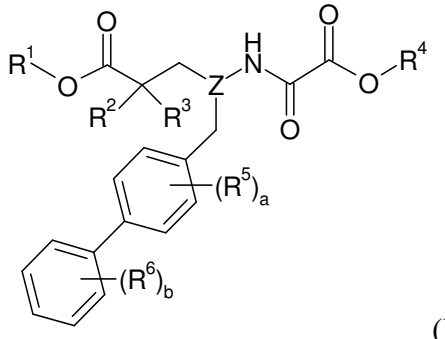
CLAIMS

WHAT IS CLAIMED IS:

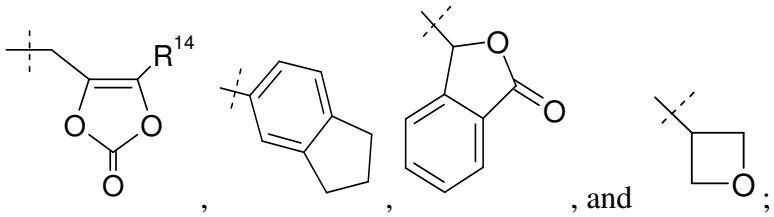
1. A compound of formula I:



(I)

where:

R^1 is selected from H, -C_{1-8}alkyl, -C_{1-3}alkylene-C_{6-10}aryl, -C_{1-3}alkylene-C_{1-9}heteroaryl, -C_{3-7}cycloalkyl, -$[(CH_2)_2O]_{1-3}CH_3$, -C_{1-6}alkylene-$OC(O)R^{10}$, -C_{1-6}alkylene-$NR^{11}R^{12}$, -C_{1-6}alkylene-$C(O)R^{13}$, -C_{0-6}alkylenemorpholinyl, -C_{1-6}alkylene-SO_2-C_{1-6}alkyl,

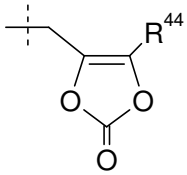
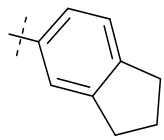
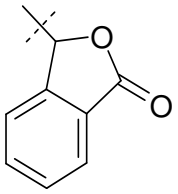
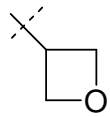


; R^{10} is selected from -C_{1-6}alkyl, -O-C_{1-6}alkyl, -C_{3-7}cycloalkyl, -O-C_{3-7}cycloalkyl, phenyl, -O-phenyl, -$NR^{11}R^{12}$, -$CH(R^{15})$-NH_2, -$CH(R^{15})$-NHC(O)O-C_{1-6}alkyl, and -$CH(NH_2)CH_2COOCH_3$; and R^{11} and R^{12} are independently selected from H, -C_{1-6}alkyl, and benzyl; or R^{11} and R^{12} are taken together as -$(CH_2)_{3-6}$-, -C(O)-$(CH_2)_3$-, or -$(CH_2)_2O(CH_2)_2$-; R^{13} is selected from -O-C_{1-6}alkyl, -O-benzyl, and -$NR^{11}R^{12}$; and R^{14} is -C_{1-6}alkyl or -C_{0-6}alkylene-C_{6-10}aryl; R^{15} is H, -CH_3, -$CH(CH_3)_2$, phenyl, or benzyl;

R^2 is CH_2OR^{21}; and R^3 is -CH_3; where R^{21} is H, -C(O)-C_{1-6}alkyl, -C(O)-$CH(R^{22})$-NH_2, -C(O)-$CH(R^{22})$-NHC(O)O-C_{1-6}alkyl, or -$P(O)(OR^{23})_2$; R^{22} is H, -CH_3, -$CH(CH_3)_2$, phenyl, or benzyl; R^{23} is H, -C_{1-6}alkyl, or phenyl; or

Z is selected from -CH- and -N-;

R^4 is selected from H, -C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{1-8}alkyl, -C_{1-3}alkylene-C_{6-10}aryl, -C_{1-3}alkylene-O-C_{6-10}aryl, -C_{1-3}alkylene-C_{1-9}heteroaryl, -C_{3-7}cycloalkyl, -$[(CH_2)_2O]_{1-3}CH_3$, -C_{1-6}alkylene-$OC(O)R^{40}$, -C_{1-6}alkylene-$NR^{41}R^{42}$, -C_{1-6}alkylene-$C(O)R^{43}$, -C_{0-6}alkylenemorpholinyl, -C_{1-6}alkylene-SO_2-C_{1-6}alkyl,

R^{40} is selected from -C_{1-6}alkyl, -O-C_{1-6}alkyl, -C_{3-7}cycloalkyl, -O-C_{3-7}cycloalkyl, phenyl, -O-phenyl, -$NR^{41}R^{42}$, -$CH(R^{45})$-NH_2, -$CH(R^{45})$-NHC(O)O-C_{1-6}alkyl, and -$CH(NH_2)CH_2COOCH_3$; and R^{41} and R^{42} are independently selected from H, -C_{1-6}alkyl, and benzyl; or R^{41} and R^{42} are taken together as -$(CH_2)_{3-6}$-, -C(O)-$(CH_2)_3$-, or -$(CH_2)_2O(CH_2)_2$-; R^{43} is selected from -O-C_{1-6}alkyl, -O-benzyl, and -$NR^{41}R^{42}$; and R^{44} is -C_{1-6}alkyl or -C_{0-6}alkylene-C_{6-10}aryl; R^{45} is H, -CH_3, -$CH(CH_3)_2$, phenyl, or benzyl;

a is 0 or 1; R^5 is selected from halo, –CH_3, –CF_3, and -CN;

b is 0 or an integer from 1 to 3; each R^6 is independently selected from halo, -OH, -CH_3, –OCH_3, -CN, and -CF_3;

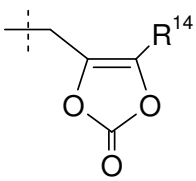
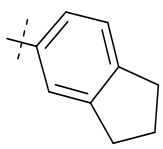
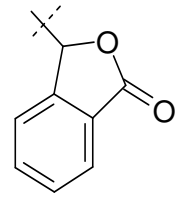
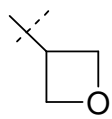
where each alkyl group in R^1 and R^4 is optionally substituted with 1 to 8 fluoro atoms; and

where the methylene linker on the biphenyl is optionally substituted with one or two -C_{1-6}alkyl groups or cyclopropyl;

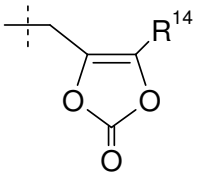
or a pharmaceutically acceptable salt thereof.

2. The compound of Claim 1, where R^1 is H.

3. The compound of Claim 1, where R^1 is selected from -C_{1-8}alkyl, -C_{1-3}alkylene-C_{6-10}aryl, -C_{1-3}alkylene-C_{1-9}heteroaryl, -C_{3-7}cycloalkyl, -$[(CH_2)_2O]_{1-3}CH_3$, -C_{1-6}alkylene-OC(O)R^{10}, -C_{1-6}alkylene-$NR^{11}R^{12}$, -C_{1-6}alkylene-C(O)R^{13}, -C_{0-6}alkylenemorpholinyl, -C_{1-6}alkylene-SO_2-C_{1-6}alkyl,

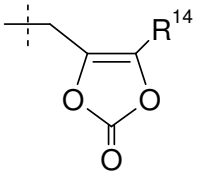





4. The compound of Claim 1, where R^1 is selected from H, -C_{1-8}alkyl, -C_{1-6}alkylene-OC(O)R^{10}, and



where R^{10} is -C_{1-6}alkyl, -O-C_{1-6}alkyl, or -CH[R^{15}]-NHC(O)O-C_{1-6}alkyl; R^{14} is -C_{1-6}alkyl; R^{15} is -$CH(CH_3)_2$; and each alkyl group in R^1 is optionally substituted with 1 to 8 fluoro atoms.

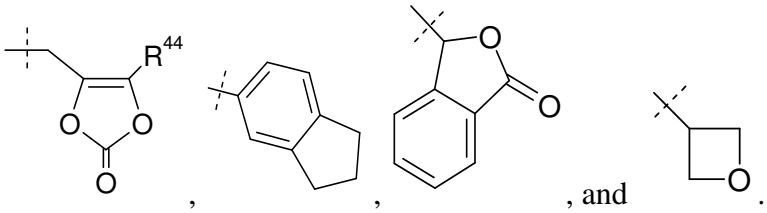
5. The compound of Claim 4, where R^1 is selected from H, -CH_2CH_3, -$CH(CH_3)_2$, -$CH_2CH(CH_3)_2$, -$(CH_2)_3CH_3$, -$(CH_2)_6CH_3$, -CH_2CF_3, -$(CH_2)_2CF_3$, -$CH_2CF_2CH_3$, -$CH_2CF_2CF_3$, -$CH_2OC(O)CH_3$, -$CH_2OC(O)CH_2CH_3$, -$CH_2OC(O)(CH_2)_2CH_3$, -$CH_2OC(O)OCH_2CH_3$, -$CH_2OC(O)$-CH[$CH(CH_3)_2$]-NHC(O)O-CH_3, and



where R^{14} is -CH_3.

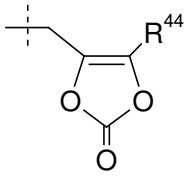
6. The compound of Claim 1, where R^4 is H.

7. The compound of Claim 1, where R^4 is selected from -C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{1-8}alkyl, -C_{1-3}alkylene-C_{6-10}aryl, -C_{1-3}alkylene-O-C_{6-10}aryl, -C_{1-3}alkylene-C_{1-9}heteroaryl, -C_{3-7}cycloalkyl, -$[(CH_2)_2O]_{1-3}CH_3$, -C_{1-6}alkylene-OC(O)R^{40}, -C_{1-6}alkylene-$NR^{41}R^{42}$, -C_{1-6}alkylene-C(O)R^{43}, -C_{0-6}alkylenemorpholinyl, -C_{1-6}alkylene-SO_2-C_{1-6}alkyl,



, and .

8. The compound of Claim 1, where R^4 is selected from H, -C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{6-10}aryl, -$[(CH_2)_2O]_{1-3}CH_3$, and



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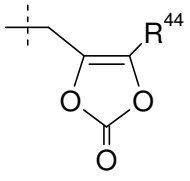
where R^{44} is -C_{1-6}alkyl; and each alkyl group in R^4 is optionally substituted with 1 to 7 fluoro atoms.

9. The compound of Claim 8, where R^4 is selected from H, -CH_2CH_3, -$CH(CH_3)_2$, -$CH_2CH(CH_3)_2$, -$(CH_2)_3CH_3$, -$C(CH_3)_3$, -$(CH_2)_2CF_3$, -$CH_2CF_2CH_3$, -$(CH_2)_3$-O-CH_2CH_3, -$(CH_2)_2$-O-phenyl, -$(CH_2)_2OCH_3$, and



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where R^{44} is -CH_3.

10. The compound of claim 1, where a is 0, or a is 1 and R^5 is halo.

11. The compound of claim 1, where b is 0, or b is 1 and R^6 is halo, or b is 2 and each R^6 is independently selected from halo and —CH_3.

12. The compound of claim 1, where:

a is 0 and b is 0; or

a is 0, b is 1, and R^6 is 2′-fluoro, 3′-fluoro, 3′-chloro, or 4′-flouro; or

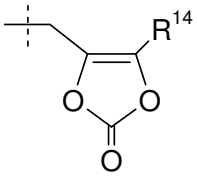
a is 0, b is 2, and R^6 is 2′-fluoro, 5′-chloro or 2′-methyl, 5′-chloro or 2′,5′-dichloro; or

a is 1, R^5 is 3-chloro, and b is 0; or

a is 1, R^5 is 3-chloro, b is 1, and R^6 is 3′-chloro; or

a is 1, R^5 is 3-chloro, b is 2, and R^6 is 2′-fluoro, 5′-chloro.

13. The compound of Claim 1, where R^1 is selected from H, -C_{1-8}alkyl, -C_{1-6}alkylene-$OC(O)R^{10}$, and



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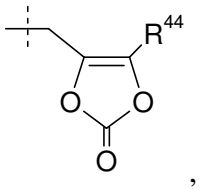
where R^{10} is -C_{1-6}alkyl, -O-C_{1-6}alkyl, or -$CH[R^{15}]$-$NHC(O)O$-C_{1-6}alkyl; R^{14} is -C_{1-6}alkyl; R^{15} is $-CH(CH_3)_2$; and each alkyl group in R^1 is optionally substituted with 1 to 8 fluoro atoms;

R^4 is selected from H, -C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{1-8}alkyl, -C_{1-3}alkylene-O-C_{6-10}aryl, -$[(CH_2)_2O]_{1-3}CH_3$, and



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where R^{44} is -C_{1-6}alkyl; and each alkyl group in R^4 is optionally substituted with 1 to 8 fluoro atoms;

a is 0 and b is 0; or a is 0, b is 1, and R^6 is halo; or a is 0, b is 2, and one R^6 is halo and the other R^6 is halo or $-CH_3$; or a is 1, R^5 is halo, and b is 0; or a is 1, R^5 is halo, b is 1, and R^6 is halo; or a is 1, R^5 is halo, b is 2, and each R^6 is halo; and

where the methylene linker on the biphenyl is optionally substituted with two $-CH_3$ groups.

14. (2S,4R)-5-(5'-chloro-2'-fluorobiphenyl-4-yl)-2-hydroxymethyl-2-methyl-4-(oxalyl-amino)pentanoic acid or a pharmaceutically acceptable salt thereof.

15. The compound of claim 1, where Z is –CH-.

16. The compound of claim 1, where R^4 is -C_{1-8}alkyl.

17. The compound of claim 1, where R^4 is –CH_2CH_3.

18. The compound of claim 1, where a is 0.

19. The compound of claim 1, where b is 2.

20. The compound of claim 1, where a is 0; b is 2; and R^6 is 2'-fluoro, 5'-chloro.

21. The compound of claim 13, where Z is –CH-.

22. The compound of claim 13, where R^4 is -C_{1-8}alkyl.

23. The compound of claim 13, where R^4 is –CH_2CH_3.

24. The compound of claim 13, where a is 0.

25. The compound of claim 13, where b is 2.

26. The compound of claim 13, where a is 0; b is 2; and R^6 is 2'-fluoro, 5'-chloro.

27. A pharmaceutical composition comprising a compound as of any one of Claims 1-5, 6-12, 13 and 14- 26 and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of Claim 27, wherein the pharmaceutical composition further comprises an AT_1 receptor antagonist.

29. Use of a compound of any one of Claims 1-5, 6-12, 13 and 14-26, in the manufacture of a medicament for treating hypertension, heart failure, or renal disease in a patient.