of Formula I wherein R^1 or R^3 is ω-$H_2NC(=O)(C_1$-$C_6)$alkyl or ω-{(C_1-C_6)alkylNHC(=O)}(C_1-C_6)alkyl .

(4) a compound of Formula I wherein R^1 or R^3 is ω-hydroxy(C_1-C_6)alkyl can be converted to its methanesulfonate or trifluoromethanesulfonate, treated with sodium azide and reduced to give a compound of Formula I, wherein R^1 or R^3 is ω-amino(C_1-C_6)alkyl.

(5) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with acetic anhydride or acetyl chloride to give a compound of Formula I wherein R^1 or R^3 is {acetylamino}(C_1-C_6)alkyl.

(6) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with methanesulfonyl chloride to give a compound of Formula I wherein R^1 or R^3 is {methanesulfonylamino}(C_1-C_6)alkyl.

(7) a compound of Formula I, wherein R^1 is (C_2-C_6)alkenyl, is hydroborated to afford a compound of Formula I wherein R^1 is hydroxy(C_2-C_6)alkyl,.

(8) a compound of Formula I, wherein R^3 is (C_2-C_6)alkenyl, is hydroborated to afford a compound of Formula I wherein R^3 is hydroxy(C_2-C_6)alkyl.

(9) a compound of Formula I, wherein R^1 is (C_2-C_6)alkenyl, can be reacted with osmium tetroxide and N-methylmorpholine-N-oxide to afford a compound of Formula I wherein R^1 is vicinal dihydroxy(C_2-C_6)alkyl,.

(10) a compound of Formula I, wherein R^3 is (C_2-C_6)alkenyl, can be reacted with osmium tetroxide and N-methylmorpholine-N-oxide to afford a vicinal diol compound of Formula I wherein R^3 is vicinal dihydroxy(C_2-C_6)alkyl,.

(11) a compound of Formula I, wherein R^1 is H_2C=CH(C_0-C_4)alkyl-, can be reacted with ozone followed by $NaBH_4$ to give a compound of Formula I wherein R^1 is ω-hydroxy(C_1-C_5)alkyl.

(12) a compound of Formula I, wherein R^3 is H_2C=CH(C_0-C_4)alkyl-, can be reacted with ozone followed by $NaBH_4$ to give a compound of Formula I wherein R^3 is ω-hydroxy(C_1-C_5)alkyl.

(13) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with an (C_1-C_6)alkyl isocyanate to give a compound of Formula I wherein R^1 or R^3 is (C_1-C_6)alkylaminocarbonylamino(C_1-C_6)alkyl.

(14) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with an (C_1-C_6)alkyl chloroformate to give a compound of Formula I wherein R^1 or R^3 is (C_1-C_6)alkoxycarbonylamino(C_1-C_6)alkyl.

(15) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with chlorosulfonyl isocyanate or sulfamide to give a compound of Formula I wherein R^1 or R^3 is aminosulfonylamino(C_1-C_6)alkyl.

(16) a compound of Formula I wherein R^1 or R^3 is amino(C_1-C_6)alkyl can be reacted with a (C_1-C_6)alkylsulfamoyl chloride to give a compound of Formula I wherein R^1 or R^3 is (C_1-C_6)alkylaminosulfonylamino(C_1-C_6)alkyl.

(17) a compound of Formula I wherein R^1 or R^3 is hydroxy(C_1-C_6)alkyl can be reacted with chlorosulfonyl isocyanate to give a compound of Formula I wherein R^1 or R^3 is aminosulfonyloxy(C_1-C_6)alkyl.

(18) a compound of Formula I wherein R^1 or R^3 is hydroxy(C_1-C_6)alkyl can be reacted with p-nitrophenyl chloroformate, pentafluorophenyl chloroformate or carbonyl diimidazole, followed by ammonia, a (C_1-C_6)alkylamine or a di(C_1-C_6)alkylamine to give a compound of Formula I wherein R^1 or R^3 is aminocarboxy(C_1-C_6)alkyl, (C_1-C_6)alkyl aminocarboxy(C_1-C_6)alkyl or di(C_1-C_6)alkyl aminocarboxy(C_1-C_6)alkyl.

(19) a compound of Formula I wherein R^1 or R^3 is hydroxy(C_1-C_6)alkyl can be reacted with $POCl_3$ to give a compound of Formula I wherein R^1 or R^3 is $(HO)_2P(=O)O(C_1$-$C_6)$alkyl.

(20) a compound of Formula I wherein Cy^1 is substituted with bromine or iodine, A^2 is a bond and Cy^2 is hydrogen can be reacted with a cyclic amine in the presence of a palladium catalyst to give a compound of Formula I wherein A^2 is a bond and Cy^2 is a cyclic amino moiety attached through its nitrogen atom.

(21) a compound of Formula I wherein Q is NR^5 and R^5 is H can be reacted with an (C_1-C_6)alkyl halide in the presence of a strong base such as sodium hydride to afford a compound of Formula I wherein Q is NR^5 and R^5 is (C_1-C_6)alkyl.

(22) a compound of Formula I wherein R^1 or R^3 is ω-$H_2NCO(C_1$-$C_5)$alkyl can be reacted with TFAA in the presence of pyridine to afford a compound of Formula I wherein R^1 or R^3 is ω-cyano(C_1-C_5)alkyl.

(23) a compound of Formula I, wherein R^1 or R^3 is ω-$MeO_2C(C_1$-$C_5)$alkyl can be reacted with at least 2 equivalents of MeMgBr to afford a compound of Formula I, wherein R^1 or R^3 is $HOC(Me)_2(C_1$-$C_5)$alkyl.

(24) a compound of Formula I wherein R^1 or R^3 is ω-hydroxy(C_1-C_6)alkyl can be converted to its methanesulfonate or trifluoromethanesulfonate and reacted with morpholine to give a compound of Formula I, wherein R^1 or R^3 is ω-(4-morpholino)(C_1-C_6)alkyl.

PURIFICATION METHODS

Compounds of the invention can be purified by high pressure liquid chromatography (prep HPLC). Unless otherwise specified, prep HPLC refers to

preparative reverse phase HPLC on a C-18 column eluted with a water/acetonitrile gradient containing 0.01% TFA run on a Gilson 215 system.

LC-MS METHODS

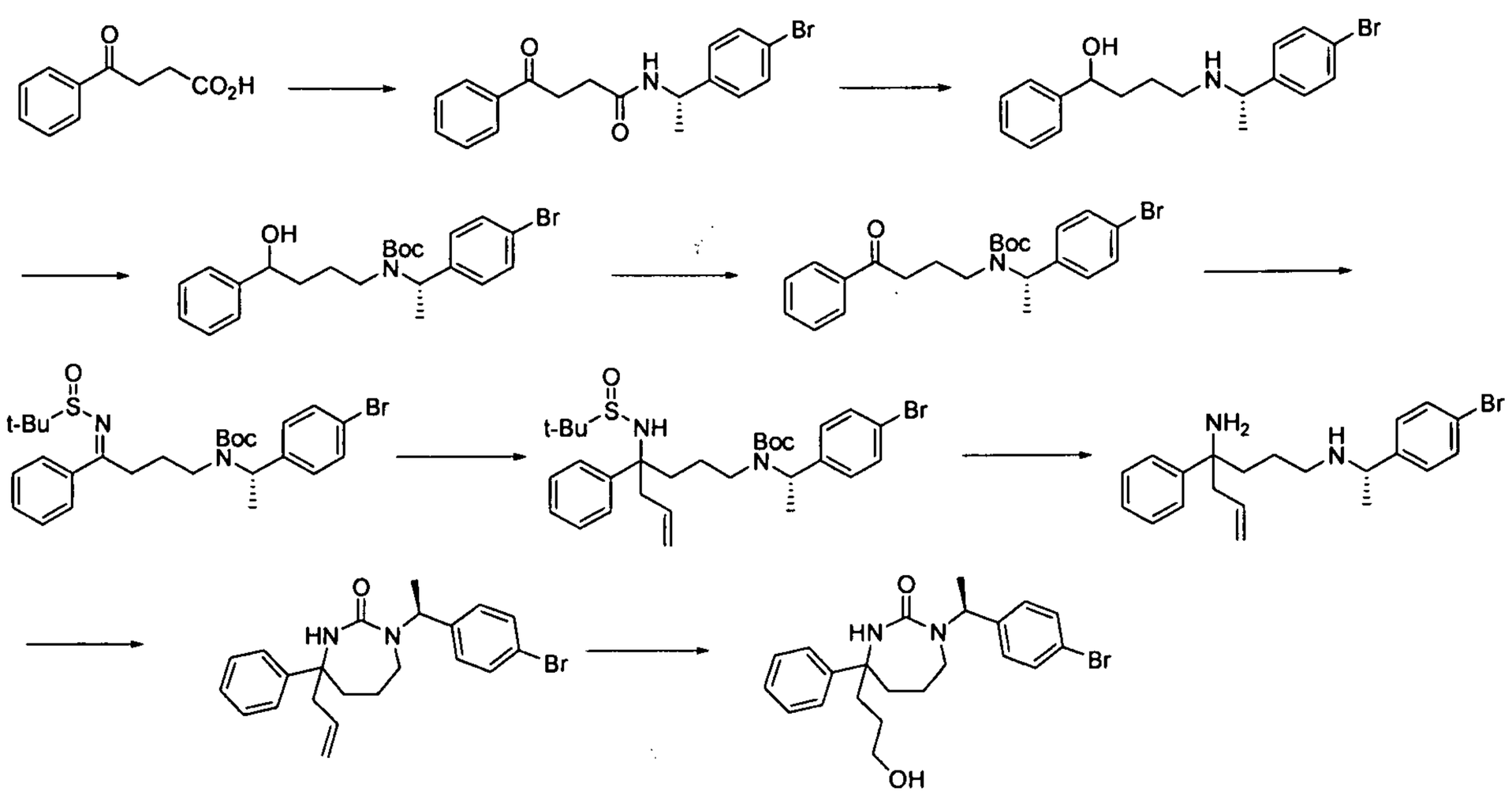
Method 1 [LC-MS (3 min)]

Column: Chromolith SpeedRod, RP-18e, 50 x 4.6 mm; Mobil phase: A: 0.01%TFA/water, B: 0.01%TFA/CH_3CN; Flow rate: 1 mL/min; Gradient:

Time (min)	A%	B%
0.0	90	10
2.0	10	90
2.4	10	90
2.5	90	10
3.0	90	10

EXAMPLE 1

1-((S)-1-(4-bromophenyl)ethyl)-4-(3-hydroxypropyl)-4-phenyl-1,3-diazepan-2-one



Step 1

To a stirred solution of benzoylpropionic acid (2.00 g, 11.2 mmol), (S)-1-(4-bromophenyl)ethanamine (2.25 g, 11.2 mmol), HOBt (1.72 g, 11.2 mmol) and i-Pr_2NEt (2.2 mL, 12.3 mmol) in CH_2Cl_2 (40 mL) was added EDC.HCl (2.37 g, 12.3 mmol). The mixture was stirred at rt for 4 h and diluted with EtOAc (140 mL) and 5%

aq HCl (50 mL). The mixture was filtered and (S)-N-(1-(4-bromophenyl)ethyl)-4-oxo-4-phenylbutanamide (3.80 g, 93%) was collected as a white solid. ^{1}H NMR (d_6-DMSO) δ 1.28 (d, 3H), 2.50 (m, 2H), 3.19 (m, 2H), 4.82 (m, 1H), 7.23 (d, 2H), 7.47 (4H), 7.59 (m, 1H), 7.92 (d, 2H), 8.38 (d, 1H).

Step 2

A 250-mL RBF equipped with a magnetic stirbar was charged with solid (S)-N-(1-(4-bromophenyl)ethyl)-4-oxo-4-phenylbutanamide (2.85 g, 7.9 mmol) and placed in an ice bath. To the stirred solid was added 1.0 M BH_3 in THF (30 mL, 30 mmol). The ice bath was removed and the mixture was stirred at rt for 2.5 h. The mixture was poured into 5% aq HCl (100 mL) and concentrated under reduced pressure to remove the THF. The aqueous residue was basified to pH 14 by portionwise addition of NaOH pellets. The mixture was extracted with CH_2Cl_2 (2 x 100 mL). The combined CH_2Cl_2 extracts were dried over Na_2SO_4. Removal of the solvent afforded crude 4-((S)-1-(4-bromophenyl)ethylamino)-1-phenylbutan-1-ol (2.58 g, 94%) as an oil. LC-MS Method 1 t_R = 1.20 min, m/z = 348, 350.

Step 3

To a stirred solution of crude 4-((S)-1-(4-bromophenyl)ethylamino)-1-phenylbutan-1-ol (2.46 g, 7.1 mmol) in THF (40 mL) was added 10% aq K_2CO_3 (40 mL), followed by di-t-butyl dicarbonate (1.90 g, 8.5 mmol). The mixture was stirred overnight at rt and concentrated to remove THF. The aqueous residue was extracted with EtOAc (2 x 80 mL). The combined EtOAc extracts were washed with brine (40 mL) and dried over $MgSO_4$. Removal of the solvent left tert-butyl (S)-1-(4-bromophenyl)ethyl(4-hydroxy-4-phenylbutyl)carbamate (3.24 g, quant). LC-MS Method 1 t_R = 1.20 min, m/z = 472, 470, 350, 348.

Step 4

To a stirred solution of tert-butyl (S)-1-(4-bromophenyl)ethyl(4-hydroxy-4-phenylbutyl)carbamate (3.24 g, 7.1 mmol) in CH_2Cl_2 (20 mL) at rt was added 15% Dess-Martin periodinane solution in CH_2Cl_2 (23 mL, 10.8 mmol). The mixture was stirred overnight at rt. Satd aq $NaHCO_3$ (50 mL) was added and the mixture was stirred for 10 min. Solid $Na_2S_2O_3$ (5 g) was added and stirring was continued for 1 h. The mixture was extracted with CH_2Cl_2 (2 x 100 mL) and the combined organic layer was washed with brine (35 mL) and dried over Na_2SO_4. Removal of the solvent left an amber oil (3.19 g) which was purified by chromatography on a 40-g silica cartridge

eluted with a 0-100% EtOAc in hexanes gradient to afford (S)-tert-butyl 1-(4-bromophenyl)ethyl(4-oxo-4-phenylbutyl)carbamate (2.32 g, 72%) as a yellow oil. LC-MS Method 1 t_R = 2.40 min, m/z = 470, 468, 348, 346.

Step 5

A stirred mixture of (S)-tert-butyl 1-(4-bromophenyl)ethyl(4-oxo-4-phenylbutyl)carbamate (2.16 g, 4.84 mmol), t-BuSONH$_2$ (586 mg, 4.84 mmol), $Ti(OEt)_4$ (2.21 g, 9.67 mmol) and dry THF (30 mL) was heated at reflux for 24 h. The mixture was concentrated and the residue was diluted with EtOAc (90 mL) and brine (30 mL). The mxiture was filtered through Celite and the organic layer of the filtrate was separated, washed with brine (20 mL) and dried over Na_2SO_4. Removal of the solvent afforded a yellow oil (2.39 g) which was purified by chromatography on silica gel to afford tert-butyl (S)-1-(4-bromophenyl)ethyl(4-(tert-butylsulfinylimino)-4-phenylbutyl)carbamate (1.35 g, 51%) as a yellow solid. LC-MS (3 min) t_R = 2.45 min, m/z = 551, 549.

Step 6

A stirred solution of tert-butyl (S)-1-(4-bromophenyl)ethyl(4-(tert-butylsulfinylimino)-4-phenylbutyl)carbamate (926 mg, 1.69 mmol) in dry THF (25 mL) was cooled in a dry ice/i-PrOH bath and 1 M allylmagnesium bromide (4.2 mL, 4.2 mmol) was added dropwise over 2 min. The mixture was stirred in the cooling bath for 3 h, diluted with satd aq NH_4Cl (50 mL) and extracted with EtOAc (2 x 50 mL). The combined EtOAc extracts were washed with brine (15 mL), dried over Na_2SO_4 and concentrated to afford tert-butyl (S)-1-(4-bromophenyl)ethyl(4-(1,1-dimethylethylsulfinamido)-4-phenylhept-6-enyl)carbamate (990 mg, 99%) as an oil. LC-MS (3 min) t_R = 2.47 min, m/z = 593, 591.

Step 7

To an ice-cold, stirred solution of tert-butyl (S)-1-(4-bromophenyl)ethyl(4-(1,1-dimethylethylsulfinamido)-4-phenylhept-6-enyl)carbamate (990 mg, 1.67 mmol) in CH_2Cl_2 (5 mL) was added 4 M HCl in dioxane (10 mL, 40 mmol). The mixture was stirred overnight at rt and concentrated to afford an off-white solid (940 mg). The solid was redissolved in 5% aq HCl (25 mL), washed with ether (75 mL) and basified with NaOH. The basic aqueous solution was extracted with CH_2Cl_2 (2 x 60 mL). The combined CH_2Cl_2 extracts were dried over Na2SO4 and concentrated to afford N^1-

((S)-1-(4-bromophenyl)ethyl)-4-phenylhept-6-ene-1,4-diamine (522 mg, 80%) as an oil. LC-MS (3 min) t_R = 0.97 min, m/z = 389, 387.

Step 8

To a stirred, ice-cold solution of N^1-((S)-1-(4-bromophenyl)ethyl)-4-phenylhept-6-ene-1,4-diamine (284 mg, 0.73 mmol) in CH_2Cl_2 (50 mL) was added i-Pr_2NEt (0.39 mL, 2.2 mmol), followed by a solution of triphosgene (72 mg, 0.24 mmol) in CH_2Cl_2 (4 mL). The mixture was allowed to warm to rt and stirred overnight. The mixture was concentrated and the residue was taken up in ether (90 mL) and 5% aq HCl (20 mL). The organic layer was separated, washed with brine, dried over Na_2SO_4 and concentrated to leave a 1:1 mixture of the diastereomers of 4-allyl-1-((S)-1-(4-bromophenyl)ethyl)-4-phenyl-1,3-diazepan-2-one (292 mg). This material was combined with product from another similar reaction (total weight 554 mg). Chromatography on a 40-g silica gel cartridge eluted with a 0-60% EtOAc in hexanes gradient afforded the two diastereomers of 4-allyl-1-((S)-1-(4-bromophenyl)ethyl)-4-phenyl-1,3-diazepan-2-one.

Isomer 1 (160 mg, 29%): LC-MS (3 min) t_R = 2.20 min, m/z = 415, 413. ^1H NMR ($CDCl_3$) [*selected resonances*] 1.22 (d, 3H), 5.51 (q, 1H).

Isomer 2 (154 mg, 28%): LC-MS (3 min) t_R = 2.20 min, m/z = 415, 413. ^1H NMR ($CDCl_3$) 1.15 (m, 1H), 1.39 (m, 1H), 1.43 (d, 3H), 1.84 (m, 1H), 2.40 (m, 2H), 2.45 (m, 1H), 2.78 (m, 2H), 4.99 (s, 1H), 4.18 (m, 2H), 5.26 (q, 1H), 5.43 (m, 1H), 6.62 (d, 2H), 7.18 (d, 2H), 7.28 (m, 1H), 7.39 (m, 4H).

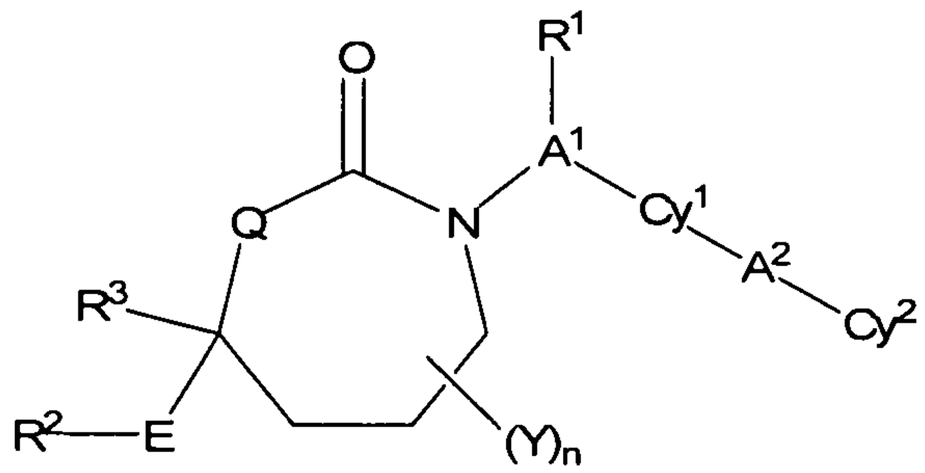
Step 9

A stirred solution of 4-allyl-1-((S)-1-(4-bromophenyl)ethyl)-4-phenyl-1,3-diazepan-2-one isomer 2 (70 mg, 0.17 mmol) in dry THF (2 mL) was cooled in an ice bath and 0.5 M disiamylborane (2 mL, 1.0 mmol) was added dropwise over 2 min. The ice bath was allowed to melt and the mixture was stirred overnight at rt. Water (5 mL) was added, followed by solid $NaBO_3.H_2O$ (180 mg, 1.8 mmol). The mixture was stirred at rt for 2 h and concentrated. The aqueous residue was extracted with EtOAc (2 x 60 mL). The combined EtOAc extracts were dried over Na_2SO_4 and concentrated to afford an oil (94 mg). Preparative HPLC afforded 1-((S)-1-(4-bromophenyl)ethyl)-4-(3-hydroxypropyl)-4-phenyl-1,3-diazepan-2-one (47 mg, 64%) as an oil. LC-MS (16 min) t_R = 8.55 min, m/z = 433, 431. ^1H NMR ($CDCl_3$) 1.23 (m, 1H), 1.44 (d, 3H), 1.52 (m, 3H), 1.81 (m, 2H), 1.95 (m, 1H), 2.39 (m, 1H), 2.80 (m,

2H), 3.57 (m, 2H), 4.38 (1H), 5.30 (q, 1H), 5.90 (1H), 6.68 (d, 2H), 7.23 (d, 2H), 7.33 (m, 1H), 7.40 (4H).

PROPHETIC COMPOUND TABLES

TABLE 1



I

n = 0, Q = O

Prophetic Example No.	A^1-R^1	Cy^1	A^2	Cy^2	E	R^2	R^3
1a	bond	3-Me-Ph	bond	H	bond	Ph	Me
2a	bond	3-Br-Ph	bond	H	bond	Ph	Me
3a	bond	1,3-C_6H_4	bond	Ph	bond	Ph	Me
4a	bond	1,3-C_6H_4	bond	2-Cl-Ph	bond	Ph	Me
5a	bond	1,3-C_6H_4	bond	2-NC-Ph	bond	Ph	Me
6a	CH	1,3-C_6H_4	bond	2-MeO-Ph	bond	Ph	Me
7a	bond	1,3-C_6H_4	bond	2,6-diCl-Ph	bond	Ph	Me
8a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	Me
9a	bond	1,3-C_6H_4	bond	3-Cl-Ph	bond	Ph	Me
10a	bond	1,3-C_6H_4	bond	3-F-Ph	bond	Ph	Me
11a	bond	1,3-C_6H_4	bond	2,5-diF-Ph	bond	Ph	Me
12a	bond	1,3-C_6H_4	bond	3,5-diF-Ph	bond	Ph	Me
13a	bond	1,3-C_6H_4	bond	4-F-Ph	bond	Ph	Me
14a	bond	1,3-C_6H_4	bond	2-F-Ph	bond	Ph	Me
15a	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$

16a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)CH_2$
17a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
18a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	allyl
19a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2$
20a	bond	1,3-(4-F)C_6H_3	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
21a	bond	1,3-(4-F)C_6H_3	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
22a	bond	1,3-C_6H_4	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
23a	bond	1,3-C_6H_4	bond	2,6-diCl-Ph	bond	Ph	$HOCH_2CH_2$
24a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$H_2NC(=O)CH_2$
25a	CH	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
26a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
27a	bond	1,3-C_6H_4	bond	Ph	bond	3-Cl-Ph	Me
28a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	2-pyridyl	Me
29a	CHMe	Ph	bond	H	bond	Ph	Me
30a	CHMe	3-MeO-Ph	bond	H	bond	Ph	Me
31a	CHMe	4-MeO-Ph	bond	H	bond	Ph	Me
32a	CHMe	Ph	bond	H	bond	2-Me-Ph	Me
33a	CHMe	Ph	bond	H	bond	4-Me-Ph	Me
34a	CHMe	Ph	bond	H	bond	4-MeS-Ph	Me
35a	CHMe	Ph	bond	H	bond	4-F-Ph	allyl
36a	bond	1,3-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
37a	CHMe	Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
38a	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$MeSO_2NHCH_2CH_2$
39a	bond	1,3-(4-F)C_6H3	bond	2-Cl-4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
40a	bond	1,3-C_6H_4	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
41a	bond	2,6-pyridyl	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
42a	bond	2,6-pyridyl	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
43a	bond	2,6-pyridyl	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
44a	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
45a	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
46a	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2$

47a	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
48a	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
49a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	allyl
50a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	allyl
51a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
52a	CHMe	Ph	bond	H	bond	4-F-Ph	vinyl
53a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
54a	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
55a	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
56a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
57a	CHMe	c-hex	bond	H	bond	4-F-Ph	allyl
58a	CHMe	c-hex	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
59a	CHMe	1,4-C_6H_4	bond	c-Pr	bond	4-F-Ph	allyl
60a	CHMe	4-MeO_2C-Ph	bond	H	bond	4-F-Ph	allyl
61a	CHMe	1,3-C_6H_4	bond	c-Pr	bond	4-F-Ph	$HOCH_2CH_2CH_2$
62a	CHMe	4-MeO_2C-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
63a	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	allyl
64a	bond	2,6-(5-Cl)-pyridyl	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
65a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2CH_2$
66a	bond	2,6-(5-Cl)-pyridyl	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
67a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
68a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCH(OH)CH_2$
69a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeC(=O)CH_2$
70a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOC(Me)_2CH_2$
71a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeOCH_2CH_2$
72a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)NHCH_2CH_2$
73a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
74a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
75a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCOCH_2CH_2$
76a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)CH_2CH_2$
77a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCONHCH_2CH_2$

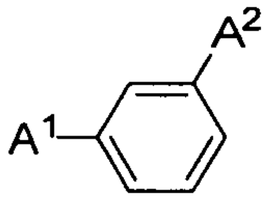
78a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)OCH_2CH_2$
79a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NSO_2NHCH_2CH_2$
80a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NSO_2OCH_2CH_2$
81a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$(HO)_2P(=O)OCH_2CH_2$
82a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2C(=O)NHCH_2CH_2$
83a	CHMe	4-$HOCH_2$-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
84a	CHMe	4-$HOC(Me)_2$-Ph	bond	H	bond	4-F-Ph	allyl
85a	CHMe	4-Br-Ph	bond	H	bond	2-thienyl	allyl
86a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
87a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	allyl
88a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
89a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	HOCH2CH2
90a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	allyl
91a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
92a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$MeCH(OH)CH_2$
93a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
94a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
95a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$MeCH(OH)CH_2$
96a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
97a	CHMe	Ph	bond	2,4-diF-Ph	bond	4-F-Ph	$NCCH_2CH_2$
98a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
99a	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
100a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOC(=O)CH_2CH_2$
101a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2NHCH_2CH_2$
102a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH2C(=O)NHCH_2CH_2$
103a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	MeOC(=O)NHCH2CH2
104a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(4-morpholino)ethyl
105a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$EtNHCONHCH_2CH_2$
106a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=NCN)NHCH_2CH_2$
107a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$
108a	CH2Me	4-Cl-Ph	bond	H	bond	i-Pr	$HOCH_2CH_2CH_2$

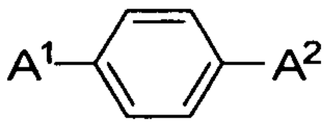
109a	CH2Me	4-Me-Ph	bond	H	bond	4-F-Ph	allyl
110a	CH2Me	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH_2$
111a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	allyl
112a	CHMe	4-$HOCH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
113a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
114a	CHMe	4-Cl-Ph	bond	H	bond	4-F-Ph	allyl
115a	CHMe	c-hex	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
116a	CHMe	4-$HOCH_2CH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
117a	CHMe	4-$MeOCH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
118a	CHMe	4-Br-Ph	bond	H	bond	i-Pr	$HOCH_2CH_2CH_2$
119a	CHMe	4-Cl-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
120a	CH2Me	4-Cl-Ph	bond	H	bond	4-F-Ph	MeCH(OH)CH2
121a	CHMe	4-Br-Ph	bond	H	bond	Ph	allyl
122a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$HOCH_2CH_2$
123a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
124a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH_2$
125a	bond	1-(*t*-BuOC(=O))pyrrolidin-3-yl	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
126a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH_2$
127a	CHMe	1,4-C_6H_4	bond	4-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
128a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
129a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH_2CH_2$
130a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2$
131a	CHMe	1,4-C_6H_4	bond	2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
132a	CHMe	1,4-C_6H_4	bond	4-morpholinyl	bond	4-F-Ph	allyl
133a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2$
134a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$NCCH_2CH_2$
135a	CHEt	4-Br-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
136a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
137a	CHMe	1,4-C_6H_4	bond	1-oxo-3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
138a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH(OH)CH_2$
139a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$MeCH(OH)CH_2$

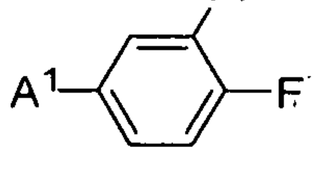
140a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
141a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	Pr
142a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
143a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2CH_2CH_2$
144a	CHMe	1,4-C_6H_4	bond	5-Me-1,3,4-thiadiazol-2-yl	bond	4-F-Ph	allyl
145a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
146a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	$HOCH_2CH2$
147a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$H_2NCOCH_2CH_2$
148a	CHMe	1,4-C_6H_4	bond	2-MeO-5-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
149a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$H_2NCOCH_2CH_2$
150a	CHEt	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
151a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOC(Me)_2CH_2$
152a	CHEt	4-Br-Ph	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
153a	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
154a	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
155a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$NCCH_2$
156a	CHMe	1,4-C_6H_4	bond	2,4-diMe-5-thiazolyl	bond	4-F-Ph	allyl
157a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
158a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2CH_2$
159a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	3-F-Ph	$HOCH_2CH_2CH_2$
160a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOC(Me)_2CH_2CH_2$
161a	CHMe	1,4-C_6H_4	bond	5-MeCO-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
162a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$H_2NCOCH_2CH_2$
163a	CHMe	1,4-C_6H_4	bond	5-(H_2NCHMe)-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
164a	CHEt	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
165a	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
166a	CHMe	1,4-C_6H_4	bond	5-(HOCHMe)-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
167a	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
168a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2CH_2CH_2$
169a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHCH_2CH_2$
170a	CHMe	1,4-C_6H_4	bond	3-(CF_3)-1-pyrazolyl	bond	4-F-Ph	allyl

171a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOC(Me)_2CH_2CH_2$
172a	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
173a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSCH_2CH_2$
174a	CHMe	Ph	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH_2$
175a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)OCH_2CH_2$
176a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2OCH_2CH_2$
177a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(1-imidazolyl)ethyl
178a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCONMeCH_2CH_2$
179a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$MeSO_2NHCH_2CH_2CH_2$
180a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH_2CH_2$
181a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)OCH_2CH_2CH_2$
182a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(1-aminoimidazol-1-yl)ethyl
183a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)NHCH_2CH_2CH_2$
184a	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH(OH)CH_2$
185a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH(OH)CH_2$
186a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$MeSO_2NMeCH_2CH(OH)CH_2$
187a	CHMe	1,4-C_6H_4	bond	6-CF_3-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
188a	CHMe	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
189a	CHMe	3-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
190a	CHMe	2-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
191a	CHMe	4-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
192a	CHMe	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
193a	CHMe	4-Cl-Ph	bond	H	bond	Ph	$H_2NCOCH_2CH_2$
194a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
195a	CHMe	4-F_2HCO-Ph	bond	H	bond	4-F-Ph	allyl
196a	CHMe	Ph	bond	3-pyrazolyl	bond	Ph	$HOCH_2CH_2CH_2$
197a	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	Ph	allyl
198a	CHMe	3-CF_3-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
199a	CHMe	4-CF_3-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
200a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$
201a	CHMe	1,4-C_6H_4	bond	4-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$

202a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
203a	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
204a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2$
205a	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
206a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	NCC(Me)2CH2
207a	CHMe	1,4-C_6H_4	bond	6-MeO-3-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$
208a	CHMe	1,4-C_6H_4	bond	5-MeO-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
209a	CHMe	1,4-C_6H_4	bond	5-Cl-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
210a	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$MeSO_2NHCH_2CH_2$
211a	CHMe	4-F_2HCO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
212a	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$(HO)_2P(=O)OCH_2CH_2CH_2$
213a	CHMe	1,4-C_6H_4	bond	2-Me-4-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
214a	CHMe	1,4-C_6H_4	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
215a	CHMe	1,4-C_6H_4	bond	1-Me-6-oxo-3-(1,6-dihydropyridyl)	bond	Ph	$HOCH_2CH_2CH_2$
216a	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$
217a	CHMe	4-MeO-Ph	bond	H	bond	Ph	$H_2NCOCH_2CH_2$
218a	CHMe	4-F-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
219a	CHMe	c-hex	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
220a	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
221a	CHMe	c-hex	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$

[a] Cy^1 = 1,3-C_6H_4 means 

Cy^1 = 1,4-C_6H_4 means 

Cy^1 = 1,3-(4-F)C_6H_3 means 

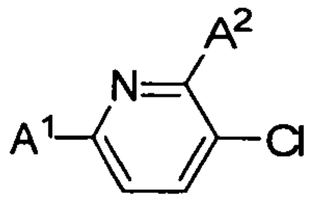
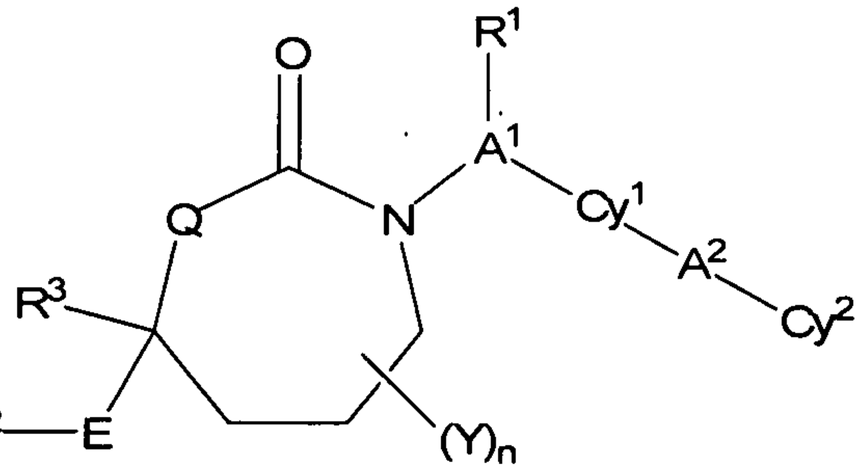
Cy^1 = 2,6-(5-Cl)-pyridyl means 

TABLE 2



I

n = 0, Q = NH

Prophetic Example No.	A^1-R^1	Cy^1	A^2	Cy^2	E	R^2	R^3
1b	bond	3-Me-Ph	bond	H	bond	Ph	Me
2b	bond	3-Br-Ph	bond	H	bond	Ph	Me
3b	bond	1,3-C_6H_4	bond	Ph	bond	Ph	Me
4b	bond	1,3-C_6H_4	bond	2-Cl-Ph	bond	Ph	Me
5b	bond	1,3-C_6H_4	bond	2-NC-Ph;	bond	Ph	Me
6b	CH	1,3-C_6H_4	bond	2-MeO-Ph	bond	Ph	Me
7b	bond	1,3-C_6H_4	bond	2,6-diCl-Ph	bond	Ph	Me
8b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	Me
9b	bond	1,3-C_6H_4	bond	3-Cl-Ph	bond	Ph	Me
10b	bond	1,3-C_6H_4	bond	3-F-Ph	bond	Ph	Me
11b	bond	1,3-C_6H_4	bond	2,5-diF-Ph	bond	Ph	Me
12b	bond	1,3-C_6H_4	bond	3,5-diF-Ph	bond	Ph	Me
13b	bond	1,3-C_6H_4	bond	4-F-Ph	bond	Ph	Me
14b	bond	1,3-C_6H_4	bond	2-F-Ph	bond	Ph	Me
15b	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
16b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)CH_2$
17b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
18b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	allyl
19b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2$

20b	bond	1,3-(4-F)C_6H_3	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
21b	bond	1,3-(4-F)C_6H_3	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
22b	bond	1,3-C_6H_4	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
23b	bond	1,3-C_6H_4	bond	2,6-diCl-Ph	bond	Ph	$HOCH_2CH_2$
24b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$H_2NC(=O)CH_2$
25b	CH	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
26b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
27b	bond	1,3-C_6H_4	bond	Ph	bond	3-Cl-Ph	Me
28b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	2-pyridyl	Me
29b	CHMe	Ph	bond	H	bond	Ph	Me
30b	CHMe	3-MeO-Ph	bond	H	bond	Ph	Me
31b	CHMe	4-MeO-Ph	bond	H	bond	Ph	Me
32b	CHMe	Ph	bond	H	bond	2-Me-Ph	Me
33b	CHMe	Ph	bond	H	bond	4-Me-Ph	Me
34b	CHMe	Ph	bond	H	bond	4-MeS-Ph	Me
35b	CHMe	Ph	bond	H	bond	4-F-Ph	allyl
36b	bond	1,3-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
37b	CHMe	Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
38b	bond	1,3-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$MeSO_2NHCH_2CH_2$
39b	bond	1,3-(4-F)C_6H3	bond	2-Cl-4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
40b	bond	1,3-C_6H_4	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
41b	bond	2,6-pyridyl	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
42b	bond	2,6-pyridyl	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
43b	bond	2,6-pyridyl	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
44b	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
45b	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
46b	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2$
47b	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
48b	bond	2,6-pyridyl	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
49b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	allyl
50b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	allyl

51b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
52b	CHMe	Ph	bond	H	bond	4-F-Ph	vinyl
53b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
54b	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	Ph	$HOCH_2CH_2$
55b	bond	2,6-pyridyl	bond	2-Cl-4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
56b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2$
57b	CHMe	c-hex	bond	H	bond	4-F-Ph	allyl
58b	CHMe	c-hex	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
59b	CHMe	1,4-C_6H_4	bond	c-Pr	bond	4-F-Ph	allyl
60b	CHMe	4-MeO_2C-Ph	bond	H	bond	4-F-Ph	allyl
61b	CHMe	1,3-C_6H_4	bond	c-Pr	bond	4-F-Ph	$HOCH_2CH_2CH_2$
62b	CHMe	4-MeO_2C-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
63b	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	allyl
64b	bond	2,6-(5-Cl)-pyridyl	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2$
65b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2CH_2$
66b	bond	2,6-(5-Cl)-pyridyl	bond	2,4-diF-Ph	bond	2-F-Ph	$HOCH_2CH_2$
67b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
68b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCH(OH)CH_2$
69b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeC(=O)CH_2$
70b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOC(Me)_2CH_2$
71b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeOCH_2CH_2$
72b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)NHCH_2CH_2$
73b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
74b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
75b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCOCH_2CH_2$
76b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)CH_2CH_2$
77b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCONHCH_2CH_2$
78b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)OCH_2CH_2$
79b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NSO_2NHCH_2CH_2$
80b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NSO_2OCH_2CH_2$
81b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$(HO)_2P(=O)OCH_2CH_2$

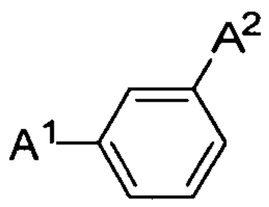
82b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2C(=O)NHCH_2CH_2$
83b	CHMe	4-$HOCH_2$-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
84b	CHMe	4-$HOC(Me)_2$-Ph	bond	H	bond	4-F-Ph	allyl
85b	CHMe	4-Br-Ph	bond	H	bond	2-thienyl	allyl
86b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2$
87b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	allyl
88b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
89b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	HOCH2CH2
90b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	allyl
91b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
92b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$MeCH(OH)CH_2$
93b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
94b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
95b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$MeCH(OH)CH_2$
96b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
97b	CHMe	Ph	bond	2,4-diF-Ph	bond	4-F-Ph	$NCCH_2CH_2$
98b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH(OH)CH_2$
99b	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
100b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOC(=O)CH_2CH_2$
101b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2NHCH_2CH_2$
102b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	HOCH2C(=O)$NHCH_2CH_2$
103b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	MeOC(=O)NHCH2CH2
104b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(4-morpholino)ethyl
105b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$EtNHCONHCH_2CH_2$
106b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=NCN)NHCH_2CH_2$
107b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$
108b	CH2Me	4-Cl-Ph	bond	H	bond	i-Pr	$HOCH_2CH_2CH_2$
109b	CH2Me	4-Me-Ph	bond	H	bond	4-F-Ph	allyl
110b	CH2Me	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH_2$
111b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	allyl
112b	CHMe	4-$HOCH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$

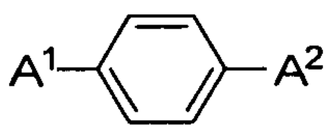
113b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2$
114b	CHMe	4-Cl-Ph	bond	H	bond	4-F-Ph	allyl
115b	CHMe	c-hex	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
116b	CHMe	4-$HOCH_2CH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
117b	CHMe	4-$MeOCH_2$-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
118b	CHMe	4-Br-Ph	bond	H	bond	i-Pr	$HOCH_2CH_2CH_2$
119b	CHMe	4-Cl-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
120b	CH2Me	4-Cl-Ph	bond	H	bond	4-F-Ph	MeCH(OH)CH2
121b	CHMe	4-Br-Ph	bond	H	bond	Ph	allyl
122b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$HOCH_2CH_2$
123b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
124b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH_2$
125b	bond	1-(*t*-BuOC(=O))pyrrolidin-3-yl	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
126b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH_2$
127b	CHMe	1,4-C_6H_4	bond	4-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
128b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
129b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH_2CH_2$
130b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2$
131b	CHMe	1,4-C_6H_4	bond	2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
132b	CHMe	1,4-C_6H_4	bond	4-morpholinyl	bond	4-F-Ph	allyl
133b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2$
134b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$NCCH_2CH_2$
135b	CHEt	4-Br-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
136b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
137b	CHMe	1,4-C_6H_4	bond	1-oxo-3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
138b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	i-Pr	$HOCH_2CH(OH)CH_2$
139b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$MeCH(OH)CH_2$
140b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
141b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	Pr
142b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
143b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSO_2CH_2CH_2$

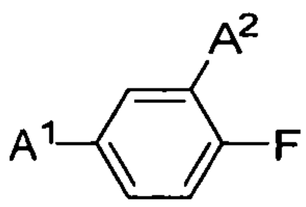
144b	CHMe	1,4-C_6H_4	bond	5-Me-1,3,4-thiadiazol-2-yl	bond	4-F-Ph	allyl
145b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-thienyl	$HOCH_2CH_2CH_2$
146b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	2-thienyl	$HOCH_2CH2$
147b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$H_2NCOCH_2CH_2$
148b	CHMe	1,4-C_6H_4	bond	2-MeO-5-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
149b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	4-F-Ph	$H_2NCOCH_2CH_2$
150b	CHEt	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
151b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOC(Me)_2CH_2$
152b	CHEt	4-Br-Ph	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
153b	CHMe	4-Br-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
154b	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
155b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$NCCH_2$
156b	CHMe	1,4-C_6H_4	bond	2,4-diMe-5-thiazolyl	bond	4-F-Ph	allyl
157b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
158b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	2-F-Ph	$HOCH_2CH_2CH_2$
159b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	3-F-Ph	$HOCH_2CH_2CH_2$
160b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOC(Me)_2CH_2CH_2$
161b	CHMe	1,4-C_6H_4	bond	5-MeCO-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
162b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$H_2NCOCH_2CH_2$
163b	CHMe	1,4-C_6H_4	bond	5-(H_2NCHMe)-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
164b	CHEt	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
165b	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOCH_2CH_2CH_2$
166b	CHMe	1,4-C_6H_4	bond	5-(HOCHMe)-2-thienyl	bond	Ph	$HOCH_2CH_2CH_2$
167b	CHEt	4-Br-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH(OH)CH_2$
168b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NCH_2CH_2CH_2$
169b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHCH_2CH_2$
170b	CHMe	1,4-C_6H_4	bond	3-(CF_3)-1-pyrazolyl	bond	4-F-Ph	allyl
171b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	Ph	$HOC(Me)_2CH_2CH_2$
172b	CHEt	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2CH_2$
173b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeSCH_2CH_2$
174b	CHMe	Ph	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH_2$

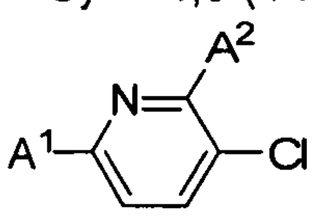
175b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)OCH_2CH_2$
176b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2OCH_2CH_2$
177b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(1-imidazolyl)ethyl
178b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeCONMeCH_2CH_2$
179b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$MeSO_2NHCH_2CH_2CH_2$
180b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH_2CH_2$
181b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)OCH_2CH_2CH_2$
182b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	2-(1-aminoimidazol-1-yl)ethyl
183b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$MeNHC(=O)NHCH_2CH_2CH_2$
184b	CHMe	1,4-C_6H_4	bond	2,4-diF-Ph	bond	4-F-Ph	$H_2NC(=O)NHCH_2CH(OH)CH_2$
185b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$MeSO_2NHCH_2CH(OH)CH_2$
186b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	4-F-Ph	$MeSO_2NMeCH_2CH(OH)CH_2$
187b	CHMe	1,4-C_6H_4	bond	6-CF_3-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
188b	CHMe	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
189b	CHMe	3-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
190b	CHMe	2-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
191b	CHMe	4-F-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
192b	CHMe	4-MeO-Ph	bond	H	bond	Ph	$HOCH_2CH(OH)CH_2$
193b	CHMe	4-Cl-Ph	bond	H	bond	Ph	$H_2NCOCH_2CH_2$
194b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
195b	CHMe	4-F_2HCO-Ph	bond	H	bond	4-F-Ph	allyl
196b	CHMe	Ph	bond	3-pyrazolyl	bond	Ph	$HOCH_2CH_2CH_2$
197b	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	Ph	allyl
198b	CHMe	3-CF_3-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
199b	CHMe	4-CF_3-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
200b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$
201b	CHMe	1,4-C_6H_4	bond	4-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$
202b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$HOCH_2CH_2CH_2$
203b	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	Ph	$HOCH_2CH_2CH_2$
204b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2$
205b	CHMe	1,4-C_6H_4	bond	5-F-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$

206b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	NCC(Me)2CH2
207b	CHMe	1,4-C_6H_4	bond	6-MeO-3-pyridyl	bond	Ph	$H_2NCOCH_2CH_2$
208b	CHMe	1,4-C_6H_4	bond	5-MeO-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
209b	CHMe	1,4-C_6H_4	bond	5-Cl-3-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
210b	CHMe	1,4-C_6H_4	bond	3-pyridyl	bond	Ph	$MeSO_2NHCH_2CH_2$
211b	CHMe	4-F_2HCO-Ph	bond	H	bond	4-F-Ph	$HOCH_2CH_2CH_2$
212b	CHMe	1,4-C_6H_4	bond	4-F-Ph	bond	Ph	$(HO)_2P(=O)OCH_2CH_2CH_2$
213b	CHMe	1,4-C_6H_4	bond	2-Me-4-pyridyl	bond	4-F-Ph	$HOCH_2CH_2CH_2$
214b	CHMe	1,4-C_6H_4	bond	H	bond	Ph	$HOCH_2CH_2CH_2$
215b	CHMe	1,4-C_6H_4	bond	1-Me-6-oxo-3-(1,6-dihydropyridyl)	bond	Ph	$HOCH_2CH_2CH_2$
216b	CHMe	4-MeO-Ph	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$
217b	CHMe	4-MeO-Ph	bond	H	bond	Ph	$H_2NCOCH_2CH_2$
218b	CHMe	4-F-Ph	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
219b	CHMe	c-hex	bond	H	bond	4-F-Ph	$H_2NCOCH_2CH_2$
220b	bond	1,3-(4-F)C_6H_3	bond	2,4-diF-Ph	bond	4-F-Ph	$HOCH_2CH_2$
221b	CHMe	c-hex	bond	H	bond	4-F-Ph	$MeSO_2NHCH_2CH_2CH_2$

[a] Cy^1 = 1,3-C_6H_4 means 

Cy^1 = 1,4-C_6H_4 means 

Cy^1 = 1,3-(4-F)C_6H_3 means 

Cy^1 = 2,6-(5-Cl)-pyridyl means 

The compounds of the invention are useful for ameliorating or treating disorders or diseases in which decreasing the level of cortisol is effective in treating a disease state. Thus, the compounds of the invention can be used in the treatment or prevention of diabetes mellitus, obesity, symptoms of metabolic syndrome, glucose intolerance, hyperglycemica, hypertension, hyperlipidemia, insulin resistance,

cardiovascular disease, dyslipidemia, atherosclerosis, lipodystrophy, osteoporosis, glaucoma, Cushing's syndrome, Addison's Disease, visceral fat obesity associated with glucocorticoid therapy, depression, anxiety, Alzheimer's disease, dementia, cognitive decline (including age-related cognitive decline), polycystic ovarian syndrome, infertility and hypergonadism. In addition, the compounds modulate the function of B and T cells of the immune system and can therefore be used to treat diseases such as tuberculosis, leprosy and psoriasis. They can also be used to promote wound healing, particularly in diabetic patients.

The disclosed compounds can be used alone (i.e. as a monotherapy) or in combination with another therapeutic agent effective for treating any of the above indications. The pharmaceutical compositions can comprise the disclosed compounds alone as the the only pharmaceutically active agent or can comprise one or more additional pharmaceutically active agents.

A pharmaceutical composition of the invention may, alternatively or in addition to a compound of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), or (Ig) comprise a pharmaceutically acceptable salt of a compound of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig) or a prodrug or pharmaceutically active metabolite of such a compound or salt and one or more pharmaceutically acceptable carriers therefore. Alternatively, a pharmaceutical composition of the invention may comprise a compound of Formula (I), (Ia), (Ib), (Ic), (Id), (Ie), (If), (Ig) or a pharmaceutical salt thereof as the only pharmaceutically active agent in the pharmaceutical composition.

A pharmaceutical composition of the invention may, alternatively or in addition to a compound of Formula I, comprise a pharmaceutically acceptable salt of a compound of Formula I or a prodrug or pharmaceutically active metabolite of such a compound or salt and one or more pharmaceutically acceptable carriers therefore.

The compositions of the invention are 11β-HSD1 inhibitors. Said compositions contain compounds having a mean inhibition constant (IC_{50}) against 11β-HSD1 of below about 1,000 nM; preferably below about 100 nM; more preferably below about 50 nM; even more preferably below about 5 nM; and most preferably below about 1 nM.

The invention includes a therapeutic method for treating or ameliorating an 11β-HSD1 mediated disorder in a subject in need thereof comprising administering to a subject in need thereof an effective amount of a compound of Formula I, or an enantiomer, diastereomer, or pharmaceutically acceptable salt thereof of composition thereof. As used herein, "treating" or "treatment" includes both therpaeutic and prophylactic treatment. Therapeutic treatment includes reducing the symptoms

associated with a disease or condition and/or increasing the longevity of a subject with the disease or condition. Prophylactic treatment includes delaying the onset of a disease or condition in a subject at risk of developing the disease or condition or reducing the liklihood that a subject will then develop the disease or condition in a subject that is at risk for developing the disease or condition.

An embodiment of the invention includes administering an 11β-HSD1 inhibiting compound of Formula I or composition thereof in a combination therapy with one or more additional agents for the treatment of diabetes, dyslipidemia, cardiovascular disease, hypertension, obesity, cancer or glaucoma. Agents for the treatment of diabetes include insulins, such as Humulin® (Eli Lilly), Lantus® (Sanofi Aventis), Novolin (Novo Nordisk), and Exubera® (Pfizer); PPAR gamma agonists, such as Avandia® (rosiglitizone maleate, GSK) and Actos® (pioglitazone hydrochloride, Takeda/Eli Lilly); sulfonylureas, such as Amaryl® (glimepiride, Sanofi Aventis), Diabeta® (glyburide, Sanofi Aventis), Micronase®/Glynase® (glyburide, Pfizer), and Glucotrol®/Glucotrol XL® and (glipizide, Pfizer); meglitinides, such as Prandin®/NovoNorm® (repaglinide, Novo Nordisk), Starlix® (nateglinide, Novartis), and Glufast® (mitiglinide, Takeda); biguanides, such as Glucophase®/Glucophase XR® (metformin HCl, Bristol Myers Squibb) and Glumetza (metformin HCl, Depomed); thiazolidinediones; amylin analogs, GLP-1 analogs; DPP-IV inhibitors; PTB-1B inhibitors; protein kinase inhibitors (including AMP-activated protein kinase inhibitors); glucagon antagonists, glycogen synthase kinase-3 beta inhibitors; glucose-6-phoshatase inhibitors; glycogen phosphorylase inhibitors; sodium glucose co-transporter inhibitors, and alpha-glucosidase inhibitors, such as Precose®/Glucobay®/Prandase®/Glucor® (acarbose, Bayer) and Glyset® (miglitol, Pfizer). Agents for the treatment of dyslipidemia and cardiovascular disease include statins, fibrates, and ezetimbe. Agents for the treatment of hypertension include alpha-blockers, beta-blockers, calcium channel blockers, diuretics, angiotensin converting enzyme (ACE) inhibitors, dual ACE and neutral endopeptidase (NEP) inhibitors, angiotensin-receptor blockers (ARBs), aldosterone synthase inhibitor, aldosterone-receptor antagonists, or endothelin receptor antagonist. Agents for the treatment of obesity include orlistat, phentermine, sibutramine and rimonabant.

An embodiment of the invention includes administering an 11β-HSD1 inhibiting compound of Formula I or composition thereof in a combination therapy with one or more other 11β-HSD1 inhibitors (whether such inhibitors are also compounds of Formula I or are compounds of a different class/genus), or with combination products, such as Avandamet® (metformin HCl and rosiglitazone

maleate, GSK); Avandaryl® (glimepiride and rosiglitazone maleate, GSK); Metaglip® (glipizide and metformin HCl, Bristol Myers Squibb); and Glucovance® (glyburide and metformin HCl, Bristol Myers Squibb).

The compounds of the present invention can be prepared and administered in a wide variety of oral and parenteral dosage forms. Thus, the compounds of the present invention can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Additionally, the compounds of the present invention can be administered intranasally or transdermally. It will be obvious to those skilled in the art that the following dosage forms may comprise as the active ingredient, either compounds or a corresponding pharmaceutically acceptable salt of a compound of the present invention.

For preparing pharmaceutical compositions from the compounds of the present invention, pharmaceutically acceptable carriers can either be solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier can be one or more substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material. In powders, the carrier is a finely divided solid which is in a mixture with the finely divided active ingredient.

In tablets, the active ingredient is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

The powders and tablets preferably contain from about one to about seventy percent of the active ingredient. Suitable carriers are magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium caboxymethylcellulose, a low-melting wax, cocoa butter, and the like. Tablets, powders, cachets, lozenges, fast-melt strips, capsules and pills can be used as solid dosage forms containing the active ingredient suitable for oral administration.

For preparing suppositories, a low-melting wax, such as a mixture of fatty acid glycerides or cocoa butter, is first-melted and the active ingredient is dispersed homogeneously therein, as by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, retention enemas, and emulsions, for example, water or water propylene glycol solutions. For

parenteral injection, liquid preparations can be formulated in solution in aqueous polyethylene glycol solution.

Aqueous solutions suitable for oral administration can be prepared by dissolving the active ingredient in water and adding suitable colorants, flavors, stabilizing, and thickening agents as desired. Aqueous suspensions for oral administration can be prepared by dispersing the finely divided active ingredient in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well-known suspending agents.

The pharmaceutical composition is preferably in unit dosage form. In such form, the composition is subdivided into unit doses containing appropriate quantities of the active ingredient. The unit dosage form can be a packaged preparation, the package containing discrete quantities of, for example, tablets, powders, and capsules in vials or ampules. Also, the unit dosage form can be a tablet, cachet, capsule, or lozenge itself, or it can be the appropriate amount of any of these in packaged form.

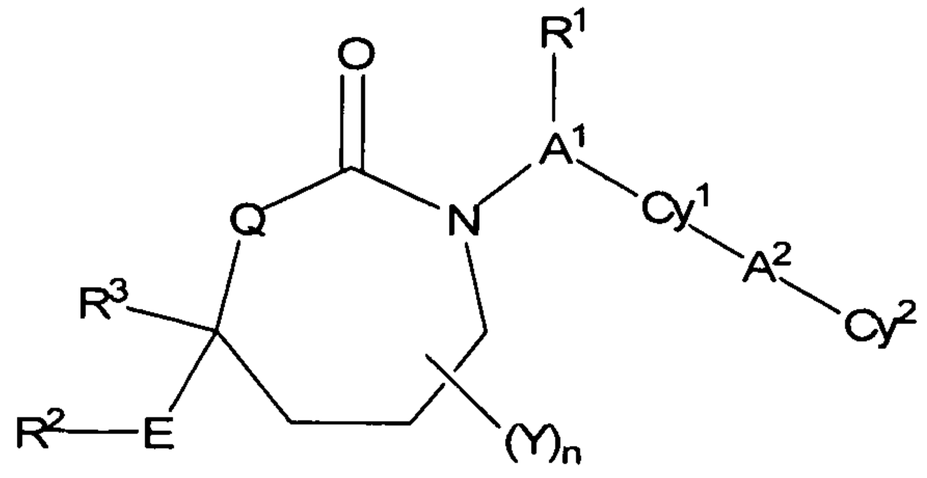
The quantity of active ingredient in a unit dose preparation may be varied or adjusted from about 0.1 mg to about 1000.0 mg, preferably from about 0.1 mg to about 100 mg. The dosages, however, may be varied depending upon the requirements of the patient, the severity of the condition being treated, and the compound being employed. Determination of the proper dosage for a particular situation is within the skill in the art. Also, the pharmaceutical composition may contain, if desired, other compatible therapeutic agents.

In therapeutic treatment or as a method-of-use as an inhibitor of 11β-HSD1 or an inhibitor in the production of cortisol in the cell, the active ingredient is preferably administered orally in a solid dosage form as disclosed above in an amount of about 0.1 mg to about 100 mg per daily dose where the dose is administered once or more than once daily.

All publications, patents and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application were specifically and individually designated as having been incorporated by reference. It is understood that the examples and embodiments described herein are for illustrative purposes only, and it will be appreciated that the invention is susceptible to modification, variation and change without departing from the proper scope or fair meaning of the appended claims.

What is claimed is:

1. A compound of Formula (I)



I

; wherein

R^1 is (a) absent or (b) is selected from $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl or $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

A^1 is (a) a bond, or (b) $(C_1\text{-}C_3)$alkylene, CH_2CH_2O, wherein the oxygen is attached to Cy^1, or $CH_2C(=O)$, wherein the carbonyl carbon is attached to Cy^1;

Cy^1 is aryl, heteroaryl, monocyclic cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}C_7)$cycloalkylalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy,

(C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

A^2 is (a) a bond, O, S or NR^4; or (b) (C_1-C_3)alkylene or (C_1-C_2)alkyleneoxy, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo;

Cy^2 is (a) hydrogen or (b) aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkyl-alkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-

C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

Y is (C_1-C_6)alkyl or halo(C_1-C_6)alkyl;

n is 0, 1 or 2;

E is (a) a bond or (b) (C_1-C_3)alkylene or (C_1-C_2)alkylenyloxy, wherein the O is attached to R^2, each of which is optionally substituted with 1 to 4 groups independently selected from methyl, ethyl, trifluoromethyl or oxo;

R^2 is (C_1-C_6)alkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with up to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkyl-alkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-

C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

R^3 is selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl and (C_1-C_3)alkoxy(C_1-C_3)alkyl, wherein each is optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-

substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

Q is O or NR^5;

R^4 is independently selected from H; (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl and (C_1-C_6)alkoxy(C_1-C_6)alkyl;

R^5 is H, (C_1-C_6)alkyl, halo(C_1-C_6)alkyl, or hydroxy(C_1-C_6)alkyl;
or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

2. The compound of Claim 1; wherein
R^3 is selected from substituted (C_1-C_6)alkyl, or optionally substituted (C_2-C_6)alkenyl, optionally substituted (C_2-C_6)alkynyl and optionally substituted (C_1-C_3)alkoxy(C_2-C_3)alkyl, wherein each substituted group represented by R^3 has up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which

in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

3. The compound of Claim 1; wherein

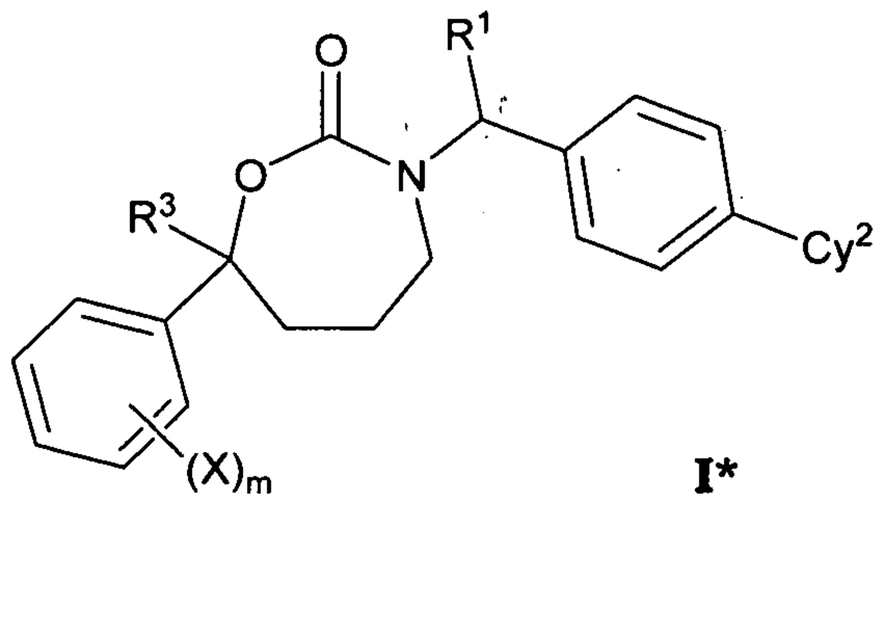
E is a bond;

R^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}C_7)$cycloalkylalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, $(C_4\text{-}C_7)$cycloalkylalkoxy, halo$(C_1\text{-}C_6)$alkoxy, halo$(C_3\text{-}C_6)$cycloalkoxy, halo$(C_4\text{-}C_7)$cycloalkylalkoxy, $(C_1\text{-}C_6)$alkylthio, $(C_3\text{-}C_6)$cycloalkythio, $(C_4\text{-}C_7)$cycloalkylalkylthio, halo$(C_1\text{-}C_6)$alkylthio, halo$(C_3\text{-}C_6)$cycloalkythio, halo$(C_4\text{-}C_7)$cycloalkylalkylthio, $(C_1\text{-}C_6)$alkanesulfinyl, $(C_3\text{-}C_6)$cycloalkanesulfinyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, halo$(C_1\text{-}C_6)$alkanesulfinyl, halo$(C_3\text{-}C_6)$cycloalkanesulfinyl, halo$(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, $(C_1\text{-}C_6)$alkanesulfonyl, $(C_3\text{-}C_6)$cycloalkanesulfonyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfonyl, halo$(C_1\text{-}C_6)$alkanesulfonyl, halo$(C_3\text{-}C_6)$cycloalkanesulfonyl, halo$(C_4\text{-}C_7)$cycloalkylalkanesulfonyl, $(C_1\text{-}C_6)$alkylamino, di$(C_1\text{-}C_6)$alkylamino, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1\text{-}C_6)$alkylaminocarbonyl, di$(C_1\text{-}C_6)$alkylaminocarbonyl, $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1\text{-}C_6)$alkylaminosulfonyl, di$(C_1\text{-}C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1\text{-}C_6)$alkylcarbonylamino, $(C_1\text{-}C_6)$alkylcarbonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylsulfonylamino, $(C_1\text{-}C_6)$alkylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkoxy, heteroaryl, oxo, amino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl, di$(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl amino$(C_2\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylamino$(C_2\text{-}C_6)$alkoxy, di$(C_1\text{-}C_6)$alkylamino$(C_2\text{-}C_6)$alkoxyl and $(C_1\text{-}C_6)$alkylcarbonyl;

R^3 is selected from substituted $(C_1\text{-}C_6)$alkyl, or optionally substituted $(C_2\text{-}C_6)$alkenyl, optionally substituted $(C_2\text{-}C_6)$alkynyl and optionally substituted $(C_1\text{-}C_3)$alkoxy$(C_2\text{-}C_3)$alkylwherein each substituted group represented by R^3 has up to four groups independently selected from cyano, R^4, $(R^4)_2N$-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

4. The compound of claim 1 wherein the compound is of Formula (I*)



I*

; wherein

R^1 is $(C_1\text{-}C_6)$alkyl, optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

Cy^2 is aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1\text{-}C_6)$alkyl, hydroxy$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, hydroxy$(C_3\text{-}C_6)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkylalkyl, $(C_2\text{-}C_6)$alkenyl, halo$(C_2\text{-}C_6)$alkenyl, hydroxy$(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_6)$cycloalkyl$(C_2\text{-}C_4)$alkynyl, halo$(C_1\text{-}C_6)$alkyl, halo$(C_3\text{-}C_6)$cycloalkyl, halo$(C_4\text{-}C_7)$cycloalkylalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_3\text{-}C_6)$cycloalkoxy, $(C_4\text{-}C_7)$cycloalkylalkoxy, halo$(C_1\text{-}C_6)$alkoxy, halo$(C_3\text{-}C_6)$cycloalkoxy, halo$(C_4\text{-}C_7)$cycloalkylalkoxy, $(C_1\text{-}C_6)$alkylthio, $(C_3\text{-}C_6)$cycloalkythio, $(C_4\text{-}C_7)$cycloalkyl-alkylthio, halo$(C_1\text{-}C_6)$alkylthio, halo$(C_3\text{-}C_6)$cycloalkythio, halo$(C_4\text{-}C_7)$cycloalkylalkylthio, $(C_1\text{-}C_6)$alkanesulfinyl, $(C_3\text{-}C_6)$cycloalkanesulfinyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, halo$(C_1\text{-}C_6)$alkane-sulfinyl, halo$(C_3\text{-}C_6)$cycloalkanesulfinyl, halo$(C_4\text{-}C_7)$cycloalkylalkanesulfinyl, $(C_1\text{-}C_6)$alkanesulfonyl, $(C_3\text{-}C_6)$cycloalkanesulfonyl, $(C_4\text{-}C_7)$cycloalkylalkanesulfonyl, halo$(C_1\text{-}C_6)$alkanesulfonyl, halo$(C_3\text{-}C_6)$cycloalkanesulfonyl, halo$(C_4\text{-}C_7)$cyclo-alkylalkanesulfonyl, $(C_1\text{-}C_6)$alkylamino, di$(C_1\text{-}C_6)$alkylamino, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1\text{-}C_6)$alkylaminocarbonyl, di$(C_1\text{-}C_6)$alkylaminocarbonyl, $(C_1\text{-}C_3)$alkoxy$(C_1\text{-}C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1\text{-}C_6)$alkylaminosulfonyl, di$(C_1\text{-}C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1\text{-}C_6)$alkylcarbonylamino, $(C_1\text{-}C_6)$alkylcarbonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylsulfonylamino, $(C_1\text{-}C_6)$alkylsulfonylamino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxycarbonyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, halo$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}$

C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

X is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

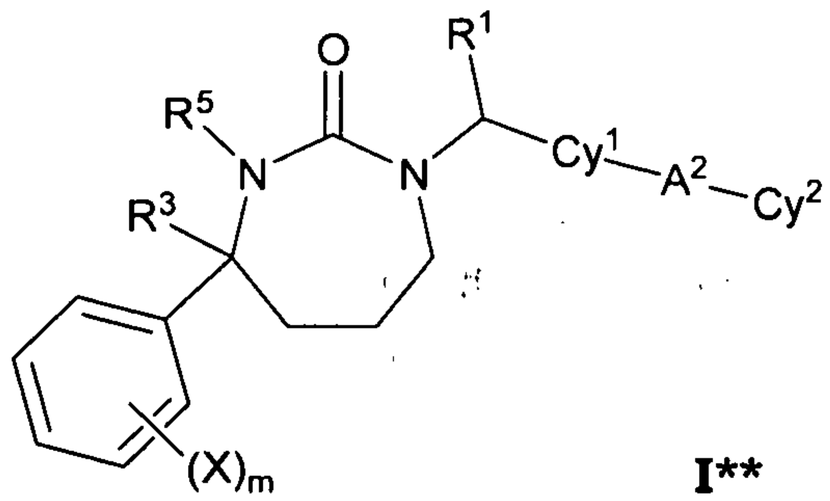
m is 0, 1, 2, 3, 4;

R^3 is (C_1-C_6)alkyl substituted with up to four groups independently selected from cyano, oxo, HO-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-,

$(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

5. The compound of claim 1 wherein the compound is of Formula (I**)



I** ; wherein

R^1 is $(C_1$-$C_6)$alkyl, optionally substituted with up to four groups independently selected from fluorine, cyano, oxo, R^4, R^4O-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$-, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$-, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$-, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$-, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$-,

$(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$-, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$-, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$-, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$-, aryl, cycloalkyl, heterocyclyl, heteroaryl, arylamino and heteroarylamino;

Cy^1 is aryl, heteroaryl, monocyclic cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

A^2 is a bond;

Cy^2 is (a) hydrogen or (b) aryl, heteroaryl, cycloalkyl or heterocyclyl, wherein each is optionally substituted with 1 to 4 groups independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkyl-alkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkane-sulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

X is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-

C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

m is 0, 1, 2, 3, 4; and

R^3 is (C_1-C_6)alkyl substituted with up to four groups independently selected from cyano, oxo, R^4, HO-, $(R^4)_2N$-, R^4O_2C-, R^4S, $R^4S(=O)$-, $R^4S(=O)_2$-, $R^4C(=O)NR^4$, $(R^4)_2NC(=O)$-, $(R^4)_2NC(=O)O$-, $(R^4)_2NC(=O)NR^4$-, $R^4OC(=O)NR^4$-, $(R^4)_2NC(=NCN)NR^4$, $(R^4O)_2P(=O)O$-, $(R^4O)_2P(=O)NR^4$-, $R^4OS(=O)_2NR^4$-, $(R^4)_2NS(=O)_2O$-, $(R^4)_2NS(=O)_2NR^4$, $R^4S(=O)_2NR^4$-, $R^4S(=O)_2NHC(=O)$-, $R^4S(=O)_2NHC(=O)O$-, $R^4S(=O)_2NHC(=O)NR^4$, $R^4OS(=O)_2NHC(=O)$-, $R^4OS(=O)_2NHC(=O)O$-, $R^4OS(=O)_2NHC(=O)NR^4$, $(R^4)_2NS(=O)_2NHC(=O)$-, $(R^4)_2NS(=O)_2NHC(=O)O$-, $(R^4)_2NS(=O)_2NHC(=O)NR^4$, $R^4C(=O)NHS(=O)_2$-, $R^4C(=O)NHS(=O)_2O$-, $R^4C(=O)NHS(=O)_2NR^4$, $R^4OC(=O)NHS(=O)_2$-, $R^4OC(=O)NHS(=O)_2O$-, $R^4OC(=O)NHS(=O)_2NR^4$, $(R^4)_2NC(=O)NHS(=O)_2$-, $(R^4)_2NC(=O)NHS(=O)_2O$-, $(R^4)_2NC(=O)NHS(=O)_2NR^4$, heterocyclyl (which in turn may be optionally substituted with alkyl, haloalkyl or oxo), heteroaryl (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo), arylamino (which in turn may be optionally substituted with alkyl, alkoxy, alkylthio,

alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido and N,N-dialkyl-substituted amido) and heteroarylamino (which in turn may be optionally substituted with alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, halogen, trifluoromethyl, dialkylamino, nitro, cyano, CO_2H, $CONH_2$, N-monoalkyl-substituted amido, N,N-dialkyl-substituted amido, or oxo);

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

6. The compound of any of claims 1-5, wherein A^1 is a bond.

7. The compound of any of claims 1-6, wherein A^1 is $(C_1\text{-}C_3)$alkylene.

8. The compound of any of claims 1-7, wherein A^1 is methylene.

9. The compound of any of claims 1-8, wherein A^1 is CH and R^1 is present.

10. The compound of any of claims 1-9, wherein R^1 is $(C_1\text{-}C_6)$alkyl.

11. The compound of any of claims 1-10, wherein R^1 is an optionally substituted methyl or ethyl.

12. The compound of any of claims 1-11, wherein R^1 is unsubstituted methyl or ethyl.

13. The compound of any of claims 1-12, wherein Cy^1 is optionally substituted aryl or optionally substituted heteroaryl.

14. The compound of any of claims 1-13, wherein Cy^1 is optionally substituted phenyl or optionally substituted pyridyl.

15. The compound of any of claims 1-14, wherein Cy^1 is optionally substituted monocyclic cycloalkyl.

16. The compound of any of claims 1-13, wherein Cy^1 is optionally substituted cyclohexyl.

17. The compound of any of claims 1-16, wherein Cy^1 is optionally substituted phenyl.

18. The compound of any of claims 1-17, wherein Cy^1 is substituted with fluorine, chlorine, bromine, methoxy, methoxycarbonyl, carboxy, or methyl.

19. The compound of any of claims 1-18, wherein A^2 is a bond and Cy^2 is hydrogen.

20. The compound of any of claims 1-19, wherein A^2 is a bond and Cy^2 is hydrogen.

21. The compound of any of claims 1-20, wherein A^2 is a bond and Cy^2 is hydrogen.

22. The compound of any of claims 1-21, wherein A^2 is a bond and Cy^2 is hydrogen.

23. The compound of any of claims 1-22, wherein A^2 is a bond and Cy^2 is cyclopropyl.

24. The compound of any of claims 1-23, wherein A^2 is a bond and Cy^2 is optionally substituted aryl or optionally substituted heteroaryl.

25. The compound of any of claims 1-24, wherein A^2 is a bond and Cy^2 is optionally substituted phenyl or optionally substituted pyridyl.

26. The compound of any of claims 1-25, wherein Cy^2 is optionally substituted phenyl.

27. The compound of any of claims 1-26, wherein Cy^2 is substituted with 1 to 4 groups independently selected from chlorine or fluorine.

28. The compound of any of claims 1-27, wherein Cy^2 is difluorophenyl.

29. The compound of any of claims 1-28, wherein Cy^2 is fluorophenyl.

30. The compound of any of claims 1-29, wherein R^3 is hydroxy(C_2-C_4)alkyl.

31. The compound of any of claims 1-30, wherein R^3 is dihydroxy(C_3-C_4)alkyl.

32. The compound of any of claims 1-31, wherein R^3 is ω-$H_2NCO(C_1$-$C_3)$alkyl.

33. The compound of any of claims 1-32, wherein R^3 is $H_2NC(=O)CH_2CH_2$.

34. The compound of any of claims 1-33, wherein R^3 is (C_1-C_2)alkoxy(C_1-C_3)alkyl.

35. The compound of any of claims 1-34, wherein R^3 is $H_2NSO_2O(C_2$-$C_4)$alkyl.

36. The compound of any of claims 1-35, wherein R^3 is $H_2NSO_2NH(C_2$-$C_4)$alkyl.

37. The compound of any of claims 1-36, wherein R^3 is oxo(C_2-C_4)alkyl.

38. The compound of any of claims 1-37, wherein R^3 is alkenyl.

39. The compound of any of claims 1-38, wherein R^3 is allyl.

40. The compound of any of claims 1-39, wherein R^3 is $MeC(=O)NH(C_2$-$C_4)$alkyl.

41. The compound of any of claims 1-40, wherein R^3 is $MeOC(=O)NH(C_2$-$C_4)$alkyl.

42. The compound of any of claims 1-41, wherein R^3 is cyanoalkyl.

43. The compound of any of claims 1-42, wherein R^3 is alkylsulfonylaminoalkyl.

44. The compound of any of claims 1-43, wherein R^3 is $MeS(=O)_2NH(C_2-C_4)$alkyl.

45. The compound of any of claims 1-44, wherein R^3 is $MeS(=O)_2NHCH_2CH_2CH_2$.

46. The compound of any of claims 1-45, wherein R^3 is alkylhydroxyalkyl.

47. The compound of any of claims 1-46, wherein R^3 is hydroxyalkoxyalkyl.

48. The compound of any of claims 1-47, wherein R^3 is aminocarbonylaminoalkyl.

49. The compound of any of claims 1-48, wherein R^3 is aminocarboxyalkyl.

50. The compound of any of claims 1-49, wherein R^3 is 2-(4-morpholino)ethyl.

51. The compound of any of claims 1-50, wherein R^3 is 2-(1-imidazolyl)ethyl.

52. The compound of any of claims 1-51, wherein R^2 is optionally substituted aryl, optionally substituted heteroaryl or optionally substituted cycloalkyl.

53. The compound of any of claims 1-52, wherein R^2 is optionally substituted phenyl, optionally substituted thienyl or optionally substituted pyridyl.

54. The compound of any of claims 1-53, wherein R^2 is optionally substituted phenyl.

55. The compound of any of claims 1-54, wherein E is a bond.

56. The compound of any of claims 1-55, wherein R^2 is fluorophenyl.

57. The compound of any of claims 1-56, wherein R^2 is an optionally substituted alkyl.

58. The compound of any of claims 1-57, wherein R^2 is an optionally substituted isopropyl.

59. The compound of claim 1; wherein

R^1 is absent or is methyl or ethyl;

A^1 is a bond or CH_2 or if R^1 is present, then A^1 is CH;

Cy^1 is phenyl, cyclopropyl, cyclohexyl, pyrrolidinyl, pyridyl, N-oxo-pyridyl, thiazolyl or pyrimidinyl each optionally substituted with 1 to 4 groups independently selected from halo, methyl, trifluoromethyl, hydroxy, methoxy, methoxycarbonyl, carboxy, ethoxycarbonylmethoxy 2-hydroxy-2-methylpropoxy, cyano, difluoromethoxy, t-butoxycarbonyl, hydroxy, hydroxymethyl, 2-hydroxyethyl, 2-hydroxy-2-propyl, methoxymethyl, methylsulfonyl and methylsulfonylamino;

A^2 is a bond, O, OCH_2CO or C=O;

Cy^2 is (a) hydrogen or (b) phenyl, thienyl, pyridyl, N-oxo-pyridyl, cyclopropyl, piperidinyl, piperazinyl, morpholinyl, thiazolyl, oxadiazolyl, thiadiazolyl, pyrazolyl, S,S-dioxothiazinyl, 2-oxo-1,2-dihydropyridyl each optionally substituted by 1 to 4 groups independently selected fromaminomethyl, 1-aminoethyl, halo, hydroxy, methoxy, hydroxymethyl, methoxycarbonyl, amino, carbamoyl, methylcarbamoyl, dimethylcarbamoyl, (2-methoxyethyl)aminocarbonyl, acetylaminomethyl, methyl-sulfonyl, methylsulfonylamino, methylaminosulfonyl, isopropylaminosulfonyl,

dimethylaminosulfonyl, pyrrolidine-1-sulfonyl, methylsulfonylaminomethyl, tetrazolyl, methyl, trifluoromethyl, acetyl, 2-hydroxyethyl and 1-aminoethyl;

n is 0;

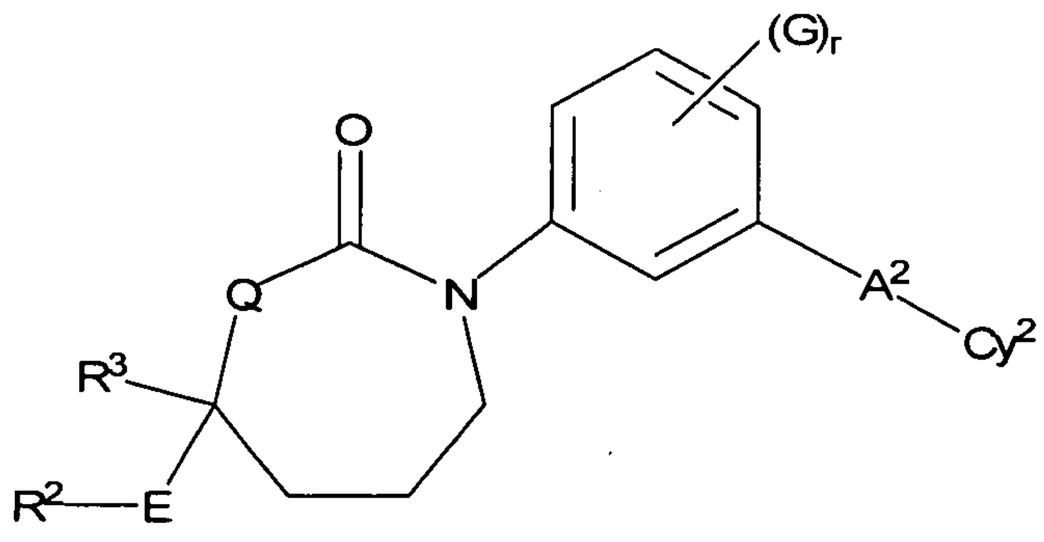
E is a bond or CH_2;

R^2 is cyclohexyl, isopropyl, thienyl, phenyl or pyridyl, each optionally substituted with one group selected from halo, methyl, methylthio or (4-morpholino)methyl;

R^3 is methyl, ethyl, propyl, butyl, vinyl, allyl or ethoxyethyl, each optionally substituted with up to two groups independently selected from methyl, $H_2C=CH$, HO-, MeO-, MeC(=O), H_2N-, MeC(=O)NH-, $MeS(=O)_2NH$-, $H_2NC(=O)$-, MeNHC(=O)-, HO_2C-, $HO-(CH_2)_2O$-, $(HO)_2P(=O)O$-, $H_2NS(=O)_2O$-, $H_2NS(=O)_2NH$-, MeNHC(=O)NH-, MeNHC(=O)O-, cyano, HO_2C-, $HOCH_2CH_2NH$-, 4-morpholino, $HOCH_2C(=O)NH$-, $H_2NCH_2C(=O)NH$-, EtNHC(=O)NH, $H_2NHC(=O)NH$, $H_2NHC(=O)O$-, $CH_3C(=O)$-, MeOC(=O)NH-, MeNHC(=NC≡N)NH-, Me-, MeS-, $MeSO_2$- $MeSO_2N(Me)$-, $MeS(=O)_2NHC(=O)$-, imidazolylamino-, imidazolyl, morpholino, tetrazolyl, H_2NCONH-, H_2NCO_2-, $HOCH_2CH_2O$-, MeNH-, Me_2N- and MeCONMe; and

R^5 is hydrogen or methyl.

60. The compound of claim 1 wherein the compound is of Formula (Ia)



Ia

; wherein

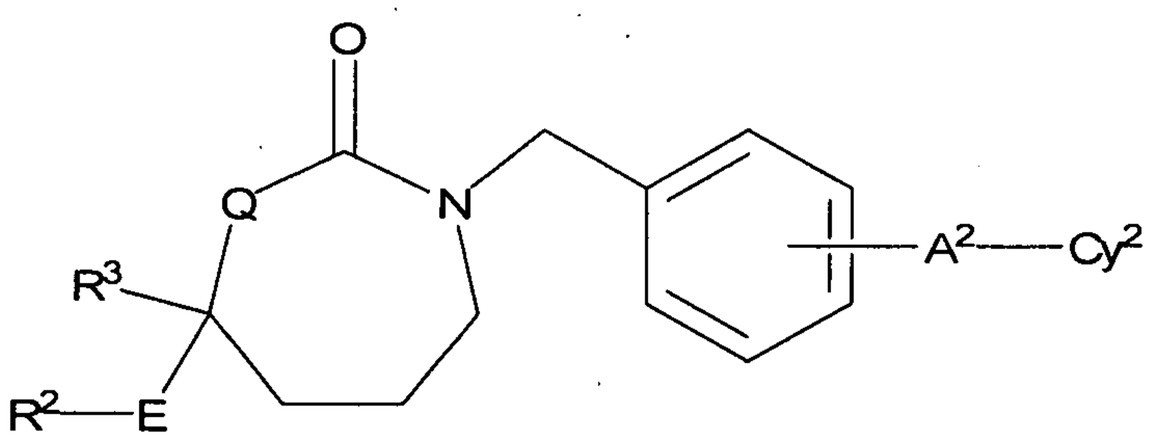
r is 0, 1, 2, 3 or 4; and

G is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl$(C_2-$

C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO, H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl or (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

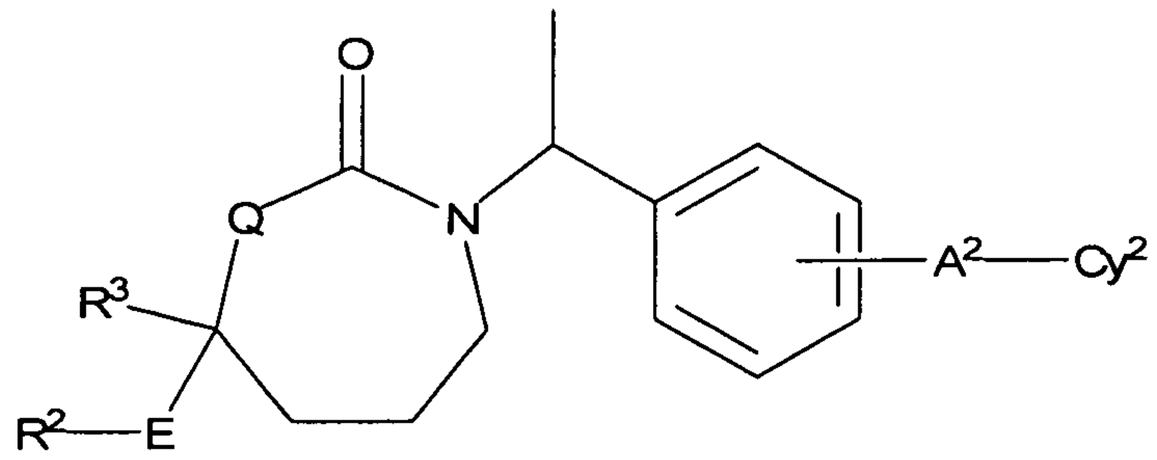
61. The compound of claim 1 wherein the compound is of Formula (Ib)



Ib

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

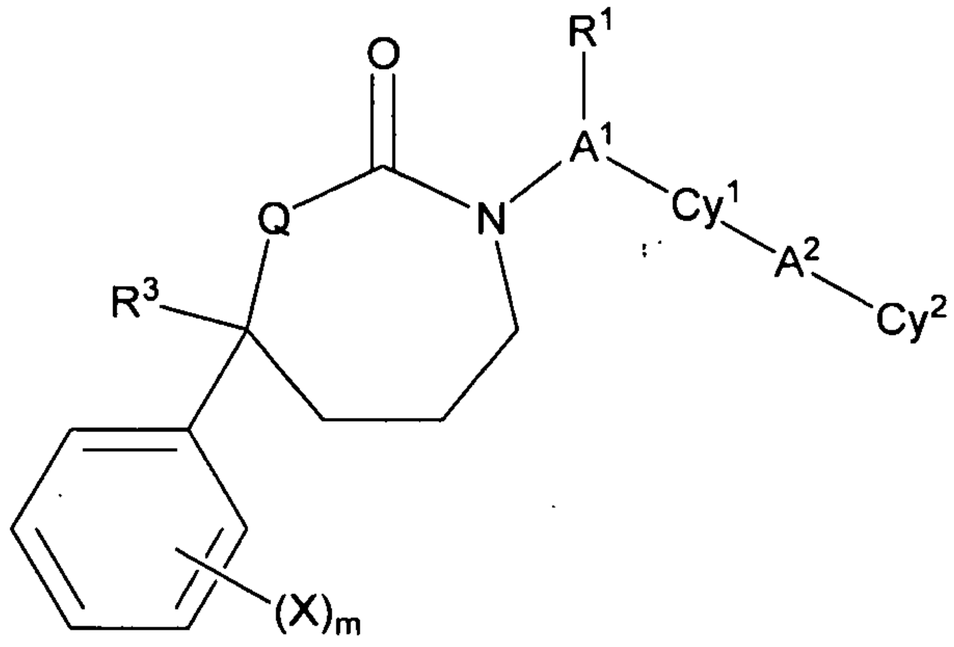
62. The compound of claim 1 wherein the compound is of Formula (Ic)



Ic

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

63. The compound of claim 1 wherein the compound is of Formula (Id)



Id

; wherein

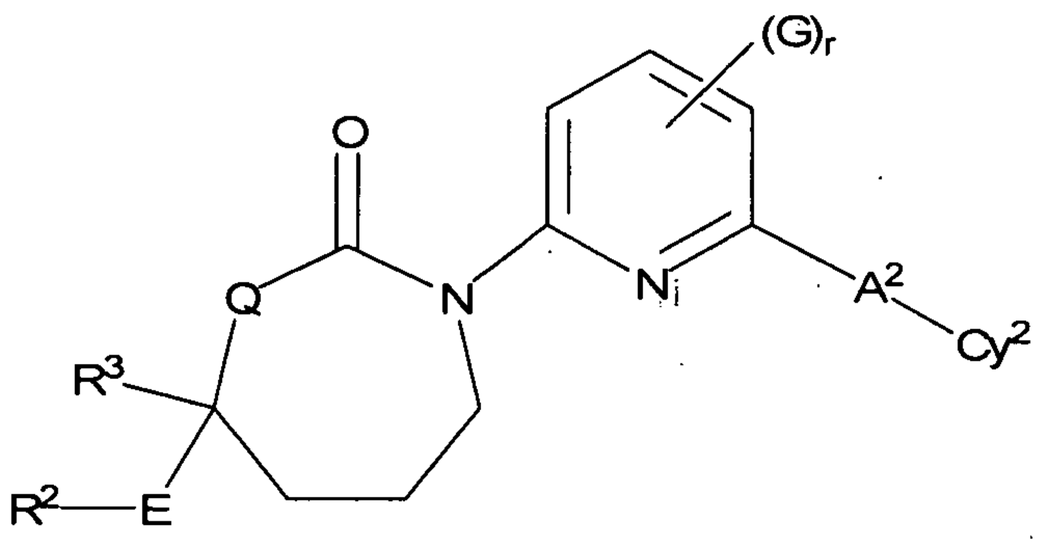
m is 0, 1, 2, 3 or 4;

X is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkanesulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-

C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

64. The compound of claim 1 wherein the compound is of Formula (Ie)



Ie

; wherein

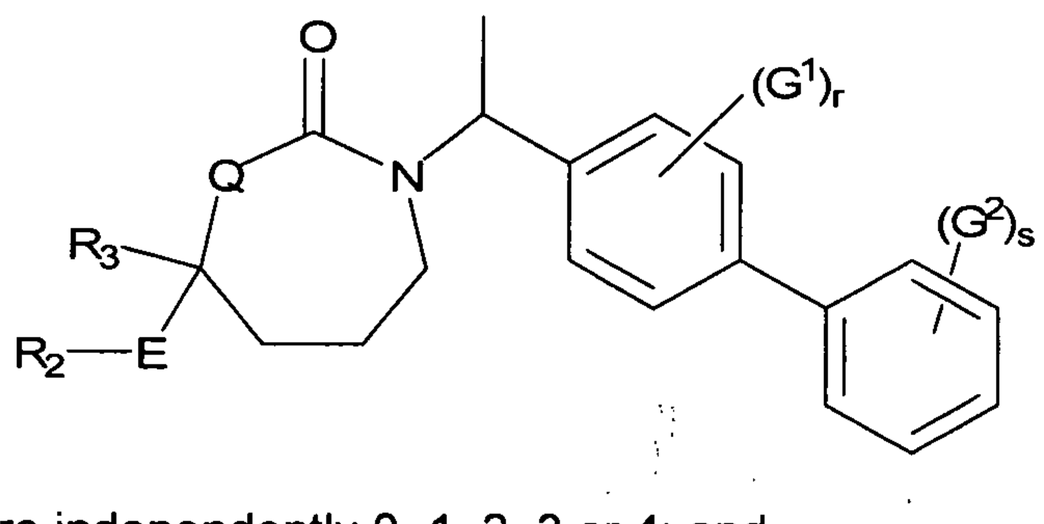
r is 0, 1, 2, 3 or 4;

G is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cycloalkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO,

H_2NSO_2, (C_1-C_6)alkylaminocarbonyl, di(C_1-C_6)alkylaminocarbonyl, (C_1-C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy-carbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl,, hydroxy(C_1-C_6)alkoxy, heteroaryl, oxo, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

65. The compound of claim 1 wherein the compound is of Formula (If)



If

; wherein

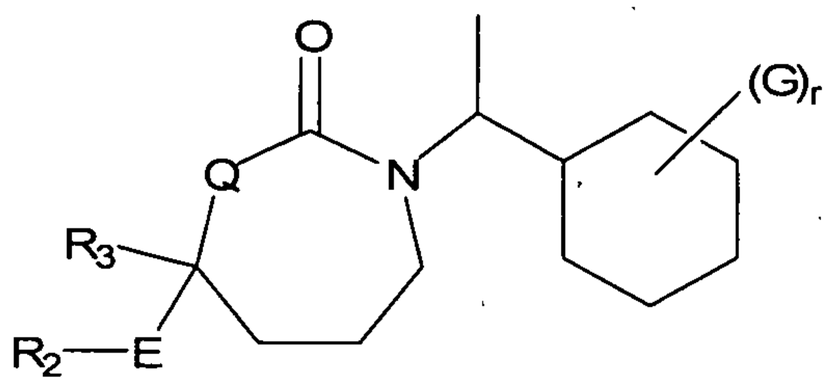
r and s are independently 0, 1, 2, 3 or 4; and

G^1 and G^2 are independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, (C_1-C_6)alkyl, hydroxy(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, hydroxy(C_3-C_6)cycloalkyl, (C_4-C_7)cycloalkylalkyl, (C_2-C_6)alkenyl, halo(C_2-C_6)alkenyl, hydroxy(C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_6)cycloalkyl(C_2-C_4)alkynyl, halo(C_1-C_6)alkyl, halo(C_3-C_6)cycloalkyl, halo(C_4-C_7)cycloalkylalkyl, (C_1-C_6)alkoxy, (C_3-C_6)cycloalkoxy, (C_4-C_7)cycloalkylalkoxy, halo(C_1-C_6)alkoxy, halo(C_3-C_6)cycloalkoxy, halo(C_4-C_7)cycloalkylalkoxy, (C_1-C_6)alkylthio, (C_3-C_6)cycloalkythio, (C_4-C_7)cycloalkylalkylthio, halo(C_1-C_6)alkylthio, halo(C_3-C_6)cycloalkythio, halo(C_4-C_7)cycloalkylalkylthio, (C_1-C_6)alkanesulfinyl, (C_3-C_6)cycloalkanesulfinyl, (C_4-C_7)cycloalkylalkanesulfinyl, halo(C_1-C_6)alkanesulfinyl, halo(C_3-C_6)cycloalkanesulfinyl, halo(C_4-C_7)cycloalkylalkanesulfinyl, (C_1-C_6)alkanesulfonyl, (C_3-C_6)cycloalkanesulfonyl, (C_4-C_7)cycloalkylalkanesulfonyl, halo(C_1-C_6)alkanesulfonyl, halo(C_3-C_6)cycloalkanesulfonyl, halo(C_4-C_7)cyclo-alkylalkanesulfonyl, (C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, halo(C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxycarbonyl, H_2NCO,

H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-$C_3)$alkoxy$(C_1$-$C_3)$alkylaminocarbonyl, heterocyclylcarbonyl, $(C_1$-$C_6)$alkylaminosulfonyl, di$(C_1$-$C_6)$alkylaminosulfonyl, heterocyclsulfonyl, $(C_1$-$C_6)$alkylcarbonylamino, $(C_1$-$C_6)$alkylcarbonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonylamino, $(C_1$-$C_6)$alkylsulfonylamino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-carbonyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl,, hydroxy$(C_1$-$C_6)$alkoxy, heteroaryl, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, di$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl amino$(C_2$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxy, di$(C_1$-$C_6)$alkylamino$(C_2$-$C_6)$alkoxyl and $(C_1$-$C_6)$alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

66. The compound of claim 1 wherein the compound is of Formula (Ig)



Ig

; wherein

r is 0, 1, 2, 3 or 4; and

G is independently selected from fluorine, chlorine, bromine, iodine, cyano, nitro, amino, hydroxy, carboxy, $(C_1$-$C_6)$alkyl, hydroxy$(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, hydroxy$(C_3$-$C_6)$cycloalkyl, $(C_4$-$C_7)$cycloalkylalkyl, $(C_2$-$C_6)$alkenyl, halo$(C_2$-$C_6)$alkenyl, hydroxy$(C_2$-$C_6)$alkenyl, $(C_2$-$C_6)$alkynyl, $(C_3$-$C_6)$cycloalkyl$(C_2$-$C_4)$alkynyl, halo$(C_1$-$C_6)$alkyl, halo$(C_3$-$C_6)$cycloalkyl, halo$(C_4$-$C_7)$cycloalkylalkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkoxy, $(C_4$-$C_7)$cycloalkylalkoxy, halo$(C_1$-$C_6)$alkoxy, halo$(C_3$-$C_6)$cycloalkoxy, halo$(C_4$-$C_7)$cycloalkylalkoxy, $(C_1$-$C_6)$alkylthio, $(C_3$-$C_6)$cycloalkythio, $(C_4$-$C_7)$cycloalkylalkylthio, halo$(C_1$-$C_6)$alkylthio, halo$(C_3$-$C_6)$cycloalkythio, halo$(C_4$-$C_7)$cycloalkylalkylthio, $(C_1$-$C_6)$alkanesulfinyl, $(C_3$-$C_6)$cycloalkanesulfinyl, $(C_4$-$C_7)$cycloalkylalkanesulfinyl, halo$(C_1$-$C_6)$alkanesulfinyl, halo$(C_3$-$C_6)$cycloalkanesulfinyl, halo$(C_4$-$C_7)$cycloalkylalkanesulfinyl, $(C_1$-$C_6)$alkanesulfonyl, $(C_3$-$C_6)$cycloalkanesulfonyl, $(C_4$-$C_7)$cycloalkylalkanesulfonyl, halo$(C_1$-$C_6)$alkanesulfonyl, halo$(C_3$-$C_6)$cycloalkanesulfonyl, halo$(C_4$-$C_7)$cyclo-alkylalkanesulfonyl, $(C_1$-$C_6)$alkylamino, di$(C_1$-$C_6)$alkylamino, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxycarbonyl, H_2NCO, H_2NSO_2, $(C_1$-$C_6)$alkylaminocarbonyl, di$(C_1$-$C_6)$alkylaminocarbonyl, $(C_1$-

C_3)alkoxy(C_1-C_3)alkylaminocarbonyl, heterocyclylcarbonyl, (C_1-C_6)alkylaminosulfonyl, di(C_1-C_6)alkylaminosulfonyl, heterocyclsulfonyl, (C_1-C_6)alkylcarbonylamino, (C_1-C_6)alkylcarbonylamino(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonylamino, (C_1-C_6)alkylsulfonylamino(C_1-C_6)alkyl, (C_1-C_6)alkoxy-carbonyl(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy(C_1-C_6)alkyl, hydroxy(C_1-C_6)alkoxy, heteroaryl, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl amino(C_2-C_6)alkoxy, (C_1-C_6)alkylamino(C_2-C_6)alkoxy, di(C_1-C_6)alkylamino(C_2-C_6)alkoxyl and (C_1-C_6)alkylcarbonyl;

or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.

67. A method of treating a subject with a disease associated with the activity or expression of 11β-HSD1, comprising the step of administering to the subject an effective amount of a compound of claims 1-66.

68. A method of inhibiting 11β-HSD1 activity comprising the step of administering to a mammal in need of such treatment an effective amount of a compound of claims 1-66.

69. A pharmaceutical composition comprising: i) a pharmaceutically acceptable carrier or diluent; and ii) the compound in any one of claims 1-66; or a pharmaceutically acceptable salt, enantiomer or diastereomer thereof.