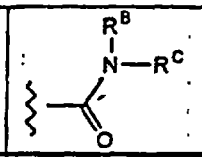
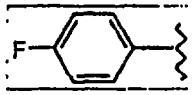
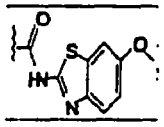
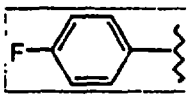
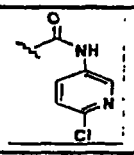
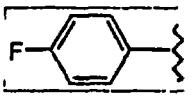
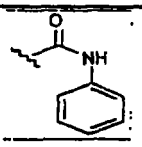
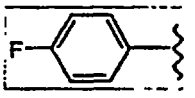
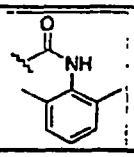
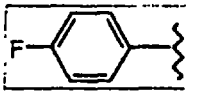
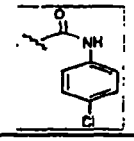
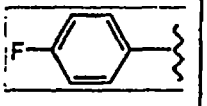
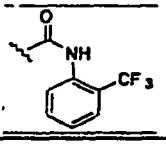
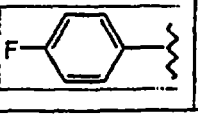
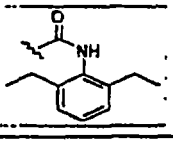
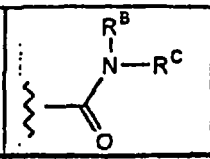
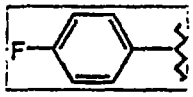
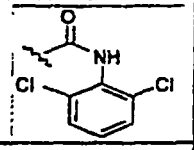
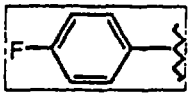
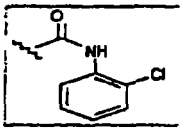
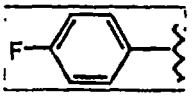
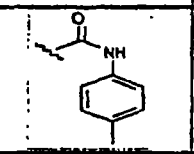
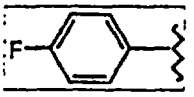
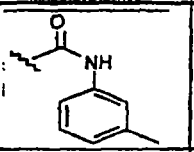
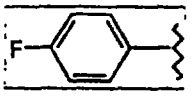
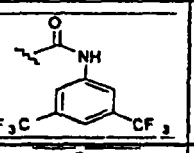
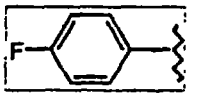
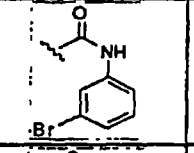
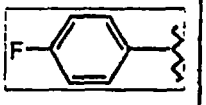
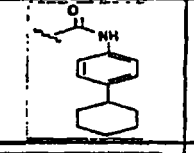
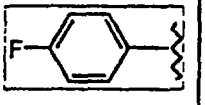
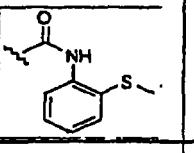
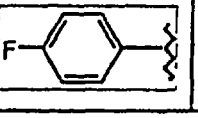
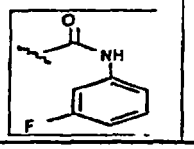
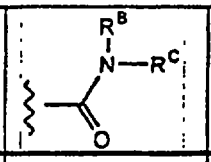
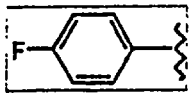
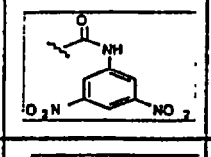
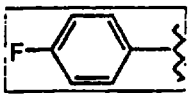
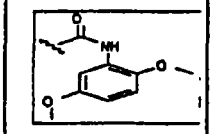
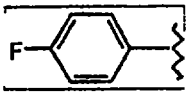
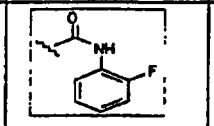
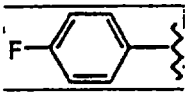
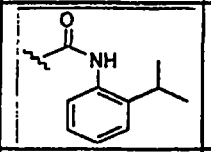
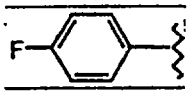
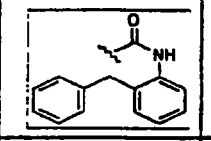
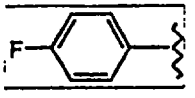
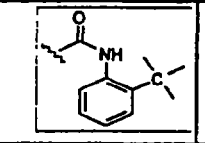
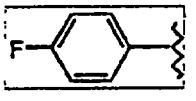
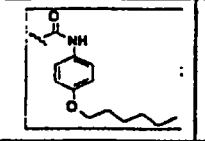
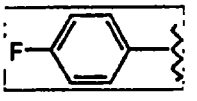
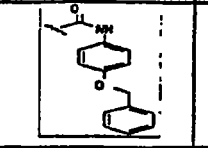
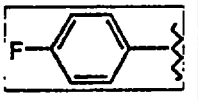
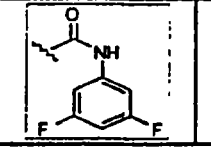
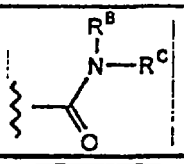
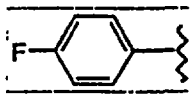
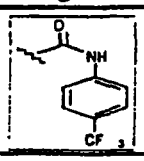
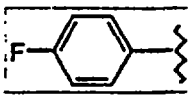
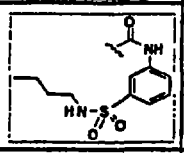
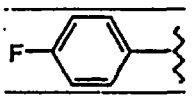
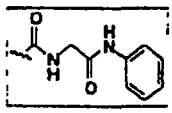
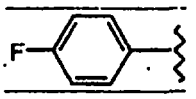
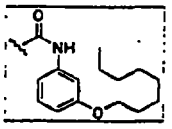
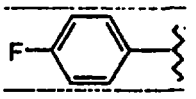
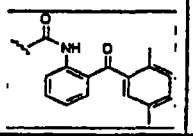
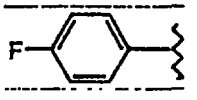
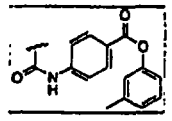
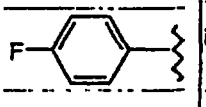
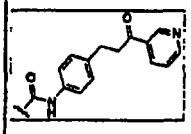
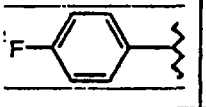
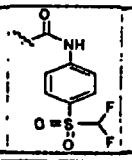
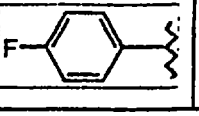
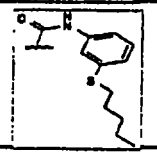


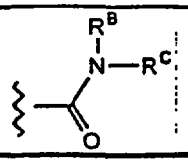
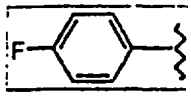
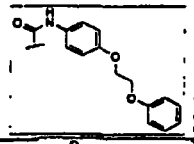
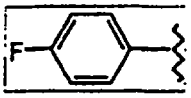
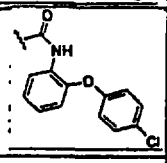
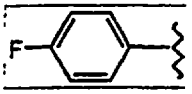
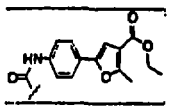
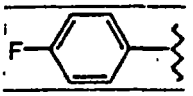
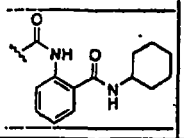
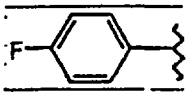
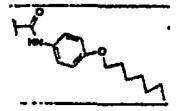
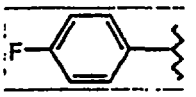
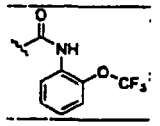
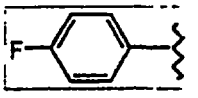
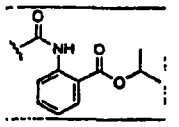
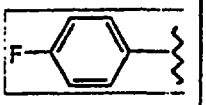
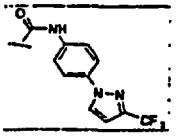
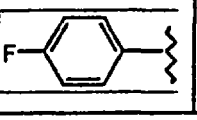
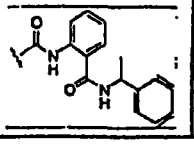
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B-2414			14	473	474
B-2415			19	421	422
B-2416			13	386	387
B-2417			29	414	415
B-2418			6	420	421
B-2419			10	454	-
B-2420			5	442	443

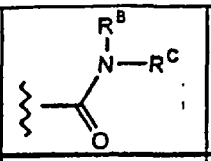
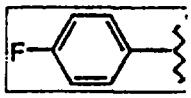
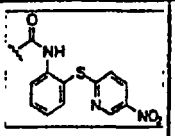
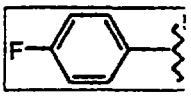
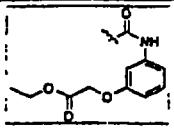
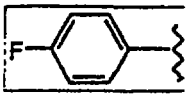
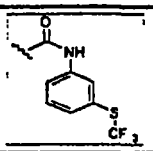
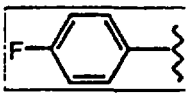
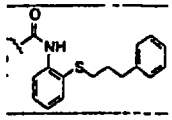
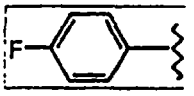
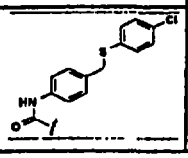
G00001

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2421			28	454	455
B-2422			47	420	421
B-2423			53	400	401
B-2424			15	400	401
B-2425			18	522	523
B-2426			38	464	465
B-2427			26	468	469
B-2428			22	432	433
B-2429			41	404	405

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2430			15	476	477
B-2431			6	446	447
B-2432			37	404	405
B-2433			8	428	429
B-2434			13	476	477
B-2435			23	442	443
B-2436			5	486	487
B-2437			4	492	493
B-2438			58	422	423

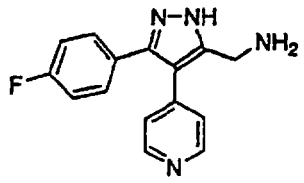
	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2439			12	454	455
B-2440			8	521	522
B-2441			6	443	444
B-2442			37	514	515
B-2443			15	518	-
B-2444			52	520	-
B-2445			33	517	518
B-2446			70	500	501
B-2447			56	488	489

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2448			51	522	523
B-2449			19	512	513
B-2450			16	538	539
B-2451			71	511	512
B-2452			71	500	501
B-2453			61	470	-
B-2454			15	472	473
B-2455			39	520	-
B-2456			51	533	534

	R^2		Yield	Calcd. Mass Spec.	Observed Mass Spec M+H
B-2457			55	540	-
B-2458			22	488	489
B-2459			8	486	487
B-2460			13	534	535
B-2461			13	542	-

Example C-1

5-AMINOMETHYL-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



1-(4-fluorophenyl)-2-(4-pyridyl)-1-ethanone. 4-picoline (40 g, 0.43 mol) was added to a LiHMDS solution (0.45 mol, 450 mL of a 1.0 M solution in THF) over 30 minutes at room temperature (a slight exotherm was observed) The resulting solution was stirred for 1 h. This solution was added to ethyl 4-fluorobenzoate (75.8 g, 0.45 mol, neat) over 1 h. The mixture was stirred overnight (16 h). Water (200 mL) was added and the mixture was extracted with EtOAc (2x200 mL). The organic layer was washed with brine (1x200 mL) and dried over

Na_2SO_4. The organic layer was filtered and the solvent was removed to leave oily solid. Hexane was added to the oil and the resulting solid was filtered and washed with hexane (cold). A yellow solid was isolated (50 g, 54%): ^1H NMR ($CDCl_3$) δ 8.58 (d, J = 5.7 Hz, 2H), 8.02 (dd, J = 5.5, 8.0, 2H), 7.12-7.21 (m, 4H), 4.23 (s, 2H); ^{19}F NMR ($CDCl_3$) δ -104.38 (m); LC/MS, t_r = 2.14 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 216; High Resolution MS Calcd for $C_{23}H_{20}N_4O_2F$ (M+H): 216.0825. Found: 216.0830 (Δ mmu = 0.5).

N-benzyloxycarbonyl-5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. A 3L round bottom flask fitted with a mechanical stirrer, N_2 inlet and an addition funnel was was charged wtih 557 mL (0.56 mol) of 1 M t-BuOK in THF and 53 mL (0.56 mol) of t-BuOH. The ketone, **1** (60 g, 0.28 mol) was dissolved in 600 mL of THF and added to the stirred mixture at room temperature. A yellow precipitate formed and the mixture was stirred for 1 h. N-benzyloxycarbonyl-glycinyl N-hydroxysuccinimide (128.6 g, 0.42 mol) was dissolved in 600 mL of THF and added dropwise at r.t. over 1h. The mixture was stirred for another 5 minutes and 150 mL of water was added. the pH was adjusted to 6.7 with 70 mL of AcOH. Hydrazine monohydrate (41 mL in100 mL of water) was added via an addition funnel. The mixture was stirred for 1 h and was diluted with 500 mL of water and 500 mL of ethyl acetate. The biphasic mixture was transferred to a sep funnel and the layers were separated. The aqueous layer was extracted with EtOAc (3x300 mL). The organic layer was

dried (Na_2SO_4), filtered and evaporated to leave 157 g of a crude reddish oil.

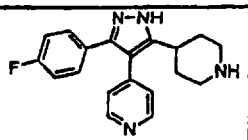
The oil was suspended in CH_2Cl_2 and filtered to remove any insoluble material (DCU, hydrazone of the monoketone). The solution was split into two portions and each portion was chromatographed (Biotage 75L, 3% EtOH/CH_2Cl_2 then 6% EtOH/CH_2Cl_2). The appropriate fractions were concentrated (some contamination from the monoketone and the hydrazone) from each portion to leave a yellow solid. The solid was suspended in ethyl acetate and heated to boiling for 10 minutes. The solution was allowed to cool to R.T. overnight. The precipitate was filtered to give 30 g of a white solid (27% yield of **2**): ^1H NMR (DMF-d_7) δ 13.36 (s, 1H), 8.57 (d, J = 5.8 Hz, 2H), 7.16-7.52 (m, 11H), 5.11 (s, 2H), 4.48 (d, J = 5.4 Hz, 2H); ^{19}F NMR (DMF-d_7) δ -114.9 (m), -116.8 (m) (split fluorine signal is due to the pyrazole tautomers); LC/MS, t_r = 3.52 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 403; High Resolution MS Calcd for $C_{23}H_{20}N_4O_2F$ (M+H): 403.1570. Found: 403.1581 (Δ mmu = 1.1).

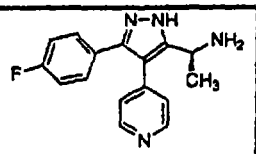
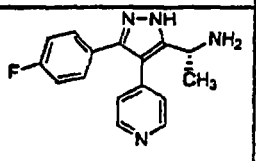
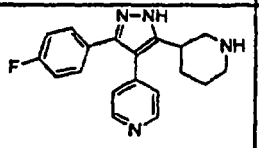
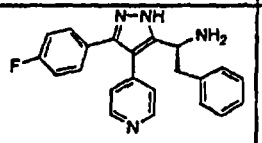
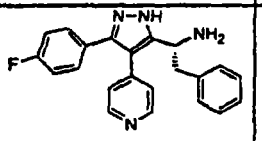
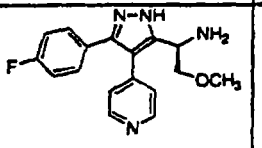
5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a 1L Parr bottle was added 7 g (17.4 mmol) of 2 and 180 mL of MeOH and 90 mL of THF to give a clear solution. The bottle was purged with nitrogen and 1.5 g of 10% Pd/C (wet Degussa type E101) was added. The Parr bottle was pressured to 40 psi (H_2) and was agitated. Hydrogen uptake was 5 psi after 5 h. The bottle was repressured to 42 psi and was agitated overnight. The bottle was purged with N2 and was filtered through Celite. The Celite was washed with MeOH (3x50 mL) and

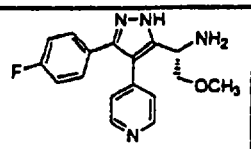
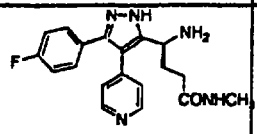
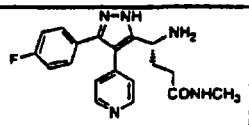
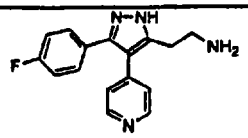
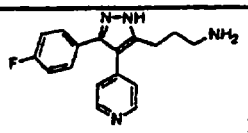
the filtrate was concentrated to give 4.5 g of an off-white solid (94%). ^{1}H NMR (DMSO-d_6) δ 8.52 (d, J = 4.63 Hz, 2H), 7.36 (dd, J = 5.64, 8.1 Hz, 2H), 7.16-7.30 (m, 4H), 3.79 (s, 2H); ^{19}F NMR (DMSO-d_6) δ -114.56 (m); LC/MS, t_r = 1.21 minutes (5 to 95% acetonitrile/water over 15 minutes at 1 mL/min, at 254 nm at 50°C), M+H = 269 m/z; High Resolution MS Calcd for $C_{15}H_{14}N_4F$ (M+H): 269.1202. Found: 269.1229 (Δ mmu = 2.7).

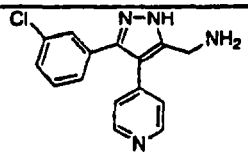
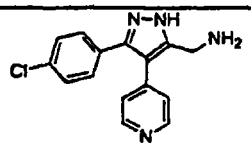
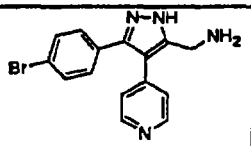
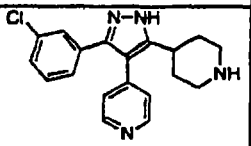
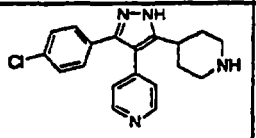
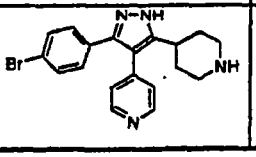
The following pyridylpyrazoles (**C-2** through **C-21**, Table C-1) were prepared according to the experimental procedure described above for example **C-1**.

Table C-1.

Example No.	Structure	MW, M + H Calculated Found	^{1}H NMR (solvent), ppm
C-2		323.1672 323.1670	(DMF-d_7): 8.77 (t, J = 4.4 Hz, 2H), 7.60 (m, 2H), 7.44 (t, J = 4.4 Hz, 2H), 7.35 (m, 2H), 3.22 (bd, 2H), 3.01 (septet, J = 5.3 Hz, 1H), 2.74 (m, 2H), 1.95 (m, 4H)

C-3		282.127 (M) 282.1245 (M, EI)	(DMF-d_7): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.34 (m, 2H), 4.40-4.37 (m, 1H), 1.56 (br s, 3H)
C-4		282.127 (M) 282.1147 (M, EI)	(DMF-d_7): 8.77 (br s, 2H), 7.64-7.62 (m, 2H), 7.50 (br s, 2H), 7.38-7.35 (m, 2H), 4.40-4.37 (m, 1H), 1.57 (br s, 3H)
C-5		323.1672 323.1687	(DMSO-d_6): 8.56 (br, 2H), 7.32 (m, 2H), 7.18 (m, 4H), 2.91 (m, 2H), 2.71 (m, 2H) 1.88 (m, 1H), 1.65 (m, 2H), 1.40 (m, 2H)
C-6		359 359	(DMSO-d_6): 8.46 (d, J = 4.6 Hz, 2H), 7.32-7.13 (m, 7H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.95 (m, 2H)
C-7		359 359	(DMSO-d_6): 8.46 (d, J = 5.4 Hz, 2H), 7.32-7.28 (m, 2H), 7.20-7.12 (m, 5H), 6.98-6.96 (m, 4H), 4.06 (t, J = 7.0 Hz, 1H), 2.98-2.94 (m, 2H)
C-8		313.1465 313.1492	(DMSO-d_6): 13.83 (bs, 1H), 8.61 (d, J = 5.7 Hz, 2H), 8.33 (bs, 1H), 7.33 (m, 6H), 4.44 (m, 1H), 3.63 (m, 2H), 3.27 (s, 3H)

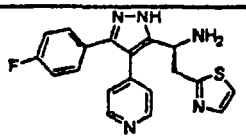
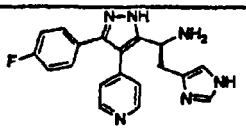
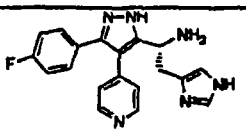
C-9		313.1465 313.1457	(DMSO-d_6): 8.55 (dd, J = 1.5, 4.4 Hz, 2H), 7.37-7.32 (m, 2H), 7.26 (dd, J = 1.6, 4.4 Hz, 2H), 7.22-7.16 (m, 2H), 4.06 (t, J = 6.5 Hz, 1H), 3.49 (d, J = 6.6 Hz, 2H), 3.20 (s, 3H)
C-10		354 354	(DMSO-d_6): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-11		354 354	(DMSO-d_6): 13.03 (bs, 1H), 8.50 (dd, J=1.6, 2.7 Hz, 2H), 7.58 (bq, J=4.3 Hz, 1H), 7.3 (m, 2H), 7.12-7.21 (m, 4H), 3.77 (t, J= 6.3 Hz, 1H), 2.45 (d, J=4.5 Hz, 3H), 1.97 (t, J= 7.4 Hz, 2H), 1.85 (dt, J=7.3, 7.1 Hz, 2H)
C-12		283.1359 283.1363	(DMSO-d_6): 8.53 (d, J = 5.0 Hz, 2H), 7.37-7.32 (m, 2H), 7.21-7.17 (m, 4H), 2.83(d, J = 6.0 Hz, 2H), 2.77 (d, J = 6.0 Hz, 2H)
C-13		297.1515 297.1515	(DMSO-d_6): 8.53 (d, J = 5.4 Hz, 2H), 7.34 (dd, J = 5.8, 8.2 Hz, 2H), 7.18

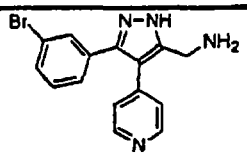
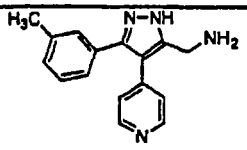
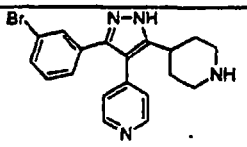
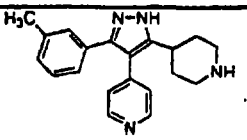
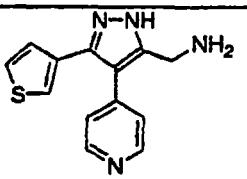
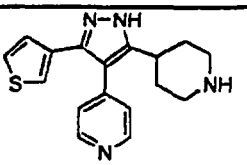
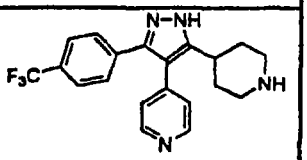
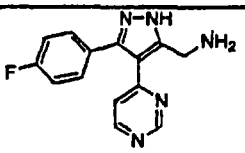
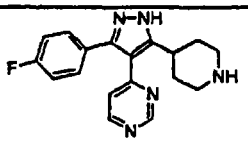
			(dd, J = 5.8, 9.8 Hz, 4H), 2.68 (t, J = 7.3 Hz, 2H), 2.52 (m, 2H), 1.64 (m, 2H)
C-14		284.0829 284.0806	(CD_3OD): 8.74 (br, 2H), 7.77 (br, 2H), 7.45-7.58 (m, 3H), 7.30-7.40 (m, 1H), 4.43 (s, 2H)
C-15		285 285	(DMSO-d_6): 8.53 (br, 2H), 7.56 (br, 2H), 7.26 (m, 4H), 3.75 (br, 2H)
C-16		329, 331 329, 331	(DMSO-d_6): 8.53 (d, J = 4.4 Hz, 2H), 7.42 (d, J = 7.9 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 4.6 Hz, 2H), 3.76 (bs, 2H)
C-17		339 339	(DMSO-d_6): 8.53 (t, J = 4.3 Hz, 2H), 7.33 (m, 3H), 7.19 (t, J = 4.6 Hz, 2H), 7.14 (d, J = 7.3 Hz, 1H), 3.23 (m, 2H), 2.88, (m, 3H), 1.92, (m, 3H), 1.70 (m, 1H)
C-18		339 339	(DMSO-d_6): 8.57 (d, J = 4.6 Hz, 2H), 7.41 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 4.8 Hz, 2H), 3.18 (bd, 2H), 2.88 (m, 1H), 2.76 (m, 2H), 1.82 (br, 4H)
C-19		383, 385 383, 385	(DMSO-d_6): 8.56 (br, 2H), 7.52 (br, 2H), 7.14-7.29 (m, 4H), 2.99 (br, 2H),

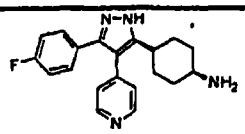
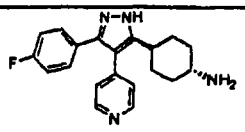
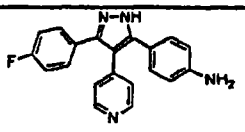
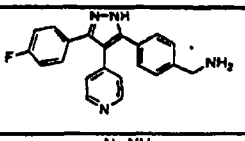
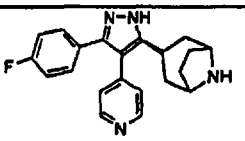
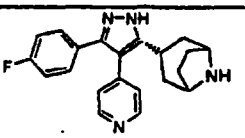
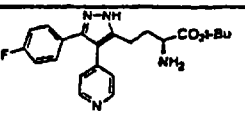
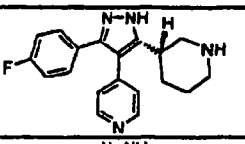
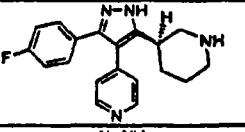
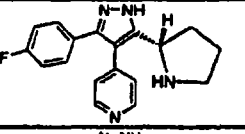
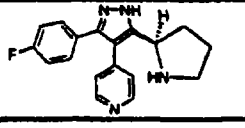
			2.71 (br, 1H), 2.51 (br, 2H), 1.68 (br, 4H)

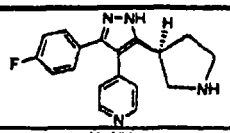
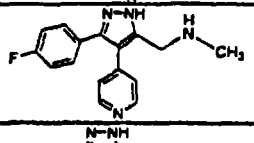
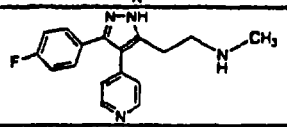
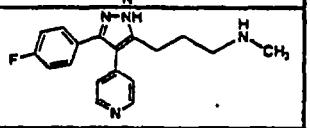
The following pyridylpyrazoles (**C-22** through **C-40**, Table C-2) are prepared utilizing the general schemes C-1 and C-2 and the experimental procedure described for example **C-1** above.

Table C-2

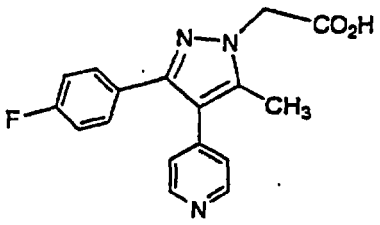
Cmpd. No.	Structure
C-22	
C-23	
C-24	

C-25	
C-26	
C-27	
C-28	
C-29	
C-30	
C-31	
C-32	
C-33	

C-34	
C-35	
C-36	
C-37	
C-38	
C-39	
C-40	
C-41	
C-42	
C-43	
C-44	

C-45	
C-46	
C-47	
C-48	

Example C-49



Step A

The pyrazole (2.60 g, 10.3 mmol) from example C-4 was suspended in 52 mL of dichloroethane and 52 mL of 2.5 M

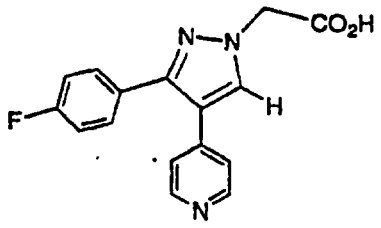
NaOH. Tetrabutylammonium hydroxide (0.5 mL of a 1 M aqueous solution) was added to the stirred mixture. To this mixture was added t-butyl bromoacetate (2.10 g, 10.8 mmol). The reaction mixture was stirred at room temperature for 4 h. The mixture was poured onto 200 mL of CH_2Cl_2 and 200 mL of H_2O. The phases were separated and the organic phase was washed with water (1x100 mL) and brine (1x100 mL). The organic layer was dried over Na_2SO_4 and was filtered. The solvent was removed to leave an off-white solid. This solid was triturated with hexane and the resulting solid isolated by filtration. The solid was washed with hexane to leave 3.4 g of a white solid (90%).

Step B

The alkylated pyrazole (3.7 g, 10.1 mmol) from Step A was treated with 57 mL of 4 N HCL in dioxane. The solution was stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was dissolved in THF. The solution was treated with propylene oxide (10.3 mmol) and was stirred for 1h at room temperature. The solvent was removed to leave an oil. The residual solvent was chased with several portions of EtOH. The resulting solid was triturated with Et_2O and the title compound Example **C-49** was isolated by filtration to afford 3.0 g of an off-white solid (95%). Mass spec: M+H cald: 312; found 312. ^1H NMR (DMSO-d6): 8.81 (d, J = 6.4 Hz, 2H), 7.73 (d, J =

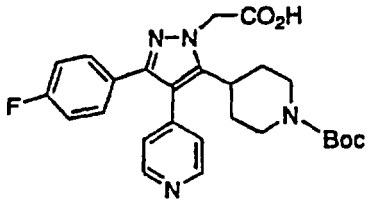
5.8 Hz, 2H), 7.40 (m, 2H), 7.23 (t, J = 8.5 Hz, 1H), 5.16 (s, 2H), 2.40 (s, 3H).

Example C-50



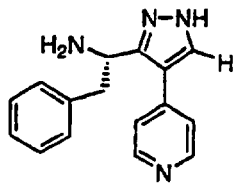
According to the procedure described above in Example C-49, Example C-50 was also prepared starting from 4-[3-(4-fluorophenyl)-1H-pyrazole-4-yl]pyridine. Mass spec: M+H cald: 298; found 298. ^{1}H NMR (DMSO-d6): 8.75 (d, J = 6.4 Hz, 2H), 8.68 (s, 1H), 7.78 (d, J = 6.6 Hz, 2H), 7.52 (dd, J = 5.4, 8.5 Hz, 2H), 7.31 (t, J = 8.9 Hz, 2H), 5.16 (s, 2H).

Example C-51

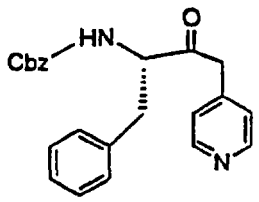


Starting with the N-Boc-piperidinyl analog of Example C-2, Example C-51 is also prepared according to the methods described in Scheme C-1.

Example C-52

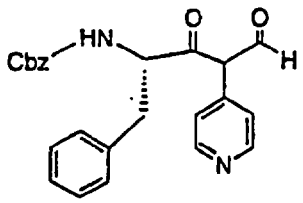


Step A: Picoline is treated with a base chosen from but not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH in an organic solvent such as THF, ether, t-BuOH or dioxane from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. The picoline solution is then added to a solution of N-Cbz-(L)-phenylalaninyl N-hydroxysuccinimide. The reaction is allowed to stir from 30 minutes to 48 hours during which time the temperature may range from -20 °C to 120 °C. The mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the pyridyl monoketone is isolated as a crude solid which could be purified by crystallization and/or chromatography.

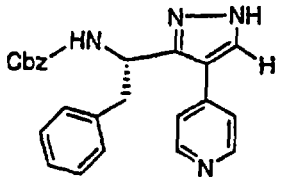


Step B: A solution of the pyridyl monoketone in ether, THF, tBuOH, or dioxane is added to a base chosen from but

not limited to n-BuLi, LDA, LiHMDS, tBuOK, or NaH contained in hexane, THF, ether, dioxane, or tBuOH from -78 °C to 50 °C for a period of time from 10 minutes to 3 hours. Formyl acetic anhydride is then added as a solution in THF, ether, or dioxane to the monoketone anion while the temperature is maintained between -50 °C and 50 °C. The resulting mixture is allowed to stir at the specified temperature for a period of time from 5 minutes to several hours. The resulting pyridyl diketone intermediate is utilized without purification in Step C.

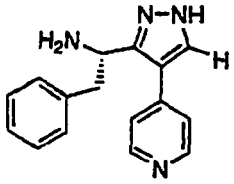


Step C: The solution containing the pyridyl diketone is quenched with water and the pH is adjusted to between 4 and 8 utilizing an inorganic or organic acid chosen from HOAc, H_2SO_4, HCl, or HNO_3. The temperature during this step is maintained between -20 °C and room temperature. Hydrazine or hydrazine hydrate is then added to the mixture while maintaining the temperature between -20 °C and 40 °C for a period of 30 minutes to several hours. The mixture is then poured into water and extracted with an organic solvent. The N-Cbz-protected pyridyl pyrazole is obtained as a crude solid which is purified by chromatography or crystallization.



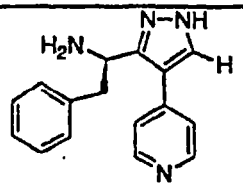
Step: D

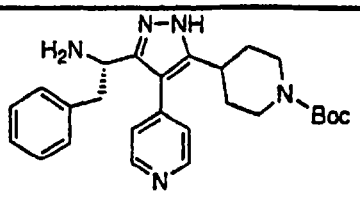
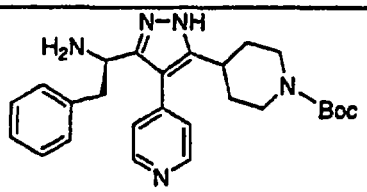
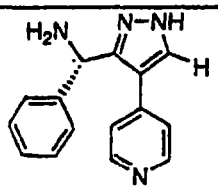
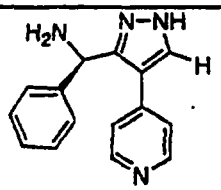
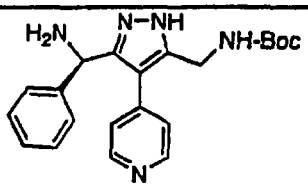
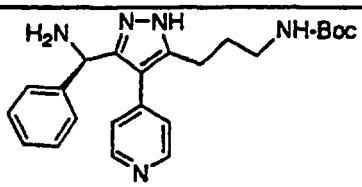
The CBZ protecting group is cleaved using hydrogen gas under pressure and Pd-C in an alcohol solvent, affording scaffold **C-52** after filtration and concentration.



The following compounds **C-53** through **C-59** in Table C-3 are prepared according to the general procedure described above for the preparation of **C-52**.

Table C-3

Example No.	Structure
C-53	

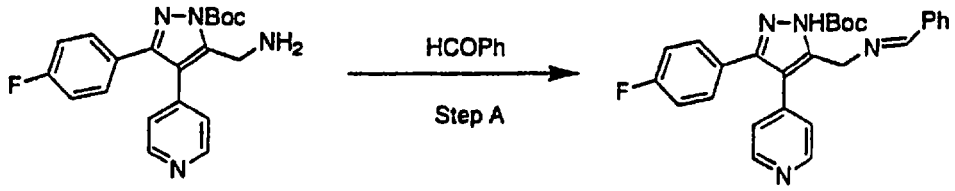
C-54	
C-55	
C-56	
C-57	
C-58	
C-59	

Example C-60

Step A:

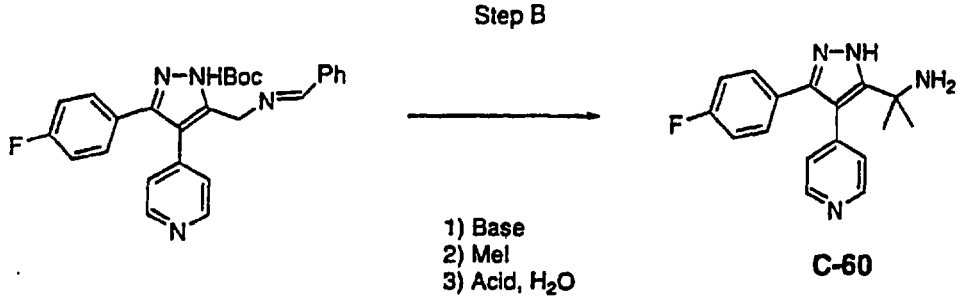
A Boc protected pyridylpyrazole is treated with benzaldehyde in methylene chloride at room temperature in

the presence of a drying agent for a period of time ranging from 1-24 h. Solvent is then evaporated and the resulting imine is used in step B without further purification.

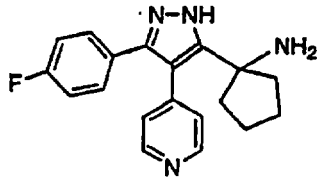


Step B:

The pyridylpyrazole imine is dissolved in THF and stirred under nitrogen at temperatures ranging from -78 to -20 °C. A base such as LDA, n-BuLi, or LiHMDS is added dropwise to the mixture which is then stirred for an additional 10 minutes to 3 h. Two equivalents of a methyl iodide are then added to the mixture and stirring is continued for several hours. The mixture is then quenched with acid and allowed to warm to room temperature and stirred several hours until cleavage of the Boc and the imine functions is complete. The pH is adjusted to 12 and then the mixture is extracted with an organic solvent, which is dried and evaporated. The crude pyridylpyrazole is then crystallized and/or chromatographed to give purified **C-60.**

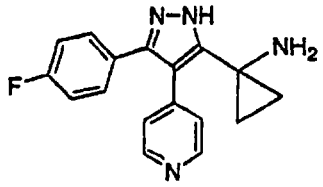


Example C-61



Example C-61 is prepared according to the method described in example C-60, substituting 1,4-dibromobutane for methyl iodide.

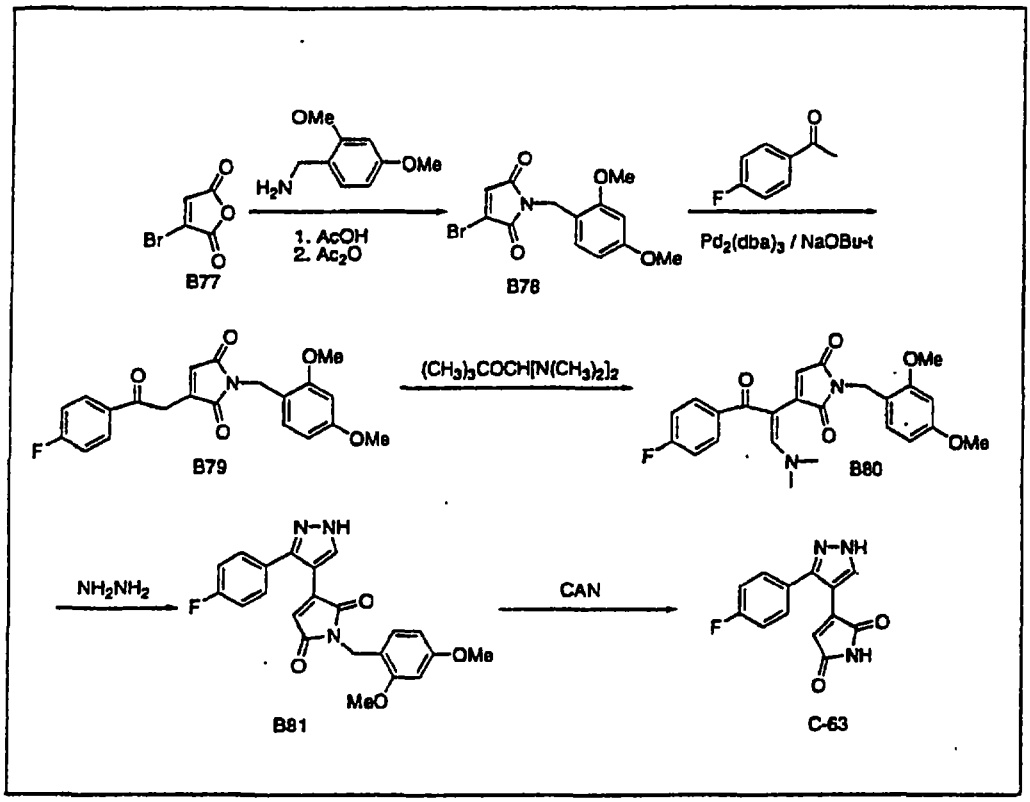
Example C-62



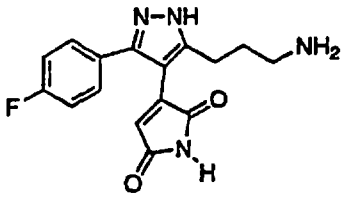
Example C-62 is prepared according to the method described in example C-60, substituting 1,3-dibromoethane for methyl iodide.

Example C-63

The synthesis of compound **C-63** starts with the condensation reaction of bromomaleic anhydride **B77** with 2, 4-dimethoxybenzylamine in acetic acid and acetic anhydride. The maleimide **B78** is then treated with 4'-fluoroacetophenone in the presence of catalytic amount $Pd_2(dba)_3$ and sodium t-butoxide to form the fluoroacetophenone substituted maleimide **B79**. **B79** is then treated with *tert*-butoxybis(dimethylamino)methane to yield the a-ketoenamine **B80**. The a-ketoenamine **B80** is condensed with hydrazine to form the N-protected maleimide pyrazole **B81**. The 2,4-dimethoxybenzyl group is cleaved with ceric ammonium nitrate (CAN) to give the title compound **C-63**.

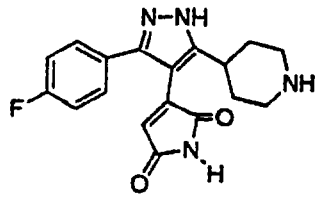


Example C-64



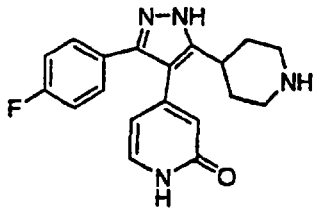
Using the method described in Schemes C-6 and C-7, Example 64 is prepared.

Example C-65



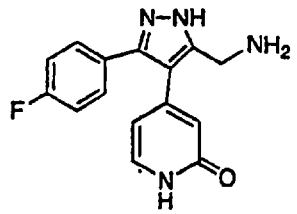
Using the method described in Schemes C-6 and C-7, Example 65 is prepared.

Example C-66



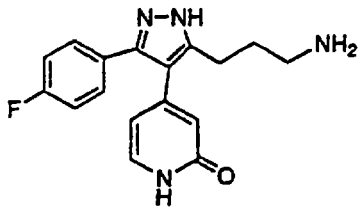
Using the method described in Schemes C-6 and C-7, Example C-66 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**.

Example C-67



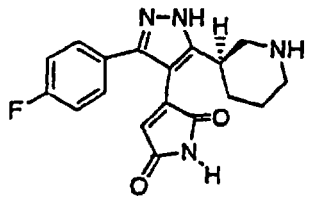
Using the method described in Schemes C-6 and C-7, Example C-67 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**, and substituting N-Boc-glycyl N-hydroxysuccinimide for **B82**.

Example C-68



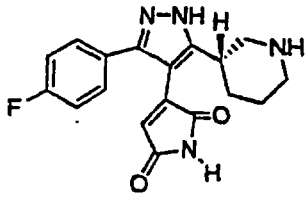
Using the method described in Schemes C-6 and C-7, Example C-68 is synthesized, substituting N-2,4-dimethoxybenzyl-4-bromopyridone for **B78**.

Example C-69



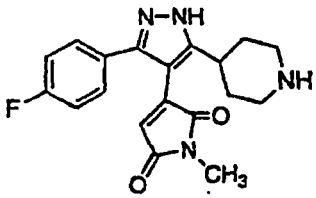
Using the method described in Schemes C-6 and C-7, Example 69 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

Example C-70



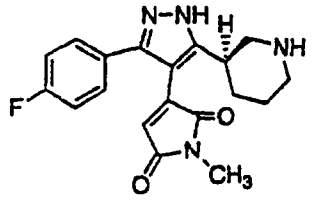
Using the method described in Schemes C-6 and C-7, Example 70 is prepared, substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

Example C-71



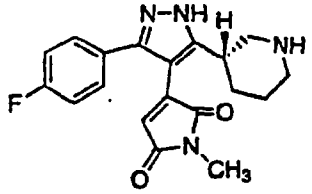
Using the method described in Schemes C-6 and C-7, Example 71 is prepared, substituting N-methyl-3-bromomaleimide for **B78**.

Example C-72



Using the method described in Schemes C-6 and C-7, Example 72 is prepared, substituting N-methyl-3-bromomaleimide for **B78**, and substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

Example C-73

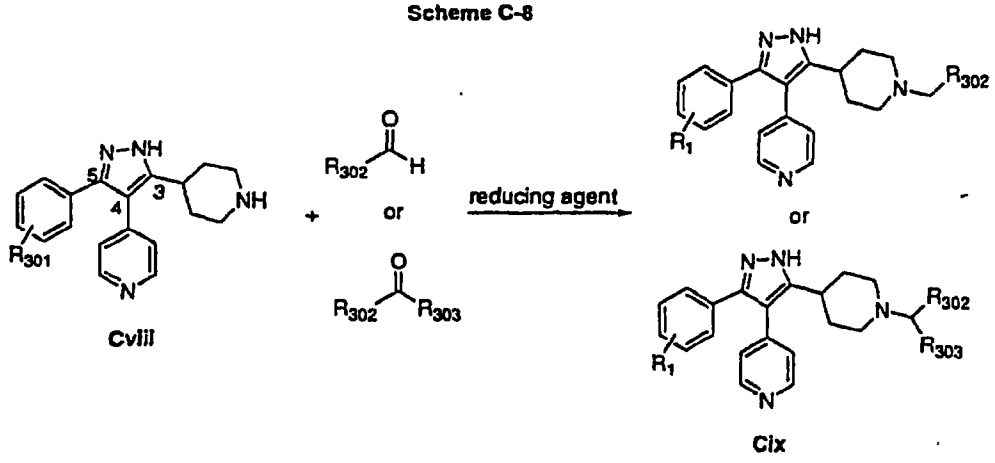


Using the method described in Schemes C-6 and C-7, Example 73 is prepared, substituting N-methyl-3-bromomaleimide for **B78** and substituting N-Boc-nipecotyl N-hydroxysuccinimide for **B83**.

General Synthetic Procedures

Scheme C-8 illustrates a general method that can be used for the introduction of various groups on an unsubstituted nitrogen atom that is present as part of pyrazole (**Cviii**) with appropriately substituted aldehydes ($R_{302}CHO$) or ketones ($R_{302}COR_{303}$) in the presence of a reducing agent such as sodium cyanoborohydride or sodium triacetoxyborohydride affords the desired products (**Cix**). Typical conditions for the reductive alkylation include the use of an alcoholic solvent at temperatures ranging from 20 °C to 80 °C. In Scheme C-8, R_{302} and R_{303} are selected from but not limited to alkyl, benzyl, substituted benzyl, arylalkyl, heteroarylalkyl.

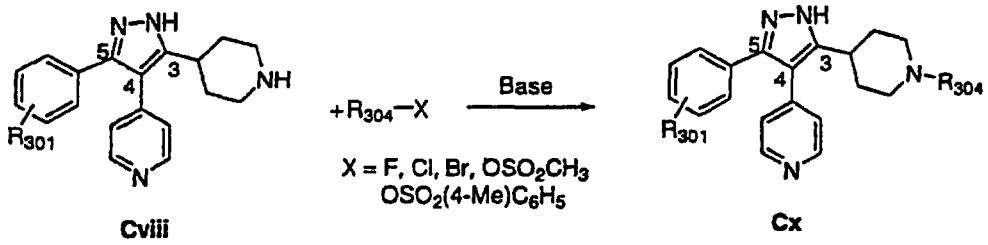
Scheme C-8



Scheme C-9 illustrates another method for introduction of substituents on the unsubstituted nitrogen atom present as part of the C-3 position of the pyrazole (**Cviii**). Treatment of the pyrazole (**Cviii**) with

a suitable alkylating agent ($R_{304}X$) such as an alkyl chloride, alkyl bromide, alkyl iodide or with an alkyl methanesulfonate or alkyl p-toluenesulfonate in the presence of a suitable base affords the desired alkylated pyrazoles (**Cx**). Examples of suitable bases include diisopropylethylamine, triethylamine, N-methylmorpholine, potassium carbonate and potassium bicarbonate.

Scheme C-9



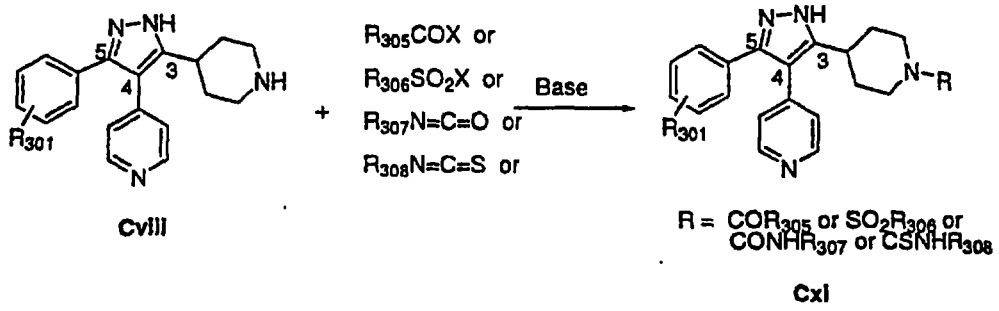
Cviii **Cx**

Typical conditions for the alkylation include reaction with the suitable base in a polar aprotic solvent such as acetonitrile, dimethylformamide, dimethylacetamide or dimethyl sulfoxide at temperatures ranging from 20 °C to 150 °C. Typical R_{304} substituents are selected from but are not limited to alkyl, substituted benzyl, heteroaromatic, substituted heteroalkyl and substituted heteroarylalkyl groups.

Compounds containing acyl, sulfonyl or ureidyl groups at the nitrogen atom can be prepared as shown in Scheme C-10. Treatment of the pyrazole **Cviii** with a suitable acylating agent in the presence of a base such as N-methylmorpholine, triethylamine, diisopropylethylamine or dimethylamino pyridine in an

organic solvent such as dichloromethane, dichloroethane or dimethylformamide at temperatures ranging from 20 °C to 120 °C affords the desired acylated pyrazoles (**Cxi**). Suitable acylating agents include acid halides, activated esters of acids such as the N-hydroxysuccinimde esters, p-nitrophenyl esters, pentafluorophenyl esters, sulfonyl halides, isocyanates, and isothiocyanates.

Scheme C-10



Cviii

R = COR_{305} or SO_2R_{306} or $CONHR_{307}$ or $CSNHR_{308}$

Cxi

A general synthesis of 2-substituted pyrimidinylpyrazole compounds of type **Cxv** is shown in Scheme C-11.

Step A:

4-Methyl-2-methylmercaptopyrimidine is treated with a base selected from but not limited to n-BuLi, LDA, LiHMDS, t-BuOK, NaH in an organic solvent such as THF, ether, t-BuOH, dioxane from -78 °C to 50 °C for a period of time from 30 minutes to 5 hours. The resulting 4-methyl anion is then added to a solution of an appropriate ester **B88**. The reaction is allowed to stir from 30 minutes to 48 hours during which time the

temperature may range from 0 °C to 100 °C. The reaction mixture is then poured into water and extracted with an organic solvent. After drying and removal of solvent the desired monoketone **B89** is isolated as a crude solid which can be recrystallized or purified by chromatography.

Step B:

Monoketone **B89** is treated with a base selected from but not limited to n-BuLi, LDA, LiHMDS, t-BuOK, NaH, K_2CO_3 or Cs_2CO_3 in an organic solvent such as THF, ether, t-BuOH, dioxane, toluene or DMF from -78 °C to 50 °C for a period of time from 30 minutes to 5 hours. A solution of an appropriately activated ester of a carboxylic acid $CbzNR''-(CH_2)_nCR'(R^6)-COOH$ or $BocNR''-(CH_2)_nCR'(R^6)-COOH$, preferably but not limited to the N-hydroxysuccinimide ester **B90** is then added to the monoketone anion while maintaining the temperature between 0 °C to 100 °C. The reaction is allowed to stir at the specified temperature for a period of time ranging from 30 minutes to 48 hours. The resulting pyrimidine diketone intermediate **B91** is utilized without further purification in Step C.

Step C:

The solution or suspension containing the diketone intermediate **B91** is quenched with water and the pH adjusted to between 4 and 8 using an acid chosen from AcOH, H_2SO_4, HCl or HNO_3 while maintaining the temperature between 0 °C to 40 °C. Hydrazine or hydrazine monohydrate is then added to the mixture while maintaining the temperature between 0 °C to 40 °C. The mixture is stirred

for a period of 30 minutes to 16 hours maintaining the temperature between 20 °C to 50 °C, poured into water and extracted with an organic solvent. The pyrimidinyl pyrazole **CxiiBoc** or **CxiiCbz** is obtained as crude solid which is purified by chromatography or crystallization.

Step D:

The 2-methylmercapto group in the pyrimidinyl pyrazole (**CxiiBoc** or **CxiiCbz**) is oxidized to the 2-methylsulfone (where n =2) or the 2-methylsulfoxide (where n = 1) using either Oxone or m-chloroperbenzoic acid as an oxidizing agent in a suitable solvent at temperatures ranging from 25 °C to 100 °C. Solvents of choice for the oxidation include dichloromethane, acetonitrile, tetrahydrofuran or hydroalcoholic mixtures. The 2-methylsulfone (n = 2) or the 2-methylsulfoxide (n = 1) (**CxiiiBoc** or **CxiiiCbz**) is purified by crystallization or chromatography.

Step E:

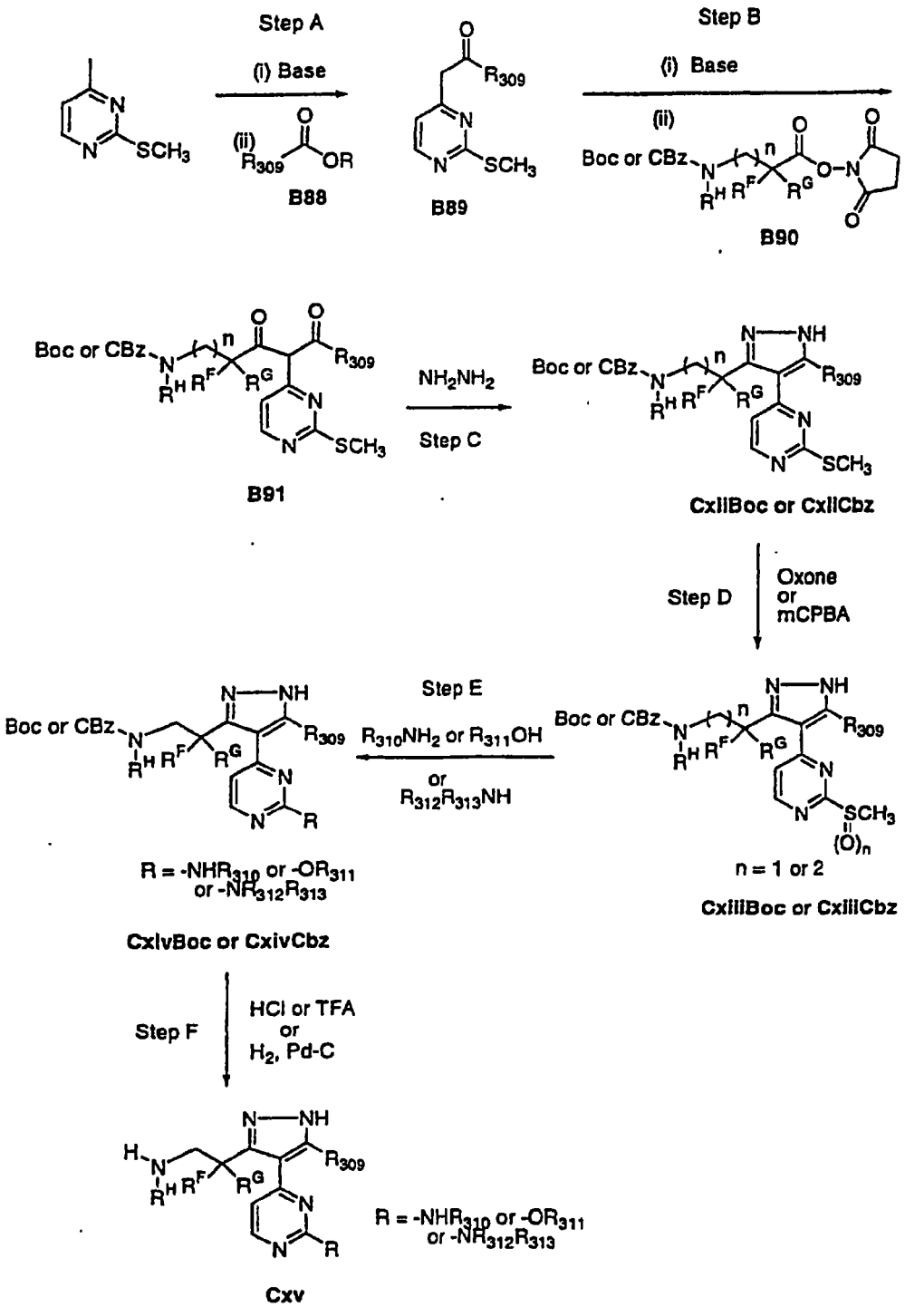
The 2-methylsulfone/2-methylsulfoxide group in **CxiiiBoc** or **CxiiiCBz** is conveniently displaced with various amines or alkoxides at temperatures ranging from 20 °C to 200 °C in solvents that include but are not limited to dimethylformamide, acetonitrile, tetrahydrofuran and dioxane. The alkoxides can be generated from their alcohols by treatment with a base selected from but not limited to sodium hydride, lithium hexamethyldisilazide, potassium tertiary-butoxide in solvents such as tetrahydrofuran, dimethylformamide and

dioxane at temperatures ranging from 0 °C to 100 °C. The resulting 2-amino or 2-oxo derivatives (**CxivBoc** or **CxivCbz**) are purified by either chromatography or crystallization.

Step F:

The carbamate protecting groups from **CxivBoc** or **CxivCbz** are removed to afford the desired compounds **Cxv** containing either a free primary amine ($R^{''}$ is hydrogen) or a free secondary amine ($R^{''}$ is not equal to hydrogen). The Boc protecting groups are cleaved utilizing either trifluoroacetic acid in methylene chloride or hydrochloric acid in dioxane at room temperature for several hours. The Cbz protecting groups are cleaved using hydrogen gas at atmospheric or higher pressures and a catalyst (palladium on charcoal) in an alcoholic solvent. The resulting amines **Cxv** are then crystallized or purified by chromatography.

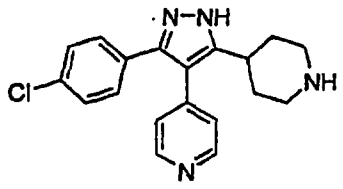
SCHEME C-11


Step A
(i) Base
(ii)
B88
B89
Step B
(i) Base
(ii)
B90
B91
NH2NH2
Step C
CxiiBoc or CxiiCbz
Step D
Oxone
or
mCPBA
Step E
R310NH2 or R311OH
or
R312R313NH
CxiiiBoc or CxiiiCbz
n = 1 or 2
R = -NHR310 or -OR311
or -NR312R313
CxivBoc or CxivCbz
Step F
HCl or TFA
or
H2, Pd-C
Cxv
R = -NHR310 or -OR311
or -NR312R313

The following examples contain detailed descriptions of the methods of preparation of compounds that form part of the invention. These descriptions are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All compounds showed NMR spectra consistant with their assigned structures.

Example C-74

5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

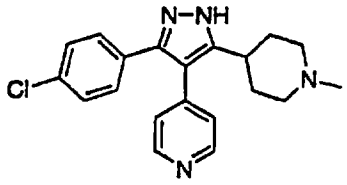


By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: ^{1}HNMR (d_6-DMSO) δ 8.57 (d, *J* = 4.83 Hz, 2 H), 7.41 (d, *J* = 8.26 Hz, 2 H), 7.29 (d, *J* = 8.26 Hz, 2 H), 7.20 (d, *J* = 4.63 Hz, 2 H), 3.18 (bd, *J* =

12.08 Hz, 2 H), 2.88 (m, 1 H), 2.76 (m, 2 H), 1.82 (bs, 4 H). MS (M+H): 339 (base peak).

Example C-75

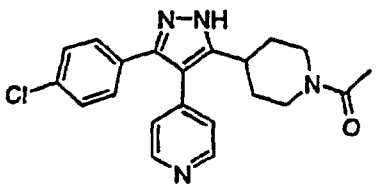
5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



To a solution of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (25 g, 61 mmol) in 140 mL of formic acid (96%) was added 50 g of formaldehyde (37%). The solution was stirred at 75 °C for 48 h and was cooled to room temperature. The excess formic acid was removed under reduced pressure and the residue was dissolved in 100 mL of water. The solution was added to concentrated NH_4OH/H_2O and the mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were washed with brine (1 x 250 mL) and was dried over Na_2SO_4. The solution was filtered and concentrated to leave a white solid. The solid was triturated with ether and was filtered to afford the title compound: MS (M+H): 353 (base peak).

Example C-76

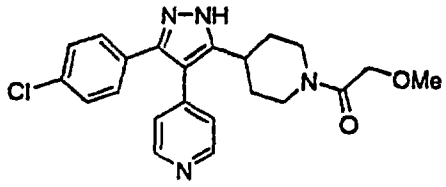
5-(*N*-ACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (1 g, 2.4 mmol) in 24 mL of CH_2Cl_2 was added 4-dimethylamino pyridine (0.88 g, 7.2 mmol) and acetyl chloride (0.21 g, 2.6 mmol). The solution was stirred for 3 h and the solvent was removed under reduced pressure. The residue was treated with saturated NH_4OH (20 mL) and the suspension was extracted with ethyl acetate (3 x 30 mL). The combined extracts were washed with brine (1 x 50 mL), dried over $MgSO_4$, filtered and concentrated to leave a solid. The solid was triturated with ether and was filtered to leave the title compound: MS (M+H): 381 (base peak).

Example C-77

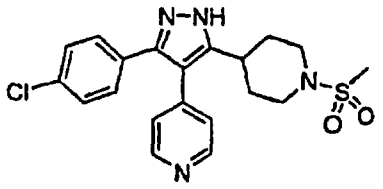
5-(*N*-METHOXYACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting methoxy acetyl chloride for acetyl chloride the title compound was prepared: ^{1}HNMR (DMSO-d_6) δ 8.75 (d, J = 6.72 Hz, 2 H), 7.70 (d, J = 6.72 Hz, 2 H), 7.38 (d, J = 8.60 Hz, 2 H), 7.29 (dd, J = 6.72, 1.88 Hz, 2 H), 4.40 (d, J = 11.8 Hz, 1 H), 4.05 (m, 2 H), 3.70 (d, J = 12.70 Hz, 1 H), 3.25 (s, 3 H), 3.0 (m, 2 H), 2.55 (m, 1 H), 1.7 (m, 4 H). MS (M+H): 411 (base peak).

Example C-78

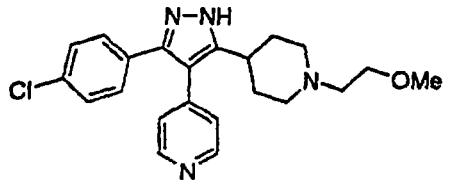
5-(*N*-METHYLSULFONYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting methylsulfonyl chloride (2.0 equivalents) for acetyl chloride the title compound was prepared: ^{1}HNMR (DMSO-d_6) δ 8.70 (d, J = 6.72 Hz, 2 H), 7.72 (d, J = 6.72 Hz, 2 H), 7.38 (d, J = 7.66 Hz, 2 H), 7.30 (dd, J = 6.72, 1.88 Hz, 2 H), 3.58 (bd, J = 11.8 Hz, 2 H), 2.87 (m, 1 H), 2.82 (s, 3 H), 2.72 (m, 2 H), 1.85 (m, 4 H). MS (M+H): 417 (base peak).

Example C-79

5-[*N*-METHOXYETHYL-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

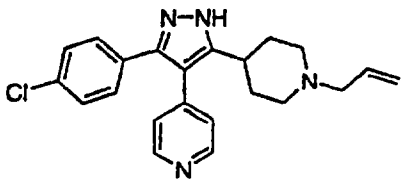


To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) (500 mg, 1.2 mmol) in 12 mL of DMF was added Hunig's base (790 mg, 6.1 mmol) and 2-bromoethyl methyl ether (850 mg, 6.1 mmol). The solution was stirred at room temperature for 5 days. The solution was poured onto 2.5 N NaOH and was extracted with ethyl acetate (3 x 100 mL). The combined extracts were washed with water (3 x 100 mL) and brine (1 x 100 mL). The organic phase was dried over Na_2SO_4 and was filtered. The

solvent was removed under reduced pressure to leave a solid. The solid was triturated and filtered to leave the title compound: ^{1}HNMR ($CDCl_3$) δ 8.63 (d, J = 4.23 Hz, 2 H), 7.28 (m, 4 H), 7.14 (d, J = 4.43 Hz, 2 H), 3.57 (t, J = 5.24 Hz, 2 H), 3.38 (s, 3 H), 3.14 (bd, J = 10.1 Hz,. 2 H), 2.79 (m, 1 H), 2.68 (t, J = 5.04, 2 H), 2.08 (m, 4 H), 1.92 (m, 2 H). MS (M+H): 397 (base peak).

Example C-80

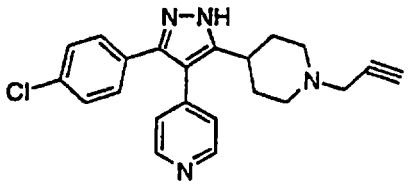
5-(*N*-ALLYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of example C-79 and substituting allyl bromide for 2-bromoethyl methyl ether the title compound was prepared: MS (M+H): 379 (base peak)

Example C-81

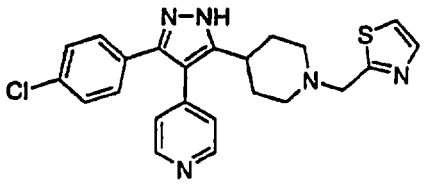
5-(*N*-PROPARGYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of example C-79 and substituting propargyl bromide for 2-bromoethyl methyl ether the title compound was prepared: MS (M+H): 377 (base peak)

Example C-82

5-[*N*-(2-METHYLTHIAZOLYL)-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

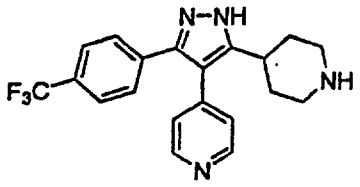


To a suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) in 12 mL of MeOH was added trimethyl orthoformate (2.6 g,

24.4 mmol) and 2-thiazolecarboxaldehyde (1.4 g, 12.2 mmol). The suspension was stirred at room temperature for 2 h. To this mixture was added $NaCNBH_3$ (1.5 g, 24.4 mmol) and the resulting suspension was stirred at room temperature for 7 days. The mixture was poured onto 2.5 N NaOH and was extracted with ethyl acetate (2 x 100 mL). The combined extracts were washed with brine (1 x 100 mL), dried over Na_2SO_4, filtered and concentrated to leave a solid. This solid was triturated with ether and filtered to afford the title compound: MS (M+H): 436 (base peak).

Example C-83

5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE

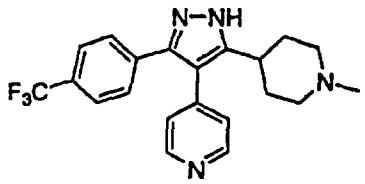


By following the method of Example C-1 and substituting methyl-4-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate

was accomplished with 4 N HCl in dioxane to afford the title compound as its hydrochloride salt: MS (M+H): 373 (base peak).

Example C-84

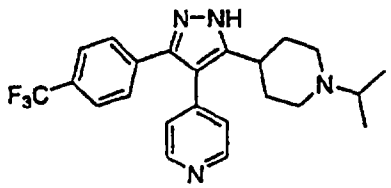
5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole hydrochloride (Example C-83) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 387 (base peak).

Example C-85

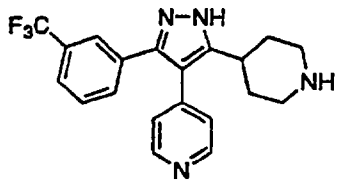
5-[*N*-(2-PROPYL)-4-PIPERIDYL]-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



To a solution of 5-(4-piperidyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole (Example C-83) (300 mg, 0.7 mmol) in 50 mL of acetone was added 1 mL of AcOH and $NaBH(OAc)_3$ (15 g, 70.8 mmol). The mixture was warmed to reflux and was stirred for 5 days. The reaction mixture was poured onto 100 mL of 2.5 N NaOH and was extracted with ethyl acetate (2 x 100 mL). The extracts were combined and washed with brine (1 x 100 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated to afford the title compound: MS (M+H): 415 (base peak).

Example C-86

5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE

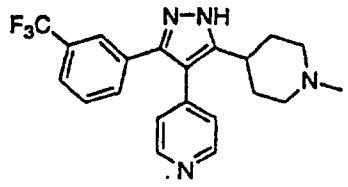


By following the method of Example C-1 and substituting methyl-3-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the

title compound as its hydrochloride salt: MS (M+H): 373 (base peak).the pyrazole C-3 substituent (**Cviii**). Treatment of the

Example C-87

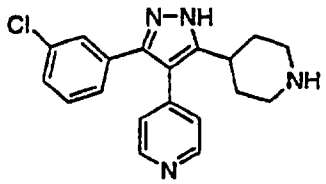
5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-[3-(trifluoromethyl)phenyl] pyrazole hydrochloride (Example C-86) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 387 (base peak).

Example C-88

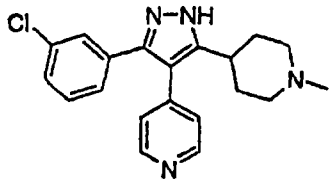
5-(4-PIPERIDYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting methyl-3-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 339 (base peak).

Example C-89

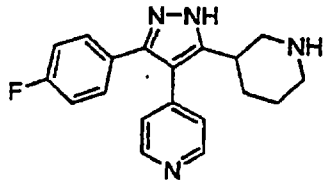
5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(3-chlorophenyl) pyrazole hydrochloride (Example C-88) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 353 (base peak).

Example C-90

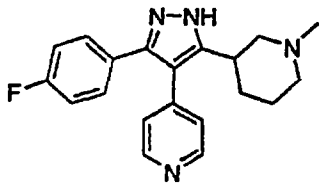
5-(3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-nipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as its hydrochloride salt: MS (M+H): 323 (base peak).

Example C-91

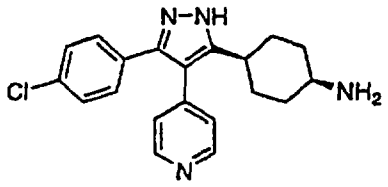
5-(*N*-METHYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole hydrochloride (Example C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 337 (base peak).

Example C-92

5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

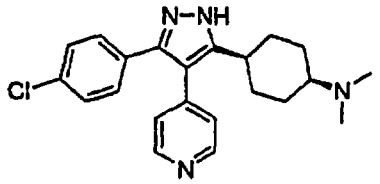


By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-

fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: ^{1}HNMR (d_6-DMSO) δ 8.56 (d, *J* = 6.04 Hz, 2 H), 7.39 (d, *J* = 8.66 Hz, 2 H), 7.31 (d, *J* = 8.46 Hz, 2 H), 7.17 (d, *J* = 5.84 Hz, 2 H), 3.05 (m, 1 H), 2.62 (m, 1 H), 1.99 (m, 2 H), 1.53 (m, 6 H). MS (M+H): 353 (base peak).

Example C-93

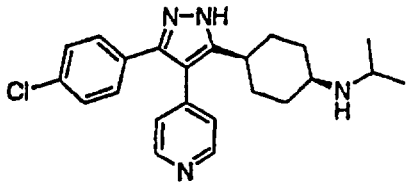
5-*cis*-(4-*N*,*N*-DIMETYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 381 (base peak).

Example C-94

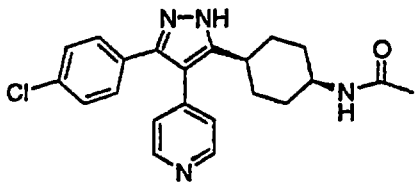
5-[*cis*-4-*N*-(2-PROPYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



To a slurry of 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) (1.0 g, 2.8 mmol, 1.0 eq) in methylene chloride (28 mL) was added acetone (0.5 mL), acetic acid (0.5 mL) and solid sodium triacetoxyborohydride. The slurry was stirred for 5 h and the volatiles were removed. The residue was partitioned between 2.5 M NaOH (25 mL) and ethyl acetate (25 mL) and the aqueous layer was extracted with ethyl acetate (3 x 25 mL). The combined organic layer was washed with brine (50 mL), dried over $MgSO_4$ and evaporated. The residue was triturated with ether to yield the title compound as a white powder: ^{1}HNMR (d_6-DMSO) δ 8.56 (d, *J* = 5.84 Hz, 2H), 7.40 (d, *J* = 8.26 Hz, 2H), 7.30 (d, *J* = 8.66 Hz, 2H), 7.18 (d, *J* = 5.64 Hz, 2H), 2.95 (m, 2H), 2.72 (m, 1H), 1.90 (m, 2H), 1.73 (m, 2H), 1.55 (m, 4H), 1.07 (d, *J* = 5.64 Hz, 6H). MS (M+H): 395 (base peak).

Example C-95

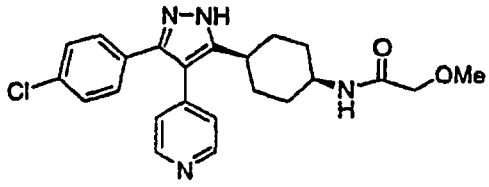
5-*cis*-[4-*N*-(ACETYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 395 (base peak).

Example C-96

5-*cis*-[4-*N*-(METHOXYACETYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

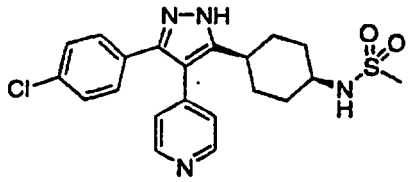


By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-

(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) and methoxy acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 425 (base peak).

Example C-97

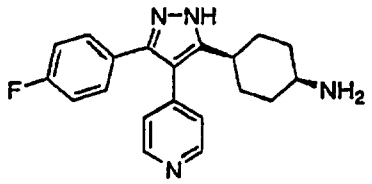
5-*cis*-[4-*N*-(METHYLSULFONYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) and methylsulfonyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 431 (base peak).

Example C-98

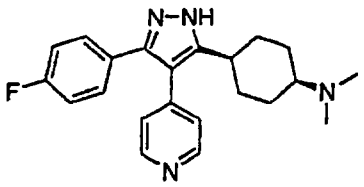
5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 337 (base peak).

Example C-99

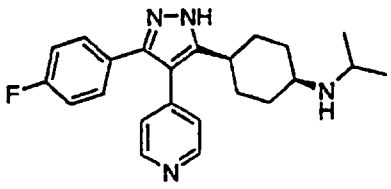
5-(*cis*-4-*N*,*N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-98) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 365 (base peak).

Example C-100

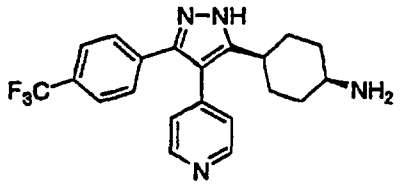
5-*cis*-[4-*N*-(2-PROPYL)AMINOCYCLOHEXYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-94 and substituting *cis*-5-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-98) for 5-(*cis*-4-n-(2-propyl)aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-92) the title compound was prepared: MS (M+H): 379 (base peak).

Example C-101

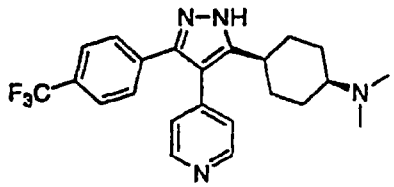
5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-1 and substituting methyl-4-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 387 (base peak).

Example C-102

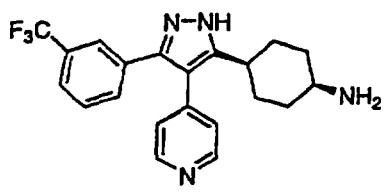
5-*cis*-(4-*N*,*N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[4-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-[4-(trifluoromethyl)phenyl] pyrazole (Example C-101) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 415 (base peak).

Example C-103

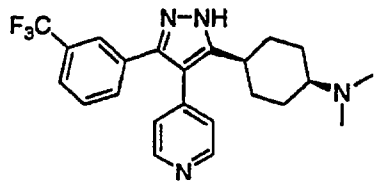
5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-1 and substituting methyl-3-(trifluoromethyl)benzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-t-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 387 (base peak).

Example C-104

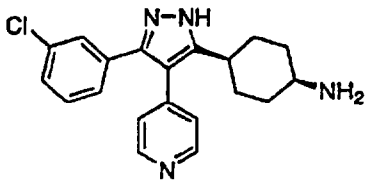
5-*cis*-(4-*N*,*N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-[3-(TRIFLUOROMETHYL)PHENYL] PYRAZOLE



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(3-(trifluoromethyl)phenyl) pyrazole (Example C-103) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 415 (base peak).

Example C-105

5-*cis*-(4-AMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE

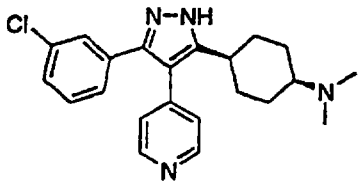


By following the method of Example C-1 and substituting methyl-3-chlorobenzoate for ethyl-4-

fluorobenzoate and *N*-*t*-butoxycarbonyl-*cis*-4-aminocyclohexanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 353 (base peak).

Example C-106

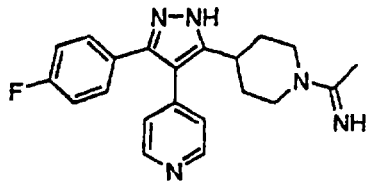
5-*cis*-(4-*N*,*N*-DIMETHYLAMINOCYCLOHEXYL)-4-(4-PYRIDYL)-3-(3-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-*cis*-(4-aminocyclohexyl)-4-(4-pyridyl)-3-(3-chlorophenyl) pyrazole hydrochloride (Example C-105) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 381 (base peak).

Example C-107

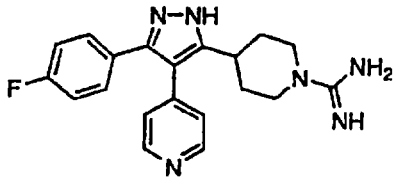
5-(*N*-ACETIMIDO-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



To a suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) (0.11 g, 0.35 mmol) in 2 mL EtOH was added ethyl acetamidate hydrochloride (0.065 g, 0.53 mmol) and the mixture was refluxed for 30 minutes. The solution was left at 5-10 °C for 16 h and filtered to obtain the title compound as a white solid: MS (M+H): 364 (base peak).

Example C-108

5-(*N*-CARBOXAMIDINO-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

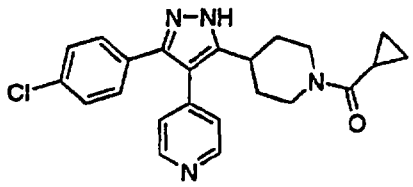


To a stirred suspension of 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-2) (1.5 g, 4.7

mmol) in 47 mL of DMF was added Hunig's base (0.60 g, 4.7 mmol) and pyrazole carboxamide hydrochloride (0.68 g, 4.7 mmol). The slurry was allowed to stir at room temperature for 4 days. The reaction mixture was poured onto 300 mL of ether. The resulting precipitate was filtered to leave the title compound as the hydrochloride salt: MS (M+H): 365 (base peak).

Example C-109

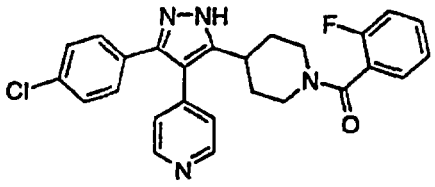
5-(*N*-CYCLOPROPANOYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting cyclopropanoyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 407 (base peak).

Example C-110

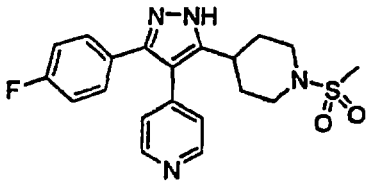
5-[*N*-(2-FLUORO)BENZOYL-4-PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 2-fluorobenzoyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 461 (base peak).

Example C-111

5-(*N*-METHYLSULFONYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

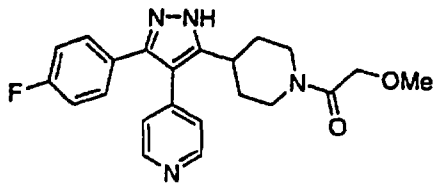


By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-74)

and methylsulfonyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 401 (base peak).

Example C-112

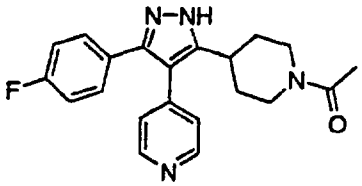
5-(*N*-METHOXYACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-74) and methoxy acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 395 (base peak).

Example C-113

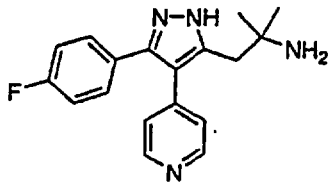
5-(*N*-ACETYL-4-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole Example (C-2) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole Example (C-74) the title compound was prepared: MS (M+H): 365 (base peak).

Example C-114

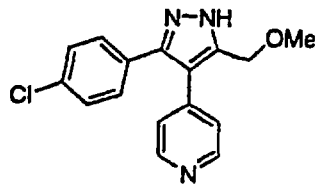
5-[2-(1,1-DIMETHYL)AMINOETHYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting *N*-*t*-butoxycarbonyl-2-amino-2,2-dimethylpropanoyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: MS (M+H): 327 (base peak).

Example C-115

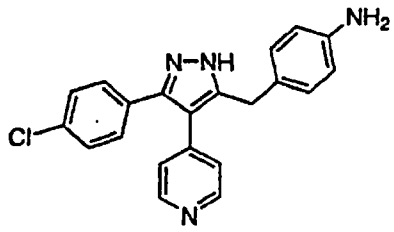
5-(METHOXYMETHYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and 2-methoxyacetyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 300 (base peak).

Example C-116

5-(4-AMINOBENZYL)-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

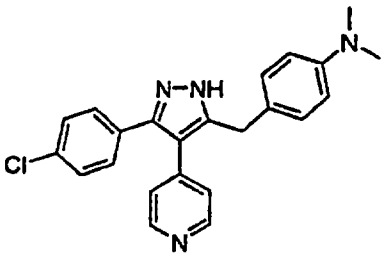


By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and *N*-*t*-butoxycarbonyl-4-aminophenyl

acetyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: MS (M+H): 361 (base peak).

Example C-117

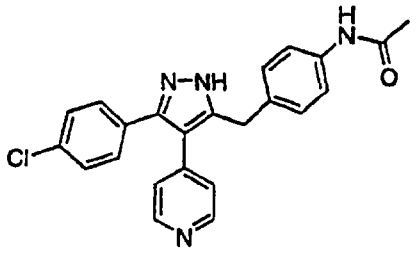
5-[4-(*N*,*N*-DIMETHYL)AMINOBENZYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-(4-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-116) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 389 (base peak).

Example C-118

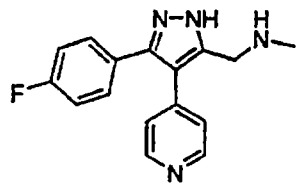
5-[4-(*N*-ACETYL)AMINOBENZYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-(4-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-116) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 403 (base peak).

Example C-119

5-(*N*-METHYLAMINOMETHYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



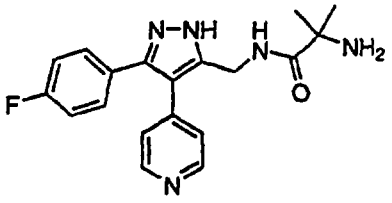
5-(*N*-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a suspension of 5-aminomethyl-

4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) (8.04 g, 30 mmol) in 120 mL dichloromethane was added p-nitrophenylformate (6.01 g, 36 mmol) as a solid. The suspension was stirred for 24 h at room temperature and the solvents removed under reduced pressure. The residue was triturated with ether and filtered to obtain the desired 5-(*N*-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole derivative as a white solid: MS (M+H): 297 (base peak).

5-(*N*-methylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a suspension of 5-(*N*-formylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (8.74 g, 29.5 mmol) in 90 mL anhydrous tetrahydrofuran was added a 1.0 M solution of borane in tetrahydrofuran (90 mL, 90 mmol) and the mixture was stirred at room temperature for 24 h. 1 N aqueous hydrochloric acid (100 mL) was then added to this mixture and the solution was refluxed for 5 hours and cooled to room temperature. The solution was extracted with ether (2 x 250 mL) and the pH of the aqueous layer adjusted to 9 by addition of concentrated ammonium hydroxide. The aqueous layers (pH ~ 9) were then extracted with ethyl acetate (4 x 150 mL). The organic extracts were dried over sodium sulfate, filtered and evaporated to dryness under reduced pressure. The residue was triturated with acetonitrile and filtered to obtain the title compound as a white solid: MS (M+H): 283 (base peak).

Example C-120

5-[*N*-(2-AMINO-2,2-DIMETHYLACETYL)AMINOMETHYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



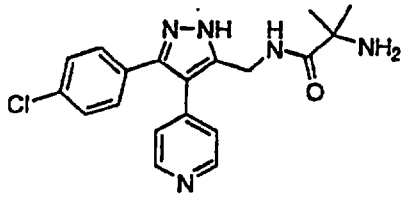
5-(*N*-*t*-butoxycarbonylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a solution of 5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) (0.27 g, 1 mmol) in anhydrous dimethylformamide (4 mL) was added *N*-tert-butoxycarbonyl aminoisobutyric acid *N*-hydroxysuccinimide ester (0.33 g, 1.1 mmol) and the mixture stirred at 40 °C for 24 h. The resulting solution was evaporated to dryness under reduced pressure. The residue was dissolved in dichloromethane (30 mL) and washed with a saturated solution of sodium bicarbonate (2 x 20 mL) and brine (20 mL). The organic layers were dried over sodium sulfate, filtered and evaporated under reduced pressure to dryness to afford 5-(*N*-*t*-butoxycarbonylaminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole as a white solid.

5-(*N*-(2-amino-2,2-dimethylacetyl)aminomethyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole. To a solution of the above compound in acetonitrile (2 mL) was added 1 mL of a 4.0 M solution of hydrochloric acid in dioxane. The

reaction mixture was stirred at room temperature for 6 hours. The suspension was evaporated to dryness under reduced pressure. The resulting residue was stirred in acetonitrile (5 mL), filtered and dried in a vacuum dessicator to afford the title compound as a hydrochloride salt: MS (M+H): 354 (base peak).

Example C-121

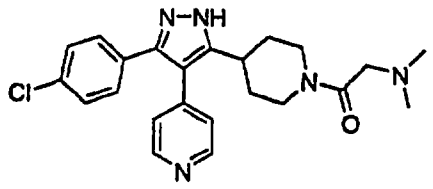
5-[*N*-(2-AMINO-2,2-DIMETHYLACETYL)AMINOMETHYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-120 and substituting 5-aminomethyl-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (Example C-15) for 5-aminomethyl-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-1) the title compound was prepared: MS (M+H): 370 (base peak).

Example C-122

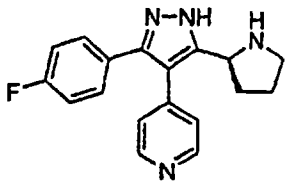
5-[4-*N*-(2-DIMETHYLAMINOACETYL)PIPERIDYL]-4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



To a solution of N,N-dimethylglycine hydrochloride (0.28 g, 2 mmol) in dimethylformamide (4 mL) was added hydroxybenzotriazole (0.27 g, 2 mmol), N,N-diisopropylethyl amine (0.7 mL, 4 mmol) and polymer supported ethyl carbodimide (Example B-49) (1 g, 2.39 mmol). To this solution after 30 minutes at room temperature was added 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74), 0.41 g, 1 mmol). The suspension was agitated on a labtop orbital shaker for 24 h. The suspension was filtered, washed with dimethylformamide (2 x 5 mL) and the filtrates evaporated under high pressure. The residue was dissolved in dichloromethane (30 mL), washed with a saturated solution of sodium bicarbonate (50 mL) and brine (50 mL). The organic layers were dried over sodium sulfate, filtered and evaporated under high vacuum to afford the title compound as a white solid: MS (M+H): 424 (base peak).

Example C-123

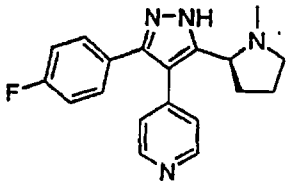
(*S*)-5-(2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting (*S*)-*N*-*t*-butoxycarbonyl-prolinyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 309 (base peak).

Example C-124

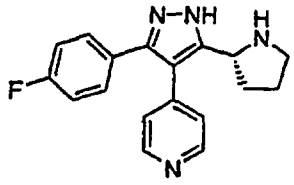
(*S*)-5-(*N*-METHYL-2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting (*S*)-5-(2-pyrolidinyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-123) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 323 (base peak).

Example C-125

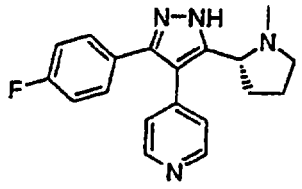
(*R*)-5-(2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-1 and substituting (*R*)-*N*-*t*-butoxycarbonyl-prolinyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 309 (base peak).

Example C-126

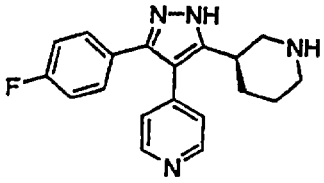
(*R*)-5-(*N*-METHYL-2-PYROLIDINYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting (*R*)-5-(2-pyrolidinyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-125) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 323 (base peak).

Example C-127

(*R*)-5-(3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

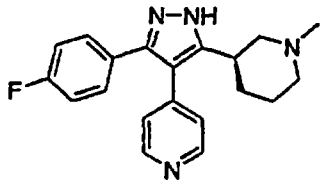


By following the method of Example C-1 and substituting (*R*)-*N*-*t*-butoxycarbonyl-nipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-

hydroxysuccinimide the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound: MS (M+H): 323 (base peak).

Example C-128

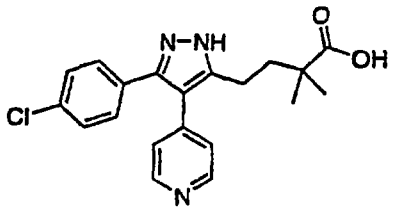
(*R*)-5-(*N*-METHYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting (*R*)-5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (Example C-125) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: MS (M+H): 337 (base peak).

Example C-129

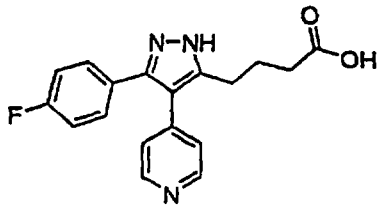
2,2-DIMETHYL-4-[4-(4-PYRIDYL)-3-(4-CHLOROPHENYL) PYRAZOLYL] BUTYRIC ACID



By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate and 2,2-dimethyl glutaric anhydride for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 370 (base peak).

Example C-130

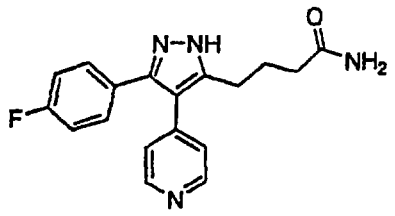
4-[4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL] BUTYRIC ACID



By following the method of Example C-1 and substituting glutaric anhydride for *N*-benzyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 326 (base peak).

Example C-131

4-[4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL] BUTYRAMIDE



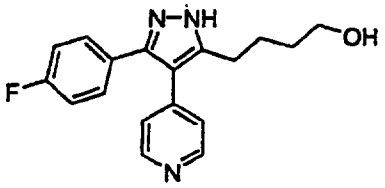
Methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate. To a solution of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyric acid (Example C-130) (40 g, 123 mmol) in 650 mL of MeOH was added 20 mL of concentrated H_2SO_4. The solution was stirred overnight at room temperature. The solution was concentrated and diluted with 200 mL of water. The solution was cooled with an ice/water bath and to the solution was added 150 mL of saturated $NaHCO_3$. The solution was neutralized further with 50% NaOH to pH 7. The resulting slurry was extracted with CH_2Cl_2 (3 x 250 mL). The combined extracts were washed with water (1 x 300 mL) and saturated $NaHCO_3$ (1 x 500 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated to afford methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate: MS (M+H): 340 (base peak).

4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyramide. A solution of methyl 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyrate (39 g, 120 mmol) in 600 mL of MeOH was saturated with NH_3. The solution was

periodically treated with additional NH_3 over a 24 h period. The solution was degassed with a stream of nitrogen and the solution was concentrated to leave a yellow solid. The solid was slurried in ether and filtered to leave the title compound: MS (M+H): 325 (base peak).

Example C-132

5-[4-(1-HYDROXY)BUTYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

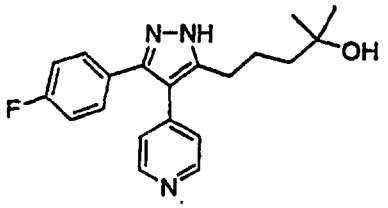


A stirred suspension of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyric acid (Example C-130) (2 g, 6.15 mmol) in 100 ml of anhydrous ether was cooled to 0 °C under nitrogen. Lithium aluminum hydride (467 mg, 12.3 mmol) was added to this suspension slowly. After the addition was complete, the mixture was warmed to room temperature and stirred for additional 2 h. The reaction was quenched slowly with 1N $KHSO_4$ (80 ml). The mixture was transferred to a separatory funnel and the aqueous layer was removed. The aqueous layer was then made basic with K_2CO_3 (pH 8). The aqueous solution was extracted with ethyl acetate (2 x 100 mL). The combined ethyl acetate extracts were washed with water (1 x 100

mL), dried over $MgSO_4$, filtered and concentrated to give the title compound: MS (M+H): 312 (base peak).

Example C-133

5-[4-(1,1-DIMETHYL-1-HYDROXY)BUTYL]-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE

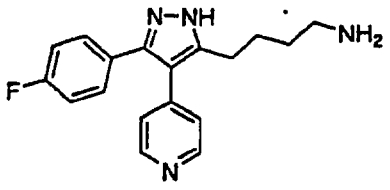


A solution of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyric acid (Example C-130) (200 mg, 0.615 mmol) in 50 ml of MeOH was treated with 10 ml of 4 N HCl/dioxane. The reaction mixture was stirred for 5 hours and evaporated to dryness. To this residue was added 15 ml of 1N methyl magnesium bromide in butyl ether and 5 ml of anhydrous THF. The reaction was heated to reflux under nitrogen for 64 h.

The reaction was quenched with 20 ml of saturated ammonium chloride. This mixture was transferred to a separatory funnel and was extracted with 100 ml ethyl acetate (2 x 100 mL). The combined ethyl acetate extracts were washed with water (1 x 100 mL), dried over $MgSO_4$, filtered and concentrated to afford a crude oil. The crude oil was subjected to column chromatography by using 3.5 % MeOH/CH_2Cl_2 followed by 6 % MeOH/CH_2Cl_2 to give the title compound: MS (M+H): 340 (base peak).

Example C-134

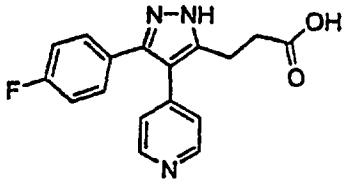
5-(4-(1-AMINO)BUTYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



To a suspension of 4-(4-(4-pyridyl)-3-(4-fluorophenyl) pyrazolyl) butyramide (Example C-131) (2 g, 6.2 mmol) in 100 ml of anhydrous ether was added lithium aluminum hydride (467 mg, 12.3 mmol). After the addition was complete, the mixture was warmed to room temperature and stirred for additional 2 h. The reaction was quenched with 20 mL of ethyl acetate and was poured onto 100 mL of 2.5 N NaOH. The mixture was extracted with ethyl acetate (3 x 50 mL). The combined extracts were washed with brine (1 x 100 mL), dried over Na_2SO_4, filtered and concentrated to afford the title compound: MS (M+H): 311 (base peak).

Example C-135

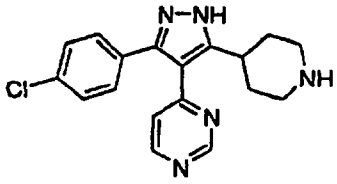
4-(4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLYL) PROPIONIC ACID



By following the method of Example C-1 and substituting succinic anhydride for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide the title compound was prepared: MS (M+H): 312 (base peak).

Example C-136

5-(4-PIPERIDYL)-4-(4-PYRIMIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE

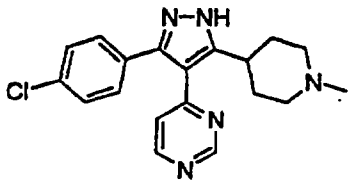


By following the method of Example C-1 and substituting methyl-4-chlorobenzoate for ethyl-4-fluorobenzoate, *N*-*t*-butoxycarbonyl-isonipecotyl *N*-hydroxysuccinimide for *N*-benyloxycarbonyl-glycinyl *N*-hydroxysuccinimide and 4-methylpyrimidine for 4-picoline

the title compound was prepared as the *N*-*t*-butoxycarbonyl protected compound. The deprotection of the *N*-*t*-butoxycarbonyl intermediate was accomplished with 4 N HCl in dioxane to afford the title compound as the hydrochloride salt: ^{1}H NMR ($CDCl_3$) δ 9.2 (s, 1 H), 8.48 (d, J = 5.19 Hz, 1 H), 7.31 (m, 4 H), 6.94 (d, J = 4.79 Hz, 1 H), (3.69 (m, 3 H), 3.12 (m, 2 H), 2.3 (m, 3 H), 1.24 (m, 2 H). MS (M+H): 340 (base peak).

Example C-137

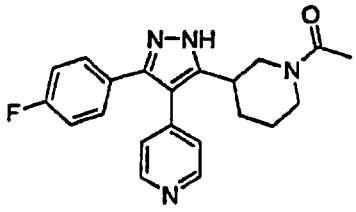
5-(*N*-METHYL-4-PIPERIDYL)-4-(4-PYRIMIDYL)-3-(4-CHLOROPHENYL) PYRAZOLE



By following the method of Example C-75 and substituting 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-136) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole hydrochloride (Example C-74) the title compound was prepared: ^{1}H NMR ($CDCl_3$) δ 9.2 (d, J = 1.2 Hz, 1 H), 8.48 (d, J = 5.59 Hz, 1 H), 7.31 (m, 4 H), 6.95 (dd, J= 1.2, 5.6 Hz, 1 H), 3.39 (m, 1 H), 3.03 (d, J = 11.6 Hz, 2 H), 2.38 (s, 3 H), 2.06 (m, 4 H), 1.24 (m, 2 H). MS (M+H): 354 (base peak).

Example C-138

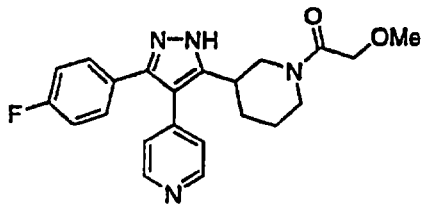
5-(*N*-ACETYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



By following the method of Example C-76 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (C-74) the title compound was prepared: MS (M+H): 365 (base peak).

Example C-139

5-(*N*-METHOXYACETYL-3-PIPERIDYL)-4-(4-PYRIDYL)-3-(4-FLUOROPHENYL) PYRAZOLE



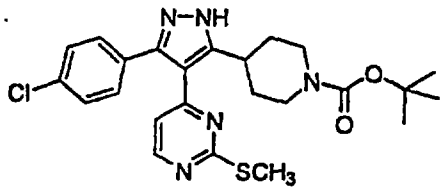
By following the method of Example C-76 and substituting 5-(3-piperidyl)-4-(4-pyridyl)-3-(4-fluorophenyl) pyrazole (C-90) for 5-(4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl) pyrazole (C-74) and methoxy

acetyl chloride for acetyl chloride the title compound was prepared: MS (M+H): 395 (base peak).

Additional compounds of the present invention which could be prepared using one or more of the reaction schemes set forth in this application include, but are not limited to, the following:

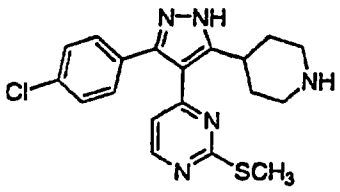
Example C-140

5-(4-*N*-t-butoxycarbonylpiperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



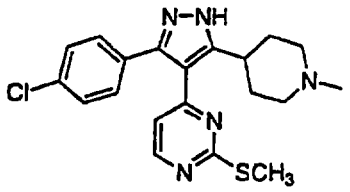
Example C-141

5-(4-piperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



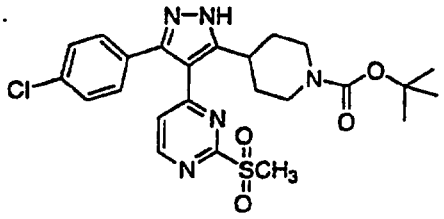
Example C-142

5-(4-*N*-methylpiperidinyl)-4-[4-(2-thiomethyl)pyrimidinyl]-3-4-(chlorophenyl)pyrazole



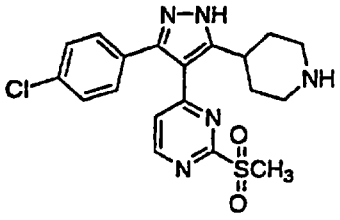
Example C-143

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



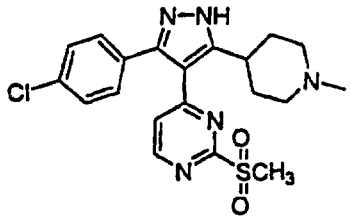
Example C-144

5-(4-piperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



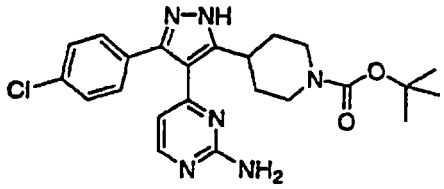
Example C-145

5-(4-*N*-methylpiperidinyl)-4-[4-(2-methanesulfonyl)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



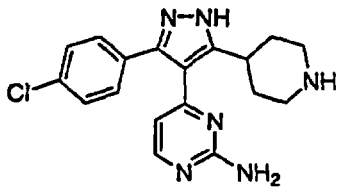
Example C-146

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



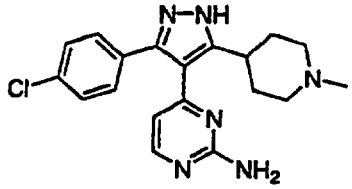
Example C-147

5-(4-piperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



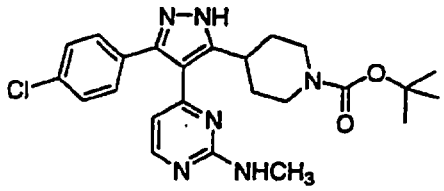
Example C-148

5-(4-*N*-methylpiperidinyl)-4-[4-(2-amino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



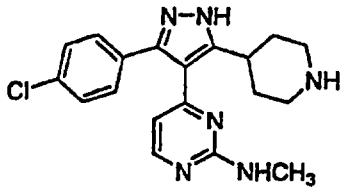
Example C-149

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



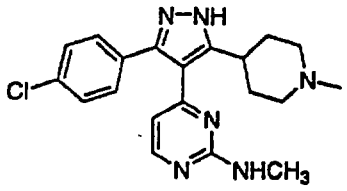
Example C-150

5-(4-piperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



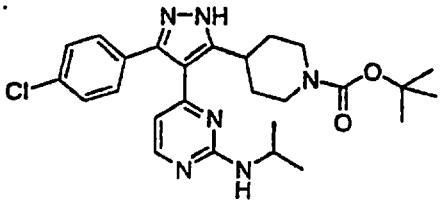
Example C-151

5-(4-*N*-methylpiperidinyl)-4-[4-(2-methylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



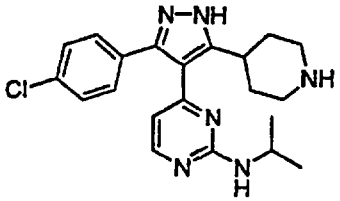
Example C-152

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



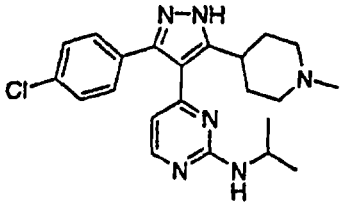
Example C-153

5-(4-piperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



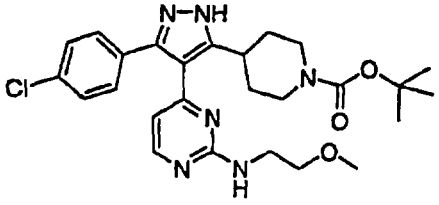
Example C-154

5-(4-*N*-methylpiperidinyl)-4-[4-(2-isopropylamino)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



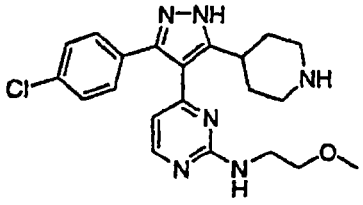
Example C-155

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole



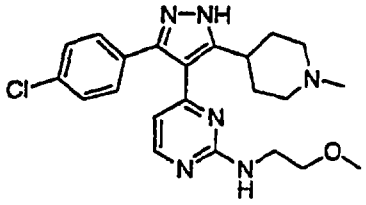
Example C-156

5-(4-piperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole



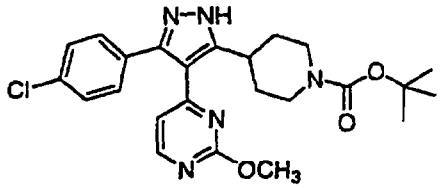
Example C-157

5-(4-*N*-methylpiperidinyl)-4-[4-(2-(2-methoxyethylamino))pyrimidinyl]-3-(4-chlorophenyl)pyrazole



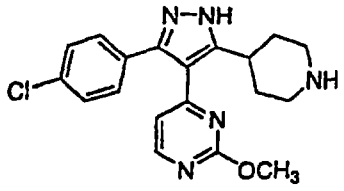
Example C-158

5-(4-*N*-t-butoxycarbonylpiperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



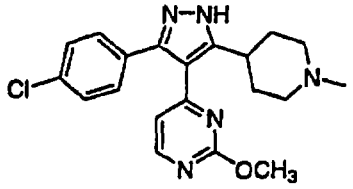
Example C-159

5-(4-piperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



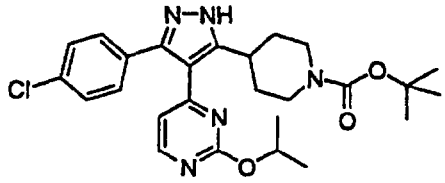
Example C-160

5-(4-*N*-methylpiperidinyl)-4-[4-(2-methoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



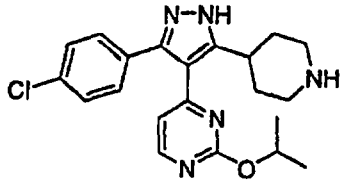
Example C-161

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



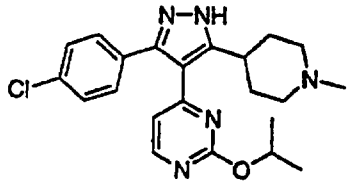
Example C-162

5-(4-piperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



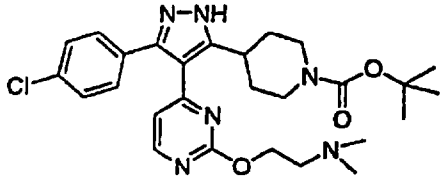
Example C-163

5-(4-*N*-methylpiperidinyl)-4-[4-(2-isopropoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



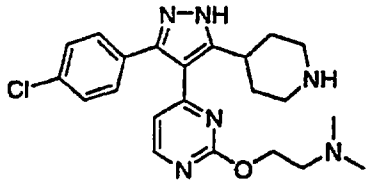
Example C-164

5-(4-*N*-*t*-butoxycarbonylpiperidinyl)-4-[4-(2-(2-*N*,*N*-dimethylamino)ethoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



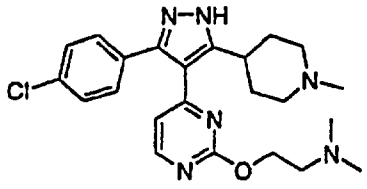
Example C-165

5-(4-piperidinyl)-4-[4-(2-(2-*N*,*N*-dimethylamino)ethoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



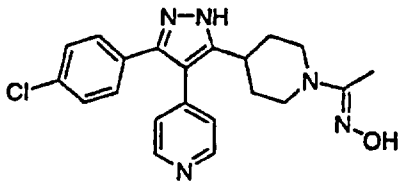
Example C-166

5-(4-*N*-methylpiperidinyl)-4-[4-(2-(2-*N*,*N*-dimethylamino)ethoxy)pyrimidinyl]-3-(4-chlorophenyl)pyrazole



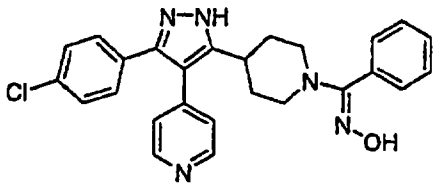
Example C-167

5-(*N*-acetylhydroxylimido-4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



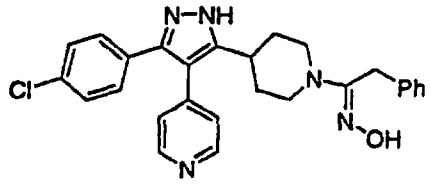
Example C-168

5-(*N*-benzylhydroxylimido-4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



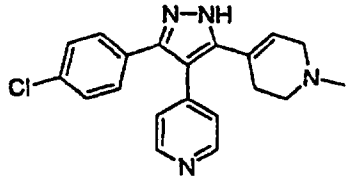
Example C-169

5-(*N*-phenylacethydroxylimido-4-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



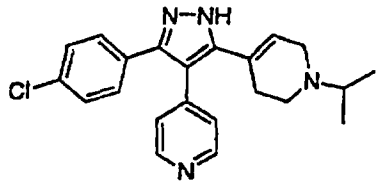
Example C-170

5-[*N*-methyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



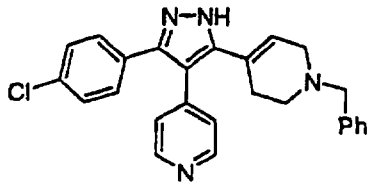
Example C-171

5-[*N*-isopropyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



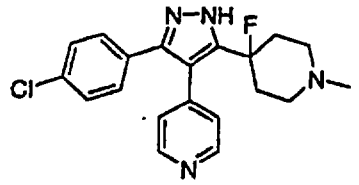
Example C-172

5-[*N*-benzyl-4-(3,4-dehydro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



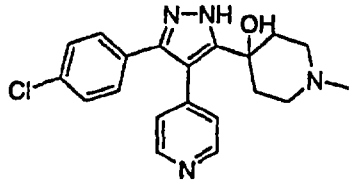
Example C-173

5-[*N*-methyl-4-(4-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



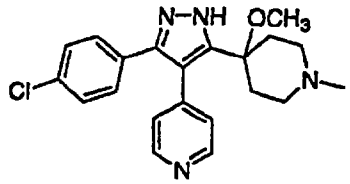
Example C-174

5-[*N*-methyl-4-(4-hydroxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



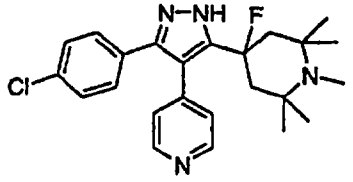
Example C-175

5-[*N*-methyl-4-(4-methoxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



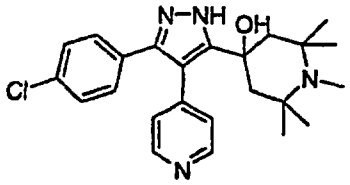
Example C-176

5-[*N*-methyl-4-(2,5-tetramethyl-4-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



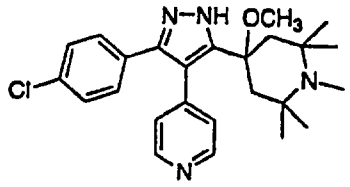
Example C-177

5-[*N*-methyl-4-(2,5-tetramethyl-4-hydroxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



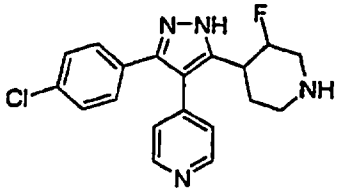
Example C-178

5-[*N*-methyl-4-(2,5-tetramethyl-4-methoxy)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



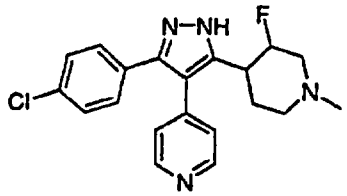
Example C-179

5-[4-(3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



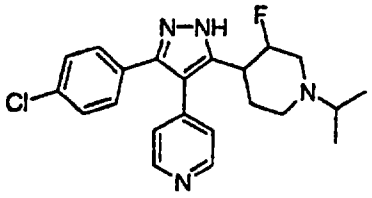
Example C-180

5-[4-(*N*-methyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



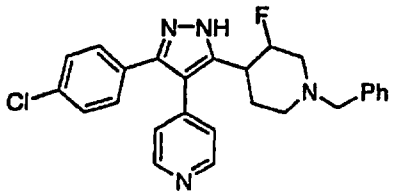
Example C-181

5-[4-(*N*-isopropyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



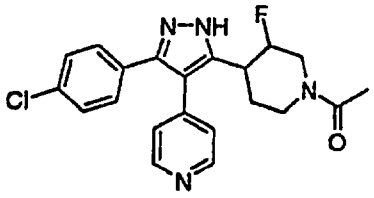
Example C-182

5-[4-(*N*-benzyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



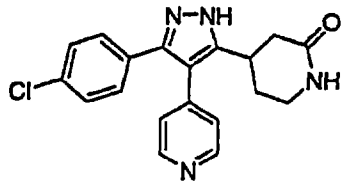
Example C-183

5-[4-(*N*-acetyl-3-fluoro)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



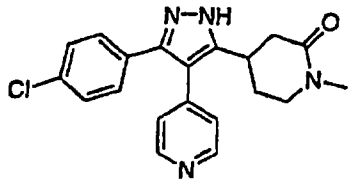
Example C-184

5-[4-(2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



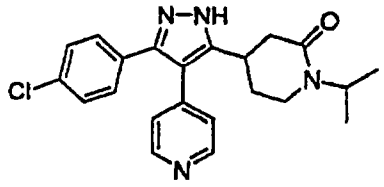
Example C-185

5-[4-(*N*-methyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



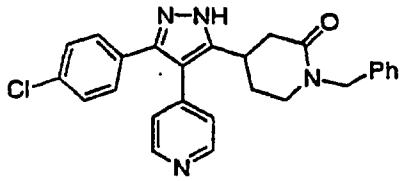
Example C-186

5-[4-(*N*-isopropyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



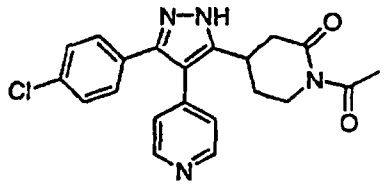
Example C-187

5-[4-(*N*-benzyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



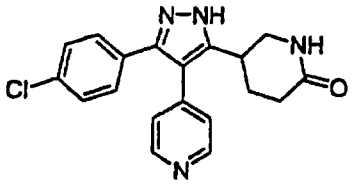
Example C-188

5-[4-(*N*-acetyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



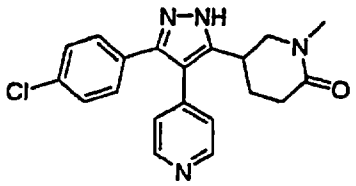
Example C-189

5-[5-(2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



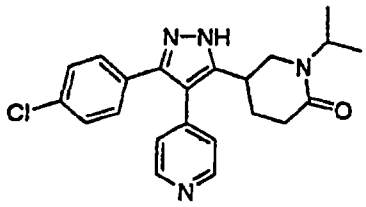
Example C-190

5-[5-(*N*-methyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



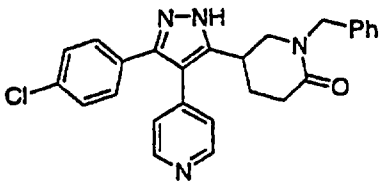
Example C-191

5-[5-(*N*-isopropyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



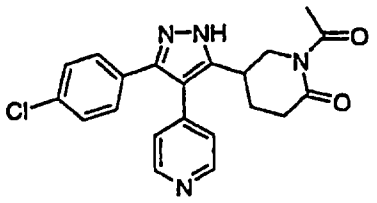
Example C-192

5-[5-(*N*-benzyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



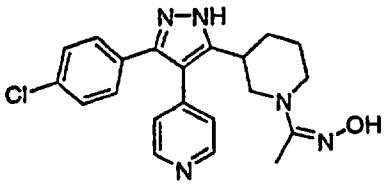
Example C-193

5-[5-(*N*-acetyl-2-oxo)piperidyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



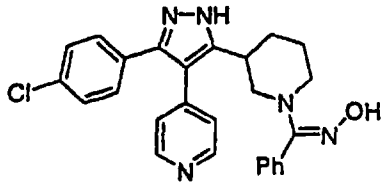
Example C-194

5-(*N*-acethydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



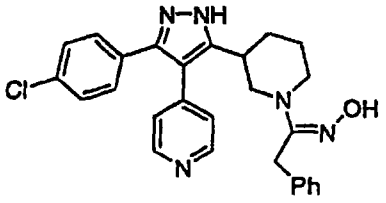
Example C-195

5-(*N*-benzhydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



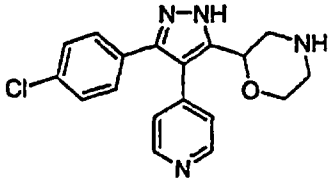
Example C-196

5-(*N*-phenacethydroxylimido-3-piperidyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



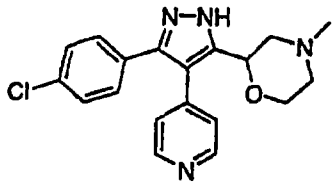
Example C-197

5-(2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



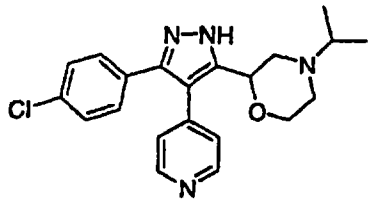
Example C-198

5-(*N*-methyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



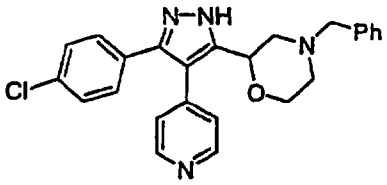
Example C-199

5-(*N*-isopropyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



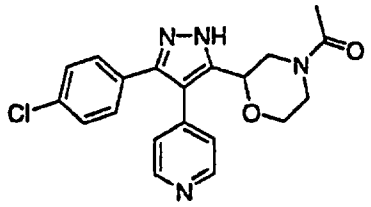
Example C-200

5-(*N*-benzyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



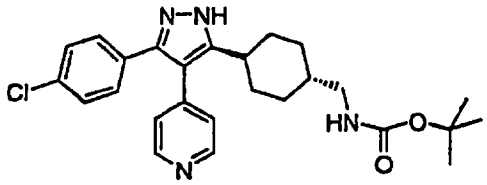
Example C-201

5-(*N*-acetyl-2-morpholinyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



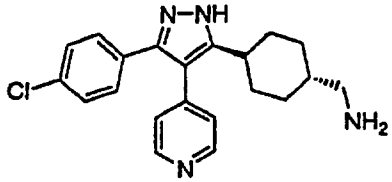
Example C-202

5-[*trans*-4-(*N*-t-butoxycarbonylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



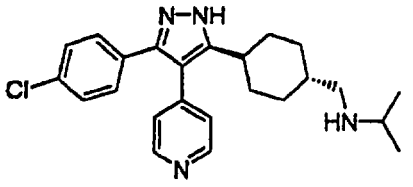
Example C-203

5-(*trans*-4-aminomethylcyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



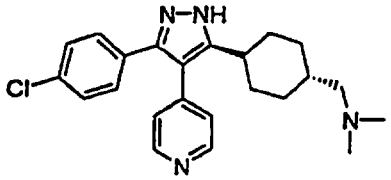
Example C-204

5-[*trans*-4-(*N*-isopropylamino)methylcyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



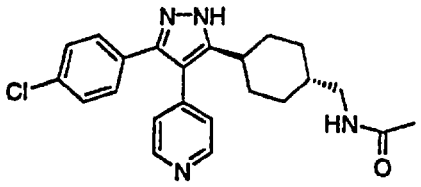
Example C-205

5-[*trans*-4-(*N,N*-dimethylamino)methylcyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



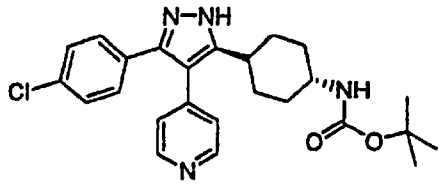
Example C-206

5-[*trans*-4-(*N*-acetylamino)methylcyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



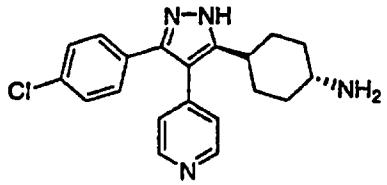
Example C-207

5-[*trans*-4-(*N*-t-butoxycarbonylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



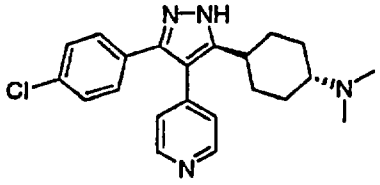
Example C-208

5-(*trans*-4-aminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



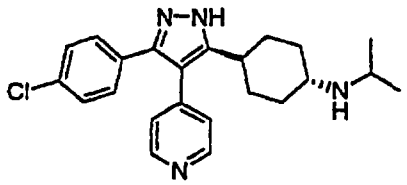
Example C-209

5-[*trans*-4-(*N,N*-dimethylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



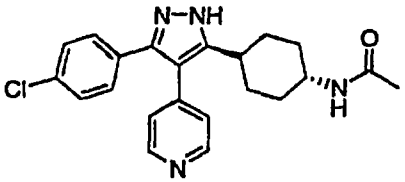
Example C-210

5-[*trans*-4-(*N*-isopropylamino)cyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



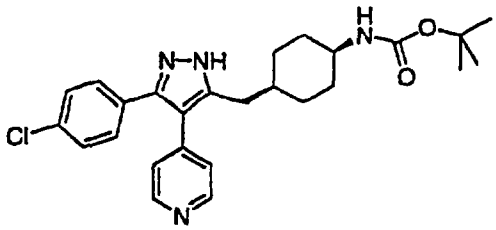
Example C-211

5-[*trans*-4-(*N*-acetylamino)cyclohexyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



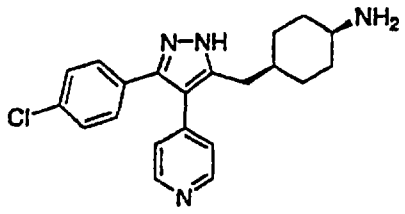
Example C-212

5-[*cis*-4-(*N*-t-butoxycarbonyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



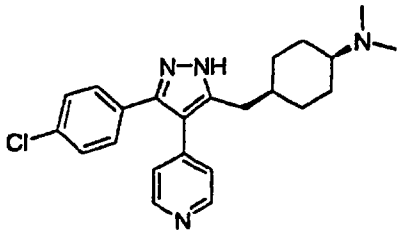
Example C-213

5-(*cis*-4-methylaminocyclohexyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



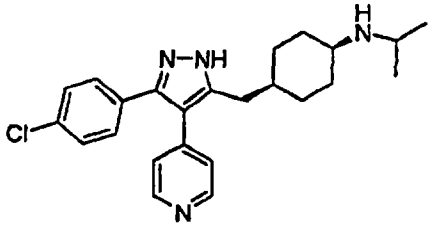
Example C-214

5-[*cis*-4-(*N,N*-dimethyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



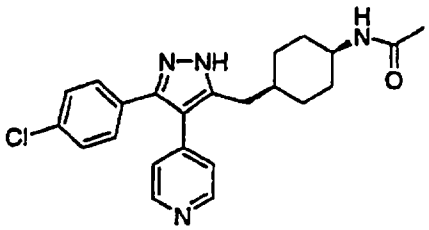
Example C-215

5-[*cis*-4-(*N*-isopropyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



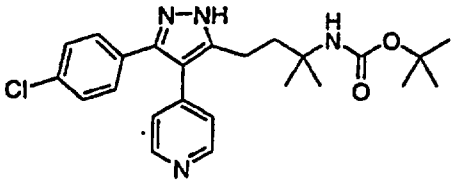
Example C-216

5-[*cis*-4-(*N*-acetyl)methylaminocyclohexyl)]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



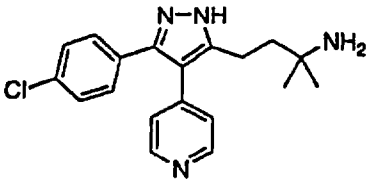
Example C-217

5-[3-(1,1-dimethyl-1-(*N*-*t*-butoxycarbonylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



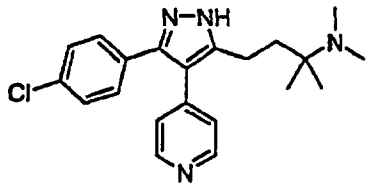
Example C-218

5-[3-(1,1-dimethyl-1-amino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



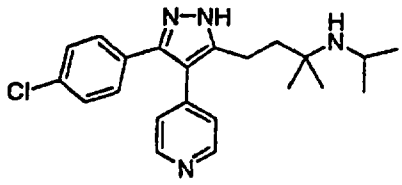
Example C-219

5-[3-(1,1-dimethyl-1-(*N*,*N*-dimethylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



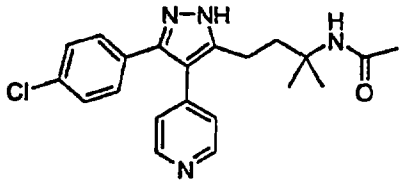
Example C-220

5-[3-(1,1-dimethyl-1-(*N*-isopropylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



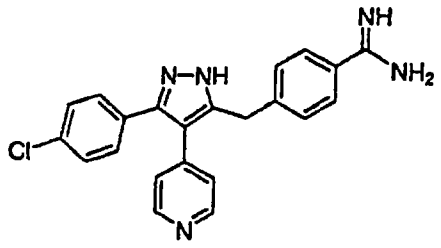
Example C-221

5-[3-(1,1-dimethyl-1-(*N*-acetylamino)propyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



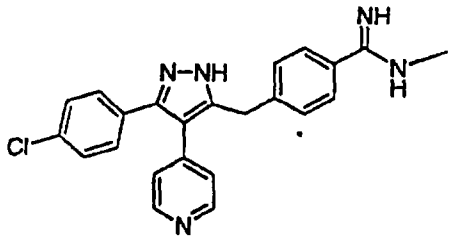
Example C-222

5-[4-(1-carboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



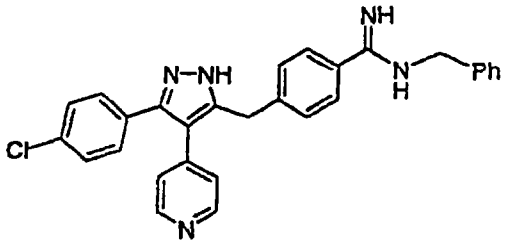
Example C-223

5-[4-(1-*N*-methylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



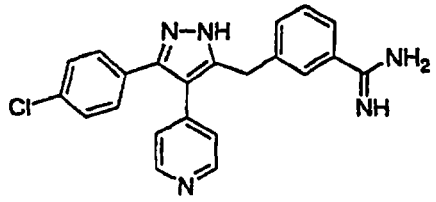
Example C-224

5-[4-(1-*N*-benzylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



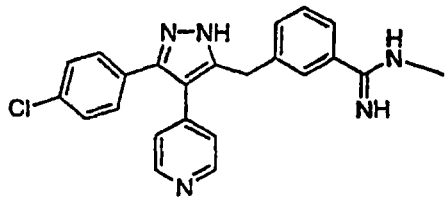
Example C-225

5-[3-(1-carboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



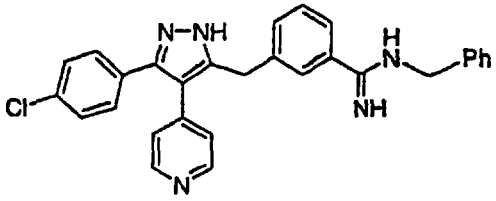
Example C-226

5-[3-(1-*N*-methylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



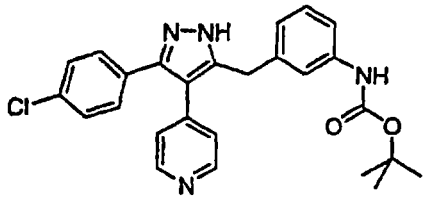
Example C-227

5-[3-(1-*N*-benzylcarboxamidino)benzyl-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



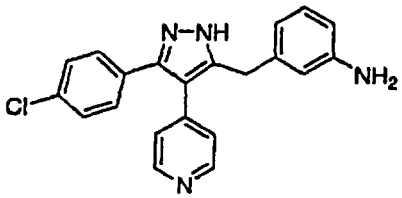
Example C-228

5-[3-(*N*-*t*-butoxycarbonyl)aminobenzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



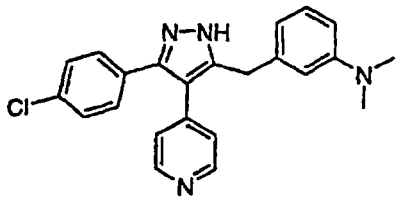
Example C-229

5-(3-aminobenzyl)-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



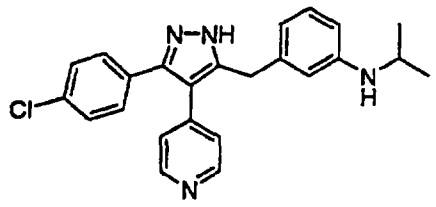
Example C-230

5-[3-(*N*,*N*-dimethylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



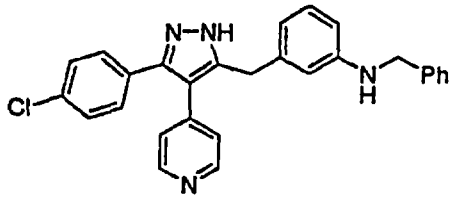
Example C-231

5-[3-(*N*-isopropylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



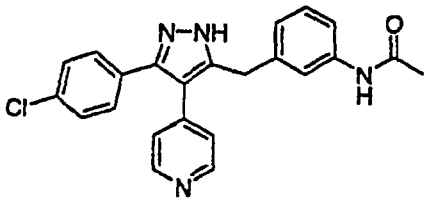
Example C-232

5-[3-(*N*-benzylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



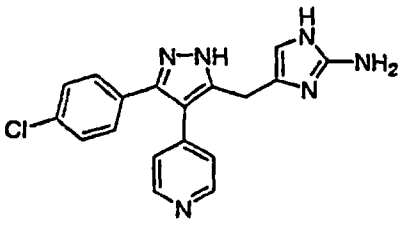
Example C-233

5-[3-(*N*-acetylamino)benzyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



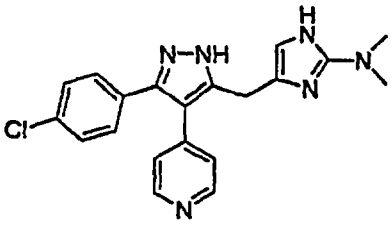
Example C-234

5-[4-(2-amino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



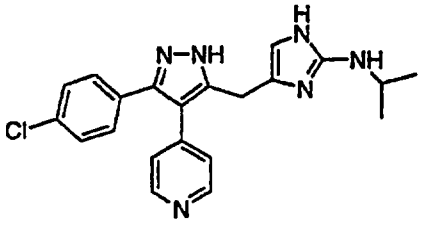
Example C-235

5-[4-(2-*N*,*N*-dimethylamino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



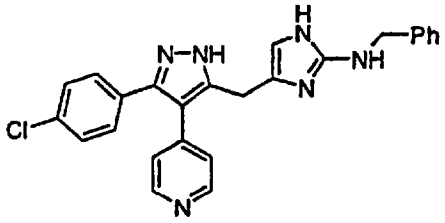
Example C-236

5-[4-(2-*N*-isopropylamino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



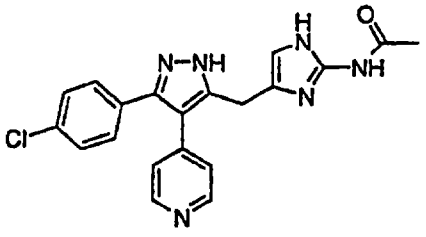
Example C-237

5-[4-(2-*N*-benzylamino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



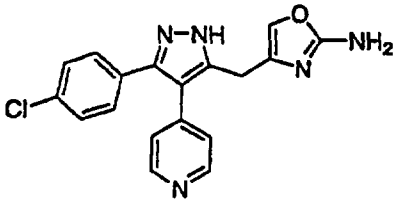
Example C-238

5-[4-(2-*N*-acetylamino)methylimidazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



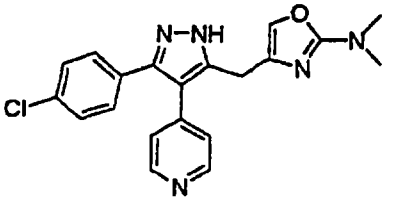
Example C-239

5-[4-(2-amino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



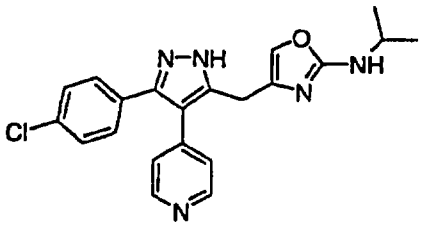
Example C-240

5-[4-(2-*N,N*-dimethylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



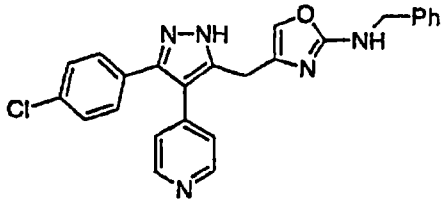
Example C-241

5-[4-(2-*N*-isopropylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



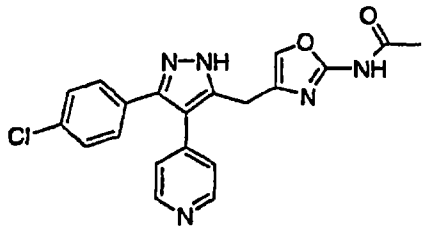
Example C-242

5-[4-(2-*N*-benzylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



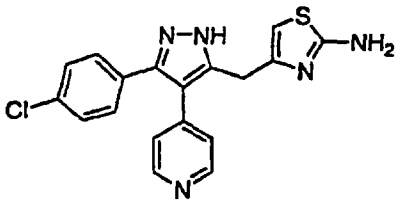
Example C-243

5-[4-(2-*N*-acetylamino)methyloxazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



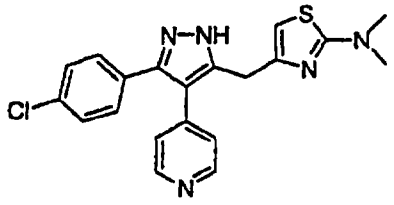
Example C-244

5-[4-(2-amino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



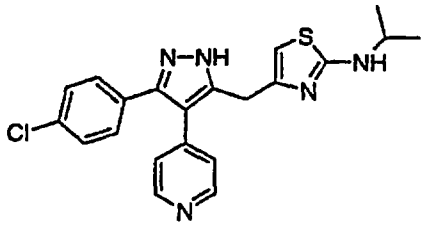
Example C-245

5-[4-(2-*N*,*N*-dimethylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



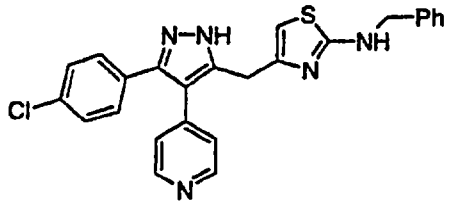
Example C-246

5-[4-(2-*N*-isopropylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



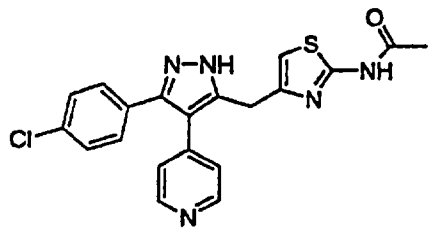
Example C-247

5-[4-(2-*N*-benzylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



Example C-248

5-[4-(2-*N*-acetylamino)methylthiazolyl]-4-(4-pyridyl)-3-(4-chlorophenyl)pyrazole



Biological data from compounds of Examples B-0001 through B-1573 and of Examples B-2270 through B-2462 are shown in the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

"P38 alpha kinase IC_{50}, uM or % inhib @ conc. (uM)"

In vitro whole cell assay for measuring the ability of the compounds to inhibit TNF production in human U937 cells stimulated with LPS are shown in the column identified as:

"U937 Cell IC_{50}, uM or % inhib @ conc., (uM)"

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the mouse is shown in the column identified as:

"Mouse LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when the compound is administered.

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

"Rat LPS Model, % TNF inhib @ dose @ predose time"

wherein in the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time

indicates the number of hours before LPS challenge when the compound is administered.

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0001	53.0%@1.0uM	40.0% @1.0uM		
B-0002	71.0%@1.0uM	28.0%@10.0uM		
B-0003	70.0%@1.0uM	76.0% 10.0uM		
B-0004	80.0%@1.0uM	4.61uM		
B-0005	95.0%@1.0uM	2.97uM		
B-0006	82.0%@1.0uM	80%@10.0uM		
B-0007	74.0%@1.0uM	85.0%@10.0uM		
B-0008	42.0%@1.0uM	65.0%@10.0uM		
B-0009	0.04 uM	0.72uM		
B-0010	0.52 uM	0.65uM		
B-0011	0.03 uM	4.47uM		
B-0012	30.0%@1.0uM	44.0% @1.0uM		
B-0013	70.0%@1.0uM	84.0%@10.0uM		
B-0014	79.0%@1.0uM	80.0%@10.0uM		
B-0015	82.0%@1.0uM	80.0%@10.0uM		
B-0016	94.0%@1.0uM	3.98uM		
B-0017	56.0%@1.0uM	79.0%@10.0uM		
B-0018	60.0%@1.0uM	59.0%@10.0uM		
B-0019	84.0%@1.0uM	100.0%@10.0uM		
B-0020	73.0%@1.0uM	81.0%@10.0uM		
B-0021	68.0%@1.0uM	76.0%@10.0uM		
B-0022	69.0%@1.0uM	44.0@1.0uM		
B-0023	90.0%@1.0uM	77.0%@10.0uM		
B-0024	94.0%@1.0uM	52.0%@1.0uM		
B-0025	89.0%@1.0uM	79.0%@10.0uM		
B-0026	96.0%@1.0uM	3.27uM		
B-0027	94.0%@1.0uM	11.0uM		
B-0028	69.0%@1.0uM	45.0%@10.0uM		
B-0029	91.0%@1.0uM	58.0%@10.0uM		
B-0030	92.0%@1.0uM	75.0%@10.0uM		
B-0031	94.0%@1.0uM	100.0%@10.0uM		
B-0032	94.0%@1.0uM	78.0%@10.0uM		
B-0033	97.0%@1.0uM	10.0uM		
B-0034	95.0%@1.0uM	10.0uM		
B-0035	94.0%@1.0uM	10.0uM		
B-0036	92.0%@1.0uM	8.24uM		
B-0037	91.0%@1.0uM	86.0%@10.0uM		
B-0038	71.0%@1.0uM	84.0%@10.0uM		
B-0039	89.0%@1.0uM	72.0%@10.0uM		
B-0040	93.0%@1.0uM	2.3uM		
B-0041	65.0%@1.0uM	66.0%@10.0uM		
B-0042	94.0%@1.0uM	2.76uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0043	0.22 uM	0.54uM		
B-0044	0.14 uM	0.19uM		
B-0045	94.0%@1.0uM	1.01uM		
B-0046	96.0%@1.0uM	54.0%@1.0uM		
B-0047	94.0%@1.0uM	74.0%@10.0uM		
B-0048	94.0%@1.0uM	76.0%@10.0uM		
B-0049	88%@1.0uM	33.0%@1.0uM		
B-0050	73%@1.0uM	34.0%@1.0uM		
B-0051	3.3uM	2.15uM	47%@100mpk@-6h	79%@3mpk@-4h
B-0052	92%@1.0uM	15.0%@1.0uM		
B-0053	95%@1.0uM	34.0%@1.0uM		
B-0054	90%@1.0uM	30.0%@1.0uM		
B-0055	93%@1.0uM	>1.0uM		
B-0056	96%@1.0uM	21.0%@1.0uM		
B-0057	96%@1.0uM	29.0%@1.0uM		
B-0058	79%@1.0uM	18.0%@1.0uM		
B-0059	83%@1.0uM	35.0%@1.0uM		
B-0060	73%@1.0uM	22.0%@1.0uM		
B-0061	62%@1.0uM	27.0%@1.0uM		
B-0062	94%@1.0uM	36.0%@1.0uM		
B-0063	96%@1.0uM	40.0%@1.0uM		
B-0064	90%@1.0uM	4.0%@1.0uM		
B-0065	83%@1.0uM	21.0%@1.0uM		
B-0066	94%@1.0uM	28.0%@1.0uM		
B-0067	91%@1.0uM	1.0%@1.0uM		
B-0068	72%@1.0uM	22.0%@1.0uM		
B-0069	96%@1.0uM	37.0%@1.0uM		
B-0070	92%@1.0uM	30.0%@1.0uM		
B-0071	86%@1.0uM	31.0%@1.0uM		
B-0072	77%@1.0uM	32.0%@1.0uM		
B-0073	91%@1.0uM	24.0%@1.0uM		
B-0074	92%@1.0uM	42.0%@1.0uM		
B-0075	91%@1.0uM	35.0%@1.0uM		
B-0076	58%@1.0uM	21.0%@1.0uM		
B-0077	0.8uM	10.0uM		
B-0078	80%@1.0uM	20.0%@1.0uM		
B-0079	93%@1.0uM	13.0%@1.0uM		
B-0080	73%@1.0uM	73.0%@1.0uM		
B-0081	92%@1.0uM	13.0%@1.0uM		
B-0082	47%@1.0uM	27.0%@1.0uM		
B-0083	0.22uM	6.51uM		
B-0084	56%@1.0uM	30.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0085	83%@1.0uM	21.0%@1.0uM		
B-0086	91%@1.0uM	37.0%@1.0uM		
B-0087	0.55uM	2.26uM	38%@30mpk@-6h	
B-0088	96%@1.0uM	9.0%@1.0uM		
B-0089	0.04uM	3.33uM		
B-0090	98%@1.0uM	52.0%@1.0uM		
B-0091	96%@1.0uM	40.0%@1.0uM		
B-0092	97%@1.0uM	34.0%@1.0uM		
B-0093	3.18 uM	1.25uM	30%@30mpk@-6h	
B-0094	96%@1.0uM	52.0%@1.0uM		
B-0095	98%@1.0uM	38.0%@1.0uM		
B-0096	91%@1.0uM	22.0%@1.0uM		
B-0097	72.0%@10.0uM	38.0%@1.0uM		
B-0098	66.0%@10.0uM	12.0%@1.0uM		
B-0099	43.0% @1.0uM	>1.0uM		
B-0100	75.0% @1.0uM	5.0uM		
B-0101	71.0% @1.0uM	2.11uM		
B-0102	81.0%@1.0uM	15.0%@1.0uM		
B-0103	71.0%@1.0uM	6.0%@1.0uM		
B-0104	56.0% @1.0uM	2.78uM		
B-0105	78.0%@1.0uM	5.0uM		
B-0106	62.0%@1.0uM	5.0uM		
B-0107	0.27uM	5.0uM		
B-0108	61.0%@1.0uM	4.85uM		
B-0109	45.0%@1.0uM	19.0%@1.0uM		
B-0110	66.0%@1.0uM	13.0%@1.0uM		
B-0111	57.0%@1.0uM	>1.0uM		
B-0112	97.0%@1.0uM	1.12uM		
B-0113	75.0%@1.0uM	43.0%@1.0uM		
B-0114	45.0%@1.0uM	3.92uM		
B-0115	47.0%@1.0uM	2.0%@1.0uM		
B-0116	73.0%@1.0uM	35.0%@1.0uM		
B-0117	0.46 uM	1.78 uM	30%@30mpk@-6h	
B-0118	1.18 uM	1.29 uM		
B-0119	89.0%@10.0uM	2.78uM		
B-0120	0.008 uM	0.21 uM	77%@100mpk@-6h	70%@3mpk@-4h
B-0121	79.0%@1.0uM	1.22uM		
B-0122	79.0%@10.0uM	2.0%@1.0uM		
B-0123	59.0%@1.0uM	>1.0uM		
B-0124	73.0%@1.0uM	15.0%@1.0uM		
B-0125	70.0%@10.0uM	17.0%@1.0uM		
B-0126	66.0%@1.0uM	1.57uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0127	82.0%@1.0uM	0.96uM		
B-0128	78.0%@1.0uM	1.81uM		
B-0129	51.0%@1.0uM	31.0%@1.0uM		
B-0130	69.0%@1.0uM	58.0%@1.0uM		
B-0131	43.0%@1.0uM	46.0%@1.0uM		
B-0132	76.0%@1.0uM	8.0%@1.0uM		
B-0133	51.0%@1.0uM	42.0%@1.0uM		
B-0134	60.0%@1.0uM	2.17uM		
B-0135	78.0%@1.0uM	58.0%@1.0uM		
B-0136	77.0%@1.0uM	44.0%@1.0uM		
B-0137	41.0%@1.0uM	37.0%@1.0uM		
B-0138	50.0%@1.0uM	32.0%@1.0uM		
B-0139	54.0%@10.0uM	17.0%@1.0uM		
B-0140	67%@10.0uM	9.0%@1.0uM		
B-0141	78.0%@1.0uM	10.0%@1.0uM		
B-0142	86.0%@1.0uM	12.0%@1.0uM		
B-0143	42.0% @1.0uM	3.63uM		
B-0144	86.0% @1.0uM	43.0%@1.0uM		
B-0145	54.0% @10.0uM	12.0% @1.0uM		
B-0146	77.0% @10.0uM	28.0% @1.0uM		
B-0147	44.0% @1.0uM	22.0% @1.0uM		
B-0148	51.0% @1.0uM	>1.0uM		
B-0149	1.15 uM	10.0 uM		
B-0150	27.0% @10.0uM	35.0% @1.0uM		
B-0151	43.0% @1.0uM	30.0% @1.0uM		
B-0152	51.0% @1.0uM	24.0% @1.0uM		
B-0153	57.0% @1.0uM	21.0% @1.0uM		
B-0154	65.0% @10.0uM	14.0% @1.0uM		
B-0155	40.0% @10.0uM	26.0% @1.0uM		
B-0156	42.0% @10.0uM	13.0% @1.0uM		
B-0157	48.0% @10.0uM	9.0% @1.0uM		
B-0158	58.0% @10.0uM	39.0% @1.0uM		
B-0159	54.0% @10.0uM	5.0% @1.0uM		
B-0160	59.0% @10.0uM	26.0% @1.0uM		
B-0161	72.0% @10.0uM	13.0% @1.0uM		
B-0162	23%@1.0uM	2.05 uM		
B-0163	20.0% @10.0uM	10.0% @1.0uM		
B-0164	37.0% @10.0uM	20.0% @1.0uM		
B-0165	70.0% @10.0uM	19.0% @1.0uM		
B-0166	45.0% @10.0uM	37.0% @1.0uM		
B-0167	40.0% @1.0uM	37.0% @1.0uM		
B-0168	44%@1.0uM	2.36 uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0169	43.0% @1.0uM	21.0% @1.0uM		
B-0170	43.0% @1.0uM	30.0% @1.0uM		
B-0171	61.0% @10.0uM	21.0% @1.0uM		
B-0172	16.0% @10.0uM	11.0% @1.0uM		
B-0173	33.0% @10.0uM	48.0% @1.0uM		
B-0174	54.0% @10.0uM	43.0% @1.0uM		
B-0175	41.0% @10.0uM	31.0% @1.0uM		
B-0176	50.0% @1.0uM	30.0% @1.0uM		
B-0177	70.0% @10.0uM	27.0% @1.0uM		
B-0178	12.0% @10.0uM	35.0% @1.0uM		
B-0179	27.0% @10.0uM	37.0% @1.0uM		
B-0180	34.0% @10.0uM	23.0% @1.0uM		
B-0181	5.0%@1.0uM	2.0% @1.0uM		
B-0182	39.0% @10.0uM	40.0% @1.0uM		
B-0183	12.0% @10.0uM	34.0% @1.0uM		
B-0184	66.0% @10.0uM	17.0% @1.0uM		
B-0185	65.0% @10.0uM	25.0% @1.0uM		
B-0186	40.0% @1.0uM	25.0% @1.0uM		
B-0187	4.0% @10.0uM	14.0% @1.0uM		
B-0188	70.0% @10.0uM	35.0% @1.0uM		
B-0189	42.0% @10.0uM	9.0% @1.0uM		
B-0190	59.0% @10.0uM	31.0% @1.0uM		
B-0191	40.0% @1.0uM	29.0% @1.0uM		
B-0192	12.0% @10.0uM	47.0% @1.0uM		
B-0193	0.54 uM	6%@1.0uM		
B0194	1.31 uM	22%@1.0uM		
B-0195	1.03 uM	55%@1.0uM		
B-0196	2.24 uM	>1.0uM		
B-0197	2.0 uM	14%@1.0uM		
B-0198	1.2 uM	2%@1.0uM		
B-0199	1.34 uM	3%@1.0uM		
B-0200	1.31 uM	16%@1.0uM		
B-0201	0.29 uM	59%@1.0uM		
B-0202	0.55 uM	2.26 uM		
B-0203	0.16 uM	65%@1.0uM		
B-0204	0.21 uM	48%@1.0uM		
B-0205	0.096 uM	54%@1.0uM		
B-0206	5.76 uM	14%@1.0uM		
B-0207	0.12 uM	52%@1.0uM		
B-0208	0.067 uM	>1.0uM		
B-0209	0.29 uM	8%@1.0uM		
B-0210	0.057 uM	67%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0211	0.25 uM	30%@1.0uM		
B-0212	0.12 uM	28%@1.0uM		
B-0213	0.31 uM	39%@1.0uM		
B-0214	0.16 uM	50%@1.0uM		
B-0215	0.11 uM	51%@1.0uM		
B-0216	0.56 uM	>1.0uM		
B-0217	0.55 uM	>1.0uM		
B-0218	0.53 uM	18%@1.0uM		
B-0219	0.91 uM	18%@1.0uM		
B-0220	0.13 uM	40%@1.0uM		
B-0221	2.4 uM	>1.0uM		
B-0222	0.4uM	29.0%@1.0uM		
B-0223	0.2uM	1.0%@1.0uM		
B-0224	<0.1uM	93.0%@1.0uM		
B-0225	0.047uM	37.0%@1.0uM		
B-0226	0.074uM	20.0%@1.0uM		
B-0227	0.045uM	1.0%@1.0uM		
B-0228	0.15uM	44.0%@1.0uM		
B-0229	<0.1uM	61.0%@1.0uM		
B-0230	0.041uM	30.0%@1.0uM		
B-0231	0.055uM	40.0%1.0uM		
B-0232	0.048uM	24.0%@1.0uM		
B-0233	0.095uM	43.0%@1.0uM		
B-0234	0.11uM	68.0%@1.0uM		
B-0235	1.31uM	90.0%@1.0uM		
B-0236	0.077uM	46.0%@1.0uM		
B-0237	0.13uM	60.0%@1.0uM		
B-0238	0.47uM	82.0%@1.0uM		
B-0239	5.73uM	84.0%@1.0uM		
B-0240	0.2uM	70.0%@1.0uM		
B-0241	0.1uM	45.0%@1.0uM		
B-0242	<0.1uM	78.0%@1.0uM		
B-0243	0.039uM	53.0%@1.0uM		
B-0244	0.02uM	57.0%@1.0uM		
B-0245	0.13uM	24.0%@1.0uM		
B-0246	<0.1uM	>1.0uM		
B-0247	0.082uM	75.0%@1.0uM		
B-0248	<0.1uM	11.0%@1.0uM		
B-0249	<0.1uM	75.0%@1.0uM		
B-0250	0.28uM	36.0%@1.0uM		
B-0251	0.31uM	1.0%@1.0uM		
B-0252	0.041uM	54.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0253	0.061uM	74.0%@1.0uM		
B-0254	0.12uM	59.0%@1.0uM		
B-0255	0.32uM	68.0%@1.0uM		
B-0256	<0.1uM	88.0%@1.0uM		
B-0257	1.71uM	11.0%@1.0uM		
B-0258	0.37uM	63.0%@1.0uM		
B-0259	0.35uM	58.0%@1.0uM		
B-0260	0.56uM	23.0%@1.0uM		
B-0261	0.49uM	23.0%@1.0uM		
B-0262	0.41uM	89.0%@1.0uM		
B-0263	0.62uM	64.0%@1.0uM		
B-0264	0.14uM	18.0%@1.0uM		
B-0265	0.92uM	24.0%@1.0uM		
B-0266	0.25uM	24.0%@1.0uM		
B-0267	0.48uM	11.0%@1.0uM		
B-0268	3.39uM	19.0%@1.0uM		
B-0269	9.81uM	19.0%@1.0uM		
B-0270	5.79uM	13.0%@1.0uM		
B-0271	7.55uM	12.0%@1.0uM		
B-0272	1.81uM	48.0%@1.0uM		
B-0273	5.03uM	13.0%@1.0uM		
B-0274	2.68uM	25.0%@1.0uM		
B-0275	2.67uM	33.0%@1.0uM		
B-0276	1.25uM	26.0%@1.0uM		
B-0277	0.68uM	34.0%@1.0uM		
B-0278	1.26uM	36.0%@1.0uM		
B-0279	1.39uM	33.0%@1.0uM		
B-0280	0.86uM	18.0%@1.0uM		
B-0281	7.37uM	24.0%@1.0uM		
B-0282	0.75uM	38.0%@1.0uM		
B-0283	6.66uM	29.0%@1.0uM		
B-0284	0.083uM	65.0%@1.0uM		
B-0285	4.57uM	29.0%@1.0uM		
B-0286	0.33uM	50.0%@1.0uM		
B-0287	4.0uM	22.0%@1.0uM		
B-0288	4.46uM	26.0%@1.0uM		
B-0289	0.15uM	55.0%@1.0uM		
B-0290	0.66uM	44.0%@1.0uM		
B-0291	1.33uM	20.0%@1.0uM		
B-0292	0.22uM	28.0%@1.0uM		
B-0293	0.66uM	53.0%@1.0uM		
B-0294	0.68uM	45.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0295	0.82uM	45.0%@1.0uM		
B-0296	8.03uM	36.0%@1.0uM		
B-0297	0.78uM	30.0%@1.0uM		
B-0298	0.58uM	48.0%@1.0uM		
B-0299	0.87uM	54.0%@1.0uM		
B-0300	0.78uM	32.0%@1.0uM		
B-0301	0.19uM	50.0%@1.0uM		
B-0302	4.02uM	24.0%@1.0uM		
B-0303	0.22uM	10.0%@1.0uM		
B-0304	0.56uM	28.0%@1.0uM		
B-0305				
B-0306				
B-0307				
B-0308				
B-0309				
B-0310				
B-0311				
B-0312				
B-0313				
B-0314				
B-0315				
B-0316				
B-0317				
B-0318				
B-0319				
B-0320				
B-0321				
B-0322				
B-0323				
B-0324				
B-0325				
B-0326				
B-0327				
B-0328				
B-0329				
B-0330				
B-0331				
B-0332				
B-0333				
B-0334				
B-0335				
B-0336				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0337				
B-0338				
B-0339				
B-0340				
B-0341				
B-0342				
B-0343				
B-0344				
B-0345				
B-0346				
B-0347				
B-0348				
B-0349				
B-0350				
B-0351				
B-0352				
B-0353	1.37uM	55%@1.0uM		
B-0354	1.0uM	0.66uM	51%@30mpk@-6h	54%@3mpk@-4h
B-0355	0.75uM	40.0%@1.0uM		
B-0356	0.66uM	24.0%@1.0uM		
B-0357	1.46uM	0.66uM		
B-0358	0.37uM	17.0%@1.0uM		
B-0359	0.45uM	47.0%@1.0uM		
B-0360	1.6uM	19.0%@1.0uM		
B-0361	0.33uM	46.0%@1.0uM		
B-0362	0.52uM	27.0%@1.0uM		
B-0363	4.67uM	25.0%@1.0uM		
B-0364	1.44uM	27.0%@1.0uM		
B-0365	0.96uM	27.0%@1.0uM		
B-0366	0.7uM	46.0%@1.0uM		
B-0367	1.0uM	23.0%@1.0uM		
B-0368	1.0uM	0.64uM	37%@30mpk@-6h	
B-0369	0.16uM	57.0%@1.0uM		
B-0370	0.65uM	28.0%@1.0uM		
B-0371	0.49uM	28.0%@1.0uM		
B-0372	0.35uM	29.0%@1.0uM		
B-0373	0.45uM	18.0%@1.0uM		
B-0374	1.38uM	12.0%@1.0uM		
B-0375	1.0uM	19.0%@1.0uM		
B-0376	2.99uM	12.0%@1.0uM		
B-0377	1.29uM	36.0%@1.0uM		
B-0378	1.1uM	36.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0379	0.53uM	24.0%@1.0uM		
B-0380	1.41uM	32.0%@1.0uM		
B-0381	0.22uM	47.0%@1.0uM		
B-0382	0.41uM	32.0%@1.0uM		
B-0383	1.43uM	10.0%@1.0uM		
B-0384	4.02uM	16.0%@1.0uM		
B-0385	0.057uM	0.9uM	30%@30mpk@-6h	0%@3mpk@-4h
B-0386	0.13uM	54.0%@1.0uM		
B-0387	0.41uM	52.0%@1.0uM		
B-0388	<0.1uM	36.0%@1.0uM		
B-0389	0.01uM	0.05uM		62%@3mpk@-4h
B-0390	0.089uM	55.0%@1.0uM		
B-0391	0.86uM	18.0%@1.0uM		
B-0392	0.13uM	57.0%@1.0uM		
B-0393	0.043uM	66.0%@1.0uM		
B-0394	0.13uM	45.0%@1.0uM		
B-0395	0.087uM	48.0%@1.0uM		
B-0396	0.097uM	0.44uM		
B-0397	0.17uM	41.0%@1.0uM		
B-0398	0.054uM	66.0%@1.0uM		
B-0399	0.14uM	39.0%@1.0uM		
B-0400	0.16uM	25.0%@1.0uM		
B-0401	0.46uM	52.0%@1.0uM		
B-0402	0.14uM	1.51uM		
B-0403	1.77uM	2.42uM		
B-0404	0.31uM	48.0%@1.0uM		
B-0405	0.79uM	30.0%@1.0uM		
B-0406	0.54uM	35.0%@1.0uM		
B-0407	0.76uM	27.0%@1.0uM		
B-0408	0.5uM	50.0%@1.0uM		
B-0409	0.53uM	30.0%@1.0uM		
B-0410	0.38uM	44.0%@1.0uM		
B-0411	0.62uM	50.0%@1.0uM		
B-0412	0.24uM	48.0%@1.0uM		
B-0413	0.18uM	55.0%@1.0uM		
B-0414	2.54uM	25.0%@1.0uM		
B-0415	0.42uM	43.0%@1.0uM		
B-0416	0.32uM	34.0%@1.0uM		
B-0417	0.91uM	28.0%@1.0uM		
B-0418	0.22uM	27.0%@1.0uM		
B-0419	0.85uM	41.0%21.0uM		
B-0420	0.83uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0421	0.46uM	57.0%@1.0uM		
B-0422	<0.1uM	40.0%@1.0uM		
B-0423	0.18uM	33.0%@1.0uM		
B-0424	0.083uM	32.0%@1.0uM		
B-0425	0.26uM	54.0%@1.0uM		
B-0426	0.055uM	0.74uM		41%@3mpk@-4h
B-0427	0.63uM	39.0%@1.0uM		
B-0428	0.99uM	27.0%@1.0uM		
B-0429	0.27uM	45.0%@1.0uM		
B-0430	0.29uM	75.0%@1.0uM		
B-0431	0.21uM	64.0%@1.0uM		
B-0432	<0.1uM	89.0%@1.0uM		
B-0433	<0.1uM	92.0%@1.0uM		
B-0434	0.12uM	65.0%@1.0uM		
B-0435	0.3uM	61.0%@1.0uM		
B-0436	1.11uM	71.0%@1.0uM		
B-0437	0.58uM	59.0%@1.0uM		
B-0438	<0.1uM	91.0%@1.0uM		
B-0439	2.12uM	65.0%@1.0uM		
B-0440	0.66uM	63.0%@1.0uM		
B-0441	0.8uM	58.0%@1.0uM		
B-0442	<0.1uM	91.0%@1.0uM		
B-0443	2.01uM	71.0%@1.0uM		
B-0444	1.01uM	51.0%@1.0uM		
B-0445	<0.1uM	83.0%@1.0uM		
B-0446	0.78uM	80.0%@1.0uM		
B-0447	0.19uM	71.0%@1.0uM		
B-0448	0.4uM	79.0%@1.0uM		
B-0449	0.83uM	81.0%@1.0uM		
B-0450	0.26uM	81.0%@1.0uM		
B-0451	0.071uM	83.0%@1.0uM	42%@30mpk@-6h	
B-0452	0.7uM	75.0%@1.0uM		
B-0453	0.47uM	75.0%@1.0uM		
B-0454	0.11uM	80.0%@1.0uM		
B-0455	<0.1uM	95.0%@1.0uM		36%@3mpk%-4h
B-0456	1.81uM	67.0%@1.0uM		
B-0457	0.089uM	81.0%@1.0uM		
B-0458	0.033uM	70.0%@1.0uM		
B-0459	0.099uM	76.0%@1.0uM		
B-0460	0.061uM	92.0%@1.0uM		
B-0461	0.025uM	96.0%@1.0uM		
B-0462	<0.1uM	97.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0463	0.052uM	95.0%@1.0uM		
B-0464	<0.1uM	91.0%@1.0uM		
B-0465	0.084uM	98.0%@1.0uM		
B-0466	<0.1uM	98.0%@1.0uM		0%@3mpk@-4h
B-0467	<0.1uM	77.0%@1.0uM		
B-0468	0.031uM	93.0%@1.0uM		
B-0469	0.056uM	92.0%@1.0uM		
B-0470	0.063uM	92.0%@1.0uM		
B-0471	0.027uM	97.0%@1.0uM		
B-0472	0.19uM	54.0%@1.0uM		
B-0473	0.004uM	95.0%@1.0uM		
B-0474	0.024uM	86.0%@1.0uM		
B-0475	0.21uM	74.0%@1.0uM		
B-0476	0.56uM	69.0%@1.0uM		
B-0477	1.48uM	96.0%@1.0uM		
B-0478	0.034uM	87.0%@1.0uM		
B-0479	0.031uM	90.0%@1.0uM		15%@3mpk@-4h
B-0480	0.12uM	88.0%@1.0uM		
B-0481	0.014uM	95.0%@1.0uM		56%@3mpk@-4h
B-0482	0.97uM	68.0%@1.0uM		
B-0483	0.57uM	68.0%@1.0uM		
B-0484	0.28uM	62.0%@1.0uM		
B-0485	0.04uM	95.0%@1.0uM		
B-0486	0.24uM	80.0%@1.0uM		
B-0487	0.11uM	89.0%@1.0uM		54%@3mpk@-4h
B-0488	0.62uM	88.0%@1.0uM		
B-0489	0.3uM	80.0%@1.0uM		
B-0490	0.91uM	74.0%@1.0uM		
B-0491	0.43uM	66.0%@1.0uM		
B-0492	0.069uM	42.0%@1.0uM		
B-0493	0.3uM	36.0%@1.0uM		
B-0494	0.13uM	30.0%@1.0uM		
B-0495	0.12uM	25.0%@1.0uM		
B-0496	0.83uM	16.0%@1.0uM		
B-0497	0.44uM	31.0%@1.0uM		
B-0498	0.33uM	11.0%@1.0uM		
B-0499	0.39uM	37.0%@1.0uM		
B-0500	0.26uM	41.0%@1.0uM		
B-0501	0.049uM	52.0%@1.0uM		
B-0502	0.065uM	48.0%@1.0uM		
B-0503	0.16uM	73.0%@1.0uM		
B-0504	0.4uM	43.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0505	0.28uM	44.0%@1.0uM		
B-0506	0.94uM	43.0%@1.0uM		
B-0507	0.18uM	75.0%@1.0uM		
B-0508	2.0uM	48.0%@1.0uM		
B-0509	0.1uM	86.0%@1.0uM		
B-0510	0.69uM	61.0%@1.0uM		
B-0511	0.007uM	90.0%@1.0uM		
B-0512	1.0uM	53.0%@1.0uM		
B-0513	0.72uM	52.0%@1.0uM		
B-0514	0.14uM	87.0%@1.0uM		
B-0515	0.42uM	61.0%@1.0uM		
B-0516	0.37uM	84.0%@1.0uM		
B-0517	0.094uM	52.0%@1.0uM		
B-0518	0.11uM	64.0%@1.0uM		
B-0519	0.043uM	87.0%@1.0uM		
B-0520	0.4uM	67.0%@1.0uM		
B-0521	1.37uM	52.0%@1.0uM		
B-0522	0.15uM	75.0%@1.0uM		
B-0523	0.19uM	83.0%@1.0uM		
B-0524	0.4uM	77.0%@1.0uM		
B-0525	0.16uM	76.0%@1.0uM		
B-0526	0.031uM	87.0%@1.0uM		
B-0527	1.09uM	63.0%@1.0uM		
B-0528	0.14uM	70.0%@1.0uM		
B-0529	0.11uM	73.0%@1.0uM		
B-0530	5.53uM	45.0%@1.0uM		
B-0531	0.5uM	48.0%@1.0uM		
B-0532	0.45uM	1.01uM	41%@30mpk@-6h	
B-0533	1.23uM	47.0%@1.0uM		
B-0534	0.41uM	54.0%@1.0uM		
B-0535	0.44uM	0.87uM		
B-0536	0.46uM	0.15uM		
B-0537	3.44uM	51.0%@1.0uM		
B-0538	1.13uM	45.0%@1.0uM		
B-0539	2.84uM	21.0%@1.0uM		
B-0540	3.62uM	54.0%@1.0uM		
B-0541	3.24uM	28.0%@1.0uM		
B-0542	1.55uM	50.0%@1.0uM		
B-0543	1.56uM	43.0%@1.0uM		
B-0544	1.12uM	27.0%@1.0uM		
B-0545	1.06uM	41.0%@1.0uM		
B-0546	1.04uM	18.0%@1.0uM		
B-0547	1.24uM	21.0%@1.0uM		
B-0548	1.77uM	28.0%@1.0uM		
B-0549	2.22uM	22.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0550	2.41uM	14.0%@1.0uM		
B-0551	1.08uM	56.0%@1.0uM		
B-0552	0.13uM	46.0%@1.0uM		
B-0553	1.44uM	47.0%@1.0uM		
B-0554	2.58uM	20.0%@1.0uM		
B-0555	1.87uM	34.0%@1.0uM		
B-0556	0.49uM	39.0%@1.0uM		
B-0557	1.37uM	32.0%@1.0uM		
B-0558	0.85uM	33.0%@1.0uM		
B-0559	0.53uM	49.0%@1.0uM		
B-0560	2.57uM	31.0%@1.0uM		
B-0561	2.07uM	40.0%@1.0uM		
B-0562	0.22uM	0.3uM		5%@3mpk@-4h
B-0563	0.18uM	0.13uM		
B-0564	0.82uM	58%@1.0uM		
B-0565	0.23uM	0.59uM		
B-0566	<0.1uM	0.17uM		0%@3mpk@-4h
B-0567	0.14uM	0.28uM		
B-0568	1.22uM	46.0%@1.0uM		
B-0569	0.15uM	0.26uM		
B-0570	0.27uM	46.0%@1.0uM		
B-0571	0.38uM	44.0%@1.0uM		
B-0572	0.27uM	41.0%@1.0uM		
B-0573	0.36uM	1.7uM		
B-0574	0.13uM	0.66uM		37%@3mpk@-4h
B-0575	0.032uM	0.17uM		
B-0576	0.068uM	0.39uM		65%@3mpk@-4h
B-0577	0.091uM	66.0%@1.0uM		
B-0578	1.88uM	47.0%@1.0uM		
B-0579	0.11uM	79.0%@1.0uM		
B-0580	2.23uM	0.84uM		
B-0581	0.26uM	2.17uM		
B-0582	1.03uM	37.0%@1.0uM		
B-0583	3.93uM	26.0%@1.0uM		
B-0584	0.66uM	54.0%@1.0uM		
B-0585	0.83uM	79.0%@1.0uM	50%@30mpk@-6h	
B-0586	0.81uM	51.0%@1.0uM		
B-0587	6.84uM	38%@1.0uM		
B-0588	12.8uM	42%@1.0uM		
B-0589	1.71uM	42%@1.0uM		
B-0590	1.57uM	38.0uM		
B-0591	3.59uM	29.0%@1.0uM		
B-0592	1.62uM	45.0%@1.0uM		
B-0593	1.22uM	36.0%@1.0uM		
B-0594	-	41.0%@1.0uM		
B-0595	2.42uM	22.0%@1.0uM		
B-0596	20.0uM	41.0%@1.0uM		
B-0597	1.68uM	63.0%@1.0uM		
B-0598	2.12uM	50.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0599	4.16uM	21.0%@1.0uM		
B-0600	0.002uM	28.0%@1.0uM		
B-0601	0.089uM	1.31uM		43%@3mpk%-4h
B-0602	0.97uM	61.0%@1.0uM		
B-0603	0.09uM	51.0%@1.0uM		
B-0604	0.3uM	20.0%@1.0uM		
B-0605	0.18uM	47.0%@1.0uM		
B-0606	0.17uM	53.0%@1.0uM		
B-0607	2.79uM	70.0%@1.0uM		
B-0608	0.059uM	73.0%@1.0uM		
B-0609	<0.1uM	87.0%@1.0uM		
B-0610	<0.1uM	88.0%@1.0uM		
B-0611	0.65uM	60.0%@1.0uM		
B-0612	0.16uM	60.0%@1.0uM		
B-0613	0.17uM	76.0%@1.0uM		
B-0614	0.76uM	70.0%@1.0uM		0%@3mpk@-4h
B-0615	0.08uM	83.0%@1.0uM		
B-0616	0.38uM	87.0%@1.0uM		
B-0617	0.045uM	92.0%@1.0uM		
B-0618	0.37uM	80.0%@1.0uM		
B-0619	<0.1uM	88.0%@1.0uM		
B-0620	1.59uM	58.0%@1.0uM		
B-0621	0.36uM	68.0%@1.0uM		
B-0622	0.076uM	78.0%@1.0uM		
B-0623	0.12uM	76.0%@1.0uM		
B-0624	0.085uM	54.0%@1.0uM		
B-0625	0.023uM	88.0%@1.0uM		
B-0626	<0.1uM	85.0%@1.0uM		
B-0627	0.25uM	69.0%@1.0uM		
B-0628	0.023uM	72.0%@1.0uM		
B-0629	0.2uM	79.0%@1.0uM		
B-0630	0.06uM	77.0%@1.0uM		
B-0631	0.065uM	81.0%@1.0uM		
B-0632	<0.1uM	79.0%@1.0uM		
B-0633	0.6uM	80.0%@1.0uM		
B-0634	0.6uM	40.0%@1.0uM		
B-0635	0.15uM	55.0%@1.0uM		
B-0636	<0.1uM	86.0%@1.0uM		
B-0637	0.11uM	92.0%@1.0uM		
B-0638	0.25uM	89.0%@1.0uM		
B-0639	0.051uM	93.0%@1.0uM		50%@3mpk@-4h
B-0640	0.36uM	94.0%@1.0uM		
B-0641	0.58uM	65.0%@1.0uM		
B-0642	0.49uM	90.0%@1.0uM		
B-0643	0.069uM	85.0%@1.0uM		0%@3mpk@-4h
B-0644	0.058uM	89.0%@1.0uM		
B-0645	0.58uM	80.0%@1.0uM		
B-0646	0.26uM	94.0%@1.0uM		
B-0647	1.61uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-0648	<0.1uM	83.0%@1.0uM		
B-0649	0.83uM	39.0%@1.0uM		
B-0650	0.006uM	95.0%@1.0uM		8%@3mpk@-4h
B-0651	1.78uM	81.0%@1.0uM		
B-0652	0.19uM	83.0%@1.0uM		
B-0653	2.01uM	74.0%@1.0uM		
B-0654	5.97uM	78.0%@1.0uM		
B-0655	1.25uM	76.0%@1.0uM		
B-0656	0.007uM	95.0%@1.0uM		28%@3mpk@-4h
B-0657	0.17uM	83.0%@1.0uM		
B-0658	1.14uM	91.0%@1.0uM		
B-0659	2.64uM	87.0%@1.0uM		
B-0660	0.088uM	92.0%@1.0uM		
B-0661	<0.1uM	90.0%@1.0uM		
B-0662	<0.1uM	95.0%@1.0uM		
B-0663	0.88uM	74.0%@1.0uM		
B-0664	0.39uM	80.0%@1.0uM		
B-0665	0.47uM	72.0%@1.0uM		
B-0666	0.17uM	73.0%@1.0uM		
B-0667	0.83uM	75.0%@1.0uM		
B-0668	0.27uM	78.0%@1.0uM		
B-0669	0.89uM	34.0%@1.0uM		
B-0670	3.15uM	32.0%@1.0uM		
B-0671	6.38uM	36.0%@1.0uM		
B-0672	6.59uM	32.0%@1.0uM		
B-0673	8.54uM	48.0%@1.0uM		
B-0674	2.81uM	42.0%@1.0uM		
B-0675	5.42uM	3.0%@1.0uM		
B-0676	2.09uM	22.0%@1.0uM		
B-0677	1.63uM	25.0%@1.0uM		
B-0678	0.38uM	52.0%@1.0uM		
B-0679	0.062uM	45.0%@1.0uM		
B-0680	0.42uM	67.0%@1.0uM		
B-0681	1.96uM	17.0%@1.0uM		
B-0682	0.76uM	39.0%@1.0uM		
B-0683	13.0uM	32.0%@1.0uM		
B-0684	0.54uM	68.0%@1.0uM		
B-0685	15.4uM	33.0%@1.0uM		
B-0686	0.42uM	59.0%@1.0uM		
B-0687	10.1uM	15.0%@1.0uM		
B-0688	0.66uM	58.0%@1.0uM		
B-0689	14.6uM	27.0%@1.0uM		
B-0690	27.1uM	36.0%@1.0uM		
B-0691	0.16uM	48.0%@1.0uM		
B-0692	0.38uM	29.0%@1.0uM		
B-0693	0.39uM	28.0%@1.0uM		
B-0694	0.62uM	21.0%@1.0uM		
B-0695	0.23uM	32.0%@1.0uM		
B-0696	0.085uM	35.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0697	0.45uM	44.0%@1.0uM		
B-0698	2.33uM	43.0%@1.0uM		
B-0699	0.34uM	31.0%@1.0uM		
B-0700	0.24uM	56.0%@1.0uM		
B-0701	0.39uM	45.0%@1.0uM		
B-0702	0.036uM	39.0%@1.0uM		
B-0703	0.12uM	39.0%@1.0uM		
B-0704	2.19uM	29.0%@1.0uM		
B-0705	0.44uM	21.0%@1.0uM		
B-0706	0.44uM	32.0%@1.0uM		
B-0707	1.7uM			
B-0708	2.1uM			
B-0709	0.84uM			
B-0710	1.99uM			
B-0711	1.99uM			
B-0712	2.9uM			
B-0713	4.3uM			
B-0714	3.7uM			
B-0715	3.2uM			
B-0716	4.6uM			
B-0717	4.3uM			
B-0718	1.4uM			
B-0719	3.4uM			
B-0720	1.3uM			
B-0721	3.8uM			
B-0722	0.07uM	>1.0uM		
B-0723	0.47uM			
B-0724	0.06uM	17.0%@1.0uM		
B-0725	9.7uM			
B-0726	1.4uM			
B-0727	0.51uM			
B-0728	20.0uM			
B-0729	0.87uM			
B-0730	0.25uM	11.0%@1.0uM		
B-0731	0.87uM	>1.0uM		
B-0732	14.0uM			
B-0733	32.0uM			
B-0734	0.92uM			
B-0735	1.0uM			
B-0736	26.0uM			
B-0737	2.6uM			
B-0738	2.7uM			
B-0739	4.1uM			
B-0740	4.4uM			
B-0741	26.0uM			
B-0742	2.2uM			
B-0743	1.2uM			
B-0744	23.0uM			
B-0745	6.0uM			

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0746	0.01uM	22.0%@1.0uM		
B-0747	1.1uM			
B-0748	1.2uM			
B-0749	4.4uM			
B-0750	0.92uM			
B-0751	1.6uM			
B-0752	0.33uM			
B-0753	0.37uM			
B-0754	0.55uM			
B-0755	2.3uM			
B-0756	0.94uM			
B-0757	0.54uM	16.0%@1.0uM		
B-0758	1.5uM			
B-0759	0.3uM			
B-0760	0.01uM	13.0%@1.0uM		
B-0761	<0.1uM			
B-0762	0.13uM	5.0%@1.0uM		
B-0763	0.015uM	17.0%@1.0uM		
B-0764	0.67uM	26.0%@1.0uM		
B-0765	0.3uM	29.0%@1.0uM		
B-0766	0.95uM			
B-0767	0.08uM			
B-0768	1.4uM			
B-0769	12.7uM			
B-0770	2.3uM			
B-0771	0.5uM			
B-0772	0.8uM			
B-0773	14.0uM			
B-0774	1.5uM			
B-0775	0.6uM	>1.0uM		
B-0776	0.9uM	>1.0uM		
B-0777	21.0uM			
B-0778	51.0uM			
B-0779	0.5uM			
B-0780	1.1uM			
B-0781	48.0uM			
B-0782	22.0uM			
B-0783	8.0uM			
B-0784	7.0uM			
B-0785	23.0uM			
B-0786	24.0uM			
B-0787	1.5uM			
B-0788	1.2uM			
B-0789	33.0uM			
B-0790	1.0uM	4.0%@1.0uM		
B-0791	0.3uM	>1.0uM		
B-0792	1.1uM			
B-0793	0.3uM			
B-0794	2.9uM	2.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0795	1.9uM	11.0%@1.0uM		
B-0796	1.4uM			
B-0797	1.04uM	-		
B-0798	1.73uM	-		
B-0799	-	>1.0uM		
B-0800	1.01uM	>1.0uM		
B-0801	0.67uM	>1.0uM		
B-0802	-	>1.0uM		
B-0803	0.057uM	53.0%@1.0uM		
B-0804	0.3uM	32.0%@1.0uM		
B-0805	0.71uM	>1.0uM		
B-0806	3.28uM	>1.0uM		
B-0807	10.8uM	-		
B-0808	3.09uM	>1.0uM		
B-0809	1.22uM	7.0%@1.0uM		
B-0810	1.11uM	>1.0uM		
B-0811	2.79uM	2.0%@1.0uM		
B-0812	2.12uM	>1.0uM		
B-0813	3.02uM	>1.0uM		
B-0814	-	>1.0uM		
B-0815	2.11uM	>1.0uM		
B-0816	3.46uM	>1.0uM		
B-0817	3.07uM	33.0%@1.0uM		
B-0818	4.97uM	>1.0uM		
B-0819	1.08uM	>1.0uM		
B-0820	1.64uM	3.0%@1.0uM		
B-0821	1.44uM	-		
B-0822	1.33uM	-		
B-0823	2.39uM	>1.0uM		
B-0824	3.41uM	-		
B-0825	-	-		
B-0826	1.74uM	-		
B-0827	15.6uM	-		
B-0828	7.9uM	-		
B-0829	0.61uM	65.0%@1.0uM		
B-0830	0.54uM	34.0%@1.0uM		
B-0831	0.9uM	>1.0uM		
B-0832	1.49uM	-		
B-0833	0.95uM	23.0%@1.0uM		
B-0834	1.25uM	-		
B-0835	-	-		
B-0836	1.24uM	-		
B-0837	1.96uM	>1.0uM		
B-0838	3.1uM	-		
B-0839	4.3uM	-		
B-0840	0.63uM	47.0%@1.0uM		
B-0841	0.32uM	36.0%@1.0uM		
B-0842	0.74uM	63.0%@1.0uM		
B-0843	0.61uM	>1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0844	0.4uM	25.0%@1.0uM		
B-0845	1.78uM	-		
B-0846	1.8uM	-		
B-0847	0.73uM	21.0%@1.0uM		
B-0848	1.56uM	-		
B-0849	1.25uM	-		
B-0850	1.81uM	-		
B-0851	0.91uM	39.0%@1.0uM		
B-0852	1.02uM	-		
B-0853	-	38.0%@1.0uM		
B-0854	-	25.0%@1.0uM		
B-0855	-	8.0%@1.0uM		
B-0856	-	38.0%@1.0uM		
B-0857	6.25uM	-		
B-0858	2.1uM	48.0%@1.0uM		
B-0859	39.5uM	-		
B-0860	38.1uM	-		
B-0861	1.32uM	12.0%@1.0uM		
B-0862	2.15uM	4.0%@1.0uM		
B-0863	0.81uM	25.0%@1.0uM		
B-0864	0.39uM	40.%@1.0uM		
B-0865	0.66uM	46.0%@1.0uM		
B-0866	1.38uM	28.0%@1.0uM		
B-0867	0.62uM	>1.0uM		
B-0868	3.28uM	8.0%@1.0uM		
B-0869	4.19uM	>1.0uM		
B-0870	3.13uM	>1.0uM		
B-0871	1.9uM	>1.0uM		
B-0872	3.13uM	3.0%@1.0uM		
B-0873	6.92uM	>1.0uM		
B-0874	1.92uM	>1.0uM		
B-0875	2.13uM	8%@1.0uM		
B-0876	0.89uM	>1.0uM		
B-0877	1.17uM	13.0%@1.0uM		
B-0878	0.65uM	19.0%@1.0uM		
B-0879	0.87uM	1.0%@1.0uM		
B-0880	0.15uM	40.0%@1.0uM		
B-0881	1.36uM	>1.0uM		
B-0882	1.48uM	9%@1.0uM		
B-0883	1.06uM	>1.0uM		
B-0884	1.89uM	-		
B-0885				
B-0886				
B-0887				
B-0888				
B-0889				
B-0890				
B-0891				
B-0892				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0893				
B-0894				
B-0895				
B-0896				
B-0897				
B-0898				
B-0899				
B-0900				
B-0901				
B-0902				
B-0903				
B-0904				
B-0905				
B-0906				
B-0907				
B-0908				
B-0909				
B-0910				
B-0911				
B-0912				
B-0913				
B-0914				
B-0915				
B-0916				
B-0917				
B-0918				
B-0919				
B-0920				
B-0921				
B-0922				
B-0923				
B-0924				
B-0925				
B-0926				
B-0927				
B-0928				
B-0929				
B-0930				
B-0931				
B-0932				
B-0933	47.0%@1.0uM	37.0%@1.0uM		
B-0934	67.0%@1.0uM	36.0%@1.0uM		
B-0935	69.0%@1.0uM	54.0%@1.0uM		
B-0936	69.0%@1.0uM	>1.0uM		
B-0937	64.0%@1.0uM	1.74uM		
B-0938	51.0%@1.0uM	29.0%@1.0uM		
B-0939	78.0%@1.0uM	14.0%@1.0uM		
B-0940	56.0%@1.0uM	22.0%@1.0uM		
B-0941	81.0%@1.0uM	25.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0942	82.0%@1.0uM	2.0%@1.0uM		
B-0943	63.0% @10.0uM	24.0%@1.0uM		
B-0944	45.0%@1.0uM	27.0%@1.0uM		
B-0945	96.0%@1.0uM	0.93uM		
B-0946	76.0%@1.0uM	31.0%@1.0uM		
B-0947	69.0%@1.0uM	34.0%@1.0uM		
B-0948	68.0%@1.0uM	1.81uM		
B-0949	90.0%@1.0uM	17.0%@1.0uM		
B-0950	81.0%@1.0uM	0.58uM		
B-0951	82.0%@1.0uM	20.0%@1.0uM		
B-0952	44.0%@1.0uM	21.0%@1.0uM		
B-0953	63.0%@1.0uM	25.0%@1.0uM		
B-0954	62.0%@1.0uM	0.52uM		
B-0955	49.0%@1.0uM	0.54uM		
B-0956	56.0%@1.0uM	1.33uM		
B-0957	79.0%@1.0uM	22.0%@1.0uM		
B-0958	74.0%@1.0uM	0.38uM		
B-0959	83.0%@1.0uM	39.0%@1.0uM		
B-0960	48.0%@1.0uM	4.0%@1.0uM		
B-0961	79.0%@1.0uM	23.0%@1.0uM		
B-0962	85.0%@1.0uM	2.71uM		
B-0963	76.0%@1.0uM	39.0%@1.0uM		
B-0964	94.0%@1.0uM	5.0uM		
B-0965	74.0%@1.0uM	1.1uM		
B-0966	50.0%@1.0uM	5.0%@1.0uM		
B-0967	80.0%@1.0uM	29.0%@1.0uM		
B-0968	35.0%@1.0uM	26.0%@1.0uM		
B-0969	63.0%@1.0uM	35.0%@1.0uM		
B-0970	76.0%@10.0uM	0.88uM		
B-0971	61.0%@1.0uM	39.0%@1.0uM		
B-0972	85.0%@1.0uM	2.0%@1.0uM		
B-0973	66.0%@10.0uM	48.0%@1.0uM		
B-0974	57.0%@1.0uM	47.0%@1.0uM		
B-0975	82.0%@1.0uM	32.0%@1.0uM		
B-0976	79.0%@1.0uM	36.0%@1.0uM		
B-0977	60.0%@1.0uM	26.0%@1.0uM		
B-0978	59.0%@1.0uM	36.0%@1.0uM		
B-0979	56.0%@10.0uM	23.0%@1.0uM		
B-0980	68.0%@1.0uM	31.0%@1.0uM		
B-0981	62.0%@1.0uM	57.0%@1.0uM		
B-0982	65.0%@1.0uM	23.0%@1.0uM		
B-0983	75.0%@1.0uM	0.8uM		
B-0984	60.0%@1.0uM	51.0%@1.0uM		
B-0985	86.0%@1.0uM	0.75uM		
B-0986	70.0%@1.0uM	71.0%@1.0uM		
B-0987	78.0%@1.0uM	79.0%@1.0uM		
B-0988	72.0%@1.0uM	65.0%@1.0uM		
B-0989	85.0%@1.0uM	0.85uM		
B-0990	-	26.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-0991	58.0%@1.0uM	33.0%@1.0uM		
B-0992	77.0%@1.0uM	45.0%@1.0uM		
B-0993	57.0%@1.0uM	73.0%@1.0uM		
B-0994	55.0%@1.0uM	43.0%@1.0uM		
B-0995	53.0%@1.0uM	14.0%@1.0uM		
B-0996	54.0%@1.0uM	27.0%@1.0uM		
B-0997	69.0%@1.0uM	22.0%@1.0uM		
B-0998	67.0%@1.0uM	25.0%@1.0uM		
B-0999	61.0%@1.0uM	24.0%@1.0uM		
B-1000	55.0%@1.0uM	42.0%@1.0uM		
B-1001	63.0%@1.0uM	31.0%@1.0uM		
B-1002	70.0%@1.0uM	41.0%@1.0uM		
B-1003	74.0%@1.0uM	29.0%@1.0uM		
B-1004	79.0%@1.0uM	45.0%@1.0uM		
B-1005	58.0%@1.0uM	23.0%@1.0uM		
B-1006	69.0%@1.0uM	38.0%@1.0uM		
B-1007	52.0%@1.0uM	34.0%@1.0uM		
B-1008	54.0%@1.0uM	23.0%@1.0uM		
B-1009	80.0%@1.0uM	55.0%@1.0uM		
B-1010	75.0%@1.0uM	1.0uM		
B-1011	72.0%21.0uM	17.0%@1.0uM		
B-1012	-	20.0%@1.0uM		
B-1013	85.0%@1.0uM	7.0%@1.0uM		
B-1014	88.0%@1.0uM	20.0%@1.0uM		
B-1015	77.0%@1.0uM	34.0%@1.0uM		
B-1016	58.0%@1.0uM	10.0%@1.0uM		
B-1017	96.0%@1.0uM	58.0%@1.0uM		
B-1018	88.0%@1.0uM	34.0%@1.0uM		
B-1019	82.0%@1.0uM	66.0%@1.0uM		
B-1020	87.0%@1.0uM	36.0%@1.0uM		
B-1021	82.0%@1.0uM	35.0%@1.0uM		
B-1022	84.0%@1.0uM	53.0%@1.0uM		
B-1023	93.0%@1.0uM	70.0%@1.0uM		
B-1024	89.0%@1.0uM	57.0%@1.0uM		
B-1025	61.0%@1.0uM	23.0%@1.0uM		
B-1026	87.0%@1.0uM	53.0%@1.0uM		
B-1027	58.0%@1.0uM	18.0%@1.0uM		
B-1028	70.0%@1.0uM	17.0%@1.0uM		
B-1029	69.0%@1.0uM	54.0%@1.0uM		
B-1030	76.0%@1.0uM	60.0%@1.0uM		
B-1031	69.0%@1.0uM	42.0%@1.0uM		
B-1032	76.0%@1.0uM	37.0%@1.0uM		
B-1033	86.0%@1.0uM	34.0%@1.0uM		
B-1034	66.0%@1.0uM	39.0%@1.0uM		
B-1035	75.0%@1.0uM	52.0%@1.0uM		
B-1036	68.0%@1.0uM	68.0%@1.0uM		
B-1037	-	41.0%@1.0uM		
B-1038	57.0%@1.0uM	0.57uM		
B-1039	-	1.33uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1040	72.0%@1.0uM	0.38uM		
B-1041	70.0%@1.0uM	73.0%@1.0uM		
B-1042	79.0%@1.0uM	12.0%@1.0uM		
B-1043	64.0%@1.0uM	53.0%@1.0uM		
B-1044	94.0%@1.0uM	0.93uM		
B-1045	78.0%@1.0uM	25.0%@1.0uM		
B-1046	72.0%@1.0uM	66.0%@1.0uM		
B-1047	72.0%@1.0uM	58.0%@1.0uM		
B-1048	67.0%@1.0uM	19.0%@1.0uM		
B-1049	67.0%@1.0uM	65.0%@1.0uM		
B-1050	-	0.54uM		
B-1051	68.0%@1.0uM	41%@1.0uM		
B-1052	69.0%@1.0uM	66%@1.0uM		
B-1053	78.0%@1.0uM	0.4uM		
B-1054	79.0%@1.0uM	55.0%@1.0uM		
B-1055	89.0%@1.0uM	63.0%@1.0uM		
B-1056	89.0%@1.0uM	0.76uM		
B-1057	85.0%@1.0uM	0.72uM		
B-1058	0.66uM	43.0%@1.0uM		
B-1059	0.18uM	24.0%@1.0uM		
B-1060	0.11uM	32.0%@1.0uM		
B-1061	0.03uM	19.0%@1.0uM		
B-1062	<0.1uM	26.0%@1.0uM		
B-1063	0.16uM	44.0%@1.0uM		
B-1064	0.39uM	50.0%@1.0uM		
B-1065	0.56uM	40.0%@1.0uM		
B-1066	<0.1uM	39.0%@1.0uM		
B-1067	1.6uM	32.0%@1.0uM		
B-1068	0.48uM	24.0%@1.0uM		
B-1069	0.22uM	27.0%@1.0uM		
B-1070	<0.1uM	44.0%@1.0uM		
B-1071	<0.1uM	48.0%@1.0uM		
B-1072	0.38uM	28.0%@1.0uM		
B-1073	<0.1uM	21.0%@1.0uM		
B-1074	0.23uM	33.0%@1.0uM		
B-1075	0.03uM	29.0%@1.0uM		
B-1076	0.08uM	31.0%@1.0uM		
B-1077	<0.1uM	38.0%@1.0uM		
B-1078	0.26uM	48.0%@1.0uM		
B-1079	<0.1uM	40.0%@1.0uM		
B-1080	0.19uM	28.0%@1.0uM		
B-1081	<0.1uM	37.0%@1.0uM		
B-1082	<0.1uM	54.0%@1.0uM		
B-1083	<0.1uM	23.0%@1.0uM		
B-1084	0.43uM	29.0%@1.0uM		
B-1085	<0.1uM	29.0%@1.0uM		
B-1086	<0.1uM	42.0%@1.0uM		
B-1087	0.05uM	32.0%@1.0uM		
B-1088	0.73uM	49.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1089	<0.1uM	39.0%@1.puM		
B-1090	<0.1uM	90.0%@1.0uM		
B-1091	<0.1uM	73.0%@1.0uM		
B-1092	0.27uM	85.0%@1.0uM		
B-1093	0.33uM	36.0%@1.0uM		
B-1094	0.013uM	69.0%@1.0uM		
B-1095	<0.1uM	70.0%@1.0uM		
B-1096	<0.1uM	32.0%@1.0uM		
B-1097	<0.1uM	44.0%@1.07uM		
B-1098	<0.1uM	82.0%@1.0uM		
B-1099	0.26uM	74.0%@1.0uM		
B-1100	0.22uM	56.0%@1.0uM		
B-1101	0.026uM	82.0%@1.0uM		
B-1102	0.035uM	83.0%@1.0uM		
B-1103	0.094uM	90.0%@1.0uM		
B-1104	0.12uM	69.0%@1.0uM		
B-1105	<0.1uM	84.0%@1.0uM		
B-1106	<0.1uM	86.0%@1.0uM		
B-1107	0.057uM	84.0%@1.0uM		
B-1108	0.22uM	81.0%@1.0uM		
B-1109	0.054uM	80.0%@1.0uM		
B-1110	0.47uM	64.0%@1.0uM		
B-1111	0.19uM	64.0%@1.0uM		
B-1112	0.58uM	43.0%@1.0uM		
B-1113	<0.1uM	72.0%@1.0uM		
B-1114	0.069uM	51.0%@1.0uM		
B-1115	0.024uM	89.0%@1.0uM		
B-1116	0.41uM	81.0%@1.0uM		
B-1117	0.13uM	73.0%@1.0uM		
B-1118	0.33uM	91.0%@1.0uM		
B-1119	0.35uM	80.0%@1.0uM		
B-1120	0.47uM	9.0%@1.0uM		
B-1121	3.58uM	29.0%@1.0uM		
B-1122	1.84uM	32.0%@1.0uM		
B-1123	2.93uM	27.0%@1.0uM		
B-1124	1.49uM	52.0%@1.0uM		
B-1125	0.56uM	41.0%@1.0uM		
B-1126	1.5uM	>1.0uM		
B-1127	0.71uM	7.0%@1.0uM		
B-1128	2.55uM	26.0%@1.0uM		
B-1129	1.07uM	46.0%@1.0uM		
B-1130	0.5uM	29.0%@1.0uM		
B-1131	0.076uM	34.0%@1.0uM		
B-1132	0.72uM	11.0%@1.0uM		
B-1133	0.38uM	33.0%@1.0uM		
B-1134	1.71uM	33.0%@1.0uM		
B-1135	0.23uM	38.0%@1.0uM		
B-1136	1.17uM	40.0%@1.0uM		
B-1137	0.038uM	35.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1138	1.82uM	>1.0uM		
B-1139	0.041uM	29.0%@1.0uM		
B-1140	1.68uM	39.0%@1.0uM		
B-1141	2.47uM	32.0%@1.0uM		
B-1142	0.11uM	37.0%@1.0uM		
B-1143	0.17uM	40.0%@1.0uM		
B-1144	0.44uM	72.0%@1.0uM		
B-1145	1.07uM	71.0%@1.0uM		
B-1146	0.47uM	61.0%@1.0uM		
B-1147	0.095uM	53.0%@1.0uM		
B-1148	0.43uM	61.0%@1.0uM		
B-1149	1.55uM	48.0%@1.0uM		
B-1150	0.47uM	75.0%@1.0uM		
B-1151	0.32uM	72.0%@1.0uM		
B-1152	0.73uM	53.0%@1.0uM		
B-1153	2.22uM	52.0%@1.0uM		
B-1154	0.085uM	46.0%@1.0uM		
B-1155	3.22uM	30.0%@1.0uM		
B-1156	0.27uM	78.0%@1.0uM		
B-1157	0.26uM	66.0%@1.0uM		
B-1158	74%@1.0uM	0.68uM	53%@30mpk@-6h	
B-1159	66.0%@1.0uM	1.03uM	60%@30mpk@-6h	
B-1160	79.0%@1.0uM	0.38uM		
B-1161	64.0%21.0uM	0.93uM	40%@30mpk@-6h	45%@3mpk@-4h
B-1162	79.0%@1.0uM	0.59uM	40%@30mpk@-6h	
B-1163	74.0%@1.0uM	0.37uM		
B-1164	-	0.35uM		
B-1165	66.0%@1.0uM	0.99uM		
B-1166	77.0%@1.0uM	0.39uM	50%@30mpk@-6h	50%@3mpk@-4h
B-1167	70.0%@1.0uM	1.06uM		
B-1168	66.0%@1.0uM	0.63uM		
B-1169	80.0%@1.0uM	0.11uM		
B-1170	82.0%@1.0uM	0.57uM		
B-1171	78.0%@1.0uM	0.23uM		
B-1172	68.0%@1.0uM	1.95uM		
B-1173	65.0%@1.0uM	62%@1.0uM		
B-1174	80.0%@1.0uM	0.86uM		
B-1175	72.0%@1.0uM	1.83uM		
B-1176	67.0%@1.0uM	67.0%@1.0uM		
B-1177	70.0%@1.0uM	1.16uM		
B-1178	92.0%@1.0uM	1.61uM		
B-1179	86.0%@1.0uM	0.41uM		
B-1180	78.0%@1.0uM	0.53uM		
B-1181	79.0%@1.0uM	66%@1.0uM		
B-1182	72.0%@1.0uM	0.65uM		
B-1183	77.0%@1.0uM	0.2uM		
B-1184	69.0%@1.0uM	0.63uM		
B-1185	71.0%@1.0uM	0.79uM		
B-1186	83.0%@1.0uM	60%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1187	76.0%@1.0uM	1.89uM		
B-1188	-	36.0%@1.0uM		
B-1189	68.0%@1.0uM	0.83uM		
B-1190	78.0%@1.0uM	62.0%@1.0uM		
B-1191	74.0%@1.0uM	57.0%@1.0uM		
B-1192	84.0%@1.0uM	0.47uM		
B-1193	69.0%@1.0uM	65.0%@1.0uM		
B-1194	87.0%@1.0uM	0.58uM		
B-1195	52.0%@1.0uM	60.0%@1.0uM		
B-1196	74.0%@1.0uM	68.0%@1.0uM		
B-1197	77.0%@1.0uM	45.0%@1.0uM		
B-1198	92.0%@1.0uM	0.46uM		
B-1199	87.0%@1.0uM	49.0%@1.0uM		
B-1200	95.0%@1.0uM	0.64uM		
B-1201	84.0%@1.0uM	0.51uM		
B-1202	71.0%@1.0uM	58.0%@1.0uM		
B-1203	84.0%@1.0uM	58.0%@1.0uM		
B-1204	68.0%@1.0uM	59.0%@1.0uM		
B-1205	74.0%@1.0uM	46.0%@1.0uM		
B-1206	81.0%@1.0uM	0.34uM		
B-1207	90.0%@1.0uM	58.0%@1.0uM		
B-1208	82.0%@1.0uM	51.0%@1.0uM		
B-1209	86.0%@1.0uM	55.0%@1.0uM		
B-1210	82.0%@1.0uM	57.0%@1.0uM		
B-1211	88.0%@1.0uM	59.0%@1.0uM		
B-1212	90.0%@1.0uM	57.0%@1.0uM		
B-1213	84.0%@1.0uM	0.62uM		
B-1214	76.0%@1.0uM	58.0%@1.0uM		
B-1215	86.0%@1.0uM	0.23uM		
B-1216	88.0%@1.0uM	0.18uM		
B-1217	87.0%@1.0uM	0.46uM		
B-1218	88.0%@1.0uM	76.0%@1.0uM		
B-1219	85.0%@1.0uM	37.0%@1.0uM		
B-1220	81.0%@1.0uM	53.0%@1.0uM		
B-1221	82.0%@1.0uM	44.0%@1.0uM		
B-1222	65.0%@1.0uM	9.0%@1.0uM		
B-1223	80.0%@1.0uM	61.0%@1.0uM		
B-1224	82.0%@1.0uM	74.0%@1.0uM		
B-1225	89.0%@1.0uM	73.0%@1.0uM		
B-1226	89.0%@1.0uM	0.18uM		
B-1227	83.0%@1.0uM	0.22uM		
B-1228	90.0%@1.0uM	0.72uM		
B-1229	87.0%@1.0uM	0.65uM		
B-1230	90.0%@1.0uM	0.25uM		
B-1231	94.0%@1.0uM	0.56uM		
B-1232	81.0%@1.0uM	54.0%@1.0uM		
B-1233	85.0%@1.0uM	0.36uM		
B-1234	89.0%@1.0uM	0.49uM		
B-1235	0.04uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1236	0.1uM	53.0%@1.0uM		
B-1237	0.22uM	39.0%@1.0uM		
B-1238	0.14uM	16.0%@1.0uM		
B-1239	<0.1uM	38.0%@1.0uM		
B-1240	<0.1uM	59.0%@1.0uM		
B-1241	0.04uM	81.0%@1.0uM		
B-1242	0.08uM	83.0%@1.0uM		
B-1243	0.04uM	47.0%@1.0uM		
B-1244	0.26uM	44.0%@1.0uM		
B-1245	0.49uM	42.0%@1.0uM		
B-1246	0.27uM	40.0%@1.0uM		
B-1247	<0.1uM	58.0%@1.0uM		
B-1248	<0.1uM	68.0%@1.0uM		
B-1249	0.24uM	60.0%@1.0uM		
B-1250	0.14uM	18.0%@1.0uM		
B-1251	0.41uM	38.0%@1.0uM		
B-1252	0.17uM	46.0%@1.0uM		
B-1253	0.15uM	57.0%@1.0uM		
B-1254	0.16uM	68.0%@1.0uM		
B-1255	12.9uM	75.0%@1.0uM		
B-1256	0.12uM	41.0%@1.0uM		
B-1257	1.48uM	40.0%@1.0uM		
B-1258	0.07uM	56.0%@1.0uM		
B-1259	<0.1uM	0.48uM		
B-1260	0.11uM	48.0%@1.0uM		
B-1261	0.74uM	44.0%@1.0uM		
B-1262	<0.1uM	63.0%@1.0uM		
B-1263	1.05uM	57.0%@1.0uM		
B-1264	0.32uM	47.0%@1.0uM		
B-1265	0.43uM	51.0%@1.0uM		
B-1266	<0.1uM	58.0%@1.0uM		
B-1267	<0.1uM	73.0%@1.0uM		
B-1268	<0.1uM	79.0%@1.0uM		
B-1269	0.46uM	84.0%@1.0uM		
B-1270	0.47uM	83.0%@1.0uM		
B-1271	0.13uM	74.0%@1.0uM		
B-1272	0.014uM	38.0%@1.0uM		
B-1273	<0.1uM	36.0%@1.0uM		
B-1274	<0.1uM	41.0%@1.0uM		
B-1275	<0.1uM	50.0%@1.0uM		
B-1276	0.062uM	11.0%@1.0uM		
B-1277	<0.1uM	47.0%@1.0uM		
B-1278	0.12uM	85.0%@1.0uM		
B-1279	<0.1uM	79.0%@1.0uM		
B-1280	0.039uM	83.0%@1.0uM		
B-1281	<0.1uM	85.0%@1.0uM		
B-1282	<0.1uM	75.0%@1.0uM		
B-1283	<0.1uM	64.0%@1.0uM		
B-1284	<0.1uM	75.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1285	0.057uM	80.0%@1.0uM		
B-1286	0.15uM	78.0%21.0uM		
B-1287	0.25uM	55.0%@1.0uM		
B-1288	0.15uM	74.0%@1.0uM		
B-1289	0.73uM	35.0%@1.0uM		
B-1290	0.26uM	75.0%@1.0uM		
B-1291	0.097uM	55.0%@1.0uM		
B-1292	0.01uM	74.0%@1.0uM		
B-1293	0.31uM	48.0%@1.0uM		
B-1294	0.013uM	54.0%@1.0uM		
B-1295	0.079uM	74.0%@1.0uM		
B-1296	0.038uM	48.0%@1.0uM		
B-1297	0.02uM	>1.0uM		
B-1298	0.055uM	20.0%@1.0uM		
B-1299	0.091uM	>1.0uM		
B-1300	0.071uM	18.0%@1.0uM		
B-1301	0.12uM	15.0%@1.0uM		
B-1302	0.023uM	11.0%@1.0uM		
B-1303	0.08uM	>1.0uM		
B-1304	0.11uM	10.0%@1.0uM		
B-1305	0.64uM	9.0%@1.0uM		
B-1306	0.11uM	>1.0uM		
B-1307	0.009uM	16.0%@1.0uM		
B-1308	<0.1uM	>1.0uM		
B-1309	0.045uM	>1.0uM		
B-1310	0.12uM	11.0%@1.0uM		
B-1311	0.05uM	57.0%@1.0uM		
B-1312	0.35uM	>1.0uM		
B-1313	0.035uM	37.0%@1.0uM		
B-1314	0.045uM	24.0%@1.0uM		
B-1315	0.055uM	12.0%@1.0uM		
B-1316	0.026uM	36.0%@1.0uM		
B-1317	0.019uM	9.0%@1.0uM		
B-1318	<0.1uM	1.0%@1.0uM		
B-1319	0.24uM	>1.0uM		
B-1320	0.047uM	43.0%@1.0uM		
B-1321	0.47uM	66.0%@1.0uM		
B-1322	0.12uM	87.0%@1.0uM		
B-1323	0.013uM	85.0%@1.0uM		
B-1324	0.16uM	83.0%@1.0uM		
B-1325	0.27uM	95.0%@1.0uM		
B-1326	0.092uM	84.0%@1.0uM		
B-1327	0.13uM	65.0%@1.0uM		
B-1328	0.032uM	86.0%@1.0uM		
B-1329	0.66uM	54.0%@1.0uM		
B-1330	0.053uM	85.0%@1.0uM		
B-1331	0.004uM	85.0%@1.0uM		
B-1332	0.007uM	81.0%@1.0uM		
B-1333	0.45uM	76.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1334	0.13uM	73.0%@1.0uM		
B-1335	0.097uM	63.0%@1.0uM		
B-1336	0.072uM	83.0%@1.0uM		
B-1337	0.4uM	90.0%@1.0uM		
B-1338	0.18uM	73.0%@1.0uM		
B-1339	0.12uM	67.0%@1.0uM		
B-1340	0.043uM	63.0%@1.0uM		
B-1341	0.42uM	52.0%@1.0uM		
B-1342	0.25uM	59.0%@1.0uM		
B-1343	0.065uM	83.0%@1.0uM		
B-1344	0.014uM	86.0%@1.0uM		
B-1345	0.27uM	73.0%@1.0uM		
B-1346	0.043uM	86.0%@1.0uM		
B-1347	0.021uM	84.0%@1.0uM		
B-1348	0.009uM	69.0%@1.0uM		
B-1349	0.037uM	86.0%@1.0uM		
B-1350	0.019uM	78.0%@1.0uM		
B-1351	0.068uM	78.0%@1.0uM		
B-1352	0.013uM	76.0%@1.0uM		
B-1353	0.062uM	80.0%@1.0uM		
B-1354	0.013uM	83.0%@1.0uM		
B-1355	0.07uM	75.0%@1.0uM		
B-1356	0.059uM	91.0%@1.0uM		
B-1357	0.18uM	84.0%@1.0uM		
B-1358	0.16uM	76.0%@1.0uM		
B-1359	0.005	84.0%@1.0uM		
B-1360	0.11	0.15uM		54%@3mpk@-4h
B-1361	0.03	0.29uM		
B-1362	0.003	0.29uM		
B-1363	0.009	0.28uM	51.0%@30pmk @-6H	53%@3mpk@-4h
B-1364	0.009	0.27uM	53.0%@30mpk@-6.0H	17%@3mpk@-4h
B-1365	0.17	88.0%@1.0uM		
B-1366	0.04	0.27uM		
B-1367	<0.1	0.22uM		
B-1368	0.031	0.33uM	44.0%@30mpk @-	
B-1369	<0.1	0.29uM		
B-1370	<0.1	0.77uM		
B-1371	0.06	83.0%@1.0uM		
B-1372	<0.1	0.41uM	48.0%@30mpk @-	
B-1373	0.016	0.17uM		
B-1374	<0.1	0.28uM		
B-1375	0.01	0.25uM		
B-1376	0.009	0.26uM	3.0%@30mpk @-6H	
B-1377	0.12	5.0uM		
B-1378	0.02	1.04uM		
B-1379	<0.1	0.092uM		
B-1380	<0.1	0.26uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1381	0.055	0.73uM		
B-1382	<0.1	0.44uM		
B-1383	0.0012	0.15uM		
B-1384	0.57	0.37uM		
B-1385	<0.1	0.11uM		
B-1386	<0.1	0.25uM		
B-1387	<0.1	0.1uM		
B-1388	0.57	1.38uM		
B-1389	0.06	0.57uM		
B-1390	<0.1	71.0%@1.0uM		
B-1391	0.016uM	82.0%@1.0uM		
B-1392	0.059uM	82.0%@1.0uM		
B-1393	3.17uM	80.0%@1.0uM		
B-1394	0.32uM	78.0%@1.0uM		
B-1395	1.48	61.0%@1.0uM		
B-1396	1.55	73.0%@1.0uM		
B-1397	0.92	85.0%@1.0uM		
B-1398	0.67	83.0%@1.0uM		
B-1399	0.14	74.0%@1.0uM		
B-1400	0.024	83.0%@1.0uM		
B-1401	0.033	75.0%@1.0uM		
B-1402	0.12	76.0%@1.0uM		
B-1403	4.54	71%@1.0uM		
B-1404	0.6	70%@1.0uM		
B-1405	0.28	70%@1.0uM		
B-1406	1.39	56.0%@1.0uM		
B-1407	0.4	71.0%@1.0uM		
B-1408	0.27	69.0%@1.0uM		
B-1409	<0.1	72.0%@1.0uM		
B-1410	<0.1	69%@1.0uM		
B-1411	<0.1	81.0%@1.0uM		
B-1412	0.097	80.0%@1.0uM		
B-1413	0.016	78.0%@1.0uM		
B-1414	0.025	83.0%@1.0uM		
B-1415	1.41	79.0%@1.0uM		
B-1416	0.14	81.0%@1.0uM		
B-1417	0.069	69.0%@1.0uM		
B-1418	1.01	82.0%@1.0uM		
B-1419	0.3	84.0%@1.0uM		
B-1420	<0.1	82.0%@1.0uM		
B-1421	0.014	75.0%@1.0uM		
B-1422	0.58	68.0%@1.0uM		
B-1423	1.58	84.0%@1.0uM		
B-1424	0.86	76.0%@1.0uM		
B-1425	0.09	83.0%@1.0uM		
B-1426	0.19	80.0%@1.0uM		
B-1427	<0.1	84.0%@1.0uM		
B-1428	<0.1	86.0%@1.0uM		
B-1429	<0.1	87.0%@1.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1430	0.75uM	35.0% @1.0uM		
B-1431	0.36uM	58.0% @1.0uM		
B-1432	0.11uM	51.0% @1.0uM		
B-1433	0.26uM	21.0% @1.0uM		
B-1434	0.19uM	28.0% @1.0uM		
B-1435	1.8uM	45.0% @1.0uM		
B-1436	1.0uM	20.0% @1.0uM		
B-1437	0.3uM	23.0% @1.0uM		
B-1438	2.01uM	27.0% @1.0uM		
B-1439	1.7uM	17.0% @1.0uM		
B-1440	0.87uM	3.0% @1.0uM		
B-1441	1.95uM	66.0% @1.0uM		
B-1442	1.54uM	18.0% @1.0uM		
B-1443	0.014uM	83.0% @1.0uM		
B-1444	0.3uM	24.0% @1.0uM		
B-1445	0.43uM	27.0% @1.0uM		
B-1446	0.77uM	36.0% @1.0uM		
B-1447	0.5uM	34.0% @1.0uM		
B-1448	1.43uM	22.0% @1.0uM		
B-1449	1.61uM	50.0%@1.0uM		
B-1450	2.1uM	49.0%@1.0uM		
B-1451	2.88uM	50% @1.0uM		
B-1452	2.41uM	47.0%@1.0uM		
B-1453	2.53uM	49.0% @1.0uM		
B-1454	1.6uM	12.0% @1.0uM		
B-1455	1.21uM	8.0% @1.0uM		
B-1456	1.29uM	>1.0uM		
B-1457	0.43uM	43.0% @1.0uM		
B-1458	0.95uM	65.0% @1.0uM		
B-1459	0.67uM	46.0% @1.0uM		
B-1460	0.96uM	29.0% @1.0uM		
B-1461	0.4uM	39.0% @1.0uM		
B-1462	0.22uM	50.0% @1.0uM		
B-1463	2.34uM	26.0% @1.0uM		
B-1464	1.18uM	27.0% @1.0uM		
B-1465	3.23uM	31.0% @1.0uM		
B-1466	1.69uM	>1.0uM		
B-1467	1.22uM	1.0% @1.0uM		
B-1468	1.61uM	10.0% @1.0uM		
B-1469	0.37uM	14.0% @1.0uM		
B-1470	0.6uM	28.0% @1.0uM		
B-1471	0.85uM	25.0% @1.0uM		
B-1472	0.93uM	12.0%@1.0uM		
B-1473	1.24uM	14.0% @1.0uM		
B-1474	1.23uM	31.0% @1.0uM		
B-1475	2.1uM	24.0% @1.0uM		
B-1476	0.047uM	42.0% @1.0uM		
B-1477	2.5uM	34.0% @1.0uM		
B-1478				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-1479				

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2270	0.72uM	31%@10.0uM		
B-2271	0.93uM	38%@10.0uM		
B-2272	0.26uM	53.0%@10.0uM		
B-2273	1.92uM	39.0%@10.0uM		
B-2274	0.26uM	59.0%@10.0uM		
B-2275	2.16uM	53.0%@10.0uM		
B-2276	11.5uM	37.0%@10.0uM		
B-2277	14.9uM	44.0%@10.0uM		
B-2278	0.8uM	51.0%@10.0uM		
B-2279	0.32uM	36.0%@10.0uM		
B-2280	0.4uM	57.0%@10.0uM		
B-2281	0.81uM	60.0%@10.0uM		
B-2282	0.91uM	41.0%@10.0uM		
B-2283	0.04uM	53.0%@10.0uM		
B-2284	4.61uM	62.0%@10.0uM		
B-2285	2.29uM	49.0%@10.0uM		
B-2286	0.017uM	0.78uM	25%@30mpk@-1h	
B-2287	2.56uM	61.0%@10.0uM		
B-2288	6.51uM	46.0%@10.0uM		
B-2289	3.0uM	30.0%@10.0uM		
B-2290	2.37uM	59.0%@10.0uM		
B-2291	0.019uM	41%@10.0uM		
B-2292	8.82uM	57.0%@10.0uM		
B-2293	2.11uM	56.0%@10.0uM		
B-2294	1.68uM	50.0%@10.0uM		
B-2295	1.79uM	56.0%@10.0uM		
B-2296	17.3uM	63.0%@10.0uM		
B-2297	3.59uM	57.0%@10.0uM		
B-2298	0.29uM	4.22uM		
B-2299	1.97uM	62.0%@10.0uM		
B-2300	0.07uM	43.0%@10.0uM		
B-2301	0.18uM	44.0%@10.0uM		
B-2302	1.0uM	58.0%@1.0uM		
B-2303	0.011uM	54.0%@10.0uM		
B-2304	1.41uM	50.0%@10.0uM		
B-2305	0.54uM	60.0%@10.0uM		
B-2306	5.88uM	39.0%@10.0uM		
B-2307	2.29uM	69.0%@10.0uM		
B-2308	0.66uM	56.0%@10.0uM		
B-2309	0.29uM	47.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % Inhib@conc. (uM)	U937 Cell IC50,uM or % Inhib@conc. (uM)	Mouse LPS Model % TNF Inhib @ dose @predose time	Rat LPS Model % Inhib @dose @predose time
B-2310	0.12uM	1.2uM	50%@30mpk@-6h	
B-2311	7.18uM	60%@10.0uM		
B-2312	2.93uM	43.0%@10.0uM		
B-2313	42.3uM	58.0%@10.0uM		
B-2314	11.0uM	66.0%@10.0uM		
B-2315	0.49uM	36.0%@10.0uM		
B-2316	0.46uM	58.0%@10.0uM		
B-2317	1.0uM	60.0%@10.0uM		
B-2318	73.0%@10.0uM	25.0%@10.0uM		
B-2319	75.0%@10.0uM	40.0%@10.0uM		
B-2320	44.0%@10.0uM	35.0%@10.0uM		
B-2321	69.0%@10.0uM	27.0%@10.0uM		
B-2322	76.0%@10.0uM	38.0%@10.0uM		
B-2323	69.0%@10.0uM	46.0%@10.0uM		
B-2324	58.0%@10.0uM	36.0%@10.0uM		
B-2325	60.0%@10.0uM	51.0%@10.0uM		
B-2326	76.0%@10.0uM	33.0%@10.0uM		
B-2327	76.0%@10.0uM	23.0%@10.0uM		
B-2328	65.0%@10.0uM	28.0%@10.0uM		
B-2329	72.0%@10.0uM	53.0%@10.0uM		
B-2330	81.0%@10.0uM	37.0%@10.0uM		
B-2331	74.0%@10.0uM	44.0%@10.0uM		
B-2332	70.0%@10.0uM	47.0%@10.0uM		
B-2333	58.0%@10.0uM	36.0%@10.0uM		
B-2334	81.0%@10.0uM	45.0%@10.0uM		
B-2335	82.0%@10.0uM	50.0%@10.0uM		
B-2336	48.0%@10.0uM	35.0%@10.0uM		
B-2337	46.0%@10.0uM	59.0%@10.0uM		
B-2338	73.0%@10.0uM	50.0%@10.0uM		
B-2339	84.0%@10.0uM	>10.0uM		
B-2340	35.0%@10.0uM	12.0%@10.0uM		
B-2341	75.0%@10.0uM	50.0%@10.0uM		
B-2342	83.0%@10.0uM	46.0%@10.0uM		
B-2343	43.0%@10.0uM	27.0%@10.0uM		
B-2344	71.0%@10.0uM	50.0%@10.0uM		
B-2345	64.0%@10.0uM	38.0%@10.0uM		
B-2346	45.0%@10.0uM	48.0%@10.0uM		
B-2347	49.0%@10.0uM	50.0%@10.0uM		
B-2348	76.0%@10.0uM	48.0%@10.0uM		
B-2349	75.0%@10.0uM	27.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2350	38.0%@10.0uM	56.0%@10.0uM		
B-2351	77.0%@10.0uM	1.0%@10.0uM		
B-2352	37.0%@10.0uM	19.0%@10.0uM		
B-2353	38.0%@10.0uM	33.0%@10.0uM		
B-2354	65.0%@10.0uM	25.0%@10.0uM		
B-2355	84.0%@10.0uM	50.0%@10.0uM		
B-2356	77.0%@10.0uM	45.0%@10.0uM		
B-2357	47.0%@10.0uM	41.0%@10.0uM		
B-2358	17.0%@10.0uM	52.0%@10.0uM		
B-2359	76.0%@10.0uM	35.0%@10.0uM		
B-2360	45.0%@10.0uM	>10.0uM		
B-2361	19.0%@10.0uM	46.0%@10.0uM		
B-2362	60%@100.0uM	39.0%@10.0uM		
B-2363	44.0%@10.0uM	1.0%@10.0uM		
B-2364	47.0%@10.0uM	4.0%@10.0uM		
B-2365	82.0%@10.0uM	43.0%@10.0uM		
B-2366	70.0%@10.0uM	59.0%@10.0uM		
B-2367	46.0%@10.0uM	40.0%@1.0uM		
B-2368	65.0%@10.0uM	55.0%@10.0uM		
B-2369	32.0%@10.0uM	>10.0uM		
B-2370	73%@100.0uM	20.0%@10.0uM		
B-2371	54.0%@10.0uM	36.0%@10.0uM		
B-2372	55.0%@100.0uM	>10.0uM		
B-2373	50.0%@100.0uM	6%@10.0uM		
B-2374	35.0%@10.0uM	20.0%@10.0uM		
B-2375	62.0%@100.0uM	>10.0uM		
B-2376	32.0%@10.0uM	17.0%@10.0uM		
B-2377	34.0%@10.0uM	17.0%@10.0uM		
B-2378	48.0%@10.0uM	61.0%@10.0uM		
B-2379	73.0%@100.0uM	45.0%@1.0uM		
B-2380	81%@100.0uM	53.0%@10.0uM		
B-2381	68%@100.0uM	2.0%@10.0uM		
B-2382	51.0%@10.0uM	24.0%@10.0uM		
B-2383	63.0%@10.0uM	35.0%@10.0uM		
B-2384	49%@100.0uM	10.0%@10.0uM		
B-2385	79.0%@10.0uM	19.0%@10.0uM		
B-2386	38.0%@10.0uM	19.0%@10.0uM		
B-2387	50.0%@100.0uM	>10.0uM		
B-2388	42.0%@10.0uM	24.0%@10.0uM		
B-2389	39.0%@10.0uM	29.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2390	34.0%@10.0uM	27.0%@1.0uM		
B-2391	40.0%@10.0uM	59.0%@10.0uM		
B-2392	63.0%@10.0uM	46.0%@10.0uM		
B-2393	43.0%@10.0uM	>10.0uM		
B-2394	37.0%@10.0uM	22.0%@10.0uM		
B-2395	32.0%@10.0uM	28.0%@10.0uM		
B-2396	75.0%@10.0uM	>10.0uM		
B-2397	83.0%@10.0uM	22.0%@10.0uM		
B-2398	55%@100.0uM	10.0%@10.0uM		
B-2399	69.0%@10.0uM	18.0%@10.0uM		
B-2400	60.0%@10.0uM	40.0%@10.0uM		
B-2401	78.0%@10.0uM	44.0%@10.0uM		
B-2402	43.0%@10.0uM	52.0%@10.0uM		
B-2403	72%@100.0uM	52.0%@10.0uM		
B-2404	58%@100.0uM	52.0%@10.0uM		
B-2405	47%@100.0uM	>10.0uM		
B-2406	45.0%@10.0uM	24.0%@10.0uM		
B-2407	47%@100.0uM	27.0%@10.0uM		
B-2408	39.0%@10.0uM	10.0%@10.0uM		
B-2409	78.0%@10.0uM	26.0%@10.0uM		
B-2410	33.0%@10.0uM	32.0%@10.0uM		
B-2411	26%@100.0uM	13.0%@10.0uM		
B-2412	40.0%@10.0uM	31.0%@10.0uM		
B-2413	75.0%@10.0uM	37.0%@10.0uM		
B-2414	86.0%@10.0uM	38.0%@10.0uM		
B-2415	94.0%@10.0uM	50.0%@10.0uM		
B-2416	85.0%@10.0uM	43.0%@1.0uM		
B-2417	83.0%@10.0uM	18.0%@10.0uM		
B-2418	88.0%@10.0uM	34.0%@10.0uM		
B-2419	86.0%@10.0uM	66.0%@10.0uM		
B-2420	70.0%@10.0uM	34.0%@10.0uM		
B-2421	89.0%210.0uM	38.0%@10.0uM		
B-2422	90.0%@10.0uM	17.0%@10.0uM		
B-2423	85.0%@10.0uM	>10.0uM		
B-2424	86.0%@10.0uM	43.0%@10.0uM		
B-2425	79.0%@10.0uM	42.0%@10.0uM		
B-2426	88.0%@10.0uM	53.0%@10.0uM		
B-2427	87.0%@10.0uM	59.0%@10.0uM		
B-2428	82.0%@10.0uM	50.0%@10.0uM		
B-2429	92.0%@10.0uM	32.0%@10.0uM		

Example#	P38 alpha kinase IC50,uM or % inhib@conc. (uM)	U937 Cell IC50,uM or % inhib@conc. (uM)	Mouse LPS Model % TNF inhib @ dose @predose time	Rat LPS Model % inhib @dose @predose time
B-2430	90.0%@10.0uM	61.0%@10.0uM		
B-2431	85.0%210.0uM	68.0%@10.0uM		
B-2432	86.0%210.0uM	40.0%@10.0uM		
B-2433	94.0%@10.0uM	84.0%@10.0uM		
B-2434	92.0%@10.0uM	63.0%@10.0uM		
B-2435	84.0%@10.0uM	4.0%@10.0uM		
B-2436	80.0%@10.0uM	54.0%@10.0uM		
B-2437	82.0%@10.0uM	41.0%@10.0uM		
B-2438	75.0%@10.0uM	40.0%@10.0uM		
B-2439	81.0%@10.0uM	44.0%@10.0uM		
B-2440	77.0%@10.0uM	78.0%@10.0uM		
B-2441	86.0%@10.0uM	46.0%@10.0uM		
B-2442	86.0%@10.0uM	>10.0uM		
B-2443	84.0%@10.0uM	44.0%@10.0uM		
B-2444	89.0%@10.0uM	7.0%@10.0uM		
B-2445	94.0%@10.0uM	15.0%@10.0uM		
B-2446	90.0%@10.0uM	28.0%@10.0uM		
B-2447	94.0%@10.0uM	>10.0uM		
B-2448	75.0%@10.0uM	30.0%@10.0uM		
B-2449	86.0%@10.0uM	42.0%@10.0uM		
B-2450	87.0%@10.0uM	46.0%@1.0uM		
B-2451	87.0%@10.0uM	45.0%@10.0uM		
B-2452	89.0%@10.0uM	33.0%@10.0uM		
B-2453	91.0%@10.0uM	>10.0uM		
B-2454	88.0%@10.0uM	40.0%@10.0uM		
B-2455	87.0%@10.0uM	54.0%@10.0uM		
B-2456	86.0%@10.0uM	53.0%@10.0uM		
B-2457	90.0%@10.0uM	18.0%@10.0uM		
B-2458	83.0%@10.0uM	36.0%@10.0uM		
B-2459	82.0%@10.0uM	81.0%@10.0uM		
B-2460	80.0%@10.0uM	79.0%@10.0uM		
B-2461	67.0%@10.0uM	59.0%@10.0uM		

Biological data from a number of compounds of Examples C-74 through C-139 are shown in the following tables.

In vitro P38-alpha kinase inhibitory data are shown in the column identified as:

"P38 alpha kinase IC50, μM"

In vitro human whole blood assay data for measuring the ability of the compounds to inhibit TNF production in human whole blood stimulated with LPS are shown in the column identified as:

"Human Whole Blood IC50, μM or %Inhib@conc. (μM)"

In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF release in the rat is shown in the column identified as:

"Rat LPS Model % Inhibition@dose@predose time"

wherin the dose is milligram per kilogram (mpk) administered by oral gavage and the predose time indicates the number of hours before LPS challenge when the compound is administered.

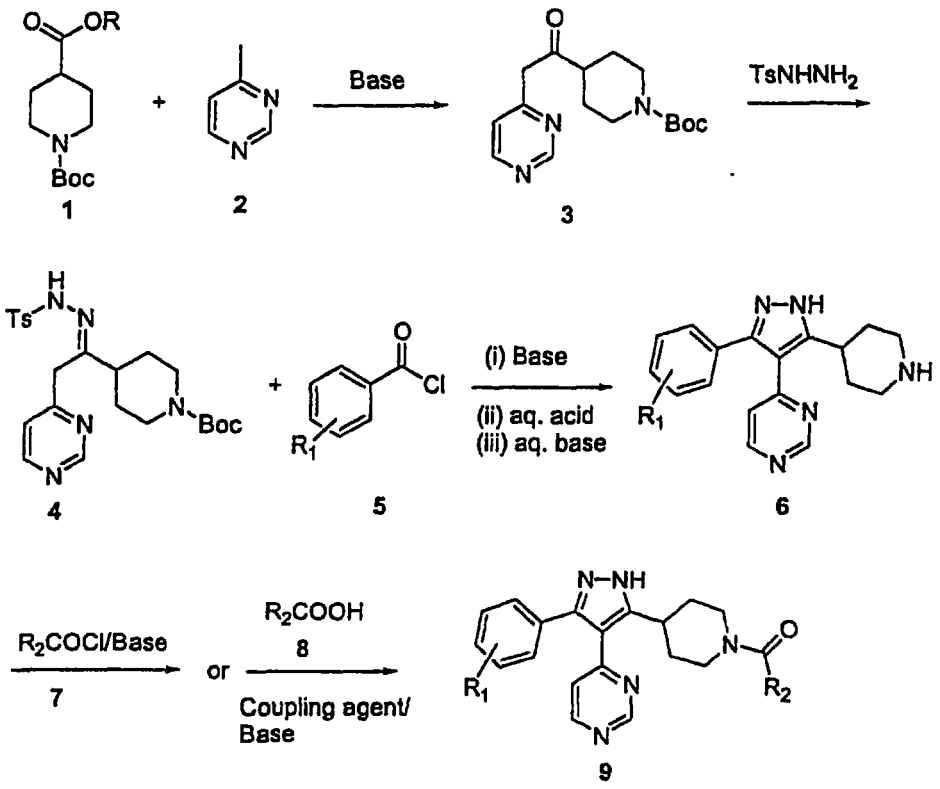
Example#	P38 alpha kinase IC50, μM	Human Whole Blood IC50, μM or %Inhib@conc. (μM)	Rat LPS Model % Inhibition@ dose@predose time
C-74	0.037	0.56	54%@5mpk@-4h
C-75	0.045	0.4	71%@5mpk@-4h
C-76	0.07	3.24	66%@5mpk@-4h
C-77	0.071	8.2	92%@5mpk@-4h
C-78	0.068	10.5	87%@5mpk@-4h
C-79	0.045	0.52	83%@5mpk@-4h

Example#	P38 alpha kinase IC50, μM	Human Whole Blood IC50, μM or %Inhib@conc. (μM)	Rat LPS Model % Inhibition@ dose@predose time
C-80	0.008	51%@ 5 μM	
C-81	0.037	40%@ 5 μM	
C-82	0.15	7.31	
C-83	0.24	1.23	25%@5mpk@-4h
C-84	0.048	0.88	22%@5mpk@-4h
C-85	0.57	>25	
C-86	0.007	0.19	66%@5mpk@-4h
C-87	0.027	0.34	
C-88	0.012	0.3	59%@5mpk@-4h
C-89	0.039	0.12	27%@5mpk@-4h
C-90	0.037	0.48	
C-91	0.054	2.31	63%@5mpk@-4h
C-92	0.024	0.28	66%@5mpk@-4h
C-93	0.009	0.38	50%@5mpk@-4h
C-94	0.02	0.27	73%@5mpk@-4h
C-95	0.13	3.91	32%@5mpk@-4h
C-96	0.077	2.1	38%@5mpk@-4h
C-97	0.025	3.83	21%@5mpk@-4h
C-98	0.016	0.64	78%@5mpk@-4h
C-99	0.062	0.38	36%@5mpk@-4h
C-100	0.027	0.27	44%@5mpk@-4h
C-101	0.083	3.71	52%@5mpk@-4h
C-102	0.29	7.56	72%@5mpk@-4h
C-105	0.033	0.13	46%@5mpk@-4h
C-106	0.026	0.44	23%@5mpk@-4h
C-107	0.014	0.38	11%@5mpk@-4h
C-108	0.02	0.73	0%@5mpk@-4h
C-111	0.21	6.05	39%@5mpk@-4h
C-112	0.54	6.36	89%@5mpk@-4h
C-113	0.082	2.72	77%@5mpk@-4h
C-114	0.11	1.73	39%@5mpk@-4h
C-115	0.042	10.2	39%@5mpk@-4h
C-116	0.429	0.50	53%@5mpk@-4h
C-117	3.42	7.26	71%@5mpk@-4h
C-118	0.298	>25	39%@5mpk@-4h
C-120	0.7	18.6	26%@5mpk@-4h
C-121	0.11	15.3	39%@5mpk@-4h
C-122	0.025		55%@5mpk@-4h
C-123	0.67	>25.0	

Example#	P38 alpha kinase IC50, μM	Human Whole Blood IC50, μM or %Inhib@conc. (μM)	Rat LPS Model % Inhibition@ dose@predose time
C-124	0.17	4.56	51%@20mpk@-4h
C-125	7.22	>25.0	
C-126	0.71	>25.0	6%@20mpk@-4h
C-127	0.038	0.27	53%@5mpk@-4h
C-128	0.09	2.22	63%@5mpk@-4h
C-132	0.086	44%@ 5 μM	
C-133	0.16	4.54	55%@5mpk@-4h
C-135	6.0		
C-136	0.032		
C-137	0.051		58%@5mpk@-4h
C-138	0.28	0.68	26%@5mpk@-4h
C-139	0.2	3.66	46%@5mpk@-4h

Additional compounds of interest can be prepared as set forth above and as described below in Scheme D-1, wherein the R_1 and R_2 substituents are as defined previously.

Scheme D-1



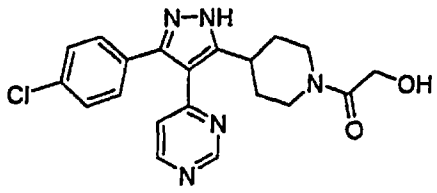
The synthesis begins with the treatment of 4-methylpyrimidine 2 with a base such as LiHMDS, LDA or tBuOK in an organic solvent such as THF or ether which is cooled in an ice bath (0-10 °C). To the resulting 4-methylanion is added a solution of a suitably protected (Boc is shown) ethyl ester of isonipecotic acid 1 in THF or ether. The reaction is allowed to warm to room

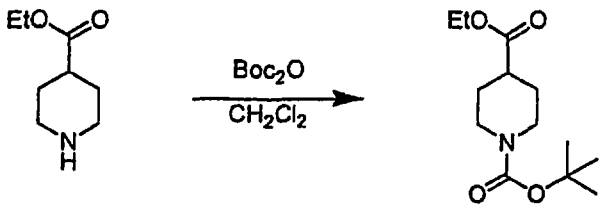
temperature and stirred for a period of 4 hours to 20 hours at which time the desired ketone 3 is isolated after aqueous work up. Condensation of the ketone 3 with tosylhydrazide in toluene or benzene as a solvent at refluxing temperatures for a period of 1 hour to 5 hours affords the hydrazone 4. The hydrazone 4 is reacted with a suitably substituted benzoyl chloride 5, in the presence of a base such as LiHMDS or LDA or tBuOK or triethylamine at temperatures ranging from 0 °C to 70 °C. The reaction is stirred for a period of 3-6 hours. Acidic hydrolysis of the protecting groups with an aqueous acid such as HCl or H_2SO_4 and subsequent neutralization with an aqueous base such as NaOH or KOH affords the desired pyrazole 6. Treatment of the pyrazole 6 with an acid chloride 7 in the presence of base or with an acid 8 under standard peptide coupling conditions (EDC or DCC or PyBrOP with an additive such as HOBt or HATU and base such as N-methylmorpholine or diisopropylethylamine or triethylamine) affords the desired pyrazole amide 9. In most instance the desired products can be obtained pure by direct trituration with solvents such as methanol, ethyl acetate, acetonitrile or ether and/or recrystallization from suitable solvents.

The following examples contain detailed descriptions of the methods of preparation of these additional compounds that form part of the invention. These detailed descriptions are presented for illustrative purposes only and are not intended as a restriction on the scope of the invention. All compounds showed NMR spectra consistent with their assigned structures.

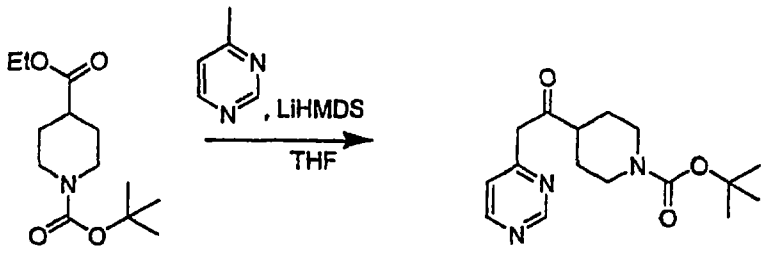
Example D-1

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

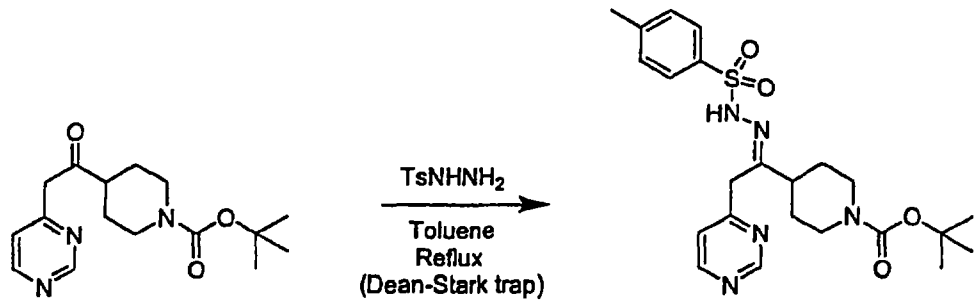




Step 1: A 5 L 4-necked round bottom flask fitted with an overhead mechanical stirrer, N_2 inlet and a thermocouple was charged with 600 g (2.75 mol) of di-*tert*-butyl-dicarbonate and 1.5 L of CH_2Cl_2. The solution was cooled to 0 °C and 428 g (2.73 mol) of ethyl isonipecotate was added dropwise via an addition funnel. The addition took 45 minutes and the temperature rose from 0 °C to 17.4 °C. The reaction mixture was stirred for an additional 2 hours at ambient temperature. The solvent was removed *in vacuo* to afford 725 g of a yellow oil (residual solvent remained).



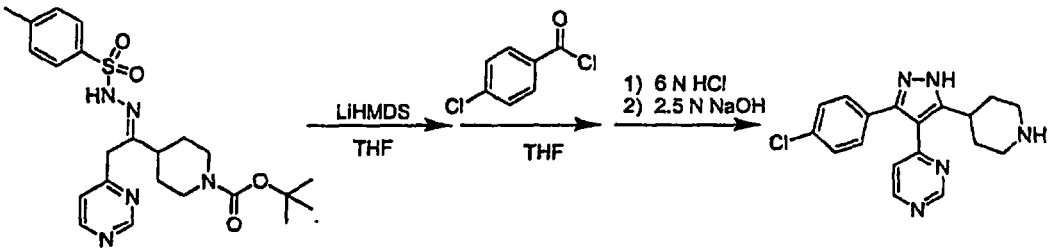
Step 2: A 3 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a N_2 inlet, an addition funnel and a thermocouple was charged with 1850 mL (1.85 mol) of a 1.0 M solution of LiHMDS in THF. The flask was cooled to 5 °C and 68 mL (0.74 mol) of 4-methylpyrimidine was added (neat) to the stirred solution. To this solution was added 198 g (0.77 mol) of Ethyl-N-t-butylcarbonyl isonipecotate dissolved in 160 mL of THF. The ice bath was removed and the reaction was allowed to stir for 18 hours. The reaction was quenched with 500 mL of saturated NH_4Cl and was extracted with 500 mL of ethyl acetate. The organic phase was washed with 500 mL of brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford 235 g of a brown oil.



Step 3: A 2 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a Dean-Stark trap and

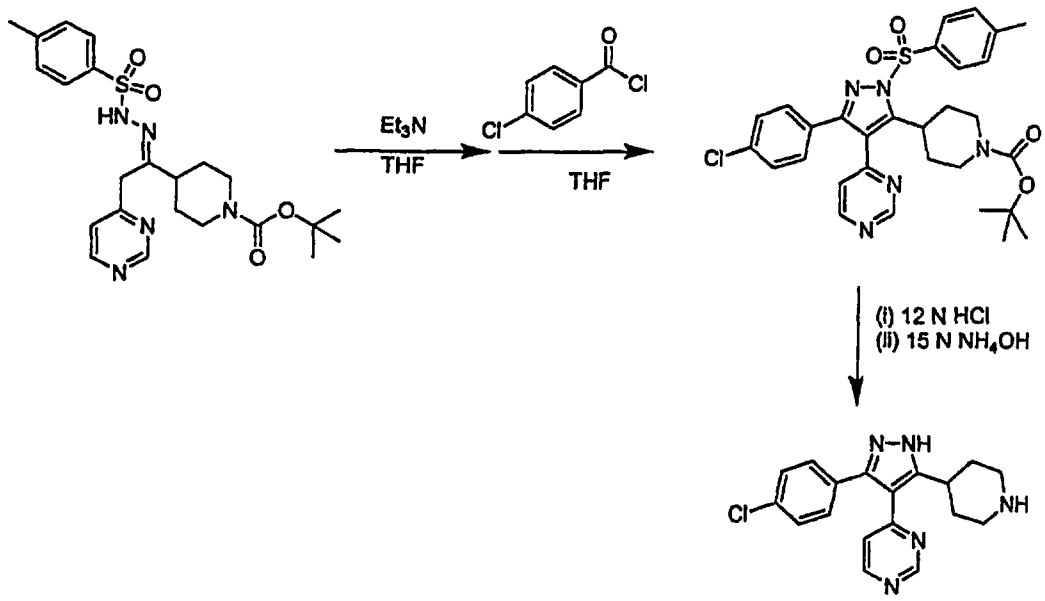
a thermocouple was charged with 1.5 L of toluene, 226 g (0.742 mol) of N-t-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone and 138.4 g (0.743 mol) of tosyl hydrazide. The mixture was warmed to reflux. The solution was allowed to reflux for 2 hours and was cooled to ambient temperature. The reaction was allowed to stand overnight. A fine precipitate formed and was removed by filtration. The filtrate was concentrated *in vacuo* to afford a brown solid. The solid was suspended in 500 mL of ethyl acetate and the resulting mixture was placed in a sonication bath for 5 hours. The mixture was cooled in an ice bath and was filtered to afford 310 g of a wet solid. The solid was dried in a vacuum oven (40 °C, 5 mm) overnight to afford 248 g of the desired hydrazone (71%). ^{1}H NMR ($CDCl_3$) δ 9.03 (d, *J* = 1.2 Hz, 1H), 8.72 (d, *J* = 5.2 Hz, 2H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.26 (dd, *J* = 5.2, 1.0 Hz, 1H), 4.03 (d, *J* = 12.1 Hz, 2H), 3.76 (s, 2H), 2.71 (t, *J* = 12.1 Hz, 2H), 2.43 (s, 3H), 2.34 (m, 1H), 1.66 (d, *J* = 13.5 Hz, 2H), 1.47 (s, 9H), 1.38 (m, 2H); MS (M + H): 474 (base peak).

Step 4:



Method A. A 2 L 3-necked round bottom flask fitted with an overhead mechanical stirrer, a N_2 inlet, an addition funnel and a thermocouple was charged with 400 mL (400 mmol) of a 1.0 M solution of LiHMDS in THF. The solution was cooled to -21.9 °C and a solution of 62 g (131 mmol) of N-*t*-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone p-toluenesulfonyl hydrazone in 400 mL of THF was added slowly. The temperature never exceeded -11 °C throughout the addition. The solution was re-cooled to -19.6 °C and 23.0 g (131 mmol in 250 mL of THF) of p-chlorobenzoylchloride was added slowly. The temperature never exceeded -13 °C throughout the addition. The cooling bath was removed and the reaction was allowed to warm to ambient temperature. After 3 hours the reaction was quenched with 600 mL of 3 N HCl. The reaction was warmed to reflux and was held at reflux for 2 hours. The reaction was allowed to cool to ambient temperature overnight. The reaction mixture was washed with 1.4 L of Et_2O and the aqueous phase was neutralized with 1 L of 2.5 N NaOH. The aqueous phase was extracted with ethyl acetate (2 x 1000 mL). The combined organic phases were washed with brine (1 x 500 mL), dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to afford 21 g of a yellow solid. The solid was suspended in 500 mL of 2:1 Et_2O/hexane. After sonication the solid was isolated by filtration to leave a wet solid. The solid was dried in a vacuum oven to afford 13.8 g of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole. ^1H NMR (DMSO-d_6) 9.18 (s, 1H), 8.65 (d, J = 5.2, 1H), 7.44 (d, J = 8.5, 2H), 7.37 (d, J = 7.7 Hz, 2H), 7.15 (d,

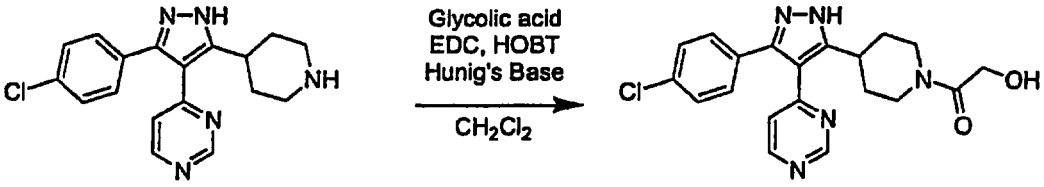
J = 5.2 Hz, 1H), 3.16 (m, 1H), 3.00 (d, J = 11.9 Hz, 2H), 2.52 (m, 2H), 1.69 (m, 4H); MS (M + H): 340 (base peak).



Method B: To a solution of 200 g (423 mmol) of N-t-butylcarbonyl-1-(4-piperidyl)-2-(4-pyrimidyl)-1-ethanone p-toluenesulfonyl hydrazone in 800 mL THF was added 70 mL (500 mmol) of triethylamine in a 3 L three necked flask. The solution was cooled in an ice/salt/water bath to 0-5 °C. To this cold solution was added a solution of 4-chlorobenzoyl chloride (74 g, 423 mmol) in 100 mL THF dropwise, maintaining the temperature below 10 °C. After the addition was complete the ice-bath was removed and replaced with a heating mantle. 4-N, N-dimethylaminopyridine (5 g, 40 mmol) was added and the reaction mixture was heated to 50 °C for 15-30 minutes. The reaction mixture was filtered and the residue washed

with THF (100 mL). The combined filtrates were evaporated under reduced pressure to a semisolid.

The semisolid residue was dissolved in 450 mL THF and 180 mL of 12 N HCl was added to this solution rapidly. The reaction mixture was heated to 65 °C for 1.5-2 hours and transferred to a separatory funnel. The organic layer was discarded and the aqueous phase was washed twice with 200 mL of THF. The aqueous phase was transferred back to a 2 L flask and cooled to 0-10 °C in an ice bath. The pH of the solution was adjusted to between ~ 9-10 by dropwise addition of 15 N ammonium hydroxide (~ 180 mL). This mixture was transferred back to a separatory funnel and extracted with warm n-butanol (3 X 150 mL). The combined n-butanol phases were evaporated under reduced pressure to dryness. The residue was then stirred with methanol (200 mL), filtered and dried to obtain 129 g (90%) of the desired 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole as a off-white solid. This material was identical in all respects to the material prepared by Method A.

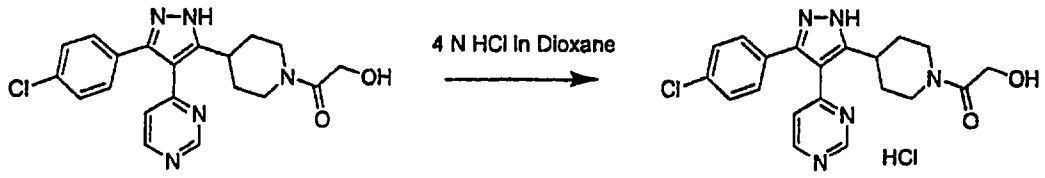


Step 5: A 1 L round bottom flask was charged with 34.2 g (102 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole, 500 mL of CH_2Cl_2 and 26.6 mL (153 mmol) of Hunig's base. To this suspension was added 16.5

g (122 mmol) of 1-hydroxybenzotriazole and 8.1 g (106 mmol) of glycolic acid. The addition of glycolic acid was followed by the addition of 23.7 g (122 mmol) of 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride. The reaction was allowed to stir at ambient temperature overnight. The reaction was concentrated *in vacuo* to leave an oily residue. The residue was dissolved in 400 mL of methanol and 50 mL of 2.5 N NaOH. The reaction mixture was stirred at ambient temperature for 1 hour. The mixture was acidified to pH 5 with 2 N HCl and was extracted with CH_2Cl_2 (6 x 200 mL). The combined organic phases were filtered through phase paper and the filtrate was concentrated *in vacuo* to leave a yellow residue. The residue was treated with 75 mL of acetonitrile. A precipitate formed. The solid was filtered and washed with additional acetonitrile and Et_2O to afford 31.4 g of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole. ^1H NMR (DMSO-d_6) 9.20 (s, 1H), 8.67 (d, J = 4.8, 1H), 7.40 (m, 4H), 7.17 (d, J = 4.0, 1H), 4.53 (m, 2H), 4.13 (s, 2H), 3.77 (m, 1H), 3.05 (t, J = 12.7 Hz, 1H), 2.69 (m, 1H), 1.90 (m, 2H), 1.73 (m, 2H); MS (M +H): 398 (base peak).

Example D-2

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride

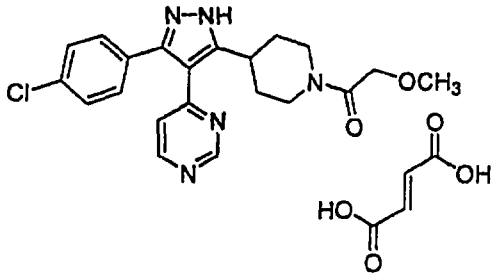


A 25 mL round bottom flask was charged with 65 mg (0.164 mmol) of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole and 2.5 mL of dioxane. To this suspension was added 0.082 mL of 4 N HCl in dioxane. The mixture was stirred for 2 hours. The mixture was diluted with 5 mL of Et_2O and filtered. The solid was dried over solid $CaSO_4$ under vacuum for 12 h to afford 68 mg of N-(2-hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole hydrochloride. ^1H NMR (DMSO-d_6) 9.18(s, 1H), 8.63(d, J=5.37 Hz, 1H), 7.40(d, J=8.59 Hz, 2H), 7.33(d, J=8.59 Hz, 2H), 7.15(m, 1H), 4.40(m, 1H), 4.06(m, 2H), 3.72(m, 1H), 3.33(m, 1H), 2.97(m, 1H), 2.62(m, 1H), 1.83(m, 2H), 1.64(m, 2H); MS (M+H): 398

Example D-3

N-(2-Methoxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole (fumarate salt)

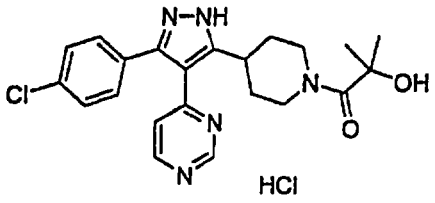
1064



To a suspension of 250 mg (0.74 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-1, Step 3) and 180 mg (1.48 mmol) of N,N-dimethylamino pyridine in 20 mL of CH_2Cl_2 was added 88 mg (0.81 mmol) of 2-methoxyacetyl chloride. The reaction was stirred for 5 hours. The reaction was quenched with 20 mL of saturated NH_4Cl. The mixture was extracted with n-butyl alcohol and the organic layer was washed with brine. The solvent was removed to afford 72 mg of an oil. This oil was dissolved in 1 mL of warm MeOH. This solution was combined with a warm solution of 1 equivalent of fumaric acid in warm MeOH. The solution was cooled to ambient temperature and the reaction was allowed to stir for 1 hour. The solvent was removed *in vacuo* and the residue was triturated with Et_2O. The resulting solid was isolated by filtration to yield 56 mg of an off-white powder. ^1H NMR (DMSO-d_6) 13.23 (bs, 1H), 9.19 (d, J = 1.2 Hz, 1H), 8.65 (d, J = 5.1 Hz, 1H), 7.41 (m, 4H), 7.16 (dd, J = 5.4, 1.2 Hz, 1H), 4.45 (bd, J = 11.1 Hz, 1H), 4.11 (q_{AB}, J = 39.0, 13.8 Hz, 2H), 3.86 (bd, J = 12.9 Hz, 1H), 3.32 (m, 4H), 3.04 (bt, J = 12.3 Hz, 1H), 2.63 (bt, J = 12.0 Hz, 1H), 1.77 (m, 4H); MS (M + H): 411 (base peak).

Example D-4

N-(2-Hydroxy-2-methylpropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride



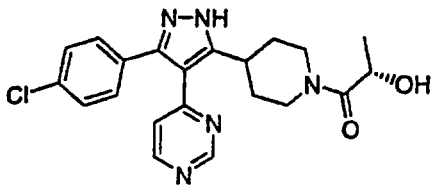
Step 1: To a suspension of 2.05 g (6.1 mmol) of 5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl) pyrazole (Example C-1, Step 3) and 3.7 g (30.5 mmol) of N,N-dimethylamino pyridine in 30 mL of CH_2Cl_2 was added 1.06 mL (7.3 mmol) of 2-acetoxy-2-methylpropionyl chloride. The reaction was allowed to stir overnight at ambient temperature. The reaction was quenched with saturated NH4Cl and water. The resulting aqueous phase was extracted with CH_2Cl_2. The combined organic layers were concentrated *in vacuo* to leave an oily solid. The residue was treated with CH_3CN and allowed to stand for 15 minutes. The resulting suspension was diluted with Et20 and was filtered to afford 2.2 g of a solid. Analysis by LC/MS indicated that the solid was a mixture of the hydroxy derivative and the acetoxy derivative. This solid was carried on to the next step without further purification.

Step 2: A solution of 1 g of the solid from step 1 in 10 mL of MeOH was treated with 500 mg of solid K_2CO_3. The mixture was allowed to stir overnight at ambient

temperature. The suspension was treated with water and the resulting solution was extracted with ethyl acetate. The organic phase was filtered through phase separation paper (to remove the residual water) and was concentrated *in vacuo* to leave an oily solid. The solid was dried under vacuum and was treated with CH_3CN. The suspension was filtered to afford 825 mg of an off-white solid. This solid was suspended in 5 mL of dioxane and 0.5 mL of 4 N HCl in dioxane was added. The suspension was stirred for 1 hour and the suspension was filtered to leave a solid. The solid was washed with Et_2O and the resulting suspension was filtered to give 900 mg of the title compound. ^1H NMR (DMSO-d_6) 9.23 (s, 1H), 8.69 (s, 1H), 7.45 (m, 4H), 7.19 (s, 1H), 4.8 (br m, 4H), 3.85 (m, 2H), 3.38 (m, 1H), 1.89 (m, 2H), 1.72 (m, 2H), 1.37 (s, 6H); MS (M + H): 426 (base peak).

Example D-5

(*S*)-N-(2-Hydroxypropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride

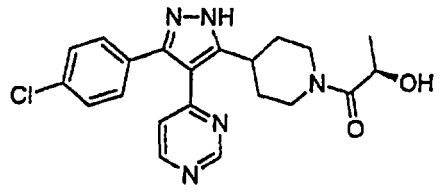


By following the method of Example C-1 and substituting (*S*)-lactic acid for glycolic acid the title compound was prepared. ^1H NMR (DMSO-d_6) 13.15(s, br, 1H), 9.12(d, *J*=1.07 Hz, 1H), 8.59(d, *J*=5.37Hz, 1H),

7.39(d, J=7.79Hz, 2H), 7.31(d, J=8.33, 2H), 7.10(dd, J=1.34, 5.1Hz, 1H), 4.76(m, 1H), 4.41(m, 2H), 3.99(m, 1H), 2.97(m, 1H), 2.45(m, 1H), 1.83(m, 2H), 1.64(m, 2H), 1.15(m, 3H); MS (M+H): 412 (base peak).

Example D-6

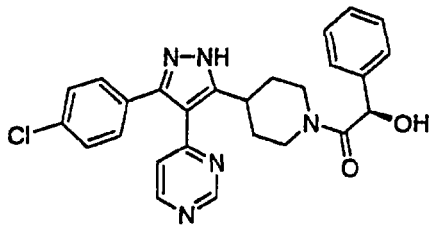
(*R*)-N-(2-Hydroxypropionyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole hydrochloride



By following the method of Example C-1 and substituting (*R*)-lactic acid for glycolic acid the title compound was prepared. ^{1}H NMR ($CDCl_3$) 9.24(s, 1H), 8.52(d, J = 5.0 Hz, 1H), 7.32-7.36(m, 4H), 6.98(d, J = 5.3 Hz, 1H), 4.72(d, J = 10.5 Hz, 1H), 4.55(br, 1H), 3.88(d, J = 13.1 Hz, 1H), 3.66(br, 1H), 3.19(br, 1H), 2.82(t, J = 12.4 Hz, 1H), 2.10(br, 2H), 1.37(d, J = 6.2 Hz, 3H), 1.81-1.90(m, 2H); MS (M + H): 412 (base peak).

Example D-7

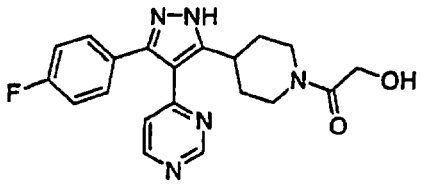
(*R*)-N-(2-Hydroxy-2-phenylacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



By following the method of Example C-1 and substituting (*R*)-phenylacetic acid for glycolic acid the title compound was prepared. ^{1}H NMR (DMSO-d_6) 9.15 (d, J = 0.9 Hz, 1H), 8.63 (d, J = 5.4 Hz, 1H), 7.40 (m, 9H), 7.13 (t, J = 6.6 Hz, 1H), 5.43 (d, J = 19.5 Hz, 1H), 4.51 (s, 1H), 4.04 (m, 1H), 3.33 (m, 4H), 2.8 (m, 2H), 1.68 (m, 3H); MS (M + H): 474 (base peak).

Example D-8

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-fluorophenyl)pyrazole

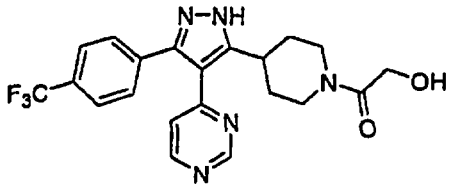


By following the method of Example C-1 and substituting 4-fluorobenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d_7) 13.48(s, 1H), 9.40(s, 1H), 8.86(d, J = 5.1 Hz, 1H), 7.71(br, 2H), 7.42(bd, J = 5.2 Hz, 3H), 4.78(br, 1H), 4.43(s, 2H), 4.04(br, 1H), 3.79(br, 1H), 3.70(s, 1H),

3.34(t, J = 12.2 Hz, 1H), 3.0(br, 1H), 2.21(d, J = 10.9 Hz, 2H), 2.08(br, 1H); MS (M + H): 382 (base peak).

Example D-9

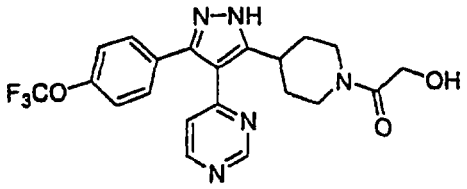
N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-trifluoromethylphenyl)pyrazole



By following the method of Example C-1 and substituting 4-trifluoromethylbenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d$_7$) 13.47(s, 1H), 9.24(s, 1H), 8.73(d, J = 4.0 Hz, 1H), 7.77(bd, J = 13.3 Hz, 4H), 7.34(d, J = 4.3 Hz, 1H), 4.61(br, 1H), 4.26(s, 2H), 3.87(br, 1H), 3.52(s, 2H), 3.17(t, J = 12.0 Hz, 1H), 2.8 (br, 1H), 2.02(br, 2H), 1.91(br, 1H); MS (M + H): 432 (base peak).

Example D-10

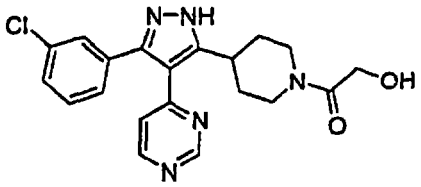
N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(4-trifluoromethoxyphenyl)pyrazole



By following the method of Example C-1 and substituting 4-trifluoromethoxybenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d_7) 13.55(s, 1H), 9.40(s, 1H), 8.88(d, J = 4.6 Hz, 1H), 7.81(d, J = 7.7 Hz, 2H), 7.64(br, 2H), 7.47(d, J = 4.4 Hz, 1H), 4.75(br, 1H), 4.42(s, 2H), 4.04(d, J = 12.5 Hz, 1H), 3.69(br, 2H), 3.34(t, J = 12.0 Hz, 1H), 3.0(br, 1H), 2.20(d, J = 11.7 Hz, 2H), 2.05(br, 1H); MS (M + H): 448 (base peak).

Example D-11

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-chlorophenyl)pyrazole

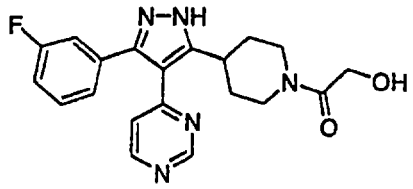


By following the method of Example C-1 and substituting 3-chlorobenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d_7) 13.41(s, 1H), 9.24(s, 1H), 8.73(d, J = 4.9 Hz, 1H), 7.56(s, 1H), 7.49(br, 2H), 7.41(br, 1H), 7.32(d, J = 4.2

Hz, 1H), 4.60(d, J = 11.7 Hz, 1H), 4.25(s, 2H), 3.87(d, J = 12.7 Hz, 1H), 3.52(bs, 2H), 3.17(t, J = 12.1 Hz, 1H), 2.84(d, J = 12.5 Hz, 1H), 2.03(d, J = 11.9 Hz, 2H), 1.87(br, 1H); MS (M + H): 398 (base peak).

Example D-12

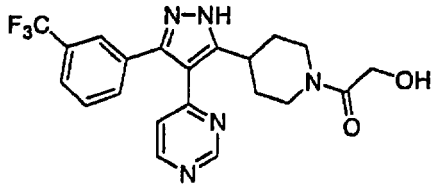
N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-fluorophenyl)pyrazole



By following the method of Example C-1 and substituting 3-fluorobenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d$_7$) 13.38(s, 1H), 9.24(s, 1H), 8.72(d, J = 5.2 Hz, 1H), 7.49(dd, J = 8.0 and 6.2 Hz, 1H), 7.24-7.32(m, 4H), 4.60(d, J = 13.1 Hz, 1H), 4.25(s, 2H), 3.87(d, J = 13.3 Hz, 1H), 3.55-3.60(m, 1H), 3.52(s, 1H), 3.17(t, J = 12.2 Hz, 1H), 2.82(d, J = 12.9 Hz, 1H), 2.03(d, J = 10.9 Hz, 2H), 1.83-1.96(m, 1H); MS (M + H): 382 (base peak).

Example D-13

N-(2-Hydroxyacetyl)-5-(4-piperidyl)-4-(4-pyrimidyl)-3-(3-trifluoromethylphenyl)pyrazole

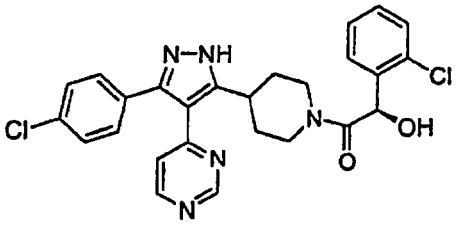


By following the method of Example C-1 and substituting 3-trifluoromethylbenzoyl chloride for 4-chlorobenzoyl chloride the title compound was prepared. ^{1}H NMR (DMF-d_7) 13.76(s, 1H), 9.41(s, 1H), 8.91(d, J = 5.3 Hz, 1H), 8.02(s, 1H), 7.95(t, J = 6.5 Hz, 2H), 7.85(t, J = 7.5 Hz, 1H), 7.53(d, J = 4.6 Hz, 1H), 4.78(d, J = 11.9 Hz, 1H), 4.45(d, J = 16.3 Hz, 2H), 4.06(d, J = 12.5 Hz, 1H), 3.69(bs, 2H), 3.34(t, J = 11.3 Hz, 1H), 3.01(d, J = 13.1 Hz, 1H), 2.20(d, J = 11.1 Hz, 2H), 2.12(br, 1H); MS (M + H): 432 (base peak).

The following examples can be prepared in a manner similar to that described above for the synthesis of Examples C1-C13.

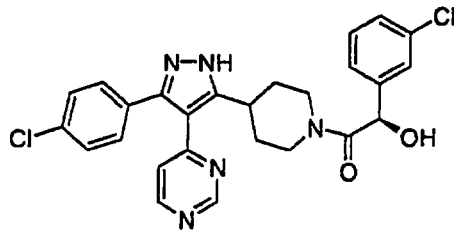
Example D-14

5-[4-*N*-(2-hydroxy-2-(2-chlorophenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



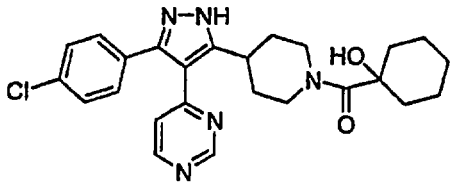
Example D-15

5-[4-*N*-(2-hydroxy-2-(3-chlorophenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



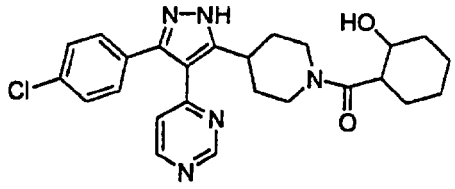
Example D-16

5-[4-*N*-(1-hydroxy-1-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



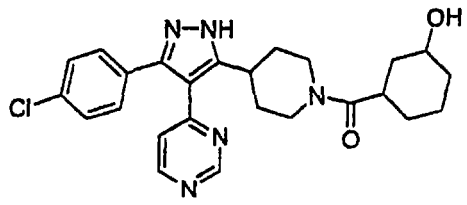
Example D-17

5-[4-*N*-(2-hydroxy-1-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



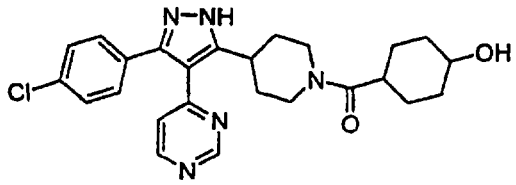
Example D-18

5-[4-*N*-(3-hydroxy-1-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



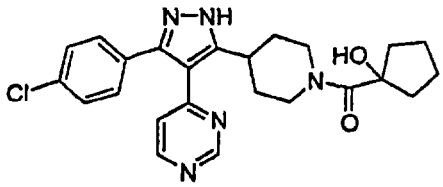
Example D-19

5-[4-*N*-(4-hydroxy-1-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



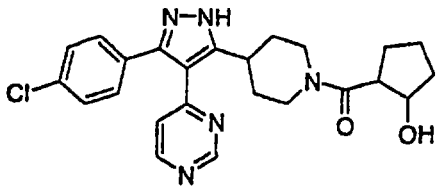
Example D-20

5-[4-*N*-(1-hydroxy-1-cyclopentylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



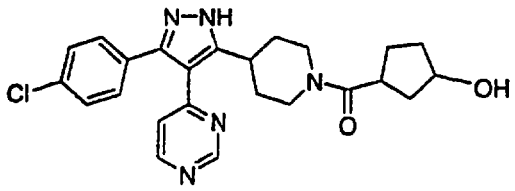
Example D-21

5-[4-*N*-(2-hydroxy-1-cyclopentylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



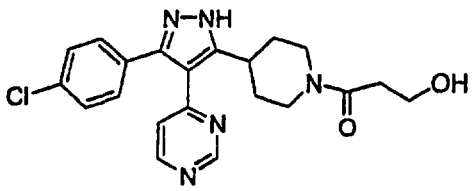
Example D-22

5-[4-*N*-(3-hydroxy-1-cyclopentylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



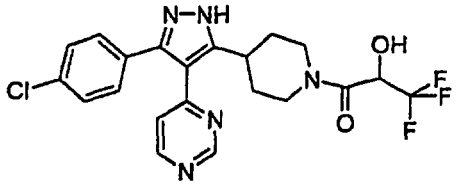
Example D-23

5-[4-*N*-(3-hydroxypropionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



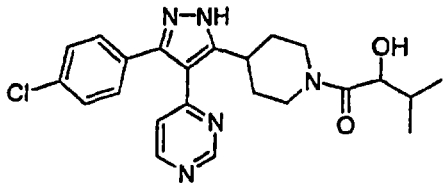
Example D-24

5-[4-*N*-(2-hydroxy-3,3,3-trifluoropropionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



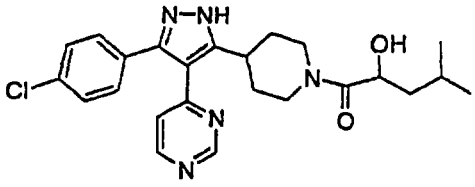
Example D-25

5-[4-*N*-(2-hydroxy-3-methylbutyryl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



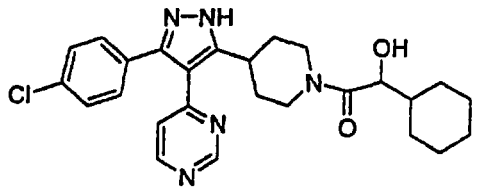
Example D-26

5-[4-*N*-(2-hydroxyisocaproyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



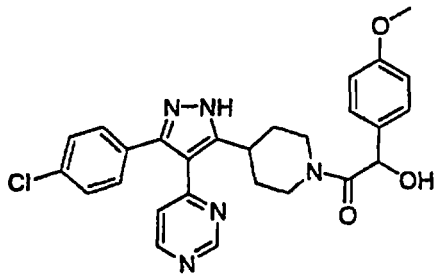
Example D-27

5-[4-*N*-(2-hydroxy-2-cyclohexylacetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



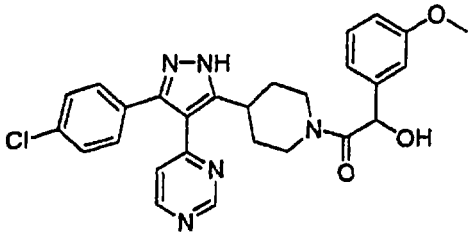
Example D-28

5-[4-*N*-(2-hydroxy-2-(4-methoxyphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



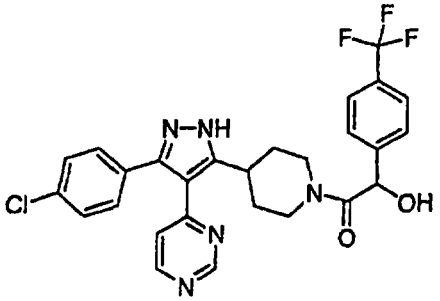
Example D-29

5-[4-*N*-(2-hydroxy-2-(3-methoxyphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



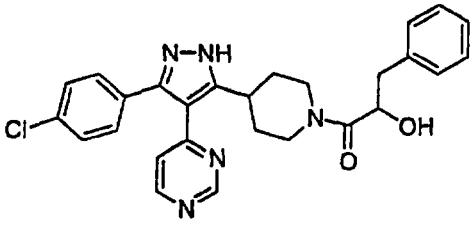
Example D-30

5-[4-*N*-(2-hydroxy-2-(4-trifluoromethylphenyl)acetyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



Example D-31

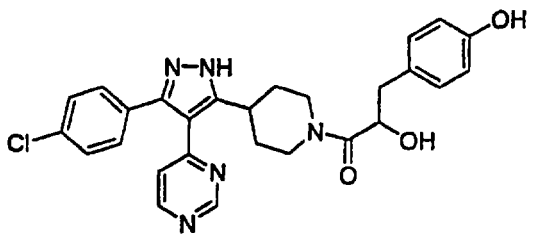
5-[4-*N*-(2-hydroxy-3-phenylpropionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



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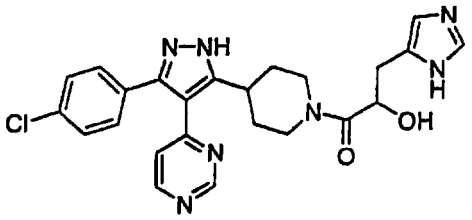
Example D-32

5-[4-*N*-(2-hydroxy-3-(4-hydroxyphenyl)propionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole



Example D-33

5-[4-*N*-(2-hydroxy-3-imidazolpropionyl)piperidyl]-4-(4-pyrimidyl)-3-(4-chlorophenyl)pyrazole

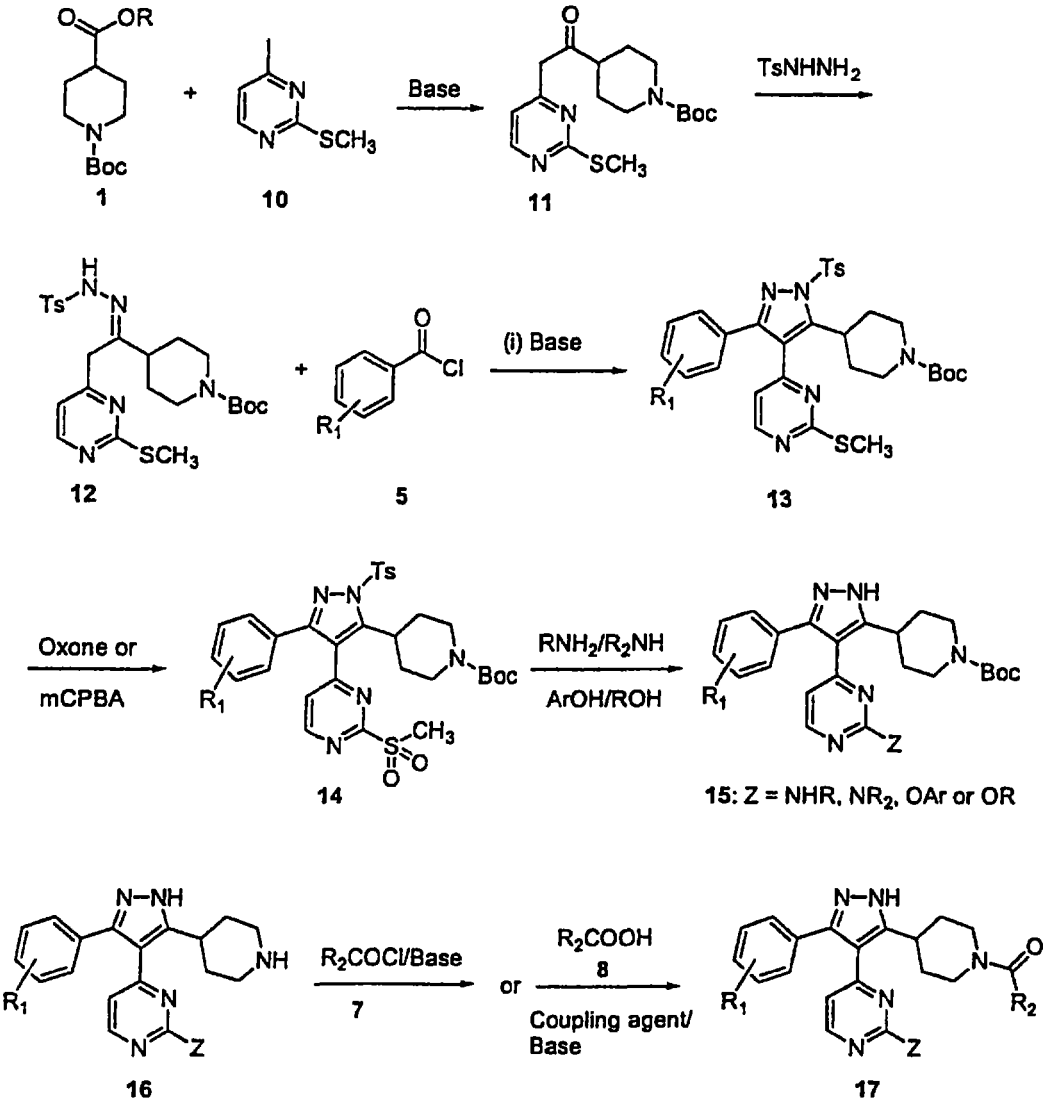


The synthesis of 2-substituted pyrimidinyl pyrazoles is shown in Scheme 2. Reaction of 2-methylmercapto-4-methyl pyrimidine 10 with N-Boc methyl ester of isonipecotic acid (1) under basic (base selected from LiHMDS or LDA or tBuOK) conditions in an anhydrous solvent such as tetrahydrofuran or ether affords the desired ketone 11. Condensation of the ketone 11 with tosyl hydrazine under refluxing conditions in either toluene or

benzene affords the hydrazone 12. The hydrazone 12 is deprotonated under basic (base selected from LiHMDS or LDA or tBuOK) conditions in an anhydrous solvent such as tetrahydrofuran or ether and the anion is reacted in situ with a suitably substituted benzoyl chloride 5 to afford, after mild aqueous work up, the desired and fully protected pyrazole 13. Oxidation of the 2-mercaptomethyl group present in 13 with oxidants selected from but not limited to Oxone®, H_2O_2 or mCPBA in solvents such as dichloromethane, acetonitrile or tetrahyrofuran affords the 2-methane sulfonyl pyrazole 14. The 2-methanesulfone group in 14 is conveniently displaced with various amines, aryloxides or alkoxides in solvents such as tetrahydrofuran, dioxane, dimethylformamide or acetonitrile at temperatures ranging from 20 °C to 200 °C. Under these reaction conditions the tosyl protecting group on the pyrazole is also simultaneously deprotected. Aqueous workup affords the desired tosyl deprotected, 2-alkoxy, or 2-aryloxy or 2-amino substituted pyrazoles 15. The alkoxides or aryloxides are generated from their respective alcohols or phenols with suitable bases such as LiHMDS, NaH, LDA or tBuOK in solvents such as tetrahydrofuran, dioxane or dimethylformamide. Deprotection of the remaining N-Boc group in 15 is accomplished with trifluoroacetic acid or hydrochloric acid in solvents such as dichloromethane or dioxane to afford the pyrazole 16. Treatment of the pyrazole 16 with an acid chloride 7 in the presence of base or with an acid 8 under standard peptide coupling conditions (EDC or DCC or PyBrOP with an additive such as HOBt or HATU and base

such as N-methylmorpholine or diisopropyl ethylamine) affords the desired final products 17.

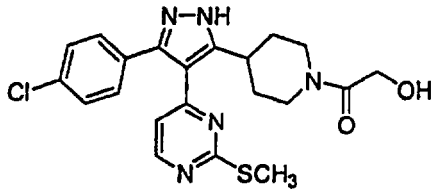
Scheme D-2



The following 2-substituted pyrimidine compounds can be prepared as set forth above, particularly in a manner similar to that outlined above in Scheme D-2.

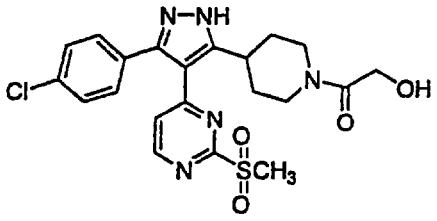
Example D-34

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-thiomethyl)pyrimidyl]-3-(4-chlorophenyl)pyrazole



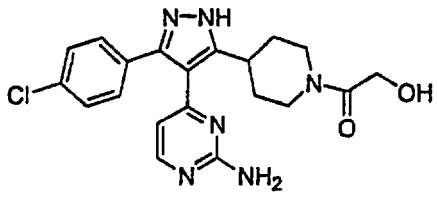
Example D-35

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methanesulfonyl)pyrimidyl]-3-(4-chlorophenyl)pyrazole



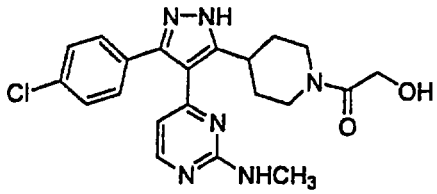
Example D-36

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-amino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



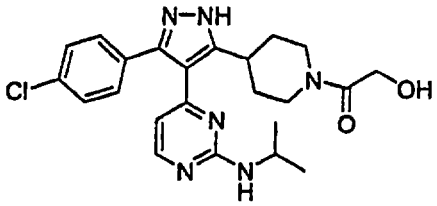
Example D-37

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



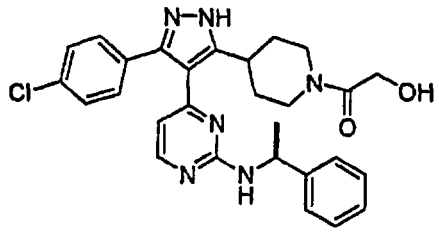
Example D-38

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-isopropylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



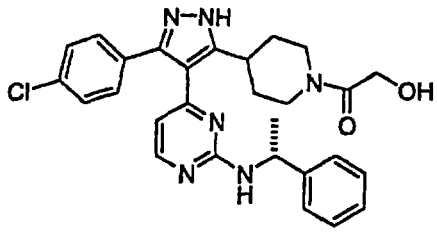
Example D-39

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-*S*-methylbenzylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



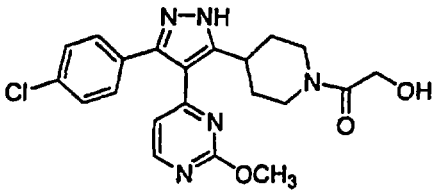
Example D-40

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-*R*-methylbenzylamino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



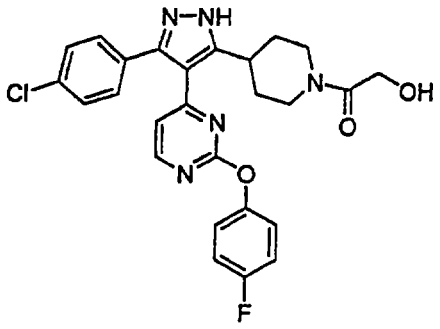
Example D-41

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(2-methoxy)pyrimidyl]-3-(4-chlorophenyl)pyrazole



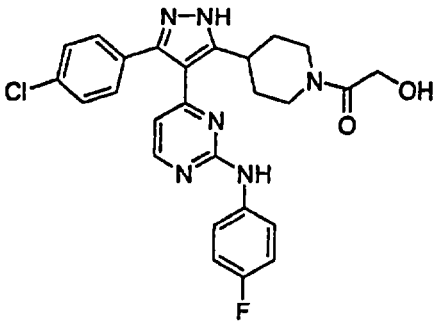
Example D-42

5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(p-fluorophenoxy)pyrimidyl]-3-(4-chlorophenyl)pyrazole



Example D-43

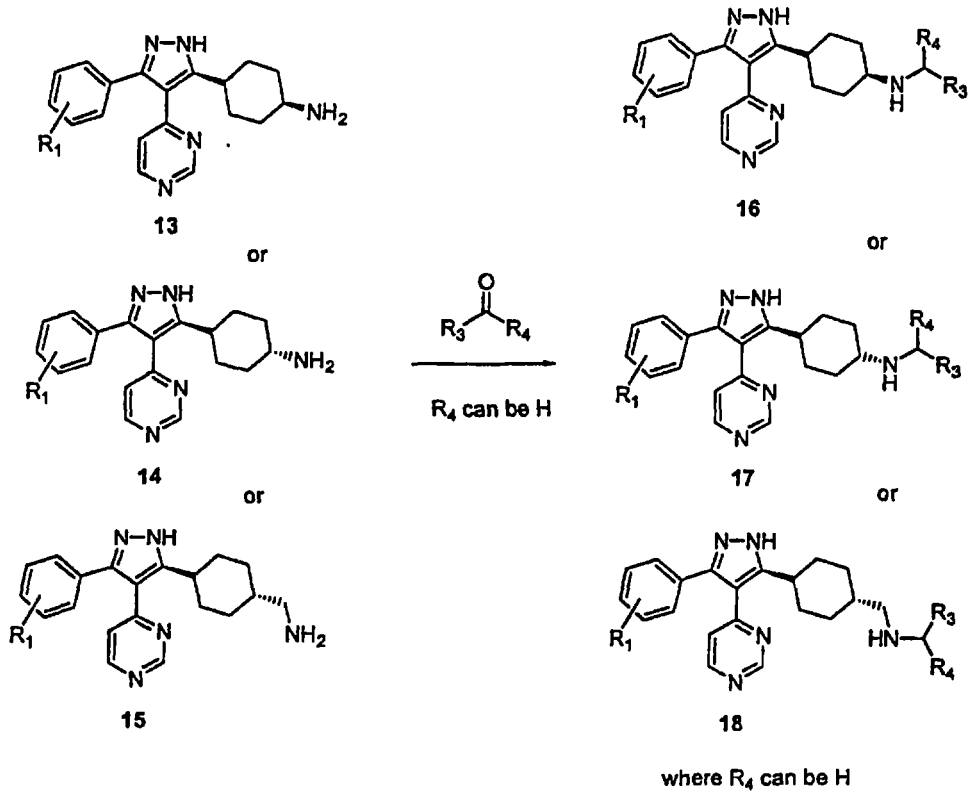
5-[4-*N*-(2-hydroxyacetyl)piperidyl]-4-[4-(p-fluoroanilino)pyrimidyl]-3-(4-chlorophenyl)pyrazole



In a manner similar to that outlined above in Scheme D-1, for the synthesis of the piperidine analogs 6, the aminocyclohexane analogs are prepared by substitution of 1 in Scheme D-1 with a suitably protected (Boc is shown) methyl or ethyl ester of cis-aminocyclohexane carboxylic acid 10 or trans-aminocyclohexane carboxylic acid 11 or trans-aminomethylcyclohexane carboxylic acid 12, which

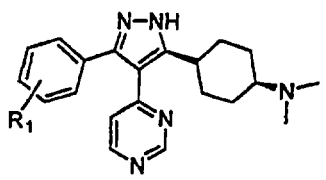
affords the cis-aminocyclohexane 13, or trans-aminocyclohexane 14 or the trans-aminomethylcyclohexane 15 respectively (Scheme 3). Suitable reductive alkylations on 13, 14 or 15 with 1-1.5 equivalents of aldehydes or ketones in the presence of a reducing agent like sodium cyanoborohydride or sodium triacetoxyborohydride in solvents such as methanol, ethanol, acetic acid, tetrahydrofuran or dichloromethane lead to the desired mono-alkylated derivatives 16, 17 or 18 respectively.

Scheme 3

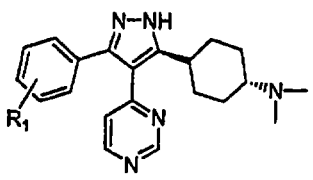


The dimethyl derivatives 19, 20 or 21 can be prepared by heating a solution of the aminocyclohexanes 13, 14 or 15

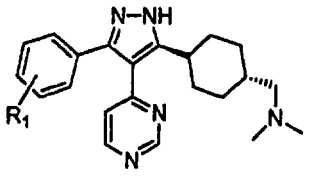
respectively in a mixture of formaldehyde and formic acid at temperatures ranging from 40 °C to 110 °C.



19

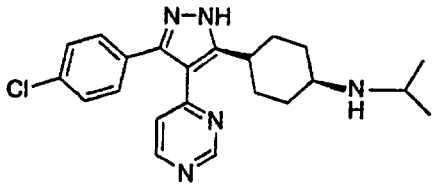


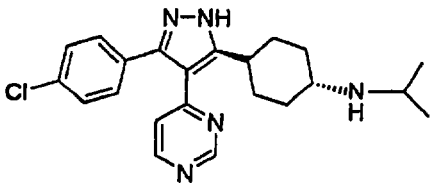
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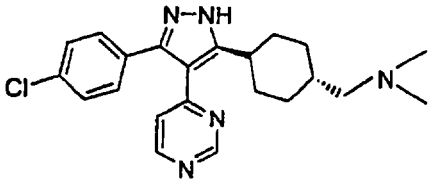


21

An additional group of compounds of interest includes the following:







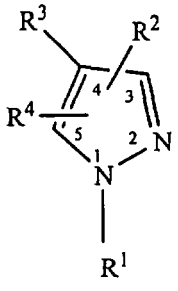
Biological data for a number of compounds are shown in the following table. In vitro p38 alpha kinase inhibitory data are shown in the column identified as *"p38 alpha IC_{50} (μM)"*. In vitro human whole blood assay data for measuring the ability of the compounds to inhibit TNF production in human whole blood stimulated with LPS are shown in the column identified as: *"HWB IC_{50} (μM)"*. In vivo assessment of the ability of the compounds to inhibit LPS-stimulated TNF-release in the rat is shown in the column identified as: *"ratLPS/%Inh@dose(mg/kg)"* wherein the dose is in milligram per kilogram (mg/kg) administered by oral gavage, 4 hours before LPS challenge.

Example	p38 alpha IC_{50} (uM)	HWB IC_{50} (uM)	ratLPS/%Inh @1.0(mg/kg)	ratLPS/%Inh @5.0(mg/kg)	ratLPS/%Inh @20.0(mg/kg)
D-1	0.17		83.0		
D-2	0.084	1.79	89.0	95.0	
D-3	0.095	0.46	69.0	88.0	91.0
D-4	0.91	1.55	42.3	83.0	99.0
D-5	0.14	4.09	65.0	78.5	83.0
D-6	0.083	1.33	82.0	96.0	100
D-7	0.44	>25.0		0	
D-8	0.18	1.3	65	85	
D-9	1.63	15.8	5	86	
D-10	3.95	14.8		80	
D-11	0.16	1.5	43	86	
D-12	0.82	7.06	71	91	
D-13	0.33	8.36	53	87	

Appendix A
Allowed Claims from the Corresponding European Application

1. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IB:

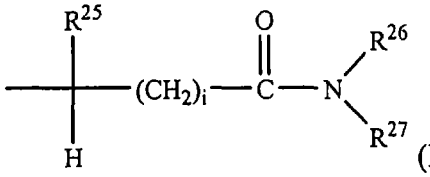


(IB); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl, or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$, alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl, wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

the arylalkyl and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is piperidinyl substituted with:

one or more substituents independently selected from the group consisting of hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, and hydroxyacyl, wherein:

said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, and hydroxyacyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

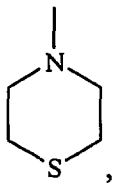
said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy, or

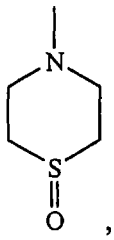
one or more substituents independently selected from the group consisting of hydroxycycloalkyl and alkoxycycloalkyl, wherein:

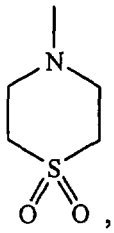
said hydroxycycloalkyl and alkoxycycloalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



,


, and


, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

2. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 1, wherein:

R^2 is piperidinyl substituted with:

one or more substituents independently selected from the group consisting of hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl, wherein:

said hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, alkoxyalkyl, alkoxyalkenyl, alkoxyalkynyl, hydroxyalkylcarbonyl, hydroxyalkenylcarbonyl, and hydroxyalkynylcarbonyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy, or

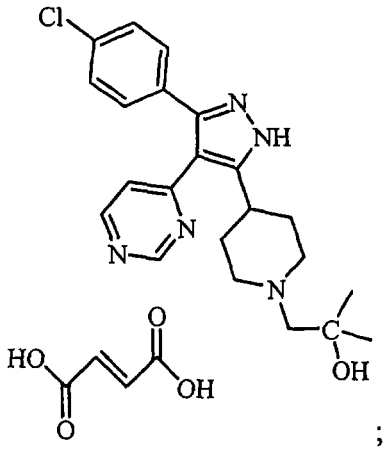
one or more substituents independently selected from the group consisting of hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl, wherein:

said hydroxycycloalkyl, alkoxycycloalkyl, and hydroxycycloalkylcarbonyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

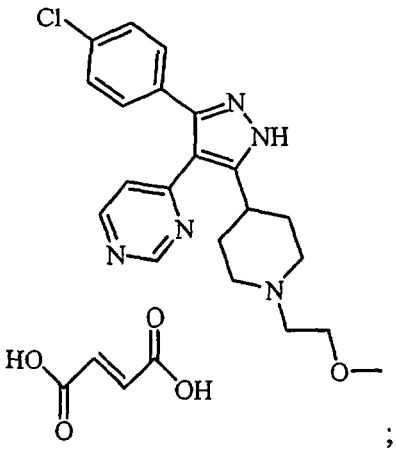
said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and

heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

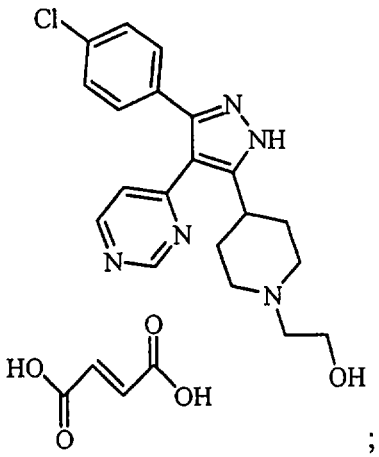
3. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 1, wherein the compound, tautomer or salt is selected from the group consisting of:



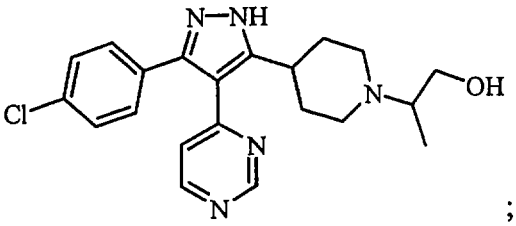
;



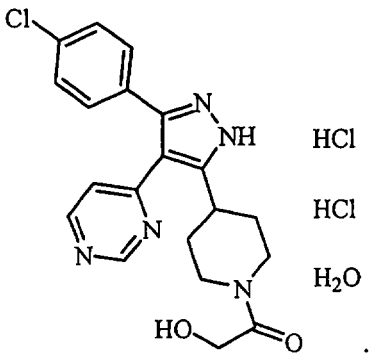
;



;



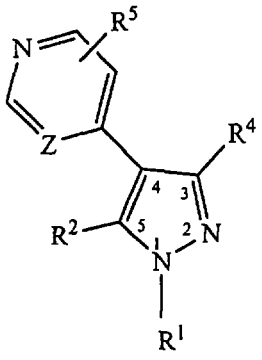
; and



.

4. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 1, wherein:

the compound corresponds in structure to Formula XB:



(XB);

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; and

R^2 is piperidinyl substituted with:

one or more substituents independently selected from the group consisting of hydroxyalkyl, hydroxyalkenyl, alkoxyalkyl, alkoxyalkenyl, hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl, wherein:

said hydroxyalkyl, hydroxyalkenyl, alkoxyalkyl, alkoxyalkenyl, hydroxyalkylcarbonyl, and hydroxyalkenylcarbonyl substituents may be

optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy, or

one or more substituents independently selected from the group consisting of hydroxycycloalkyl and hydroxycycloalkylcarbonyl, wherein:

said hydroxycycloalkyl and hydroxycycloalkylcarbonyl substituents may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^4 is selected from the group consisting of cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^5 represents one or more substituents independently selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

5. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^2 is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

6. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein Z is =C(H)-.

7. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein Z is =N-.

8. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^1 is selected from the group consisting of hydrido, alkyl, hydroxyalkyl, and alkynyl.

9. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^1 is hydrido.

10. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^2 is piperidinyl substituted with at least one substituent selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and hydroxycycloalkylcarbonyl.

11. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^4 is optionally-substituted phenyl.

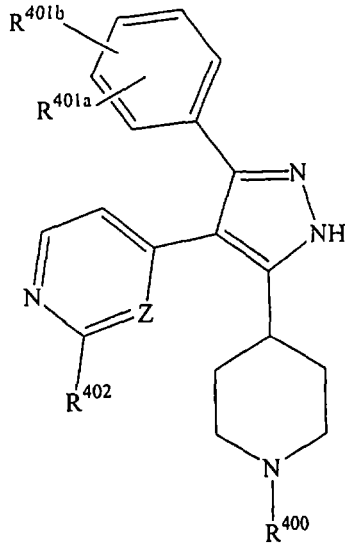
12. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of chloro, fluoro, bromo, and iodo.

13. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^4 is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

14. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 4, wherein R^5 is hydrido.

15. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 1, wherein:

the compound corresponds in structure to Formula XX:



(XX); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^{400} is selected from the group consisting of hydroxyalkyl, hydroxyalkylcarbonyl and alkoxyalkyl, wherein:

said hydroxyalkyl, hydroxyalkylcarbonyl, and alkoxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; or

R^{400} is hydroxycycloalkylcarbonyl that may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl, wherein:

said cycloalkyl, alkyl, aryl, arylalkyl, haloalkyl, and heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^{401a} and R^{401b} are independently selected from the group consisting of hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^{402} is selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

16. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkoxyalkyl, wherein:

said lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkoxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein:

said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy; or

R^{400} is hydroxycycloalkylcarbonyl that may be optionally substituted with one or more substituents independently selected from the group consisting of cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl, wherein:

said cycloalkyl, lower alkyl, phenyl, lower phenylalkyl, lower haloalkyl, and lower heteroarylalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, aryloxy, heterocyclyl, and lower heteroarylalkoxy; and

R^{401a} and R^{401b} are independently selected from the group consisting of hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein:

said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl,

phenyloxy, heterocyclyl, and lower heteroarylalkoxy; and

R^{402} is selected from the group consisting of hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein:

said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy.

17. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein Z is =C(H)-.

18. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein Z is =N-.

19. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{400} is optionally-substituted hydroxyalkylcarbonyl.

20. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{400} is optionally-substituted hydroxycycloalkylcarbonyl.

21. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{400} is optionally-substituted alkoxyalkyl.

22. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{400} is optionally-substituted hydroxyalkyl.

23. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{401} represents one or more substituents independently selected from the group consisting of chloro, fluoro, bromo, and iodo.

24. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{401} is meta-chloro or para-chloro.

25. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein R^{402} is hydrido.

26. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is optionally-substituted lower hydroxyalkylcarbonyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

27. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is selected from the group consisting of optionally-substituted 2-hydroxyacetyl, 2-hydroxy-proprionyl, 2-hydroxy-2-methylpropionyl, 2-hydroxy-2-phenylacetyl, 3-hydroxyproprionyl, 2-hydroxy-3-methylbutyryl, 2-hydroxyisocapropyl, 2-hydroxy-3-phenylproprionyl, and 2-hydroxy-3-imidazolylproprionyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

28. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 27, wherein R^{401a} is meta-chloro or para-chloro.

29. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 27, wherein:

R^{401a} is para-chloro, and

R^{401b} is hydrogen.

30. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is optionally-substituted lower hydroxycycloalkylcarbonyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

31. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is selected from the group consisting of optionally-substituted 1-hydroxy-1-cyclohexylacetyl, 2-hydroxy-1-cyclohexylacetyl, 3-hydroxy-1-cyclohexylacetyl, 4-hydroxy-1-cyclohexylacetyl, 1-hydroxy-1-cyclopentylacetyl, 2-hydroxy-1-cyclopentylacetyl, and 3-hydroxy-1-cyclopentylacetyl, 2-hydroxy-2-cyclohexylacetyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

32. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 31, wherein R^{401a} is meta-chloro or para-chloro.

33. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is optionally-substituted lower hydroxyalkyl; and

R^{401} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

34. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is selected from the group consisting of optionally-substituted hydroxymethyl, hydroxyethyl, hydroxypropyl, and hydroxyisopropyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

35. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 34, wherein R^{401a} is meta-chloro or para-chloro.

36. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is optionally-substituted lower alkoxyalkyl; and

R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

37. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 15, wherein:

R^{400} is selected from the group consisting of optionally-substituted methoxymethyl, methoxyethyl, methoxypropyl, methoxyisopropyl, ethoxymethyl, ethoxyethyl, ethoxypropyl, and ethoxyisopropyl.

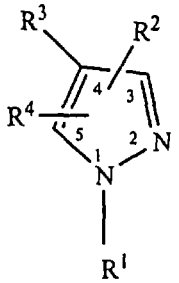
R^{401a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{402} is hydrido.

38. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 37, wherein R^{401a} is meta-chloro or para-chloro.

39. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IC:

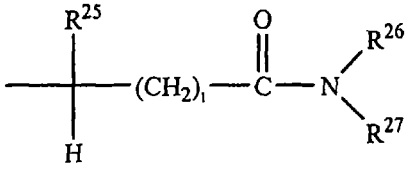


(IC); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl, or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$, alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl,

alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl; wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino; wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

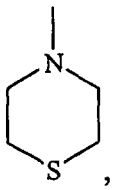
R^{28} is alkoxycarbonyl; and

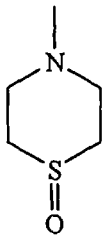
R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl; wherein:

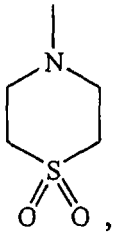
said arylalkyl and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is cyclohexyl substituted with one or more substituents independently selected from the group consisting of optionally-substituted hydroxyalkyl, alkylaminoalkyl, and cycloalkylamino; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



,


, and


, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

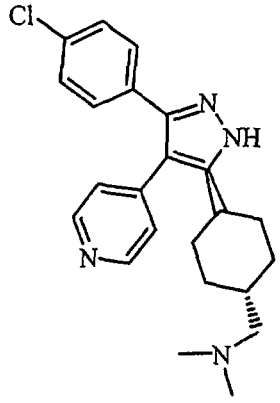
said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

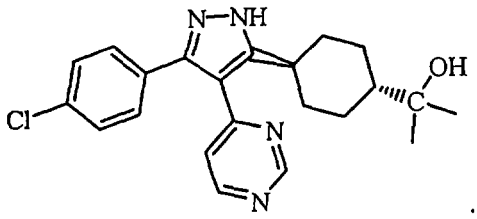
said alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

40. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 39, wherein the compound is selected from the group consisting of :

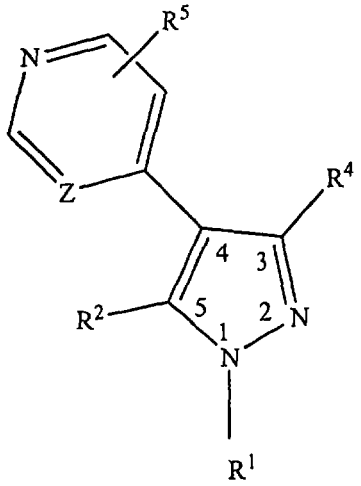


; and



41. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 39, wherein:

the compound corresponds in structure to Formula XC:



(XB); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl,

cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; and

R^2 is cyclohexyl substituted with one or more substituents independently selected from the group consisting of optionally-substituted hydroxyalkyl, alkylaminoalkyl, and cycloalkylamino; and

R^4 is selected from the group consisting of cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^5 represents one or more substituents independently selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently

selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

42. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^2 is cyclohexyl substituted with at least one substituent attached to the 4-position carbon ring atom of the cyclohexyl ring.

43. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein Z is =C(H)-.

44. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein Z is =N-.

45. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^1 is selected from the group consisting of hydrido, alkyl, hydroxyalkyl, and alkynyl.

46. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^1 is hydrido.

47. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^2 is cyclohexyl substituted with one or more substituents independently selected from the group consisting of optionally-substituted lower hydroxyalkyl, lower alkylaminoalkyl, and cycloalkylamino.

48. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^4 is optionally-substituted phenyl.

49. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^4 is phenyl optionally substituted

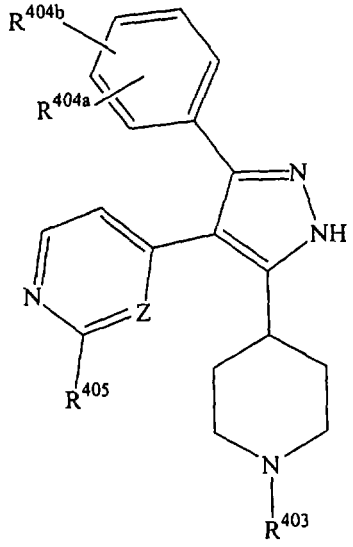
with one or more substituents independently selected from the group consisting of chloro, fluoro, bromo, and iodo.

50. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^4 is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

51. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein R^5 is hydrido.

52. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 41, wherein:

the compound corresponds in structure to Formula XXIA:



(XXIA); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^{403} is selected from the group consisting of hydroxyalkyl, alkylaminoalkyl, and cycloalkylamino; and

R^{404a} and R^{404b} are independently selected from the group consisting of hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino,

nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^{405} is selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

53. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is selected from the group consisting of lower hydroxyalkyl, lower alkylaminoalkyl, and cycloalkylamino; and

R^{404a} and R^{404b} are independently selected from the group consisting of hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein:

said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy; and

R^{405} is selected from the group consisting of hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein:

said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy.

54. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein Z is =C(H)-.

55. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein Z is =N-.

56. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{403} is optionally-substituted hydroxyalkyl.

57. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{403} is optionally-substituted alkylaminoalkyl.

58. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 57, wherein R^{403} is optionally-substituted dialkylaminoalkyl.

59. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{403} is optionally substituted-cycloalkylamino.

60. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo.

61. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{404a} is meta-chloro or para-chloro.

62. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein R^{405} is hydrido.

63. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is optionally-substituted lower hydroxyalkyl; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

64. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is selected from the group consisting of optionally-substituted hydroxymethyl, hydroxyethyl, hydroxypropyl, and hydroxybutyl; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

65. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 64, wherein R^{404a} is meta-chloro or para-chloro.

66. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is optionally-substituted lower alkylaminoalkyl; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

67. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is selected from the group consisting of optionally-substituted methylaminomethyl, methylaminoethyl, methylaminopropyl, ethylaminomethyl, ethylaminoethyl, ethylaminopropyl, propylaminomethyl, propylaminoethyl, propylaminopropyl, dimethylaminomethyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminomethyl, diethylaminoethyl, diethylaminopropyl, dipropylaminomethyl, dipropylaminoethyl, and dipropylaminopropyl; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

68. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 67, wherein R^{404a} is meta-chloro or para-chloro.

69. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

R^{403} is optionally-substituted cycloalkylamino; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

70. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 52, wherein:

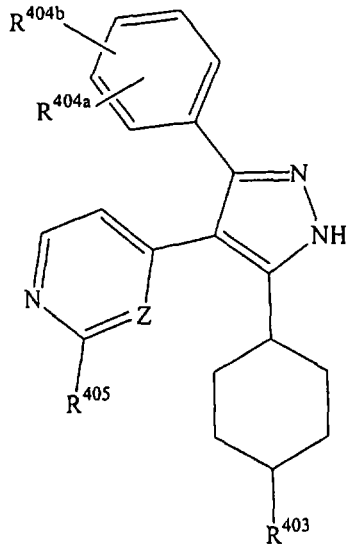
R^{403} is selected from the group consisting of optionally-substituted cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

71. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula XXIB:



(XXIB); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^{403} is alkylamino; and

R^{404a} and R^{404b} are independently selected from the group consisting of hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy; and

R^{405} is selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

72. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein:

R^{403} is lower alkylamino; and

R^{404a} and R^{404b} are independently selected from the group consisting of hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein:

said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy; and

R^{405} is selected from the group consisting of hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein:

said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or

more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy.

73. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein Z is =C(H)-.

74. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein Z is =N-.

75. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein R^{403} is optionally-substituted dialkylamino.

76. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo.

77. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein R^{404a} is meta-chloro or para-chloro.

78. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein R^{405} is hydrido.

79. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein:

R^{403} is optionally-substituted lower alkylamino; and

R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

80. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein:

R^{403} is selected from the group consisting of optionally-substituted methylamino, ethylamino, n-propylamino, isopropylamino, n-butylamino, sec-butylamino, t-butylamino, isobutylamino, dimethylamino, diethylamino, di-n-propylamino, di-isopropylamino, di-n-butylamino, di-sec-butylamino, di-t-butylamino, and di-isobutylamino; and

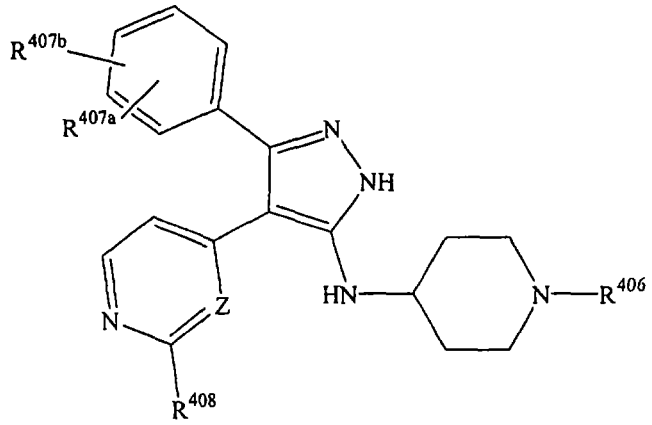
R^{404a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{405} is hydrido.

81. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 80, wherein R^{404a} is meta-chloro or para-chloro.

82. A compound , a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula XXII:



(XXII); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^{406} is alkynyl; and

R^{407a} and R^{407b} are independently selected from the group consisting of hydrogen, halo, haloalkyl, haloalkoxy, alkoxy, cyano, hydroxy, alkyl, alkenyl, and alkynyl, wherein:

said haloalkyl, haloalkoxy, alkoxy, hydroxy, alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl,

and heteroarylalkoxy; and

R^{408} is selected from the group consisting of hydrogen, aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy, wherein:

said aryl, alkylamino, alkylthio, alkyloxy, aryloxy, arylamino, arylthio, and arylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, alkenyl, hydroxy, halo, haloalkyl, alkoxy, keto, amino, nitro, cyano, alkylsulfonyl, alkylsulfinyl, alkylthio, alkoxyalkyl, aryloxy, heterocyclyl, and heteroarylalkoxy.

83. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein:

R^{406} is selected from the group consisting of lower alkynyl; and

R^{407a} and R^{407b} are independently selected from the group consisting of hydrogen, halo, lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl, wherein:

said lower haloalkyl, lower haloalkoxy, lower alkoxy, cyano, hydroxy, lower alkyl, lower alkenyl, and lower alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, lower alkynyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy; and

R^{408} is selected from the group consisting of hydrogen, phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy, wherein:

said phenyl, lower alkylamino, lower alkylthio, lower alkyloxy, phenyloxy, phenylamino, phenylthio, and phenylalkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of lower alkyl, lower alkenyl, hydroxy, halo, lower haloalkyl, lower alkoxy, keto, amino, nitro, cyano, lower alkylsulfonyl, lower alkylsulfinyl, lower alkylthio, lower alkoxyalkyl, phenyloxy, heterocyclyl, and lower heteroarylalkoxy.

84. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of

the compound or tautomer according to Claim 82, wherein Z is =C(H)-.

85. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein Z is =N-.

86. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein R^{407a} is selected from the group consisting of chloro, fluoro, bromo, and iodo.

87. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein R^{407a} is meta-chloro or para-chloro.

88. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein R^{408} is hydrido.

89. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein:

R^{406} may be optionally substituted lower alkynyl; and

R^{407a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^{408} is hydrido.

90. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein:

R^{406} is selected from the group consisting of optionally-substituted ethynyl, propynyl, and butynyl; and

R^{407a} is selected from the group consisting of chloro, fluoro, bromo, and iodo; and

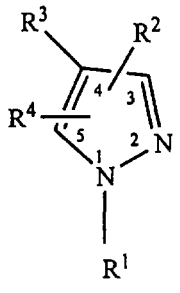
R^{408} is hydrido.

91. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein R^{406} is propargyl.

92. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 82, wherein R^{407a} is meta-chloro or para-chloro.

93. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:

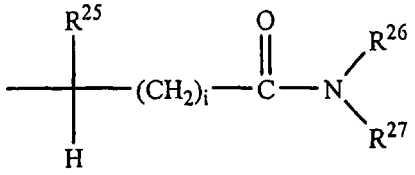


(IA); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$, alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, and alkylaminosulfonylaryl; wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

said arylalkyl and heterocylcyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is selected from the group consisting of R^{200}-heterocyclyl-R^{201}, R^{200}-aryl-R^{201}, R^{200}-cycloalkyl-R^{201}, -$NHCR^{204}R^{205}$, -$C(NR^{206})R^{207}$, mercapto, aryl(hydroxyalkyl)amino, N-alkyl-N-alkynylamino, aminocarbonylalkyl, aminoalkylcarbonylaminoalkyl, alkylaminoalkylcarbonylamino, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, alkoxyalkyl, alkoxyalkylthio, alkoxycarbonylaminoalkoxy, arylalkythio, heterocyclylalkylthio, aminoalkoxy, cyanoalkoxy, carboxyalkoxy, aryloxy, arylalkoxy, alkenyloxy, alkynyloxy, and heterocyclylalkyloxy; and

R^{200} is selected from the group consisting of:

-$(CR^{202}R^{203})_y$-,

-C(O)-,

-C(O)-$(CH_2)_y$-,

-C(O)-O-$(CH_2)_y$-,

-$(CH_2)_y$-C(O)-,

-O-$(CH_2)_y$-C(O)-,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{202}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxyalkyl, cycloalkyl, hydroxyalkylcarbonyl, alkoxyalkyl, alkoxyaryl, carboxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, aminoalkyl, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, and guanidinoalkyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

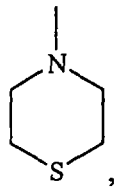
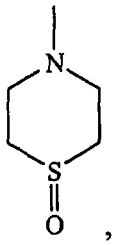
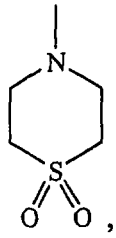
R^{204} is alkylaminoalkyl; and

R^{205} is aryl; and

R^{206} is selected from the group consisting of hydrogen and hydroxy; and

R^{207} is selected from the group consisting of alkyl, aryl, and arylalkyl; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,


,

, and

, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl,

alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

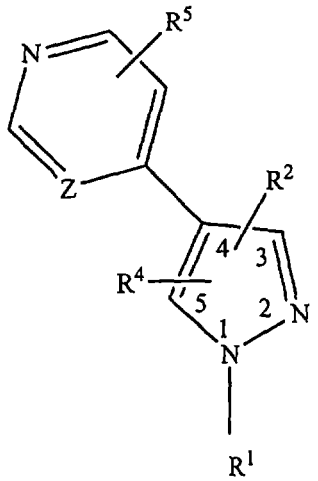
R^3 is not 2-pyridinyl when R^4 is a phenyl ring containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^2 is selected from the group consisting of -R^{200}-heterocyclyl-R^{201}, -R^{200}-aryl-R^{201}, and -R^{200}-unsubstituted cycloalkyl-R^{201} when R^4 is hydrido; and

R^1 is not methylsulfonylphenyl.

94. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IXA:



(IXA); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, lower alkyl, lower hydroxyalkyl, lower alkynyl, lower arylalkyl, lower aminoalkyl, and lower alkylaminoalkyl; and

R^2 is selected from the group consisting of lower hydroxyalkylamino, R^{200}-heterocyclyl-R^{201}, and R^{200}-cycloalkyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{202}-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, lower hydroxyalkyl, lower cycloalkyl, lower hydroxyalkylcarbonyl, lower cycloalkylcarbonyl (except cyclopropylcarbonyl), lower alkoxyalkyl, lower alkoxyaryl, lower carboxyalkylcarbonyl, lower alkoxyalkylcarbonyl (except methoxymethylcarbonyl), lower heterocyclylalkylcarbonyl, lower alkylsulfonylalkyl, lower aminoalkyl, lower arylalkylamino, lower alkylaminoalkyl, aminocarbonyl, lower alkylcarbonylamino (except methylcarbonylamino and propylcarbonylamino), lower alkylcarbonylaminoalkyl, lower alkylaminoalkylcarbonyl, lower alkylaminoalkylcarbonylamino, lower aminoalkylcarbonylaminoalkyl, lower alkoxycarbonylamino, lower alkoxyalkylcarbonylamino (except methoxymethylcarbonylamino), lower alkoxycarbonylaminoalkyl, lower alkylimidocarbonyl, amidino, lower alkylamidino, lower arylalkylamidino, guanidino, lower guanidinoalkyl, and lower alkylsulfonylamino (except methylsulfonylamino and ethylsulfonylamino); and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, lower alkyl, aryl, and lower arylalkyl; and

y is selected from the group consisting of zero, 1, 2, and 3; and

R^4 is selected from the group consisting of phenyl, biphenyl, and naphthyl, wherein:

said phenyl, biphenyl, and naphthyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, aryloxy, lower arylalkoxy, lower haloalkyl, lower alkylthio, lower alkylamino, nitro, and hydroxy; and

R^5 is selected from the group consisting of hydrido, halo, amino, cyano, aminocarbonyl, lower alkyl, lower alkoxy, hydroxy, lower aminoalkyl, lower arylalkyl, lower arylalkyloxy, lower arylalkylamino, lower alkoxycarbonyl, lower alkylamino, lower hydroxyalkylamino, lower alkylcarbonyl, lower arylalkenyl, lower arylheterocyclyl, carboxy, lower cycloalkylamino, lower hydroxycycloalkylamino, lower alkoxycarbonylamino, lower alkoxyarylalkylamino, lower alkylaminoalkylamino, lower heterocyclylamino, lower heterocyclylalkylamino, lower arylalkylheterocyclylamino, lower alkylaminocarbonyl, lower alkylcarbonyl, lower alkoxyarylalkylamino, hydrazinyl, and lower alkylhydrazinyl, and $-NR^{62}R^{63}$; and

R^{62} is selected from the group consisting of lower alkylcarbonyl and amino; and

R^{63} is selected from the group consisting of lower alkyl and lower phenylalkyl.

95. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^2 is R^{200}-heterocyclyl-R^{201}.

96. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^2 is R^{200}-cycloalkyl-R^{201}.

97. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein:

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is selected from the group consisting of R^{200}-piperidinyl-R^{201}, R^{200}-piperazinyl-R^{201}, and R^{200}-cyclohexyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-

dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, ethoxycarbonylaminomethyl, methylimidocarbonyl, ethylimidocarbonyl, amidino, methylamidino, methylamidino, benzylamidino, guanidino, guanidinomethyl, and guanidinoethyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, phenyl, and benzyl; and

y is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl, wherein:

said phenyl may be optionally substituted with one or more substituents independently selected from the group consisting of methylthio, fluoro, chloro, bromo, iodo, methyl, ethyl, methoxy, ethoxy, phenoxy, benzyloxy, trifluoromethyl, nitro, dimethylamino, and hydroxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, iodo, hydroxy, methyl, ethyl, propyl, benzyl, fluorophenylethyl, fluorophenylethenyl, fluorophenylpyrazolyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino,

hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, ethylcarbonyl, hydrazinyl, and 1-methylhydrazinyl, and $-NR^{62}R^{63}$; and

R^{62} is selected from the group consisting of methylcarbonyl and amino; and

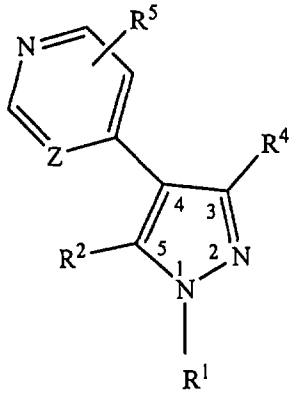
R^{63} is selected from the group consisting of methyl and benzyl.

98. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 97, wherein R^2 is R^{200}-piperidinyl-R^{201}.

99. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 97, wherein R^2 is R^{200}-pyrazinyl-R^{201}.

100. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 97, wherein R^2 is R^{200}-cyclohexyl-R^{201}.

101. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, having the Formula XA:



(XA); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-piperidinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, N-methylamino, N,N-

dimethylamino, N-ethylamino, N,N-diethylamino, N-propylamino, N,N-dipropylamino, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, ethoxycarbonylaminomethyl, methylimidocarbonyl, ethylimidocarbonyl, amidino, methylamidino, methylamidino, benzylamidino, guanidino, guanidinomethyl, and guanidinoethyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, phenyl, and benzyl; and

y is is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

102. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 101, wherein:

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-piperidinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-CH_2-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-dimethyl)ethyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethyl, aminocarbonyl, methoxycarbonylamino, and ethoxycarbonylamino; and

R^{202} is selected from the group consisting of hydrido, methyl, ethyl, phenyl, and benzyl; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino,

phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

103. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 101, wherein:

R^1 is hydrido; and

R^2 is R^{200}-piperidinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-CH_2-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, methoxyethylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, aminomethyl, aminoethyl, aminopropyl, N-benzylamino, methylaminomethyl, aminocarbonyl, methoxycarbonylamino, and ethoxycarbonylamino; and

R^{202} is selected from the group consisting of hydrido, methyl phenyl, and benzyl; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, and methoxy; and

R^5 is selected from the group consisting of hydrido, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino,

hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, dimethylaminoethylamino, dimethylaminopropylamino, dimethylaminobutylamino, dimethylaminopentylamino, diethylaminoethylamino, diethylaminopropylamino, diethylaminobutylamino, and diethylaminopentylamino.

104. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 101, wherein:

R^1 is hydrido; and

R^2 is R^{200}-piperidinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-CH_2-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

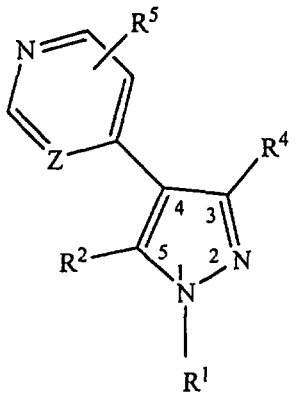
R^{201} represents one or more substituents independently selected from the group consisting of methoxyethyl, methylcarbonyl, and hydroxymethylcarbonyl; and

R^{202} is selected from the group consisting of hydrido and methyl; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, and methoxy; and

R^5 is selected from the group consisting of hydrido, hydroxypropylamino, hydroxycyclohexylamino, diethylaminoethylamino.

105. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, having the Formula XA:



(XA); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-piperazinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino,

methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, ethoxycarbonylaminomethyl, methylimidocarbonyl, ethylimidocarbonyl, amidino, methylamidino, methylamidino, benzylamidino, guanidino, guanidinomethyl, and guanidinoethyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, phenyl, and benzyl; and

y is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

106. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 105, wherein:

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-piperazinyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, ethoxyethyl, methoxyphenyl, ethoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, and ethoxycarbonylaminomethyl; and

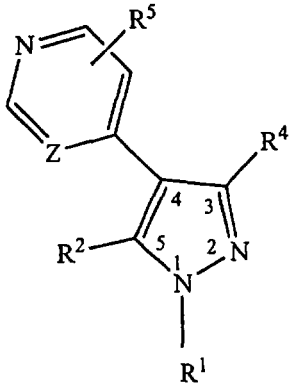
R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, phenyl, and benzyl; and

y is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, cthylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

107. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, having the Formula XA:



(XA); and

Z is selected from the group consisting of =N- and =C(H)-; and

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-cyclohexyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, ethoxycarbonylaminomethyl, methylimidocarbonyl, ethylimidocarbonyl, amidino, methylamidino, methylamidino, benzylamidino, guanidino, guanidinomethyl, and guanidinoethyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, propyl, butyl, phenyl, and benzyl; and

y is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl, wherein:

said phenyl may be optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, propyl, benzyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl,

acetyl, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, imidazolylamino, morpholinylethylamino, (1-ethyl-2-hydroxy)ethylamino, piperidinylamino, pyridinylmethylamino, phenylmethylpiperidinylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

108. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 107, wherein:

R^1 is selected from the group consisting of hydrido, methyl, ethyl, hydroxyethyl, and propargyl; and

R^2 is R^{200}-cyclohexyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, hydroxymethyl, hydroxyethyl, hydroxypropyl, (1-hydroxy-1,1-dimethyl)ethyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, methoxymethyl, methoxyethyl, methoxypropyl, ethoxyethyl, ethoxypropyl, propoxyethyl, propoxypropyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl,

carboxymethylcarbonyl, carboxyethylcarbonyl, carboxypropylcarbonyl, methoxyethylcarbonyl, methoxypropylcarbonyl, ethoxymethylcarbonyl, ethoxyethylcarbonyl, ethoxypropylcarbonyl, propoxymethylcarbonyl, propoxyethylcarbonyl, propoxypropylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, propoxyphenylcarbonyl, piperidinylmethylcarbonyl, piperazinylmethylcarbonyl, morpholinylcarbonyl, methylsulfonylmethyl, aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, and ethoxycarbonylaminomethyl; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, methyl, ethyl, phenyl, and benzyl; and

y is selected from the group consisting of zero, 1, and 2; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, ethyl, methoxy, and ethoxy; and

R^5 is selected from the group consisting of hydrido, fluoro, chloro, bromo, hydroxy, methyl, ethyl, cyano, carboxy, methoxy, methoxycarbonyl, aminocarbonyl, acetyl, methylamino, dimethylamino, ethylamino, dimethylaminoethylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, ethoxycarbonylamino, methoxyphenylmethylamino, phenylmethylamino, fluorophenylmethylamino, fluorophenylethylamino, methylaminoethylamino, dimethylaminoethylamino, methylaminopropylamino, dimethylaminopropylamino, methylaminobutylamino, dimethylaminobutylamino, methylaminopentylamino, dimethylaminopentylamino, ethylaminoethylamino, diethylaminoethylamino, ethylaminopropylamino, diethylaminopropylamino, ethylaminobutylamino, diethylaminobutylamino, ethylaminopentylamino, methylaminocarbonyl, methylcarbonyl, and ethylcarbonyl.

109. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 107, wherein:

R^1 is hydrido; and

R^2 is R^{200}-cyclohexyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-CH_2-$,

$-NR^{202}-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of aminomethyl, aminoethyl, aminopropyl, phenylamino, benzylamino, methylaminomethyl, ethylaminomethyl, methylaminoethyl, ethylaminoethyl, aminocarbonyl, ethylcarbonylamino, methylaminomethylcarbonyl, ethylaminomethylcarbonyl, methylcarbonylaminomethyl, ethylcarbonylaminomethyl, aminomethylcarbonylaminocarbonylmethyl, methoxycarbonylamino, ethoxycarbonylamino, methoxyethylcarbonylamino, ethoxymethylcarbonylamino, ethoxyethylcarbonylamino, methoxycarbonylaminomethyl, and ethoxycarbonylaminomethyl; and

R^{202} is selected from the group consisting of hydrido, methyl, phenyl, and benzyl; and

R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of fluoro, chloro, methyl, and methoxy; and

R^5 is selected from the group consisting of hydrido, methylamino, dimethylamino, 2-methylbutylamino, ethylamino, dimethylaminoethylamino, hydroxypropylamino, hydroxyethylamino, hydroxypropylamino, hydroxybutylamino, hydroxycyclopropylamino, hydroxycyclobutylamino, hydroxycyclopentylamino, hydroxycyclohexylamino, (1-ethyl-2-hydroxy)ethylamino, aminomethyl, cyclopropylamino, amino, dimethylaminoethylamino, dimethylaminopropylamino, dimethylaminobutylamino, dimethylaminopentylamino, diethylaminoethylamino, diethylaminopropylamino, diethylaminobutylamino, and diethylaminopentylamino.

110. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^2 is selected from the group consisting of piperidinyl and piperazinyl, wherein:

the piperidinyl or piperazinyl is substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine or piperazine ring.

111. A compound Claim 94, wherein R^2 is piperidinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperidine ring.

112. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^2 is piperazinyl substituted with at least one substituent attached to the distal nitrogen heteroatom or to a carbon ring atom adjacent to the distal nitrogen heteroatom of the piperazine ring.

113. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein Z is =C(H)-.

114. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein Z is =N-.

115. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^1 is hydrido.

116. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^{200} is a bond.

117. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^{201} represents one or more substituents independently selected from the group consisting of lower hydroxyalkyl, lower

hydroxyalkylcarbonyl, and lower alkylaminoalkyl.

118. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^{201} represents one or more substituents independently selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethyl, ethylaminomethyl, methylaminoethyl, and ethylaminoethyl.

119. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^4 is optionally-substituted phenyl.

120. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of chloro, fluoro, bromo, and iodo.

121. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^4 is phenyl optionally substituted at the meta or para position with one or more chloro radicals.

122. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein R^5 is hydrido.

123. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein:

R^1 is hydrido; and

R^{200} is a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of lower hydroxyalkyl, lower hydroxyalkylcarbonyl, and lower alkylaminoalkyl; and

R^4 is phenyl optionally substituted with one or more independently selected halo; and

R^5 is hydrido.

124. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 94, wherein:

R^1 is hydrido; and

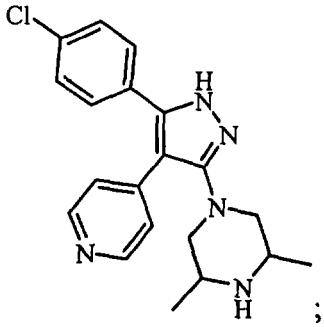
R^{200} is a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxymethyl, hydroxyethyl, hydroxypropyl, hydroxybutyl, (1-hydroxy-1,1-dimethyl)ethyl, hydroxymethylcarbonyl, hydroxyethylcarbonyl, hydroxypropylcarbonyl, methylaminomethyl, ethylaminomethyl, methylaminoethyl, and ethylaminoethyl; and

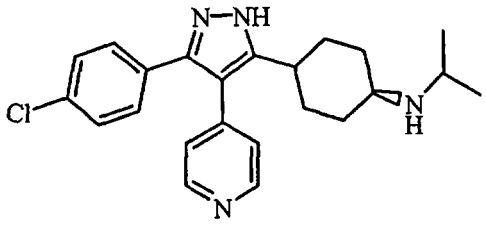
R^4 is phenyl optionally substituted with one or more substituents independently selected from the group consisting of chloro, fluoro, bromo, and iodo; and

R^5 is hydrido.

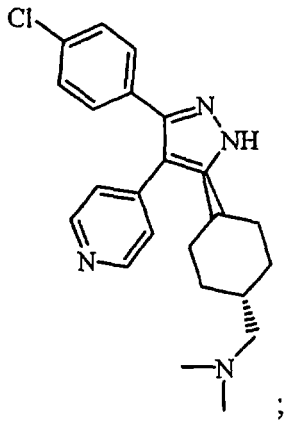
125. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound, wherein the compound is selected from the group consisting of:



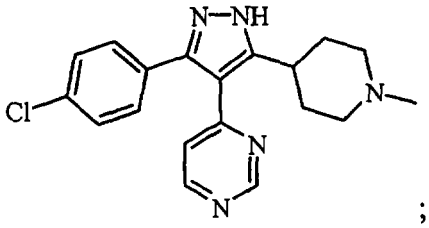
; and



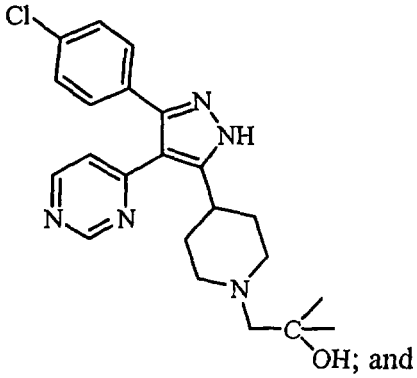
; and



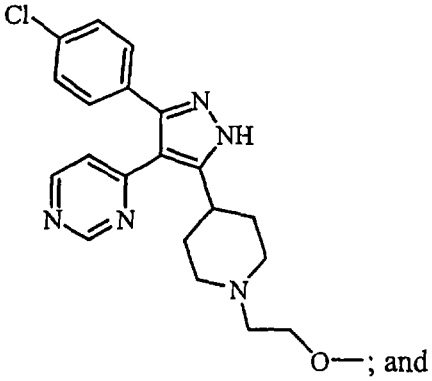
; and



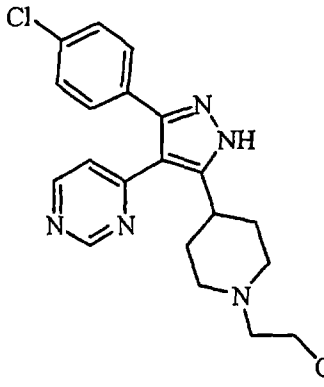
; and



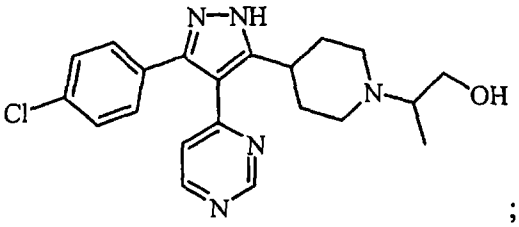
; and



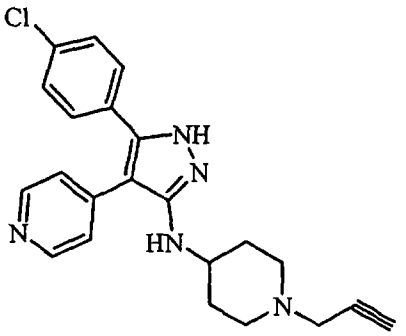
; and



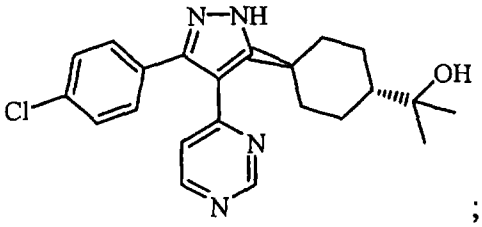
OH ; and



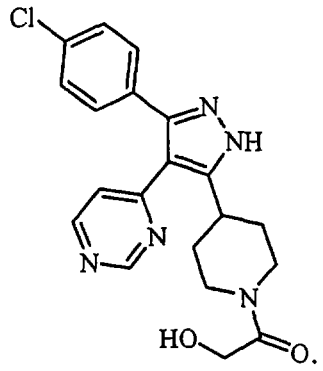
; and



; and

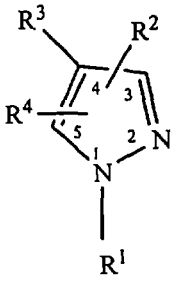


; and



126. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:



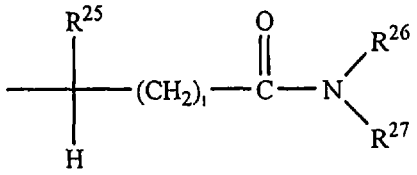
(IA); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl,

heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$, alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl, wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl,

arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

said arylalkyl and heterocylcyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is R^{200}-cycloalkyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-C(O)-$,

$-C(O)-(CH_2)_y-$,

$-C(O)-O-(CH_2)_y-$,

$-(CH_2)_y-C(O)-$,

$-O-(CH_2)_y-C(O)-$,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{202}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$,

-S-, and

-O-; and

R^{201} represents one or more substituents independently selected from the group consisting of halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, amino, aminoalkyl, alkylamino, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, guanidinoalkyl, and alkylsulfonylamino; and

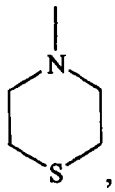
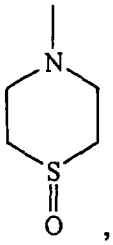
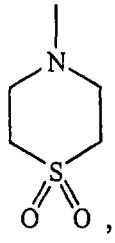
R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,

, , and , wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

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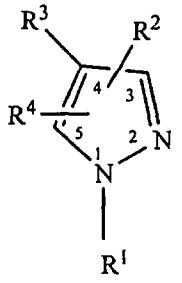
the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

R^3 is not 2-pyridinyl when R^4 is a phenyl containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^1 is not methylsulfonylphenyl.

127. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:



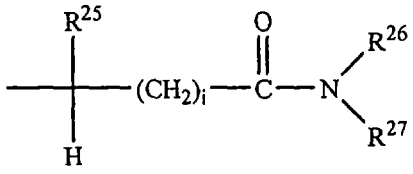
(IA); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl,

alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$ alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl,

wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27} together with the nitrogen atom to which they are attached form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

said arylalkyl and heterocylcyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is R^{200}-aryl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

-C(O)-,

$-C(O)-(CH_2)_y-$,

$-C(O)-O-(CH_2)_y-$,

$-(CH_2)_y-C(O)-$,

$-O-(CH_2)_y-C(O)-$,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{300}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_{z1}-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$, and

-O-; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, carboxy, keto, hydroxyalkyl, cycloalkyl, alkenyl, alkynyl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxyalkyl, alkoxyaryl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, amino, aminoalkyl, alkylamino, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, guanidinoalkyl, and alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

R^{300} is selected from the group consisting of alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

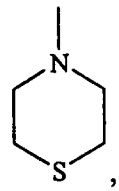
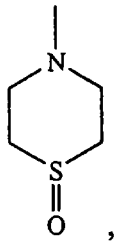
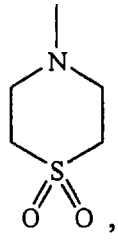
z1 is selected from the group consisting of 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

the sum of y + z1 is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,


,

, and

, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino,

alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

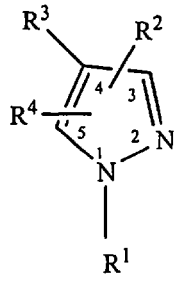
the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

R^3 is not 2-pyridinyl when R^4 is a phenyl ring containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^1 is not methylsulfonylphenyl.

128. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:

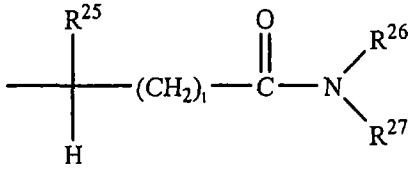


(IA); and

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl, heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl,

aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$ alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl, arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl, wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl,

alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more radicals independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

said arylalkyl and heterocylcyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

R^2 is R^{200}-heterocyclyl-R^{201}; and

R^{200} is selected from the group consisting of:

$-(CR^{301}R^{302})_y-$,

$-C(O)-(CH_2)_{y1}-$,

$-C(O)-O-(CH_2)_y-$,

$-(CH_2)_y-C(O)-$,

$-O-(CH_2)_y-C(O)-$,

$-NR^{303}-(CH_2)_y-$,

$-(CH_2)_{y1}-NR^{202}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_{z1}-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$, and

$-(CH_2)_y-O-$; and

R^{201} represents one or more substituents independently selected from the group consisting of hydroxy, carboxy, keto, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkyl, alkoxyaryl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, amino, aminoalkyl, alkylamino, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, guanidinoalkyl, and alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

R^{301} and R^{302} are independently selected from the group consisting of aryl and arylalkyl; and

R^{303} is selected from the group consisting of alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

z1 is selected from the group consisting of 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

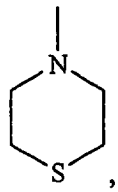
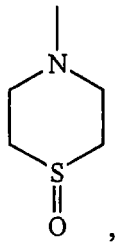
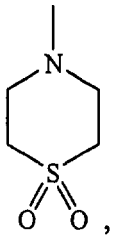
the sum of y + z1 is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

either x or y is other than zero when R^{200} is $-S(O)_x-(CR^{202}R^{203})_y-$; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl,

maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,


,

, and

, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

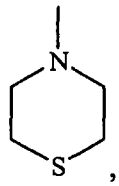
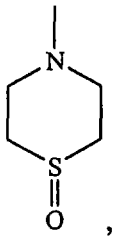
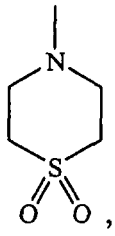
R^3 is not 2-pyridinyl when R^4 is a phenyl ring containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^2 is selected from the group consisting of aryl, heterocyclyl, unsubstituted cycloalkyl, and cycloalkenyl when R^4 is hydrido; and

R^1 is not methylsulfonylphenyl.

129. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to claim 130, wherein:

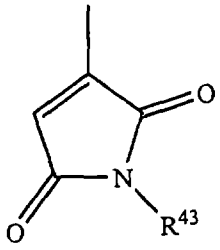
R^3 is selected from the group consisting of maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,


,

, and

, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl,

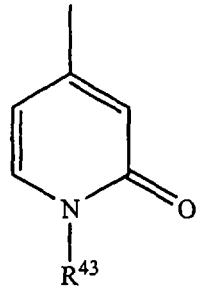
alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and $-NR^{44}R^{45}$; and

R^3 is not:



(IV)

and

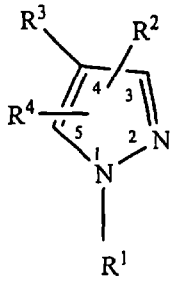


(V), wherein:

R^{43} is selected from the group consisting of hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and.

130. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:



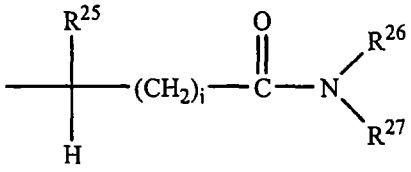
(IA); and

as to R^1:

R^1 is selected from the group consisting of hydrido, hydroxy, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl, heterocyclyl, cycloalkylalkyl, cycloalkenylalkyl, heterocyclylalkyl, haloalkyl, haloalkenyl, haloalkynyl, hydroxyalkyl, hydroxyalkenyl, hydroxyalkynyl, arylalkyl, arylalkenyl, arylalkynyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxyalkyl, alkenoxyalkyl, alkynoxyalkyl, aryloxyalkyl, alkoxyaryl,

heterocyclyloxyalkyl, alkoxyalkoxy, mercaptoalkyl, alkylthioalkyl, alkenylthioalkyl, alkylthioalkenyl, amino, aminoalkyl, alkylamino, alkenylamino, alkynylamino, arylamino, heterocyclylamino, alkylsulfinyl, alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, heterocyclylsulfinyl, alkylsulfonyl, alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, heterocyclylsulfonyl, alkylaminoalkyl, alkylsulfonylalkyl, acyl, acyloxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, heterocyclyloxycarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, heterocyclyloxycarbonylaryl, alkylcarbonylalkyl, arylcarbonylalkyl, heterocyclylcarbonylalkyl, alkylcarbonylaryl, arylcarbonylaryl, heterocyclylcarbonylaryl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, heterocyclylcarbonyloxyalkyl, alkylcarbonyloxyaryl, arylcarbonyloxyaryl, and heterocyclylcarbonyloxyaryl; or

R^1 corresponds in structure to formula (II):



(II); and

i is an integer from zero to 9; and

R^{25} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

as to R^{26} and R^{27}:

R^{26} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkylalkyl, arylalkyl, alkoxycarbonylalkyl, and alkylaminoalkyl; and R^{27} is selected from the group consisting of -$CHR^{28}R^{29}$, alkyl, cycloalkyl, alkynyl, aryl, heterocyclyl, arylalkyl, cycloalkylalkyl, cycloalkenylalkyl, cycloalkylaryl, cycloalkylcycloalkyl, heterocyclylalkyl, alkylaryl, alkylarylalkyl, arylalkylaryl, alkylheterocyclyl, alkylheterocyclylalkyl, alkylheterocyclylaryl, arylalkylheterocyclyl, alkoxyalkyl, alkoxyaryl, alkoxyarylalkyl, alkoxyheterocyclyl, alkoxyalkoxyaryl, aryloxyaryl, arylalkoxyaryl, alkoxyheterocyclylalkyl, aryloxyalkoxyaryl, alkoxycarbonylalkyl, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonylalkyl, aminoalkyl, alkylaminoalkyl, arylaminocarbonylalkyl, alkoxyarylaminocarbonylalkyl, aminocarbonylalkyl, arylaminocarbonylalkyl, alkylaminocarbonylalkyl,

arylcarbonylalkyl, alkoxycarbonylaryl, aryloxycarbonylaryl, alkylaryloxycarbonylaryl, arylcarbonylaryl, alkylarylcarbonylaryl, alkoxycarbonylheterocyclylaryl, alkoxycarbonylalkoxylaryl, heterocyclylcarbonylalkylaryl, alkylthioalkyl, cycloalkylthioalkyl, alkylthioaryl, arylalkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, arylsulfonylaminoalkyl, alkylsulfonylaryl, alkylaminosulfonylaryl, wherein:

said alkyl, cycloalkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylheterocyclylaryl, alkoxyaryl, aryloxyaryl, arylaminocarbonylalkyl, aryloxycarbonylaryl, arylcarbonylaryl, alkylthioaryl, heterocyclylthioaryl, arylthioalklylaryl, and alkylsulfonylaryl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, halo, haloalkyl, alkoxy, keto, amino, nitro, and cyano, or

R^{26} and R^{27}, together with the nitrogen atom to which they are attached, form a heterocycle, wherein:

said heterocycle may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl, aryl, heterocyclyl, heterocyclylalkyl, alkylheterocyclylalkyl, aryloxyalkyl, alkoxyaryl, alkylaryloxyalkyl, alkylcarbonyl, alkoxycarbonyl, arylalkoxycarbonyl, alkylamino, and alkoxycarbonylamino, wherein:

said aryl, heterocyclylalkyl, and aryloxyalkyl may be optionally substituted with one or more substituents independently selected from the group consisting of halogen, alkyl, and alkoxy; and

R^{28} is alkoxycarbonyl; and

R^{29} is selected from the group consisting of arylalkyl, arylalkoxyalkyl, heterocyclylalkyl, alkylheterocyclylalkyl, alkoxycarbonylalkyl, alkylthioalkyl, and arylalkylthioalkyl, wherein:

said arylalkyl and heterocylcyl may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and nitro; and

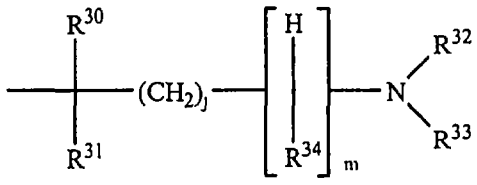
as to R^2:

R^2 is selected from the group consisting of R^{200}-heterocyclyl-R^{201}, R^{200}-aryl-R^{201}, R^{200}-cycloalkyl-R^{201}, -$NHCR^{204}R^{205}$, -$C(NR^{206})R^{207}$, -$CR^{41}R^{42}$, hydrido, halogen, mercapto, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, arylalkyl,

alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino, heterocyclylamino, heterocyclylalkylamino, arylalkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkyl, arylaminoalkyl, alkylaminoalkyl, arylaminoaryl, alkylaminoaryl, alkylaminoalkylamino, alkylcarbonylaminoalkyl, aminoalkylcarbonylaminoalkyl, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy, heterocyclyloxy, alkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, arylthio, heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl, alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino, alkoxycarbonylaminoalkyl, alkoxycarbonylaminoalkoxy, alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl, arylalkythio, heterocyclylalkylthio, aminoalkoxy, cyanoalkoxy, carboxyalkoxy, aryloxy, arylalkoxy, alkenyloxy, alkynyloxy, and heterocyclylalkyloxy, wherein:

the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl, and cycloalkenyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, arylalkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, arylsulfonyl, and arylalkylsulfonyl, or

R^2 has the formula:



(III); and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

-C(O)-,

$-C(O)-(CH_2)_y-$,

$-C(O)-O-(CH_2)_y-$,

$-(CH_2)_y-C(O)-$,

$-O-(CH_2)_y-C(O)-$,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{202}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$,

-S-,

-O-, and

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, amino, aminoalkyl, alkylamino, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, guanidinoalkyl, and alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

R^{204} is alkylaminoalkyl; and

R^{205} is aryl; and

R^{206} is selected from the group consisting of hydrogen and hydroxy; and

R^{207} is selected from the group consisting of alkyl, aryl, and arylalkyl; and

j is an integer from zero to 8; and

m is selected from the group consisting of zero and 1; and

R^{30} and R^{31} are independently selected from the group consisting of hydrogen, alkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl, alkoxyalkyl, and alkylcarbonyloxyalkyl; and

R^{32} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

R^{33} is selected from the group consisting of hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$; and

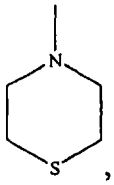
R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, and R^{40} are independently selected from the group consisting of hydrocarbon, heterosubstituted hydrocarbon, and heterocyclyl; and

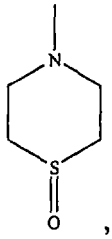
R^{34} is selected from the group consisting of hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; and

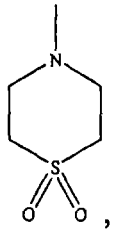
R^{41} is aryl; and

R^{42} is hydroxy; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



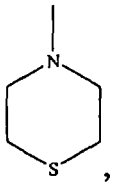
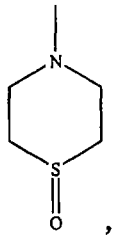
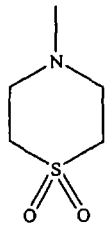
,


, and


, wherein:

the pyridinyl, pyrimidinyl, quinolinyl, and purinyl are substituted with one or more substituents independently selected from the group consisting of keto, haloarylamino, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxyarylamino, alkylsulfonylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, alkylheterocyclylalkylamino, heterocyclylheterocyclylalkylamino, and alkoxycarbonylheterocyclylamino, and

the maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,


,

, and


may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro, alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -$NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

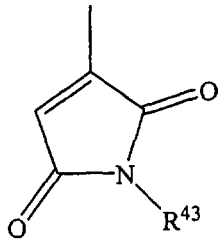
R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

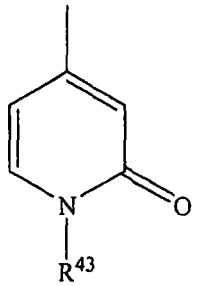
R^3 is not 2-pyridinyl when R^4 is a phenyl ring containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^3 is not:



(IV)

and



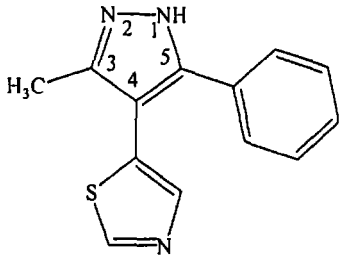
(V), wherein:

R^{43} is selected from the group consisting of hydrogen, alkyl, aminoalkyl, alkoxyalkyl, alkenoxyalkyl, and aryloxyalkyl; and

R^2 is selected from the group consisting of aryl, heterocyclyl, unsubstituted cycloalkyl, and cycloalkenyl when R^4 is hydrido; and

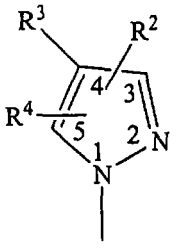
R^1 is not methylsulfonylphenyl; and

the compound does not correspond in structure to the following formula:



131. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer, wherein:

the compound corresponds in structure to Formula IA:



(IA); and

R^1 is selected from the group consisting of hydroxy and alkoxyaryl; and

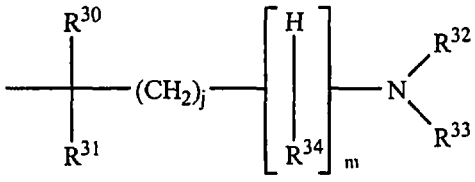
as to R^2:

R^2 is selected from the group consisting of R^{200}-heterocyclyl-R^{201}, R^{200}-aryl-R^{201}, R^{200}-cycloalkyl-R^{201}, -$NHCR^{204}R^{205}$, -$C(NR^{206})R^{207}$, -$CR^{41}R^{42}$, hydrido, halogen, mercapto, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, haloalkyl, hydroxyalkyl, arylalkyl, alkylheterocyclyl, heterocyclylalkyl, heterocyclylheterocyclyl, heterocyclylalkylheterocyclyl, alkylamino, alkenylamino, alkynylamino, arylamino, aryl(hydroxyalkyl)amino, heterocyclylamino, heterocyclylalkylamino, arylalkylamino, N-alkyl-N-alkynyl-amino, aminoalkyl, aminoaryl, aminoalkylamino, aminocarbonylalkyl, arylaminoalkyl, alkylaminoalkyl, arylaminoaryl, alkylaminoaryl, alkylaminoalkylamino, alkylcarbonylaminoalkyl, aminoalkylcarbonylaminoalkyl, alkylaminoalkylcarbonylamino, cycloalkyl, cycloalkenyl, aminoalkylthio, alkylaminocarbonylalkylthio, alkylaminoalkylaminocarbonylalkylthio, alkoxy, heterocyclyloxy, alkylthio, cyanoalkylthio, alkenylthio, alkynylthio, carboxyalkylthio, arylthio, heterocyclylthio, alkoxycarbonylalkylthio, alkylsulfinyl, alkylsulfonyl, carboxy, carboxyalkyl, alkoxyalkyl, alkoxyalkylthio, carboxycycloalkyl, carboxycycloalkenyl, carboxyalkylamino, alkoxycarbonyl, heterocyclylcarbonyl, alkoxycarbonylalkyl,

alkoxycarbonylalkylamino, alkoxycarbonylheterocyclyl, alkoxycarbonylheterocyclylcarbonyl, alkoxyalkylamino, alkoxycarbonylaminoalkyl, alkoxycarbonylaminoalkoxy, alkoxycarbonylaminoalkylamino, heterocyclylsulfonyl, arylalkythio, heterocyclylalkylthio, aminoalkoxy, cyanoalkoxy, carboxyalkoxy, aryloxy, arylalkoxy, alkenyloxy, alkynyloxy, and heterocyclylalkyloxy, wherein:

the aryl, heterocyclyl, heterocyclylalkyl, cycloalkyl, and cycloalkenyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, amino, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, epoxyalkyl, amino(hydroxyalkyl) carboxy, alkoxy, aryloxy, arylalkoxy, haloalkyl, alkylamino, alkynylamino, alkylaminoalkylamino, heterocyclylalkylamino, alkylcarbonyl, alkoxycarbonyl, arylsulfonyl, and arylalkylsulfonyl, or

R^2 has the formula:



(III); and

R^{200} is selected from the group consisting of:

$-(CR^{202}R^{203})_y-$,

$-C(O)-$,

$-C(O)-(CH_2)_y-$,

$-C(O)-O-(CH_2)_y-$,

$-(CH_2)_y-C(O)-$,

$-O-(CH_2)_y-C(O)-$,

$-NR^{202}-(CH_2)_y-$,

$-(CH_2)_y-NR^{202}-$,

$-(CH_2)_y-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-C(O)-NR^{202}-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-(CH_2)_z-$,

$-(CH_2)_y-NR^{202}-C(O)-NR^{203}-(CH_2)_z-$,

$-S(O)_x-(CR^{202}R^{203})_y-$,

$-(CR^{202}R^{203})_y-S(O)_x-$,

$-S(O)_x-(CR^{202}R^{203})_y-O-$,

$-S(O)_x-(CR^{202}R^{203})_y-C(O)-$,

$-O-(CH_2)_y-$,

$-(CH_2)_y-O-$,

-S-,

-O-,

a bond; and

R^{201} represents one or more substituents independently selected from the group consisting of hydrido, halogen, hydroxy, carboxy, keto, alkyl, hydroxyalkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, alkylcarbonyl, hydroxyalkylcarbonyl, cycloalkylcarbonyl, arylcarbonyl, haloarylcarbonyl, alkoxy, alkoxyalkyl, alkoxyaryl, alkoxycarbonyl, carboxyalkylcarbonyl, alkoxyalkylcarbonyl, heterocyclylalkylcarbonyl, alkylsulfonylalkyl, amino, aminoalkyl, alkylamino, arylalkylamino, alkylaminoalkyl, aminocarbonyl, alkylcarbonylamino, alkylcarbonylaminoalkyl, alkylaminoalkylcarbonyl, alkylaminoalkylcarbonylamino, aminoalkylcarbonylaminoalkyl, alkoxycarbonylamino, alkoxyalkylcarbonylamino, alkoxycarbonylaminoalkyl, alkylimidocarbonyl, amidino, alkylamidino, arylalkylamidino, guanidino, guanidinoalkyl, and alkylsulfonylamino; and

R^{202} and R^{203} are independently selected from the group consisting of hydrido, alkyl, aryl, and arylalkyl; and

y and z are independently selected from the group consisting of zero, 1, 2, 3, 4, 5, and 6; and

the sum of y + z is less than or equal to 6; and

x is selected from the group consisting of zero, 1, and 2; and

R^{204} is alkylaminoalkyl; and and

R^{205} is aryl; and

R^{206} is selected from the group consisting of hydrogen and hydroxy; and

R^{207} is selected from the group consisting of alkyl, aryl, and arylalkyl; and

j is an integer from zero to 8; and

m is selected from the group consisting of zero and 1; and

R^{30} and R^{31} are independently selected from the group consisting of hydrogen, alkyl, aryl, heterocyclyl, arylalkyl, heterocyclylalkyl, aminoalkyl, alkylaminoalkyl, aminocarbonylalkyl,

alkoxyalkyl, and alkylcarbonyloxyalkyl; and

R^{32} is selected from the group consisting of hydrogen, alkyl, arylalkyl, heterocyclylalkyl, alkoxyalkyl, aryloxyalkyl, aminoalkyl, alkylaminoalkyl, arylaminoalkyl, alkylcarbonylalkyl, arylcarbonylalkyl, and heterocyclylcarbonylaminoalkyl; and

R^{33} is selected from the group consisting of hydrogen, alkyl, $-C(O)R^{35}$, $-C(O)OR^{35}$, $-SO_2R^{36}$, $-C(O)NR^{37}R^{38}$, and $-SO_2NR^{39}R^{40}$; and

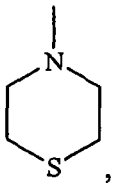
R^{35}, R^{36}, R^{37}, R^{38}, R^{39}, and R^{40} are independently selected from the group consisting of hydrocarbon, heterosubstituted hydrocarbon, and heterocyclyl; and

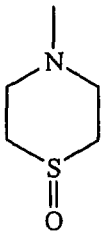
R^{34} is selected from the group consisting of hydrogen, alkyl, aminocarbonyl, alkylaminocarbonyl, and arylaminocarbonyl; and

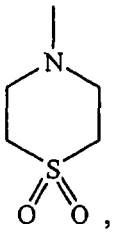
R^{41} is aryl; and

R^{42} is hydroxy; and

R^3 is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, purinyl, maleimidyl, pyridonyl, thiazolyl, thiazolylalkyl, thiazolylamino,



,


, and


, wherein:

any such substituent may be optionally substituted with one or more substituents independently selected from the group consisting of halo, keto, alkyl, arylalkyl, arylalkenyl, arylheterocyclyl, carboxy, carboxyalkyl, alkoxy, aryloxy, alkylthio, arylthio, alkylsulfinyl, arylsulfinyl, arylsulfonyl, arylalkoxy, heterocyclylalkoxy, amino, alkylamino, alkenylamino, alkynylamino, cycloalkylamino, cycloalkenylamino, arylamino, haloarylamino, heterocyclylamino, aminocarbonyl, cyano, hydroxy, hydroxyalkyl, alkoxyalkyl, alkenoxyalkyl, aryloxyalkyl, alkoxyalkylamino, alkylaminoalkoxy, alkoxycarbonyl, aryloxycarbonyl, heterocyclyloxycarbonyl, alkoxycarbonylamino, alkoxyarylamino, alkoxyarylalkylamino, aminosulfinyl, alkylsulfonylamino, alkylaminoalkylamino, hydroxyalkylamino, arylalkylamino, aryl(hydroxyalkyl)amino, alkylaminoalkylaminoalkylamino, alkylheterocyclylamino, heterocyclylalkylamino, alkylheterocyclylalkylamino, arylalkylheterocyclylamino, heterocyclylheterocyclylalkylamino, alkoxycarbonylheterocyclylamino, nitro,

alkylaminocarbonyl, alkylcarbonylamino, aminoalkyl, haloalkyl, alkylcarbonyl, hydrazinyl, alkylhydrazinyl, arylhydrazinyl, and -$NR^{44}R^{45}$; and

R^{44} is selected from the group consisting of alkylcarbonyl and amino; and

R^{45} is selected from the group consisting of alkyl and arylalkyl; and

R^4 is selected from the group consisting of hydrido, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, aryl, and heterocyclyl, wherein:

the alkyl, alkenyl, and alkynyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

the cycloalkyl, cycloalkenyl, aryl, and heterocyclyl may be optionally substituted with one or more substituents independently selected from the group consisting of halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, arylthio, alkylthioalkyl, arylthioalkyl, alkylsulfinyl, alkylsulfinylalkyl, arylsulfinylalkyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, arylalkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, and hydroxy; and

R^3 is not 2-pyridinyl when R^4 is a phenyl ring containing a 2-hydroxy substituent and when R^1 is hydrido; and

R^2 is selected from the group consisting of aryl, heterocyclyl, unsubstituted cycloalkyl, and cycloalkenyl when R^4 is hydrido.

132. A pharmaceutical composition, wherein:

the pharmaceutical composition comprises a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt of the compound; and

said compound is selected from the group consisting of the compounds recited in Claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

133. A use of a therapeutically-effective amount of a compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer to prepare a pharmaceutical composition for treating a tumor necrosis factor mediated disorder, wherein said compound is selected from the group of compounds recited in Claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

134. A use of a therapeutically-effective amount of a compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer to prepare a pharmaceutical composition for treating a p38 kinase mediated disorder, wherein said compound is selected from the group of compounds recited in Claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

135. The use according to Claim 134, wherein the p38 kinase mediated disorder is selected from the group of disorders consisting of bone resorption, graft vs. host reaction, atherosclerosis, arthritis, osteoarthritis, rheumatoid arthritis, gout, psoriasis, topical inflammatory disease state, adult respiratory distress syndrome, asthma, chronic pulmonary inflammatory disease, cardiac reperfusion injury, renal reperfusion injury, thrombus, glomerulonephritis, Crohn's disease, ulcerative colitis, inflammatory bowel disease, and cachexia.

136. The use according to Claim 134, wherein the p38 kinase mediated disorder is inflammation.

137. The use according to Claim 134, wherein the p38 kinase mediated disorder is arthritis.

138. The use according to Claim 134, wherein the p38 kinase mediated disorder is asthma.

139. A use of a therapeutically-effective amount of a compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer to prepare a pharmaceutical composition for treating inflammation, wherein said compound is selected from

the group of compounds recited in Claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

140. A use of a therapeutically-effective amount of a compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer to prepare a pharmaceutical composition for treating arthritis, wherein said compound is selected from the group of compounds recited in Claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

141. A method of preparing a pyrazole, a tautomer of the pyrazole, or a pharmaceutically-acceptable salt of the pyrazole or tautomer, wherein:

the method comprises treating a substituted ketone with an acyl hydrazide to form the pyrazole; and

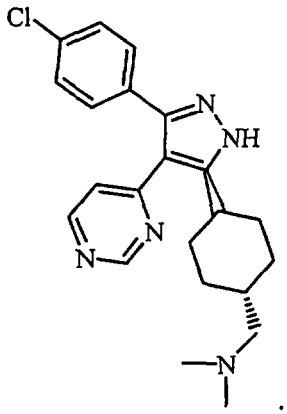
the pyrazole is selected from the group of compounds recited in claims 1, 39, 71, 82, 93, 94, 125, 126, 127, 128, 129, 131, and 150.

142. The process of Claim 141, wherein the process is carried out in an acidic solvent.

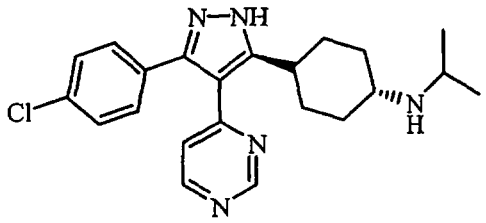
143. The process of Claim 141, wherein the acidic solvent is acetic acid.

144. The process of Claim 141, wherein the acidic solvent is an organic solvent containing an acid.

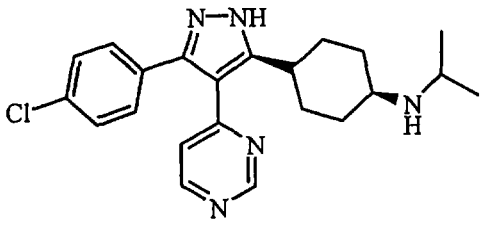
145. A compound, a tautomer of the compound, or pharmaceutically-acceptable a salt of the compound or tautomer according to Claim 42, wherein the compound corresponds in structure to the following formula:



146. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 71, wherein the compound corresponds in structure to a formula selected from the group consisting of:

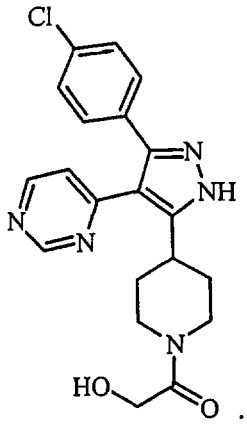


; and

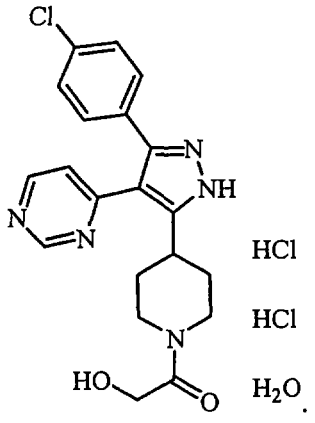


147. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 70, wherein R^{404a} is meta-chloro or para-chloro.

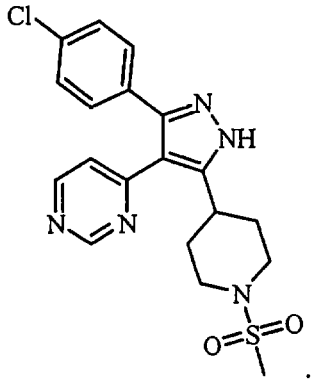
148. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to Claim 1, wherein the compound corresponds in structure to a formula selected from the group consisting of:



149. A salt according to claim 148, wherein the salt corresponds in structure to the following formula:



150. A compound or a pharmaceutically-acceptable salt of the compound, wherein the compound corresponds in structure to a formula selected from the group consisting of:



151. A compound, a tautomer of the compound, or a pharmaceutically-acceptable salt of the compound or tautomer according to claim 1, 39, 93, 126, 127, 128, 129, or 131, wherein the compound corresponds in structure to the following formula:

