unlabeled human eotaxin/CCL11. *See,* Iino *et al.*, "Molecular cloning and functional characterization of cynomolgus monkey (*Macaca fascicularis*) CC chemokine receptor, CCR3," *Cytokine* **2002**, *19*, 276-286.

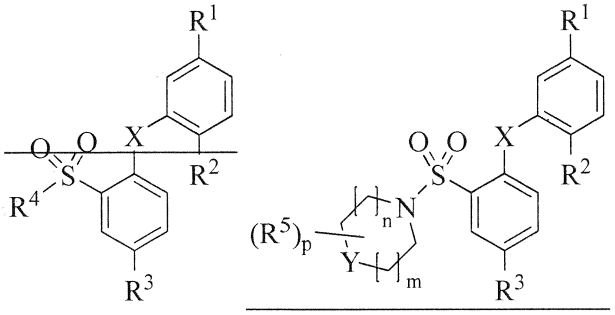
[00351] The biological results are summarized in Tables 1 and 2, wherein A represents a value no greater than 10 nM; B represents a value greater than 10 nM but no greater than 25 nM; C represents a value greater than 25 nM but no greater than 100 nM; D represents a value greater than 100 nM but no greater than 500 nM; and E represents a value greater than 500 nM.

TABLE 1

Cmpd #	K_i		Cmpd #	K_i	
	Free	HCl[a]		Free	HCl[a]
51	D	C	**52**		
53	C		**54**	D	C
55	E		**56**	C	C
57		E	**58**	E	
59	E	E	**60**	E	E
61	B		**62**		E
63	E	E	**64**	E	E
65	E		**66**	A	
67	C	D	**68**	C	C
69	C	D	**70**	D	
71	E		**72**	E	C
73		C	**74**	B	A
75		A	**76**	A	A
77	A	A	**78**	C	C
79	A	A	**80**	A	A
81	A	B	**82**	D	

What is claimed is:

1. A compound of Formula ~~I~~II:



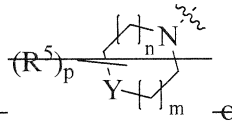
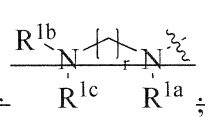
~~(I)~~ (II)

or an enantiomer, a mixture of enantiomers, a mixture of two or more diastereomers, a tautomer, or a mixture of two or more tautomers thereof; or a pharmaceutically acceptable salt, ~~solvate,~~ or hydrate thereof;

wherein:

R^1 and R^2 are each independently fluoro, chloro, or methyl; ~~(a) halo, cyano, nitro, hydroxyl, or guanidine; (b) C_{1-6} alkyl, C_{1-6} alkoxy, or C_{1-6} alkylthio, wherein the alkyl, alkoxy, and alkylthio are each independently and optionally substituted with one, two, or three halo; (c) C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, benzyl, phenoxy, benzoxy, or heterocyclyl; or (d) $C(O)R^{1a}$, $C(O)OR^{1a}$, $C(O)NR^{1b}R^{1c}$, $C(NR^{1a})NR^{1b}R^{1c}$, $OC(O)R^{1a}$, $OC(O)OR^{1a}$, $OC(O)NR^{1b}R^{1c}$, $OC(=NR^{1a})NR^{1b}R^{1c}$, $OS(O)R^{1a}$, $OS(O)_2R^{1a}$, $OS(O)NR^{1b}R^{1c}$, $OS(O)_2NR^{1b}R^{1c}$, $NR^{1b}R^{1c}$, $NR^{1a}C(O)R^{1d}$, $NR^{1a}C(O)OR^{1d}$, $NR^{1a}C(O)NR^{1b}R^{1c}$, $NR^{1a}C(=NR^{1d})NR^{1b}R^{1c}$, $NR^{1a}S(O)R^{1d}$, $NR^{1a}S(O)_2R^{1d}$, $NR^{1a}S(O)NR^{1b}R^{1c}$, $NR^{1a}S(O)_2NR^{1b}R^{1c}$, $S(O)R^{1a}$, $S(O)_2R^{1a}$, $S(O)NR^{1b}R^{1c}$, or $S(O)_2NR^{1b}R^{1c}$;~~

R^3 is ~~(a) hydrogen, halo,~~ cyano or nitro, ~~or hydroxyl; (b) C_{1-6} alkyl, C_{1-6} alkoxy, or C_{1-6} alkylthio, wherein the alkyl, alkoxy, and alkylthio are each independently and optionally substituted with one, two, or three halo; (c) C_{2-6} alkenyl, C_{2-6} alkynyl, or tetrazolyl; or (d) $C(O)R^{1a}$, $C(O)OR^{1a}$, $C(O)NR^{1b}R^{1c}$, $C(NR^{1a})NR^{1b}R^{1c}$, $OC(O)R^{1a}$, $OC(O)OR^{1a}$, $OC(O)NR^{1b}R^{1c}$, $OC(=NR^{1a})NR^{1b}R^{1c}$, $OS(O)R^{1a}$, $OS(O)_2R^{1a}$, $OS(O)NR^{1b}R^{1c}$, $OS(O)_2NR^{1b}R^{1c}$, $NR^{1b}R^{1c}$, $NR^{1a}C(O)R^{1d}$, $NR^{1a}C(O)OR^{1d}$, $NR^{1a}C(O)NR^{1b}R^{1c}$, $NR^{1a}C(=NR^{1d})NR^{1b}R^{1c}$, $NR^{1a}S(O)R^{1d}$, $NR^{1a}S(O)_2R^{1d}$, $NR^{1a}S(O)R^{1d}$, $NR^{1a}S(O)_2R^{1d}$, $S(O)R^{1a}$, $S(O)_2R^{1a}$, $S(O)NR^{1b}R^{1c}$, or $S(O)_2NR^{1b}R^{1c}$;~~

~~R^4 is~~  ~~or~~  ;

each R^5 is methyl, oxo, or methoxycarbonyl; ~~independently (a) halo, cyano, nitro, hydroxyl, oxo, or guanidine; (b) C_{1-6} alkyl, C_{1-6} alkoxy,~~ or ~~C_{1-6} alkylthio, wherein the alkyl, alkoxy, and alkylthio are each independently and optionally substituted with one, two, or three halo; (c) C_{2-6} alkenyl, C_{2-6} alkynyl, phenyl, benzyl, phenoxy, benzoxy, or heterocyclyl; or (d) $C(O)R^{1a}$, $C(O)OR^{1a}$, $C(O)NR^{1b}R^{1c}$, $C(NR^{1a})NR^{1b}R^{1c}$, $OC(O)R^{1a}$, $OC(O)OR^{1a}$, $OC(O)NR^{1b}R^{1c}$, $OC(=NR^{1a})NR^{1b}R^{1c}$, $OS(O)R^{1a}$, $OS(O)_2R^{1a}$, $OS(O)NR^{1b}R^{1c}$, $OS(O)_2NR^{1b}R^{1c}$, $NR^{1b}R^{1c}$, $NR^{1a}C(O)R^{1d}$, $NR^{1a}C(O)OR^{1d}$, $NR^{1a}C(O)NR^{1b}R^{1c}$, $NR^{1a}C(=NR^{1d})NR^{1b}R^{1c}$, $NR^{1a}S(O)R^{1d}$, $NR^{1a}S(O)_2R^{1d}$, $NR^{1a}S(O)R^{1d}$, $NR^{1a}S(O)_2R^{1d}$, $S(O)R^{1a}$, $S(O)_2R^{1a}$, $S(O)NR^{1b}R^{1c}$, or $S(O)_2NR^{1b}R^{1c}$;~~

X is O or S;

Y is –O–, –S–, –S(O)–, or $-S(O)_2-$, ~~$N(R^{1a})$, $C(R^{1a})(R^{1d})$, or $C(R^{1a})(NR^{1b}R^{1c})$~~;

m is an integer of 1~~ from 0 to 3~~;

n is an integer of 1 or 2 ~~from 1 to 3~~; and

p is an integer of 0, 1, or 2 ~~from 0 to 4~~;

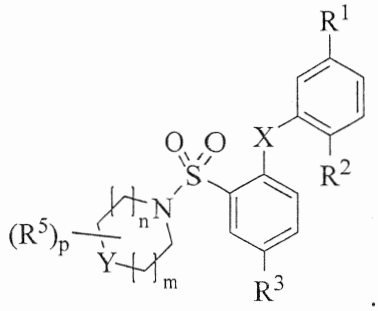
~~r is an integer from 1 to 6; and~~

~~each R^{1a}, R^{1b}, R^{1c}, and R^{1d} is independently (a) hydrogen, phenyl, or benzyl; (b) C_{3-7} cycloalkyl, heteroaryl, or heterocyclyl, each optionally substituted; or (c) C_{1-6} alkyl, optionally substituted with one, two, or three substituents, each independently selected from halo, hydroxyl, carboxy, alkoxy, carbamoyl, C_{6-14} aryl, C_{1-6} alkylcarbamoyl, di(C_{1-6} alkyl)carbamoyl, C_{3-7} cycloalkylcarbamoyl, and C_{3-7} heterocyclylcarbamoyl; or~~

~~each pair of R^{1b} and R^{1c} together with the N atom to which they are attached independently form heteroaryl or heterocyclyl;~~

~~with the proviso that when X is O; Y is $N(R^{1a})$; m and n are 1; R^1 and R^2 are each independently chloro, nitro, methyl, or isopropyl; R^3 is nitro; and p is 0; then R^{1a} is not hydrogen~~.

2. The compound of claim 1, having the structure of Formula II:



(II)

3. The compound of claim 1 or 2, wherein each R^5 is independently oxo; C_{1-6} alkyl, optionally substituted with one, two, or three halo; or $-C(O)OR^{1a}$.

4. The compound of claim 3, wherein each R^5 is independently oxo, methyl, or methoxycarbonyl.

5. The compound of any of claims 1 to 4, wherein p is 0, 1, or 2.

6. The compound of any of claims 1 to 5, wherein m is 1.

7. The compound of any of claims 1 to 6, wherein n is 1 or 2.

8. The compound of any of claims 1 to 7, wherein Y is –O–,–S–, –S(O)–, or $-S(O)_2-$.

9. The compound of any of claims 1 to 7, wherein Y is $-NR^{1a}-$.

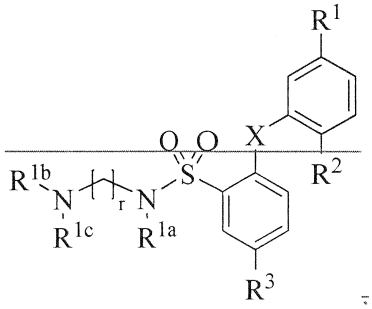
10. The compound of any of claims 1 to 7, wherein Y is $-C(R^{1a})(R^{1d})-$.

11. The compound of claim 9 or 10, wherein R^{1a} is hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, heteroaryl, or heterocyclyl.

12. The compound of claim 11, wherein R^{1a} is hydrogen, methyl, ethyl, propyl, pentyl, cyclopentyl, cyclohexyl, or 3-oxo-1*H*-imidazo[1,5-c]imidazol-2(3*H*)-yl.

13. The compound of any of claims 10 to 12, wherein R^{1d} is hydrogen.

~~14. The compound of claim 1, having the structure of Formula III:~~



~~(III)~~

~~15. The compound of claims 1 or 14, wherein R^{1a} is hydrogen or C_{1-6} alkyl.~~

~~16. The compound of claim 1, 14, or 15, wherein R^{1b} is hydrogen or C_{1-6} alkyl.~~

~~17. The compound of claim 15, wherein R^{1b} is ethyl.~~

~~18. The compound of any of claims 1 and 14 to 17, wherein R^{1c} is hydrogen or C_{1-6} alkyl.~~

~~19. The compound of claim 18, wherein R^{1c} is ethyl.~~

~~20. The compound of claim 1, 14, or 15, wherein R^{1b} and R^{1c} together with the N atom to which they are attached form heteroaryl or heterocyclyl.~~

~~21. The compound of claim 20, wherein R^{1b} and R^{1c} together with the N atom to which they are attached form 5- to 7-membered heterocyclyl.~~

~~22. The compound of claim 21, wherein the heterocyclyl is pyrrolidinyl or piperidinyl.~~

~~23. The compound of any of claims 1 to 22, wherein R^1 is halo or C_{1-6} alkyl.~~

~~24. The compound of claim 23, wherein R^1 is fluoro, chloro, or methyl.~~

~~25. The compound of any of claims 1 to 24, wherein R^2 is halo or C_{1-6} alkyl.~~

~~26. The compound of claim 25, wherein R^2 is fluoro, chloro, or methyl.~~

~~27~~2. The compound of claim ~~26~~1, wherein R^1 and R^2 are fluoro.

~~3~~28. The compound of claim 1~~2~~6, wherein R^1 and R^2 are chloro.

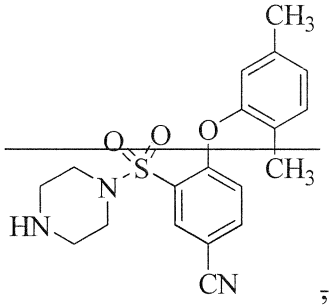
~~4~~29. The compound of claim 1~~2~~6, wherein R^1 and R^2 are methyl.

~~30. The compound of any of claims 1 to 29, wherein R^3 is cyano or nitro.~~

~~5~~31. The compound of any of claims 1 to ~~4~~30, wherein X is O.

~~6~~32. The compound of any of claims 1 to ~~4~~30, wherein X is S.

~~7~~33. The compound of claim 1 selected from the group consisting of:



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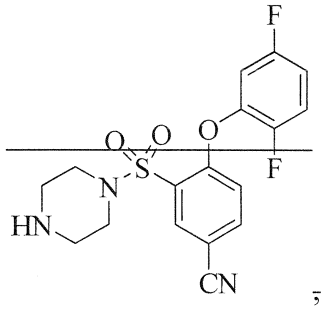

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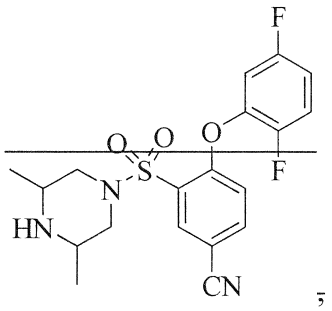

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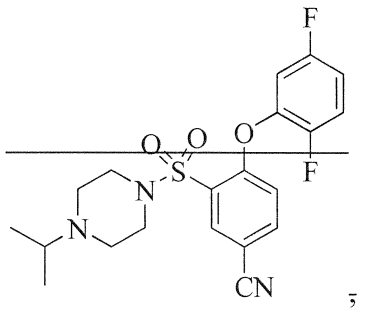

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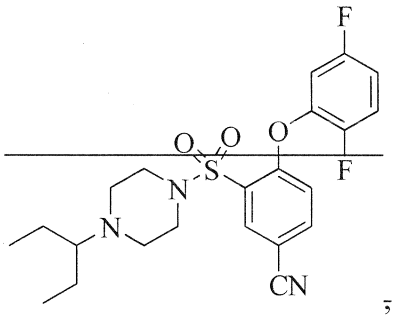

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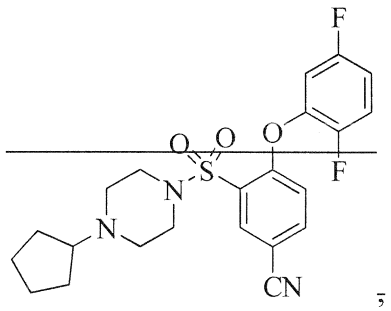

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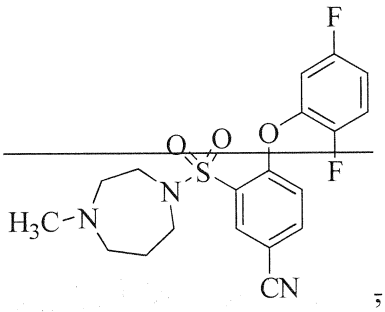

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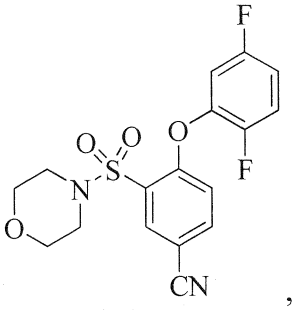

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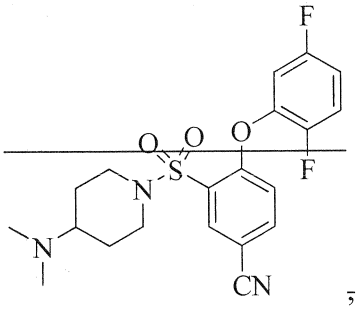

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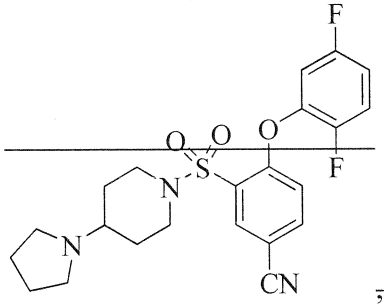

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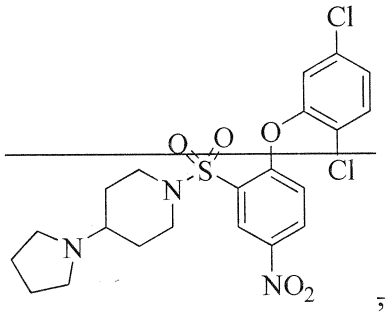

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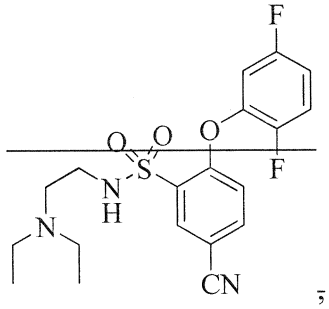

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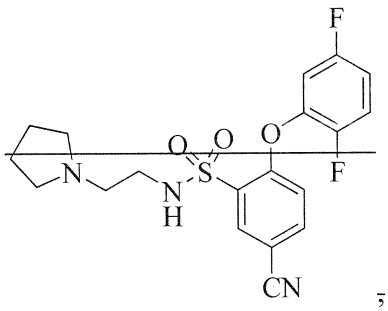

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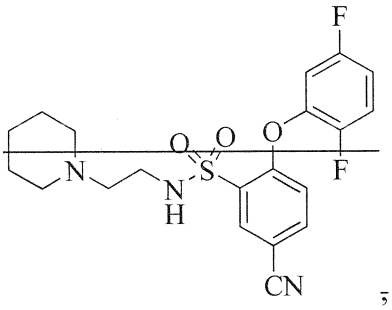

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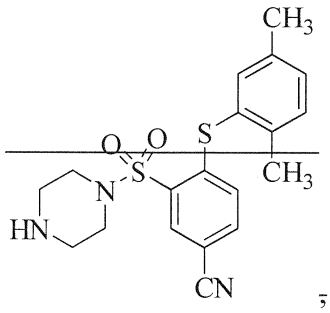

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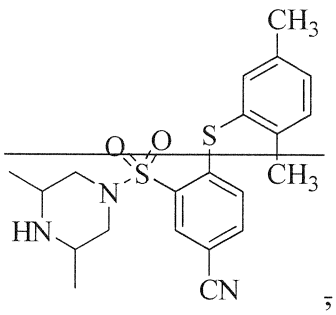

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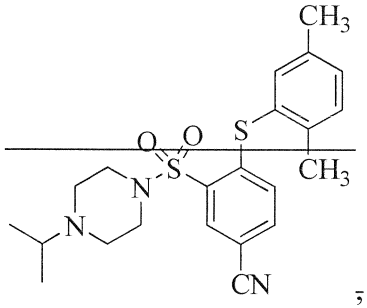

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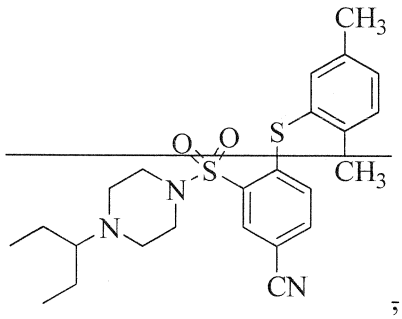

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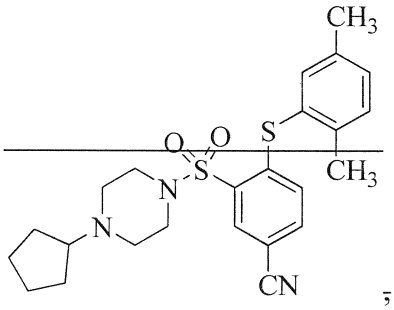

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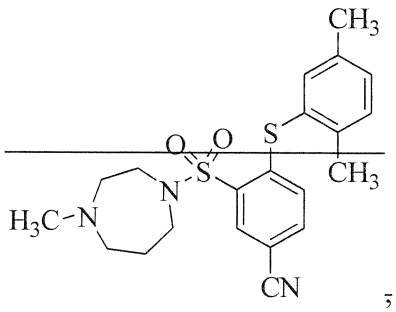

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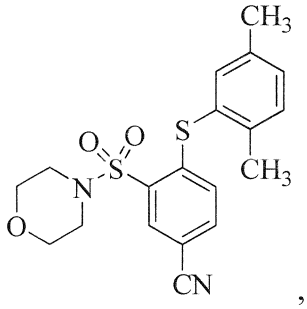

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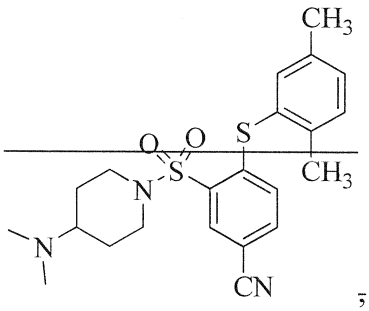

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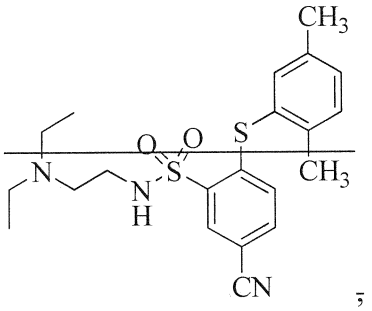

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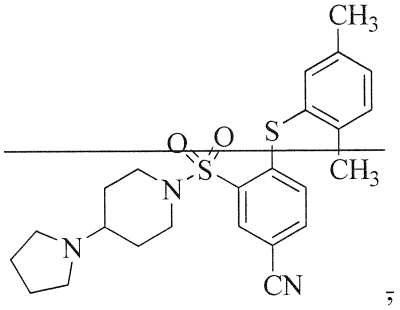

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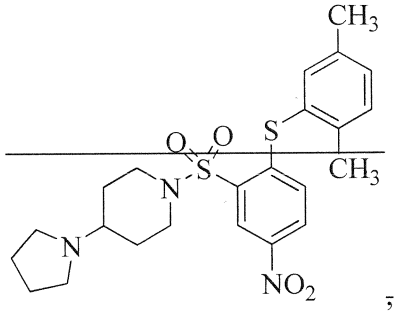

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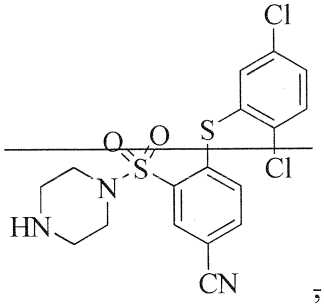

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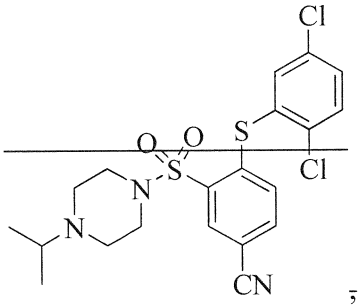

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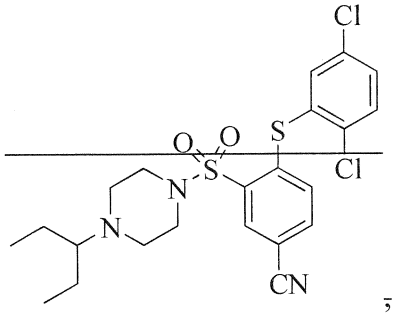

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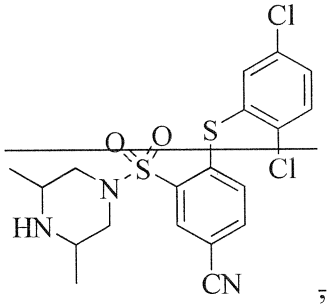

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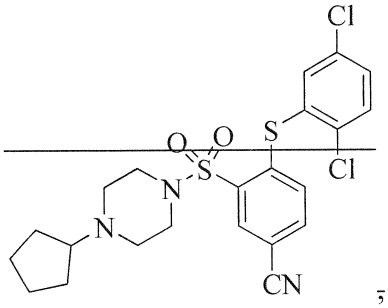

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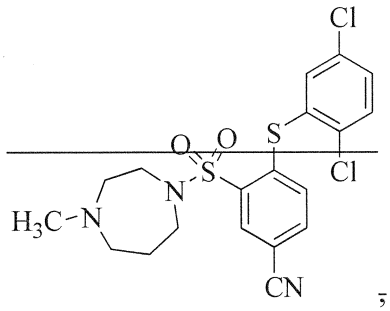

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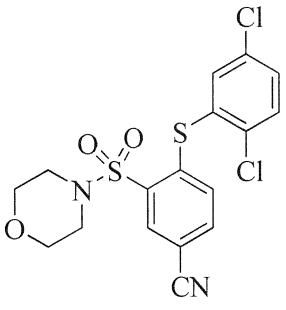

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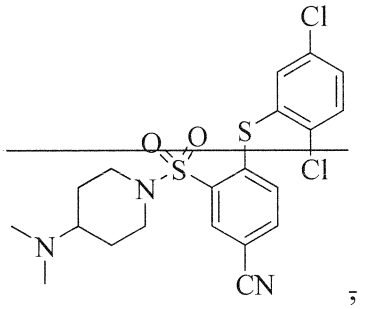

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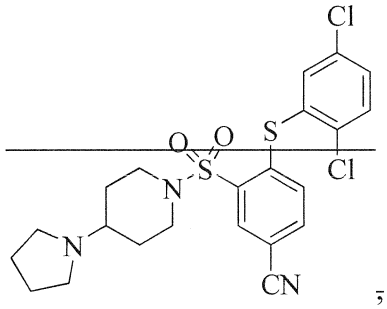

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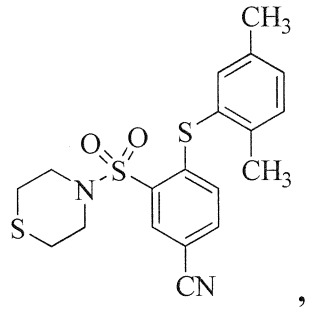

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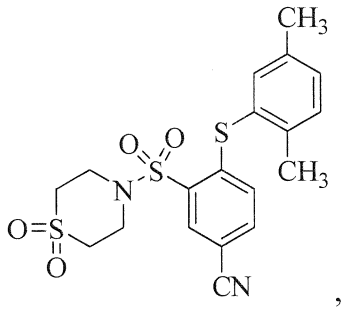

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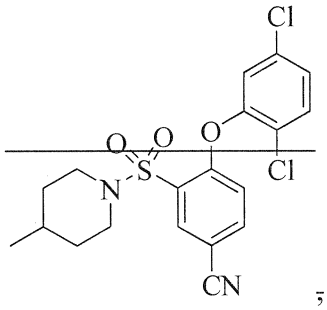

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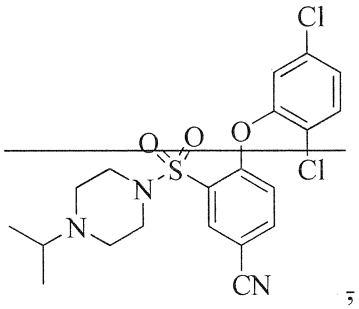

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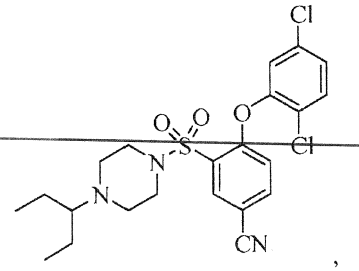

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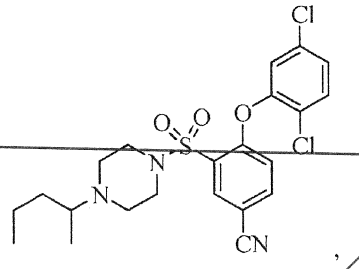

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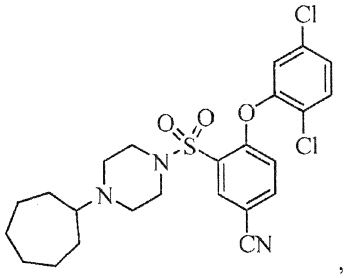

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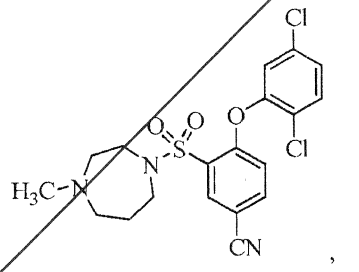

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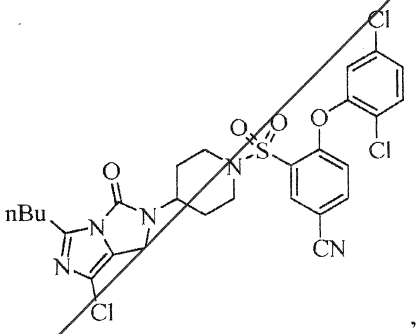

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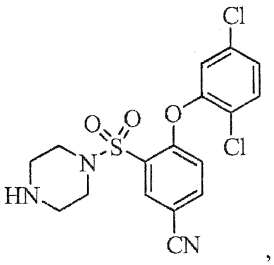

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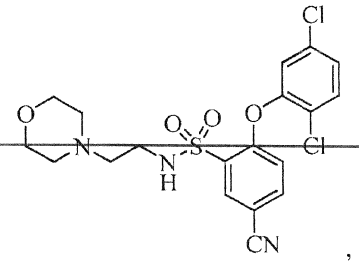

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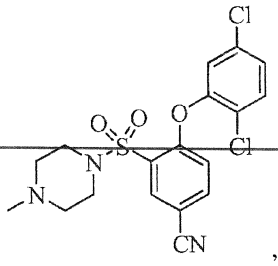

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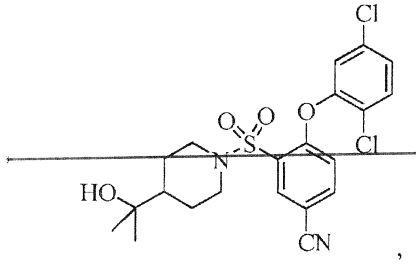

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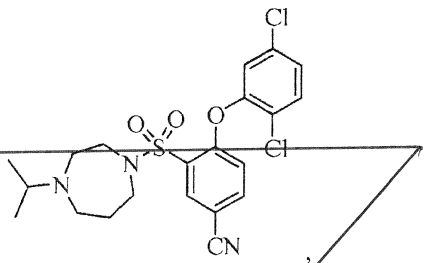

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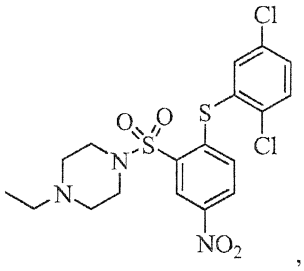

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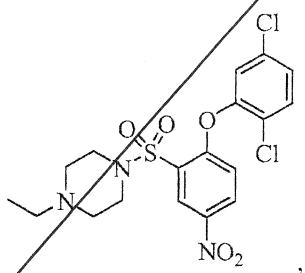

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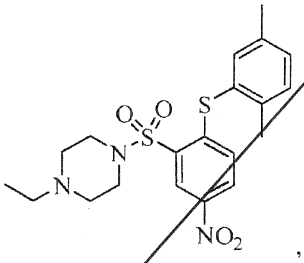

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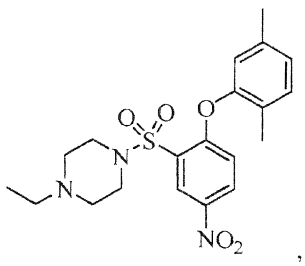

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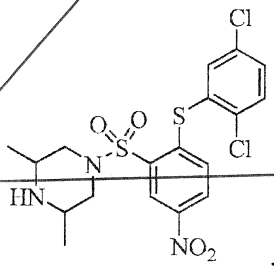

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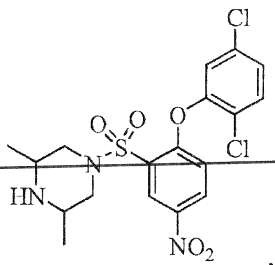

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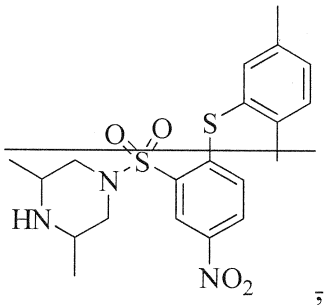

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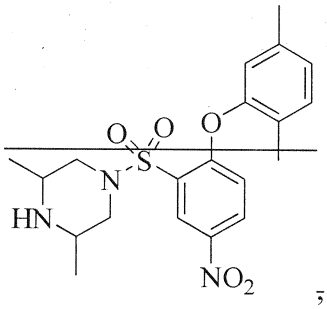

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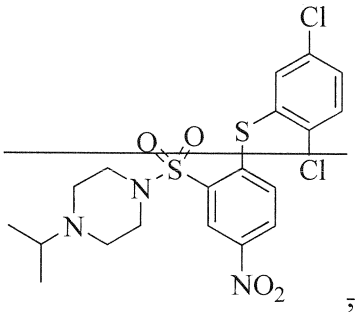

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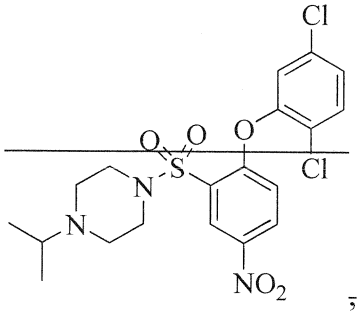

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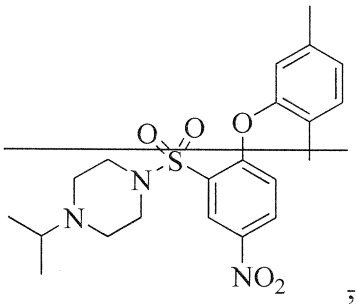

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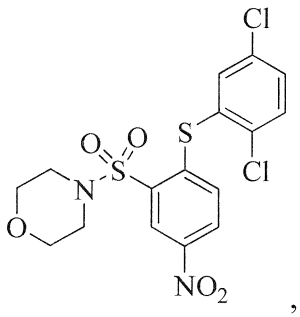

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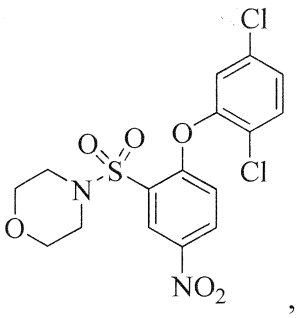

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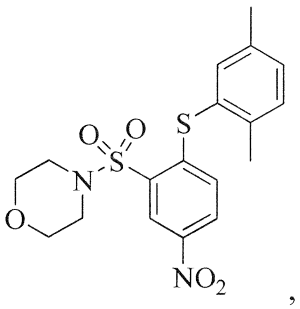

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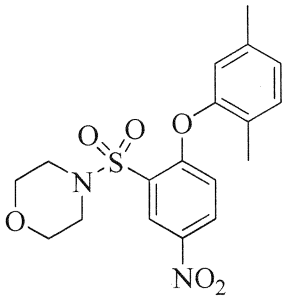

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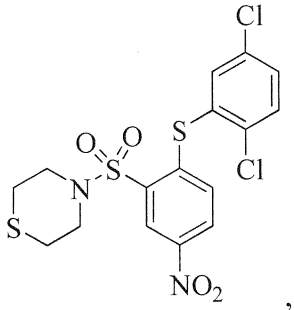

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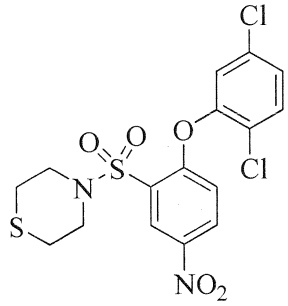

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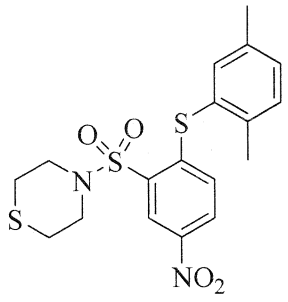

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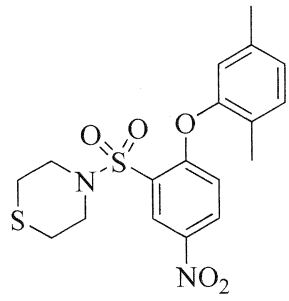

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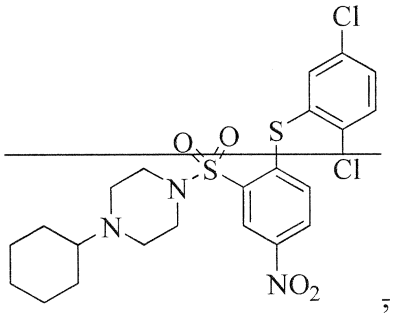

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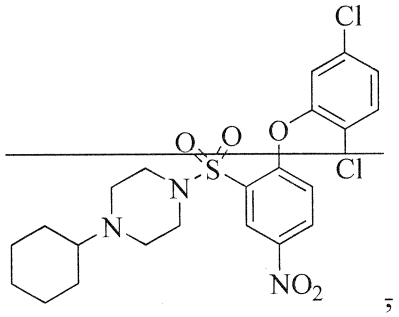

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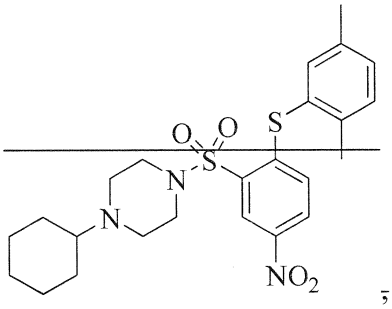

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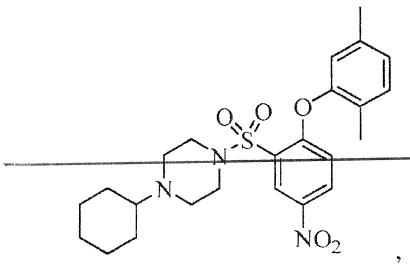

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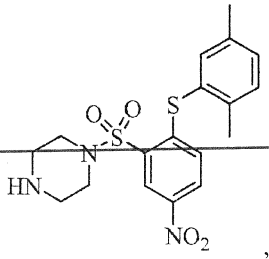

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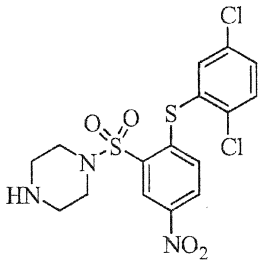

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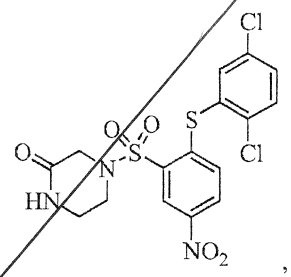

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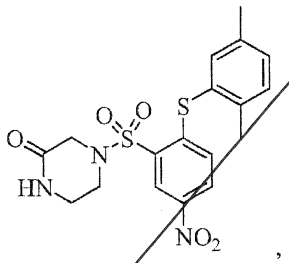

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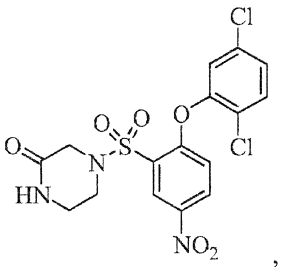

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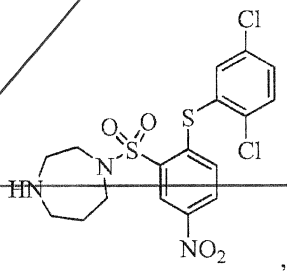

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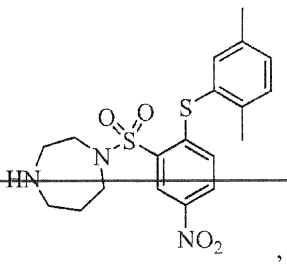

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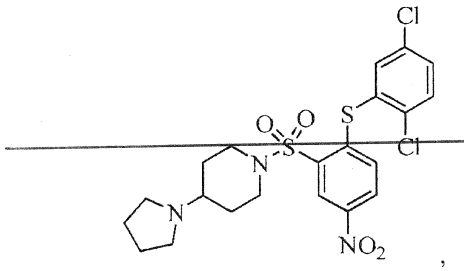

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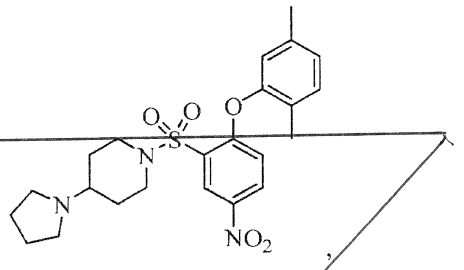

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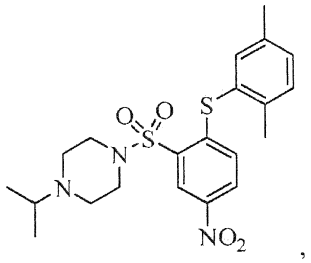

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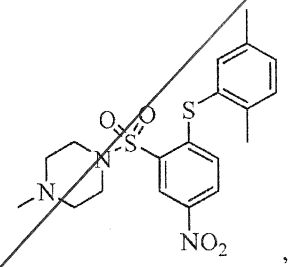

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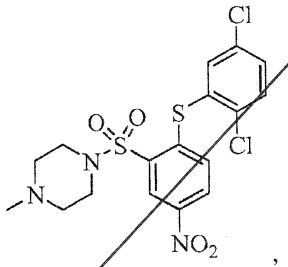

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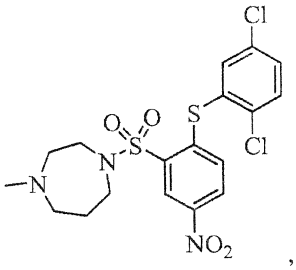

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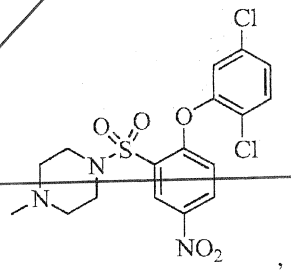

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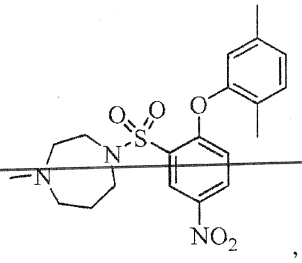

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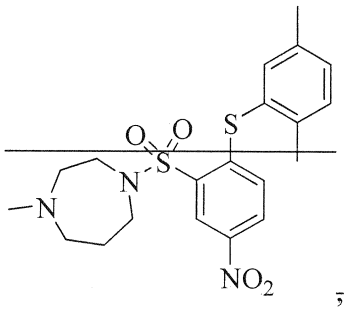

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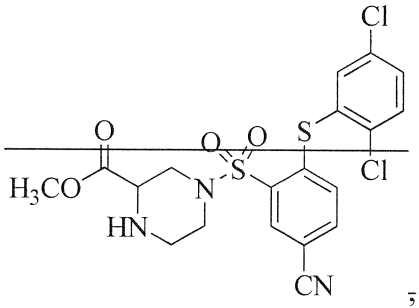

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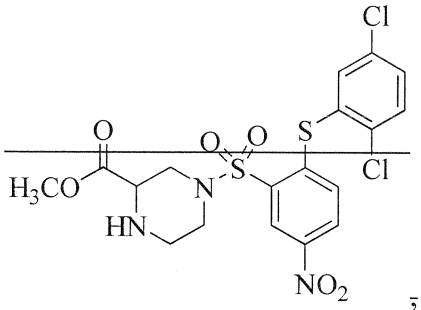

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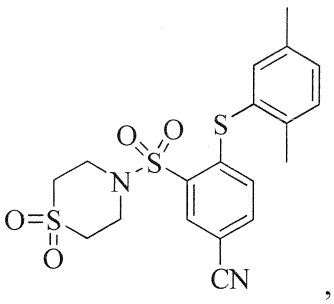

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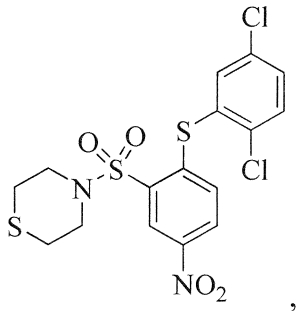

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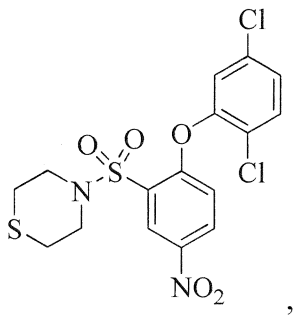

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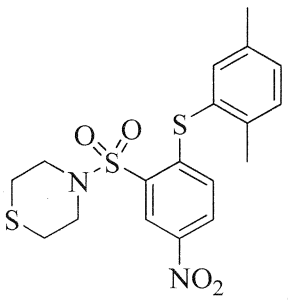

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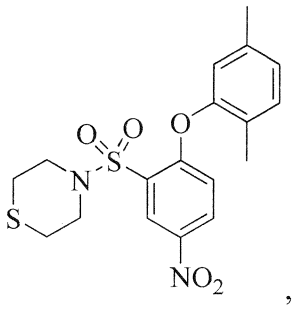

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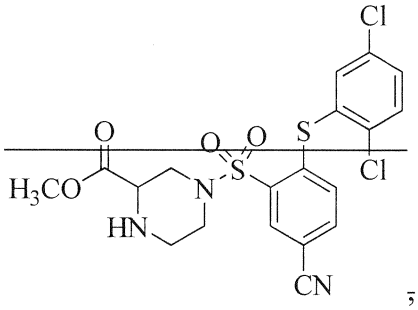

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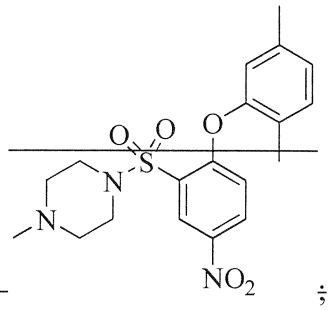

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~~145~~ ~~146~~

and enantiomers, mixtures of enantiomers, mixtures of two or more diastereomers, tautomers, and mixtures of two or more tautomers thereof; and pharmaceutically acceptable salts, ~~solvates,~~ and hydrates thereof.

8~~34~~. The compound of any of claims 1 to 7~~33~~, wherein the compound is a hydrochloride salt.

9~~35~~. A pharmaceutical composition comprising a compound of any of claims 1 to 8~~34~~, or a pharmaceutically acceptable salt, ~~solvate,~~ hydrate, stereoisomer, or tautomer thereof; and one or more pharmaceutically acceptable carriers or excipients.

10~~36~~. The pharmaceutical composition of claim 9~~35~~, further comprising a second therapeutic agent.

11~~37~~. The pharmaceutical composition of claim 9~~35~~ or 10~~36~~, wherein the composition is formulated for single dose administration.

12~~38~~. The pharmaceutical composition of claim 11~~37~~, wherein the composition is formulated as oral, parenteral, or intravenous dosage form.

13~~39~~. The pharmaceutical composition of claim 12~~38~~, wherein the oral dosage form is a tablet or capsule.

14~~40~~. Use of the compound of any of claims 1 to 8~~34~~ in the manufacture of a medicament for the treatment, prevention, or amelioration of one or more symptoms of a CCR3-mediated disorder, disease, or condition.

15~~41~~. Use of the compound of any of claims 1 to 8~~34~~ in the manufacture of a medicament for the treatment, prevention, or amelioration of one or more symptoms of an eosinophil-related disorder, disease, or condition.

1642. Use of the compound of any of claims 1 to 834 in the manufacture of a medicament for the treatment, prevention, or amelioration of one or more symptoms of a basophil-related disorder, disease, or condition.

1743. Use of the compound of any of claims 1 to 834 in the manufacture of a medicament for the treatment, prevention, or amelioration of one or more symptoms of a mast cell-related disorder, disease, or condition.

1844. Use of the compound of any of claims 1 to 834 in the manufacture of a medicament for the treatment, prevention, or amelioration of one or more symptoms of an inflammatory disease.

1945. The use of any of claims 1440 to 1844, wherein the disorder, disease, or condition is selected from the group consisting of asthma, allergic asthma, exercise induced asthma, allergic rhinitis, perennial allergic rhinitis, seasonal allergic rhinitis, atopic dermatitis, contact hypersensitivity, contact dermatitis, conjunctivitis, allergic conjunctivitis, eosinophilic bronchitis, food allergies, eosinophilic gastroenteritis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, mastocytosis, hyper IgE syndrome, systemic lupus erythematous, psoriasis, acne, multiple sclerosis, allograft rejection, reperfusion injury, chronic obstructive pulmonary disease, Churg-Strauss syndrome, sinusitis, basophilic leukemia, chronic urticaria, basophilic leukocytosis, eczema, arthritis, rheumatoid arthritis, psoriatic arthritis, osteoarthritis, and cardiovascular disorders.

2046. The use of claim 1945, wherein the disorder, disease, or condition is asthma, exercise induced asthma, allergic rhinitis, atopic dermatitis, chronic obstructive pulmonary disease, or allergic conjunctivitis.

2147. The use of any of claims 1440 to 2046, wherein the medicament is manufactured for oral, parenteral, or topical administration.

2248. The use of any of claims 1440 to 2147, wherein the medicament is manufactured for administration in combination with a second therapeutic agent.

2349. Use of the compound of any of claims 1 to 834 in the manufacture of a medicament for modulating CCR3 activity, comprising contacting a CCR3 receptor with the compound.