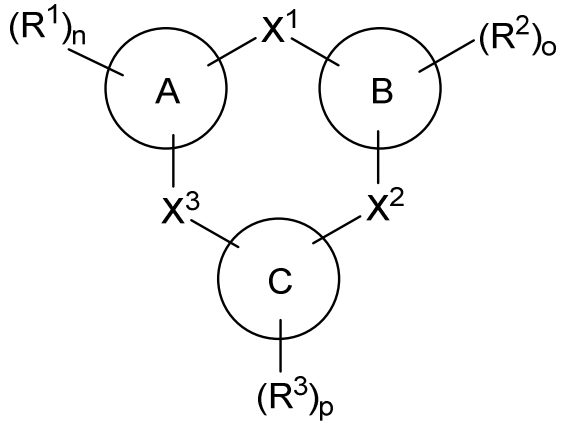
CLAIMS

WE CLAIM:

1. A compound of formula (I)



(I)

or a stereoisomer and/or a pharmaceutically acceptable salt thereof, wherein:

Ring A is phenyl, pyridinyl, or pyridonyl, wherein the nitrogen atom of the pyridonyl may optionally be substituted by C_{1-6}alkyl;

Ring B is phenyl or 5-10 membered heterocyclyl;

Ring C is phenyl, 5-10 membered heterocyclyl, or 5-10 membered heteroaryl; or

Ring C is absent;

R^1 is independently, for each occurrence, selected from the group consisting of halogen, hydroxyl, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, -O-C(O)C_{1-6}alkyl, -O-C(O)C_{3-6}cycloalkyl, and $N(R^E)_2$;

R^2 is independently, for each occurrence, selected from the group consisting of halogen, hydroxyl, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{3-6}cycloalkyl, and COOH;

R^3 is selected from the group consisting of cyano, halogen, C_{1-6}alkyl, and C_{3-6}cycloalkyl;

X^1 is selected from the group consisting of *-$S(O)_2N(R^A)$-**, -C(O)-, *-C(O)$N(R^A)$-**, *-$CH_2N(R^A)$-**, and *-$S(O)_2CH_2$-**, wherein * denotes the point of attachment to Ring A and ** denotes the point of attachment to Ring B;

X^2 is a bond or -O-;

X^3 is #-L^1-L^2-L^3-##, wherein # denotes the point of attachment to Ring A and ## denotes the point of attachment to Ring C or to Ring B when Ring C is absent;

L^1 is selected from the group consisting of -CH_2-, -O-, -C(O)-, -C(O)$N(R^B)$-, -C(O)O-, C_{1-6}alkyl-O-, -CH_2-C(O)O-, -CH_2-$N(R^B)$C(O)-, and 5-6 membered heteroaryl;

L^2 is C_{1-6}alkyl or 4-6 membered heterocyclyl, wherein the 4-6 membered heterocyclyl may be optionally substituted with oxo; or

L^2 is absent;

L^3 is selected from the group consisting of a bond, -O-, -O-C_{1-6}alkyl, C_{1-6}alkyl-O-, and 4-6 membered heterocyclyl;

R^A is hydrogen or C_{1-6}alkyl;

R^B is hydrogen or C_{1-6}alkyl;

R^E is independently, for each occurrence, hydrogen or C_{1-6}alkyl;

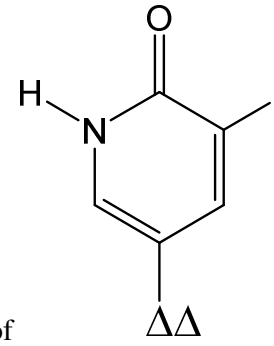
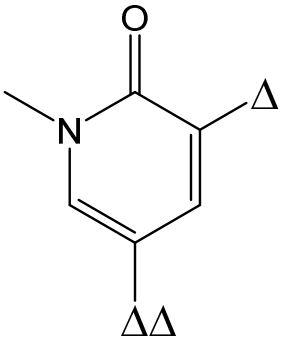
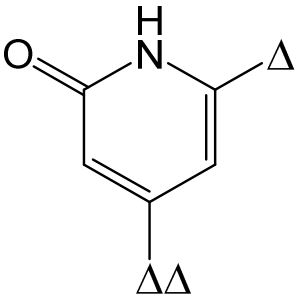
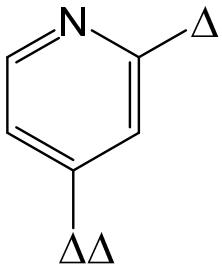
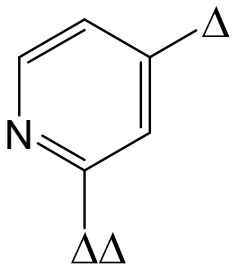
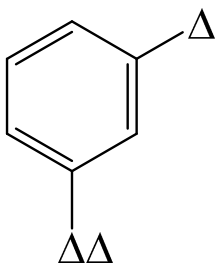
n is 0, 1, or 2;

o is 1 or 2; and

p is 0 or 1.

2. The compound of claim 1, wherein Ring A is phenyl, pyridinyl, or 2-pyridonyl, wherein the nitrogen atom of the 2-pyridonyl may optionally be substituted by C_{1-6}alkyl.

3. The compound of claim 1 or 2, wherein Ring A is phenyl, pyridinyl, or 2-pyridonyl, wherein the nitrogen atom of the 2-pyridonyl may optionally be substituted by CH_3.

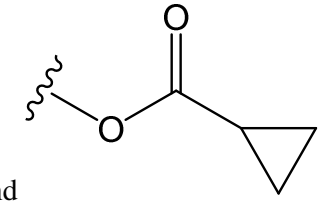
4. The compound of any one of claims 1-3, wherein Ring A is selected from the group consisting of  ,  ,  ,  ,  , and  , wherein Δ denotes the point of attachment to X^1 and ΔΔ denotes the point of attachment to X^3.

5. The compound of any one of claims 1-4, wherein n is 0.

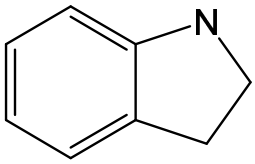
6. The compound of any one of claims 1-4, wherein n is 1.

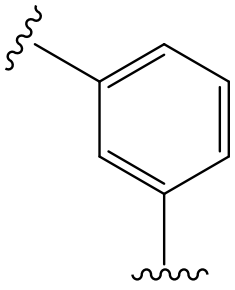
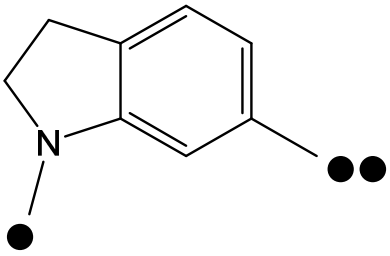
7. The compound of claim 6, wherein R^1 is selected from the group consisting of chloro, hydroxyl, CH_3, CHF_2, and NH_2.

8. The compound of any one of claims 1-4, wherein n is 2.

9. The compound of claim 8, wherein R^1 is independently, for each occurrence, selected from the group consisting of chloro, fluoro, hydroxyl, CH_3, CHF_2, -O-CH_3, -O-CHF_2, -O-$C(O)CH_3$, and  .

10. The compound of any one of claims 1-9, wherein Ring B is phenyl or 9-membered heterocyclyl.

11. The compound of any one of claims 1-10, wherein Ring B is phenyl or  .

12. The compound of any one of claims 1-10, wherein Ring B is  or 

, wherein ● denotes the point of attachment to X^1 and ●● denotes the point of attachment to X^2.

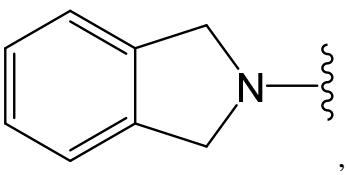
13. The compound of any one of claims 1-12, wherein o is 1.

14. The compound of claim 13, wherein R^2 is selected from the group consisting of fluoro, hydroxyl, cyclopropyl, CF_3, -O-CH_3, -O-CHF_2, -O-CF_3, and C(O)OH.

15. The compound of any one of claims 1-12, wherein o is 2.

16. The compound of claim 15, wherein R^2 is independently, for each occurrence, selected from the group consisting of chloro, fluoro, CH_3, CF_3, and -O-CH_3.

17. The compound of any one of claims 1-16, wherein Ring C is absent.

18. The compound of any one of claims 1-16, wherein Ring C is selected from the group consisting of phenyl, pyrrolidinyl, piperidinyl, pyridinyl, 

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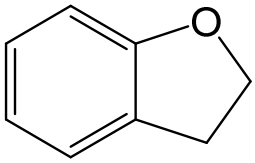
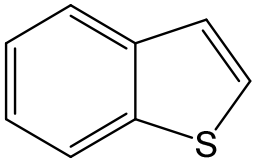
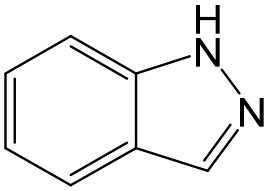
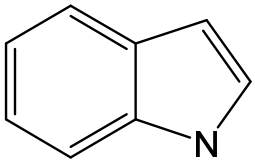
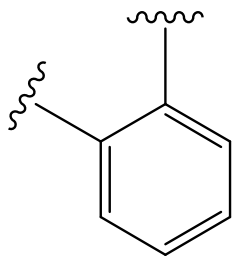
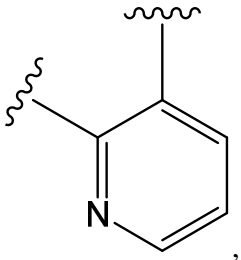
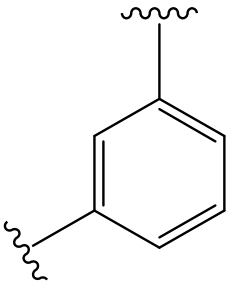
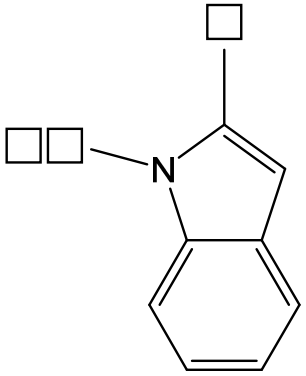
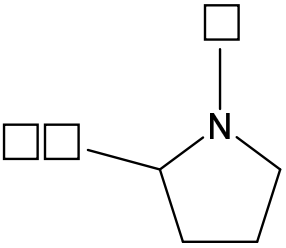
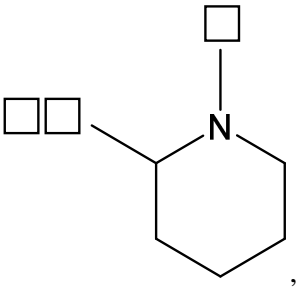
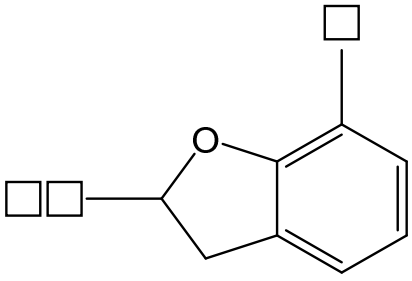
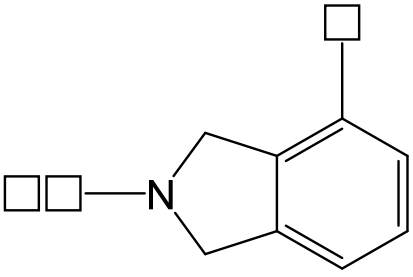
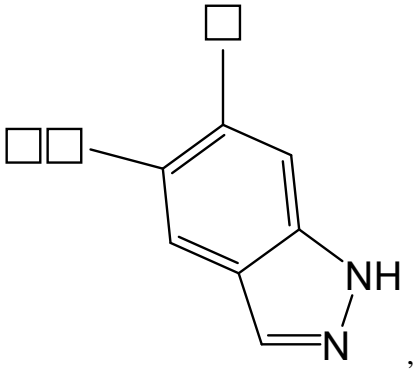
 ,  ,  , and

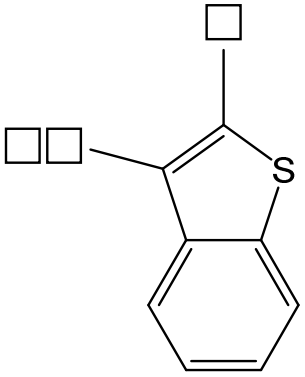
 .

19. The compound of any one of claims 1-16 or 18, wherein Ring C is selected from the group consisting of  ,  ,  ,

 ,  ,  ,

 ,  ,



, and 

, wherein □ denotes the point of attachment to X^2 and □□ denotes the point of attachment to X^3.

20. The compound of any one of claims 1-16, 18, and 19, wherein p is 1.

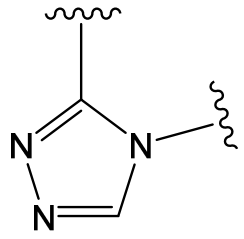
21. The compound of claim 20, wherein R^3 is selected from the group consisting of bromo, chloro, fluoro, cyano, CH_3, and cyclopropyl.

22. The compound of any one of claims 1-16, 18, and 19, wherein p is 0.

23. The compound of any one of claims 1-22, wherein X^1 is selected from the group consisting of *-$S(O)_2N(H)$-**, *-$S(O)_2N(CH_3)$-**, -C(O)-, *-C(O)N(H)-**, *-$CH_2N(H)$-**, and *-$S(O)_2CH_2$-**, wherein * denotes the point of attachment to Ring A and ** denotes the point of attachment to Ring B.

24. The compound of any one of claims 1-23, wherein X^2 is a bond.

25. The compound of any one of claims 1-23, wherein X^2 is -O-.

26. The compound of any one of claims 1-25, wherein L^1 is selected from the group consisting of -C(O)N(H)-, -C(O)N(CH_3)-, -C(O)O-, -CH_2-, -CH_2-O-, -C(O)-, -CH_2-C(O)O-, -CH_2-N(CH_3)C(O)-, -O-, and 

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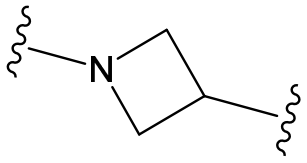
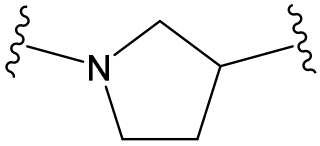
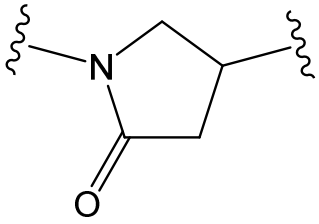
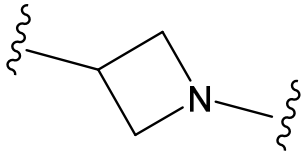
27. The compound of any one of claims 1-26, wherein L^2 is selected from the group consisting of $-CH_2CH_2-$, $-(CH_2)_3-$, $-CH_2-$, $-(CH_2)_4-$, $-CH(CH_3)CH_2-$, $-CH_2CH_2C(H)(CH_3)-$,

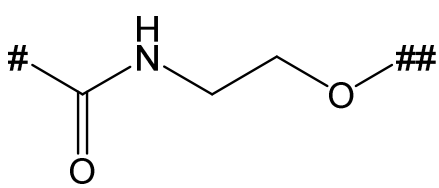
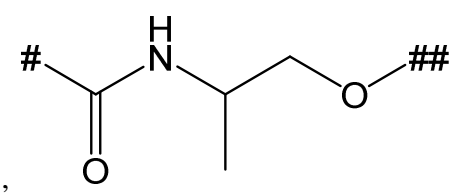
 ,  , and  .

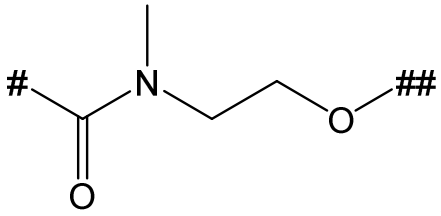
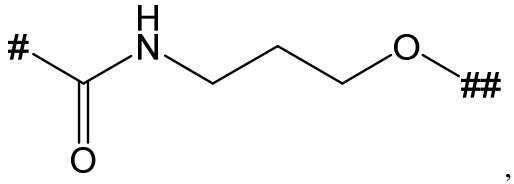
28. The compound of any one of claims 1-26, wherein L^2 is absent.

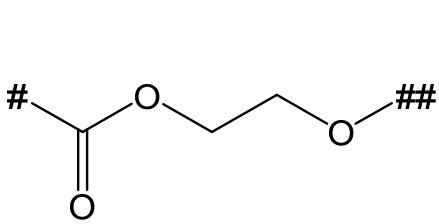
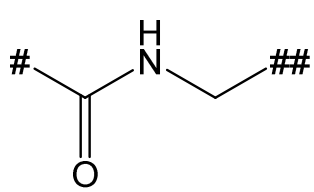
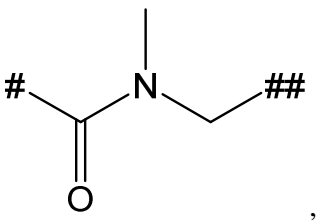
29. The compound of any one of claims 1-28, wherein L^3 is a bond.

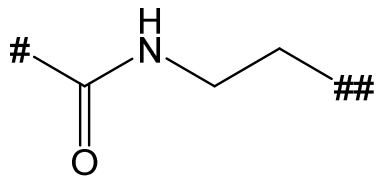
30. The compound of any one of claims 1-28, wherein L^3 is -O-, $-CH_2-O-$, or

 .

31. The compound of any one of claims 1-25, wherein X^3 is selected from the group consisting of  ,  ,

 ,  ,

 ,  ,  ,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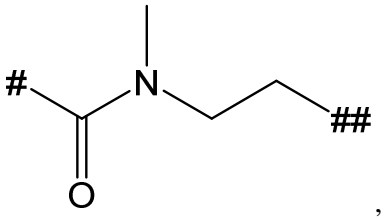
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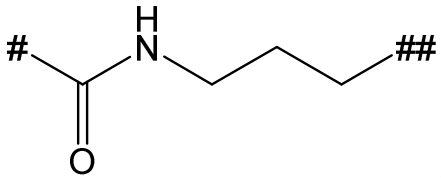
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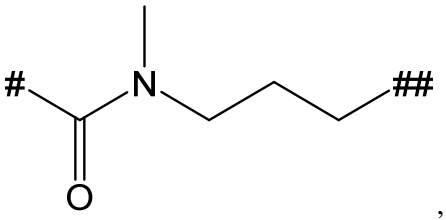
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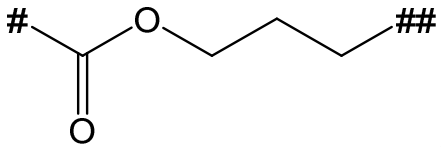
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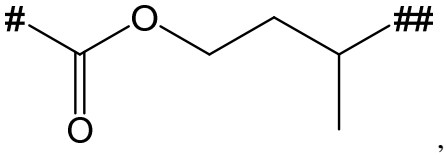
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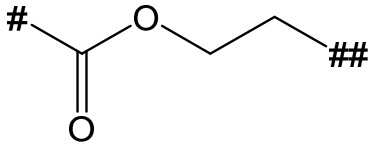
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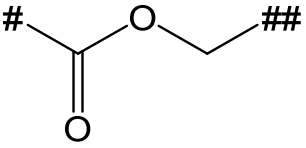
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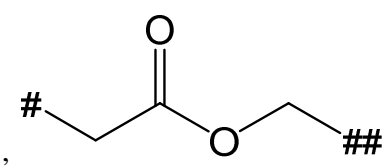
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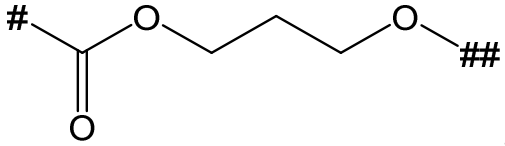
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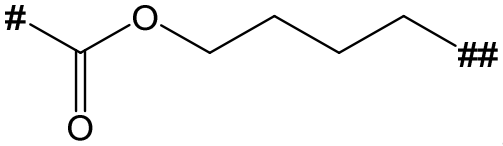
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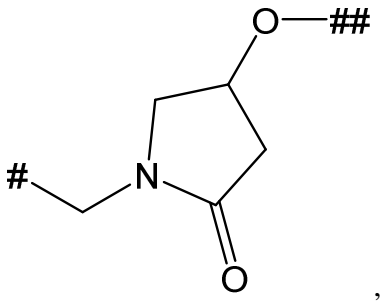
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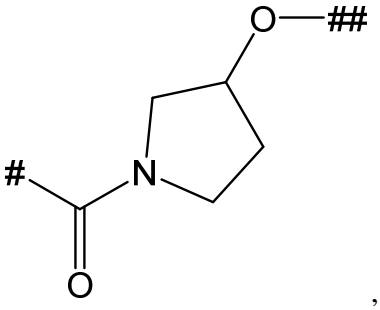
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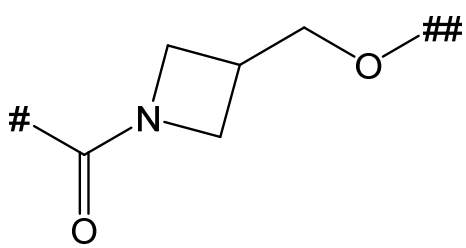
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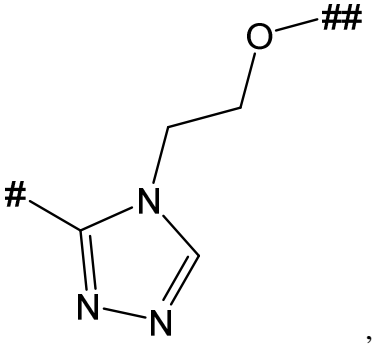
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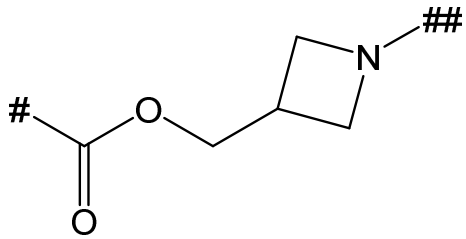
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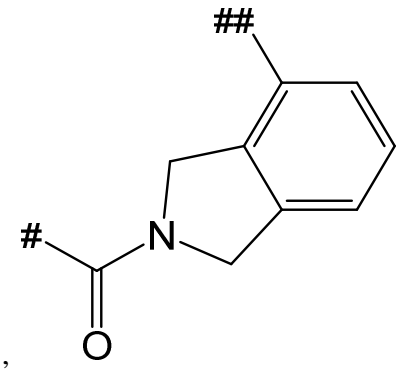
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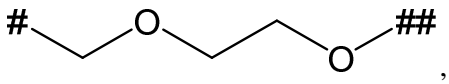
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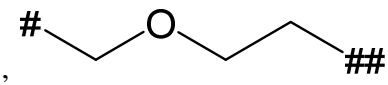
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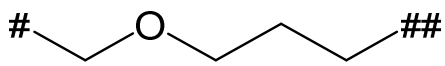
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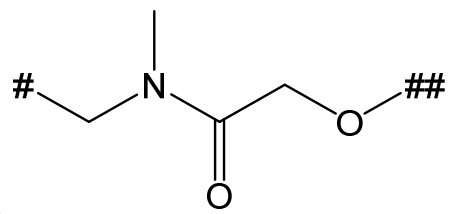
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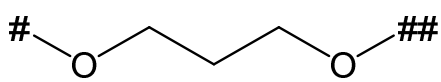
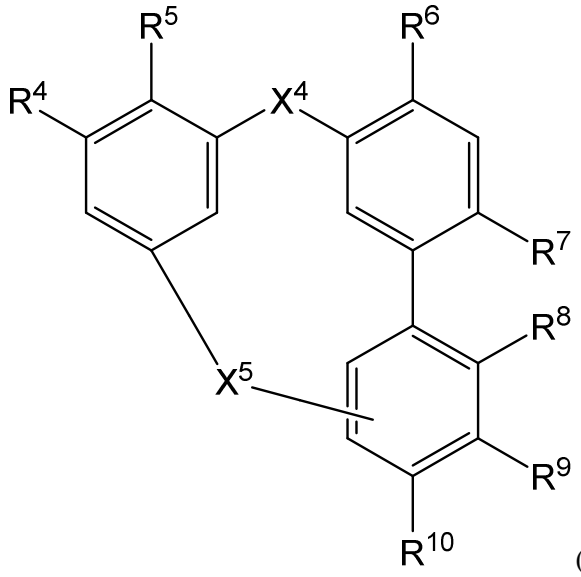

, wherein # denotes the point of attachment to Ring A and ## denotes the point of attachment to Ring C.

32. A compound of formula (Ia)


(Ia)

or a stereoisomer and/or a pharmaceutically acceptable salt thereof, wherein:

R^4 is selected from the group consisting of hydrogen, hydroxyl, halogen, and C_{1-6}alkyl;

R^5 is selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6}alkoxy, C_{1-6}haloalkyl, C_{1-6}haloalkoxy, -C(O)OC_{1-6}alkyl, and -C(O)OC_{1-6}cycloalkyl;

R^6 is selected from the group consisting of hydrogen, halogen, hydroxyl, C_{1-6}alkoxy, C_{1-6}haloalkoxy, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, and C(O)OH;

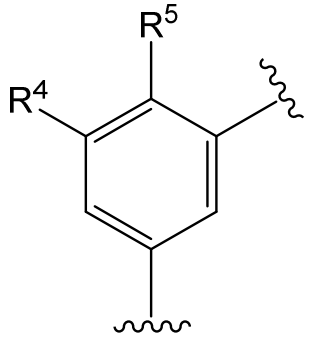
R^7 is selected from the group consisting of hydrogen, halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

R^8 is hydrogen, halogen, or C_{1-6}alkyl;

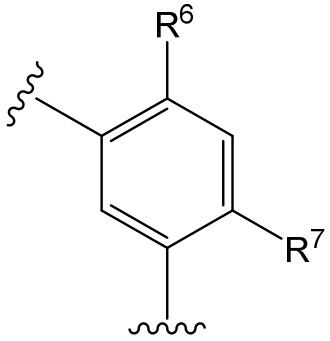
R^9 is selected from the group consisting of hydrogen, cyano, halogen, and C_{3-6}cycloalkyl;

R^{10} is hydrogen, cyano, or halogen;

X^4 is selected from the group consisting of *-$S(O)_2N(R^C)$-**, *-C(O)$N(R^C)$-**, *-$CH_2N(R^C)$-**, and *-$S(O)_2CH_2$-**, wherein * denotes the point of attachment to

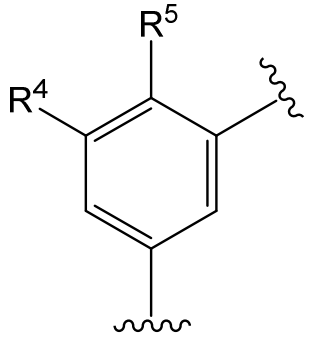


and ** denotes the point of attachment to



;

X^5 is #-L^4-L^5-L^6-##, wherein # denotes the point of attachment to



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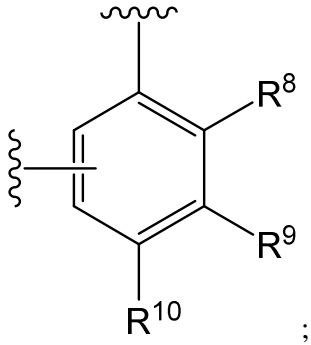


;

L^4 is selected from the group consisting of CH_2, C_{1-6}alkyl-O-, -O-, -C(O)-, -C(O)N(R^D)-, -C(O)O-, -CH_2-C(O)O-, -CH_2-N(R^D)C(O)-, and 5-6 membered heteroaryl;

L^5 is C_{1-6}alkyl or 4-6 membered heterocyclyl, wherein the 4-6 membered heterocyclyl may be optionally substituted with oxo;

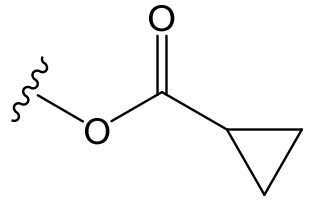
L^6 is selected from the group consisting of a bond, -O-, C_{1-6}alkyl-O-, and 4-6 membered heterocyclyl;

R^C is hydrogen or C_{1-6}alkyl; and

R^D is hydrogen or C_{1-6}alkyl.

33. The compound of claim 32, wherein R^4 is selected from the group consisting of hydrogen, hydroxyl, chloro, and CH_3.

34. The compound of claim 32 or 33, wherein R^5 is selected from the group consisting of hydrogen, fluoro, hydroxyl, CHF_2, -O-CH_3, -O-CHF_2, -O-C(O)CH_3, and



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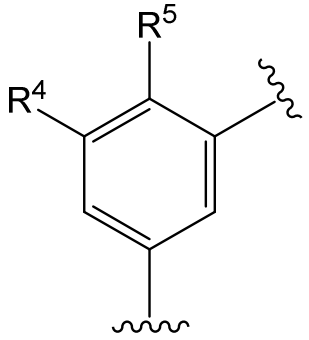
35. The compound of any one of claims 32-34, wherein R^6 is selected from the group consisting of hydrogen, hydroxyl, fluoro, chloro, cyclopropyl, CF_3, -O-CH_3, -O-CHF_2, -O-CF_3, and C(O)OH.

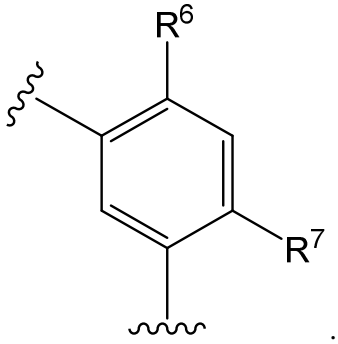
36. The compound of any one of claims 32-35, wherein R^7 is selected from the group consisting of hydrogen, chloro, fluoro, -O-CH_3, CH_3, and CF_3.

37. The compound of any one of claims 32-36, wherein R^8 is hydrogen, CH_3, or chloro.

38. The compound of any one of claims 32-37, wherein R^9 is selected from the group consisting of hydrogen, cyano, chloro, bromo, fluoro, and cyclopropyl.

39. The compound of any one of claims 32-38, wherein R^{10} is selected from the group consisting of hydrogen, cyano, chloro, and fluoro.

40. The compound of any one of claims 32-39, wherein X^4 is selected from the group consisting of *-$S(O)_2N(H)$-**, *-$S(O)_2N(CH_3)$-**, *-C(O)N(H)-**, *-$CH_2N(H)$-**, and *-$S(O)_2CH_2$-**, wherein * denotes the point of attachment to 

and ** denotes the point of attachment to 

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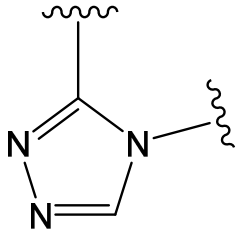
41. The compound of any one of claims 32-40, wherein L^4 is selected from the group consisting of -CH_2-, -O-, -C(O)-, -C(O)N(H)-, -C(O)$N(CH_3)$-, -C(O)O-, -CH_2-C(O)O-, -CH_2-$N(CH_3)$C(O)-, -CH_2-O-, and 

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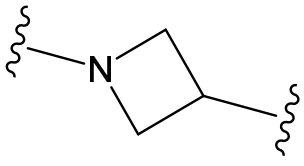
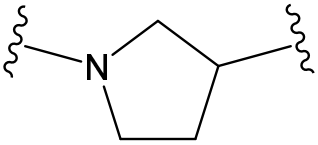
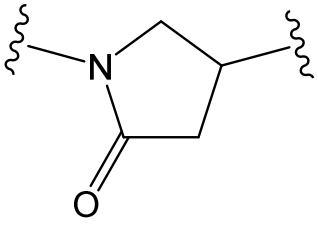
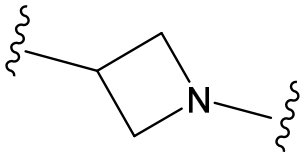
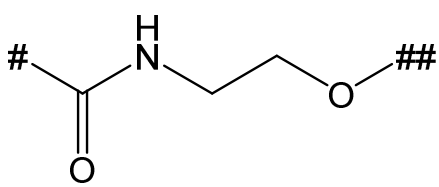
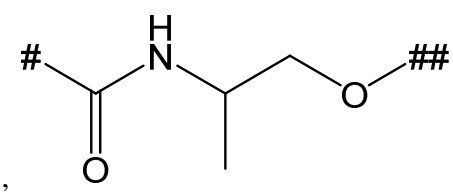
42. The compound of any one of claims 32-41, wherein L^5 is selected from the group consisting of $-CH_2-$, $-CH_2CH_2-$, $-(CH_2)_3-$, $-C(H)(CH_3)CH_2-$, $-CH_2CH_2C(H)(CH_3)-$, $-(CH_2)_4-$,

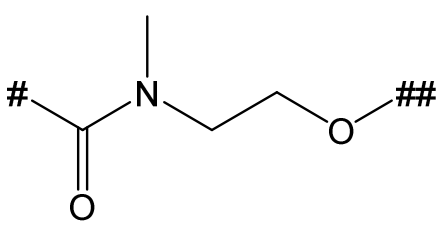
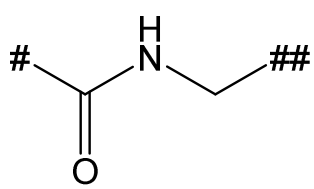
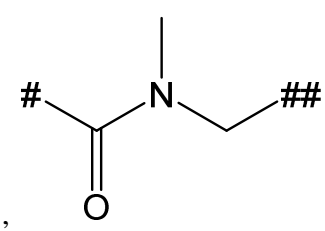
 ,  , and  .

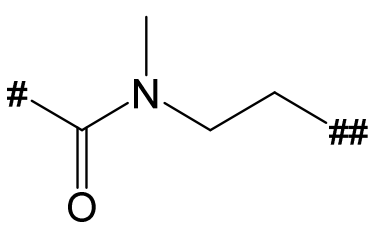
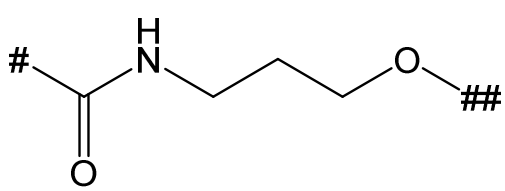
43. The compound of any one of claims 32-42, wherein L^6 is a bond.

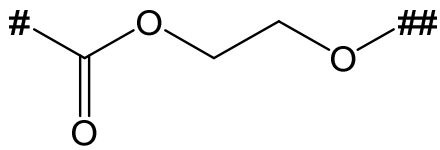
44. The compound of any one of claims 32-42, wherein L^6 is -O-, $-CH_2-O-$, or

 .

45. The compound of any one of claims 32-40, wherein X^5 is selected from the group consisting of  ,  ,

 ,  ,  ,

 ,  ,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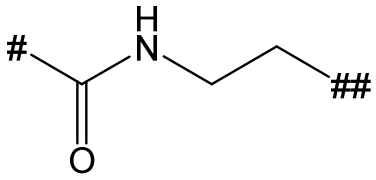
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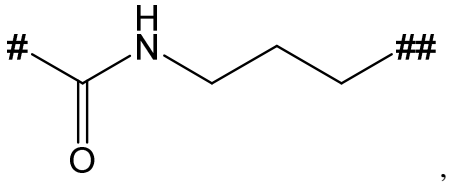
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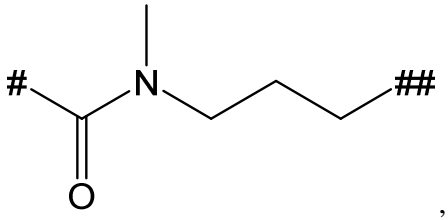
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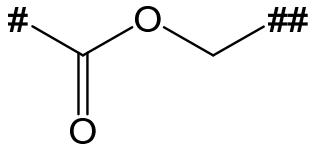
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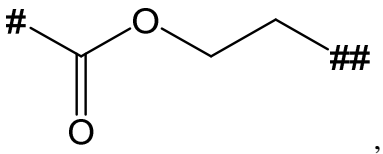
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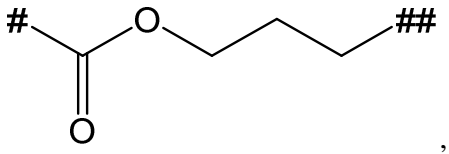
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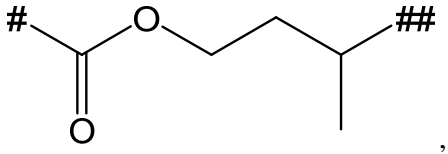
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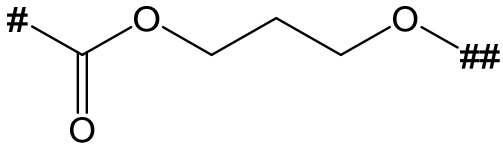
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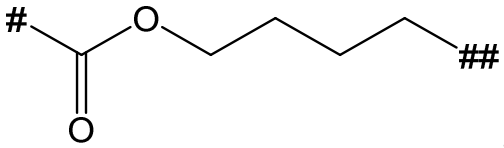
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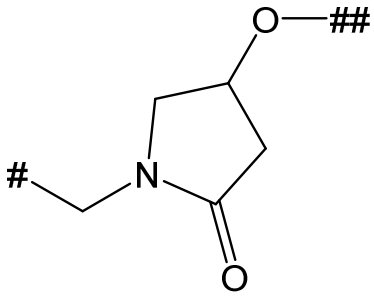
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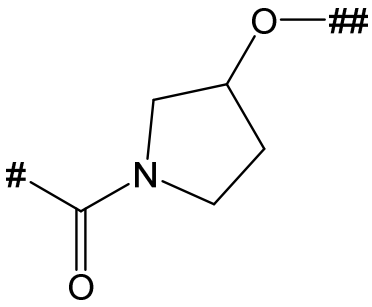
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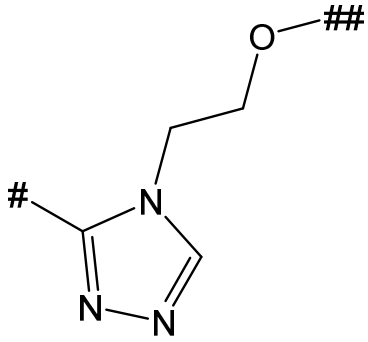
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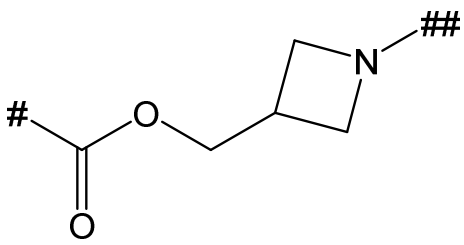
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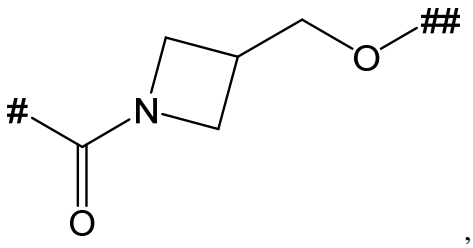
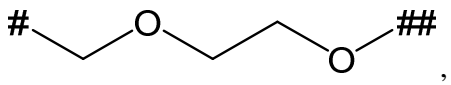
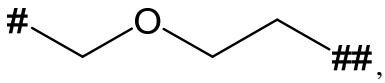
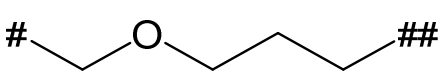
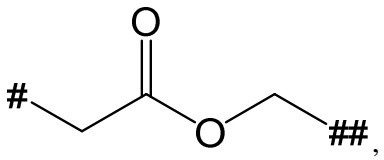
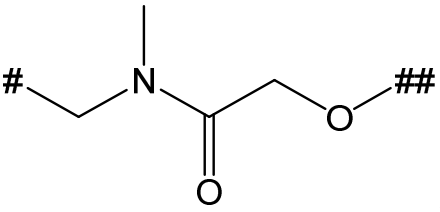


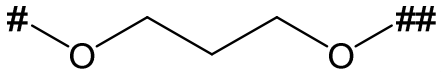
, 

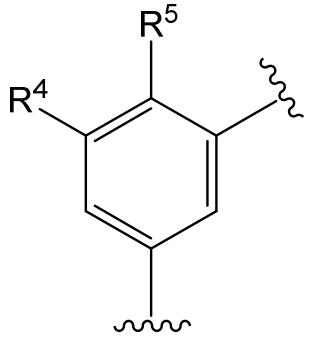
, 

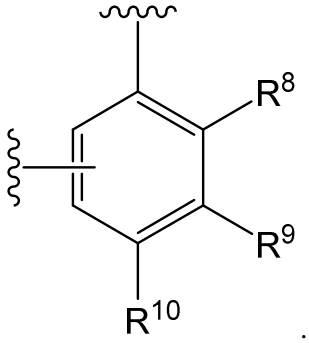
, 

, 

, 

, and 

, wherein # denotes the point of attachment to 

and ## denotes the point of attachment to 

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46. A compound selected from any compound set forth in Table 1, or a pharmaceutically acceptable salt thereof.

47. A pharmaceutical composition comprising a compound of any one of claims 1-46; and a pharmaceutically acceptable carrier.

48. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for inhibiting ACLY in a subject in need thereof.

49. The use of claim 48, wherein the subject has a liver condition, disease, or disorder.

50. The use of claim 49, wherein the liver condition, disease, or disorder is NAFLD or NASH.

51. The use of claim 48, wherein the subject has type-2 diabetes.

52. The use of claim 48, wherein the subject has inflammation.

53. The use of claim 48, wherein the subject has chronic kidney disease.

54. The use of claim 48, wherein the subject has autoimmunity.

55. The use of claim 48, wherein the subject has cancer.

56. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating NAFLD in a subject in need thereof.

57. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating NASH in a subject in need thereof.

58. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating type-2 diabetes in a subject in need thereof.

59. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating inflammation in a subject in need thereof.

60. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating chronic kidney disease in a subject in need thereof.

61. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating autoimmunity in a subject in need thereof.

62. Use of the compound of any one of claims 1-46 or the pharmaceutical composition of claim 47, in the manufacture of a medicament for treating cancer in a subject in need thereof.

63. The compound of any one of claims 1-46 or the pharmaceutical composition of claim 47 for use in therapy.