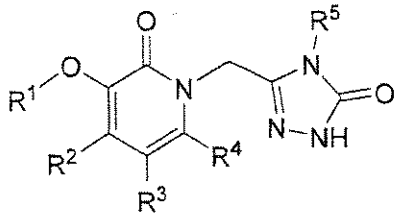
US 2007/0021442 and WO 2007/015812 disclose certain substituted aromatic compounds. The compounds are HIV reverse transcriptase inhibitors suitable, for example, for the treatment of infection by HIV.

SUMMARY ~~OF THE INVENTION~~

The present disclosure~~invention~~ is directed to certain 3-(optionally substituted phenoxy)-1-[(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methyl])-pyridin-2(1*H*)-one compounds and their use in the inhibition of HIV reverse transcriptase, the prophylaxis of infection by HIV, the treatment of infection by HIV, and the prophylaxis, treatment, and delay in the onset or progression of AIDS and/or ARC. More particularly, the present disclosure~~invention~~ includes compounds of Formula I and pharmaceutically acceptable salts thereof:



(I),

wherein:

R^1 is C_{1-10} alkyl, CycA, or AryA;

CycA is C_{3-8} cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 4 substituents, each of which is independently halogen, C_{1-6} alkyl, OH, O-C_{1-6} alkyl, C_{1-6} haloalkyl, or O-C_{1-6} haloalkyl;

AryA is aryl which is optionally substituted with a total of from 1 to 6 substituents, wherein:

(i) from zero to 6 substituents are each independently:

(1) C_{1-6} alkyl,

(2) C_{1-6} haloalkyl,

(3) C_{1-6} alkyl substituted with from 1 to 3 substituents each of which is independently OH, O-C_{1-6} alkyl, O-C_{1-6} haloalkyl, CN, NO_2, $N(R^A)R^B$, $C(O)N(R^A)R^B$, $C(O)R^A$, CO_2R^A, SR^A, $S(O)R^A$, $S(O)_2R^A$, $S(O)_2N(R^A)R^B$, $N(R^A)C(O)R^B$, $N(R^A)CO_2R^B$, $N(R^A)S(O)_2R^B$, $N(R^A)S(O)_2N(R^A)R^B$, $OC(O)N(R^A)R^B$, $N(R^A)C(O)N(R^A)R^B$, or $N(R^A)C(O)C(O)N(R^A)R^B$,

(4) C_{2-6} alkenyl,

(5) C_{2-6} alkenyl substituted with from 1 to 3 substituents each of which is independently OH, O-C_{1-6} alkyl, O-C_{1-6} haloalkyl, CN, NO_2, $N(R^A)R^B$, $C(O)N(R^A)R^B$, $C(O)R^A$, CO_2R^A, SR^A, $S(O)R^A$, $S(O)_2R^A$, $S(O)_2N(R^A)R^B$, $N(R^A)C(O)R^B$, $N(R^A)CO_2R^B$, $N(R^A)S(O)_2R^B$,

(31) $N(R^A)S(O)_2N(R^C)R^D$,

(32) $N(R^A)C(O)N(R^C)R^D$,

(33) $N(R^A)C(O)$-$C(O)N(R^C)R^D$,

(34) C_{3-8} cycloalkyl,

(35) O-C_{3-8} cycloalkyl,

(36) AryX, or

(37) HetX;

wherein AryX independently has the same definition as AryQ, and HetX independently has the same definition as HetQ;

R^4 is H, C_{1-6} alkyl, AryZ, HetZ, halogen, CN, or C_{1-6} fluoroalkyl;

AryZ independently has the same definition as AryQ;

HetZ independently has the same definition as HetQ;

R^5 is H or C_{1-6} alkyl;

each aryl is independently (i) phenyl, (ii) a 9- or 10-membered bicyclic, fused carbocylic ring system in which at least one ring is aromatic, or (iii) an 11- to 14-membered tricyclic, fused carbocyclic ring system in which at least one ring is aromatic;

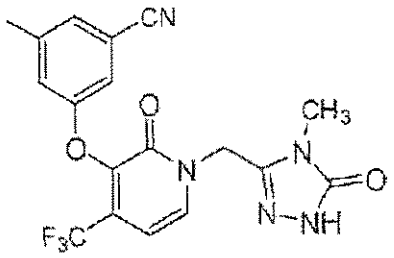
each heteroaryl is independently (i) a 5- or 6-membered heteroaromatic ring containing from 1 to 4 heteroatoms independently selected from N, O and S, wherein each N is optionally in the form of an oxide, or (ii) a 9- or 10-membered heterobicyclic, fused ring system containing from 1 to 6 heteroatoms independently selected from N, O and S, wherein either one or both of the rings contain one or more of the heteroatoms, at least one ring is aromatic, each N is optionally in the form of an oxide, and each S in a ring which is not aromatic is optionally S(O) or $S(O)_2$;

each R^A is independently H or C_{1-6} alkyl;

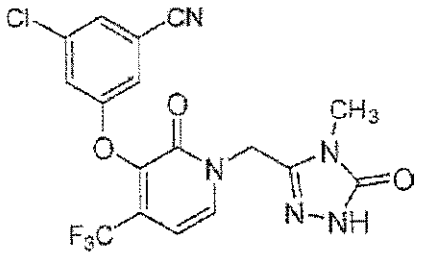
each R^B is independently H or C_{1-6} alkyl; and

each pair of R^C and R^D together with the nitrogen to which they are both attached form a 4- to 7-membered saturated or unsaturated, non-aromatic ring (e.g., a mono-unsaturated ring) which optionally contains a heteroatom in addition to the N to which R^C and R^D are attached, wherein the additional heteroatom is selected from N, O, and S; wherein the ring is optionally substituted with 1 or 2 substituents each of which is independently C_{1-6} alkyl, $C(O)R^A$, $C(O)OR^A$, $C(O)N(R^A)R^B$, or $S(O)_2R^A$; and wherein the optional S in the ring is optionally in the form of S(O) or $S(O)_2$.

In one aspect, there is provided the compound



In another aspect, there is provided the compound



or a pharmaceutically acceptable salt thereof.

The present disclosure~~invention~~ also includes pharmaceutical compositions containing a compound of Formula I or a pharmaceutically acceptable salt thereof. In another aspect, there is provided a pharmaceutical composition comprising an effective amount of the compound as defined herein and a pharmaceutically acceptable carrier. The present disclosure~~invention~~ further includes methods involving compounds of Formula I for the treatment of AIDS, the delay in the onset or progression of AIDS, the prophylaxis of AIDS, the prophylaxis of infection by HIV, and the treatment of infection by HIV.

Other embodiments, aspects, classes, sub-classes and features of the present disclosure~~invention~~ are either further described in or will be apparent from the ensuing description, examples and appended claims.

DETAILED DESCRIPTION OF THE INVENTION

The compounds of Formula I above, and pharmaceutically acceptable salts thereof, are HIV reverse transcriptase inhibitors. The compounds are useful for inhibiting HIV reverse transcriptase and for inhibiting HIV replication *in vitro* and *in vivo*. More particularly, the compounds of Formula I inhibit the polymerase function of HIV-1 reverse transcriptase. Based upon the testing of representative compounds of the invention in the assay set forth in Example 9 below, it is known that compounds of Formula I inhibit the RNA-dependent DNA polymerase activity of HIV-1 reverse transcriptase. Representative compounds of the present invention (see, e.g., the compounds of Examples 1 to 8) also exhibit activity against drug resistant forms of HIV (e.g., mutant strains of HIV-1 in which reverse transcriptase has a mutation at lysine 103 → asparagine (K103N) and/or tyrosine 181 → cysteine (Y181C)), and thus can exhibit decreased cross-resistance against currently approved antiviral therapies.

A first embodiment of the present invention (alternatively referred to herein as "Embodiment E1") is a compound of Formula I (alternatively and more simply referred to as "Compound I"), or a pharmaceutically acceptable salt thereof, wherein each CycQ is independently C_{3-8} cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 4 substituents, each of which is independently halogen, C_{1-4} alkyl, OH, O-C_{1-4} alkyl, C_{1-4} haloalkyl, or O-C_{1-4} haloalkyl; and all other variables in Formula I are as originally defined (i.e., as defined in the Summary of the Invention).

A second embodiment of the present invention (Embodiment E2) is a compound of Formula I, or a pharmaceutically acceptable salt thereof, wherein each CycQ is independently C_{3-7} cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 3 substituents, each of which is independently halogen, C_{1-4} alkyl, OH, O-C_{1-4} alkyl, C_{1-4} haloalkyl, or O-C_{1-4} haloalkyl; and all other variables are as originally defined.

A third embodiment of the present invention (Embodiment E3) is a compound of Formula I, or a pharmaceutically acceptable salt thereof, wherein each CycQ is independently C_{3-7} cycloalkyl, wherein the cycloalkyl is optionally substituted with from 1 to 3 substituents, each of which is independently Cl, Br, F, CH_3, OH, OCH_3, CF_3, or OCF_3; and all other variables are as originally defined.

A fourth embodiment of the present invention (Embodiment E4) is a compound of Formula I, or a pharmaceutically acceptable salt thereof, wherein AryQ is phenyl or naphthyl, wherein the phenyl or naphthyl is optionally substituted with from 1 to 3 substituents each of which is independently halogen, CN, NO_2, C_{1-4} alkyl, C_{1-4} haloalkyl, OH, O-C_{1-4} alkyl, O-C_{1-4} haloalkyl, $N(R^A)R^B$, $C(O)N(R^A)R^B$, $C(O)R^A$, CO_2R^A, SR^A, $S(O)R^A$, SO_2R^A,