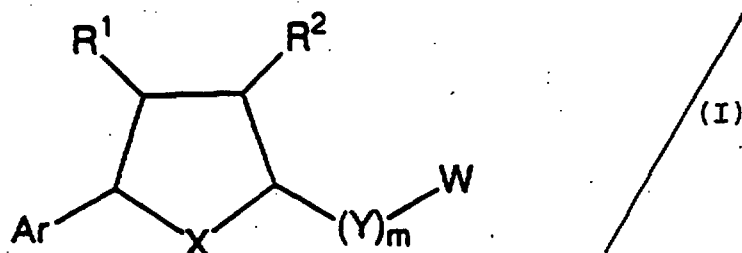


Replace with new set
of claims

We claim:

1. A compound of formula:



wherein:

Ar is an aryl or heteroaryl group that is optionally substituted with at least one group selected from the group consisting of halo (including but not limited to fluoro), lower alkoxy (including methoxy), lower aryloxy (including phenoxy), W, cyano, or R³;

m is 0;

W is independently -AN(OM)C(O)N(R³)R⁴, -AN(R³)C(O)N(OM)R⁴, -AN(OM)C(O)R⁴, -AC(O)N(OM)R⁴, -C(O)N(OM)R⁴, -C(O)NHA, or -A-B;

A is lower alkynyl, alkaryl or aralkyl groups, wherein one or more carbons optionally can be replaced by O, N, or S;

B is selected from the group consisting of pyridylimidazole and benzimidazole, either of which is optionally substituted with R₃;

M is hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable leaving group;

X is O, S, S(O), NR⁵, or CHR⁵;

Y is O, S, S(O), NR⁵, or CHR⁵;

R¹ and R² are independently hydrogen, lower alkyl including methyl, cyclopropylmethyl, ethyl, isopropyl, butyl, pentyl, hexyl, and C₃₋₈ cycloalkyl, for example, cyclopentyl; halo lower alkyl, for example, trifluoromethyl; halo; and -COOH;

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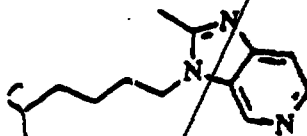
R^3 and R^4 are independently hydrogen or alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, C_{1-6} alkoxy- C_{1-10} alkyl, C_{1-6} alkylthio- C_{1-10} alkyl, heteroaryl, or heteroarylalkyl-;

R^5 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, alkaryl, $-AN(OM)C(O)N(R^3)R^4$, $-AN(R^3)C(O)N(OM)R^4$, $-AN(OM)C(O)R^4$, $-AC(O)N(OM)R^4$, $-AC(O)N(OM)R^4$, $-AS(O)_nR^3$, $-AS(O)_nCH_2C(O)R^3$, $-AS(O)_nCH_2CH(OH)R^3$, $-AC(O)NHR^3$; and

wherein n is 0-2.

2. The compound of claim 1, wherein Ar is selected from the group consisting of phenyl, trimethoxyphenyl, dimethoxyphenyl, fluorophenyl, and specifically 4-fluorophenyl, difluorophenyl, pyridyl, dimethoxypyridyl, quinoliny, furyl, imidazolyl, and thienyl.

3. The compound of claim 1, wherein -A-B is



and wherein Ar is aryl or heteroaryl substituted with at least one group selected from W, halo, hydroxyl, amino, alkylamino, arylamino, alkoxy, aryloxy, nitro, cyano, sulfonic acid, sulfate, phosphonic acid, phosphate, and phosphonate.

6. A pharmaceutical composition comprising an effective amount of the compound of claim 1, 2, 3, 4, 5, 9 or 10 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

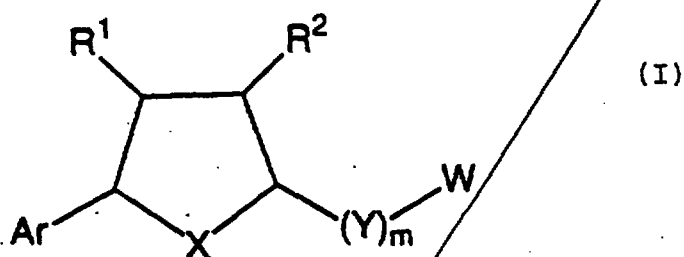
7. A method for the treatment of inflammatory disorders in a host comprising administering an effective amount of a compound of claim 1, 2, 3, 4, 5, 9 or 10 or a pharmaceutically acceptable salt thereof

8. The method of claim 7, wherein the animal

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is selected from a human, a mammal, an equine, a canine and a bovine,

9. A compound of formula:



wherein:

Ar is an aryl or heteroaryl group that is optionally substituted with at least one group selected from the group consisting of halo (including but not limited to fluoro), lower alkoxy (including methoxy), lower aryloxy (including phenoxy), W, cyano, or R^3 ;

m is 0;

W is independently $-AN(R^3)C(O)N(OM)R^4$, $-AN(OM)C(O)R^4$, $-AC(O)N(OM)R^4$, $-C(O)N(OM)R^4$, $-C(O)NHA$, or $-A-B$;

A is lower alkyl, lower alkenyl, lower alkynyl, alkaryl or aralkyl groups, wherein one or more carbons optionally can be replaced by O, N, or S;

B is selected from the group consisting of pyridylimidazole and benzimidazole, either of which is optionally substituted with R_3 ;

M is hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable leaving group;

X is O, S, $S(O)$, NR^5 , or CHR^5 ;

Y is O, S, $S(O)$, NR^5 , or CHR^5 ;

R^1 and R^2 are independently hydrogen, lower alkyl including methyl, cyclopropylmethyl, ethyl, isopropyl, butyl, pentyl, hexyl, and C_{3-8} cycloalkyl, for example, cyclopentyl; halo lower alkyl, for

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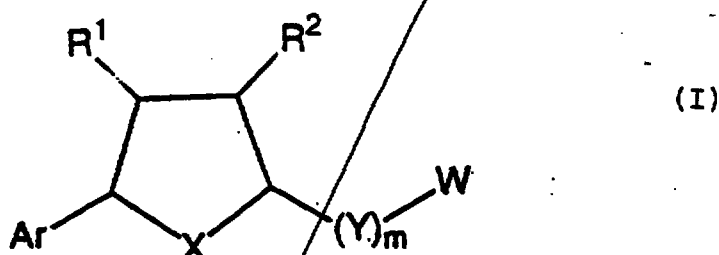
example, trifluoromethyl; halo; and -COOH;

R^3 and R^4 are independently hydrogen or alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, C_{1-4} alkoxy- C_{1-10} alkyl, C_{1-6} alkylthio- C_{1-10} alkyl, heteroaryl, or heteroarylalkyl-;

R^5 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, alkaryl, -AN(OM)C(O)N(R^3) R^4 , -AN(R^3)C(O)N(OM) R^4 , -AN(OM)C(O) R^4 , -AC(O)N(OM) R^4 , -AC(O)N(OM) R^4 , -AS(O) nR^3 , -AS(O) $nCH_2C(O)R^3$, -AS(O) $nCH_2CH(OH)R^3$, -AC(O)NHR 3 ; and

wherein n is 0-2.

10. A compound of formula:



wherein:

Ar is an aryl or heteroaryl group that is optionally substituted with at least one group selected from the group consisting of halo (including but not limited to fluoro), lower alkoxy (including methoxy), lower aryloxy (including phenoxy), W, cyano, or R^3 ;

m is 1;

W is independently -AN(OM)C(O)N(R^3) R^4 , -AN(R^3)C(O)N(OM) R^4 , -AN(OM)C(O) R^4 , -AC(O)N(OM) R^4 , -C(O)N(OM) R^4 , -C(O)NHA, or -A-B;

A is lower alkyl, lower alkenyl, lower alkynyl, alkaryl or aralkyl groups, wherein one or more carbons optionally can be replaced by O, N, or S;

B is selected from the group consisting of pyridylimidazole and benzimidazole, either of which

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is optionally substituted with R_3 ;

M is hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable leaving group;

X is O, S, S(O), or NR^5 ;

Y is O, S, S(O), NR^5 , or CHR^5 ;

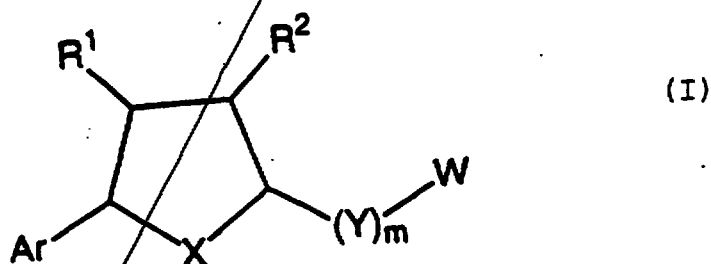
R^1 and R^2 are independently hydrogen, lower alkyl including methyl, cyclopropylmethyl, ethyl, isopropyl, butyl, pentyl, hexyl, and C_{3-8} cycloalkyl, for example, cyclopentyl; halo lower alkyl, for example, trifluoromethyl; halo; and $-COOH$;

R^3 and R^4 are independently hydrogen or alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, C_{1-6} alkoxy- C_{1-10} alkyl, C_{1-6} alkylthio- C_{1-10} alkyl, heteroaryl, or heteroarylalkyl-;

R^5 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, alkaryl, $-AN(OM)C(O)N(R^3)R^4$, $-AN(R^3)C(O)N(OM)R^4$, $-AN(OM)C(O)R^4$, $-AC(O)N(OM)R^4$, $-AC(O)N(OM)R^4$, $-AS(O)_nR^3$, $-AS(O)_nCH_2C(O)R^3$, $-AS(O)_nCH_2CH(OH)R^3$, $-AC(O)NHR^3$; and

wherein n is 0-2.

11. A compound of formula:



wherein:

Ar is an aryl or heteroaryl group that is optionally substituted with at least one group selected from the group consisting of halo (including but not limited to fluoro), lower alkoxy (including methoxy), lower aryloxy (including phenoxy), W, cyano, or R^3 ;

m is 0 or 1;

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W is independently -AN(OM)C(O)N(R³)R⁴,
 -AN(R³)C(O)N(OM)R⁴, -AN(OM)C(O)R⁴, -AC(O)N(OM)R⁴,
 -C(O)N(OM)R⁴, -C(O)NHA, or -A-B;

A is lower alkyl, lower alkenyl, lower alkynyl, alkaryl or aralkyl groups, wherein one or more carbons optionally can be replaced by O, N, or S;

B is selected from the group consisting of pyridylimidazole and benzimidazole, either of which is optionally substituted with R₃;

M is hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable leaving group;

X is O, S, S(O), NR⁵, or CHR⁵;

Y is O, S, S(O), NR⁵, or CHR⁵;

R¹ and R² are independently hydrogen, lower alkyl including methyl, cyclopropylmethyl, ethyl, isopropyl, butyl, pentyl, hexyl, and C₃₋₈ cycloalkyl, for example, cyclopentyl; halo lower alkyl, for example, trifluoromethyl; halo; and -COOH;

R³ and R⁴ are independently hydrogen or alkyl, alkenyl, alkynyl, aryl, aralkyl, alkaryl, C₁₋₆ alkoxy-C₁₋₁₀ alkyl, C₁₋₆ alkylthio-C₁₋₁₀ alkyl, heteroaryl, or heteroarylalkyl-;

R⁵ is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, alkaryl, -AN(OM)C(O)N(R³)R⁴,
 -AN(R³)C(O)N(OM)R⁴, -AN(OM)C(O)R⁴, -AC(O)N(OM)R⁴,
 -AC(O)N(OM)R⁴, -AS(O)_nR³, -AS(O)_nCH₂C(O)R³,
 -AS(O)_nCH₂CH(OH)R³, -AC(O)NHR³; and

wherein n is 0-2.

12. A pharmaceutical composition comprising an effective amount of the compound of claim 11 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

13. A method for the treatment of inflammatory disorders in a host comprising administering an effective amount of a compound of claim 11 or a pharmaceutically acceptable salt

thereof.

14. The compound of claim 1, 9, or 10 wherein X is O.

15. The compound of claim 1, 9, or 10 wherein the aryl group has a halogen substituent.

16. The compound of claim 1 or 10, wherein W is $\text{AN(OM)C(O)NR}^3\text{R}^4$.

17. The compound of claim 16, wherein R^3 and R^4 are hydrogen.

18. The compound of claim 1, 9, or 10, wherein R^1 and R^2 are hydrogen.

19. The compound of claim 1, wherein A is lower alkynyl.

20. The compound of claim 1, wherein M is H.

21. The compound of claim 11, wherein X is O.

22. The compound of claim 11, wherein the aryl group has a halogen substituent.

23. The compound of claim 22, wherein the halogen is fluorine.

24. The compound of claim 23, wherein the fluorine is in the para position.

25. The compound of claim 11, wherein W is $\text{AN(OM)C(O)NR}^3\text{R}^4$.

26. The compound of claim 25, wherein R^3 and R^4 are hydrogen.

27. The compound of claim 11, wherein R^1 and R^2 are hydrogen.

28. The compound of claim 5, wherein A is lower alkyl.

29. The compound of claim 28, wherein the lower alkyl group is butyl.

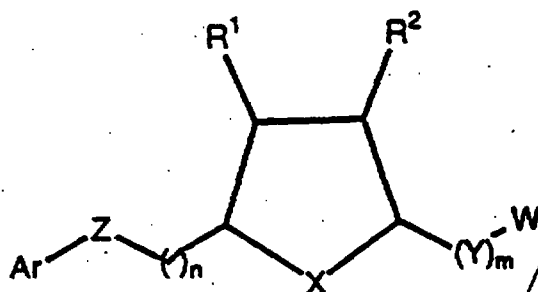
30. The compound of claim 11, wherein the lower alkyl group is isopentyl.

31. The compound of claim 1, wherein M is H.

32. A compound of formula:

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(I)



wherein:

Ar is an aryl or heteroaryl group that is optionally substituted with halo, lower alkoxy, lower aryloxy, W, cyano, or R^3 ;

m is 0 or 1;

n is 1-6;

W is independently $-AN(OM)C(O)N(R^3)R^4$, $-N(OM)C(O)N(R^3)R^4$, $-AN(R^3)C(O)N(OM)R^4$, $-N(R^3)C(O)N(OM)R^4$, $-AN(OM)C(O)R^4$, $-N(OM)C(O)R^4$, $AC(O)N(OM)R^4$, $-C(O)N(OM)R^4$, $-C(O)NHA$;

A is lower alkyl, lower alkenyl, lower alkynyl, alkylaryl or arylalkyl groups, wherein one or more carbons optionally can be replaced by O, N, or S (with valence completed with hydrogen or oxygen as necessary), however, $-Y-A-$, $-A-$, or $-AW-$ should not include two adjacent heteroatoms (i.e., $-O-O-$, $-S-S-$, $-O-S-$, etc.);

M is hydrogen, a pharmaceutically acceptable cation, or a metabolically cleavable leaving group;

X is O, S, $S(O)$, $S(O)_2$, NR^3 , or CHR^5 ;

Y is O, S, $S(O)$, $S(O)_2$, NR^3 , or CHR^5 ;

Z is O, S, $S(O)$, $S(O)_2$, NR^3 ;

R^1 and R^2 are independently hydrogen, lower alkyl, cyclopropylmethyl, ethyl, isopropyl, butyl, pentyl, hexyl, and C_{3-8} cycloalkyl, for example,

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cyclopentyl; halo lower alkyl, halo, or -COOH;

R^3 and R^4 are independently hydrogen or alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkylaryl, C_{1-6} alkoxy- C_{1-10} alkyl, C_{1-6} alkylthio- C_{1-10} alkyl, heteroaryl, or heteroarylalkyl-; and

R^5 is hydrogen, lower alkyl, lower alkenyl, lower alkynyl, arylalkyl, alkylaryl, -AN(OM)C(O)N(R^3) R^4 , -AN(R^3)C(O)N(OM) R^4 , -AN(OM)C(O) R^4 , -AC(O)N(OM) R^4 , -AS(O) xR^3 , -AS(O) $_nCH_2C(O)R^3$, -AS(O) $_nCH_2CH(OH)R^3$, or -AC(O)NHR 3 , wherein x is 0-2.

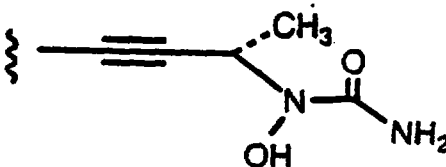
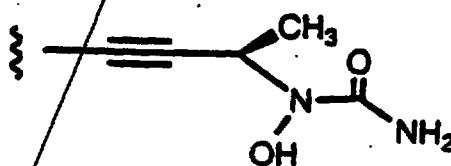
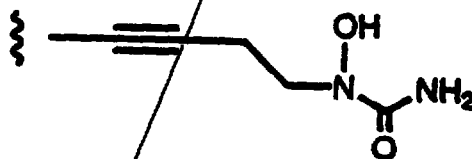
33. The compound of claim 32, wherein Ar is selected from the group consisting of phenyl, trimethoxyphenyl, dimethoxyphenyl, fluorophenyl, difluorophenyl, pyridyl, dimethoxypyridyl, quinolinyl, furyl, imidazolyl, and thienyl.

34. The compound of claim 32, wherein Ar is 4-fluorophenyl.

35. The compound of claim 32, wherein Z is O.

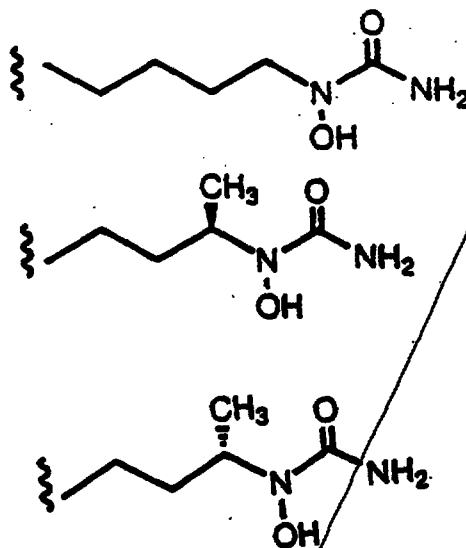
36. The compound of claim 32, wherein Z is S.

37. The compound of claim 32, wherein -(Y) $_mW$ is selected from the group consisting of:



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38. The compound of claim 2, wherein $-(Y)_mW$ is selected from the group consisting of:



39. The compound of claim 32, 33, 34, 35, 36, 37, or 38 in at least 97% enantiomerically enriched form.

40. A compound selected from the group consisting of 2S,5S-trans-2-(4-fluorophenoxymethyl)-5-(4-protected oxy-1-butynyl)tetrahydrofuran and 2S,5R-cis-2-(4-fluorophenoxymethyl)-5-(4-protected oxy-1-butynyl)tetrahydrofuran.

41. The compound of claim 32 that is 2S,5R-trans-2-(4-fluorophenoxymethyl)-5-(4-N-hydroxyureidyl-1-butyl)tetrahydrofuran.

42. The compound of claim 32 that is 2S,5S-trans-2-(4-fluorophenoxymethyl)-5-(4-N-hydroxyureidyl-1-butynyl)tetrahydrofuran.

43. The compound of claim 32 that is 2R,5S-trans-2-(4-fluorophenoxymethyl)-5-(4-N-hydroxyureidyl-1-butyl)tetrahydrofuran.

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44. The compound of claim 32 that is 2R,5R-trans-2-(4-fluorophenoxymethyl)-5-(4-N-hydroxyureidyl-1-butyryl)tetrahydrofuran.

45. A pharmaceutical composition comprising an effective antiinflammatory amount of the compound of claims 32-44 or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

46. Any of the compounds in the above claims for use in medical therapy, for example for the treatment or prophylaxis of an inflammatory disorder.

47. Use of any of the compounds in the above claims and pharmaceutically acceptable derivatives and salts thereof in the manufacture of a medicament for treatment of an inflammatory disorder.

48. Any of the compounds claimed above in combination with a pharmaceutically acceptable carrier.