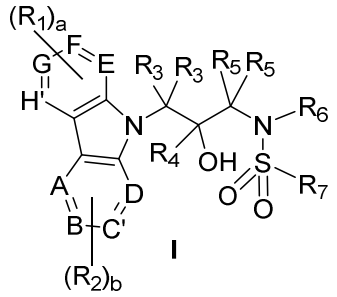
Claims

1. A compound of formula I



I

or a pharmaceutically acceptable salt or hydrate thereof, wherein

each of A, B, C', D, E, F, G, and H' is carbon;

each of R_1 and R_2 is independently selected from hydrogen or halogen;

each of R_3 and R_5 is independently hydrogen or $(C_1$-$C_6)$alkyl;

wherein each of the R_3 groups are optionally linked to each other as a 4-12 membered mono- or bicyclic ring;

wherein each of the R_5 groups are optionally linked to each other as a 4-12 membered mono- or bicyclic ring;

R_4 is hydrogen and $(C_1$-$C_6)$alkyl;

R_6 is hydrogen, $-CF_3$, $-CHF_2$, $-CH_2F$, $(C_1$-$C_6)$alkyl, $-(CR_8R_9)_d$(3-10)-membered cycloalkyl, $-(CR_8R_9)_e(C_6$-$C_{10})$aryl, $-(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_f(C{=}O)(CR_8R_9)_e(C_6$-$C_{10})$aryl, $-(CR_8R_9)_f(C{=}O)(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_eO(CR_8R_9)_f(C_6$-$C_{10})$aryl, $-(CR_8R_9)_eO(CR_8R_9)_f$(4-10)-membered heterocyclyl, $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e(C_6$-$C_{10})$aryl, and $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e$(4-10)-membered heterocyclyl;

R_5 and R_6 are optionally linked to each other as a 4-12 membered mono- or bicyclic ring;

R_7 is $-CF_3$, $-CHF_2$, $-CH_2F$, $(C_1\text{-}C_6)$alkyl, $-(CR_8R_9)_d$(3-10)-membered cycloalkyl, $-(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_f(C{=}O)(CR_8R_9)_e(C_6\text{-}C_{10})$aryl, $-(CR_8R_9)_f(C{=}O)(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_eO(CR_8R_9)_f(C_6\text{-}C_{10})$aryl, $-(CR_8R_9)_eO(CR_8R_9)_f$(4-10)-membered heterocyclyl, $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e(C_6\text{-}C_{10})$aryl, and $–(CR_8R_9)_fS(O)_d(CR_8R_9)_e$(4-10)-membered heterocyclyl;

R_6 and R_7 can be linked to each other as a 4-12 membered mono- or bicyclic ring, wherein any of the 5, 6, or 10 membered mono- or bicyclic ring is optionally substituted with one chlorine, methoxy, ethyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or one or two fluorine or methyl;

each of R_8, R_9 and R_{10} are independently selected from hydrogen, $(C_1\text{-}C_6)$alkyl, $-(CR_{11}R_{12})_e$(3-10)-membered cycloalkyl, $-(CR_{11}R_{12})_g(C_6\text{-}C_{10})$aryl, and $-(CR_{11}R_{12})_g$(4-10)-membered heterocyclyl;

any carbon atoms of the $(C_1\text{-}C_6)$alkyl, the (3-10)-membered cycloalkyl, the $(C_6\text{-}C_{10})$aryl and the (4-10)-membered heterocyclyl of the foregoing R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{15}, and R_{16} are independently optionally substituted with 1 to 3 R_{14} substituents each independently selected from halo, cyano, $-CF_3$, $-CHF_2$, $-CH_2F$, $(C_1\text{-}C_6)$alkoxy, $-(CR_8R_9)_e(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $-NR_{11}(C{=}O)\text{-}R_{13}$, $-(C{=}O)\text{-}NR_{11}R_{12}$, and $-(CR_{11}R_{12})_e$(4-10)-membered heterocyclyl;

any carbon atoms of the $(C_1\text{-}C_6)$alkyl, the (3-10)-membered cycloalkyl, the $(C_6\text{-}C_{10})$aryl and the (4-10)-membered heterocyclyl of the foregoing R_{14} are independently optionally substituted with 1 to 3 R_{16} substituents each independently selected from halo, cyano, nitro, $-CF_3$, $-CHF_2$, $-CH_2F$, trifluoromethoxy, azido, $(CH_2)_e$OH, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $-(C{=}O)\text{-}R_{11}$, $-(C{=}O)\text{-}R_{15}$, $-(C{=}O)\text{-}O\text{-}R_{11}$, $-(C{=}O)\text{-}O\text{-}R_{15}$, $-O\text{-}(C{=}O)\text{-}R_{11}$, $-O\text{-}(C{=}O)\text{-}R_{15}$, $-NR_{11}(C{=}O)\text{-}R_{13}$, $-(C{=}O)\text{-}NR_{11}R_{12}$, $-NR_{11}R_{12}$, and $–NR_{11}R_{15}$;

any nitrogen atoms of the (4-10)-membered heterocyclyl of the foregoing R_1, R_2, R_3, R_4, R_5, R_6, R_7, R_8, R_9, R_{10}, R_{14}, and R_{15} are independently optionally substituted with $(C_1\text{-}C_6)$alkyl, $(-(C{=}O)\text{-}R_{11}$, $-(C{=}O)\text{-}O\text{-}R_{11}$, $-(C{=}O)\text{-}NR_{11}R_{12}$, $-(CR_{11}R_{12})_e$(3-10)-membered cycloalkyl, $-(CR_{11}R_{12})_e(C_6\text{-}C_{10})$aryl, or $-(CR_{11}R_{12})_e$(4-10)-membered heterocyclyl;

each R_{11}, R_{12}, and R_{13} are independently hydrogen or $(C_1\text{-}C_6)$alkyl;

R_{15} is $–(CR_{11}R_{12})_e$(3-10)-membered cycloalkyl, $-(CR_{11}R_{12})_e(C_6\text{-}C_{10})$aryl, or $–(CR_{11}R_{12})_e$(4-10)-membered heterocyclyl;

a and b are each independently 1, 2, 3, or 4;

c is 1 or 2;

d is 0, 1, or 2; and

e, f, and g are each independently 0, 1, 2, 3, 4, or 5;

and wherein when R_7 is CH_3 or CH_2CH_3,

R_6 is $-CF_3$, $-CHF_2$, $-CH_2F$, $(C_{1-3}-C_6)$alkyl, $-(CR_8R_9)_d$(3-10)-membered cycloalkyl, $-(CR_8R_9)_e$(4-10)-membered non-aromatic heterocyclyl, $-(CR_8R_9)_f(C=O)(CR_8R_9)_e(C_6-C_{10})$aryl, $-(CR_8R_9)_f(C=O)(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_eO(CR_8R_9)_f(C_6-C_{10})$aryl, $-(CR_8R_9)_eO(CR_8R_9)_f$(4-10)-membered heterocyclyl, $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e(C_6-C_{10})$aryl, and $–(CR_8R_9)_fS(O)_d(CR_8R_9)_e$(4-10)-membered heterocyclyl, and wherein the (3-6)-membered cycloalkyl of the $-(CR_8R_9)_d$(3-10)-membered cycloalkyl is optionally substituted with one CF_3, CN, methoxy, or one or two fluorine or methyl.

2. The compound according to claim 1, wherein R_3 and R_5 are hydrogen; R_6 is $-CF_3$, $-CHF_2$, $-CH_2F$, (C_1-C_6)alkyl, $-(CR_8R_9)_d$(3-10)-membered cycloalkyl, $-(CR_8R_9)_e(C_6-C_{10})$aryl, $-(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_eO(CR_8R_9)_f(C_6-C_{10})$aryl, $-(CR_8R_9)_eO(CR_8R_9)_f$(4-10)-membered heterocyclyl, $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e(C_6-C_{10})$aryl, and $–(CR_8R_9)_fS(O)_d(CR_8R_9)_e$(4-10)-membered heterocyclyl; R_7 is $-CF_3$, $-CHF_2$, $-CH_2F$, (C_1-C_6)alkyl, $-(CR_8R_9)_d$(3-10)-membered cycloalkyl, $-(CR_8R_9)_e$(4-10)-membered heterocyclyl, $-(CR_8R_9)_eO(CR_8R_9)_f(C_6-C_{10})$aryl, $-(CR_8R_9)_eO(CR_8R_9)_f$(4-10)-membered heterocyclyl, $-(CR_8R_9)_fS(O)_d(CR_8R_9)_e(C_6-C_{10})$aryl, and $–(CR_8R_9)_fS(O)_d(CR_8R_9)_e$(4-10)-membered heterocyclyl.

3. The compound according to claim 1, wherein R_3 and R_5 are hydrogen; R_6 and R_7 are linked to each other as a 4-12 membered mono- or bicyclic ring wherein any of the 5, 6, or 10 membered mono- or bicyclic ring is optionally substituted with one chlorine, methoxy, ethyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or one or two fluorine or methyl.

4. The compound according to claim 1, wherein each R_3 and one R_5 are hydrogen; one R_5 and R_6 are linked to each other as a 4-12 membered mono- or bicyclic ring; and R_7 is - (C_1-C_6)alkyl.

5. The compound according to claim 3, wherein the compound is the single enantiomer bearing an (*S*)-configuration at C-3.

6. The compound according to claim 1, wherein the compound is the single enantiomer bearing an (*S*)-configuration at C-3, R_3 and R_5 are hydrogen; R_6 and R_7 are linked to each other as a 4-12 membered mono- or bicyclic ring wherein any of the 5, 6, or 10 membered mono- or bicyclic ring is optionally substituted with one chlorine, methoxy, ethyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or one or two fluorine or methyl.

7. The compound of claim 1, wherein said compound is selected from the group consisting of:

(S)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane-1,1-dioxide;

N-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-isothiazolidine-1,1-dioxide;

(S)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)isothiazolidine-1,1-dioxide;

2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-5-fluoro-isothiazolidine-1,1-dioxide;

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2,6-thiadiazinane-1,1-dioxide;

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-N-(1-methylcyclopentyl)methanesulfonamide;

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)isothiazolidine-1,1-dioxide;

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide;

N-(3-(2,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane-1,1-dioxide;

2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2,6-thiadiazinane-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

8. The compound according to claim 7 which is (S)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane-1,1-dioxide; or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 7 which is N-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-isothiazolidine-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

10. The compound according to claim 7 which is (S)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)isothiazolidine-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

11. The compound according to claim 7 which is 2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-5-fluoro-isothiazolidine-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

12. The compound according to claim 7 which is 2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2,6-thiadiazinane-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

13. The compound according to claim 7 which is N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-N-(1-methylcyclopentyl)methanesulfonamide; or a pharmaceutically acceptable salt or hydrate thereof.

14. The compound according to claim 7 which is N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)isothiazolidine-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

15. The compound according to claim 7 which is N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-2,3-dihydrobenzo[d]isothiazole-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

16. The compound according to claim 7 which is N-(3-(2,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

17. The compound according to claim 7 which is 2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2,6-thiadiazinane-1,1-dioxide; or a pharmaceutically acceptable salt or hydrate thereof.

18. A pharmaceutical composition comprising a compound according to any one of claims 1-17, or a pharmaceutically acceptable salt or hydrate thereof, and a pharmaceutically acceptable carrier, adjuvant, or diluent.

19. The pharmaceutical composition according to claim 18, further comprising one or more additional therapeutic agents.

20. Use of the pharmaceutical composition according to claim 18 in the manufacture of a medicament for the treatment of a Cry-mediated disease or disorder, wherein the Cry-mediated disease or disorder is selected from the group consisting of diabetes, obesity, metabolic syndrome, insulin resistance syndrome, Cushing's syndrome, glaucoma, psychotic depression, Alzheimer's disease, neuropathic pain, drug abuse, osteoporosis, cancer, macular degeneration, and myopathy.

21. Use of the pharmaceutical composition according to claim 18 in the manufacture of a medicament for alleviating a symptom of a Cry-mediated disease or disorder, wherein the Cry-mediated disease or disorder is selected from the group consisting of diabetes, obesity, metabolic syndrome, insulin resistance syndrome, Cushing's syndrome, glaucoma, psychotic depression, Alzheimer's disease, neuropathic pain, drug abuse, osteoporosis, cancer, macular degeneration, and myopathy.

22. The use according to claim 20 or 21, wherein the medicament further comprises one or more additional therapeutic agents.

23. The compound according to claim 1, wherein R_6 and R_7 are linked to each other as a 4-12 membered mono- or bicyclic ring, wherein any of the 5, 6, or 10 membered mono- or bicyclic ring is optionally substituted with one chlorine, methoxy, ethyl, propyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, or one or two fluorine or methyl.

24. The compound according to claim 23, wherein the compound is selected from the group consisting of:

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (33);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-3,4-dihydro-1H-benzo[d][1,2]thiazine 2,2-dioxide (35);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,3-dihydrobenzo[c]isothiazole 2,2-dioxide (36);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-3,4-dihydro-1H-benzo[c][1,2]thiazine 2,2-dioxide (37);

(R)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)isothiazolidine 1,1-dioxide (40);

(R)-N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (41);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-6-chloro-3,4-dihydro-2H-benzo[e][1,2]thiazine 1,1-dioxide (42);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-3,4-dihydro-2H-benzo[e][1,2]thiazine 1,1-dioxide (43);

N-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (86);

N-(3-(2,7-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (91);

N-(3-(2,7-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)- isothiazolidine-1,1-dioxide (92);

N-(3-(2,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (96);

N-(3-(2,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)- isothiazolidine-1,1-dioxide (97);

N-(3-(2,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)- isothiazolidine-1,1-dioxide (101);

N-(3-(4,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (105);

N-(3-(4,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)- isothiazolidine-1,1-dioxide (106);

N-(3-(3,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2-thiazinane 1,1-dioxide (107);

N-(3-(3,5-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)- isothiazolidine-1,1-dioxide (108);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-6-methyl-1,2-thiazinane-1,1-dioxide (111);

N-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-4-methoxy-1,2-thiazinane-1,1-dioxide (112);

2-(3-(9H-Carbazol-9-yl)-2-hydroxy-3-methylbutyl)-isothiazolidine-1,1-dioxide (114);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-isothiazolidine-1,1-dioxide (115);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)- 1,2-thiazinane 1,1-dioxide (116);

2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-6-fluoro-1,2-thiazinane-1,1-dioxide (121);

2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-6,6-difluoro-1,2-thiazinane-1,1-dioxide (122);

2-(3-(9H-Carbazol-9-yl)-2-hydroxypropyl)-6-methyl-1,2,6-thiadiazinane-1,1-dioxide (124);

N-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-4-methoxy-1,2-thiazinane-1,1-dioxide (155);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-methyl-1,2,6-thiadiazinane-1,1-dioxide (169);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-methyl-1,2,6-thiadiazinane-1,1-dioxide (170);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)- 1,2,6-thiadiazinane-1,1-dioxide (172);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-methyl-1,2,5-thiadiazinane-1,1-dioxide (173);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-5-methyl-1,2,5-thiadiazinane-1,1-dioxide (174);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-1,2,5-thiadiazinane-1,1-dioxide (175);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-1,2,5-thiadiazinane-1,1-dioxide (176);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-5-methylisothiazolidine-1,1-dioxide (177);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5,5-dimethylisothiazolidine-1,1-dioxide (178);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-5-methylisothiazolidine-1,1-dioxide (179);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-5,5-dimethylisothiazolidine-1,1-dioxide (180);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-4-methoxyisothiazolidine-1,1-dioxide (181);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-4-methoxyisothiazolidine-1,1-dioxide (182);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-fluoroisothiazolidine-1,1-dioxide (183);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-5-fluoroisothiazolidine-1,1-dioxide (184);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5,5-difluoroisothiazolidine-1,1-dioxide (185);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-4-methylisothiazolidine-1,1-dioxide (194);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxy-2-methylpropyl)-4-methylisothiazolidine-1,1-dioxide (195);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-ethyl-1,2,5-thiadiazinane-1,1-dioxide (216);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-isopropyl-1,2,6-thiadiazinane-1,1-dioxide (217);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-isopropyl-1,2,6-thiadiazinane-1,1-dioxide (218);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-5-ethyl-1,2,5-thiadiazinane-1,1-dioxide (219);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-cyclopentyl-1,2,6-thiadiazinane-1,1-dioxide (220);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-cyclopentyl-1,2,6-thiadiazinane-1,1-dioxide (221);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-cyclohexyl-1,2,6-thiadiazinane-1,1-dioxide (222);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-cyclohexyl-1,2,6-thiadiazinane-1,1-dioxide (223);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-isopropyl-1,2,5-thiadiazinane-1,1-dioxide (224);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-5-isopropyl-1,2,5-thiadiazinane-1,1-dioxide (225);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-ethyl-1,2,6-thiadiazinane-1,1-dioxide (226);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-ethyl-1,2,6-thiadiazinane-1,1-dioxide (227);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-6-cyclobutyl-1,2,6-thiadiazinane-1,1-dioxide (228);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-6-cyclobutyl-1,2,6-thiadiazinane-1,1-dioxide (229);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-cyclopropyl-1,2,5-thiadiazinane-1,1-dioxide (230);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-cyclopentyl-1,2,5-thiadiazinane-1,1-dioxide (231);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-5-cyclopentyl-1,2,5-thiadiazinane-1,1-dioxide (232);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-cyclohexyl-1,2,5-thiadiazinane-1,1-dioxide (233);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)-2-hydroxypropyl)-5-cyclobutyl-1,2,5-thiadiazinane-1,1-dioxide (234);

2-(3-(3,6-Difluoro-9H-carbazol-9-yl)- 2-hydroxy-2-methylpropyl)-5-cyclobutyl-1,2,5-thiadiazinane-1,1-dioxide (235);

2-(4-(9H-Carbazol-9-yl)-3-hydroxy-2-methylbutan-2-yl)-isothiazolidine-1,1-dioxide (243);

2-(4-(3,6-Difluoro-9H-carbazol-9-yl)-3-hydroxy-2-methylbutan-2-yl)isothiazolidine-1,1-dioxide (244);

2-(4-(3,6-Difluoro-9H-carbazol-9-yl)-3-hydroxy-2,3-dimethylbutan-2-yl)isothiazolidine-1,1-dioxide (245);

or a pharmaceutically acceptable salt or hydrate thereof.

25. A pharmaceutical composition comprising a compound according to claim 23 or 24, or a pharmaceutically acceptable salt or hydrate thereof, and a pharmaceutically acceptable carrier, adjuvant, or diluent.

26. The pharmaceutical composition according to claim 25, further comprising one or more additional therapeutic agents.

27. Use of the pharmaceutical composition according to claim 25 in the manufacture of a medicament for the treatment of a Cry-mediated disease or disorder, wherein the Cry-mediated disease or disorder is selected from the group consisting of diabetes, obesity, metabolic syndrome, insulin resistance syndrome, Cushing's syndrome, glaucoma, psychotic depression, Alzheimer's disease, neuropathic pain, drug abuse, osteoporosis, cancer, macular degeneration, and myopathy.

28. Use of the pharmaceutical composition according to claim 25 in the manufacture of a medicament for alleviating a symptom of a Cry-mediated disease or disorder, wherein the Cry-mediated disease or disorder is selected from the group consisting of diabetes, obesity, metabolic syndrome, insulin resistance syndrome, Cushing's syndrome, glaucoma, psychotic depression, Alzheimer's disease, neuropathic pain, drug abuse, osteoporosis, cancer, macular degeneration, and myopathy.

29. The use according to claim 27 or 28, wherein the medicament further comprises one or more additional therapeutic agents.