optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo;

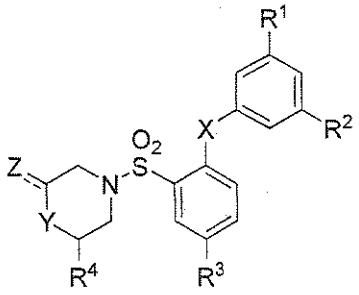
R^1 and R^2 are independently halogen, C_{1-6} alkyl, or C_{1-6} haloalkyl;

R^4 is hydrogen or C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo; and

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

with the proviso that when Y is CH_2, at least one of Z and R^4 is C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo.

[0006a] In one aspect, there is provided a compound of formula **Ia**, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer or tautomer thereof:



Ia

wherein

X is S, SO, or SO_2;

Y and Z are

Y is NR^5; Z is =O, CO_2R^6, or C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo;

R^1 and R^2 are each independently halogen, C_{1-6} alkyl, or C_{1-6} haloalkyl;

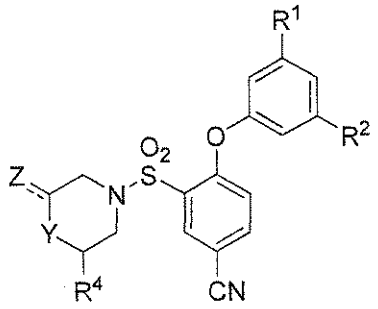
R^3 is CN or NO_2;

R^4 is hydrogen or C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo;

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

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

[0006b] In another aspect, there is provided a compound of the formula **II**, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer or tautomer thereof:



II

wherein

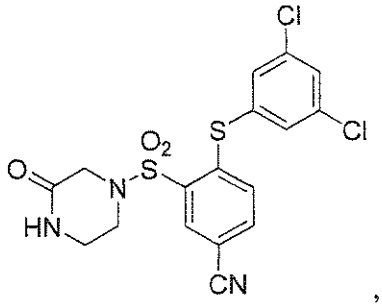
Y is NR^5; Z is =O or C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo;

R^1 and R^2 are each independently halogen, C_{1-6} alkyl, or C_{1-6} haloalkyl;

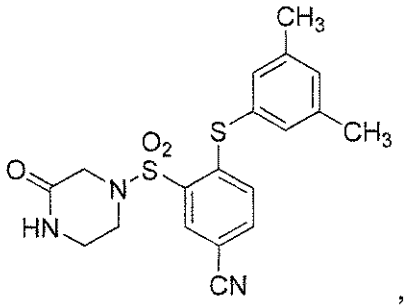
R^4 is hydrogen or C_{1-6} alkyl optionally substituted by aryl, hydroxy, carboxy, alkoxy, carbamoyl, or halo; and

R^5 is hydrogen or C_{1-6} alkyl.

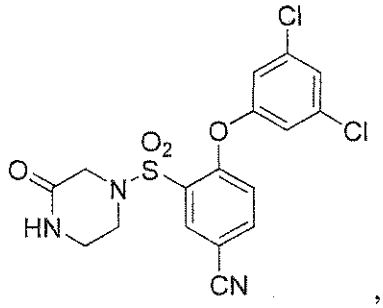
[0006c] In another aspect, there is provided a compound selected from the group consisting of:



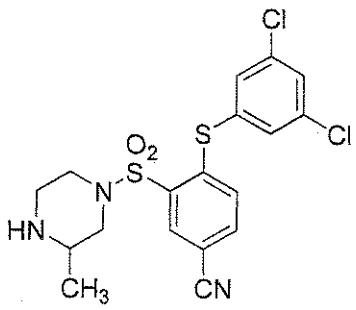
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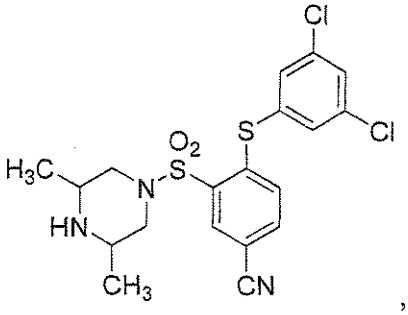


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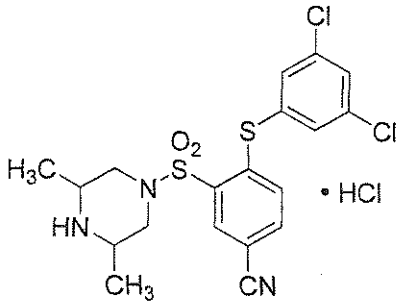


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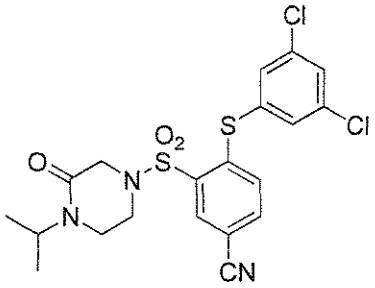




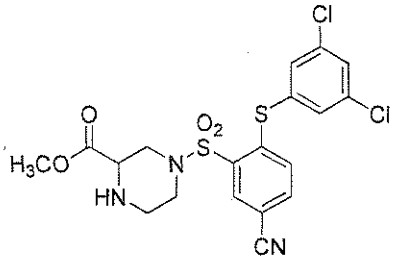
,



,



; and



or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, or tautomer thereof.

[0007] Also provided herein are pharmaceutical compositions comprising a compound disclosed herein, *e.g.*, a compound of Formula Ia, Formula I, or Formula II, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer or tautomer thereof, in combination with one or more pharmaceutically acceptable carriers or excipients.

[0007a] In another aspect, there is provided a pharmaceutical composition comprising the compound as defined above and one or more pharmaceutically acceptable carriers or excipients.

[0008] Further provided herein is a method for modulating CCR3 activity, comprising contacting a CCR3 with a therapeutically effective amount of a compound disclosed herein, *e.g.*, a compound of Formula Ia, Formula I, or Formula II, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer or tautomer thereof.

[0009] Additionally provided herein is a method for treating, preventing, or ameliorating one or more symptoms of a CCR3-mediated disorder, disease, or condition in a subject, comprising administering to the subject a therapeutically effective amount of a compound disclosed herein, *e.g.*, a compound of Formula Ia, Formula I or Formula II, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer or tautomer thereof.

[0009a] In another aspect, there is provided the use of a compound as defined above or the composition as defined above in the manufacture of a medicament for treating, preventing, or ameliorating one or more symptoms of a CCR3-related disorder, disease, or condiiton in a subject.

[0009b] In another aspect, there is provided the use of a compound as defined above or the composition as defined above in the manufacture of a medicament for modulating CCR3 activity, wherein the use comprises contacting a CCR3 receptor with the medicament.

DETAILED DESCRIPTION

[0010] To facilitate understanding of the disclosure set forth herein, a number of terms are defined below.

[0011] Generally, the nomenclature used herein and the laboratory procedures in organic chemistry, medicinal chemistry, and pharmacology described herein are those well known and commonly employed in the art. Unless defined otherwise, all technical and scientific terms used herein generally have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. In the event that there is a plurality of definitions for a term used herein, those in this section prevail unless stated otherwise.

[0012] The term "subject" refers to an animal, including, but not limited to, a primate