

SUBSTITUTED DIHYDRO-BENZIMIDAZOLE COMPOUNDS AS ROR GAMMA MODULATORS

Related Applications

This application claims the benefit of Indian Provisional Application No.
5 3207/MUM/2013 filed on October 10, 2013; which is hereby incorporated by reference in its entirety.

Technical Field

The present patent application is directed to substituted dihydro-benzimidazole
compounds which may be useful as retinoid-related orphan receptor gamma t (ROR γ t)
10 modulators.

Background of the invention

Retinoid-related orphan receptors (RORs) are transcription factors which belong to the
steroid hormone nuclear receptor super family. The ROR family consists of three members,
15 ROR alpha (ROR α), ROR beta (ROR β) and ROR gamma (ROR γ), also known as NR1F1,
NR1F2 and NR1F3 respectively (and each encoded by a separate gene RORA, RORB and
RORC, respectively). RORs contain four principal domains shared by the majority of nuclear
receptors: an *N*-terminal A/B domain, a DNA-binding domain, a hinge domain, and a ligand
binding domain. Each ROR gene generates several isoforms which differ only in their *N*-
20 terminal A/B domain. Two isoforms of ROR γ , ROR γ 1 and ROR γ t (also known as ROR γ 2)
have been identified.

ROR γ t is a truncated form of ROR γ , lacking the first *N*-terminal 21 amino acids and is
exclusively expressed in cells of the lymphoid lineage and embryonic lymphoid tissue
inducers (Sun et al., *Science*, **2000**, 288, 2369-2372; Eberl et al., *Nat Immunol.*, **2004**, 5: 64-
25 73) in contrast to ROR γ which is expressed in multiple tissues (heart, brain, kidney, lung,
liver and muscle).

ROR γ t has been identified as a key regulator of Th17 cell differentiation. Th17 cells are
a subset of T helper cells which produce IL-17 and other proinflammatory cytokines and have
been shown to have key functions in several mouse autoimmune disease models including
30 experimental autoimmune encephalomyelitis (EAE) and collagen-induced arthritis (CIA). In
addition, Th17 cells have also been associated in the pathology of a variety of human
inflammatory and autoimmune disorders including multiple sclerosis, rheumatoid arthritis,
psoriasis, Crohn's disease and asthma (Jetten et al., *Nucl. Recept. Signal*, **2009**, 7:e003; Manel

et al., *Nat. Immunol.*, **2008**, 9: 641-649). The pathogenesis of chronic autoimmune diseases including multiple sclerosis and rheumatoid arthritis arises from the break in tolerance towards self-antigens and the development of auto-aggressive effector T cells infiltrating the target tissues. Studies have shown that Th17 cells are one of the important drivers of the inflammatory process in tissue-specific autoimmunity (Steinman et al., *J. Exp. Med.*, **2008**, 205: 1517-1522; Leung et al., *Cell. Mol. Immunol.*, **2010**, 7: 182-189). Th17 cells are activated during the disease process and are responsible for recruiting other inflammatory cells types, especially neutrophils, to mediate pathology in the target tissues (Korn et al., *Annu. Rev. Immunol.*, **2009**, 27:485-517) and ROR γ t has been shown to play a critical role in the pathogenic responses of Th17 cells (Ivanov et al., *Cell*, **2006**, 126: 1121-1133). ROR γ t deficient mice have shown no Th17 cells and also resulted in amelioration of EAE. The genetic disruption of ROR γ in a mouse colitis model also prevented colitis development (Buonocore et al., *Nature*, **2010**, 464: 1371-1375). The role of ROR γ t in the pathogenesis of autoimmune or inflammatory diseases has been well documented in the literature. (Jetten et al., *Adv. Dev. Biol.*, **2006**, 16:313-355; Meier et al. *Immunity*, **2007**, 26:643-654; Aloisi et al., *Nat. Rev. Immunol.*, **2006**, 6:205-217; Jager et al., *J. Immunol.*, **2009**, 183:7169-7177; Serafmi et al., *Brain Pathol.*, **2004**, 14: 164-174; Magliozzi et al., *Brain*, **2007**, 130: 1089-1104; Barnes et al., *Nat. Rev. Immunol.*, **2008**, 8: 183-192).

In addition, ROR γ t is also shown to play a crucial role in other non-Th17 cells, such as mast cells (Hueber et al., *J Immunol.*, **2010**, 184: 3336-3340). ROR γ t expression and secretion of Th17-type of cytokines has also been reported in NK T-cells (Eberl et al., *Nat. Immunol.*, **2004**, 5: 64-73) and gamma-delta T-cells (Sutton et al, *Nat. Immunol.*, **2009**, 31: 331-341; Louten et al., *J Allergy Clin. Immunol.*, **2009**, 123: 1004-1011), suggesting an important function for ROR γ t in these cells.

In view of the above, a need exists for therapeutic agents that could modulate the activity of ROR γ t and thus will open new methods for treating diseases or condition associated with the modulation of ROR γ t.

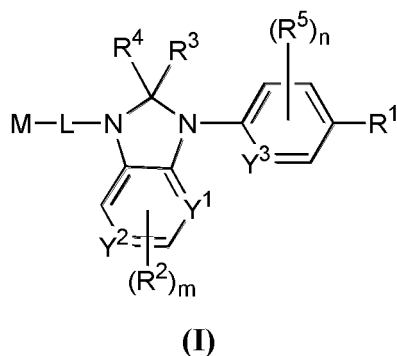
PCT publication numbers WO2012/139775, WO2012/027965, WO2012/028100, WO2012/100732, WO2012/100734, WO2012/064744 and WO2013/171729 disclose numerous heterocyclic compounds which are shown to be modulators of retinoid-related orphan receptor gamma (ROR γ) receptor activity.

The present application is directed to compounds that may be modulators of the ROR γ t receptor. Thus in light of the role ROR γ t plays in the pathogenesis of diseases, it is

desirable to prepare compounds that modulate ROR γ t activity, which can be used in the treatment of diseases mediated by ROR γ t.

Summary of the Invention

5 In one aspect, the present invention relates to compound of formula (I)



or a pharmaceutically acceptable salt thereof,

wherein,

10 L is selected from -C(O)-, -CH₂-, -S(O)₂- and -S(O)-;

M is C₆₋₁₄ aryl, 5 to 14-membered heteroaryl or 3 to 15 membered heterocyclyl, each being optionally substituted with one or more R⁶;

Y¹ and Y² are each independently selected from CH and N;

Y³ is selected from CH and N;

15 R¹ is selected from cyano, -C(O)OR⁹, -C(O)NR⁷R⁸, -S(O)₂NR⁷R⁸, -S(O)₂R¹⁰, -P(O)(OR¹¹)₂, 5 to 14 membered heteroaryl and 3 to 15 membered heterocyclyl;

each occurrence of R² is independently selected from cyano, halogen, hydroxyl, C₁₋₈alkyl, C₁₋₈alkoxy, haloC₁₋₈alkyl, hydroxyC₁₋₈alkyl, C₁₋₈alkoxyC₁₋₈alkyl, C₃₋₁₂cycloalkyl, -NR^yR^z and -CH₂NR^yR^z;

20 R³ and R⁴ are each independently selected from hydrogen, hydroxyl, C₁₋₈alkyl and haloC₁₋₈alkyl; or R³ and R⁴ together with the carbon atom to which they are attached, form a cyclic ring which is substituted or unsubstituted and wherein the cyclic ring optionally contains one or more hetero atoms selected from O, N or S; or R³ and R⁴ together form a oxo (=O) group;

25 each occurrence of R⁵ is independently selected from cyano, halogen, hydroxyl, C₁₋₈alkyl, C₁₋₈alkoxy, haloC₁₋₈alkyl, C₃₋₁₂cycloalkyl and -C(O)OH;

each occurrence of R⁶ is independently selected from cyano, halogen, hydroxyl, C₁₋₈alkyl, C₁₋₈alkoxy, haloC₁₋₈alkyl and C₃₋₁₂cycloalkyl;

R^7 and R^8 are each independently selected from hydrogen, C_{1-8} alkyl and C_{3-6} cycloalkyl;

R^9 is selected from hydrogen, C_{1-8} alkyl, halo C_{1-8} alkyl, C_{3-6} cycloalkyl, C_{6-14} aryl C_{1-8} alkyl and $-(CH_2)_qCOOR^x$;

5 R^{10} is selected from C_{1-8} alkyl and halo C_{1-8} alkyl;

R^{11} is selected from hydrogen and C_{1-8} alkyl;

R^x is selected from hydrogen and C_{1-4} alkyl;

R^y and R^z are each independently selected from hydrogen, C_{1-4} alkyl and C_{3-6} cycloalkyl;

10 'm' is an integer ranging from 0 to 2, both inclusive;

'n' is an integer ranging from 0 to 3, both inclusive; and

'q' is an integer ranging from 1 to 4, both inclusive.

The compounds of formula (I) may involve one or more embodiments. Embodiments of formula (I) includes compounds of formula (Ia) as described hereinafter. It is to be understood that the embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified. It is also to be understood that the embodiments defined herein may be used independently or in conjunction with any definition, any other embodiment defined herein. Thus the invention contemplates all possible combinations and permutations of the various independently described
15 embodiments. For example, the invention provides compounds of formula (I) as defined above wherein L is $-C(O)-$ (according to an embodiment defined below), Y^1 and Y^2 are CH (according to another embodiment defined below), 'm' is 0 or 1 (according to yet another embodiment defined below) and 'n' is 0 or 1 (according to yet another embodiment defined below).
20

25 According to one embodiment, specifically provided are compounds of formula (I), in which L is $-C(O)-$.

According to another embodiment, specifically provided are compounds of formula (I), in which L is $-C(O)-$, $-CH_2-$ or $-S(O)_2-$.

According to yet another embodiment, specifically provided are compounds of
30 formula (I), in which M is C_{6-14} aryl (e.g. phenyl or naphthyl) or 5- to 14- membered heteroaryl (e.g. pyridinyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is phenyl, naphthyl or pyridinyl; each being optionally substituted with one or more of R^6 .

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is phenyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which each occurrence of R⁶ is independently halogen (e.g. F, Cl or Br), C₁₋₈alkyl (e.g. methyl or ethyl), C₁₋₈alkoxy (e.g. methoxy), haloC₁₋₈alkyl (e.g. CHF₂ or CF₃) or C₃₋₁₂cycloalkyl (e.g. cyclopropyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is phenyl optionally substituted with one or two R⁶ substituent(s) independently selected from halogen (e.g. F, Cl or Br), C₁₋₄alkyl (e.g. methyl or ethyl), C₁₋₈alkoxy (e.g. methoxy), haloC₁₋₈alkyl (e.g. CHF₂ or CF₃) and C₃₋₆cycloalkyl (e.g. cyclopropyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is phenyl or pyridine, each being optionally substituted with one or two R⁶ substituent(s) independently selected from F, Cl, Br, OCH₃, CHF₂, CF₃ and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is phenyl or pyridin-4-yl, each being optionally substituted at 2 or 6 position with one or more of R⁶ substituent(s) independently selected from F, Cl, Br, OCH₃, CHF₂, CF₃ and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which M is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl, 1-naphthyl or 3,5-dichloropyridin-4-yl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which L-M is 2,6-dichlorobenzoyl, 2-bromo-6-chlorobenzoyl, 2-chloro-6-methoxybenzoyl, 2-fluoro-6-methoxybenzoyl, 2-chloro-6-(difluoromethyl)benzoyl, 2-chloro-6-(trifluoromethyl)benzoyl, 2-chloro-6-cyclopropylbenzoyl, 1-naphthoyl, (3,5-dichloropyridin-4-yl)carbonyl, 2,6-dichlorobenzyl or [2-(trifluoromethyl)phenyl]sulfonyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R¹ is -C(O)OH.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R¹ is -C(O)OR⁹. In this embodiment R⁹ is hydrogen or C₁₋₄alkyl (e.g. methyl, ethyl, propyl or *tert*-butyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^1 is $-C(O)NR^7R^8$ or $-S(O)_2NR^7R^8$. In this embodiment R^7 is hydrogen or C_{3-6} cycloalkyl (e.g. cyclopropyl) and R^8 is hydrogen.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^1 is $-P(O)(OR^{11})_2$. In this embodiment R^{11} is hydrogen or C_{1-4} alkyl (e.g. methyl or ethyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^1 is 5- to 14-membered heteroaryl (e.g. tetrazolyl or oxadiazolyl).

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^1 is cyano, $-C(O)OH$, $-C(O)OCH_3$, $-C(O)OC_2H_5$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which 'm' is 0 or 1.

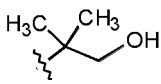
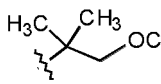
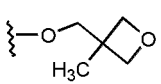
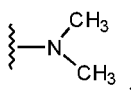
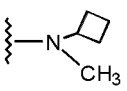
According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^1 and Y^2 are CH.

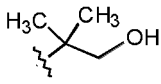
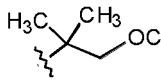
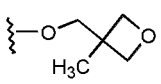
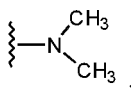
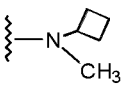
According to yet another embodiment, specifically provided are compounds of formula (I), in which one of the Y^1 and Y^2 is N and other is CH.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^2 is optional substituent present on Y^1 or Y^2 when Y^1 or Y^2 is CH.

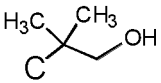
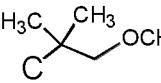
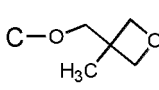
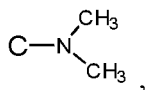
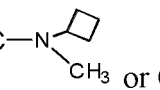
According to yet another embodiment, specifically provided are compounds of formula (I), in which R^2 is cyano, halogen (e.g. Cl or F), hydroxy C_{1-8} alkyl (e.g. hydroxymethyl or 2-hydroxy-1,1-dimethyl-ethyl), C_{1-8} alkoxy C_{1-8} alkyl (e.g. 2-methoxy-1,1-dimethyl-ethyl), C_{1-8} alkoxy (e.g. 3-methyl-oxetan-3-ylmethoxy), $-NR^yR^z$ and $-CH_2NR^yR^z$. In this embodiment R^y and R^z are each independently selected from C_{1-4} alkyl (e.g. methyl or ethyl) or C_{3-6} cycloalkyl (e.g. cyclopropyl or cyclobutyl).

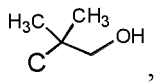
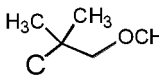
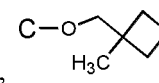
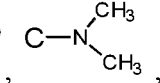
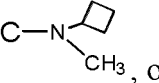
According to yet another embodiment, specifically provided are compounds of formula (I), in which R^2 is CN, halogen (e.g. Cl or F), hydroxy C_{1-8} alkyl (e.g. hydroxymethyl or 2-hydroxy-1,1-dimethyl-ethyl), C_{1-8} alkoxy C_{1-8} alkyl (e.g. 2-methoxy-1,1-dimethyl-ethyl), C_{1-8} alkoxy (e.g. 3-methyl-oxetan-3-ylmethoxy), $-CH_2N(CH_3)_2$, $-N(CH_3)_2$ or ; and 'm' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^2 is CN, F, $-CH_2OH$, , , , ,  or $-CH_2N(CH_3)_2$.

5 According to yet another embodiment, specifically provided are compounds of formula (I), in which R^2 is CN, F, $-CH_2OH$, , , , ,  or $-CH_2N(CH_3)_2$; and 'm' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^1 is N, C-H or C-F.

10 According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^2 is N, C-H, C-F, C-CN, C- CH_2OH , , , , ,  or C- $CH_2N(CH_3)_2$.

According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^1 is N, C-H or C-F; Y^2 is N, C-H, C-F, C-CN, C- CH_2OH , , , , , , or C- $CH_2N(CH_3)_2$; and m is 0 or 1.

15 According to yet another embodiment, specifically provided are compounds of formula (I), in which R^3 and R^4 together form a oxo (=O) group.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^3 is hydrogen and R^4 is C_{1-4} alkyl (e.g. methyl or ethyl).

20 According to yet another embodiment, specifically provided are compounds of formula (I), in which 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^5 is halogen (e.g. Cl or F).

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^5 is F or Cl.

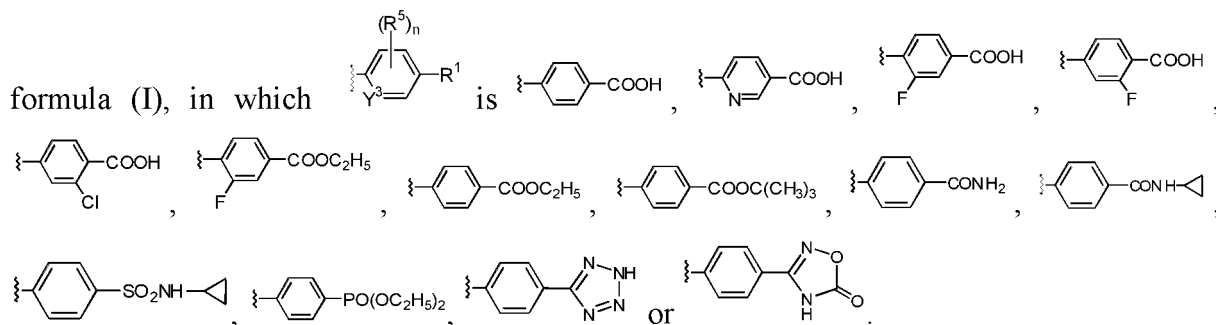
25 According to yet another embodiment, specifically provided are compounds of formula (I), in which R^5 is optional substituent present on Y^3 , when Y^3 is CH.

According to yet another embodiment, specifically provided are compounds of formula (I), in which R^5 is F or Cl; and 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^3 is N, C-H or C-F.

5 According to yet another embodiment, specifically provided are compounds of formula (I), in which Y^3 is N, C-H or C-F; and 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of



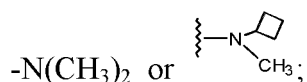
According to yet another embodiment, specifically provided are compounds of formula (I), in which

Y^1 and Y^2 are each independently selected from CH and N;

Y^3 is selected from CH and N;

15 R^1 is cyano, -C(O)OH, -C(O)OCH₃, -C(O)OC₂H₅, -C(O)OC(CH₃)₃, -C(O)NH₂, -C(O)NH-cyclopropyl, -S(O)₂NH-cyclopropyl, -P(O)(OC₂H₅)₂, 2H-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;

R^2 is CN, halogen, hydroxyC₁₋₈alkyl, C₁₋₈alkoxyC₁₋₈alkyl, C₁₋₈alkoxy, -CH₂N(CH₃)₂,



L is -C(O)-;

M is phenyl, naphthyl or pyridinyl; each being optionally substituted with one or two R^6 ;

R^3 and R^4 together form a oxo (=O) group;

R^5 is F or Cl;

25 R^6 is F, Cl, Br, OCH₃, CHF₂, CF₃ or cyclopropyl;

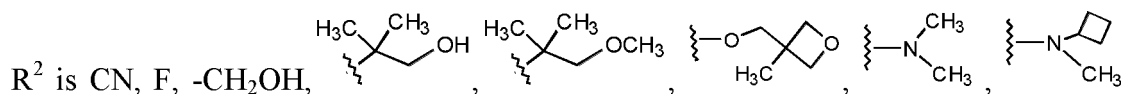
'm' is 0 or 1; and 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (I), in which

Y^1 and Y^2 are each independently selected from CH and N;

30 Y^3 is selected from CH and N;

R^1 is cyano, $-C(O)OH$, $-C(O)OCH_3$, $-C(O)OC_2H_5$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;



5 or $-CH_2N(CH_3)_2$;

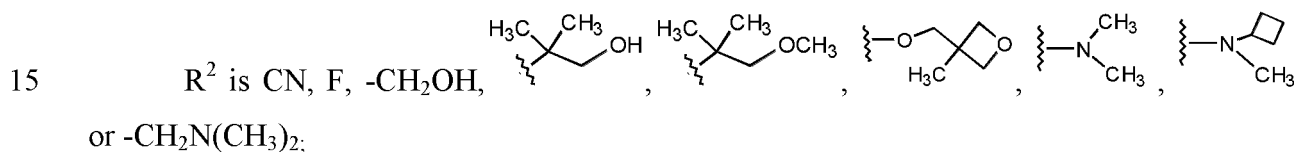
R^3 and R^4 together form a oxo ($=O$) group;

R^5 is F or Cl; 'm' is 0 or 1; 'n' is 0 or 1; and

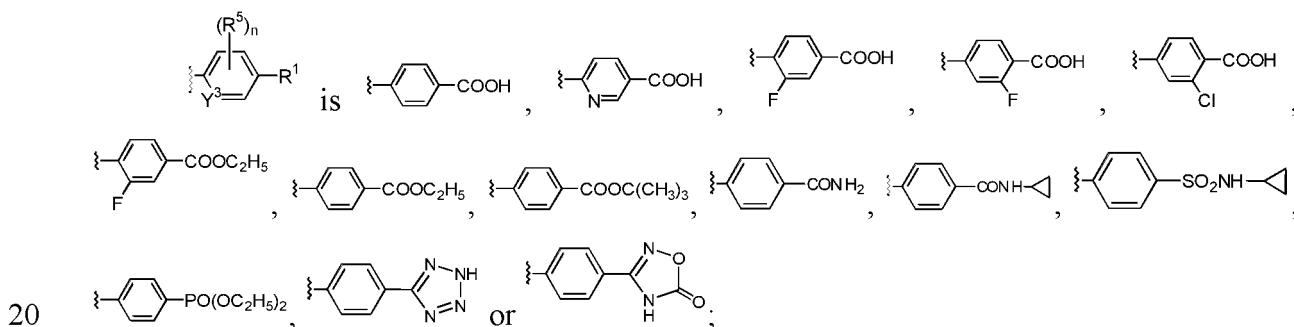
L-M is 2,6-dichlorobenzoyl, 2-bromo-6-chlorobenzoyl, 2-chloro-6-methoxybenzoyl, 2-fluoro-6-methoxybenzoyl, 2-chloro-6-(difluoromethyl)benzoyl, 2-chloro-6-(trifluoromethyl)benzoyl, 2-chloro-6-cyclopropylbenzoyl, 1-naphthoyl, (3,5-dichloropyridin-4-yl)carbonyl, 2,6-dichlorobenzyl or [2-(trifluoromethyl)phenyl]sulfonyl.

According to yet another embodiment, specifically provided are compounds of formula (I), in which

Y^1 and Y^2 are each independently selected from CH and N;



'm' is 0 or 1;



R^3 and R^4 together form a oxo ($=O$) group; and

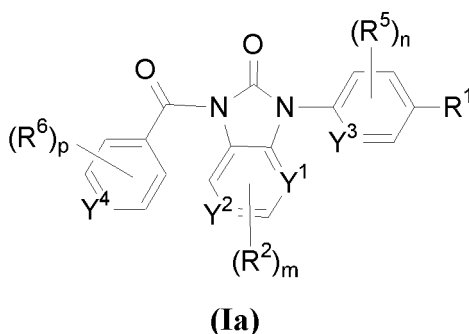
L-M is 2,6-dichlorobenzoyl, 2-bromo-6-chlorobenzoyl, 2-chloro-6-methoxybenzoyl, 2-fluoro-6-methoxybenzoyl, 2-chloro-6-(difluoromethyl)benzoyl, 2-chloro-6-(trifluoromethyl)benzoyl, 2-chloro-6-cyclopropylbenzoyl, 1-naphthoyl, (3,5-dichloropyridin-4-yl)carbonyl, 2,6-dichlorobenzyl or [2-(trifluoromethyl)phenyl]sulfonyl.

According to an embodiment, specifically provided are compounds of formula (I) with an IC_{50} value of less than 500 nM, preferably less than 100 nM, more preferably less than 50 nM with respect to ROR γ t activity.

Further embodiments relating to groups R^1 , R^2 , R^3 , R^4 , R^5 , L, M, Y^1 , Y^2 , Y^3 , m and n (and groups defined therein) are described hereinafter in relation to the compounds of formula (Ia) or formula (Ib). It is to be understood that these embodiments are not limited to use in conjunction with formula (Ia) or formula (Ib), but apply independently and individually to the compounds of formula (I). For example, in an embodiment described hereinafter, the invention specifically provides compounds of formula (Ia) or formula (Ib), in which 'n' is 0 or 1 and consequently there is also provided a compound of formula (I) in which 'n' is 0 or 1.

The invention also provides a compound of formula (Ia), which is an embodiment of a compound of formula (I).

Accordingly the invention provides compound of formula (Ia)



or a pharmaceutically acceptable salt thereof,
wherein,

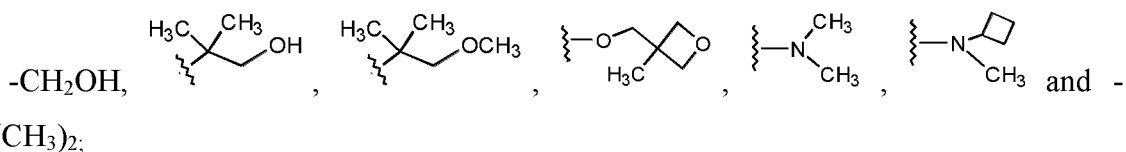
Y^1 and Y^2 are each independently selected from CH and N;

Y^3 is selected from CH and N;

Y^4 is selected from CH and N;

R^1 is selected from cyano, $-C(O)OR^9$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2*H*-tetrazol-5-yl and 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;

each occurrence of R^2 is independently selected from cyano, halogen,



each occurrence of R^5 is independently selected from cyano, halogen, hydroxyl, C_{1-8} alkyl and halo C_{1-8} alkyl;

each occurrence of R^6 is independently selected from halogen, C_{1-8} alkyl, C_{1-8} alkoxy, halo C_{1-8} alkyl and C_{3-6} cycloalkyl;

R^9 is selected from hydrogen and C_{1-8} alkyl;

'm' is an integer ranging from 0 to 2, both inclusive;

'n' is an integer ranging from 0 to 3, both inclusive; and

'p' is an integer ranging from 1 to 4, both inclusive.

The compound of formula (Ia) may involve one or more embodiments. It is to be understood that the embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified. It is also to be understood that the embodiments defined herein may be used independently or in conjunction with any definition of any other embodiment defined herein. Thus, the invention contemplates all possible combinations and permutations of the various independently described embodiments. For example, the invention provides compounds of formula (Ia) as defined above wherein Y¹ and Y² are CH (according to an embodiment defined below), 'm' is 0 or 1 (according to another embodiment defined below) and 'n' is 0 or 1 (according to yet another embodiment defined below).

According to one embodiment, specifically provided are compounds of formula (Ia), in which R¹ is -C(O)OH.

According to another embodiment, specifically provided are compounds of formula (Ia), in which R¹ is -C(O)OR⁹. In this embodiment R⁹ is hydrogen or C₁₋₈alkyl (e.g. methyl, ethyl, propyl or *tert*-butyl).

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R¹ is -C(O)NH₂, -C(O)NH-cyclopropyl, -S(O)₂NH-cyclopropyl, -P(O)(OC₂H₅)₂, 2*H*-tetrazol-5-yl and 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl.

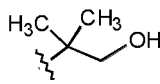
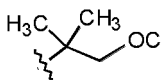
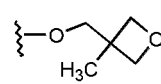
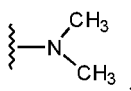
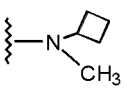
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R¹ is cyano, -C(O)OH, -C(O)OCH₃, -C(O)OC₂H₅, -C(O)OC(CH₃)₃, -C(O)NH₂, -C(O)NH-cyclopropyl, -S(O)₂NH-cyclopropyl, -P(O)(OC₂H₅)₂, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl.

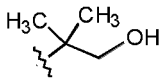
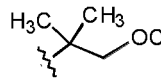
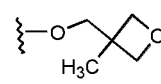
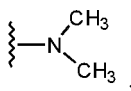
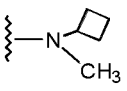
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which 'm' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y¹ and Y² are CH.

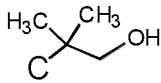
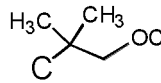
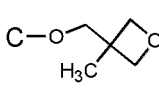
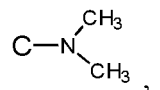
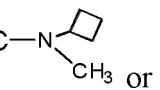
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which one of the Y¹ and Y² is N and other is CH.

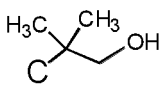
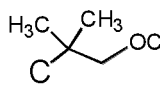
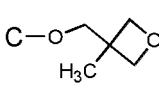
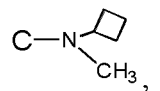
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R² is optional substituent present on Y¹ or Y² when Y¹ or Y² is CH.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^2 is CN, F, $-\text{CH}_2\text{OH}$, , , , ,  or $-\text{CH}_2\text{N}(\text{CH}_3)_2$.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^2 is CN, F, $-\text{CH}_2\text{OH}$, , , , ,  or $-\text{CH}_2\text{N}(\text{CH}_3)_2$; and 'm' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y^1 is N, C-H or C-F.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y^2 is N, C-H, C-F, C-CN, C- CH_2OH , , , , ,  or C- $\text{CH}_2\text{N}(\text{CH}_3)_2$.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y^1 is N, C-H or C-F; Y^2 is N, C-H, C-F, C-CN, C- CH_2OH , , , , , C- $\text{N}(\text{CH}_3)_2$, or C- $\text{CH}_2\text{N}(\text{CH}_3)_2$; and m is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^5 is halogen (e.g. Cl or F).

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^5 is F or Cl.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^5 is an optional substituent present on Y^3 , when Y^3 is CH.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^5 is F or Cl; and 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y^3 is N, C-H or C-F.

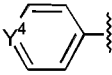
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which Y^3 is N, C-H or C-F; and 'n' is 0 or 1.

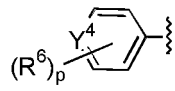
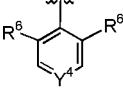
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which each occurrence of R^6 is independently halogen (e.g. F, Cl or Br), C_{1-8} alkyl (e.g. methyl or ethyl), C_{1-8} alkoxy (e.g. methoxy), halo C_{1-8} alkyl (e.g. CHF_2 or CF_3) or C_{3-6} cycloalkyl (e.g. cyclopropyl).

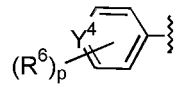
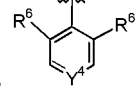
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which each occurrence of R^6 is independently halogen (e.g. F, Cl or Br), C_{1-8} alkyl (e.g. methyl or ethyl), C_{1-8} alkoxy (e.g. methoxy), halo C_{1-8} alkyl (e.g. CHF_2 or CF_3) or C_{3-6} cycloalkyl (e.g. cyclopropyl); and 'p' is 1 or 2.

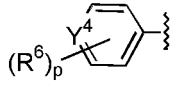
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl; and 'p' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which  ring is optionally substituted at 2 or 6 position with one or two R^6 substituent(s) independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which  is . In this embodiment R^6 is independently halogen (e.g. F, Cl or Br), C_{1-8} alkyl (e.g. methyl or ethyl), C_{1-8} alkoxy (e.g. methoxy), halo C_{1-8} alkyl (e.g. CHF_2 or CF_3) or C_{3-6} cycloalkyl (e.g. cyclopropyl).

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which  is . In this embodiment R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

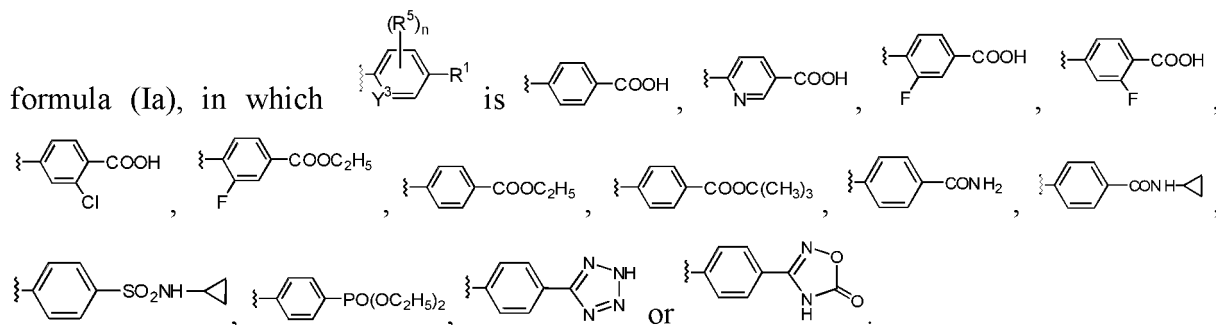
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-

6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl.

According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R⁹ is hydrogen or C₁₋₄alkyl (e.g. methyl, ethyl, propyl or *tert*-butyl).

5 According to yet another embodiment, specifically provided are compounds of formula (Ia), in which R⁹ is hydrogen, methyl, ethyl, propyl or *tert*-butyl.

According to yet another embodiment, specifically provided are compounds of



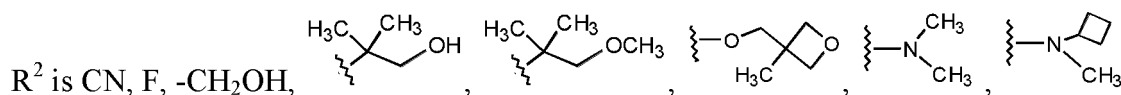
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which

Y¹ and Y² are each independently selected from CH and N;

Y³ is selected from CH and N;

15 Y⁴ is selected from CH and N;

R¹ is cyano, -C(O)OH, -C(O)OCH₃, -C(O)OC₂H₅, -C(O)OC(CH₃)₃, -C(O)NH₂, -C(O)NH-cyclopropyl, -S(O)₂NH-cyclopropyl, -P(O)(OC₂H₅)₂, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;



20 or -CH₂N(CH₃)₂;

R⁵ is F or Cl;

R⁶ is F, Cl, Br, OCH₃, CHF₂, CF₃ or cyclopropyl;

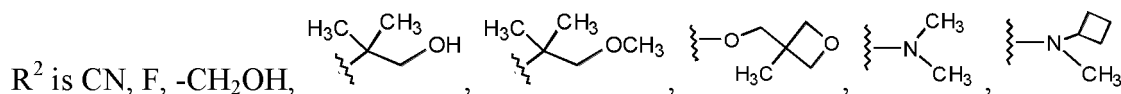
'm' is 0 or 1; 'n' is 0 or 1; and 'p' is 1 or 2.

25 According to yet another embodiment, specifically provided are compounds of formula (Ia), in which

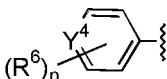
Y¹ and Y² are each independently selected from CH and N;

Y³ is selected from CH and N;

R^1 is cyano, $-C(O)OH$, $-C(O)OCH_3$, $-C(O)OC_2H_5$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;



5 or $-CH_2N(CH_3)_2$;

 is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl;

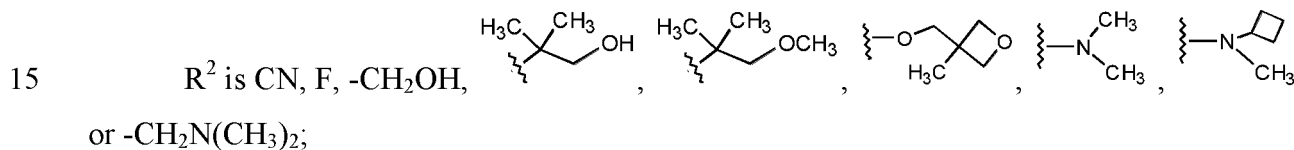
R^5 is F or Cl;

10 'm' is 0 or 1; and

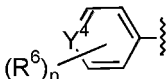
'n' is 0 or 1.

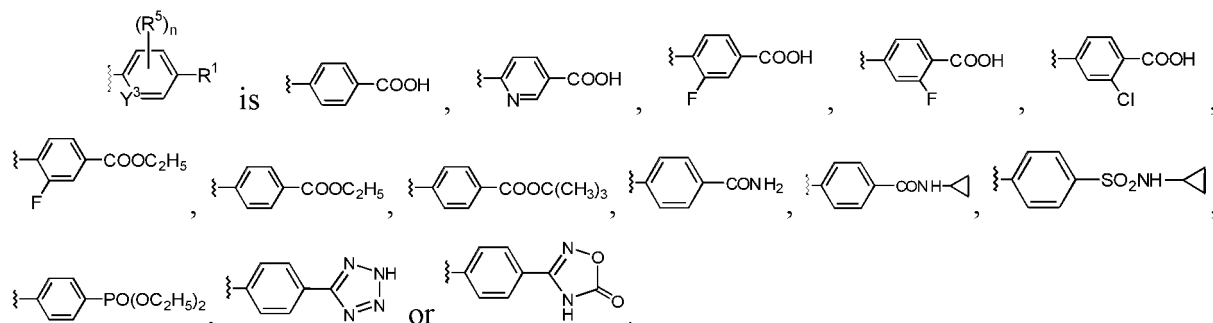
According to yet another embodiment, specifically provided are compounds of formula (Ia), in which

Y^1 and Y^2 are each independently selected from CH and N;



'm' is 0 or 1;

20  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl; and

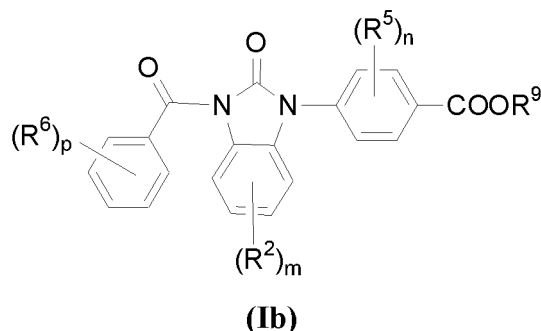


25 According to an embodiment, specifically provided are compounds of formula (Ia) with an IC_{50} value of less than 500 nM, preferably less than 100 nM, more preferably less than 50 nM with respect to ROR γ t activity.

Further embodiments relating to groups R^1 , R^2 , R^5 , R^6 , R^9 , Y^1 , Y^2 , Y^3 , Y^4 , m , n and p (and groups defined therein) are described hereinafter in relation to the compounds of formula (Ib). It is to be understood that these embodiments are not limited to use in conjunction with formula (Ib), but apply independently and individually to the compounds of Formula (I) or Formula (Ia). For example, in an embodiment described hereinafter, the invention specifically provides compounds of formula (Ib), in which 'n' is 0 or 1 and consequently there is also provided a compound of Formula (I) or Formula (Ia) in which 'n' is 0 or 1.

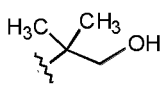
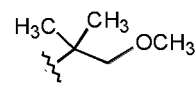
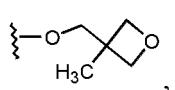
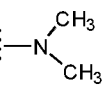
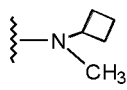
The invention also provides a compound of formula (Ib), which is an embodiment of a compound of formula (I).

Accordingly the invention provides compound of formula (Ib)



or a pharmaceutically acceptable salt thereof,

wherein,

each occurrence of R^2 is independently selected from cyano, F, $-\text{CH}_2\text{OH}$, , , , ,  and $-\text{CH}_2\text{N}(\text{CH}_3)_2$;

each occurrence of R^5 is independently selected from cyano, halogen, hydroxyl, C_{1-8} alkyl and haloC_{1-8} alkyl;

each occurrence of R^6 is independently selected from halogen, C_{1-8} alkyl, C_{1-8} alkoxy, haloC_{1-8} alkyl and C_{3-6} cycloalkyl;

R^9 is selected from hydrogen and C_{1-8} alkyl;

'm' is an integer ranging from 0 to 2, both inclusive;

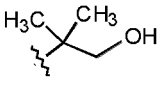
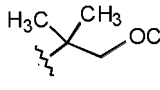
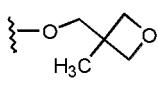
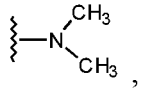
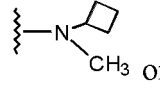
'n' is an integer ranging from 0 to 3, both inclusive; and

'p' is an integer ranging from 1 to 4, both inclusive.

The compounds of formula (Ib) may involve one or more embodiments. It is to be understood that the embodiments below are illustrative of the present invention and are not

intended to limit the claims to the specific embodiments exemplified. It is also to be understood that the embodiments defined herein may be used independently or in conjunction with any definition of any other embodiment defined herein. Thus, the invention contemplates all possible combinations and permutations of the various independently described
 5 embodiments. For example, the invention provides compounds of formula (Ib) as defined above wherein R^5 is F or Cl (according to an embodiment defined below), 'm' is 0 or 1 (according to another embodiment defined below) and 'n' is 0 or 1 (according to yet another embodiment defined below).

According to one embodiment, specifically provided are compounds of formula (Ib),
 10 in which 'm' is 0 or 1.

According to another embodiment, specifically provided are compounds of formula (Ib), in which R^2 is CN, F, $-CH_2OH$, , , , , , or $-CH_2N(CH_3)_2$; and 'm' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of
 15 formula (Ib), in which 'n' is 0 or 1.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which R^5 is halogen (e.g. Cl or F).

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which R^5 is F or Cl.

According to yet another embodiment, specifically provided are compounds of
 20 formula (Ib), in which R^5 is F or Cl; and 'n' is 0 or 1.

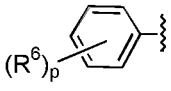
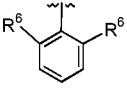
According to yet another embodiment, specifically provided are compounds of formula (Ib), in which each occurrence of R^6 is independently halogen (e.g. F, Cl or Br), C_{1-8} alkyl (e.g. methyl or ethyl), C_{1-8} alkoxy (e.g. methoxy), halo C_{1-8} alkyl (e.g. CHF_2 or CF_3) or
 25 C_{3-6} cycloalkyl (e.g. cyclopropyl).

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which each occurrence of R^6 is independently halogen (e.g. F, Cl or Br), C_{1-8} alkyl (e.g. methyl or ethyl), C_{1-8} alkoxy (e.g. methoxy), halo C_{1-8} alkyl (e.g. CHF_2 or CF_3) or C_{3-6} cycloalkyl (e.g. cyclopropyl); and 'p' is 1 or 2.

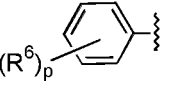
According to yet another embodiment, specifically provided are compounds of
 30 formula (Ib), in which R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl; and 'p' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which  ring is optionally substituted at 2 or 6 position with one or two R^6 substituent(s) independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which $(R^6)_p$  is . In this embodiment R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl.

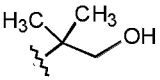
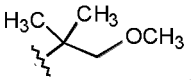
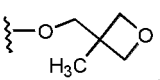
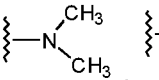
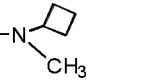
According to yet another embodiment, specifically provided are compounds of

formula (Ib), in which $(R^6)_p$  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl or 2-chloro-6-cyclopropylphenyl.

According to yet another embodiment, specifically provided are compounds of formula (Ib), R^9 is hydrogen or C_{1-8} alkyl (e.g. methyl, ethyl, propyl or *tert*-butyl).

According to yet another embodiment, specifically provided are compounds of formula (Ib), R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which

R^2 is CN , F, $-CH_2OH$, , , , , , or $-CH_2N(CH_3)_2$;

R^5 is F or Cl;

R^6 is F, Cl, Br, OCH_3 , CHF_2 , CF_3 or cyclopropyl;

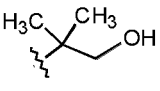
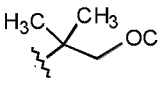
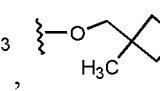
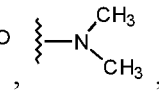
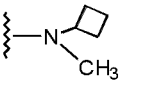
R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl;

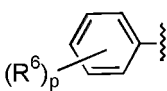
'm' is 0 or 1;

'n' is 0 or 1; and

'p' is 1 or 2.

According to yet another embodiment, specifically provided are compounds of formula (Ib), in which

R^2 is CN, F, $-\text{CH}_2\text{OH}$, , , , , ,
or $-\text{CH}_2\text{N}(\text{CH}_3)_2$;

$(R^6)_p$  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, or 2-chloro-6-cyclopropylphenyl;

R^5 is F or Cl;

R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl;

'm' is 0 or 1;

and 'n' is 0 or 1.

According to an embodiment, specifically provided are compounds of formula (Ia) with an IC_{50} value of less than 500 nM, preferably less than 100 nM, more preferably less than 50 nM with respect to ROR γ t activity.

Compounds of the present invention include the compounds in Examples 1-44.

It should be understood that the formulas (I), (Ia) and (Ib) (structurally encompasses all geometrical isomers, stereoisomers, enantiomers and diastereomers, *N*-oxides, and pharmaceutically acceptable salts that may be contemplated from the chemical structure of the genera described herein.

As disclosed herein, esters of the compounds of present invention refer to a modified version or a precursor of a parent compound, designed to enhance the delivery properties and be converted to the parent compound in the body.

Ester of the compounds of present invention are entities structurally related to parent acidic drug compound ($-\text{COOH}$), which, after administration, release the parent drug *in vivo* as the result of some metabolic process, such as enzymatic or chemical hydrolysis of a susceptible functionality.

R^1 is $-\text{COOR}^9$ Ester (wherein R^9 is C_{1-8} alkyl) of the compounds of present invention are entities structurally related to parent acidic drug compound (R^9 is $-\text{COOH}$), which, after administration, release the parent drug *in vivo* as the result of some metabolic process, such as enzymatic or chemical hydrolysis of a susceptible functionality.

The present application also provides a pharmaceutical composition that includes at least one compound described herein and at least one pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the pharmaceutical composition comprises a therapeutically effective amount of at least one compound described

herein. The compounds described in the present patent application may be associated with a pharmaceutically acceptable excipient (such as a carrier or a diluent) or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container.

5 The compounds and pharmaceutical compositions of the present invention are useful for inhibiting the activity of ROR γ t, which is believed to be related to a variety of disease states.

 The present patent application further provides a method of inhibiting ROR γ t in a subject in need thereof by administering to the subject one or more compounds described
10 herein in the amount effective to cause inhibition of such receptor.

Detailed Description of the Invention

Definitions

 The terms “halogen” or “halo” means fluorine (fluoro), chlorine (chloro), bromine
15 (bromo), or iodine (iodo).

 The term “alkyl” refers to a hydrocarbon chain radical that includes solely carbon and hydrogen atoms in the backbone, containing no unsaturation, having from one to eight carbon atoms (i.e. C₁₋₈alkyl), and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl, and 1,1-dimethylethyl (t-
20 butyl). The term “C₁₋₆ alkyl” refers to an alkyl chain having 1 to 6 carbon atoms. The term “C₁₋₄alkyl” refers to an alkyl chain having 1 to 4 carbon atoms. Unless set forth or recited to the contrary, all alkyl groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

 The term “alkenyl” refers to a hydrocarbon chain containing from 2 to 10 carbon
25 atoms (i.e. C₂₋₁₀alkenyl) and including at least one carbon-carbon double bond. Non-limiting examples of alkenyl groups include ethenyl, 1-propenyl, 2-propenyl (allyl), *iso*-propenyl, 2-methyl-1-propenyl, 1-butenyl, and 2-butenyl. Unless set forth or recited to the contrary, all alkenyl groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

30 The term “alkynyl” refers to a hydrocarbonyl radical having at least one carbon-carbon triple bond, and having 2 to about 12 carbon atoms (with radicals having 2 to about 10 carbon atoms being preferred i.e. C₂₋₁₀alkynyl). Non-limiting examples of alkynyl groups include ethynyl, propynyl, and butynyl. Unless set forth or recited to the contrary, all alkynyl groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

The term “alkoxy” denotes an alkyl group attached via an oxygen linkage to the rest of the molecule (i.e. C₁₋₈ alkoxy). Representative examples of such groups are -OCH₃ and -OC₂H₅. Unless set forth or recited to the contrary, all alkoxy groups described or claimed herein may be straight chain or branched, substituted or unsubstituted.

5 The term “alkoxyalkyl” or “alkyloxyalkyl” refers to an alkoxy or alkyloxy group as defined above directly bonded to an alkyl group as defined above (i.e. C₁₋₈alkoxyC₁₋₈alkyl or C₁₋₈alkyloxyC₁₋₈alkyl). Example of such alkoxyalkyl moiety includes, but are not limited to, -CH₂OCH₃ and -CH₂OC₂H₅. Unless set forth or recited to the contrary, all alkoxyalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

10 The term “haloalkyl” refers to at least one halo group (selected from F, Cl, Br or I), linked to an alkyl group as defined above (i.e. haloC₁₋₈alkyl). Examples of such haloalkyl moiety include, but are not limited to, trifluoromethyl, difluoromethyl and fluoromethyl groups. Unless set forth or recited to the contrary, all haloalkyl groups described herein may be straight chain or branched, substituted or unsubstituted.

15 The term “haloalkoxy” refers to an alkoxy group substituted with one or more halogen atoms (i.e. haloC₁₋₈alkoxy). Examples of “haloalkoxy” include but are not limited to fluoromethoxy, difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy, pentachloroethoxy, chloromethoxy, dichloromethoxy, trichloromethoxy and 1-bromoethoxy. Unless set forth or recited to the contrary, all haloalkoxy groups described herein may be
20 straight chain or branched, substituted or unsubstituted.

The term “hydroxyalkyl” refers to an alkyl group as defined above wherein one to three hydrogen atoms on different carbon atoms is/are replaced by hydroxyl groups (i.e. hydroxyC₁₋₈alkyl). Examples of hydroxyalkyl moieties include, but are not limited to -CH₂OH, -C₂H₄OH and -CH(OH)C₂H₄OH.

25 The term “cycloalkyl” denotes a non-aromatic mono or multicyclic ring system of 3 to about 12 carbon atoms, (i.e. C₃₋₁₂cycloalkyl). Examples of monocyclic cycloalkyl include but are not limited to cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Examples of multicyclic cycloalkyl groups include, but are not limited to, perhydronaphthyl, adamantyl and norbornyl groups, bridged cyclic groups or spirobicyclic groups, e.g., spiro(4,4)non-2-yl. The
30 term “C₃₋₆cycloalkyl” refers to the cyclic ring having 3 to 6 carbon atoms. Unless set forth or recited to the contrary, all cycloalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “cycloalkylalkyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms directly attached to an alkyl group (i.e. C₃₋₈cycloalkylC₁₋₈alkyl). The

cycloalkylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Non-limiting examples of such groups include cyclopropylmethyl, cyclobutylethyl, and cyclopentylethyl. Unless set forth or recited to the contrary, all cycloalkylalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “cycloalkenyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms with at least one carbon-carbon double bond, (i.e. C₃₋₈cycloalkenyl). Examples of “cycloalkenyl” include but are not limited to cyclopropenyl, cyclobutenyl, and cyclopentenyl. Unless set forth or recited to the contrary, all cycloalkenyl groups described or claimed herein may be substituted or unsubstituted.

The term “cycloalkenylalkyl” refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms with at least one carbon-carbon double bond, directly attached to an alkyl group, (i.e. C₃₋₈cycloalkenylC₁₋₈alkyl). The cycloalkenylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all cycloalkenylalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “aryl” refers to an aromatic radical having 6 to 14 carbon atoms (i.e. C₆₋₁₄aryl), including monocyclic, bicyclic and tricyclic aromatic systems, such as phenyl, naphthyl, tetrahydronaphthyl, indanyl, and biphenyl. Unless set forth or recited to the contrary, all aryl groups described or claimed herein may be substituted or unsubstituted.

The term “aryloxy” refers to an aryl group as defined above attached via an oxygen linkage to the rest of the molecule (i.e. C₆₋₁₄aryloxy). Examples of aryloxy moieties include, but are not limited to phenoxy and naphthoxy. Unless set forth or recited to the contrary, all aryloxy groups described herein may be substituted or unsubstituted.

The term “arylalkyl” refers to an aryl group as defined above directly bonded to an alkyl group as defined above, i.e. C₆₋₁₄arylC₁₋₈alkyl, such as -CH₂C₆H₅ and -C₂H₄C₆H₅. Unless set forth or recited to the contrary, all arylalkyl groups described or claimed herein may be substituted or unsubstituted.

The term “heterocyclic ring” or “heterocyclyl” unless otherwise specified refers to non-aromatic 3 to 15 membered ring radical (i.e. 3 to 15 membered heterocyclyl) which consists of carbon atoms and from one to five hetero atoms selected from nitrogen, phosphorus, oxygen and sulfur. The heterocyclic ring radical may be a mono-, bi- or tricyclic ring system, which may include fused, bridged or spiro ring systems, and the nitrogen, phosphorus, carbon, oxygen or sulfur atoms in the heterocyclic ring radical may be optionally

oxidized to various oxidation states. In addition, the nitrogen atom may be optionally quaternized; also, unless otherwise constrained by the definition the heterocyclic ring or heterocyclyl may optionally contain one or more olefinic bond(s). Examples of such heterocyclic ring radicals include, but are not limited to azepinyl, azetidiny, benzodioxolyl, benzodioxanyl, chromanyl, dioxolanyl, dioxaphospholanyl, decahydroisoquinolyl, indanyl, 5 indoliny, isoindoliny, isochromanyl, isothiazolidiny, isoxazolidiny, morpholiny, oxazoliny, oxazolidiny, 2-oxopiperaziny, 2-oxopiperidiny, 2-oxopyrrolidiny, 2-oxoazepiny, octahydroindolyl, octahydroisoindolyl, perhydroazepiny, piperaziny, 4-piperidony, pyrrolidiny, piperidiny, phenothiaziny, phenoxaziny, quinuclidiny, 10 tetrahydroisquinolyl, tetrahydrofuryl or tetrahydrofuranyl, tetrahydropyranyl, thiazoliny, thiazolidiny, thiamorpholiny, thiamorpholiny sulfoxide and thiamorpholiny sulfone. The heterocyclic ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heterocyclyl groups described or claimed herein may be substituted or 15 unsubstituted.

The term "heterocyclylalkyl" refers to a heterocyclic ring radical directly bonded to an alkyl group (i.e. 3 to 15 membered heterocyclylC₁₋₈alkyl). The heterocyclylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heterocyclylalkyl 20 groups described or claimed herein may be substituted or unsubstituted.

The term "heteroaryl" unless otherwise specified refers 5 to 14 membered aromatic heterocyclic ring radical with one or more heteroatom(s) independently selected from N, O or S (i.e. 5 to 14 membered heteroaryl). The heteroaryl may be a mono-, bi- or tricyclic ring system. The heteroaryl ring radical may be attached to the main structure at any heteroatom or 25 carbon atom that results in the creation of a stable structure. Examples of such heteroaryl ring radicals include, but are not limited to oxazolyl, isoxazolyl, imidazolyl, furyl, indolyl, isoindolyl, pyrrolyl, triazolyl, triazinyl, tetrazoyl, thienyl, oxadiazolyl, thiazolyl, isothiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, pyrazolyl, benzofuranyl, benzothiazolyl, benzoxazolyl, benzimidazolyl, benzothienyl, benzopyranyl, carbazolyl, quinoliny, 30 isoquinoliny, quinazoliny, cinnoliny, naphthyridiny, pteridiny, puriny, quinoxaliny, quinolyl, isoquinolyl, thiadiazolyl, indoliziny, acridiny, phenaziny and phthalaziny. Unless set forth or recited to the contrary, all heteroaryl groups described or claimed herein may be substituted or unsubstituted.

The term “heteroarylalkyl” refers to a heteroaryl ring radical directly bonded to an alkyl group (i.e. 5 to 14 membered heterarylC₁₋₈alkyl). The heteroarylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure. Unless set forth or recited to the contrary, all heteroarylalkyl groups described or claimed herein may be substituted or unsubstituted.

Unless otherwise specified, the term “substituted” as used herein refers to substitution with any one or any combination of the following substituents: hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted hydroxyl alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted guanidine, -COOR^{x'}, -C(O)R^{x'}, -C(S)R^{x'}, -C(O)NR^{x'}R^{y'}, -C(O)ONR^{x'}R^{y'}, -NR^{x'}CONR^{y'}R^{z'}, -N(R^{x'})SOR^{y'}, -N(R^{x'})SO₂R^{y'}, -(=N-N(R^{x'})R^{y'}), -NR^{x'}C(O)OR^{y'}, -NR^{x'}R^{y'}, -NR^{x'}C(O)R^{y'}, -NR^{x'}C(S)R^{y'}, -NR^{x'}C(S)NR^{y'}R^{z'}, -SONR^{x'}R^{y'}, -SO₂NR^{x'}R^{y'}, -OR^{x'}, -OC(O)NR^{y'}R^{z'}, -OC(O)OR^{y'}, -OC(O)R^{x'}, -OC(O)NR^{x'}R^{y'}, -SR^{x'}, -SOR^{x'}, -SO₂R^{x'}, and -ONO₂, wherein each occurrence of R^{x'}, R^{y'} and R^{z'} are independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted heterocyclalkyl ring, substituted or unsubstituted heteroarylalkyl, and substituted or unsubstituted heterocyclic ring. The substituents in the aforementioned “substituted” groups cannot be further substituted. For example, when the substituent on “substituted alkyl” is “substituted aryl”, the substituent on “substituted aryl” can be unsubstituted alkenyl but cannot be “substituted alkenyl”.

The term “pharmaceutically acceptable salt” includes salts prepared from pharmaceutically acceptable bases or acids including inorganic or organic bases and inorganic or organic acids. Examples of such salts include, but are not limited to, acetate, benzenesulfonate, benzoate, bicarbonate, bisulfate, bitartrate, borate, bromide, camsylate,

carbonate, chloride, clavulanate, citrate, dihydrochloride, edetate, edisylate, estolate, esylate, fumarate, gluceptate, gluconate, glutamate, glycolylarsanilate, hexylresorcinate, hydrabamine, hydrobromide, hydrochloride, hydroxynaphthoate, iodide, isothionate, lactate, lactobionate, laurate, malate, maleate, mandelate, mesylate, methylbromide, methylnitrate, methylsulfate, mucate, napsylate, nitrate, *N*-methylglucamine ammonium salt, oleate, oxalate, pamoate (embonate), palmitate, pantothenate, phosphate, diphosphate, polygalacturonate, salicylate, stearate, sulfate, subacetate, succinate, tannate, tartrate, teoclate, tosylate, triethiodide and valerate. Examples of salts derived from inorganic bases include, but are not limited to, aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic, mangamous, potassium, sodium, and zinc.

The term “treating” or “treatment” of a state, disorder or condition includes: (a) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a subject that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition; (b) inhibiting the state, disorder or condition, i.e., arresting or reducing the development of the disease or at least one clinical or subclinical symptom thereof; or (c) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms.

The term “subject” includes mammals (especially humans) and other animals, such as domestic animals (e.g., household pets including cats and dogs) and non-domestic animals (such as wildlife).

A “therapeutically effective amount” means the amount of a compound that, when administered to a subject for treating a state, disorder or condition, is sufficient to effect such treatment. The “therapeutically effective amount” will vary depending on the compound, the disease and its severity and the age, weight, physical condition and responsiveness of the subject to be treated.

Pharmaceutical Compositions

The compounds of the invention are typically administered in the form of a pharmaceutical composition. Such compositions can be prepared using procedures well known in the pharmaceutical art and comprise at least one compound of the invention. The pharmaceutical composition of the present patent application comprises one or more compounds described herein and one or more pharmaceutically acceptable excipients. Typically, the pharmaceutically acceptable excipients are approved by regulatory authorities

or are generally regarded as safe for human or animal use. The pharmaceutically acceptable excipients include, but are not limited to, carriers, diluents, glidants and lubricants, preservatives, buffering agents, chelating agents, polymers, gelling agents, viscosifying agents, solvents and the like.

5 Examples of suitable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, peanut oil, olive oil, gelatin, lactose, terra alba, sucrose, dextrin, magnesium carbonate, sugar, amylose, magnesium stearate, talc, gelatin, agar, pectin, acacia, stearic acid, lower alkyl ethers of cellulose, silicic acid, fatty acids, fatty acid amines, fatty acid monoglycerides and diglycerides, fatty acid esters, and polyoxyethylene.

10 The pharmaceutical composition may also include one or more pharmaceutically acceptable auxiliary agents, wetting agents, suspending agents, preserving agents, buffers, sweetening agents, flavouring agents, colorants or any combination of the foregoing.

 The pharmaceutical compositions may be in conventional forms, for example, capsules, tablets, solutions, suspensions, injectables or products for topical application.

15 Further, the pharmaceutical composition of the present invention may be formulated so as to provide desired release profile.

 Administration of the compounds of the invention, in pure form or in an appropriate pharmaceutical composition, can be carried out using any of the accepted routes of administration of pharmaceutical compositions. The route of administration may be any route
20 which effectively transports the active compound of the patent application to the appropriate or desired site of action. Suitable routes of administration include, but are not limited to, oral, nasal, buccal, dermal, intradermal, transdermal, parenteral, rectal, subcutaneous, intravenous, intraurethral, intramuscular, or topical.

 Solid oral formulations include, but are not limited to, tablets, capsules (soft or hard
25 gelatin), dragees (containing the active ingredient in powder or pellet form), troches and lozenges.

 Liquid formulations include, but are not limited to, syrups, emulsions, and sterile injectable liquids, such as suspensions or solutions.

 Topical dosage forms of the compounds include ointments, pastes, creams, lotions,
30 powders, solutions, eye or ear drops, impregnated dressings, and may contain appropriate conventional additives such as preservatives, solvents to assist drug penetration.

 The pharmaceutical compositions of the present patent application may be prepared by conventional techniques, e.g., as described in *Remington: The Science and Practice of Pharmacy*, 20th Ed., 2003 (Lippincott Williams & Wilkins).

Suitable doses of the compounds for use in treating the diseases and disorders described herein can be determined by those skilled in the relevant art. Therapeutic doses are generally identified through a dose ranging study in humans based on preliminary evidence derived from the animal studies. Doses must be sufficient to result in a desired therapeutic benefit without causing unwanted side effects. Mode of administration, dosage forms, and suitable pharmaceutical excipients can also be well used and adjusted by those skilled in the art. All changes and modifications are envisioned within the scope of the present patent application.

Methods of Treatment

Compounds of the present invention are particularly useful because they may inhibit the activity of Retinoid-related orphan receptor gamma {and particularly Retinoid-related orphan receptor gamma t (ROR γ t)}, i.e., they prevent, inhibit, or suppress the action of ROR γ t, and/or may elicit ROR γ t modulating effect. Compounds of the invention are thus useful in the treatment of those conditions in which inhibition of a ROR gamma activity, and particularly ROR γ t, is required.

The compounds of the present patent application are modulators of ROR γ t and can be useful in the treatment of diseases/disorder mediated by ROR γ t. Accordingly, the compounds and the pharmaceutical compositions of this invention may be useful in the treatment of inflammatory, metabolic and autoimmune diseases mediated by ROR γ t.

The term "autoimmune diseases" will be understood by those skilled in the art a condition that occurs when the immune system mistakenly attacks and destroys healthy body tissue. An autoimmune disorder may result in the destruction of one or more types of body tissue, abnormal growth of an organ, and changes in organ function. An autoimmune disorder may affect one or more organ or tissue types which include blood vessels, connective tissues, endocrine glands such as the thyroid or pancreas, joints, muscles, red blood cells, and skin. Examples of autoimmune (or autoimmune-related) disorders include multiple sclerosis, arthritis, rheumatoid arthritis, psoriasis, Crohn's disease, gastrointestinal disorder, inflammatory bowel disease, irritable bowel syndrome, colitis, ulcerative colitis, Sjorgen's syndrome, atopic dermatitis, optic neuritis, respiratory disorder, chronic obstructive pulmonary disease (COPD), asthma, type I diabetes, neuromyelitis optica, Myasthenia Gavis, uveitis, Guillain- Barre syndrome, psoriatic arthritis, Gaves' disease, allergy, osteoarthritis, Kawasaki disease, mucosal leishmaniasis, Hashimoto's thyroiditis, Pernicious anemia, Addison's disease, Systemic lupus erythematosus, Dermatomyositis, Sjogren syndrome,

Lupus erythematosus, Myasthenia gravis, Reactive arthritis, Celiac disease - sprue (gluten-sensitive enteropathy), Graves's disease, thymopoiesis and Lupus.

Compounds of the present patent application may be useful in the treatment of inflammation. The term "inflammation" will be understood by those skilled in the art to include any condition characterized by a localized or a systemic protective response, which may be elicited by physical trauma, infection, chronic diseases, and/or chemical and/or physiological reactions to external stimuli (e.g. as part of an allergic response). Any such response, which may serve to destroy, dilute or sequester both the injurious agent and the injured tissue, may be manifest by, for example, heat, swelling, pain, redness, dilation of blood vessels and/or increased blood flow, invasion of the affected area by white.

The term "inflammation" is also understood to include any inflammatory disease, disorder or condition per se, any condition that has an inflammatory component associated with it, and/or any condition characterized by inflammation as a symptom, including inter alia acute, chronic, ulcerative, specific, allergic, infection by pathogens, immune reactions due to hypersensitivity, entering foreign bodies, physical injury, and necrotic inflammation, and other forms of inflammation known to those skilled in the art. The term thus also includes, for the purposes of this present patent application, inflammatory pain, pain generally and/or fever.

The compounds of the present invention may be used for treatment of arthritis, including rheumatoid arthritis, osteoarthritis, psoriatic arthritis, septic arthritis, spondyloarthropathies, gouty arthritis, systemic lupus erythematosus and juvenile arthritis, osteoarthritis, and other arthritic conditions.

The compounds of the present invention may be used for treatment of respiratory disorders such as chronic obstructive pulmonary disease (COPD), asthma, bronchospasm, and cough.

Other respiratory disorders include bronchitis, bronchiolitis, bronchiectasis, acute nasopharyngitis, acute and chronic sinusitis, maxillary sinusitis, pharyngitis, tonsillitis, laryngitis, tracheitis, epiglottitis, croup, chronic disease of tonsils and adenoids, hypertrophy of tonsils and adenoids, peritonsillar abscess, rhinitis, abscess or ulcer and nose, pneumonia, viral and bacterial pneumonia, bronchopneumonia, influenza, extrinsic allergic alveolitis, coal workers' pneumoconiosis, asbestosis, pneumoconiosis, pneumonopathy, respiratory conditions due to chemical fumes, vapors and other external agents, emphysema, pleurisy, pneumothorax, abscess of lung and mediastinum, pulmonary congestion and hypostasis, postinflammatory pulmonary fibrosis, other alveolar and parietoalveolar pneumonopathy,

idiopathic fibrosing alveolitis, Hamman-Rich syndrome, atelectasis, ARDS, acute respiratory failure, mediastinitis.

The compounds of the present invention may be used for treatment of pain conditions. The pain can be acute or chronic pain. Thus, the compounds of the present invention may be used for treatment of inflammatory pain, arthritic pain, neuropathic pain, post-operative pain, surgical pain, visceral pain, dental pain, premenstrual pain, central pain, cancer pain, pain due to burns; migraine or cluster headaches, nerve injury, neuritis, neuralgias, poisoning, ischemic injury, interstitial cystitis, viral, parasitic or bacterial infection, post-traumatic injury, or pain associated with irritable bowel syndrome.

The compounds of the present invention may be used for treatment of gastrointestinal disorder such as irritable bowel syndrome, inflammatory bowel disease, colitis, ulcerative colitis, biliary colic and other biliary disorders, renal colic, diarrhea-dominant IBS, and pain associated with gastrointestinal distension.

In addition, the compounds of the present invention may be useful in the treatment of cancer, and pain associated with cancer. Such cancers include multiple myeloma and bone disease associated with multiple myeloma, melanoma, medulloblastoma, acute myelogenous leukemia (AML), head and neck squamous cell carcinoma, hepatocellular carcinoma, gastric cancer, bladder carcinoma and colon cancer.

The compounds of the present invention may be useful in a treatment of disease, disorder, syndrome or condition selected from the group consisting of chronic obstructive pulmonary disease (COPD), asthma, cough, pain, inflammatory pain, chronic pain, acute pain, arthritis, osteoarthritis, multiple sclerosis, rheumatoid arthritis, colitis, ulcerative colitis and inflammatory bowel disease.

The methods of treatment of the present patent application comprise administering a safe and effective amount of a compound according to Formula I or a pharmaceutically-acceptable salt thereof to a patient (particularly a human) in need thereof.

The present patent application relates to the use of the compounds in the preparation of a medicament for the treatment of diseases mediated by ROR γ t.

Compounds of the invention are indicated both in the therapeutic and/or prophylactic treatment of the above-mentioned conditions. For the above-mentioned therapeutic uses the dosage administered will, of course, vary with the compound employed, the mode of administration, the treatment desired and the disorder indicated.

Compounds of the present invention are indicated both in the therapeutic and/or prophylactic treatment of the above-mentioned conditions. For the above-mentioned therapeutic uses the

dosage administered will, of course, vary with the compound employed, the mode of administration, the treatment desired and the disorder indicated. The daily dosage of the compound of the invention may be in the range from 0.05 mg/kg to 100 mg/kg.

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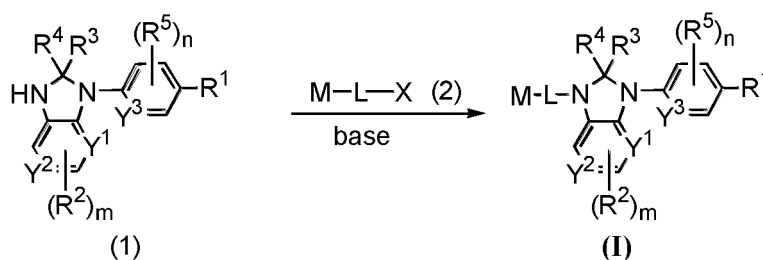
General Methods of Preparation

The compounds, described herein, are prepared according to general formula **(I)**, **(Ia)** and **(Ib)**. Suitable synthetic methods are depicted in schemes 1 to 11. Furthermore, in the following schemes, where specific acids, bases, reagents, coupling agents, solvents, etc. are mentioned, it is understood that other suitable acids, bases, reagents, coupling agents, solvents etc. may be used and are included within the scope of the present invention. The modifications to reaction conditions, for example, temperature, duration of the reaction or combinations thereof, are envisioned as part of the present invention. The compounds obtained using the general reaction sequences may be of insufficient purity. These compounds can be purified using any of the methods for purification of organic compounds known to persons skilled in the art, for example, crystallization or silica gel or alumina column chromatography using different solvents in suitable ratios. All possible geometrical isomers and stereoisomers are envisioned within the scope of this invention.

The starting materials used herein are commercially available or were prepared by methods known in the art to those of ordinary skill or by methods disclosed herein. In general, the intermediates and compounds of the present invention can be prepared through the reaction schemes as follows.

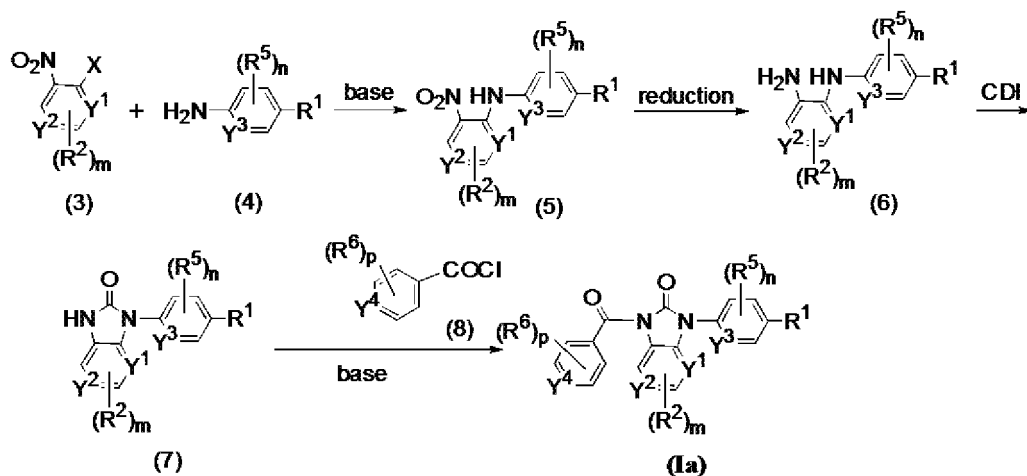
A general approach for the synthesis of compound of general formula **(I)** (wherein L, M, Y¹, Y², Y³, R¹, R², R³, R⁴, R⁵, 'm' and 'n' are as defined with respect to a compound of formula **(I)**) is shown in scheme 1. Thus benzimidazole compound of formula **(1)** on coupling with compound of formula **(2)** (wherein X is halogen (e.g. F, Cl, Br or I)) in the presence of base such as potassium carbonate, cesium carbonate, sodium hydride, etc. gives the final compound of general formula **(I)**.

Scheme 1



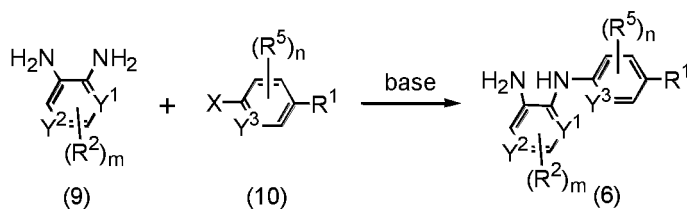
A general approach for the synthesis of compound of general formula (Ia) (wherein R^1 , R^2 , R^5 , R^6 , Y^1 , Y^2 , Y^3 , Y^4 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (Ia)) is shown in scheme 2. Thus, 2-halo nitrobenzene of formula (3) (wherein X is halogen (e.g. F, Cl, Br or I)) on aromatic nucleophilic substitution reaction with aniline of general formula (4) using base such as sodium hydride or cesium carbonate gives nitro intermediate (5). Alternatively, the Buchwald coupling reaction of 2-halo nitrobenzene derivative (3) with aniline derivative (4) using palladium catalyst such as palladium acetate in the presence of a base such as cesium carbonate also affords Intermediate (5). The reduction of the nitro intermediate (5) to amine of general formula (6) followed by cyclization using 1,1-carbodiimidazole (CDI) yields benzimidazolone Intermediate of formula (7). The coupling reaction of compound of formula (7) with the compound of formula (8) yields the compound of formula (Ia). The compound of formula (7) may be reacted with compound of formula (8) in the presence of a suitable base. The suitable base may be sodium hydride. The reaction may be carried out in a suitable solvent or mixture of solvents. The suitable solvent may be DMF. The compound of formula (Ia) may be optionally further converted to pharmaceutically acceptable salt.

Scheme 2



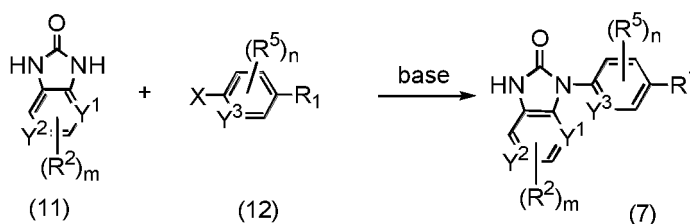
Intermediate of formula (6) (R^1 , R^2 , R^5 , Y^1 , Y^2 , Y^3 , 'm' and 'n' are as defined with respect to a compound of formula (Ia)) can be prepared from o- diamine compound of formula (9) and compound of formula (10) as depicted in scheme 3. The reaction may be carried out in the presence of base such as *N,N*-diisopropylethylamine (DIPEA) or triethylamine (TEA).

Scheme 3



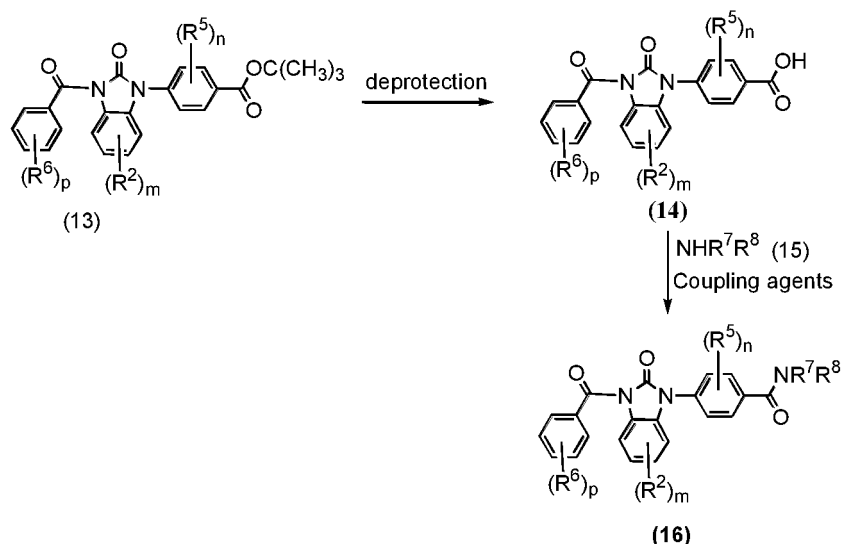
Similarly, Intermediate (7) can also be prepared from compound of general formula (11) and substituted phenyl halide of formula (12) as shown in scheme 4. The reaction may be carried out in the presence of base such as ethylene diamine and potassium hydrogen sulphate. The reaction may be carried out in the presence of catalyst such as copper iodide.

Scheme 4



A general approach for the synthesis of compound of general formula (14) (wherein R^2 , R^5 , R^6 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (1a)) and (16) (wherein R^2 , R^5 , R^6 , R^7 , R^8 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (1a)) is shown in scheme 5.

Scheme 5

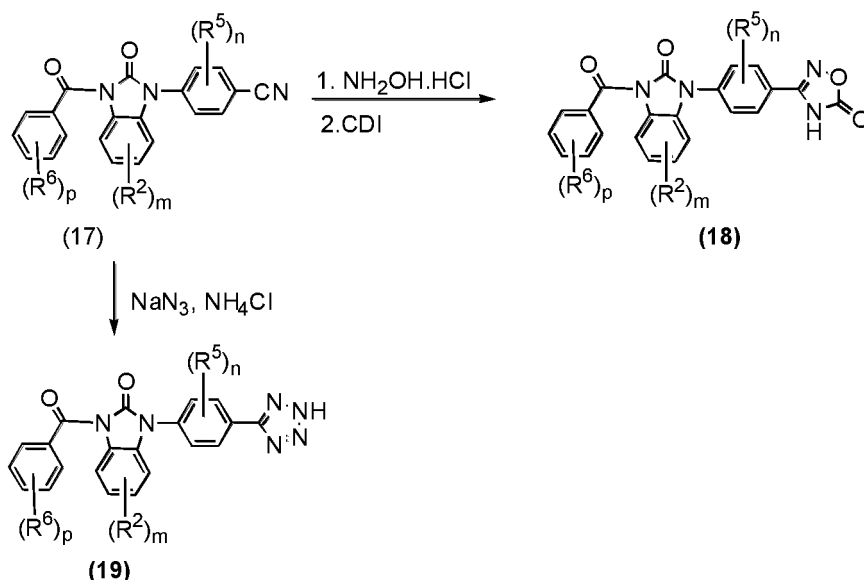


The Intermediate (13) (obtained as described in scheme 2, wherein R^1 is $\text{COOC}(\text{CH}_3)_3$) undergoes deprotection of *tert*-butyl group using acid such as trifluoroacetic acid (TFA) to yield the compound of general formula (14). The acid of general formula (14) on coupling with the amine of formula (15) using appropriate reagent such as 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI), or benzotriazol-1-

xyloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) affords the amide compound of the formula (16).

An approach for the synthesis of compound of general formula (18) (wherein R^2 , R^5 , R^6 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (1a)) and (19) (wherein R^2 , R^5 , R^6 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (1a)) is described in scheme 6. Thus, the Intermediate (17) (prepared as described in Scheme 2, wherein R^1 is CN) on reaction with hydroxylamine hydrochloride followed by cyclization using 1,1-carbodiimidazole yields the compound of the formula (18). On the other hand, the cyano intermediate (17) on reaction with sodium azide in the presence of ammonium chloride, yields final compound of the formula (19).

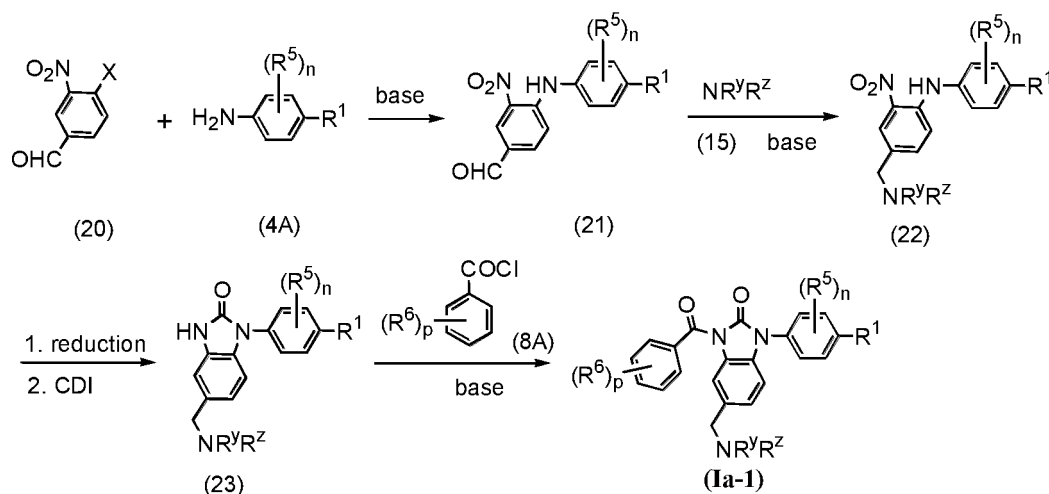
Scheme 6



An approach for the synthesis of compound of general formula (1a-1) (wherein R^1 , R^5 , R^6 , 'n' and 'p' are as defined with respect to a compound of formula (1a); R^y is CH_3 or cyclobutyl; and R^z is CH_3) is described in scheme 7. Thus, the Buchwald coupling reaction of 4-halo-3-nitrobenzaldehyde (20) (wherein X is halogen (e.g. F, Cl, Br or I)) with aniline derivative (4A) using palladium catalyst such as palladium acetate in the presence of a base such as cesium carbonate yields the Intermediate (21). The Intermediate (21) on reductive amination using sodium triacetoxy borohydride (STAB) with amine of formula (15) affords the Intermediate (22). The reduction of nitro group of the intermediate (22) followed by cyclization using CDI gives the Intermediate (23). The coupling of the acid chloride intermediate (8A) with the amine of formula (23) yields the compound of the formula (1a-1). The compound of formula (23) is reacted with compound of formula (8A) in the presence of a

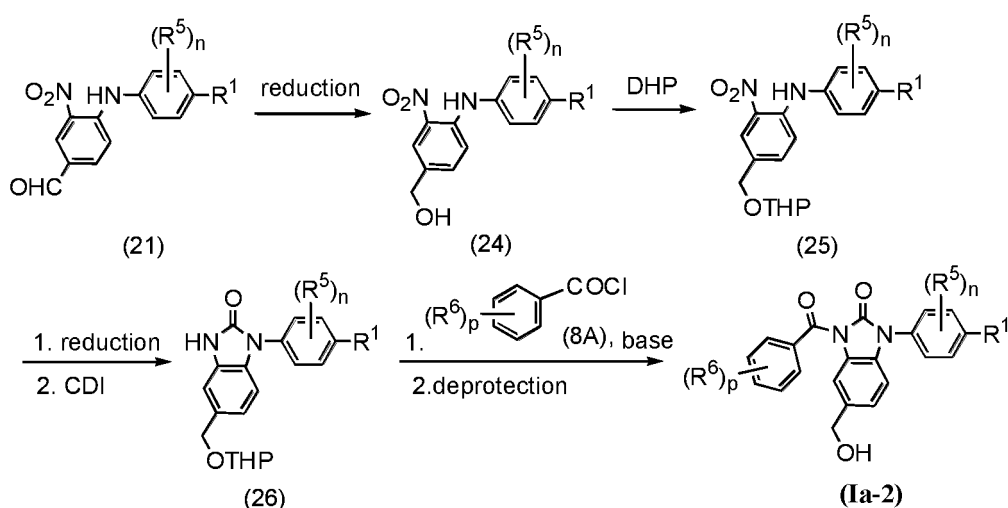
suitable base. The suitable base may be sodium hydride. The reaction may be carried out in a suitable solvent or mixture thereof. The suitable solvent may be DMF.

Scheme 7



- 5 Similarly, compound of general formula (**Ia-2**) (wherein R^1 , R^5 , R^6 , 'n' and 'p' are as defined with respect to a compound of formula (**Ia**)) can be prepared as depicted in scheme 8. Thus, the aldehyde group of the Intermediate (**21**) is reduced to corresponding alcohol (**24**) using sodium borohydride followed by the reaction with 3,4-dihydro-2H-pyran (DHP) to give the THP protected Intermediate (**25**). The nitro group reduction of the Intermediate (**25**) followed by cyclization yields the Intermediate (**26**). The coupling of the Intermediate (**26**) with the acid chloride of formula (**8A**) followed by deprotection affords the final compound of formula (**Ia-2**).

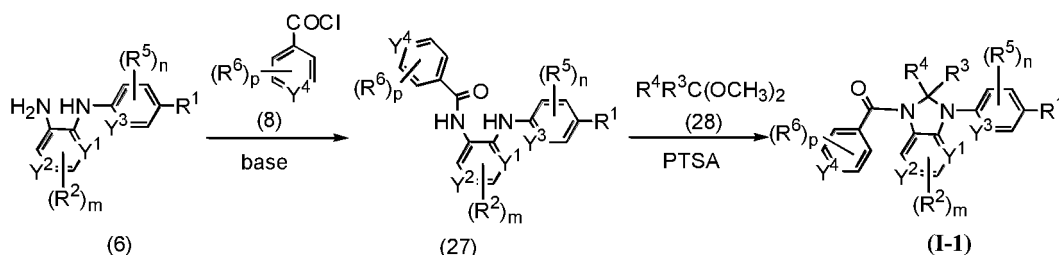
Scheme 8



- 15 An approach for the synthesis of compounds of general formula (**I-1**) (wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (**I**)) is described in scheme 9. Thus, the Intermediate (**6**) obtained as described in scheme 2, on coupling with

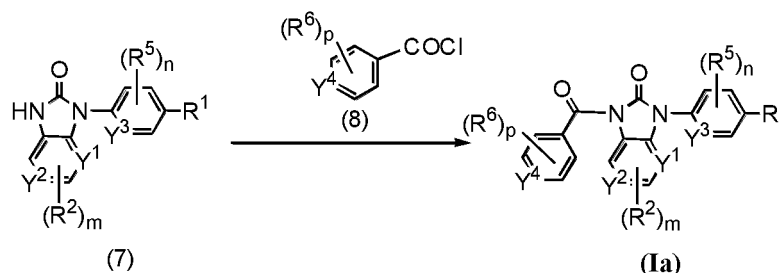
the acid chloride derivative (**8**) using base such as *N,N*-diisopropylethylamine (DIPEA) gives the amide Intermediate (**27**). The cyclization of the Intermediate (**27**) with the dimethoxy alkyl derivative (**28**) using acid such as PTSA gives the final compound of general formula (**I-1**).

5 Scheme 9



A general approach for the synthesis of compound of general formula (**Ia**) (wherein R^1 , R^2 , R^5 , R^6 , Y^1 , Y^2 , Y^3 , Y^4 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (**Ia**)) is shown in scheme 10.

10 Scheme 10



The process for the preparation of compound of formula (**Ia**) or a pharmaceutically acceptable salt thereof, which comprises:

15 reacting a compound of formula (**7**) with a compound of formula (**8**); and optionally converting the compound of formula (**Ia**) to a pharmaceutically acceptable salt thereof.

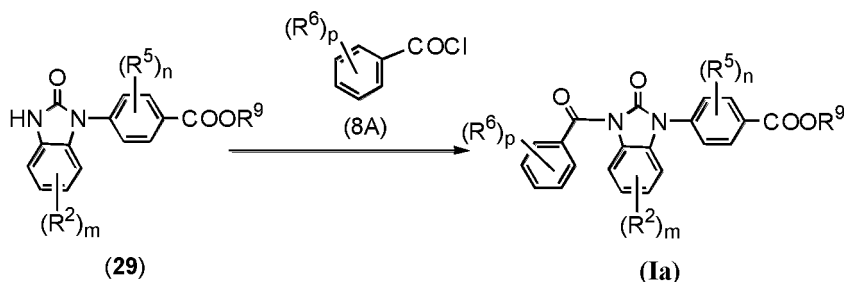
In an embodiment, the compound of formula (**7**) is reacted with compound of formula (**8**) in the presence of a suitable base. The suitable base may be sodium hydride.

In another embodiment, the reaction may be carried out in a suitable solvent. The suitable solvent may be DMF.

20 In yet another embodiment, the compound of formula (**7**) is reacted with a compound of formula (**8**) in the presence of sodium hydride in DMF.

A general approach for the synthesis of compound of general formula (**Ib**) (wherein R^2 , R^5 , R^6 , R^9 , 'm', 'n' and 'p' are as defined with respect to a compound of formula (**Ib**)) is shown in scheme 11.

25 Scheme 11



The process for the preparation of compound of formula **(Ib)** or a pharmaceutically acceptable salt thereof which comprises:

reacting a compound of formula **(29)** with a compound of formula **(8A)**; and
 5 optionally converting the compound of formula **(Ib)** to a pharmaceutically acceptable salt thereof.

In an embodiment, the compound of formula **(29)** is reacted with compound of formula **(8A)** in the presence of a suitable base. The suitable base may be sodium hydride.

In another embodiment, the reaction may be carried out in a suitable solvent. The
 10 suitable solvent may be DMF.

In yet another embodiment, the compound of formula **(29)** is reacted with a compound of formula **(8A)** in the presence of sodium hydride in DMF.

Experimental

15 Unless otherwise stated, work-up includes distribution of the reaction mixture between the organic and aqueous phase indicated within parentheses, separation of layers and drying the organic layer over sodium sulphate, filtration and evaporation of the solvent. Purification, unless otherwise mentioned, includes purification by silica gel chromatographic techniques, generally using ethyl acetate/petroleum ether mixture of a suitable polarity as the mobile
 20 phase. Use of a different eluent system is indicated within parentheses.

The abbreviations, symbols and terms used in the examples and assays have the following meanings throughout: DCM: dichloromethane; DMSO-*d*₆: Hexadeuterodimethyl sulfoxide; ¹H NMR: Proton Nuclear Magnetic Resonance; DMF: *N,N*-dimethyl formamide; DMSO: Dimethyl sulfoxide; CDI: 1,1-carbodiimidazole; BOP: (Benzotriazol-1-
 25 yloxy)tris(dimethylamino)phosphonium hexafluorophosphate; EDCI: 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide; STAB: Sodium triacetoxymethylborohydride; DMAP: 4-Dimethylaminopyridine; Xphos: 2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl; DHP: 3,4-dihydro-2*H*-pyran; THP: Tetrahydropyran; EDC: ethylene dichloride; DIPEA: *N,N*-diisopropylethylamine; DEAD: diethyl azadicarboxylate; THF: Tetrahydrofuran; TFA:

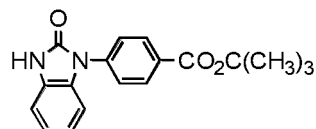
trifluoroacetic acid; Na₂SO₄: Sodium sulfate; PTSA: *p*-Toluenesulfonic acid; *J*: Coupling constant in units of Hz; h: hour(s); RT or rt: Room temperature (22-26°C); APCI-MS: Atmospheric Pressure Chemical Ionization Mass Spectrometry; Pd: Palladium; MHz: Megahertz.

5

Intermediates

Intermediate 1

tert-Butyl 4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: *tert*-Butyl 4-[(2-nitrophenyl)amino]benzoate:

- 10 To a stirred and cooled (0 °C) mixture of *tert*-butyl 4-amino benzoate (1 g, 5.175 mmol) in dry DMF (10 mL) was added sodium hydride (248 mg, 6.211 mmol) and the reaction mixture was stirred at the same temperature for 10 minutes. 1-Fluoro-2-nitrobenzene (0.5 mL, 5.175 mmol) was added to the reaction mixture and it was stirred at RT overnight. The reaction mass was diluted with water (100 mL) and the product was extracted with ethyl acetate (3 x
- 15 100 mL). The combined organic layers were washed with water (2 x 100 mL), brine (50 mL) and dried over anhydrous Na₂SO₄. The solvent was recovered under reduced pressure and the residue obtained was purified by column chromatography to afford 800 mg of the title product as off-white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.53 (s, 9H), 7.07 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 6.9 Hz, 1H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.8 Hz,
- 20 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 9.31 (s, 1H).

Step 2: *tert*-Butyl 4-[(2-aminophenyl)amino]benzoate:

- To the stirred solution of Step 1 intermediate (500 mg, 1.592 mmol) in methanol (10 mL) was added catalytic amount of 10% palladium on carbon and the mixture was stirred for 5 h under hydrogen atmosphere. The reaction mixture was filtered through celite pad and the filtrate
- 25 was concentrated to yield 370 mg of the desired product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.49 (s, 9H), 4.83 (br s, 2H), 6.56 (t, *J* = 6.9 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.92 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.82 (s, 1H).

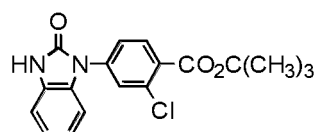
Step 3: *tert*-Butyl 4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate:

- 30 To a stirred solution of Step 2 intermediate (360 mg, 1.266 mmol) in THF (10 mL) was added CDI (313 mg, 1.90 mmol) and the reaction mixture was heated at 60 °C for 1 h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The

combined organic layers were washed with water (2 x 20 mL), brine (20 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled off under reduced pressure. The residue obtained was purified by column chromatography to afford 310 mg of the title product as off-white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 7.03-7.09 (m, 2H), 7.10-7.15 (m, 2H), 7.70 (d, *J* = 7.8 Hz, 2H), 8.06 (d, *J* = 8.4 Hz, 2H), 11.27 (br s, 1H); APCI-MS (*m/z*) 311 (M+H)⁺.

Intermediate 2

tert-Butyl 2-chloro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



10 Step 1: *tert*-Butyl 2-chloro-4-[(2-nitrophenyl)amino]benzoate:

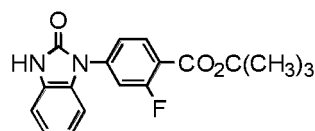
To a well stirred mixture of 1-iodo-2-nitro benzene (200 mg, 0.803 mmol) in 1,4-dioxane (10 mL) were added *tert*-butyl 4-amino-2-chlorobenzoate (218 mg, 0.963 mmol), palladium acetate (18 mg, 0.080 mmol), XPhos (56 mg, 0.090 mmol) and cesium carbonate (391 mg, 1.204 mmol). The reaction mixture was heated at 100 °C for 2h. The reaction mixture diluted with ethyl acetate (20 mL) and filtered through celite. The filtrate was concentrated under reduced pressure and residue thus obtained was purified by silica gel column chromatography to afford 300 mg of the title product as yellow oil. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.53 (s, 9H), 7.11-7.20 (m, 2H), 7.20 (s, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 8.09 (d, *J* = 8.4 Hz, 1H), 9.27 (s, 1H).

20 Step 2: *tert*-Butyl 2-chloro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate:

The title compound was prepared by platinum catalysed hydrogenation of Step 1 intermediate (280 mg, 0.8027 mmol) in a mixture of ethyl acetate (15 mL) and ethanol (3 mL) followed by cyclization of the corresponding diamine derivative (240 mg, 0.7528 mmol) in the presence of CDI (186 mg, 1.1292 mmol) in THF (10 mL) as per the process described in step 2 and 3 of the Intermediate 1 respectively to yield 140 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 7.02-7.09 (m, 1H), 7.15 (d, *J* = 7.5 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.78 (br s, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 11.31 (br s, 1H).

Intermediate 3

tert-Butyl 2-fluoro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: *tert*-Butyl 2-fluoro-4-[(2-nitrophenyl)amino]benzoate:

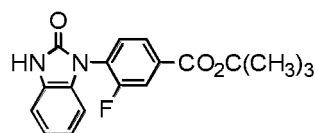
The title compound was prepared by the reaction of 1-iodo-2-nitro benzene (800 mg, 3.212 mmol) with *tert*-butyl 4-amino-2-fluorobenzoate (678 mg, 3.212 mmol) in the presence of palladium acetate (72 mg, 0.3212 mmol), XPhos (223 mg, 0.321 mmol) and cesium carbonate (1.56 g, 4.819 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of the Intermediate 2 to yield 710 mg of the product as yellow solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.51 (s, 9H), 6.97-7.04 (m, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.56-7.76 (m, 2H), 8.10 (d, *J* = 8.4 Hz, 1H), 9.30 (s, 1H).

Step 2: *tert*-Butyl 2-fluoro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (650 mg, 1.155 mmol) in methanol (15 mL) followed by cyclization of the corresponding diamine derivative (450 mg, 1.4883 mmol) in the presence of CDI (368 mg, 2.232 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 220 mg of the product as yellow solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.55 (s, 9H), 7.03-7.10 (m, 3H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.52-7.60 (m, 2H), 7.98 (t, *J* = 8.1 Hz, 1H), 11.34 (br s, 1H).

Intermediate 4

tert-Butyl 3-fluoro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: *tert*-Butyl 3-fluoro-4-[(2-nitrophenyl)amino]benzoate:

To a well stirred mixture of 1-iodo-2-nitro benzene (300 mg, 1.204 mmol) in degassed 1,4-dioxane (10 mL) were added *tert*-butyl 4-amino-3-fluorobenzoate (328 mg, 1.445 mmol), palladium acetate (27 mg, 0.1204 mmol), XPhos (84 mg, 0.1445 mmol) and cesium carbonate (588 mg, 1.807 mmol). The reaction mixture was heated at 100 °C for 2h. The reaction mixture was diluted with ethyl acetate (30 mL) and filtered through celite. The filtrate was concentrated under reduced pressure and the residue thus obtained was purified by silica gel column chromatography to afford 410 mg of the product as yellow oil. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.54 (s, 9H), 7.07 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 7.48 (t, *J* = 8.4 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.71-7.74 (m, 2H), 8.12 (d, *J* = 8.4 Hz, 1H), 9.25 (s, 1H).

Step 2: *tert*-Butyl 4-[(2-aminophenyl)amino]-3-fluorobenzoate:

A solution of step 1 intermediate (400 mg, 1.203 mmol) in methanol (10 mL) was hydrogenated in the presence of 10% palladium on carbon in a Parr apparatus for 3 hours at

RT. The reaction mixture was filtered through celite and the filtration bed was thoroughly rinsed with methanol (2 x 20 mL). The mother liquor and washings were combined and concentrated under reduced pressure to obtain 350 mg of the title product as light yellow oil.

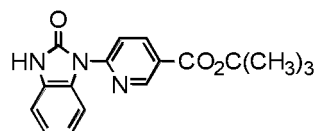
¹H NMR (300 MHz, DMSO-*d*₆) δ 1.50 (s, 9H), 5.26 (br s, 2 H), 6.48 (t, *J* = 8.7 Hz, 1H), 6.62 (t, *J* = 7.2 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.96-7.01 (m, 2H), 7.47-7.55 (m, 2H), 7.73 (s, 1H).

Step 3: *tert*-Butyl 3-fluoro-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate

To a stirred solution of Step 2 intermediate (350 mg, 1.157 mmol) in THF (10 mL) was added CDI (286 mg, 1.736 mmol) and the reaction mixture was stirred at RT for 15 h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water (2 x 15 mL), brine (20 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled off under reduced pressure. The residue obtained was purified by column chromatography to yield 300 mg of the product as brown solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.63 (s, 9H), 6.84 (d, *J* = 7.5 Hz, 1H), 7.05-7.15 (m, 3H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.91-7.98 (m, 2H), 9.93 (br s, 1H).

Intermediate 5

tert-Butyl 6-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)pyridine-3-carboxylate



Step 1: *tert*-Butyl 6-[(2-nitrophenyl)amino]pyridine-3-carboxylate:

The title compound was prepared by the reaction of 2-nitroaniline (200 mg, 1.448 mmol) and *tert*-butyl 6-chloropyridine-3-carboxylate (309 mg, 1.448 mmol) in the presence of palladium acetate (33 mg, 0.1448 mmol), XPhos (100 mg, 0.1737 mmol) and cesium carbonate (706 mg, 2.172 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of Intermediate 2 to yield 150 mg of the product as orange solid. ¹H NMR (300 MHz, CDCl₃) δ 1.60 (s, 9H), 6.92 (d, *J* = 8.7 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 8.15 (d, *J* = 9.0 Hz, 1H), 8.25 (d, *J* = 9.0 Hz, 1H), 8.83 (d, *J* = 8.4 Hz, 1H), 10.35 (br s, 1H).

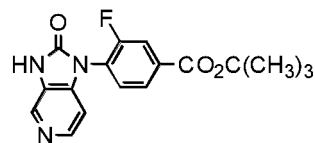
Step 2: *tert*-Butyl 6-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)pyridine-3-carboxylate:

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (600 mg, 1.9028 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (510 mg, 1.787 mmol) in the presence of CDI (442 mg, 2.681 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 400 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆)

δ 1.58 (s, 9H), 7.09-7.15 (m, 3H), 8.14 (d, J = 8.1 Hz, 1H), 8.30-8.40 (m, 2H), 9.02 (s, 1H), 11.45 (br s, 1H).

Intermediate 6

tert-Butyl 3-fluoro-4-(2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)benzoate



5

Step 1: *tert*-Butyl 3-fluoro-4-[(3-nitropyridin-4-yl)amino]benzoate:

The title compound was prepared by the reaction of 4-chloro-3-nitropyridine (450 mg, 2.840 mmol) and *tert*-butyl 4-amino-3-fluorobenzoate (600 mg, 2.8407 mmol) in the presence of palladium acetate (64 mg, 0.284 mmol), XPhos (198 mg, 0.341 mmol) and cesium carbonate (1.38 g, 4.26 mmol) in 1,4-dioxane (15 mL) as per the process described in step 1 of Intermediate 2 to yield 610 mg of the product as yellow solid. ^1H NMR (300 MHz, CDCl_3) δ 1.61 (s, 9H), 6.95 (br s, 1H), 7.80 (t, J = 6.6 Hz, 1H), 7.47 (t, J = 8.4 Hz, 1H), 7.84-7.90 (m, 2H), 8.38 (br s, 1H), 9.34 (s, 1H), 9.67 (br s, 1H).

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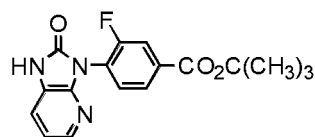
Step 2: *tert*-Butyl 3-fluoro-4-(2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)benzoate:

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (600 mg, 1.801 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (500 mg, 1.648 mmol) in the presence of CDI (408 mg, 2.472 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 400 mg of the product as light brown solid. ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 1.57 (s, 9H), 6.95 (br s, 1H), 7.80 (t, J = 6.6 Hz, 1H), 7.92 (d, J = 9.3 Hz, 1H), 8.20 (br s, 1H), 8.33 (s, 1H), 11.63 (br s, 1H).

20

Intermediate 7

tert-Butyl 3-fluoro-4-(2-oxo-1,2-dihydro-3*H*-imidazo[4,5-*b*]pyridin-3-yl)benzoate



25

Step 1: *tert*-Butyl 3-fluoro-4-[(3-nitropyridin-2-yl)amino]benzoate:

The title compound was prepared by the reaction of 2-chloro-3-nitropyridine (250 mg, 1.5768 mmol) and *tert*-butyl-4-amino-3-fluorobenzoate (332 mg, 1.5760 mmol) in the presence of palladium acetate (35 mg, 0.157 mmol), XPhos (109 mg, 0.189 mmol) and cesium carbonate (772 mg, 2.37 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of Intermediate 2 to yield 410 mg of the product as yellow solid. ^1H NMR (300 MHz, $\text{DMSO-}d_6$)

30

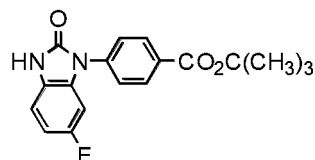
δ 1.55 (s, 9H), 7.13 (br s, 1H), 7.71-7.79 (m, 2H), 8.40 (t, $J = 7.8$ Hz, 1H), 8.60 (br s, 2H), 10.27 (br s, 1H).

Step 2: *tert*-Butyl 3-fluoro-4-(2-oxo-1,2-dihydro-3*H*-imidazo[4,5-*b*]pyridin-3-yl)benzoate

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (400 mg, 1.200 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (380 mg, 1.254 mmol) in the presence of CDI (269 mg, 1.6303 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 300 mg of the product as off white solid. ^1H NMR (300 MHz, DMSO- d_6) δ 1.61 (s, 9H), 7.09 (t, $J = 7.5$ Hz, 1H), 7.39 (d, $J = 7.8$ Hz, 1H), 7.64 (t, $J = 7.8$ Hz, 1H), 7.91-7.99 (m, 2H), 8.06 (br s, 1H), 10.41 (br s, 1H).

Intermediate 8

tert-Butyl 4-(6-fluoro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: *tert*-Butyl 4-[(5-fluoro-2-nitrophenyl)amino]benzoate:

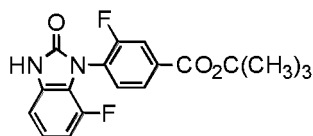
The title compound was prepared by the reaction of *tert*-butyl 4-amino benzoate (384 mg, 2.727 mmol) with 2-bromo-4-fluoro-1-nitrobenzene (500 mg, 2.272 mmol) in the presence of palladium acetate (51 mg, 0.227 mmol), XPhos (157 mg, 0.272 mmol) and cesium carbonate (1.12 g, 3.409 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of Intermediate 2 to yield 520 mg of the product as yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 1.61 (s, 9H), 6.57 (br s, 1H), 7.01 (d, $J = 11.1$ Hz, 1H), 7.27-7.32 (m, 2H), 8.05 (d, $J = 8.1$ Hz, 2H), 8.25-8.31 (m, 1H), 9.70 (s, 1H).

Step 2: *tert*-Butyl 4-(6-fluoro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate:

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (500 mg, 1.504 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (350 mg, 1.157 mmol) in the presence of CDI (286 mg, 1.736 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 230 mg of the product as off white solid. ^1H NMR (300 MHz, DMSO- d_6) δ 1.63 (s, 9H), 6.84 (br s, 2H), 7.04-7.10 (m, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 8.18 (d, $J = 8.4$ Hz, 2H), 10.21 (br s, 1H).

Intermediate 9

tert-Butyl-3-fluoro-4-(7-fluoro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: *tert*-Butyl 3-fluoro-4-[(2-fluoro-6-nitrophenyl)amino]benzoate:

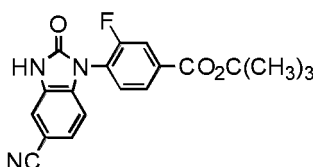
To a well stirred mixture of 2-bromo-1-fluoro-3-nitrobenzene (300 mg, 1.363 mmol) in 1,4-dioxane (10 mL) were added *tert*-butyl 4-amino-3-fluorobenzoate (287 mg, 1.3636 mmol), acetate (31 mg, 0.136 mmol), XPhos (94 mg, 0.1036 mmol) and cesium carbonate (666 mg, 2.045 mmol). The reaction mixture was heated at 100 °C for 3 h. The reaction mixture diluted with ethyl acetate (20 mL) and filtered through celite pad. The filtrate was concentrated under reduced pressure and residue thus obtained was purified by silica gel column chromatography to afford 320 mg of the title product as yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 1.58 (s, 9H), 6.84-6.89 (m, 1H), 7.10-7.13 (m, 1H), 7.41 (t, *J* = 10.2 Hz, 1H), 7.69-7.74 (m, 2H), 8.00 (d, *J* = 8.1 Hz, 1H), 8.45 (s, 1H).

Step 2: *tert*-Butyl 3-fluoro-4-(7-fluoro-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate:

To the stirred solution of Step 1 intermediate (300 mg, 0.8571 mmol) in methanol (10 mL) was added catalytic amount of 10% palladium on carbon and the mixture was stirred for 5 h under hydrogen atmosphere. The reaction mixture was filtered through celite pad and the filtrate was concentrated. The obtained solid was dissolved in THF (10 mL) and CDI (201 mg, 1.212 mmol) was added and the reaction mixture was refluxed for 18 h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water (2 x 20 mL), brine (20 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled off under reduced pressure. The residue obtained was purified by column chromatography to afford 200 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 6.89 (d, *J* = 9.0 Hz, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 7.09 (m, 1H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 7.8 Hz, 2H), 11.61 (br s, 1H).

Intermediate 10

tert-Butyl 4-(5-cyano-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-3-fluorobenzoate



Step 1: *tert*-Butyl 4-[(4-cyano-2-nitrophenyl)amino]-3-fluorobenzoate:

The title compound was prepared by the reaction of 4-bromo-3-nitrobenzonitrile (374 mg, 1.65 mmol) with *tert*-butyl 4-amino-3-fluorobenzoate (350 mg, 1.65 mmol) in the presence of

palladium acetate (18 mg, 0.082 mmol), XPhos (57 mg, 0.099 mmol) and cesium carbonate (804 mg, 2.47 mmol) in 1,4-dioxane (20 mL) as per the process described in step 1 of Intermediate 2 to yield 513 mg of the product as brown solid. ¹H NMR (300 MHz, CDCl₃) δ 1.61 (s, 9H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.86 (t, *J* = 9.3 Hz, 2H), 8.59 (s, 1H), 9.73 (br s, 1H); APCI-MS (*m/z*) 355 (M+H)⁺.

Step 2: *tert*-Butyl 4-[(2-amino-4-cyanophenyl)amino]-3-fluorobenzoate:

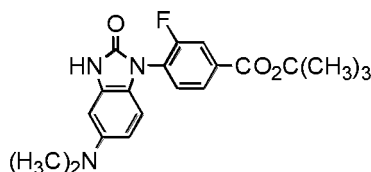
To a stirred suspension of step 1 intermediate (504 mg, 1.411 mmol) and ammonium chloride (754 mg, 14.11 mmol) in water (8 mL) and ethanol (16 mL) was added iron powder (236 mg, 4.23 mmol) at 60 °C and it was stirred at the same temperature for 2 hours. The reaction mixture was cooled to RT and diluted with ethyl acetate (50 mL). The organic mixture was washed with saturated aqueous solution of sodium bicarbonate (20 mL), brine (20 mL), the organic layer was separated and dried over anhydrous sodium sulfate. The solvent was recovered under reduced pressure to yield 448 mg of the title product as yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 1.57 (s, 9H), 6.21 (br s, 1H), 6.87-6.93 (m, 1H), 7.13-7.25 (m, 3H), 7.65-7.69 (m, 2H); APCI-MS (*m/z*) 326 (M+H)⁺.

Step 3: *tert*-Butyl 4-(5-cyano-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-3-fluorobenzoate

The title compound was prepared by the cyclization of step 2 intermediate (441 mg, 1.348 mmol) in the presence of CDI (327 mg, 2.022 mmol) in THF (10 mL) as per the process described in step 3 of Intermediate 1 to yield 324 mg of the product as pale yellow solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 7.01 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.53 (s, 1H), 7.80 (t, *J* = 8.1 Hz, 1H), 7.92 (t, *J* = 9.3 Hz, 2H), 11.79 (br s, 1H).

Intermediate 11

tert-Butyl 4-[5-(dimethylamino)-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl]-3-fluorobenzoate



Step 1: *tert*-Butyl 4-{[4-(dimethylamino)-2-nitrophenyl]amino}-3-fluorobenzoate

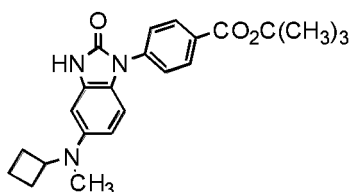
The title compound was prepared by the reaction of 4-fluoro-*N,N*-dimethyl-3-nitroaniline (694 mg, 3.030 mmol) with *tert*-butyl 4-amino-3-fluorobenzoate (767 mg, 3.636 mmol) in the presence of sodium hydride (60% w/w, 242 mg, 6.060 mmol) in DMF (20 mL) as per the process described in step 1 of Intermediate 1 to yield 700 mg of the product as brown oil; ¹H NMR (300 MHz, CDCl₃) δ 1.59 (s, 9H), 3.01 (s, 6H), 7.13 (br s, 1H), 7.31-7.39 (m, 1H), 7.52 (br s, 1H), 7.61-7.75 (m, 2H), 8.78 (s, 1H), 11.48 (br s, 1H); APCI-MS (*m/z*) 376 (M+H)⁺.

Step 2: *tert*-Butyl 4-[5-(dimethylamino)-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl]-3-fluorobenzoate

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (700 mg, 1.865 mmol) in methanol (15 mL) followed by the cyclization of the corresponding diamine derivative (226 mg, 0.650 mmol) in the presence of CDI (159 mg, 0.984 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 231 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 2.85 (s, 6H), 6.42 (d, *J* = 8.7 Hz, 1H), 6.45 (s, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 11.05 (br s, 1H).

Intermediate 12

tert-Butyl 4-[5-(cyclobutyl-methyl-amino)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate



Step 1: *N*-Cyclobutyl-4-fluoro-3-nitroaniline

A mixture of 4-fluoro-3-nitroaniline (200 mg, 1.280 mmol) and cyclobutanone (0.13 mL, 1.923 mmol) in dichloroethane (10 mL) with catalytic amount of acetic acid was stirred for 2 hours at RT. To the reaction mixture, sodium triacetoxo borohydride (542 mg, 2.560 mmol) was added and stirred for 15 hours at RT. The reaction mixture was diluted with ethyl acetate (30 mL) and washed with saturated aqueous solution of sodium bicarbonate (20 mL), water (20 mL) and brine (20 mL). The organic solution was dried over anhydrous sodium sulfate, filtered, concentrated and the residue thus obtained was purified by silica gel column chromatography to yield 107 mg of the title product as yellow oil. ¹H NMR (300 MHz, CDCl₃) δ 1.77-1.94 (m, 4H), 2.40-2.45 (m, 2H), 3.85-3.92 (m, 1H), 6.88 (br s, 1H), 7.10 (t, *J* = 9.9 Hz, 1H), 7.23-7.25 (m, 1H); APCI-MS (*m/z*) 210 (M+H)⁺.

Step 2: *N*-Cyclobutyl-4-fluoro-*N*-methyl-3-nitroaniline

A mixture of step 1 intermediate (573 mg, 2.728 mmol), potassium carbonate (564 mg, 4.092 mmol) and methyl iodide (0.25 mL, 4.092 mmol) in DMF (5 mL) was heated to 50 °C for 15 hours in a sealed tube. The reaction mixture was cooled to RT and diluted with ethyl acetate (25 mL). The organic mixture was washed with water (2 x 20 mL) followed by brine (20 mL) and dried over anhydrous sodium sulfate. The solution was filtered, concentrated and the residue thus obtained was purified by silica gel column chromatography to yield 547 mg of the title product as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ 1.74-1.79 (m, 2H), 2.07-2.14

(m, 2H), 2.25-2.30 (m, 2H), 2.86 (s, 3H), 3.89-4.00 (m, 1H), 7.00 (br s, 1H), 7.11 (t, $J = 9.9$ Hz, 1H), 7.33 (br s, 1H).

Step 3: *tert*-Butyl 4-[(4-{cyclobutyl-methyl-amino}-2-nitrophenyl)amino]benzoate

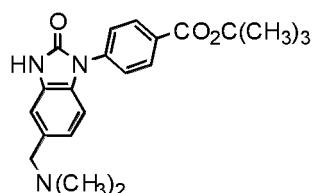
The title compound was synthesized by the reaction of step 2 intermediate (354 mg, 1.955 mmol) and *tert*-butyl 4-aminobenzoate (465 mg, 1.955 mmol) in the presence of sodium hydride (60% w/w, 117 mg, 2.932 mmol) in DMF (7 mL) as per the process described in step 1 of Intermediate 1 to yield 404 mg of the product as brown solid. APCI-MS (m/z) 398 ($M+H$)⁺.

Step 4: *tert*-Butyl 4-[5-(cyclobutyl-methyl-amino)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate

The title compound was synthesized by the catalytic hydrogenation reaction of step 3 intermediate (422 mg, 1.062 mmol) followed by the cyclization of the corresponding diamine derivative (303 mg, 0.825 mmol) by using CDI (200 mg, 1.237 mmol) in THF (10 mL) as per the process described in respective step 2 and 3 of Intermediate 1 to yield 142 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.56 (s, 9H), 1.60-1.65 (m, 2H), 2.00-2.03 (m, 2H), 2.12-2.15 (m, 2H), 2.73 (s, 3H), 3.86-3.90 (m, 1H), 6.52 (br s, 2H), 7.02 (d, $J = 9.3$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 2H), 8.05 (d, $J = 8.7$ Hz, 2H), 11.02 (br s, 1H).

Intermediate 13

tert-Butyl 4-{5-[(dimethylamino)methyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}benzoate



Step 1: *tert*-Butyl 4-[(4-formyl-2-nitrophenyl)amino]benzoate

To a stirred mixture of 4-bromo-3-nitrobenzaldehyde (2 g, 8.66 mmol) in 1,4-dioxane (30 mL) were added *tert*-butyl 4-aminobenzoate (1.84 g, 9.53 mmol), palladium acetate (97 mg, 0.433 mmol), XPhos (299 mg, 0.519 mmol) and cesium carbonate (4 g, 12.99 mmol). The reaction mixture was heated at 100 °C for 2h. The reaction mixture was diluted with water (100 mL) and extracted with ethyl acetate (2 x 100 mL). The combined organic layers were washed with water (2 x 50 mL), brine (50 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the residue thus obtained was purified by column chromatography to afford 2.5 g of the title product as off-white solid. ¹H NMR (300 MHz,

CDCl₃) δ 1.61 (s, 9H), 7.33-7.38 (m, 3H), 7.86 (d, J = 8.7 Hz, 1H), 8.09 (d, J = 7.8 Hz, 2H), 8.73 (s, 1H), 9.86 (s, 1H), 10.02 (br s, 1H).

Step 2: *tert*-Butyl 4-({4-[(dimethylamino)methyl]-2-nitrophenyl}amino)benzoate:

To a stirred solution of Step 1 intermediate (500 mg, 1.460 mmol) in EDC (10 mL) was added
5 dimethylamine hydrochloride (238 mg, 2.920 mmol) and the reaction mixture was stirred at
RT for 2 h. STAB (618 mg, 2.920 mmol) was added to the reaction mixture and it was further
stirred for 15 hours at RT. The reaction mixture was diluted with ethyl acetate (50 mL) and
washed with aqueous solution of sodium bicarbonate (2 x 25 mL) and brine (20 mL). The
solution was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The
10 residue thus obtained was purified by column chromatography to afford 660 mg of the title
product as off-white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.53 (s, 9H), 2.15 (s, 6H), 3.38 (s,
2H), 7.28 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 9.0 Hz, 1H), 7.84 (d, J =
8.4 Hz, 2H), 7.98 (s, 1H), 9.28 (s, 1H).

Step 3: *tert*-Butyl 4-({2-amino-4-[(dimethylamino)methyl]phenyl}amino) benzoate:

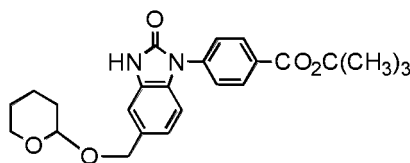
15 To the stirred solution of Step 2 intermediate (658 mg, 1.77 mmol) in methanol (10 mL) was
added catalytic amount of 10% palladium on carbon and the reaction mixture was stirred for 5
h under hydrogen atmosphere. The reaction mixture was filtered and the filtrate was
concentrated to yield 570 mg of the product. ¹H NMR (300 MHz, CDCl₃) δ 1.56 (s, 9H), 2.29
(s, 6H), 3.40 (s, 2H), 3.48 (s, 2H), 5.56 (s, 1H), 6.60-6.70 (m, 3H), 6.83 (s, 1H), 7.07 (d, J =
20 7.8 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H).

Step 4: *tert*-Butyl 4-{5-[(dimethylamino)methyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}benzoate:

To a stirred solution of Step 3 intermediate (555 mg, 1.626 mmol) in THF (10 mL) was added
CDI (395 mg, 2.43 mmol) and the reaction mixture was heated at 60 °C for 1 h. The reaction
25 mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The
combined organic layers were washed with water (2 x 50 mL), brine (50 mL) and dried over
anhydrous Na₂SO₄. The solvent was distilled out under reduced pressure and the residue thus
obtained was purified by column chromatography to afford 250 mg of the title product as
white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.57 (s, 9H), 2.25 (s, 6H), 3.56 (s, 2H), 6.98 (br
30 s, 1H), 7.07 (m, 2H), 7.70 (d, J = 8.4 Hz, 2H), 8.06 (d, J = 8.1 Hz, 2H), 11.28 (br s, 1H).

Intermediate 14

tert-Butyl 4-(2-oxo-5-{{(tetrahydro-2*H*-pyran-2-yl)oxy]methyl}-2,3-dihydro-1*H*-
benzo[d]imidazol-1-yl)benzoate



Step 1: *tert*-Butyl 4-[(4-formyl-2-nitrophenyl)amino]benzoate:

To a well stirred mixture of 4-bromo-3-nitrobenzaldehyde (2 g, 8.66 mmol) in 1,4-dioxane (20 mL) were added *tert*-butyl 4-aminobenzoate (1.84 g, 9.53 mmol), palladium acetate (97 mg, 0.433 mmol), XPhos (299 mg, 0.519 mmol) and cesium carbonate (4 g, 12.99 mmol). The reaction mixture was heated at 100 °C for 2h. The reaction mixture was diluted with water (50 mL) and product was extracted in ethyl acetate (2 x 100 mL). The combined organic layers were washed with water (2 x 50 mL), brine (25 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled off under reduced pressure. The obtained product was purified by column chromatography to afford 1.8 g of the title product as off-white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.61 (s, 9H), 7.33-7.38 (m, 3H), 7.86 (d, *J* = 8.7 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 2H), 8.73 (s, 1H), 9.86 (s, 1H), 10.02 (br s, 1H).

Step 2: *tert*-Butyl 4-{[4-(hydroxymethyl)-2-nitrophenyl]amino}benzoate:

To the stirred solution of step 1 intermediate (1 g, 2.92 mmol) in methanol (10 mL) was added sodium borohydride (143 mg, 3.79 mmol) at 0 °C and the reaction mixture was stirred at the same temperature for 30 minutes. The reaction mixture was diluted with ethyl acetate (50 mL), washed with saturated solution of ammonium chloride (50 mL) and brine (25 mL). The solvent was distilled under reduced pressure and the residue thus obtained was purified by silica gel column chromatography to yield 750 mg of the product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.60 (s, 9H), 4.67 (br s, 1H), 4.78 (br s, 2H), 7.29-7.35 (m, 2H), 7.47 (br s, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 9.86 (br s, 1H), 11.78 (br s, 1H).

Step 3: *tert*-Butyl 4-[(2-nitro-4-{[(tetrahydro-2*H*-pyran-2-yl)oxy]methyl}phenyl)amino]benzoate:

To a stirred solution of Step 2 intermediate (200 mg, 0.580 mmol) in DCM (5 mL) were added DHP (0.6 mL, 0.696 mmol) and catalytic amount of PTSA. The reaction mixture was stirred at RT for 2h. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water (2 x 50 mL), brine (25 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled out under reduced pressure and the residue thus obtained was purified by column chromatography to afford 200 mg of the title product as off-white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.60 (s, 9H), 1.75 (br

s, 5H), 3.55 (br s, 1H), 3.90 (br s, 1H), 4.45 (d, $J = 11.7$ Hz, 1H), 4.71 (br s, 2H), 7.29 (br s, 3H), 7.45 (br s, 2H), 8.00 (d, $J = 8.4$ Hz, 2H), 8.21 (s, 1H), 9.48 (br s, 1H).

Step 4: *tert*-Butyl 4-[(2-amino-4-[(tetrahydro-2H-pyran-2-yl)oxy]methyl} phenyl)amino]benzoate:

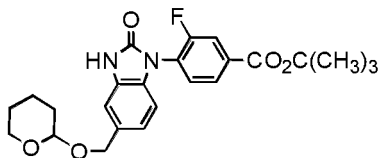
- 5 To the stirred solution of Step 3 intermediate (200 mg, 0.467 mmol) in methanol (5 mL) was added catalytic amount of 10% palladium on carbon and the reaction was stirred for 5 h under hydrogen atmosphere. The reaction mixture was filtered through celite and the filtrate was concentrated to yield 155 mg of the title product. ^1H NMR (300 MHz, CDCl_3) δ 1.56 (br s, 9H), 1.75-1.86 (m, 3H), 3.56 (br s, 4H), 3.93 (br s, 2H), 4.42 (d, $J = 11.7$ Hz, 1H), 4.70 (br s, 2H), 5.68 (br s, 1H), 6.67 (d, $J = 7.8$ Hz, 2H), 6.81 (br s, 1H), 6.89 (br s, 2H), 7.11 (br s, 1H), 7.81 (d, $J = 7.8$ Hz, 2H).

Step 5: *tert*-Butyl 4-(2-oxo-5-[(tetrahydro-2H-pyran-2-yl)oxy]methyl}-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate:

- To a well stirred solution of Step 4 intermediate (150 mg, 0.376) in THF (5 mL) was added 15 1,1-carbodiimidazole (CDI) (91 mg, 0.565 mmol) and the reaction mixture was heated to 60 °C. The reaction mixture was stirred at the same temperature for 1 hour. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with water (2 x 25 mL), brine (25 mL) and dried over anhydrous Na_2SO_4 . The solvent was recovered under reduced pressure and the residue obtained was purified by column chromatography to afford 100 mg of the title product as off-white solid. 20 ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.49 (br s, 6H), 1.57 (s, 9H), 3.50 (br s, 1H), 3.80 (br s, 1H), 4.46 (d, $J = 11.1$ Hz, 1H), 4.66 (br s, 2H), 7.02 (br s, 1H), 7.06 (br s, 2H), 7.71 (d, $J = 8.0$ Hz, 2H), 8.07 (d, $J = 8.0$ Hz, 2H), 11.26 (br s, 1H).

Intermediate 15

- 25 *tert*-Butyl 3-fluoro-4-(2-oxo-5-[(tetrahydro-2H-pyran-2-yl)oxy]methyl}-2,3-dihydro-1H-benzo[d]imidazol-1-yl)benzoate



Step 1: *tert*-Butyl 3-fluoro-4-[(4-formyl-2-nitrophenyl)amino]benzoate

- The title compound was prepared by the reaction of 4-bromo-3-nitrobenzaldehyde (1 g, 4.340 mmol) with *tert*-butyl 4-amino-3-fluorobenzoate (1 g, 4.78 mmol) in the presence of palladium acetate (48 mg, 0.217 mmol), XPhos (150 mg, 0.260 mmol) and cesium carbonate

(2.12 g, 6.51 mmol) in 1,4-dioxane (20 mL) as per the process described in step 1 of Intermediate 14 to yield 1.4 g of the product as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ 1.61 (s, 9H), 7.22 (br s, 2H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.83-7.89 (m, 2H), 7.96 (d, *J* = 9.0 Hz, 1H), 8.74 (br s, 1H), 9.89 (br s, 2H).

5 Step 2: *tert*-Butyl 3-fluoro-4-{[4-(hydroxymethyl)-2-nitrophenyl]amino}benzoate

The title compound was prepared by the aldehyde reduction of step 1 intermediate (800 mg, 2.22 mmol) by using sodium borohydride (109 mg, 2.88 mmol) in methanol (10 mL) as per the process described in step 2 of Intermediate 14 to yield 625 mg of the product as brown oil. ¹H NMR (300 MHz, CDCl₃) δ 1.60 (s, 9H), 4.69 (s, 2H), 7.33 (d, *J* = 8.7 Hz, 1H), 7.41-7.53 (m, 2H), 7.78 (br s, 2H), 8.22 (s, 1H), 9.36 (s, 1H).

10 Step 3: *tert*-Butyl 3-fluoro-4-[2-nitro-4-(tetrahydro-pyran-2-yloxymethyl)-phenylamino]-benzoate

The title compound was prepared by the reaction of Step 2 intermediate (200 mg, 0.580 mmol) with DHP (0.18 mL, 2.04 mmol) in the presence of catalytic amount of PTSA in DCM (15 mL) as per the process described in step 3 of Intermediate 14 to afford 620 mg of the product as colorless oil. ¹H NMR (300 MHz, CDCl₃) δ 1.60 (s, 9H), 1.63-1.73 (m, 3H), 1.74-7.85 (m, 2H), 3.55 (br s, 1H), 3.90 (br s, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.71 (br s, 2H), 7.27-7.34 (m, 1H), 7.42-7.51 (m, 2H), 7.80 (d, *J* = 9.3 Hz, 2H), 8.23 (s, 1H), 9.36 (br s, 1H).

15 Step 4: *tert*-Butyl 4-[2-amino-4-(tetrahydro-pyran-2-yloxymethyl)-phenylamino]-3-fluoro-benzoate

The title compound was prepared by palladium catalysed hydrogenation of step 3 intermediate in methanol (20 mL) as per the process described in step 4 of Intermediate 14 to afford 475 mg of the product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.56 (s, 9H), 1.60-1.70 (m, 5H), 3.58 (br s, 2H), 3.92 (br s, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 4.71 (br s, 2H), 6.02 (br s, 1H), 6.67 (br s, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 7.03 (br s, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.58 (br s, 2H).

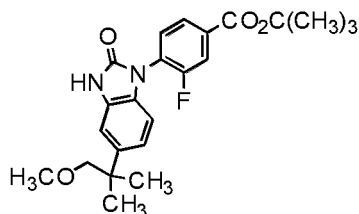
20 Step 5: *tert*-Butyl 3-fluoro-4-(2-oxo-5-{[(tetrahydro-2*H*-pyran-2-yl)oxy]methyl}-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate

The title compound was prepared by cyclization reaction of step 4 intermediate (475 mg, 1.141 mmol) in the presence of CDI (277 mg, 1.712 mmol) in THF (10 mL) as per the process described in step 5 of Intermediate 14 to yield 420 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.63 (s, 9H), 1.78 (br s, 7H), 3.58 (br s, 1H), 3.92 (br s, 1H), 4.50 (d,

$J = 11.7$ Hz, 1H), 4.71 (s, 1H), 4.79 (d, $J = 11.7$ Hz, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 7.07 (d, $J = 8.4$ Hz, 1H), 7.21 (s, 1H), 7.61 (t, $J = 7.5$ Hz, 1H), 7.91-7.98 (m, 2H), 9.84 (br s, 1H).

Intermediate 16

tert-Butyl 3-fluoro-4-[5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate



Step 1: 1-Fluoro-4-(1-methoxy-2-methylpropan-2-yl)benzene

To a cooled (0 °C) suspension of sodium hydride (60% w/w, 618 mg, 15.46 mmol) in THF (20 mL) was added a solution of 2-(4-fluorophenyl)-2-methylpropan-1-ol (1.3 g, 7.728 mmol) in THF (20 mL). After the complete addition, the resulting suspension was warmed up to RT and stirred for 1 hour under the same conditions. Methyl iodide (2.4 mL, 38.642 mmol) was added drop-wise and the mixture was continued to stir for 3 hours at RT. The reaction mixture was quenched with water (20 mL) and the aqueous solution was extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were washed with brine (25 mL) and dried over anhydrous sodium sulfate. The solution was filtered, concentrated and the residue thus obtained was purified by silica gel column chromatography to yield 1.23 g of the title product as yellow oil. ^1H NMR (300 MHz, CDCl_3) δ 6.41 (s, 6H), 3.30 (s, 3H), 3.37 (s, 2H), 6.98 (t, $J = 9.0$ Hz, 2H), 7.31-7.35 (m, 2H)

Step 2: 1-Fluoro-4-(1-methoxy-2-methylpropan-2-yl)-2-nitrobenzene

To a cooled (-30 °C) solution of step 1 intermediate (300 mg, 1.650 mmol) was added conc. sulphuric acid (2.7 mL, 50.84 mmol). To the above mixture was slowly added fuming nitric acid (0.3 mL, 6.75 mmol) in duration of 10 minutes. The resulting solution was stirred at -20 °C for 30 minutes. The reaction mixture was poured in to crushed ice and extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were washed with water (25 mL), brine (25 mL) and dried over anhydrous sodium sulfate. The solution was filtered, concentrated and the residue thus obtained was purified by silica gel column chromatography to yield 211 mg of the title product as pale yellow oil; ^1H NMR (300 MHz, CDCl_3) δ 1.36 (s, 6H), 1.30 (s, 3H), 3.38 (s, 2H), 7.18-7.25 (m, 1H), 7.62-7.67 (m, 1H), 8.02-8.07 (m, 1H).

Step 3: *tert*-Butyl 3-fluoro-4-[4-(2-methoxy-1,1-dimethyl-ethyl)-2-nitro-phenylamino]-benzoate

The title compound was synthesized by the reaction of step 2 intermediate (500 mg, 2.200 mmol) and *tert*-butyl 4-amino-3-fluorobenzoate (511 mg, 2.42 mmol) in the presence of sodium hydride (60% w/w, 132 mg, 3.30 mmol) in DMF (40 mL) as per the process described in step 1 of Intermediate 1 to yield 752 mg of the product as bright orange liquid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.26 (s, 6H), 1.54 (s, 9H), 3.22 (s, 3H), 3.39 (s, 2H), 7.22 (d, *J* = 8.7 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.65-7.72 (m, 3H), 8.02 (br s, 1H), 9.14 (s, 1H); APCI-MS (*m/z*) 417 (M+H)⁺.

Step 4: *tert*-Butyl 4-[2-amino-4-(2-methoxy-1,1-dimethyl-ethyl)-phenylamino]-3-fluorobenzoate

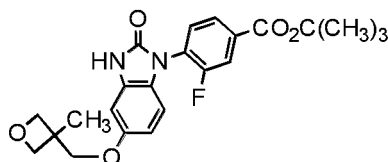
The title compound was synthesized by the palladium catalyzed hydrogenation of step 3 intermediate (746 mg, 1.780 mmol) in methanol (10 mL) as per the process described in step 2 of Intermediate 1 to yield 566 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.22 (s, 6H), 1.50 (s, 9H), 3.22 (s, 3H), 3.31 (s, 2H), 4.77 (br s, 2H), 6.42-6.45 (m, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.80 (br s, 1H), 6.90 (d, *J* = 8.1 Hz, 1H), 7.46-7.53 (m, 2H), 7.62 (br s, 1H); APCI-MS (*m/z*) 387 (M+H)⁺.

Step 5: *tert*-Butyl 3-fluoro-4-[5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate

The title compound was synthesized by the reaction of step 4 intermediate (560 mg, 1.442 mmol) and CDI (351 mg, 2.16 mmol) in THF (20 mL) as per the process described in step 3 of Intermediate 1 to yield 522 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.26 (s, 6H), 1.57 (s, 9H), 3.21 (s, 3H), 3.34 (s, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 7.01-7.05 (m, 2H), 7.75-7.79 (m, 1H), 7.91 (d, *J* = 9.0 Hz, 2H), 11.18 (br s, 1H); APCI-MS (*m/z*) 415 (M+H)⁺.

Intermediate 17

tert-Butyl-3-fluoro-4-[5-(3-methyl-oxetan-3-ylmethoxy)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate



Step 1: 3-[(4-Iodo-3-nitrophenoxy)methyl]-3-methyloxetane

To a stirred mixture of 4-iodo-3-nitrophenol (1.02 g, 3.849 mmol), 3-methyl-3-oxetane methanol (393 mg, 3.849 mmol) and triphenylphosphine (1.51 g, 5.773 mmol) in THF (20 mL) was added a diethyl azodicarboxylate (DEAD) (0.91 mL, 5.773 mmol) at 0 °C. The

reaction mixture was stirred at RT for 18 hours. The reaction mixture was concentrated under reduced pressure and the residue thus obtained was purified by silica gel column chromatography to yield 971 mg of the title product as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ 1.44 (s, 3H), 4.07 (s, 2H), 4.48 (d, *J* = 6.0 Hz, 2H), 4.60 (d, *J* = 6.0 Hz, 2H), 6.89-6.93 (m, 1H), 7.45-7.47 (m, 1H), 7.91 (d, *J* = 8.7 Hz, 1H).

Step 2: *tert*-Butyl 3-fluoro-4-[4-(3-methyl-oxetan-3-ylmethoxy)-2-nitro-phenylamino] benzoate

The title compound was synthesized by the reaction of step 1 intermediate (612 mg, 1.752 mmol) and *tert*-butyl 4-amino-3-fluorobenzoate (370 mg, 1.7529 mmol) in the presence of palladium acetate (39 mg, 0.1752 mmol), XPhos (121 mg, 0.210 mmol) and cesium carbonate (856 mg, 2.629 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of Intermediate 2 to yield 692 mg of the title product as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ 1.45 (s, 3H), 1.59 (s, 9H), 4.06 (s, 2H), 4.49 (d, *J* = 6.0 Hz, 2H), 4.64 (d, *J* = 6.0 Hz, 2H), 7.21-7.22 (m, 1H), 7.34-7.37 (m, 2H), 7.70-7.78 (m, 3H), 9.08 (br s, 1H); APCI-MS (*m/z*) 431 (M+H)⁺.

Step 3: *tert*-Butyl 4-[2-amino-4-(3-methyl-oxetan-3-ylmethoxy)-phenylamino]-3-fluorobenzoate

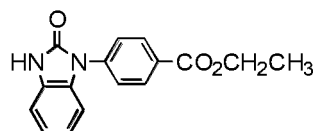
The title compound was synthesized by the catalytic hydrogenation of step 2 intermediate (673 mg, 1.556 mmol) in methanol (10 mL) as per the process described in step 2 of Intermediate 1 to yield 463 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.35 (s, 3H), 1.49 (s, 9H), 3.96 (s, 2H), 4.30 (d, *J* = 6.0 Hz, 2H), 4.48 (d, *J* = 6.0 Hz, 2H), 4.91 (br s, 2H), 6.23 (d, *J* = 8.7 Hz, 1H), 6.31-6.40 (m, 2H), 6.87 (d, *J* = 8.4 Hz, 1H), 7.44-7.51 (m, 2H), 7.58 (br s, 1H); APCI-MS (*m/z*) 401 (M+H)⁺.

Step 4: *tert*-Butyl 3-fluoro-4-[5-(3-methyl-oxetan-3-ylmethoxy)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoate

The title compound was synthesized by the reaction of step 3 intermediate (443 mg, 1.100 mmol) and CDI (272 mg, 1.65 mmol) in THF (10 mL) as per the process described in step 3 of Intermediate 1 to yield 409 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.35 (s, 3H), 1.57 (s, 9H), 4.02 (s, 2H), 4.30 (d, *J* = 6.0 Hz, 2H), 4.49 (d, *J* = 6.0 Hz, 2H), 6.66 (d, *J* = 9.0 Hz, 1H), 6.73-6.76 (m, 2H), 7.74 (t, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 11.28 (br s, 1H).

Intermediate 18

Ethyl 4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate



Step 1: Ethyl 4-[(2-nitrophenyl)amino]benzoate

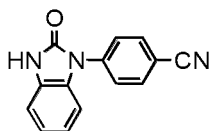
A mixture of ethyl 4-amino benzoate (1 g, 6.050 mmol) and 1-fluoro-2-nitrobenzene (0.64 mL, 6.050 mmol) was heated at 160 °C in a sealed tube for 15 hours. The reaction mixture was cooled down to RT and purified by silica gel column chromatography to yield 500 mg of the title product as yellow solid. ¹H NMR (300 MHz, CDCl₃) δ 1.40 (t, *J* = 6.9 Hz, 3H), 4.35 (q, *J* = 6.9 Hz, 2H), 6.89-6.91 (m, 1H), 7.27-7.31 (m, 2H), 7.74 (br s, 2H), 8.06 (d, *J* = 8.7 Hz, 2H), 8.21 (d, *J* = 8.4 Hz, 1H), 9.49 (br s, 1H).

Step 2: Ethyl 4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzoate

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (500 mg, 1.746 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (370 mg, 1.444 mmol) in the presence of CDI (351 mg, 2.166 mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 300 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.34 (t, *J* = 7.2 Hz, 3H), 4.35 (q, *J* = 6.9 Hz, 2H), 7.06-7.15 (m, 4H), 7.74 (d, *J* = 7.8 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 2H), 11.28 (br s, 1H).

Intermediate 19

4-(2-Oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzonitrile



Step 1: 4-[(2-Nitrophenyl)amino]benzonitrile

The title compound was prepared by the reaction of 4-aminobenzonitrile (1 g, 8.47 mmol) with 1-fluoro-2-nitrobenzene (892 mg, 8.47 mmol) in the presence of sodium hydride (60% w/w, 406 mg, 10.16 mmol) in DMF (10 mL) as described in step 1 of Intermediate 1 to yield 810 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.17 (t, *J* = 7.8 Hz, 1H), 7.30 (br s, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.61-7.73 (m, 3H), 8.10 (d, *J* = 8.7 Hz, 1H), 9.30 (s, 1H); APCI-MS (*m/z*) 238 (M+H)⁺.

Step 2: 4-(2-Oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzonitrile

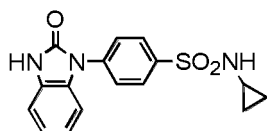
The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (800 mg, 3.344 mmol) in methanol (10 mL) followed by the cyclization of the corresponding diamine derivative (600 mg, 2.87 mmol) in the presence of CDI (697 mg, 4.30

mmol) in THF (10 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 240 mg of the product as pale yellow solid. ^1H NMR (300 MHz, DMSO- d_6) δ 7.04 (br s, 1H), 7.10 (br s, 2H), 7.15 (d, $J = 7.8$ Hz, 1H), 7.81 (d, $J = 8.1$ Hz, 2H), 8.02 (d, $J = 7.8$ Hz, 2H), 11.32 (br s, 1H); APCI-MS (m/z) 236 ($\text{M}+\text{H}$) $^+$.

5

Intermediate 20

N-Cyclopropyl-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzenesulfonamide



Step 1: *N*-Cyclopropyl-4-[(2-nitrophenyl)amino]benzenesulfonamide

The title compound was prepared by the reaction of 1-iodo-2-nitrobenzene (495 mg, 1.987 mmol) with 4-amino-*N*-cyclopropylbenzenesulfonamide (600 mg, 2.204 mmol) in the presence of palladium acetate (45 mg, 0.198 mmol), XPhos (137 mg, 0.238 mmol) and cesium carbonate (1.95 g, 5.963 mmol) in 1,4-dioxane (15 mL) as per the process described in step 1 of Intermediate 2 to yield 230 mg of the product as yellow solid. ^1H NMR (300 MHz, DMSO- d_6) δ 0.39-0.49 (s, 4H), 2.10 (br s, 1H), 7.10 (t, $J = 7.5$ Hz, 1H), 7.37 (d, $J = 8.4$ Hz, 2H), 7.50 (d, $J = 8.7$ Hz, 1H), 7.61 (t, $J = 7.2$ Hz, 1H), 7.72 (d, $J = 8.7$ Hz, 2H), 8.11 (d, $J = 8.4$ Hz, 1H), 9.31 (s, 1H); APCI-MS (m/z) 333 ($\text{M}+\text{H}$) $^+$.

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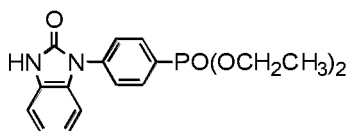
Step 2: *N*-Cyclopropyl-4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)benzenesulfonamide

The title compound was prepared by palladium catalyzed hydrogenation of step 1 intermediate (230 mg, 0.688 mmol) in methanol (8 mL) followed by the cyclization of the corresponding diamine derivative (180 mg, 0.594 mmol) in the presence of CDI (145 mg, 0.891 mmol) in THF (8 mL) as per the process described in step 2 and 3 of Intermediate 1 respectively to yield 90 mg of the product as off white solid. ^1H NMR (300 MHz, DMSO- d_6) δ 0.43 (br s, 2H), 0.53 (br s, 2H), 2.16 (br s, 1H), 7.07-7.10 (m, 3H), 7.16 (d, $J = 7.8$ Hz, 1H), 7.83 (d, $J = 8.4$ Hz, 2H), 7.97 (d, $J = 8.1$ Hz, 2H), 8.05 (br s, 1H), 11.31 (br s, 1H).

25

Intermediate 21

Diethyl [4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)phenyl]phosphonate



Step 1: Ethyl propyl {4-[(2-nitrophenyl)amino]phenyl}phosphonate

The title compound was prepared from 1-iodo-2-nitro benzene (482 mg, 1.94 mmol) and diethyl (4-aminophenyl)phosphonate (370 mg, 1.614 mmol) in the presence of palladium

30

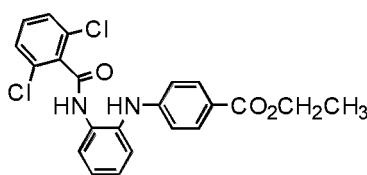
acetate (36 mg, 0.161 mmol), XPhos (112 mg, 0.194 mmol) and cesium carbonate (789 mg, 2.42 mmol) in 1,4-dioxane (10 mL) as per the process described in step 1 of Intermediate 2 to yield 416 mg of the product as brown solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.23 (t, *J* = 6.9 Hz, 6H), 3.99 (q, *J* = 6.9 Hz, 4H), 7.07 (br s, 2H), 7.36 (br s, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.60-7.68 (m, 2H), 8.09 (br s, 1H), 9.27 (br s, 1H); APCI-MS (*m/z*) 351 (M+H)⁺.

Step 2: Diethyl [4-(2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)phenyl]phosphonate

The title compound was prepared by the nitro reduction of step 1 intermediate (416 mg, 1.187 mmol) in the presence of iron powder (198 mg, 3.560 mmol) and ammonium chloride (663 mg, 11.875 mmol) in water (3.0 mL) and methanol (15 mL) as per the process described in step 2 of Intermediate 10 followed by cyclization of the diamine derivative (360 mg, 1.124 mmol) by using CDI (273 mg, 1.68 mmol) in THF (10 mL) to yield 300 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.26 (t, *J* = 6.9 Hz, 6H), 4.02-4.09 (m, 4H), 7.03-7.09 (m, 3H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.76 (br s, 2H), 7.85-7.92 (m, 2H), 11.27 (br s, 1H).

Intermediate 22

Ethyl 4-[(2-{[(2,6-dichlorophenyl)carbonyl]amino}phenyl)amino]benzoate



Step 1: Ethyl 4-[(2-nitrophenyl)amino]benzoate:

A stirred solution of ethyl 4-amino benzoate (1 g, 6.053 mmol) in 1-fluoro-2-nitrobenzene (0.64 mL, 6.053 mmol) was heated at 160 °C in sealed tube for 16 hours. The reaction mixture was cooled to RT and the residue was purified by silica gel column chromatography to yield 500 mg of the product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.40 (t, *J* = 7.2 Hz, 3H), 4.38 (d, *J* = 7.2 Hz, 2H), 6.80 (br s, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.45 (br s, 2H), 8.06 (d, *J* = 8.7 Hz, 2H), 8.22 (d, *J* = 8.4 Hz, 1H), 9.49 (br s, 1H).

Step 2: Ethyl 4-[(2-aminophenyl)amino]benzoate:

To the stirred solution of Step 1 intermediate (300 mg, 1.048 mmol) in methanol (10 mL) was added catalytic amount of 10% palladium on carbon and the reaction was stirred for 5 h under hydrogen atmosphere. The reaction mixture was filtered through celite and the filtrate was concentrated to yield 200 mg of the product. ¹H NMR (300 MHz, CDCl₃) δ 1.35 (t, *J* = 7.5 Hz, 3H), 4.33 (q, *J* = 7.2 Hz, 2H), 5.81 (br s, 1H), 6.69 (d, *J* = 8.1 Hz, 2H), 6.85 (t, *J* = 7.8 Hz,

1H), 6.91 (d, $J = 7.8$ Hz, 1H), 7.07 (t, $J = 7.8$ Hz, 1H), 7.17 (d, $J = 7.8$ Hz, 1H), 7.85 (d, $J = 8.7$ Hz, 2H).

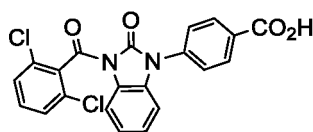
Step 3: Ethyl 4-[(2-[(2,6-dichlorophenyl)carbonyl]amino}phenyl)amino] benzoate:

To a well stirred solution of Step 2 intermediate (350 mg, 1.365 mmol) in DCM (10 ml) was added DIPEA (0.7 mL, 4.09 mmol) and the reaction mixture was cooled to 0 °C followed by the addition of 2,6-dichlorobenzoyl chloride (0.3 mL, 2.047 mmol). The reaction mixture was stirred overnight at RT. The reaction mixture was diluted with water (10 mL) and the precipitate thus obtained was filtered. The obtained product was purified by silica gel column chromatography to yield 450 mg of the title product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.35 (t, $J = 6.6$ Hz, 3H), 4.30 (q, $J = 7.2$ Hz, 2H), 6.81 (q, $J = 8.1$ Hz, 2H), 7.20-7.33 (m, 4H), 7.43 (d, $J = 7.8$ Hz, 1H), 7.82-7.90 (m, 4H).

Examples

Example 1

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid



Step 1: *tert*-Butyl 4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl]benzoate:

To a stirred and cooled (0 °C) solution of Intermediate 1 (150 mg, 0.483 mmol) in DMF (5 mL) was added sodium hydride (60% w/w, 25 mg, 0.628 mmol) and the reaction mixture was stirred for 10 minutes at the same temperature. 2,6-Dichlorobenzoyl chloride (0.08 mL, 0.580 mmol) was added to the reaction mixture and it was stirred at RT for 2 h. The reaction mixture was diluted with water (10 mL) and product was extracted in ethyl acetate (2 x 10 mL). The layers were separated. The combined organic layer was washed with water (2 x 15 mL), brine (20 ml) and dried over anhydrous Na₂SO₄. The solvent was recovered under reduced pressure. The residue was purified by column chromatography to afford 150 mg of the product as off-white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.56 (s, 9H), 7.17 (s, 1H), 7.36 (br s, 2H), 7.55-7.61 (m, 3H), 7.84 (s, 1H), 8.29 (s, 1H)

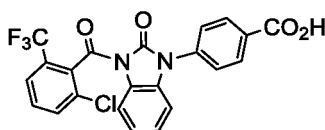
Step 2: 4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid:

To a well stirred and cooled (0 °C) solution of Step 1 product (100 mg, 0.206 mmol) in dichloromethane (3 mL) was added trifluoroacetic acid (3 mL) and the reaction mixture was

stirred at RT for 4h. The solvents were recovered under reduced pressure and the residue obtained was washed with water, triturated with diethyl ether and dried to yield 60 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.20 (br s, 1H), 7.36 (br s, 2H), 7.54-7.61 (m, 3H), 7.68 (d, *J* = 8.1 Hz, 2H), 8.07 (d, *J* = 8.1 Hz, 2H), 8.29 (br s, 1H); APCI-MS (*m/z*) 427 (M+H)⁺.

Example 2

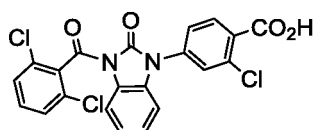
4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl}benzoic acid



The title compound was prepared by the reaction of Intermediate 1 (138 mg, 0.411 mmol) and 2-chloro-6-(trifluoromethyl)benzoyl chloride (100 mg, 0.445 mmol) in the presence of sodium hydride (60% w/w, 24 mg, 0.5788 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (110 mg, 0.212 mmol) by using TFA (3 mL) in DCM (3 mL) as per the process described in Example 1 to yield 55 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.21 (br s, 1H), 7.36 (br s, 2H), 7.66 (t, *J* = 8.4 Hz, 2H), 7.76 (t, *J* = 7.8Hz, 1H), 7.89-7.96 (m, 2H), 8.10 (t, *J* = 8.1 Hz, 2H), 8.28 (br s, 1H), 13.23 (br s, 1H); APCI-MS (*m/z*) 458 (M-H)⁺.

Example 3

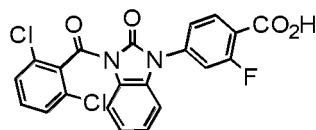
2-Chloro-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid



The title compound was prepared by the reaction of Intermediate 2 (130 mg, 0.377 mmol) with 2,6-dichlorobenzoyl chloride (0.06 mL, 0.452 mmol) in the presence of sodium hydride (60% w/w, 20 mg, 0.490 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (120 mg, 0.231 mmol) by using TFA (3 mL) in DCM (3 mL) as per the process described in Example 1 to yield 20 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.21 (br s, 1H), 7.37 (br s, 2H), 7.55-7.64 (m, 4H), 7.79 (s, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 8.28 (br s, 1H), 13.20 (br s, 1H); APCI-MS (*m/z*) 461 (M+H)⁺.

Example 4

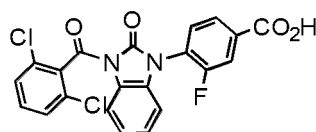
4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-2-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 3 (200 mg, 0.609 mmol) and 2,6-dichlorobenzoyl chloride (0.12 mL, 0.731 mmol) in the presence of sodium hydride (60% w/w, 32 mg, 0.7921 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (160 mg, 0.319 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 35 mg of the product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.20-7.27 (m, 2H), 7.33-7.39 (m, 5H), 7.48 (br s, 1H), 8.17 (br s, 1H), 8.48 (br s, 1H); APCI-MS (*m/z*) 445 (M)⁺.

Example 5

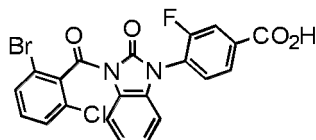
4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 4 (150 mg, 0.456 mmol) and 2,6-dichlorobenzoyl chloride (0.08 mL, 0.548 mmol) in the presence of sodium hydride (60% w/w, 24 mg, 0.593 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (120 mg, 0.239 mmol) by using TFA (3 mL) in DCM (3 mL) as per the process described in Example 1 to yield 65 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.03 (br s, 1H), 7.35 (s, 2H), 7.51-7.61 (m, 3H), 7.85 (t, *J* = 7.2 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 8.29 (m, 1H), 13.16 (br s, 1H); APCI-MS (*m/z*) 442 (M-H)⁻.

Example 6

4-[3-(2-Bromo-6-chlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



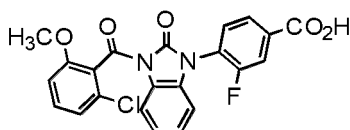
The title compound was prepared by the reaction of Intermediate 4 (300 mg, 0.914 mmol) with 2-bromo-6-chlorobenzoyl chloride (536 mg, 1.005 mmol) in the presence of sodium hydride (60% w/w, 48 mg, 1.188 mmol) in DMF (5 mL) followed by the hydrolysis of the

corresponding ester derivative (123 mg, 0.225 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 57 mg of the product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 6.91 (br s, 1H), 7.29-7.40 (m, 3H), 7.41 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.63 (t, *J* = 7.2 Hz, 1H), 8.01 (t, *J* = 8.4 Hz, 2H), 8.45 (d, *J* = 6.9 Hz, 1H);

5 APCI-MS (*m/z*) 490 (M+H)⁺.

Example 7

4-[3-(2-Chloro-6-methoxybenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl] -3-fluorobenzoic acid



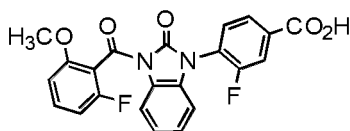
10 The title compound was prepared by the reaction of Intermediate 4 (750 mg, 2.285 mmol) with 2-chloro-6-methoxybenzoyl chloride (200 mg, 1.078 mmol) in the presence of sodium hydride (60% w/w, 43 mg, 1.078 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (210 mg, 0.4226 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 55 mg of the product as white solid. ¹H

15 NMR (300 MHz, DMSO-*d*₆) δ 3.77 (br s, 3H), 7.00 (br s, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.33 (br s, 2H), 7.46 (t, *J* = 8.4 Hz, 2H), 7.83 (t, *J* = 7.2 Hz, 1H), 7.94 (d, *J* = 9.3 Hz, 2H), 8.26 (br s, 1H); APCI-MS (*m/z*) 441 (M+H)⁺.

Example 8

3-Fluoro-4-[3-(2-fluoro-6-methoxybenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid

20

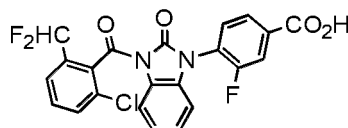


The title compound was prepared by the reaction of Intermediate 4 (150 mg, 0.457 mmol) with 2-fluoro-6-methoxybenzoyl chloride (0.08 mL, 0.594 mmol) in the presence of sodium hydride (60% w/w, 15 mg, 0.594 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (160 mg, 0.332 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 70 mg of the product as white solid. ¹H

25 NMR (300 MHz, DMSO-*d*₆) δ 3.78 (s, 3H), 6.90-7.00 (m, 3H), 7.32 (br s, 2H), 7.50 (q, *J* = 7.8 Hz, 1H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.94 (d, *J* = 9.3 Hz, 2H), 8.22 (br s, 1H), 13.62 (br s, 1H); APCI-MS (*m/z*) 425 (M+H)⁺.

Example 9

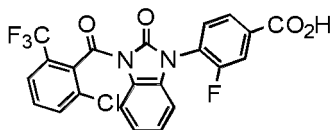
4-{3-[2-Chloro-6-(difluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 4 (200 mg, 0.609 mmol) with 2-chloro-6-(difluoromethyl)benzoyl chloride (230 mg, 1.022 mmol) in the presence of sodium hydride (60% w/w, 32 mg, 0.792 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (200 mg, 0.386 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 110 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 6.79 (t, *J* = 54.6 Hz, 1H), 6.91 (br s, 1H), 7.32 (br s, 2H), 7.53-7.61 (m, 4H), 8.01 (d, *J* = 8.7 Hz, 2H), 8.42 (br s, 1H), 13.52 (br s, 1H); APCI-MS (*m/z*) 461 (M+H)⁺.

Example 10

4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid



Step 1: *tert*-Butyl-4-{3-[2-chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoate

To a stirred solution of 2-chloro-6-(trifluoromethyl)benzoic acid (100 mg, 0.446 mmol) in dry THF (5 mL) was added DMF (20 μL) followed by 2.0 M solution of oxalyl chloride (0.33 μL, 0.667 mmol) in DCM (5 mL). The resulting mixture was stirred at RT for 2 hours. The solvents were removed under reduced pressure and the residue obtained was dried completely under *vacuo*. The sticky mass obtained was dissolved in DMF (5 mL) and slowly added to a precooled (0 °C) suspension of sodium hydride (60% w/w, 23 mg, 0.5781 mmol) and Intermediate 4 (146 mg, 0.446 mmol) in DMF (5 mL). The resulting mixture was warmed up to RT and stirred for 2 hours. The reaction mixture was quenched with water (5 mL) and extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with water (2 x 10 mL) and brine (10 mL). The solution was dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. The residue obtained was purified by silica gel column chromatography to yield 115 mg of the title product as off white solid.

¹H NMR (300 MHz, DMSO-*d*₆) δ 1.25 (s, 9H), 6.86 (d, *J* = 6.3 Hz, 1H), 7.30 (br s, 2H), 7.50-

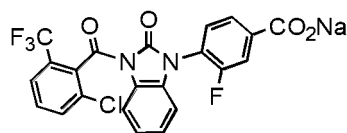
7.56 (m, 2H), 7.63-7.68 (m, 2H), 7.87 (t, $J = 8.7$ Hz, 2H), 8.41 (d, $J = 7.8$ Hz, 1H); APCI-MS (m/z) 535 (M+H)⁺.

Step 2: 4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid

- 5 A precooled (0 °C) solution of step 1 intermediate (110 mg, 0.205 mmol) in DCM (3 mL) was treated with TFA (1 mL) and the resulting mixture was stirred at RT for 4 hours. The solvent and excess of reagent were removed under reduced pressure and the residue obtained was diluted with water (10 mL). The aqueous mixture was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with brine (10 mL) and dried over anhydrous sodium sulfate. The solution was filtered and concentrated under reduced pressure. The residue thus obtained was purified by silica gel column chromatography to obtain 25 mg of the title product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 6.89 (d, $J = 6.3$ Hz, 1H), 7.32 (br s, 1H), 7.50-7.60 (m, 2H), 7.63-7.68 (m, 2H), 8.00 (t, $J = 8.7$ Hz, 2H), 8.43 (d, $J = 7.8$ Hz, 1H); APCI-MS (m/z) 479 (M+H)⁺.

15 Example 11

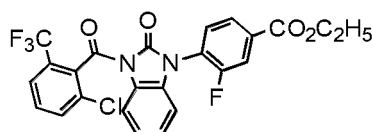
Sodium 4-(3-{[2-chloro-6-(trifluoromethyl)phenyl]carbonyl}-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)-3-fluorobenzoate



- To a well stirred and cooled (0 °C) solution of Example 10 (60 mg, 0.125 mmol) in methanol (2 mL) was added 1N aqueous solution of sodium hydroxide (0.13 mL, 0.125 mmol) and the reaction mixture was stirred at the same temperature for 1h. The solvent was recovered under reduced pressure and the residue obtained was triturated with diethyl ether to yield 38 mg of the product as white solid. ¹H NMR (300 MHz, CD₃OD) δ 6.92 (br s, 1H), 7.33 (br s, 2H), 7.50 (br s, 1H), 7.64-7.69 (m, 1H), 7.76 (br s, 2H), 7.83-7.92 (m, 2H), 8.30 (br s, 1H); APCI-MS (m/z) 479 [(M+H)-Na]⁺.

Example 12

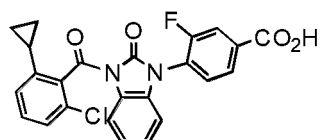
Ethyl 4-(3-{[2-chloro-6-(trifluoromethyl)phenyl]carbonyl}-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)-3-fluorobenzoate



To a well stirred solution of Example 10 (203 mg, 0.4263 mmol) in ethanol (10 mL) was added conc. sulphuric acid (0.3 mL) and the reaction mixture was refluxed for 18 h. The solvent was recovered under reduced pressure and the residue obtained was diluted with ethyl acetate (20 mL) and washed with saturated aqueous solution of sodium bicarbonate (2 x 10 mL). The solution was dried over anhydrous sodium sulphate, concentrated under reduced pressure and triturated the residue with *n*-pentane to yield 182 mg of the product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.40 (t, *J* = 6.9 Hz, 3H), 4.40 (q, *J* = 6.9 Hz, 2H), 6.86 (d, *J* = 7.2 Hz, 1H), 7.31 (br s, 2H), 7.50-7.56 (m, 2H), 7.63-7.68 (m, 2H), 7.94 (t, *J* = 9.9 Hz, 2H), 8.42 (d, *J* = 7.8 Hz, 1H); ESI-MS (*m/z*) 507 (M+H)⁺.

Example 13

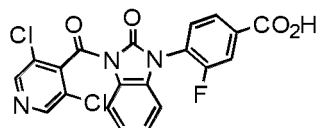
4-[3-(2-Chloro-6-cyclopropylbenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 4 (143 mg, 0.435 mmol) with 2-chloro-6-cyclopropylbenzoyl chloride (102 mg, 0.478 mmol) in the presence of sodium hydride (60% w/w, 23 mg, 0.5665 mmol) in DMF (3 mL) followed by the hydrolysis of the corresponding ester derivative (157 mg, 0.309 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 32 mg of the product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 0.74 (br s, 1H), 0.82-0.88 (m, 3H), 1.91 (br s, 1H), 6.90 (br s, 1H), 6.97 (d, *J* = 7.2 Hz, 1H), 7.28-7.35 (m, 5H), 7.62 (br s, 1H), 7.97-8.04 (m, 2H), 8.48 (d, *J* = 6.9 Hz, 1H).

Example 14

[(3,5-Dichloropyridin-4-yl)carbonyl]-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl}-3-fluorobenzoic acid

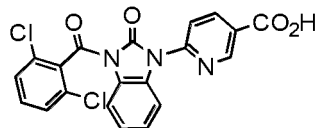


The title compound was prepared by the reaction of Intermediate 4 (100 mg, 0.304 mmol) with 3,5-dichloropyridine-4-carbonyl chloride (75 mg, 0.357 mmol) in the presence of sodium hydride (60% w/w, 18 mg, 0.456 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (65 mg, 0.129 mmol) by using TFA (1 mL) in DCM (4 mL) as per the process described in Example 1 to yield 30 mg of the product as white solid. ¹H NMR

(300 MHz, DMSO-*d*₆) δ 7.07 (br s, 1H), 7.40 (br s, 2H), 7.84-7.89 (m, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 8.27 (br s, 1H), 8.84 (s, 2H), 13.58 (br s, 1H); APCI-MS (*m/z*) 446 (M+H)⁺.

Example 15

6-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl] nicotinic acid



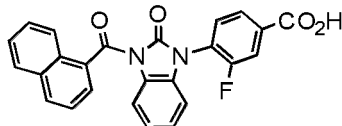
5

The title compound was prepared by the reaction of Intermediate 5 (200 mg, 0.642 mmol) with 2,6-dichlorobenzoyl chloride (0.110 mL, 0.770 mmol) in the presence of sodium hydride (60% w/w, 34 mg, 0.835 mmol) in DMF (3 mL) followed by the hydrolysis of the corresponding ester derivative (150 mg, 0.309 mmol) by using TFA (3 mL) in DCM (3 mL) as per the process described in Example 1 to yield 70 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.42 (s, 2H), 7.57-7.63 (m, 3H), 7.96 (q, *J* = 8.4 Hz, 1H), 8.05 (br s, 1H), 8.30 (br s, 1H), 8.44 (d, *J* = 8.1 Hz, 1H), 9.09 (s, 1H), 13.56 (br s, 1H); APCI-MS (*m/z*) 428 (M+H)⁺.

10

Example 16

4-[3-(1-Naphthoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



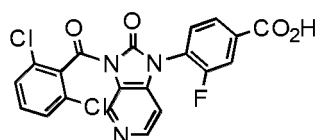
The title compound was prepared by the reaction of Intermediate 4 (100 mg, 0.304 mmol) with naphthalene-1-carbonyl chloride (0.06 mL, 0.396 mmol) in the presence of sodium hydride (60% w/w, 16 mg, 0.396 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (130 mg, 0.269 mmol) by using TFA (1 mL) in DCM (3 mL) as per the process described in Example 1 to yield 65 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 6.98 (br s, 1H), 7.35 (br s, 2H), 7.59 (br s, 3H), 7.76 (d, *J* = 7.8 Hz, 1H), 7.86-7.93 (m, 3H), 7.95-8.04 (m, 2H), 8.11 (d, *J* = 8.7 Hz, 1H), 8.21 (br s, 1H), 13.58 (br s, 1H); APCI-MS (*m/z*) 427 (M+H)⁺.

20

25

Example 17

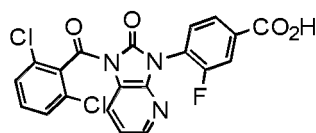
4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridin-1-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 6 (400 mg, 1.214 mmol) with 2,6-dichlorobenzoyl chloride (0.209 mL, 1.457 mmol) in the presence of sodium hydride (60% w/w, 63 mg, 1.579 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (200 mg, 0.398 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 110 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.52 (br s, 1H), 7.59-7.65 (m, 4H), 7.86 (t, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 1H), 8.56 (br s, 1H), 9.37 (s, 1H), 13.68 (br s, 1H); APCI-MS (*m/z*) 446 (M+H)⁺.

Example 18

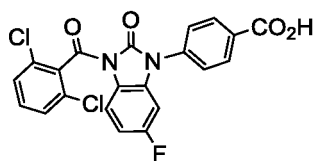
4-[1-(2,6-Dichlorobenzoyl)-2-oxo-1*H*-imidazo[4,5-*b*]pyridin-3(2*H*)-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 7 (150 mg, 0.454 mmol) and 2,6-dichlorobenzoyl chloride (0.09 mL, 0.638 mmol) in the presence of sodium hydride (60% w/w, 24 mg, 0.592 mmol) in DMF (4 mL) followed by the hydrolysis of the corresponding ester derivative (170 mg, 0.338 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 75 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.09 (br s, 1H), 7.23-7.30 (m, 3H), 7.41 (br s, 1H), 7.70-7.76 (m, 2H), 8.03 (br s, 1H), 8.37 (s, 1H), 13.50 (br s, 1H); APCI-MS (*m/z*) 446 (M+H)⁺.

Example 19

4-[3-(2,6-Dichlorobenzoyl)-6-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl]benzoic acid

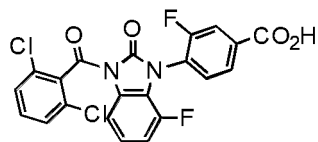


The title compound was prepared by the reaction of Intermediate 8 (210 mg, 0.639 mmol) with 2,6-dichlorobenzoyl chloride (0.12 mL, 0.766 mmol) in the presence of sodium hydride (60% w/w, 33 mg, 0.8314 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (220 mg, 0.4388 mmol) by using TFA (4 mL) in DCM (4 mL) as per the process described in Example 1 to yield 90 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.11 (d, *J* = 8.4 Hz, 1H), 7.19 (d, *J* = 8.1 Hz, 1H), 7.51-7.61

(m, 3H), 7.68 (d, $J = 8.4$ Hz, 2H), 8.10 (d, $J = 8.1$ Hz, 2H), 8.26-8.32 (m, 1H), 13.11 (br s, 1H); APCI-MS (m/z) 445 (M+H)⁺.

Example 20

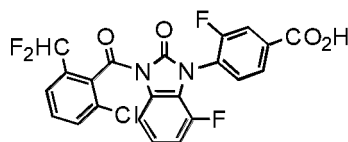
4-[3-(2,6-Dichlorobenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 9 (150 mg, 0.433 mmol) with 2,6-dichlorobenzoyl chloride (0.09 mL, 0.606 mmol) in the presence of sodium hydride (60% w/w, 23 mg, 0.5630 mmol) in DMF (4 mL) followed by the hydrolysis of the corresponding ester derivative (170 mg, 0.327 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 50 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.31-7.37 (m, 2H), 7.55-7.64 (m, 3H), 7.89-7.93 (m, 3H), 8.15 (d, $J = 7.8$ Hz, 1H), 13.61 (br s, 1H); APCI-MS (m/z) 463 (M+H)⁺.

Example 21

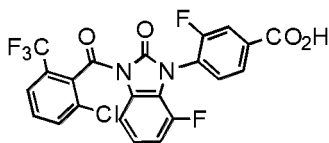
4-{3-[2-Chloro-6-(difluoromethyl)benzoyl]-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 9 (200 mg, 0.578 mmol) with 2-chloro-6-(difluoromethyl)benzoyl chloride (143 mg, 0.635 mmol) in the presence of sodium hydride (60% w/w, 18 mg, 0.7514 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (180 mg, 0.337 mmol) by using TFA (2 mL) in DCM (4 mL) as per the process described in Example 1 to yield 78 mg of the product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 6.77 (dt, $J = 10.2$ Hz, $J = 55.8$ Hz, 1H), 7.07 (t, $J = 10.2$ Hz, 1H), 7.28 (br s, 1H), 7.53-7.63 (m, 4H), 7.96 (t, $J = 9.6$ Hz, 2H), 8.23 (t, $J = 7.8$ Hz, 1H); APCI-MS (m/z) 479 (M+H)⁺.

Example 22

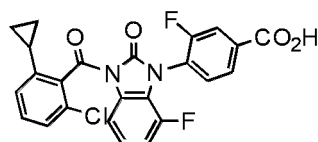
4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-7-fluoro-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 9 (200 mg, 0.577 mmol) with 2-chloro-6-(trifluoromethyl)benzoyl chloride (0.13 mL, 0.808 mmol) in the presence of sodium hydride (60% w/w, 30 mg, 0.7507 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (300 mg, 0.542 mmol) by using TFA (3 mL) in DCM (6 mL) as per the process described in Example 1 to yield 150 mg of the product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 7.08 (d, *J* = 9.3 Hz, 1H), 7.29 (br s, 2H), 7.51-7.57 (m, 2H), 7.60 (br s, 2H), 7.97 (t, *J* = 9.3 Hz, 2H), 8.28 (d, *J* = 8.1 Hz, 1H); APCI-MS (*m/z*) 497 (M+H)⁺.

Example 23

4-[3-(2-Chloro-6-cyclopropylbenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



Step 1: *tert*-Butyl 4-[3-(2-Chloro-6-cyclopropylbenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoate:

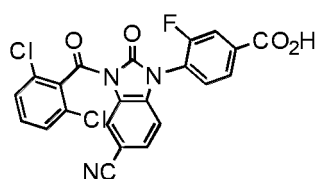
To a stirred and cooled (0 °C) solution of Intermediate 9 (183 mg, 0.528 mmol) in DMF (3 mL) was added sodium hydride (60% w/w, 28 mg, 0.686 mmol) and the reaction mixture was stirred for 10 minutes at the same temperature. A cooled solution of 2-chloro-6-cyclopropylbenzoyl chloride (183 mg, 0.851 mmol) and DIPEA (0.46 mL, 2.642 mmol) in THF (3 mL) was added to the reaction mixture and it was stirred at RT for 2 h. The reaction mixture was diluted with water (10 mL) and product was extracted with ethyl acetate (2 x 10 mL). The layers were separated. The combined organic layers were washed with water (2 x 15 mL), brine (20 mL) and dried over anhydrous Na₂SO₄. The solvent was recovered under reduced pressure. The residue was purified by column chromatography to afford 173 mg of the title product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 0.83-0.90 (m, 4H), 1.59 (s, 9H), 1.89 (br s, 1H), 6.95-7.08 (m, 2H), 7.28 (br s, 4H), 7.48-7.56 (m, 1H), 7.83 (t, *J* = 12.3 Hz, 2H), 8.28 (d, *J* = 9.0 Hz, 1H).

Step 2: 4-[3-(2-Chloro-6-cyclopropylbenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid:

To a well stirred and cooled (0 °C) solution of Step 1 intermediate (168 mg, 0.3200 mmol) in dichloromethane (4 mL) was added trifluoroacetic acid (2 mL) and the reaction mixture was stirred at RT for 3h. The solvents were recovered under reduced pressure and the residue obtained was washed with water, triturated with diethyl ether and dried to yield 54 mg of the title product as white solid. ¹H NMR (300 MHz, CDCl₃) δ 0.64-0.73 (m, 1H), 0.81-0.97 (m, 3H), 1.84-1.93 (m, 1H), 6.97 (d, *J* = 6.6 Hz, 1H), 7.06 (t, *J* = 9.3 Hz, 1H), 7.29-7.34 (m, 4H), 7.54-7.64 (m, 1H), 7.92-7.99 (m, 2H), 8.29 (d, *J* = 7.8 Hz, 1H); APCI-MS (*m/z*) 469 (M+H)⁺.

Example 24

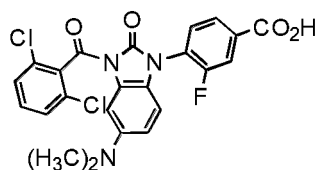
4-[5-Cyano-3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 10 (168 mg, 0.475 mmol) with 2,6-dichlorobenzoyl chloride (0.08 mL, 0.570 mmol) in the presence of sodium hydride (60% w/w, 28 mg, 0.712 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (202 mg, 0.384 mmol) by using TFA (2 mL) in DCM (6 mL) as per the process described in Example 1 to yield 112 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.25 (d, *J* = 8.4 Hz, 1H), 7.62 (br s, 2H), 7.84-7.89 (m, 3H), 7.96 (d, *J* = 8.4 Hz, 2H), 8.60 (br s, 1H), 13.66 (br s, 1H); ESI-MS (*m/z*) 467 (M-H)⁺.

Example 25

4-[3-(2,6-Dichlorobenzoyl)-5-(dimethylamino)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid

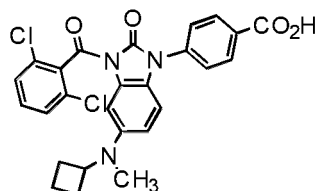


The title compound was prepared by the reaction of Intermediate 11 (100 mg, 0.269 mmol) and 2,6-dichlorobenzoyl chloride (0.05 mL, 0.323 mmol) in the presence of sodium hydride (60% w/w, 16 mg, 0.403 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (130 mg, 0.239 mmol) by using TFA (1 mL) in DCM (4 mL) as per the process described in Example 1 to yield 80 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 2.95 (br s, 6H), 6.72 (d, *J* = 8.7 Hz, 1H), 6.87 (d, *J* = 9.0 Hz,

1H), 7.50-7.60 (m, 3H), 7.37 (s, 1H), 7.79 (d, $J = 7.2$ Hz, 1H), 7.92 (d, $J = 8.7$ Hz, 2H), 13.58 (br s, 1H); APCI-MS (m/z) 488 (M+H)⁺.

Example 26

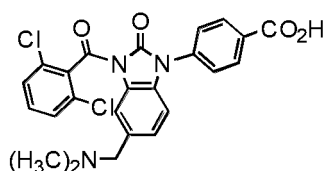
4-[5-(Cyclobutyl-methyl-amino)-3-(2,6-dichloro-benzoyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoic acid



The title compound was prepared by the reaction of Intermediate 12 (130 mg, 0.331 mmol) and 2,6-dichlorobenzoyl chloride (0.06 mL, 0.397 mmol) in the presence of sodium hydride (60% w/w, 19 mg, 0.496 mmol) in DMF (5 mL) followed by the hydrolysis of the ester derivative (143 mg, 0.253 mmol) by using TFA (1.5 mL) in DCM (4.5 mL) as per the process described in Example 1 to yield 70 mg of the product as off white solid. ¹H NMR (300 MHz, CDCl₃) δ 1.75-1.79 (m, 2H), 1.89-2.48 (m, 5H), 2.94 (br s, 3H), 4.00-4.01 (m, 1H), 6.74 (br s, 1H), 7.07 (br s, 1H), 7.38 (d, $J = 4.8$ Hz, 3H), 7.63 (d, $J = 8.7$ Hz, 2H), 8.04-8.10 (m, 1H), 8.23 (d, $J = 8.1$ Hz, 2H); APCI-MS (m/z) 510 (M+H)⁺.

Example 27

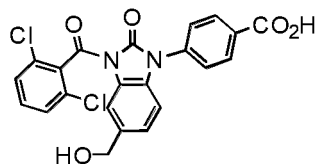
4-{3-(2,6-Dichlorobenzoyl)-5-[(dimethylamino)methyl]-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl}benzoic acid



The title compound was prepared by the reaction of Intermediate 13 (230 mg, 0.626 mmol) with 2,6-dichlorobenzoyl chloride (0.11 mL, 0.751 mmol) in the presence of sodium hydride (60% w/w, 38 mg, 0.939 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (80 mg, 0.148 mmol) by using TFA (1 mL) in DCM (4 mL) as per the process described in Example 1 to yield 60 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 2.76 (s, 6H), 4.43 (s, 2H), 7.30 (d, $J = 8.7$ Hz, 1H), 7.51 (d, $J = 8.4$ Hz, 1H), 7.56-7.64 (m, 2H), 7.68 (d, $J = 8.7$ Hz, 2H), 8.12 (d, $J = 9.0$ Hz, 2H), 8.54 (s, 1H), 9.95 (br s, 1H), 13.57 (br s, 1H); APCI-MS (m/z) 484 (M+H)⁺.

Example 28

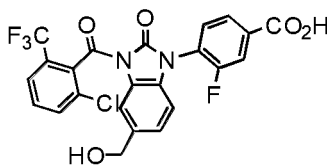
4-[3-(2,6-Dichlorobenzoyl)-5-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid



The title compound was prepared by the reaction of Intermediate 14 (150 mg, 0.353 mmol) with 2,6-dichlorobenzoyl chloride (0.06 mL, 0.424 mmol) in the presence of sodium hydride (60% w/w, 18 mg, 0.455 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (100 mg, 0.167 mmol) by using TFA (1 mL) in DCM (4 mL) as per the process described in Example 1 to yield 25 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 5.56 (s, 2H), 7.25 (br s, 1H), 7.52-7.60 (m, 4H), 7.69 (d, *J* = 7.8 Hz, 2H), 8.11 (d, *J* = 9.0 Hz, 2H), 8.45 (br s, 1H), 13.25 (br s, 1H); APCI-MS (*m/z*) 455 (M+H)⁺.

Example 29

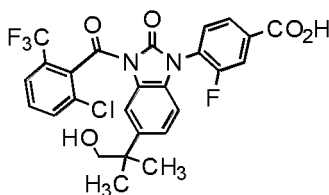
4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-5-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid



The title compound was prepared by the reaction of Intermediate 15 (420 mg, 0.949 mmol) with 2-chloro-6-(trifluoromethyl)benzoyl chloride (0.17 mL, 1.04 mmol) in the presence of sodium hydride (60% w/w, 56 mg, 1.421 mmol) in DMF (10 mL) followed by the hydrolysis and deprotection of the corresponding ester derivative (600 mg, 0.925 mmol) by using TFA (6 mL) in DCM (15 mL) as per the process described in Example 1 to yield 120 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 4.60 (s, 2H), 5.40 (br s, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.74-7.83 (m, 2H), 7.85-7.95 (m, 4H), 8.28 (s, 1H), 13.61 (br s, 1H); APCI-MS (*m/z*) 509 (M+H)⁺.

Example 30

4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(2-hydroxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid



Step 1: *tert*-Butyl 4-[3-(2-chloro-6-trifluoromethyl-benzoyl)-5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluorobenzoate

The title compound was prepared by the reaction of Intermediate 16 (321 mg, 0.774 mmol) with 2-chloro-6-(trifluoromethyl)benzoyl chloride (0.15 mL, 0.929 mmol) in the presence of sodium hydride (60% w/w, 46.5 mg, 1.160 mmol) in DMF (10 mL) as per the process described in step 1 of Example 1 to yield 573

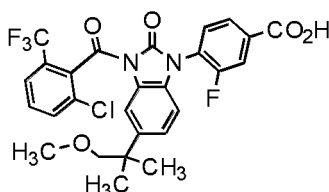
mg of the product as white solid. ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 1.32 (s, 6H), 1.56 (s, 9H), 3.24 (s, 3H), 3.42 (s, 2H), 6.97 (d, $J = 8.4$ Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.73-8.05 (m, 6H), 8.28 (s, 1H); APCI-MS (m/z) 622 ($\text{M}+\text{H}$) $^+$.

Step 2: 4-{3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(2-hydroxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl}-3-fluoro-benzoic acid

To a cooled (-78°C) solution of step 1 intermediate (72 mg, 0.116 mmol) in DCM (5 mL) was slowly added a solution of boron tribromide (1M in DCM, 1.2 mL) in DCM (5 mL). The reaction mixture was allowed to warm up to RT and it was stirred for 1 hour at RT. The reaction mixture was poured into crushed ice and extracted with ethyl acetate (2 x 10 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residue thus obtained was purified by silica gel column chromatography to yield 23 mg of the title product as yellow solid. ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 1.50 (s, 6H), 3.47 (s, 2H), 4.79 (br s, 1H), 6.97 (d, $J = 8.4$ Hz, 1H), 7.40 (d, $J = 8.4$ Hz, 1H), 7.74-7.79 (m, 2H), 7.89-7.96 (m, 4H), 8.31 (s, 1H); APCI-MS (m/z) 550 (M) $^+$.

Example 31

4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid

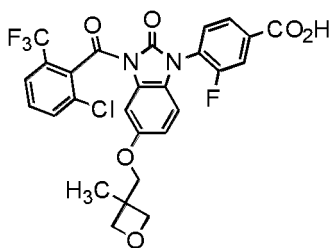


The title compound was prepared by the ester hydrolysis of *tert*-butyl 4-[3-(2-chloro-6-trifluoromethyl-benzoyl)-5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-

benzoimidazol-1-yl]-3-fluorobenzoate (80 mg, 0.129 mmol) (Step 1 product of Example 30) by using TFA (1.0 mL) in DCM (3 mL) as per the process described in step 2 of Example 1 to yield 65 mg of the product as off white solid. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 1.32 (s, 6H), 3.23 (s, 3H), 3.34 (s, 2H), 6.98 (d, $J = 8.1$ Hz, 1H), 7.42 (d, $J = 7.8$ Hz, 1H), 7.76-7.79 (m, 2H), 7.83-7.95 (m, 4H), 8.28 (s, 1H), 13.60 (br s, 1H); APCI-MS (m/z) 562 ($\text{M}+\text{H}$) $^+$.

Example 32

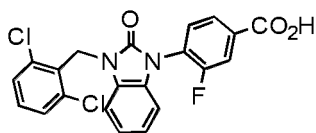
4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(3-methyl-oxetan-3-ylmethoxy)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid



The title compound was prepared by the reaction of Intermediate 17 (203 mg, 0.474 mmol) and 2-chloro-6-(trifluoromethyl)benzoyl chloride (161 mg, 0.663 mmol) in the presence of sodium hydride (60% w/w, 25 mg, 0.616 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (211 mg, 0.332 mmol) by using TFA (2.0 mL) in DCM (5 mL) as per the process described in step 1 and 2 of Example 1 respectively to yield 63 mg of the product as off white solid. ^1H NMR (300 MHz, CDCl_3) δ 1.48 (s, 3H), 4.13 (br s, 5H), 4.53 (d, $J = 5.7$ Hz, 2H), 4.72 (d, $J = 5.7$ Hz, 2H), 6.82 (d, $J = 9.0$ Hz, 1H), 6.92 (d, $J = 9.0$ Hz, 1H), 7.50-7.68 (m, 4H), 7.99 (t, $J = 10.2$ Hz, 2H), 8.11 (s, 1H); APCI-MS (m/z) 579 ($\text{M}+\text{H}$) $^+$.

Example 33

4-[3-(2,6-Dichlorobenzyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid

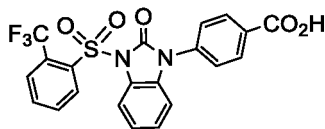


The title compound was prepared by the reaction of Intermediate 4 (100 mg, 0.304 mmol) with 2-(bromomethyl)-1,3-dichlorobenzene (102 mg, 0.426 mmol) in the presence of sodium hydride (60% w/w, 16 mg, 0.3959 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (130 mg, 0.205 mmol) by using TFA (1.5 mL) in DCM (5 mL) as per the process described in Example 1 to yield 65 mg of the product as white solid. ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 5.38 (br s, 2H), 6.88 (br s, 2H), 7.00-7.06 (m, 2H), 7.42 (t, $J =$

7.8 Hz, 1H), 7.55 (d, $J = 7.8$ Hz, 2H), 7.76 (t, $J = 7.8$ Hz, 1H), 7.97 (br s, 2H), 13.51 (br s, 1H); APCI-MS (m/z) 431 ($M+H$)⁺.

Example 34

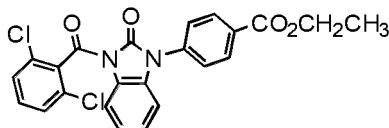
4-(2-Oxo-3-{[2-(trifluoromethyl)phenyl]sulfonyl}-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoic acid



The title compound was prepared by the reaction of Intermediate 1 (150 mg, 0.483 mmol) with 2-(trifluoromethyl)benzenesulfonyl chloride (0.12 mL, 0.725 mmol) in the presence of sodium hydride (60% w/w, 27 mg, 0.6766 mmol) in DMF (5 mL) followed by the hydrolysis of the corresponding ester derivative (170 mg, 0.327 mmol) by using TFA (3 mL) in DCM (3 mL) as per the process described in Example 1 to yield 95 mg of the product as off white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.14 (d, $J = 7.5$ Hz, 1H), 7.27-7.31 (m, 2H), 7.65 (d, $J = 8.1$ Hz, 2H), 7.82 (d, $J = 7.2$ Hz, 1H), 8.04-8.11 (m, 5H), 8.50 (br s, 1H), 13.14 (br s, 1H); APCI-MS (m/z) 463 ($M+H$)⁺.

Example 35

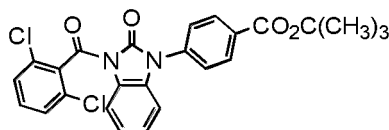
Ethyl 4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoate



The title compound was prepared by the reaction of Intermediate 18 (90 mg, 0.318 mmol) with 2,6-dichlorobenzoyl chloride (0.06 mL, 0.446 mmol) in the presence of sodium hydride (60% w/w, 17 mg, 0.414 mmol) in DMF (5 mL) as per the process described in Step 1 of Example 1 to yield 22 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.40 (t, $J = 6.9$ Hz, 3H), 4.40 (q, $J = 6.9$ Hz, 2H), 7.13 (br s, 1H), 7.31-7.38 (m, 5H), 7.59 (d, $J = 8.4$ Hz, 2H), 8.18 (d, $J = 8.4$ Hz, 2H), 8.44 (br s, 1H); APCI-MS (m/z) 455 ($M+H$)⁺.

Example 36

tert-Butyl 4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoate

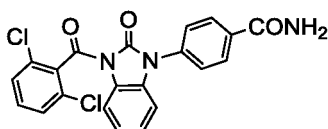


The title compound was prepared by the reaction of Intermediate 1 (80 mg, 0.251 mmol) with 2,6-dichlorobenzoyl chloride (0.05 mL, 0.309 mmol) in the presence of sodium hydride (60%

w/w, 14 mg, 0.335 mmol) in DMF (5 mL) as per the process described in step 1 of Example 1 to yield 55 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.55 (br s, 9H), 7.18 (br s, 1H), 7.36 (br s, 2H), 7.54-7.61 (m, 3H), 7.68 (d, *J* = 7.8 Hz, 2H), 8.06 (d, *J* = 8.1 Hz, 2H), 8.28 (br s, 1H); APCI-MS (*m/z*) 483 (M+H)⁺.

5 Example 37

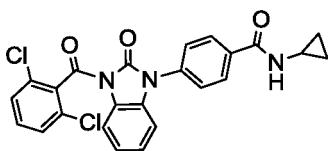
4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzamide



To a well stirred solution of Example 1 (80 mg, 0.187 mmol) in DMSO (3 mL) were added BOP (124 mg, 0.281 mmol) and ammonium chloride (100 mg, 1.877 mmol) followed by
 10 DIPEA (0.01 mL, 0.563 mmol) and the reaction mixture was stirred at RT overnight. The reaction mixture was diluted with water (10 mL) and the precipitate thus obtained was filtered. The obtained product was purified by silica gel column chromatography to yield 20 mg of the title product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.15 (br s, 1H), 7.36 (br s, 2H), 7.50-7.56 (m, 2H), 7.59-7.65 (m, 2H), 8.05 (d, *J* = 8.4 Hz, 2H), 8.12 (br s, 1H),
 15 8.28 (br s, 1H); APCI-MS (*m/z*) 426 (M+H)⁺.

Example 38

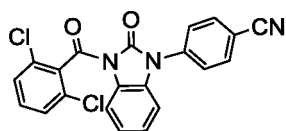
N-Cyclopropyl-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzamide



20 To a well stirred and cooled (0 °C) solution of Example 1 (100 mg, 0.234 mmol) in DMF (5 mL) were added EDCI (69 mg, 0.351 mmol) and DMAP (9 mg, 0.070 mmol) and the reaction mixture was stirred for 10 minutes. Cyclopropylamine (100 mL, 0.234 mmol) was added to the reaction mixture and it was stirred at RT overnight. The reaction mixture was diluted with water (10 mL) and the precipitate obtained was filtered and purified by silica gel column
 25 chromatography to yield 21 mg of the title product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 0.58 (br s, 2H), 0.71 (d, *J* = 5.7 Hz, 2H), 2.85 (br s, 1H), 7.12 (br s, 1H), 7.36 (br s, 2H), 7.51-7.61 (m, 5H), 7.99 (d, *J* = 8.4 Hz, 2H), 8.28 (br s, 1H), 8.60 (br s, 1H); APCI-MS (*m/z*) 466 (M+H)⁺.

Example 39

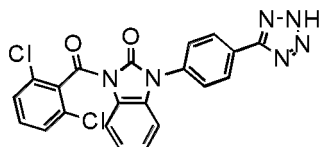
30 4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzonitrile



The title compound was prepared by the reaction of Intermediate 19 (230 mg, 0.978 mmol) with 2,6-dichlorobenzoyl chloride (0.16 mL, 1.173 mmol) in the presence of sodium hydride (60% w/w, 51 mg, 1.270 mmol) in DMF (5 mL) as per the process described in step 1 of Example 1 to yield 300 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.14 (d, *J* = 6.3 Hz, 1H), 7.37 (br s, 5H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.7 Hz, 2H), 8.47 (d, *J* = 8.1 Hz, 1H); APCI-MS (*m/z*) 408 (M)⁺.

Example 40

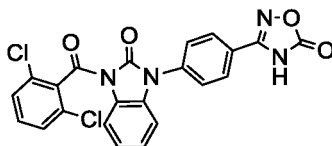
1-[4-(2H-Tetrazol-5-yl)phenyl]-3-(2,6-dichlorobenzoyl)-1H-benzo[d]imidazol-2(3H)-one



To a well stirred solution of Example 39 (168 mg, 0.411 mmol) in DMF (5 mL) were added sodium azide (34 mg, 0.534 mmol) and ammonium chloride (28 mg, 0.534 mmol) and the reaction mixture was heated at 80 °C overnight. The reaction mixture was diluted with water (20 mL) and extracted with ethyl acetate (2 x 20 mL). The combined organic layers were washed with water (3 x 25 mL), brine (25 mL) and dried over anhydrous Na₂SO₄. The solvent was distilled off under reduced pressure. The residue obtained was purified by column chromatography to afford 60 mg of the title product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.22 (br s, 1H), 7.37 (br s, 2H), 7.57-7.61 (m, 3H), 7.79 (d, *J* = 8.4 Hz, 2H), 8.22 (d, *J* = 7.8 Hz, 2H), 8.29 (br s, 1H); APCI-MS (*m/z*) 451 (M)⁺.

Example 41

3-{4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1H-benzo[d]imidazol-1-yl]phenyl}-1,2,4-oxadiazol-5(4H)-one



Step 1: 4-{3-[(2,6-Dichlorophenyl)carbonyl]-2-oxo-2,3-dihydro-1H-benzimidazol-1-yl}-*N*-hydroxy benzenecarboximidamide:

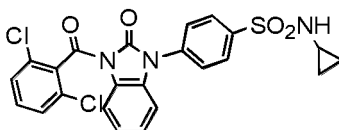
To a well stirred solution of Example 39 (100 mg, 0.244 mmol) in dry DMSO (3 mL) was added hydroxylamine hydrochloride (63 mg, 0.906 mmol) followed by DIPEA (0.15 mL, 0.906 mmol) and the reaction mixture was heated at 80 °C overnight. The reaction mixture

was diluted with water and the precipitate thus obtained was filtered and dried to obtain 65 mg of the title product as white solid. APCI-MS (m/z) 441 (M)⁺.

Step 2: 3-{4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]phenyl}-1,2,4-oxadiazol-5(4*H*)-one: To the well stirred solution of Step 1 intermediate (65 mg, 0.147 mmol) in dry DMF (2 mL) was added CDI (36 mg, 0.220 mmol) and the reaction mixture was heated at 80 °C overnight. The reaction mixture was diluted with water (25 mL) and product was extracted in ethyl acetate (2 x 100 mL). The combined organic layers were washed with water (2 x 50 mL), brine (50 mL) and dried over anhydrous Na₂SO₄. The solvent was recovered under reduced pressure. The residue obtained was purified by column chromatography to afford 30 mg of the title product as off-white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.14 (br s, 1H), 7.36 (br s, 5H), 7.70 (br s, 2H), 7.99 (br s, 2H), 8.47 (d, *J* = 6.3 Hz, 1H), 11.67 (br s, 1H); APCI-MS (m/z) 467 (M)⁺.

Example 42

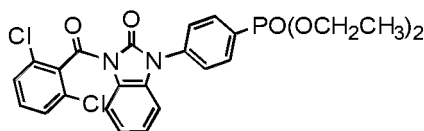
N-Cyclopropyl-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzenesulfonamide



The title compound was prepared by the reaction of Intermediate 20 (80 mg, 0.242 mmol) with 2,6-dichlorobenzoyl chloride (0.05 mL, 0.364 mmol) in the presence of sodium hydride (60% w/w, 20 mg, 0.532 mmol) in DMF (5 mL) as per the process described in step 1 of Example 1 to yield 10 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 0.81 (br s, 4H), 2.95 (br s, 1H), 7.22 (br s, 1H), 7.38 (br s, 2H), 7.56-7.62 (m, 5H), 7.88 (d, *J* = 8.4 Hz, 2H), 8.22 (br s, 1H), 8.30 (br s, 1H); APCI-MS (m/z) 503 ($M+H$)⁺.

Example 43

Diethyl {4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]phenyl}phosphonate

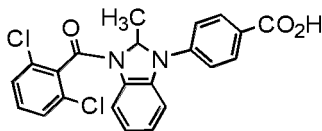


The title compound was prepared by the reaction of Intermediate 21 (300 mg, 0.866 mmol) with 2,6-dichlorobenzoyl chloride (0.15 mL, 1.039 mmol) in the presence of sodium hydride (60% w/w, 52 mg, 1.299 mmol) in DMF (10 mL) as per the process described in Step 1 of Example 1 to yield 370 mg of the product as white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ

1.24 (t, $J = 6.9$ Hz, 6H), 4.01-4.08 (m, 4H), 7.22 (br s, 1H), 7.36 (br s, 2H), 7.54-7.61 (m, 3H), 7.74 (m, 2H), 7.84-7.93 (m, 2H), 8.28 (br s, 1H); APCI-MS (m/z) 519 ($M+H$)⁺.

Example 44

4-[3-(2,6-Dichlorobenzoyl)-2-methyl-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl] benzoic acid



Step 1: Ethyl 4-(3-(2,6-dichlorobenzoyl)-2-methyl-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl)benzoate:

To the stirred solution of Intermediate 22 (150 mg, 0.349 mmol) in DCM (10 mL) was added acetaldehyde dimethyl acetal (157 mg, 1.74 mmol) followed by catalytic amount of PTSA (6.6 mg, 0.035 mmol) and the reaction mixture was stirred at RT for 15 hours. The solvent was recovered under reduced pressure and the residue thus obtained was purified by silica gel column chromatography to yield 100 mg of the title product as colourless oil. ¹H NMR (300 MHz, CDCl₃) δ 1.44 (t, $J = 6.9$ Hz, 3H), 1.73 (d, $J = 5.4$ Hz, 3H), 4.35 (q, $J = 7.2$ Hz, 2H), 5.79 (d, $J = 8.4$ Hz, 1H), 6.55-6.60 (m, 2H), 7.01 (br s, 1H), 7.15 (br s, 1H), 7.29-7.40 (m, 3H), 7.47 (br s, 1H), 8.04 (d, $J = 8.1$ Hz, 2H).

Step 2: 4-[3-(2,6-Dichlorobenzoyl)-2-methyl-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl] benzoic acid:

To the well stirred solution of Step 1 intermediate (100 mg, 0.219 mmol) in a mixture of THF (2 mL), methanol (2 mL) and water (1 mL) was added lithium hydroxide (27 mg, 0.658 mmol) and the reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with water (20 mL) and acidified by using 1*N* HCl. The product was extracted with ethyl acetate (2 x 20 mL) and the layers were separated. The combined organic layers were washed with water (2 x 20 mL), brine (20 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure. The residue thus obtained was purified by column chromatography to afford 60 mg of the title product as off-white solid. ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.61 (d, $J = 5.4$ Hz, 3H), 5.67 (d, $J = 7.8$ Hz, 1H), 6.51 (br s, 1H), 6.67 (t, $J = 7.8$ Hz, 1H), 7.05 (t, $J = 7.8$ Hz, 1H), 7.32-7.39 (m, 2H), 7.47 (d, $J = 8.1$ Hz, 2H), 7.63 (br s, 1H), 7.88 (d, $J = 8.7$ Hz, 1H), 7.94 (d, $J = 8.4$ Hz, 2H), 12.71 (br s, 1H); APCI-MS (m/z) 427 ($M+H$)⁺.

Pharmacological Activity

Biological Assay

The illustrative examples of the present patent application were screened for ROR gamma modulator activity using the TR-FRET assay by Lantha Screen as described in *JBC* **2011**, 286, 26: 22707-10; *Drug Metabolism and Disposition* **2009**, 37, 10: 2069-78.

TR-FRET assay for ROR gamma:

The assay is based on the principle that binding of the agonist to the ROR gamma causes a conformational change around helix 12 in the ligand binding domain, resulting in higher affinity for the co-activator peptide. ROR gamma being constitutively active, the Fluorescein-D22 co-activator peptide used in the assay is recruited in the absence of a ligand. Binding of the co-activator peptide, causes an increase in the TR-FRET signal while binding of an antagonist decreases the recruitment of the co-activator peptide, causing a decrease in the TR-FRET signal compared to control with no compound. The assay was performed using a two-step procedure, pre-incubation step with the compound followed by the detection step on addition of the anti-GST tagged terbium (Tb) and fluorescein tagged fluorophores as the acceptor.

Test compounds or reference compounds such as T0901317 (Calbiochem) were dissolved in dimethylsulfoxide (DMSO) to prepare 10.0 mM stock solution and diluted suitably to get the desired concentration. Final concentration of DMSO in the reaction was 4% (v/v). Assay mixture was prepared by mixing 10nM of the GST-tagged ROR gamma ligand binding domain (LBD) in the assay buffer containing 25 mM HEPES, 100 mM NaCl, 5mM DTT and 0.01% BSA with or without the desired concentration of the compound. The reaction was incubated at 22°C for 1hr. The pre-incubation step was terminated by addition of the detection mixture containing 300nM Fluorescein-D22 co-activator peptide and 10nM lantha screen Tb-anti GST antibody into the reaction mixture. After shaking for 5 minutes the reaction was further incubated for 2 hr at room temperature and read the next day at 4°C on an Infinite F500 reader as per the kit instructions (Invitrogen). The inhibition of test compound is calculated based on the TR-FRET ratio of 520/495. The activity was calculated as a percent of control reaction. IC₅₀ values were calculated from dose response curve by nonlinear regression analysis using GraphPad Prism software.

The compounds prepared were tested using the above assay procedure and the results obtained are given in Table 1. Percentage inhibition at concentrations of 1.0 µM and 10.0 µM are given in the table along with IC₅₀ (nM) details for selected examples. The compounds

prepared were tested using the above assay procedure and were found to have IC₅₀ less than 500nM, preferably less than 100nM or more preferably less than 50nM.

The IC₅₀ (nM) values of the compounds are set forth in Table 1 wherein “A” refers to an IC₅₀ value of less than 50 nM, “B” refers to IC₅₀ value in range of 50.01 to 100.0 nM and “C” refers to IC₅₀ values more than 100 nM.

Table 1: *In-vitro* screening results of compounds of present invention

Sr No.	Example	% inhibition at		IC ₅₀ Value (nM)
		1 μ M	10 μ M	
1.	Example 1	93.39	97.7	A
2.	Example 2	91.13	97.79	A
3.	Example 3	4.85	62.19	-
4.	Example 4	86.37	93.44	C
5.	Example 5	96.13	98.11	A
6.	Example 6	93.7	96.41	A
7.	Example 7	95.93	99.23	A
8.	Example 8	87.41	96.63	A
9.	Example 9	99.3	100.0	A
10.	Example 10	100.00	100.00	A
11.	Example 11	99.26	-	A
12.	Example 12	78.78	93.78	C
13.	Example 13	98.88	99.56	A
14.	Example 14	76.38	94.45	C
15.	Example 15	94.64	94.80	A
16.	Example 16	48.56	80.75	-
17.	Example 17	68.77	93.48	-
18.	Example 18	84.39	96.37	A
19.	Example 19	81.2	95.61	C
20.	Example 20	97.25	98.52	A
21.	Example 21	98.36	100	A
22.	Example 22	98.31	99.39	A
23.	Example 23	96.59	96.99	A
24.	Example 24	40.88	80.30	-

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10

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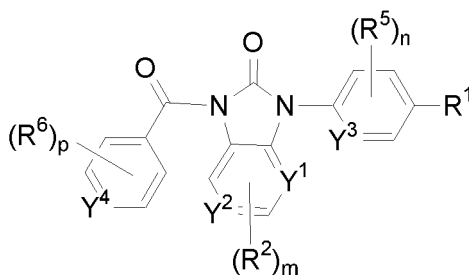
20

25.	Example 25	59.36	92.25	-
26.	Example 26	51.54	84.10	-
27.	Example 27	17.03	16.01	-
28.	Example 28	87.04	92.52	A
29.	Example 29	97.85	100.0	A
30.	Example 30	0	1.8	-
31.	Example 31	36.01	38.47	-
32.	Example 32	8.4	32.4	-
33.	Example 33	19.57	71.88	-
34.	Example 34	74.22	91.6	C
35.	Example 35	0.00	8.52	-
36.	Example 36	11.02	10.42	-
37.	Example 37	0.57	12.64	-
38.	Example 38	0.00	8.93	-
39.	Example 39	0.08	6.02	-
40.	Example 40	12.28	72.73	-
41.	Example 41	3.60	52.19	-
42.	Example 42	18.89	14.9	-
43.	Example 43	0.0	17.70	-
44.	Example 44	69.03	91.48	C

(-): Not determined

WHAT IS CLAIMED IS:

1. A compound of formula (Ia)



(Ia)

or a pharmaceutically acceptable salt thereof,

wherein,

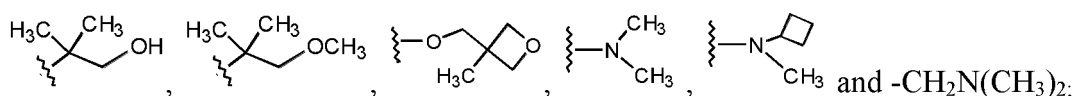
Y^1 and Y^2 are each independently selected from CH and N;

Y^3 is selected from CH and N;

Y^4 is selected from CH and N;

R^1 is selected from cyano, $-C(O)OR^9$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2H-tetrazol-5-yl and 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;

each occurrence of R^2 is independently selected from cyano, halogen, $-CH_2OH$,



each occurrence of R^5 is independently selected from cyano, halogen, hydroxyl, C_{1-8} alkyl and halo C_{1-8} alkyl;

each occurrence of R^6 is independently selected from halogen, C_{1-8} alkyl, C_{1-8} alkoxy, halo C_{1-8} alkyl and C_{3-6} cycloalkyl;

R^9 is selected from hydrogen and C_{1-8} alkyl;

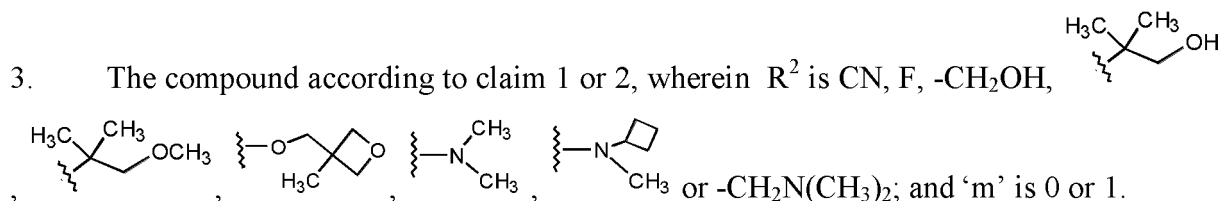
'm' is an integer ranging from 0 to 2, both inclusive;

'n' is an integer ranging from 0 to 3, both inclusive; and

'p' is an integer ranging from 1 to 4, both inclusive.

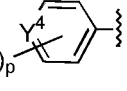
2. The compound according to claim 1, wherein R^1 is cyano, $-C(O)OH$, $-C(O)OCH_3$, $-C(O)OC_2H_5$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2H-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl.

3. The compound according to claim 1 or 2, wherein R^2 is CN, F, $-CH_2OH$,



4. The compound according to any one of claims 1 to 3, wherein R^5 is Cl or F; and 'n' is 0 or 1.

5. The compound according to any one of claims 1 to 4, wherein R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl; and 'p' is 1 or 2.

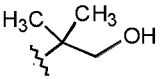
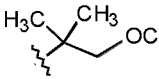
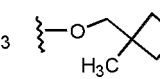
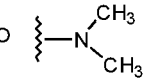
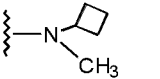
6. The compound according to any one of claims 1 to 4, wherein $(R^6)_p$  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl.

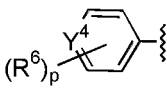
7. The compound according to claim 1, wherein

Y^1 and Y^2 are each independently selected from CH and N;

Y^3 is selected from CH and N;

R^1 is cyano, $-C(O)OH$, $-C(O)OCH_3$, $-C(O)OC_2H_5$, $-C(O)OC(CH_3)_3$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2*H*-tetrazol-5-yl or 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;

R^2 is CN, F, $-CH_2OH$, , , , , , or $-CH_2N(CH_3)_2$;

$(R^6)_p$  is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl;

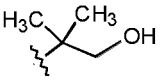
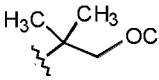
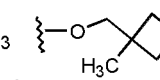
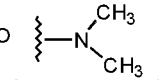
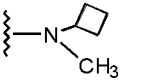
R^5 is F or Cl;

'm' is 0 or 1; and

'n' is 0 or 1.

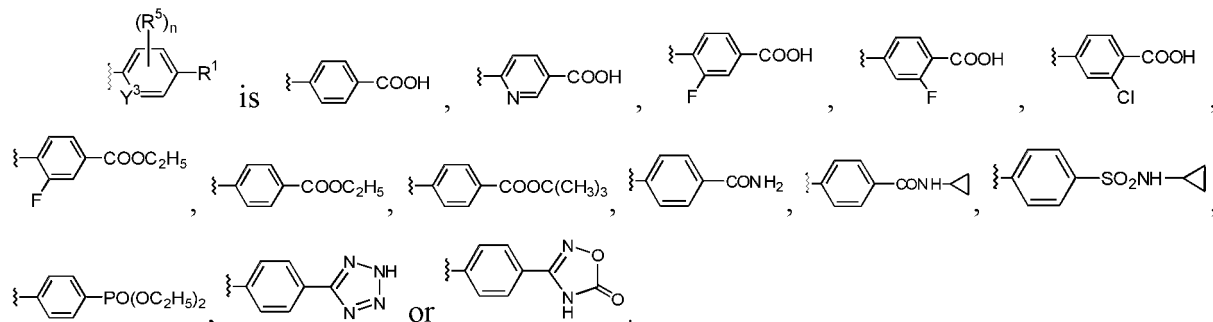
8. The compound according to claim 1, wherein

Y^1 and Y^2 are each independently selected from CH and N;

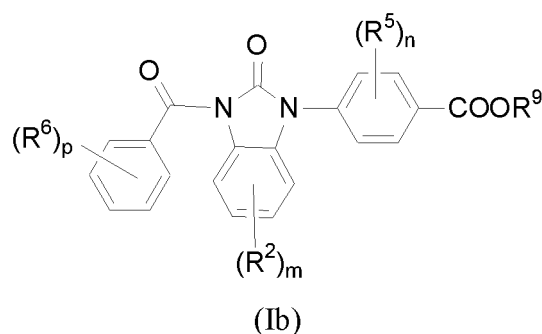
R^2 is CN, F, $-CH_2OH$, , , , , , or $-CH_2N(CH_3)_2$;

'm' is 0 or 1;

$(R^6)_p$ is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, 2-chloro-6-cyclopropylphenyl or 3,5-dichloropyridin-4-yl; and



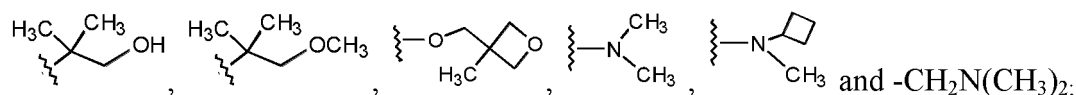
9. A compound of formula (Ib)



or a pharmaceutically acceptable salt thereof,

wherein,

each occurrence of R^2 is independently selected from cyano, F, $-CH_2OH$,



each occurrence of R^5 is independently selected from cyano, halogen, hydroxyl, C_{1-8} alkyl and halo C_{1-8} alkyl;

each occurrence of R^6 is independently selected from halogen, C_{1-8} alkyl, C_{1-8} alkoxy, halo C_{1-8} alkyl and C_{3-6} cycloalkyl;

R^9 is selected from hydrogen and C_{1-8} alkyl;

'm' is an integer ranging from 0 to 2, both inclusive;

'n' is an integer ranging from 0 to 3, both inclusive; and

'p' is an integer ranging from 1 to 4, both inclusive.

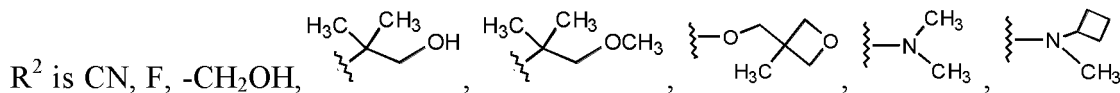
10. The compound according to claim 9, wherein R^5 is F or Cl; and 'n' is 0 or 1.

11. The compound according to claim 9 or 10, wherein 'm' is 0 or 1.

12. The compound according to any one of claims 9 to 11, wherein R^6 is independently selected from F, Cl, Br, OCH_3 , CHF_2 , CF_3 and cyclopropyl; and 'p' is 1 or 2.

13. The compound according to any one of claims 9 to 12, wherein R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl.

14. The compound according to claim 9, wherein



or $-CH_2N(CH_3)_2$;

R^5 is F or Cl;

R^6 is F, Cl, Br, OCH_3 , CHF_2 , CF_3 or cyclopropyl;

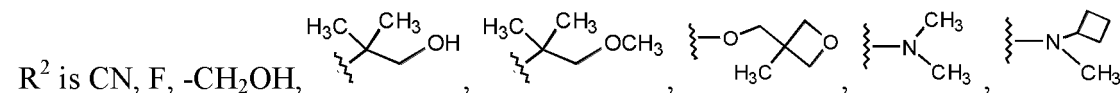
R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl;

'm' is 0 or 1;

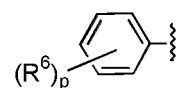
'n' is 0 or 1; and

'p' is 1 or 2.

15. The compound according to claim 9, wherein



or $-CH_2N(CH_3)_2$;



is 2,6-dichlorophenyl, 2-bromo-6-chlorophenyl, 2-chloro-6-methoxyphenyl, 2-fluoro-6-methoxyphenyl, 2-chloro-6-(difluoromethyl)phenyl, 2-chloro-6-(trifluoromethyl)phenyl, or 2-chloro-6-cyclopropylphenyl;

R^5 is F or Cl;

R^9 is hydrogen, methyl, ethyl, propyl or *tert*-butyl;

'm' is 0 or 1; and

'n' is 0 or 1.

16. A compound selected from

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid;

4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo [d]imidazol-1-yl}benzoic acid;

2-Chloro-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-2-fluorobenzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[3-(2-Bromo-6-chlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[3-(2-Chloro-6-methoxybenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

3-Fluoro-4-[3-(2-fluoro-6-methoxybenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid;

4-{3-[2-Chloro-6-(difluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid;

4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid;

Ethyl 4-(3-{[2-chloro-6-(trifluoromethyl)phenyl]carbonyl}-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-3-fluorobenzoate;

4-[3-(2-Chloro-6-cyclopropylbenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-6-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-{3-[2-Chloro-6-(difluoromethyl)benzoyl]-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid;

4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid;

4-[3-(2-Chloro-6-cyclopropylbenzoyl)-7-fluoro-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[5-Cyano-3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-5-(dimethylamino)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]-3-fluorobenzoic acid;

4-[5-(Cyclobutyl-methyl-amino)-3-(2,6-dichloro-benzoyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-benzoic acid;

4-{3-(2,6-Dichlorobenzoyl)-5-[(dimethylamino)methyl]-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}benzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-5-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoic acid;

4-{3-[2-Chloro-6-(trifluoromethyl)benzoyl]-5-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl}-3-fluorobenzoic acid;

4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(2-hydroxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid;

4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(2-methoxy-1,1-dimethyl-ethyl)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid;

4-[3-(2-Chloro-6-trifluoromethyl-benzoyl)-5-(3-methyl-oxetan-3-ylmethoxy)-2-oxo-2,3-dihydro-benzoimidazol-1-yl]-3-fluoro-benzoic acid;

Ethyl 4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoate;

tert-Butyl 4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzoate;

[(3,5-Dichloropyridin-4-yl)carbonyl]-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl}-3-fluorobenzoic acid;

6-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl] nicotinic acid;

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-imidazo[4,5-*c*]pyridin-1-yl]-3-fluorobenzoic acid;

4-[1-(2,6-Dichlorobenzoyl)-2-oxo-1*H*-imidazo[4,5-*b*]pyridin-3(2*H*)-yl]-3-fluorobenzoic acid;

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzamide;

N-Cyclopropyl-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzamide;

4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzonitrile;

1-[4-(2*H*-Tetrazol-5-yl)phenyl]-3-(2,6-dichlorobenzoyl)-1*H*-benzo[d]imidazol-2(3*H*)-one;

3-{4-[3-(2,6-Dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]phenyl}-1,2,4-oxadiazol-5(4*H*)-one;

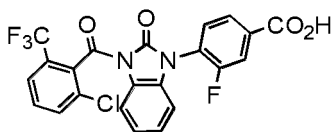
N-Cyclopropyl-4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]benzenesulfonamide;

Diethyl {4-[3-(2,6-dichlorobenzoyl)-2-oxo-2,3-dihydro-1*H*-benzo[d]imidazol-1-yl]phenyl}phosphonate;

and pharmaceutically acceptable salts thereof.

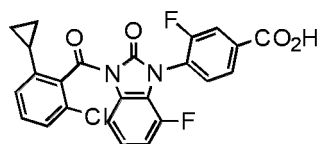
17. The compound sodium 4-(3-{[2-chloro-6-(trifluoromethyl)phenyl]carbonyl}-2-oxo-2,3-dihydro-1*H*-benzimidazol-1-yl)-3-fluorobenzoate.

18. A compound of formula



or a pharmaceutically acceptable salt thereof.

19. A compound of formula



or a pharmaceutically acceptable salt thereof.

20. A pharmaceutical composition comprising a compound according to any one of claims 1 to 19 and a pharmaceutically acceptable excipient.

21. The pharmaceutical composition according to claim 20, wherein the pharmaceutically acceptable excipient is a carrier or diluent.

22. A method of treating a ROR γ t mediated disease, disorder or syndrome in a subject comprising administering an effective amount of a compound according to any one of claims 1 to 19.

23. The method according to claim 22, wherein the disease is an inflammatory or autoimmune disease.

24. The method according to claim 23, wherein said inflammatory or autoimmune disease is selected from the group consisting of rheumatoid arthritis, psoriasis, chronic obstructive pulmonary disease (COPD), asthma, multiple sclerosis, colitis, ulcerative colitis and inflammatory bowel disease.

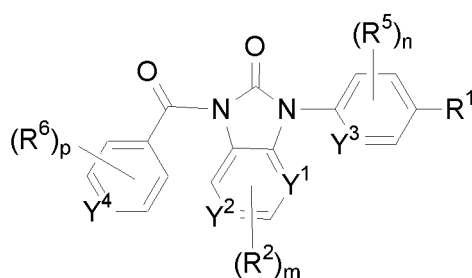
25. The method according to claim 22, wherein the disease, disorder, syndrome or condition is pain, chronic pain, acute pain, inflammatory pain, arthritic pain, neuropathic pain, post-operative pain, surgical pain, visceral pain, dental pain, premenstrual pain, central pain, cancer pain, pain due to burns, migraine or cluster headaches, nerve injury, neuritis,

neuralgias, poisoning, ischemic injury, interstitial cystitis, viral, parasitic or bacterial infection, post-traumatic injury, or pain associated with irritable bowel syndrome.

26. The method according to claim 22, wherein the disease, disorder, syndrome or condition is chronic obstructive pulmonary disease (COPD), asthma, bronchospasm or cough.

27. A method of treatment of disease, disorder, syndrome or condition selected from the group consisting of chronic obstructive pulmonary disease (COPD), asthma, cough, pain, inflammatory pain, chronic pain, acute pain, arthritis, osteoarthritis, multiple sclerosis, rheumatoid arthritis, colitis, ulcerative colitis and inflammatory bowel disease comprising administering a compound according to any one of claims 1 to 19.

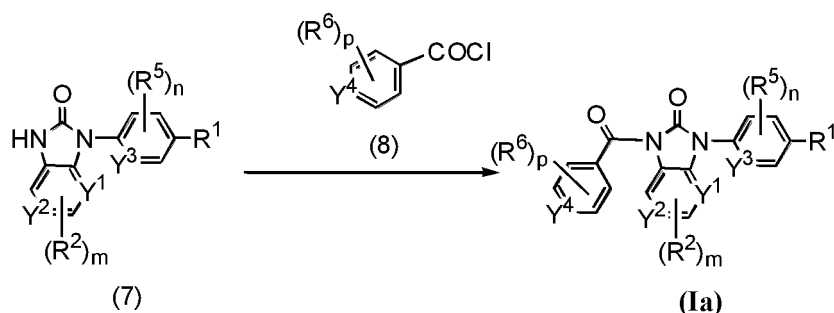
28. A process for preparing compound of formula (Ia)



(Ia)

or a pharmaceutically acceptable salt thereof, which comprises:

reacting a compound of formula (7) with a compound of formula (8); and optionally converting the compound of formula (Ia) to a pharmaceutically acceptable salt thereof:



wherein,

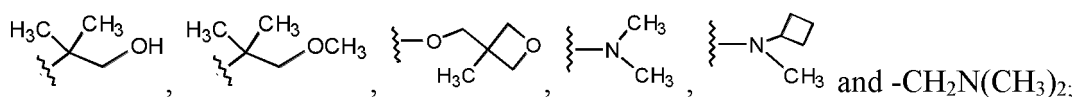
Y^1 and Y^2 are each independently selected from CH and N;

Y^3 is selected from CH and N;

Y^4 is selected from CH and N;

R^1 is selected from cyano, $-C(O)OR^9$, $-C(O)NH_2$, $-C(O)NH$ -cyclopropyl, $-S(O)_2NH$ -cyclopropyl, $-P(O)(OC_2H_5)_2$, 2H-tetrazol-5-yl and 5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl;

each occurrence of R² is independently selected from cyano, halogen, -CH₂OH,



each occurrence of R⁵ is independently selected from cyano, halogen, hydroxyl, C₁₋₈alkyl and haloC₁₋₈alkyl;

each occurrence of R⁶ is independently selected from halogen, C₁₋₈alkyl, C₁₋₈alkoxy, haloC₁₋₈alkyl and C₃₋₆cycloalkyl;

R⁹ is selected from hydrogen and C₁₋₈alkyl;

'm' is an integer ranging from 0 to 2, both inclusive;

'n' is an integer ranging from 0 to 3, both inclusive; and

'p' is an integer ranging from 1 to 4, both inclusive.

29. The process according to claim 28, wherein the compound of formula (7) is reacted with a compound of formula (8) in the presence of base.
30. The process according to claim 29, wherein the base is sodium hydride.
31. The process according to any one of claims 28 to 30, wherein the compound of formula (7) is reacted with a compound of formula (8) in a suitable solvent.
32. The process according to claim 31, wherein the solvent is DMF.
33. The process according to claim 28, wherein the compound of formula (7) is reacted with a compound of formula (8) in the presence of sodium hydride in DMF.