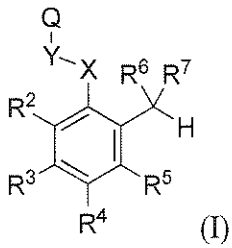
the polymer forming T state to the non-polymer forming R state (Nnamani et al. Chemistry & Biodiversity Vol. 5, 2008 pp. 1762-1769) by acting as allosteric modulators to stabilize the R state through formation of a Schiff base with an amino group on hemoglobin.

[0001] US 7,160,910 discloses 2-furfuraldehydes and related compounds that are also allosteric modulators of hemoglobin. One particular compound 5-hydroxymethyl-2-furfuraldehyde (5HMF) was found to be a potent hemoglobin modulator both *in vitro* and *in vivo*. Transgenic mice producing human HbS that were treated with 5HMF were found to have significantly improved survival times when exposed to extreme hypoxia (5% oxygen). Under these hypoxic conditions, the 5HMF treated mice were also found to have reduced amounts of hypoxia-induced sickled red blood cells as compared to the non-treated mice.

[0002] A need exists for therapeutics that can shift the equilibrium between the deoxygenated and oxygenated states of Hb to treat disorders that are mediated by Hb or by abnormal Hb such as HbS. A need also exists for therapeutics to treat disorders that would benefit from having Hb in the R state with an increased affinity for oxygen. Such therapeutics would have applications ranging, for example, from sensitizing hypoxic tumor cells that are resistant to standard radiotherapy or chemotherapy due to the low levels of oxygen in the cell, to treating pulmonary and hypertensive disorders, and to promoting wound healing.

BRIEF SUMMARY

[0003] The present disclosure provides allosteric modulators of hemoglobin. In one aspect, there is provided a compound of Formula (I):



(I)

or a tautomer or pharmaceutically acceptable salt thereof,

wherein Q is ~~selected from the group consisting of~~ aryl, ~~heteroaryl, and heterocycloalkyl, each optionally~~ substituted with one to three R^a; wherein at least one R^a is heteroaryl and is attached to said Q at the ring atom adjacent to ring atom bearing Y;

Y is O or $CR^{1a}R^{1b}$, where R^{1a} is H or halo and R^{1b} is selected from the group consisting of H, halo, and OH;

X is selected from the group consisting of O, ~~$>CH(CH_2)_nR^8$~~, and $C(R^9)_2$ where ~~n is 0 or 1, R^8 is OH, and~~ R^9 is independently H or halo; ~~or Y-X taken together is -NHC(O)- or -C(O)NH-~~;

R^2, R^3, and R^4, ~~and R^5~~ are independently selected from the group consisting of hydrogen, halo, R^b, OR^d, $-O(CH_2)_zOR^d$, $-O(CH_2)_zNR^dR^d$, $OC(O)R^e$, SR^d, CN, NO_2, CO_2R^d, $CONR^dR^d$, $C(O)R^d$, $OC(O)NR^dR^d$, NR^dR^d, $NR^dC(O)R^e$, $NR^dC(O)_2R^e$, $NR^dC(O)NR^dR^d$, $S(O)R^e$, $S(O)_2R^e$, $NR^dS(O)_2R^e$, $S(O)_2NR^dR^d$, and N_3, where z is 0, 1, 2, 3, 4, 5, or 6; ~~or R^5 is $-(CH_2)_pR^{5a}$ where p is 0 or 1 and R^{5a} is OH~~; R^5 is OH;

R^6 and R^7 together form oxo ~~or an aldehyde protecting group, or R^6 together with R^{1b}, R^8, or R^5 forms a cyclic ether where one of R^{1b}, R^8, or R^{5a} is O, R^6 is a bond, and R^7 is selected from the group consisting of OH, C_{1-8}alkoxy, and haloC_{1-8}alkoxy~~;

each R^a is independently selected from the group consisting of halo, oxo, R^b, OR^d, $O(CH_2)_uOR^d$, $O(CH_2)_uNR^dR^d$, $O(CH_2)_uNR^dC(O)R^e$, $O(CH_2)_uNR^dC(O)_2R^e$, $O(CH_2)_uNR^dS(O)_2R^e$, NH_2, $-(CH_2)_kOC(O)R^e$, $-(CH_2)_kSR^d$, CN, NO_2, $-(CH_2)_kCO_2(C_{1-8}alkyl)OH$, $-(CH_2)_kCO_2(C_{1-8}alkyl)(heteroaryl)C(O)(C_{1-8}alkyl)$, $-(CH_2)_kCO_2R^d$, $-(CH_2)_kCONR^dR^d$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^e$, $-(CH_2)_kC(O)R^d$, $-(CH_2)_kOC(O)NR^dR^d$, $-NR^d(CH_2)_uOR^d$, $-NR^d(CH_2)_uNR^dR^d$, $-NR^d(CH_2)_uNR^dC(O)R^e$, $-NR^d(CH_2)_uNR^dC(O)_2R^e$, $-NR^d(CH_2)_uNR^dS(O)_2R^e$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^d$, $-(CH_2)_kNR^dC(O)NR^dR^d$, $-(CH_2)_kS(O)R^e$, $-(CH_2)_kS(O)_2R^e$, $-(CH_2)_kNR^dS(O)_2R^e$, $-(CH_2)_kS(O)_2NR^dR^d$, N_3, $-(CH_2)_k$aryl optionally substituted with one to three R^c, $-NR^d(CH_2)_k$aryl optionally substituted with one to three R^c, $-(CH_2)_k$heteroaryl ~~optionally~~ substituted with one to three R^c, $-NR^d(CH_2)_k$heteroaryl optionally substituted with one to three R^c, $-(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c, and $-NR^d(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c where k is 0, 1, 2, 3, 4, 5, or 6 and u is 1, 2, 3, 4, 5, or 6;

each R^b is independently selected from the group consisting of C_{1-8}alkyl, C_{2-8}alkenyl, and C_{2-8} alkynyl, each optionally independently substituted with one to three halo, OR^d, or NR^dR^d;

each R^c is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8}alkenyl, haloC_{2-8} alkenyl, C_{2-8}alkynyl, haloC_{2-8}alkynyl, $(CH_2)_mOR^f$, $OC(O)R^g$, SR^f, CN, NO_2, CO_2R^f, $CONR^fR^f$, $C(O)R^f$, $OC(O)NR^fR^f$, $(CH_2)_mNR^fR^f$, $NR^fC(O)R^g$, $NR^fC(O)_2R^g$, $NR^fC(O)NR^fR^f$, $S(O)R^g$, $S(O)_2R^g$, $NR^fS(O)_2R^g$, $S(O)_2NR^fR^f$, N_3, heteroaryl optionally substituted with one to three R^h, and heterocycloalkyl optionally substituted with one to three R^h where m is selected from the group consisting of 0, 1, 2, 3, 4, 5, and 6;

each R^h is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, OR^j, OC(O)R, SR^j, NO_2, CO_2R^j, $CONR^jR^j$, $C(O)R^j$, $OC(O)NR^jR^j$, NR^jR^j, $NR^jC(O)R^t$, $NR^jC(O)_2R^t$, $NR^jC(O)NR^jR^j$, $S(O)R^t$, $S(O)_2R^t$, $NR^jS(O)_2R^t$, and $S(O)_2NR^jR^j$;

R^d, R^f, and R^j are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl; and

R^e, R^g, and R^t are each independently selected from the group consisting of C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl;

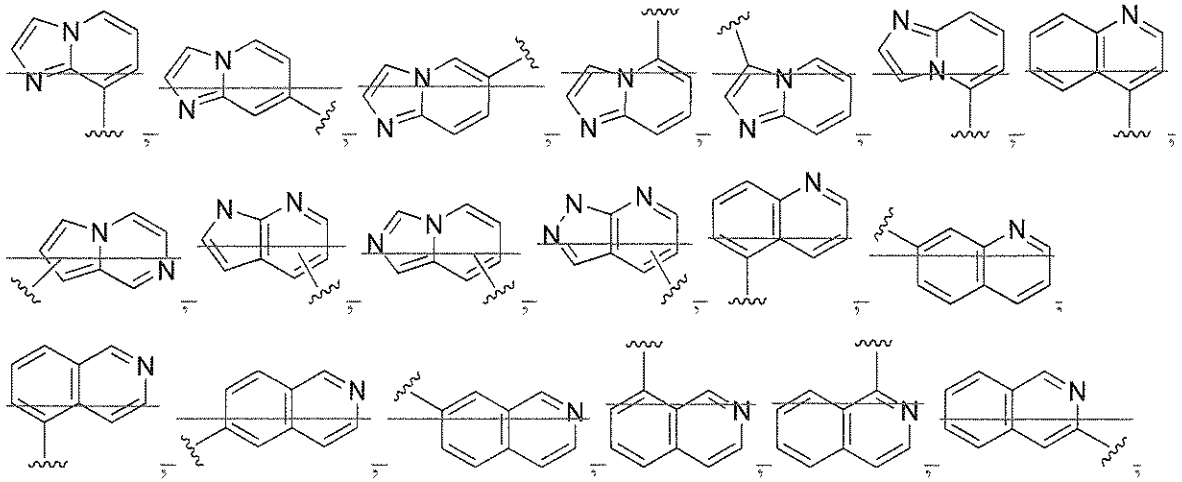
provided that X and Y are not both O; and

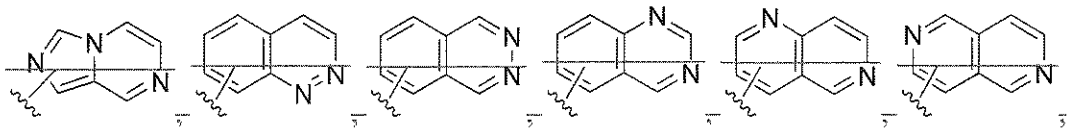
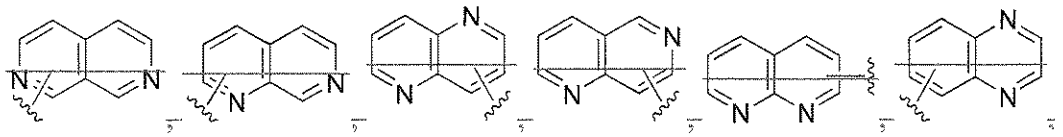
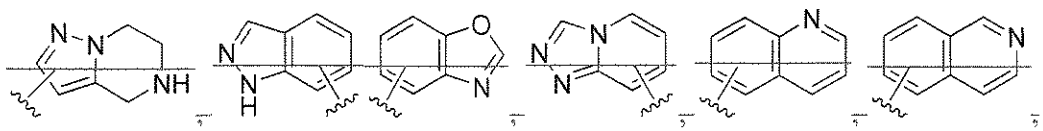
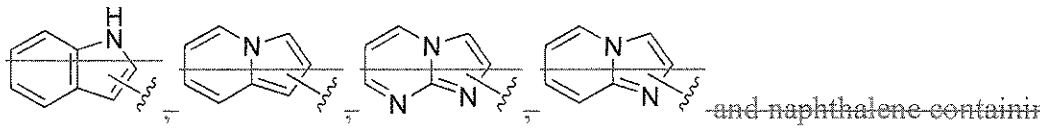
provided that when X is O, R^{1b} is not OH;

~~provided that when Y is O, and n is 0, R^8 is not OH; and~~

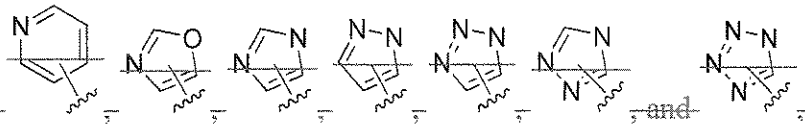
~~provided that when R^6 and R^7 together are oxo, Y is CH_2, X is O or CH_2, and R^5 is H, halo, OH, CHO, or OCH_3, then Q is V or W;~~

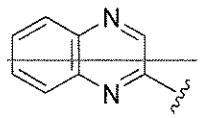
~~V is selected from the group consisting of~~



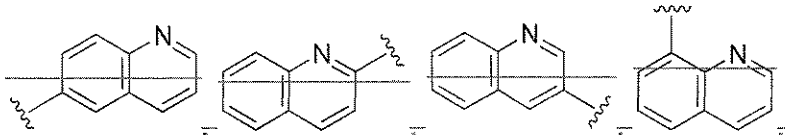
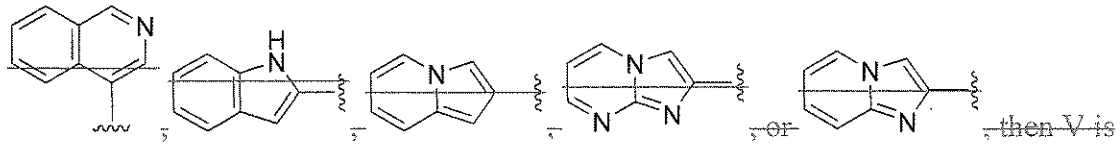





~~and naphthalene containing three to four ring nitrogen atoms; wherein V is optionally substituted with one to three R^a; and~~

~~W is selected from the group consisting of pyridin-2-yl, pyridin-3-yl, and pyridine-4-yl,~~  ~~, and~~ ~~, wherein W is optionally substituted with one to three R^a or is substituted with one to three R^a when W is pyridin-2-yl, pyridin-3-yl, or pyridine-4-yl, and wherein the wavy line signifies the point of attachment to Y, provided that when V is~~



~~optionally substituted with one R^a, then at least one of R^2, R^3, R^4, and R^5 is OR^d; and provided that when V is~~

~~, or~~ ~~, then V is substituted with one to three R^a.~~

There is also provided pharmaceutical compositions comprising the allosteric modulators disclosed herein. In another aspect, there is provided a

pharmaceutical composition comprising a compound as disclosed herein or a tautomer or a pharmaceutically acceptable salt thereof. In other embodiments, provided are methods for treating disorders mediated by hemoglobin and methods for increasing tissue oxygenation for treating disorders that would benefit from increased oxygenation, such methods comprising administering the allosteric modulators disclosed herein to a subject in need thereof. In still other embodiments, provided are methods for preparing the allosteric modulators disclosed herein. In another aspect, there is provided a compound as disclosed herein or a pharmaceutical composition as disclosed herein, or a tautomer or pharmaceutically acceptable salt thereof, for use in increasing tissue oxygenation. In yet another aspect, there is provided a compound as disclosed herein or a pharmaceutical composition disclosed herein, or a tautomer or pharmaceutically acceptable salt thereof, for use in the treatment of a condition associated with oxygen deficiency. ~~In a further aspect, there is provided use of a compound as disclosed herein or a tautomer or pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a condition selected from the group consisting of sickle cell disease, cancer, a pulmonary disorder, stroke, high altitude sickness, an ulcer, a pressure sore, Alzheimer's disease, acute respiratory disease syndrome, and a wound.~~ These and other embodiments of the disclosure are more fully described in the description that follows.

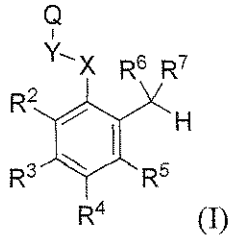
DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

[0004] As used herein, the below terms have the following meanings unless specified otherwise.

WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I)

or a tautomer or pharmaceutically acceptable salt thereof,

wherein Q is aryl substituted with one to three R^a, wherein at least one R^a is heteroaryl and is attached to said Q at the ring atom adjacent to ring atom bearing Y;

Y is O or $CR^{1a}R^{1b}$, where R^{1a} is H or halo and R^{1b} is selected from the group consisting of H, halo, and OH;

X is selected from the group consisting of O and $C(R^9)_2$ where R^9 is independently H or halo;

R^2, R^3, and R^4, are independently selected from the group consisting of hydrogen, halo, R^b, OR^d, $-O(CH_2)_zOR^d$, $-O(CH_2)_zNR^dR^d$, $OC(O)R^e$, SR^d, CN, NO_2, CO_2R^d, $CONR^dR^d$, $C(O)R^d$, $OC(O)NR^dR^d$, NR^dR^d, $NR^dC(O)R^e$, $NR^dC(O)_2R^e$, $NR^dC(O)NR^dR^d$, $S(O)R^e$, $S(O)_2R^e$, $NR^dS(O)_2R^e$, $S(O)_2NR^dR^d$, and N_3, where z is 0, 1, 2, 3, 4, 5, or 6;

R^5 is OH;

R^6 and R^7 together form oxo;

each R^a is independently selected from the group consisting of halo, oxo, R^b, OR^d, $O(CH_2)_uOR^d$, $O(CH_2)_uNR^dR^d$, $O(CH_2)_uNR^dC(O)R^e$, $O(CH_2)_uNR^dC(O)_2R^e$, $O(CH_2)_uNR^dS(O)_2R^e$, NH_2, $-(CH_2)_kOC(O)R^e$, $-(CH_2)_kSR^d$, CN, NO_2, $-(CH_2)_kCO_2(C_{1-8}alkyl)OH$, $-(CH_2)_kCO_2(C_{1-8}alkyl)(heteroaryl)C(O)(C_{1-8}alkyl)$, $-(CH_2)_kCO_2R^d$, $-(CH_2)_kCONR^dR^d$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^e$, $-(CH_2)_kC(O)R^d$, $-(CH_2)_kOC(O)NR^dR^d$, $-NR^d(CH_2)_uOR^d$, $-NR^d(CH_2)_uNR^dR^d$, $-NR^d(CH_2)_uNR^dC(O)R^e$, $-NR^d(CH_2)_uNR^dC(O)_2R^e$, $-NR^d(CH_2)_uNR^dS(O)_2R^e$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^d$, $-(CH_2)_kNR^dC(O)NR^dR^d$, $-(CH_2)_kS(O)R^e$, $-(CH_2)_kS(O)_2R^e$, $-(CH_2)_kNR^dS(O)_2R^e$, $-(CH_2)_kS(O)_2NR^dR^d$, N_3, $-(CH_2)_k$aryl optionally substituted with one to three R^c, $-NR^d(CH_2)_k$aryl

optionally substituted with one to three R^c, *-*$(CH_2)_k$*heteroaryl substituted with one to three* R^c, $-NR^d(CH_2)_k$heteroaryl optionally substituted with one to three R^c, $-(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c, and $-NR^d(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c where k is 0, 1, 2, 3, 4, 5, or 6 and u is 1, 2, 3, 4, 5, or 6;

each R^b is independently selected from the group consisting of C_{1-8}alkyl, C_{2-8}alkenyl, and C_{2-8}alkynyl, each optionally independently substituted with one to three halo, OR^d, or NR^dR^d;

each R^c is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8}alkenyl, haloC_{2-8}alkenyl, C_{2-8}alkynyl, haloC_{2-8}alkynyl, $(CH_2)_mOR^f$, $OC(O)R^g$, SR^f, CN, NO_2, CO_2R^f, $CONR^fR^f$, $C(O)R^f$, $OC(O)NR^fR^f$, $(CH_2)_mNR^fR^f$, $NR^fC(O)R^g$, $NR^fC(O)_2R^g$, $NR^fC(O)NR^fR^f$, $S(O)R^g$, $S(O)_2R^g$, $NR^fS(O)_2R^g$, $S(O)_2NR^fR^f$, N_3, heteroaryl optionally substituted with one to three R^h, and heterocycloalkyl optionally substituted with one to three R^h where m is selected from the group consisting of 0, 1, 2, 3, 4, 5, and 6;

each R^h is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, OR^j, $OC(O)R$, SR^j, NO_2, CO_2R^j, $CONR^jR^j$, $C(O)R^j$, $OC(O)NR^jR^j$, NR^jR^j, $.NR^jC(O)R^t$, $NR^jC(O)_2R^t$, $NR^jC(O)NR^jR^j$, $S(O)R^t$, $S(O)_2R^t$, $NR^jS(O)_2R^t$, and $S(O)_2NR^jR^j$;

R^d, R^f, and R^j are each independently selected from the group consisting of hydrogen, C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8}alkenyl, haloC_{2-8}alkenyl, C_{2-8}alkynyl, and haloC_{2-8}alkynyl; and

R^e, R^g, and R^t are each independently selected from the group consisting of C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8}alkenyl, haloC_{2-8}alkenyl, C_{2-8}alkynyl, and haloC_{2-8}alkynyl;

provided that X and Y are not both O; and

provided that when X is O, R^{1b} is not OH.

2. A compound according to claim 1, or a tautomer or pharmaceutically acceptable salt thereof, wherein:

Y is CH_2; and X is O.

3. A compound according to claim 1, or a tautomer or pharmaceutically acceptable salt thereof, wherein:

Y is CH_2; and X is CH_2.

4. A compound according to any one of claims 1 to 3 or a tautomer or pharmaceutically acceptable salt thereof, wherein the at least one R^a heteroaryl is substituted with at least one C_{1-8}alkyl.

5. A compound according to claim 4 or a tautomer or pharmaceutically acceptable salt thereof, wherein the at least one R^a heteroaryl is substituted with at least one methyl.

6. A compound according to claim 4 or a tautomer or pharmaceutically acceptable salt thereof, wherein the at least one R^a is pyrazolyl substituted with at least one C_{1-8}alkyl.

7. A compound according to any one of claims 1 to 6, wherein R^2 and R^3 are hydrogen.

8. A pharmaceutical composition comprising a compound of any one of claims 1 to 6 or a tautomer or pharmaceutically acceptable salt thereof.

9. A compound of any one of claims 1 to 6, or a pharmaceutical composition of claim 8, or a tautomer or a pharmaceutically acceptable salt thereof, for use in increasing tissue oxygenation.

10. A compound of any one of claims 1 to 6, or a pharmaceutical composition of claim 8, or a tautomer or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition associated with oxygen deficiency.

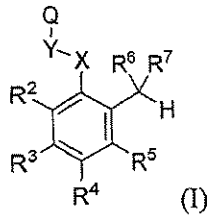
11. The compound of claim 10, wherein the condition is selected from the group consisting of sickle cell disease, cancer, a pulmonary disorder, stroke, high altitude sickness, an ulcer, a pressure sore, Alzheimer's disease, acute respiratory disease syndrome, and a wound.

12. The compound of claim 10, wherein the condition is sickle cell disease.

13. The compound of claim 10, wherein the condition is pulmonary disorder.

WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I)

or a tautomer or pharmaceutically acceptable salt thereof,

wherein Q is selected from the group consisting of aryl, heteroaryl, and heterocycloalkyl, each optionally substituted with one to three R^a;

Y is O or $CR^{1a}R^{1b}$, where R^{1a} is H or halo and R^{1b} is selected from the group consisting of H, halo, and OH;

X is selected from the group consisting of O, $>CH(CH_2)_nR^8$, and $C(R^9)_2$ where n is 0 or 1, R^8 is OH, and R^9 is independently H or halo; or Y-X taken together is -NHC(O)- or -C(O)NH-;

R^2, R^3, R^4, and R^5 are independently selected from the group consisting of hydrogen, halo, R^b, OR^d, $-O(CH_2)_zOR^d$, $-O(CH_2)_zNR^dR^d$, $OC(O)R^e$, SR^d, CN, NO_2, CO_2R^d, $CONR^dR^d$, $C(O)R^d$, $OC(O)NR^dR^d$, NR^dR^d, $NR^dC(O)R^e$, $NR^dC(O)_2R^e$, $NR^dC(O)NR^dR^d$, $S(O)R^e$, $S(O)_2R^e$, $NR^dS(O)_2R^e$, $S(O)_2NR^dR^d$, and N_3, where z is 0, 1, 2, 3, 4, 5, or 6; or R^5 is $-(CH_2)_pR^{5a}$ where p is 0 or 1 and R^{5a} is OH;

R^6 and R^7 together form oxo or an aldehyde protecting group, or R^6 together with R^{1b}, R^8, or R^5 forms a cyclic ether where one of R^{1b}, R^8, or R^{5a} is O, R^6 is a bond, and R^7 is selected from the group consisting of OH, C_{1-8}alkoxy, and haloC_{1-8}alkoxy;

each R^a is independently selected from the group consisting of halo, oxo, R^b, OR^d, $O(CH_2)_uOR^d$, $O(CH_2)_uNR^dR^d$, $O(CH_2)_uNR^dC(O)R^e$, $O(CH_2)_uNR^dC(O)_2R^e$, $O(CH_2)_uNR^dS(O)_2R^e$, NH_2, $-(CH_2)_kOC(O)R^e$, $-(CH_2)_kSR^d$, CN, NO_2, $-(CH_2)_kCO_2(C_{1-8}alkyl)OH$, $-(CH_2)_kCO_2(C_{1-8}alkyl)(heteroaryl)C(O)(C_{1-8}alkyl)$, $-(CH_2)_kCO_2R^d$, $-(CH_2)_kCONR^dR^d$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^e$, $-(CH_2)_kC(O)R^d$, $-(CH_2)_kOC(O)NR^dR^d$, $-NR^d(CH_2)_uOR^d$, $-NR^d(CH_2)_uNR^dR^d$, $-NR^d(CH_2)_uNR^dC(O)R^e$,

$-NR^d(CH_2)_uNR^dC(O)_2R^e$, $-NR^d(CH_2)_uNR^dS(O)_2R^e$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^d$, $-(CH_2)_kNR^dC(O)NR^dR^d$, $-(CH_2)_kS(O)R^e$, $-(CH_2)_kS(O)_2R^e$, $-(CH_2)_kNR^dS(O)_2R^e$, $-(CH_2)_kS(O)_2NR^dR^d$, N_3, $-(CH_2)_k$aryl optionally substituted with one to three R^c, $-NR^d(CH_2)_k$aryl optionally substituted with one to three R^c, $-(CH_2)_k$heteroaryl optionally substituted with one to three R^c, $-NR^d(CH_2)_k$heteroaryl optionally substituted with one to three R^c, $-(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c, and $-NR^d(CH_2)_k$heterocycloalkyl optionally substituted with one to three R^c where k is 0, 1, 2, 3, 4, 5, or 6 and u is 1, 2, 3, 4, 5, or 6;

each R^b is independently selected from the group consisting of C_{1-8}alkyl, C_{2-8}alkenyl, and C_{2-8} alkynyl, each optionally independently substituted with one to three halo, OR^d, or NR^dR^d;

each R^c is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8}alkenyl, haloC_{2-8} alkenyl, C_{2-8}alkynyl, haloC_{2-8}alkynyl, $(CH_2)_mOR^f$, $OC(O)R^g$, SR^f, CN, NO_2, CO_2R^f, $CONR^fR^f$, $C(O)R^f$, $OC(O)NR^fR^f$, $(CH_2)_mNR^fR^f$, $NR^fC(O)R^g$, $NR^fC(O)_2R^g$, $NR^fC(O)NR^fR^f$, $S(O)R^g$, $S(O)_2R^g$, $NR^fS(O)_2R^g$, $S(O)_2NR^fR^f$, N_3, heteroaryl optionally substituted with one to three R^h, and heterocycloalkyl optionally substituted with one to three R^h where m is selected from the group consisting of 0, 1, 2, 3, 4, 5, and 6;

each R^h is independently selected from the group consisting of halo, C_{1-8}alkyl, haloC_{1-8}alkyl, OR^j, OC(O)R, SR^j, NO_2, CO_2R^j, $CONR^jR^j$, $C(O)R^j$, $OC(O)NR^jR^j$, NR^jR^j, $NR^jC(O)R^t$, $NR^jC(O)_2R^t$, $NR^jC(O)NR^jR^j$, $S(O)R^t$, $S(O)_2R^t$, $NR^jS(O)_2R^t$, and $S(O)_2NR^jR^j$;

R^d, R^f, and R^j are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl; and

R^e, R^g, and R^t are each independently selected from the group consisting of C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl;

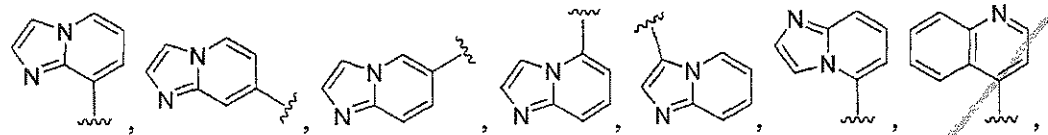
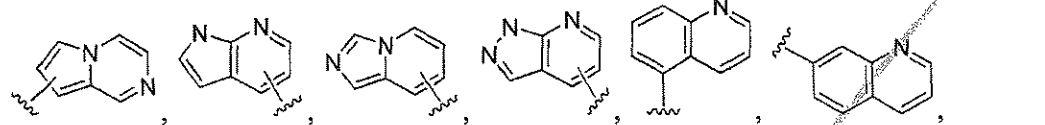
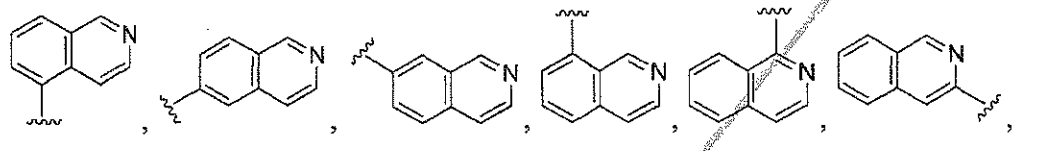
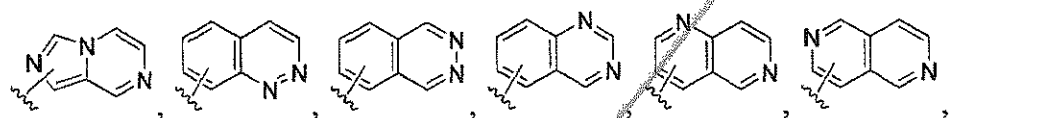
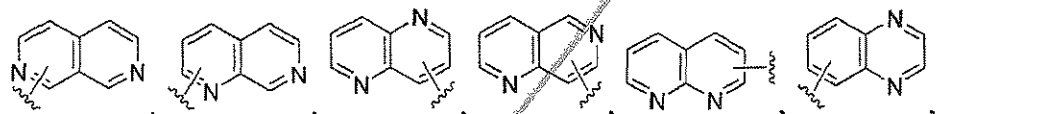
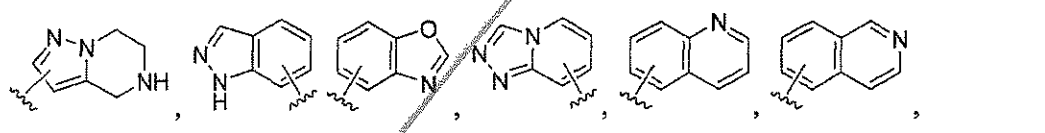
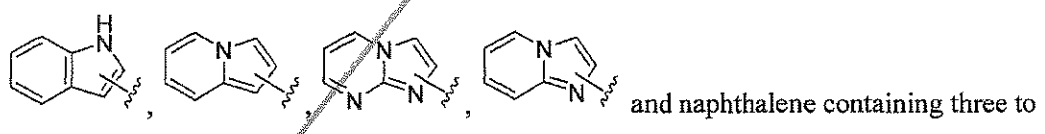
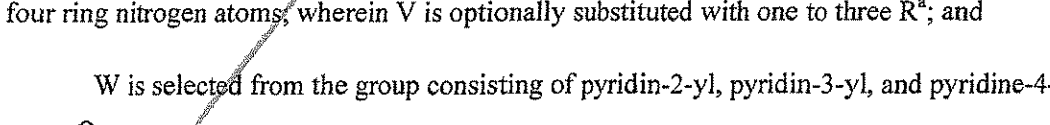
provided that X and Y are not both O;

provided that when X is O, R^{1b} is not OH;

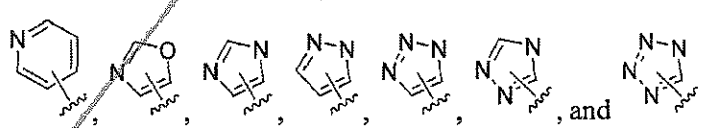
provided that when Y is O, and n is 0, R^8 is not OH; and

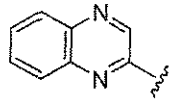
provided that when R^6 and R^7 together are oxo, Y is CH_2, X is O or CH_2, and R^5 is H, halo, OH, CHO, or OCH_3, then Q is V or W;

V is selected from the group consisting of

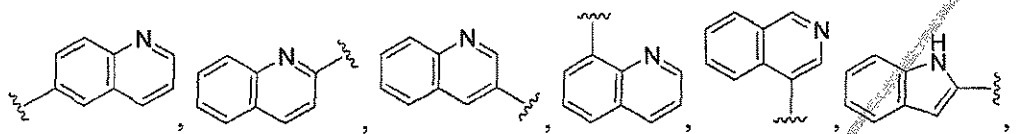









and naphthalene containing three to four ring nitrogen atoms; wherein V is optionally substituted with one to three R^a; and

W is selected from the group consisting of pyridin-2-yl, pyridin-3-yl, and pyridine-4-yl, , and , wherein W is optionally substituted with one to three R^a or is substituted with one to three R^a when W is pyridin-2-yl, pyridin-3-yl, or pyridine-4-yl, and wherein the wavy line signifies the point of attachment to Y, provided that when V is



optionally substituted with one R^a, then at least one of R^2, R^3, R^4, and R^5 is OR^d; and provided that when V is



, then V is substituted with one to three R^a.

2. A compound according to claim 1, wherein:

Y is O or CH_2;

X is O or CH_2;

Q is selected from the group consisting of:

iii) imidazopyridinyl, methylimidazopyridinyl, indazolyl, pyrrolopyridinyl, pyrrolopyrazinyl, pyrazolopyridinyl, pyrazolopyrazinyl, and quinolinyl, each of which is optionally substituted with one to three R^a; wherein

R^2, R^3, R^4, and R^5, are independently selected from the group consisting of hydrogen, halo, R^b, OR^d, $O(CH_2)_zOR^d$, $O(CH_2)_zNR^dR^d$, $OC(O)R^e$, SR^d, CN, NO_2, CO_2R^d, $CONR^dR^d$, $C(O)R^d$, $OC(O)NR^dR^d$, NR^dR^d, $NR^dC(O)R^e$, $NR^dC(O)_2R^e$, $NR^dC(O)NR^dR^d$, $S(O)R^e$, $S(O)_2R^e$, $NR^dS(O)_2R^e$, $S(O)_2NR^dR^d$, and N_3 where z is 1, 2, or 3; and

iv) pyridinyl and piperidinyl, each of which is optionally substituted with one to three R^a; wherein

R^2, R^3, and R^4 are independently selected from the group consisting of hydrogen, halo, R^b, OR^d, $O(CH_2)_zOR^d$, $O(CH_2)_zNR^dR^d$, $OC(O)R^e$, SR^d, CN, NO_2, CO_2R^d, $CONR^dR^d$, $C(O)R^d$, $OC(O)NR^dR^d$, NR^dR^d, $NR^dC(O)R^e$, $NR^dC(O)_2R^e$, $NR^dC(O)NR^dR^d$, $S(O)R^e$, $S(O)_2R^e$, $NR^dS(O)_2R^e$, $S(O)_2NR^dR^d$, and N_3 where z is 1, 2, or 3; and

R^5 is selected from the group consisting of halo and OR^d;

R^6 and R^7 together form oxo or an aldehyde protecting group;

each R^a is independently selected from the group consisting of halo, oxo, R^b, OR^d, $O(CH_2)_uOR^d$, $O(CH_2)_uNR^dR^d$, $O(CH_2)_uNR^dC(O)R^e$, $O(CH_2)_uNR^dC(O)_2R^e$, $O(CH_2)_uNR^dS(O)_2R^e$, NH_2, $-(CH_2)_kOC(O)R^e$, $-(CH_2)_kSR^d$, CN, NO_2, $-(CH_2)_kCO_2(C_{1-8}alkyl)OH$, $-(CH_2)_kCO_2(C_{1-8}alkyl)(heteroaryl)C(O)(C_{1-8}alkyl)$, $-(CH_2)_kCO_2R^d$, $-(CH_2)_kCONR^dR^d$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^e$, $-(CH_2)_kC(O)R^d$, $-(CH_2)_kOC(O)NR^dR^d$, $-NR^d(CH_2)_uOR^d$, $-NR^d(CH_2)_uNR^dR^d$, $-NR^d(CH_2)_uNR^dC(O)R^e$, $-NR^d(CH_2)_uNR^dC(O)_2R^e$, $-NR^d(CH_2)_uNR^dS(O)_2R^e$, $-(CH_2)_kNR^dC(O)R^e$, $-(CH_2)_kNR^dC(O)_2R^d$, $-(CH_2)_kNR^dC(O)NR^dR^d$, $-(CH_2)_kS(O)R^e$, $-(CH_2)_kS(O)_2R^e$, $-(CH_2)_kNR^dS(O)_2R^e$, $-C(O)(CH_2)_kNR^dS(O)_2R^e$, $-(CH_2)_kC(O)NR^dS(O)_2R^e$, $-(CH_2)_kS(O)_2NR^dR^d$, N_3, $-(CH_2)_karyl$ optionally substituted with one to three R^c, $-NR^d(CH_2)_karyl$ optionally substituted with one to three R^c, $-(CH_2)_kheteroaryl$ optionally substituted with one to three R^c, $-NR^d(CH_2)_kheteroaryl$ optionally substituted with one to three R^c, $-(CH_2)_kheterocycloalkyl$ optionally substituted with one to three R^c, and $-NR^d(CH_2)_kheterocycloalkyl$ optionally substituted with one to three R^c where k is 0, 1, 2, 3, 4, 5, or 6 and u is 1, 2, 3, 4, 5, or 6;

each R^b is independently selected from the group consisting of $C_{1-8}alkyl$, $C_{2-8}alkenyl$, and $C_{2-8}alkynyl$, each optionally independently substituted with one to three halo, OR^d, or NR^dR^d;

each R^c is independently selected from the group consisting of halo, $C_{1-8}alkyl$, $haloC_{1-8}alkyl$, $C_{2-8}alkenyl$, $haloC_{2-8}alkenyl$, $C_{2-8}alkynyl$, $haloC_{2-8}alkynyl$, $(CH_2)_mOR^f$, $OC(O)R^g$, SR^f, CN, NO_2, $(CH_2)_mCO_2R^f$, $CONR^fR^f$, $C(O)R^f$, $OC(O)NR^fR^f$, $(CH_2)_mNR^fR^f$, $NR^fC(O)R^g$, $NR^fC(O)_2R^g$, $NR^fC(O)NR^fR^f$, $S(O)R^g$, $S(O)_2R^g$, $NR^fS(O)_2R^g$, $S(O)_2NR^fR^f$, N_3, $(R^f)_mSiC_{1-8}alkyl$, heteroaryl optionally substituted with one to three R^h, cycloalkyl optionally substituted with one to three R^h, and heterocycloalkyl optionally substituted with one to three R^h where m is selected from the group consisting of 0, 1, 2, 3, 4, 5, and 6;

each R^h is independently selected from the group consisting of halo, $C_{1-8}alkyl$, $haloC_{1-8}alkyl$, OR^j, OC(O)R, SR^j, NO_2, CO_2R^j, $CONR^jR^j$, $C(O)R^j$, $OC(O)NR^jR^j$, NR^jR^j, $NR^jC(O)R^t$, $NR^jC(O)_2R^t$, $NR^jC(O)NR^jR^j$, $S(O)R^t$, $S(O)_2R^t$, $NR^jS(O)_2R^t$, and $S(O)_2NR^jR^j$;

R^d, R^f, and R^j are each independently selected from the group consisting of hydrogen, C_{1-8} alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl; and

R^e, R^g, and R^i are each independently selected from the group consisting of C_{1-8}alkyl, haloC_{1-8}alkyl, C_{2-8} alkenyl, haloC_{2-8}alkenyl, C_{2-8} alkynyl, and haloC_{2-8}alkynyl.

3. A compound according to claim 1, wherein:

Y is CH_2; and X is CH_2.

4. A compound according to claim 2, or a tautomer or pharmaceutically acceptable salt thereof, wherein Q is selected from the group consisting of imidazo[1,5-a]pyridin-8-yl, imidazo[1,5-a]pyridin-6-yl, imidazo[1,5-a]pyridin-5-yl, imidazo[1,2-a]pyridin-8-yl, imidazo[1,2-a]pyridin-7-yl, imidazo[1,2-a]pyridin-6-yl, imidazo[1,2-a]pyridin-5-yl, imidazo[1,2-a]pyridin-3-yl, 8-methylimidazo[1,2-a]pyridin-2-yl, indazol-4-yl, pyrrolo[2,3-b]pyridin-4-yl, pyrrolo[1,2-a]pyrazin-6-yl, pyrrolo[1,2-a]pyrazin-4-yl, pyrazolo[3,4-b]pyridin-4-yl, pyrazolo[1,5-a]pyrazin-3-yl, and quinolin-5-yl, each of which is optionally substituted with one to three R^a.

5. A compound according to claim 4, or a tautomer or pharmaceutically acceptable salt thereof, wherein R^2 is selected from the group consisting of H and OR^d;

R^3 is selected from the group consisting of H, CN, halo, and OR^d;

R^4 is selected from the group consisting of H, CN, and OR^d: and

R^5 is H.

6. A compound according to claim 5, or a tautomer or pharmaceutically acceptable salt thereof, wherein R^4 is methoxy.

7. A compound according to claim 3, or a tautomer or pharmaceutically acceptable salt thereof, wherein Q is selected from the group consisting of pyridine-3-yl and piperidin-1-yl.

8. A compound according to claim 7, or a tautomer or pharmaceutically acceptable salt thereof, wherein R^5 is selected from the group consisting of hydroxy and fluoro.

9. A compound according to any of the preceeding claims, or a tautomer or pharmaceutically acceptable salt thereof, wherein R^6 and R^7 together form oxo.

10. A compound according to claim 1 selected from the group consisting of:

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

4-formyl-3-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-3-ylmethoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(quinolin-5-ylmethoxy)benzaldehyde,

5-bromo-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-chloro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-fluoro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-3-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methylbenzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-4-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,5-a]pyridin-5-ylmethoxy)benzonitrile,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-ethyl-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

5-methoxy-2-((1-methyl-1H-indazol-4-yl)methoxy)benzaldehyde,

5-methoxy-2-((8-methylimidazo[1,2-a]pyridin-2-yl)methoxy)benzaldehyde,

2-((1H-indazol-4-yl)methoxy)-5-methoxybenzaldehyde,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carbonitrile,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carboxamide,

2-((1H-pyrazolo[3,4-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(pyrazolo[1,5-a]pyrazin-3-ylmethoxy)benzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

3-(imidazo[1,2-a]pyridin-8-ylmethyl)-1,3-dihydroisobenzofuran-1-ol,

2-(imidazo[1,2-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

N-(2-formyl-4-methoxyphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

N-(2-formylphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

2-formyl-N-(imidazo[1,2-a]pyridin-8-yl)benzamide,

2-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)-5-methoxybenzaldehyde,

2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde

2-((3-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-((4-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-hydroxy-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-hydroxy-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde, and

1-(2-formyl-3-hydroxyphenethyl)piperidine-4-carboxylic acid

or a tautomer or pharmaceutically acceptable salt thereof.

11. A compound according to claim 1 selected from the group consisting of:

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(quinolin-5-ylmethoxy)benzaldehyde,

5-methoxy-2-((1-methyl-1H-indazol-4-yl)methoxy)benzaldehyde,

5-methoxy-2-((8-methylimidazo[1,2-a]pyridin-2-yl)methoxy)benzaldehyde,

2-((1H-indazol-4-yl)methoxy)-5-methoxybenzaldehyde,

2-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)-5-methoxybenzaldehyde,

2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-((3-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-((4-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-hydroxy-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-hydroxy-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde, and

1-(2-formyl-3-hydroxyphenethyl)piperidine-4-carboxylic acid,

or a tautomer or pharmaceutically acceptable salt thereof.

12. A pharmaceutical composition comprising a compound of any of the preceding claims or a tautomer or pharmaceutically acceptable salt thereof.

13. A compound of any of claims 1 to 11 or a tautomer or pharmaceutically acceptable salt thereof for use in increasing tissue oxygenation.

14. A compound of any of claims 1 to 11 or a tautomer or pharmaceutically acceptable salt thereof for use in the treatment of a condition associated with oxygen deficiency.

15. The compound of claim 14, wherein the condition is selected from the group consisting of sickle cell disease, cancer, a pulmonary disorder, stroke, high altitude sickness, an ulcer, a pressure sore, Alzheimer's disease, acute respiratory disease syndrome, and a wound.

16. The compound of any of claims 13-15, wherein the compound is selected from the group consisting of:

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

4-formyl-3-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-2-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-3-ylmethoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(quinolin-5-ylmethoxy)benzaldehyde,

5-bromo-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-chloro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-fluoro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-3-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methylbenzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-4-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,5-a]pyridin-5-ylmethoxy)benzonitrile,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-ethyl-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

5-methoxy-2-((1-methyl-1H-indazol-4-yl)methoxy)benzaldehyde,

5-methoxy-2-((8-methylimidazo[1,2-a]pyridin-2-yl)methoxy)benzaldehyde,

2-((1H-indazol-4-yl)methoxy)-5-methoxybenzaldehyde,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carbonitrile,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carboxamide,

2-((1H-pyrazolo[3,4-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(pyrazolo[1,5-a]pyrazin-3-ylmethoxy)benzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

3-(imidazo[1,2-a]pyridin-8-ylmethyl)-1,3-dihydroisobenzofuran-1-ol,

2-(imidazo[1,2-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

N-(2-formyl-4-methoxyphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

N-(2-formylphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

2-formyl-N-(imidazo[1,2-a]pyridin-8-yl)benzamide,

5-methoxy-2-(pyridin-3-ylmethoxy)benzaldehyde,

4-((2-formyl-3-hydroxyphenoxy)methyl)benzoic acid,

2-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)-5-methoxybenzaldehyde,

2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-((3-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-((4-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

methyl 4-((2-formylphenoxy)methyl)benzoate,

4-((2-formylphenoxy)methyl)benzoic acid,

methyl 3-((2-formylphenoxy)methyl)benzoate,

2-hydroxy-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-hydroxy-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde, and

1-(2-formyl-3-hydroxyphenethyl)piperidine-4-carboxylic acid

or a tautomer or pharmaceutically acceptable salt thereof.

17. The compound of any of claims 13-15, wherein the compound is selected from the group consisting of:

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

4-formyl-3-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-2-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-8-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-7-ylmethoxy)-5-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-3-ylmethoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(quinolin-5-ylmethoxy)benzaldehyde,

5-bromo-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-chloro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

4-fluoro-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-3-methoxybenzaldehyde,

2-(imidazo[1,2-a]pyridin-8-ylmethoxy)-5-methylbenzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-4-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-4-methoxybenzaldehyde,

2-(imidazo[1,5-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,5-a]pyridin-5-ylmethoxy)benzonitrile,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-ethyl-2-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzaldehyde,

5-methoxy-2-((1-methyl-1H-indazol-4-yl)methoxy)benzaldehyde,

5-methoxy-2-((8-methylimidazo[1,2-a]pyridin-2-yl)methoxy)benzaldehyde,

2-((1H-indazol-4-yl)methoxy)-5-methoxybenzaldehyde,

2-((1H-pyrrolo[2,3-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carbonitrile,

6-((2-formyl-4-methoxyphenoxy)methyl)pyrrolo[1,2-a]pyrazine-7-carboxamide,

2-((1H-pyrazolo[3,4-b]pyridin-4-yl)methoxy)-5-methoxybenzaldehyde,

5-methoxy-2-(pyrazolo[1,5-a]pyrazin-3-ylmethoxy)benzaldehyde,

5-methoxy-2-(pyrrolo[1,2-a]pyrazin-6-ylmethoxy)benzaldehyde,

2-(imidazo[1,5-a]pyridin-6-ylmethoxy)-5-methoxybenzaldehyde,

3-formyl-4-(imidazo[1,2-a]pyridin-8-ylmethoxy)benzonitrile,

3-(imidazo[1,2-a]pyridin-8-ylmethyl)-1,3-dihydroisobenzofuran-1-ol,

2-(imidazo[1,2-a]pyridin-5-ylmethoxy)-5-methoxybenzaldehyde,

N-(2-formyl-4-methoxyphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

N-(2-formylphenyl)imidazo[1,2-a]pyridine-8-carboxamide,

2-formyl-N-(imidazo[1,2-a]pyridin-8-yl)benzamide,

5-methoxy-2-(pyridin-3-ylmethoxy)benzaldehyde,

4-((2-formyl-3-hydroxyphenoxy)methyl)benzoic acid,

2-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)-5-methoxybenzaldehyde,

2-hydroxy-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-((3-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

2-((4-(2H-tetrazol-5-yl)benzyl)oxy)-6-hydroxybenzaldehyde,

methyl 4-((2-formylphenoxy)methyl)benzoate,

4-((2-formylphenoxy)methyl)benzoic acid,

methyl 3-((2-formylphenoxy)methyl)benzoate,

2-hydroxy-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-hydroxy-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-(3,3,3-trifluoropropyl)-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde,

2-fluoro-6-((2-(1-isopropyl-1H-pyrazol-5-yl)pyridin-3-yl)methoxy)benzaldehyde, and

1-(2-formyl-3-hydroxyphenethyl)piperidine-4-carboxylic acid

or a tautomer or pharmaceutically acceptable salt thereof.

18. Use of a compound of any of claims 1 to 11 or a tautomer or pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a condition selected from the group consisting of sickle cell disease, cancer, a pulmonary disorder, stroke, high altitude sickness, an ulcer, a pressure sore, Alzheimer's disease, acute respiratory disease syndrome, and a wound.