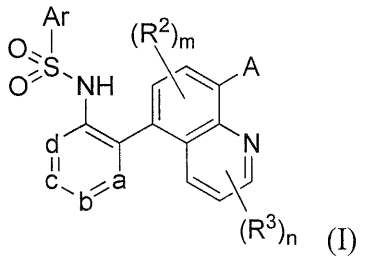
rheumatoid arthritis (Patel DD et. al., *Ann Rheum Dis* 2013), multiple sclerosis (Zepp J, Wu L, and X Li *Trends Immunol* 2011), and psoriasis (Martin DA et. al., *J Invest Dermatol* 2012). Evidence strongly linking IL17 with psoriasis include gene wide association studies that show strong association between psoriasis and genes upstream (IL-23) or downstream (NFκb) of IL17 signaling pathways as well as efficacy in targeting IL17 in a clinical setting (Martin DA et. al., *J. Invest Dermat.* 2012; Papp et. al., *NEJM*, 2012; Papp et. al., *NEJM*, 2012). In addition to enhanced CCL20-mediated chemotaxis, CCR6+ T cells isolated from psoriatic patients preferentially secrete IL-17A, IL22, and TNFα when compared to healthy controls (Kagami, et. al., *J. Invest. Dermatol.*, 2010). Lastly, ccl20 mRNA was up-regulated in lesional psoriatic skin samples (Homey, et. al., *JI*, 2000; Dieu-Nosjean, et. al., *JEM*, 2000). In mice, CCR6 knock-out mice were protected from IL-23 driven psoriasis. Thus, a multitude of evidence in both mice and men suggest a protective role for CCR6 blockade in psoriasis and psoriasis-like models.

[0009] In view of the clinical importance of CCR6, the identification of compounds that modulate CCR6 function represent an attractive avenue into the development of new therapeutic agents. Such compounds and methods for their use are provided herein.

BRIEF SUMMARY ~~OF THE INVENTION~~

[0010] Described herein are compounds having formula (I):



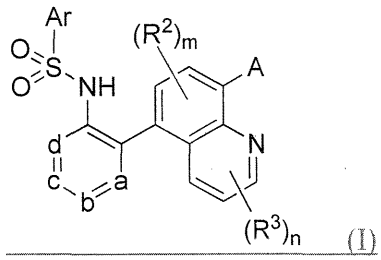
(I)

wherein the ring vertices a, b, c and d; Ar; A; R^2, R^3 and the subscripts m and n have the meanings provided in the Detailed Description below. The compounds have utility in the treatment of diseases or conditions modulated at least in part by CCR6.

[0011] Pharmaceutical compositions of the compounds of formula (I) are also provided.

[0012] Further provided in the present disclosure preparative methods for the synthesis of compounds of formula (I), as well as selected intermediates useful in the preparation.

[0012a] In one aspect of the present disclosure, there is provided a compound having formula (I):



(I)

or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, wherein

A is a carboxylic acid moiety or a carboxylic acid isostere;

ring vertices a, b, c and d are independently selected from N, CH and C(R^1);

each R^1 is independently selected from the group consisting of halogen, CN, -SF_5, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} haloalkyl, -OR^a, -SR^a, -COR^a, -NR^aR^b, and 5- or 6-membered heteroaryl, wherein the alkyl portions of R^1 are optionally further substituted with 1-3 R^a; and optionally, adjacent R^1 members are connected to form an additional 5- or 6-membered ring which is saturated or unsaturated having ring vertices selected from C, O, S and N, wherein the additional 5- or 6-membered ring is optionally substituted with one or two members selected from the group consisting of halogen, hydroxyl, C_{1-4} alkyl, C_{1-4} alkoxy and C_{1-4} haloalkyl;

the subscript m is an integer of from 0 to 2;

the subscript n is an integer of from 0 to 3;

each R^2 and R^3 is independently selected from the group consisting of halogen, CN, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} haloalkyl, aryl, -OR^a, -NR^aR^b and -$N(R^a)$-C_1-C_4 alkylene-OR^b, and wherein the alkyl or aryl portions of R^2 and R^3 are optionally further substituted with 1-3 R^a;

Ar is a 5- or 6-membered aromatic or heteroaromatic ring that is optionally substituted with from 1 to 5 R^4 substituents independently selected from the group consisting of halogen, CN, -SF_5, C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-8} haloalkyl, C_{1-8} hydroxyalkyl, -OR^a, -NR^aR^b, 5- or 6-membered heteroaryl, and 3-, 4-, 5- or 6-membered heterocycloalkane wherein the heteroatoms present as ring vertices of the heteroaryl and heterocycloalkane rings are selected from N, O and

S, and wherein the alkyl, cycloalkyl, aryl, heteroaryl and hetereocycloalkane portions of R^4 are optionally further substituted with 1-3 R^a;

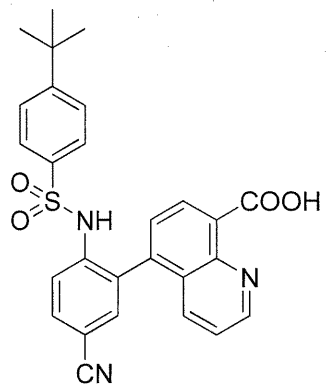
each R^a and R^b is independently selected from the group consisting of hydrogen, hydroxyl, halogen, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} haloalkyl, C_{3-6} cycloalkyl, amino, C_{1-8} alkylamino, and di C_{1-8} alkylamino, or when attached to a nitrogen atom are optionally combined to form a 4- to 7-membered saturated ring, which is optionally substituted with oxo.

[0012b] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound disclosed herein, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, with a pharmaceutically acceptable excipient.

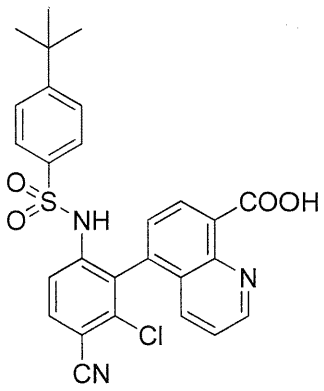
[0012c] In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, in the manufacture of a medicament for treating a disease or condition modulated at least in part by CCR6.

[0012d] In another aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, for use in treating a disease or condition modulated at least in part by CCR6.

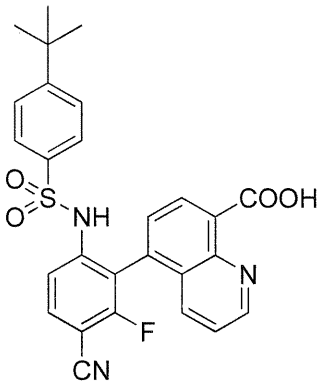
21. A compound of claim **1**, selected from the group consisting of:



,



and



or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof.

22. A pharmaceutical composition comprising a compound of any of claims **1** to **21**, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, with a pharmaceutically acceptable excipient.

23. Use of a compound of any of claims 1 to 21, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, in the manufacture of a medicament for ~~A method of~~ treating a disease or condition modulated at least in part by CCR6~~, comprising administering to a subject in need thereof, a compound of any of claims 11 to 21, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof~~.

24. The use ~~A method~~ in accordance with claim **23**, wherein said disease or condition is an inflammatory disease or condition.

25. The use ~~A method~~ in accordance with claim **23**, wherein said disease or condition is atopic dermatitis.

26. The use ~~A method~~ in accordance with claim **23**, wherein said disease or condition is psoriasis.

27. The use ~~A method~~ in accordance with any of claims **23**, **24**, **25**, or **26**, wherein said compound is a compound of claim **12**, **17**, **19**, **20** or **21**, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof.

28. The use ~~A method~~ in accordance with claim **27**, wherein the compound is a compound of claim **19**, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof.

29. The use ~~A method~~ in accordance with claim **27**, wherein the compound is a compound of claim **20**, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof.

30. A compound of any of claims **1** to **21**, or a pharmaceutically acceptable salt, hydrate, solvate, N-oxide or rotamer thereof, for use in treating a disease or condition modulated at least in part by CCR6.