

Synthesis, antimicrobial and ergosterol biosynthesis inhibition activity of clubbed 1,1'-biphenyl-pyrazole derivatives

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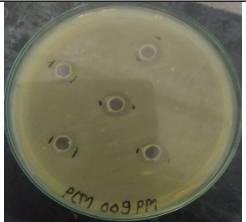


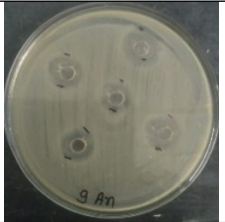

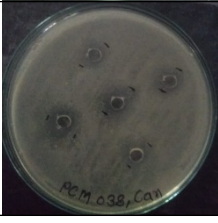


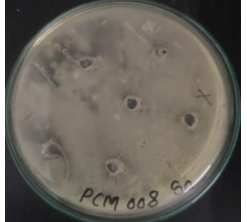

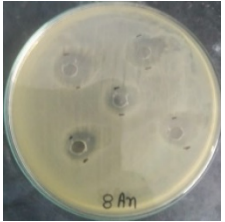




^fDepartment of Zoology, S. P. Mandali's Sir Parashurambhau College, Tilak Road, Pune, India 411 030, (Affiliated to Savitribai Phule Pune University).












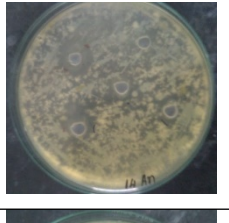

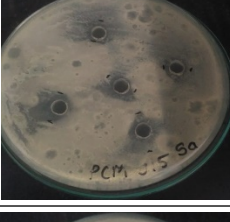

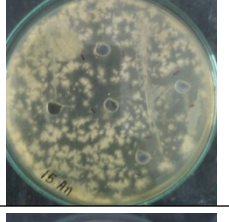



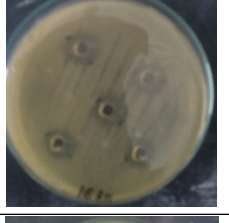







^gPost-Graduate Department of Chemistry H. P. T. Arts and R. Y. K. Science College, Nashik India 422005 (Affiliated to Savitribai Phule Pune University).











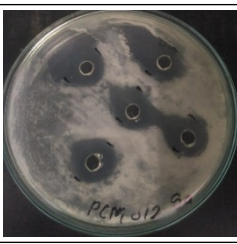

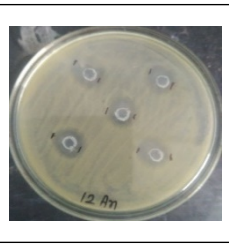




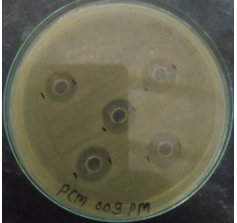


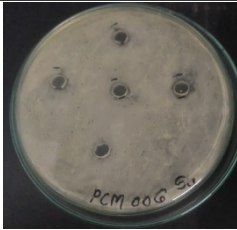


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Pravin C Mhaske (Email: mhaskepc18@gmail.com)

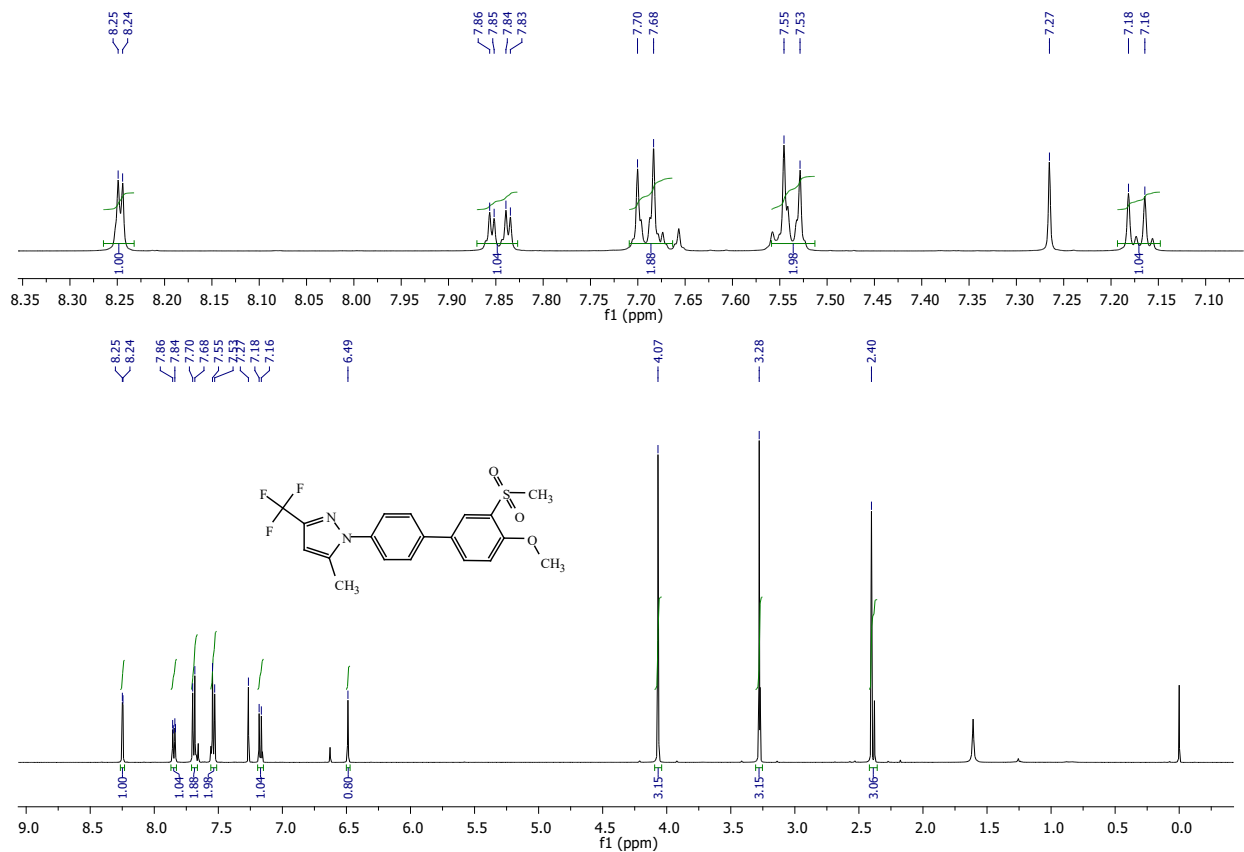
Table S1: Representative petri plates images of the antimicrobial activity of synthesized 1,1'-biphenyl-pyrazole derivatives

Petri plate no.	Compd. No	<i>P. mirabilis</i>	<i>S. albus</i>	<i>C. Albicans</i>	<i>A. Niger</i>
39	5a				
40	5b				
09	5c				
38	5d				
08	5e				
02	5f				

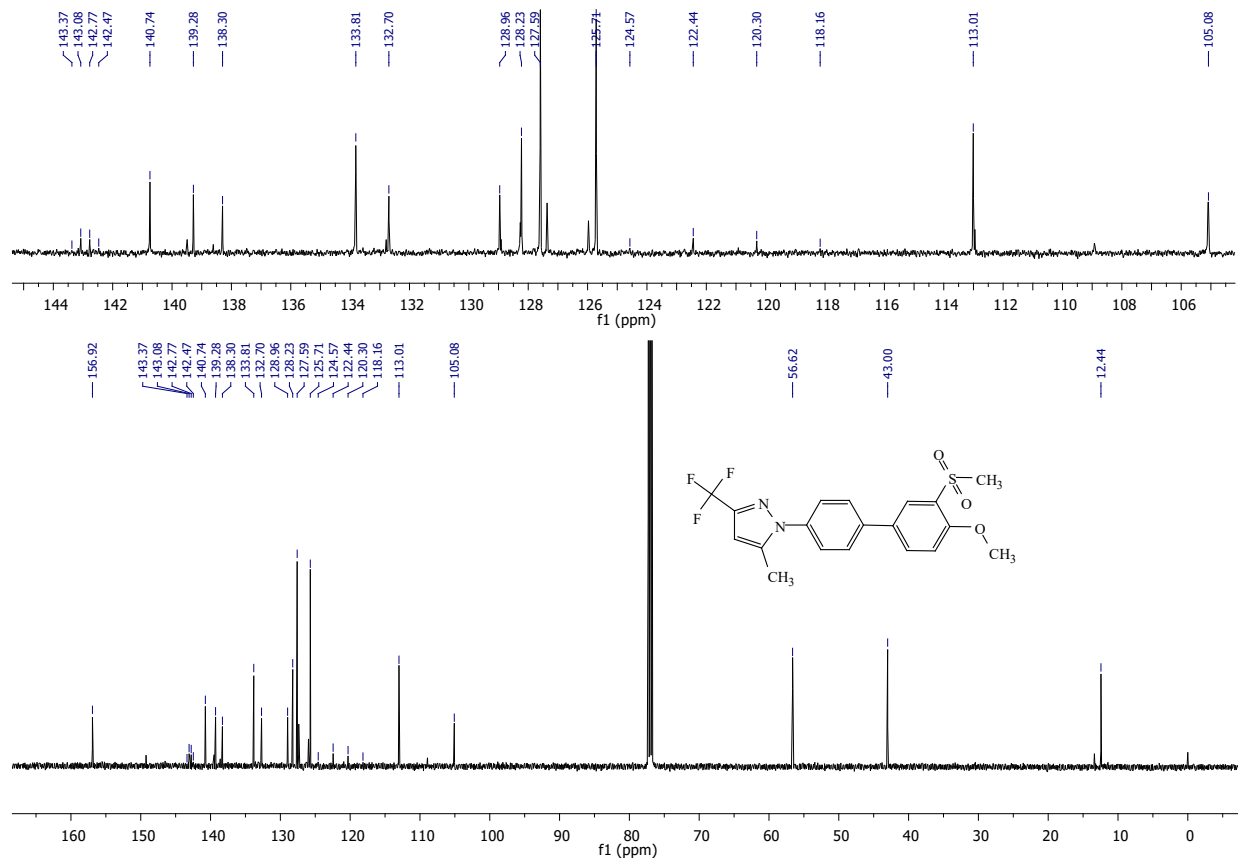
01	5g				
10	6a				
14	6b				
15	6c				
16	6d				
05	6e				
17	9a				

34	9b				
35	9c				
13	10a				
12	10b				
36	10c				
03	11a				
06	11c				

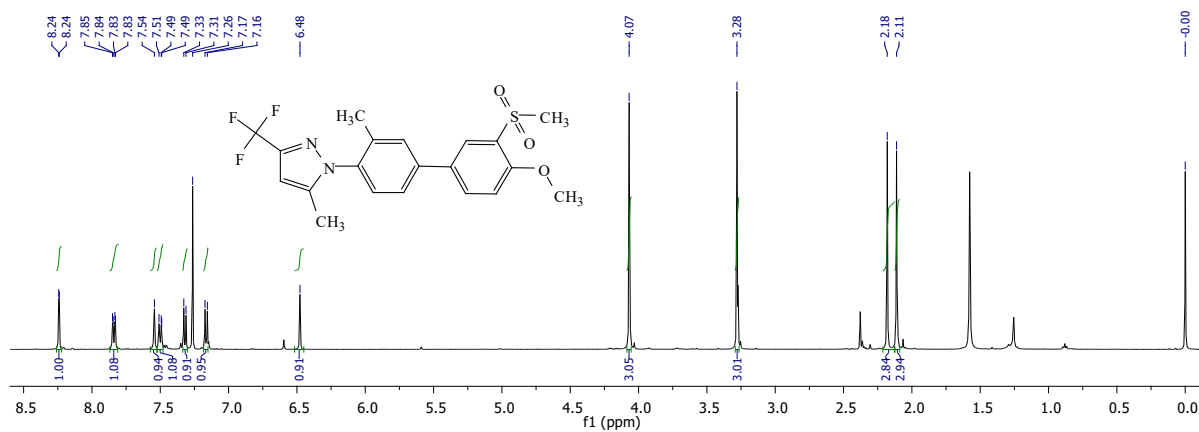
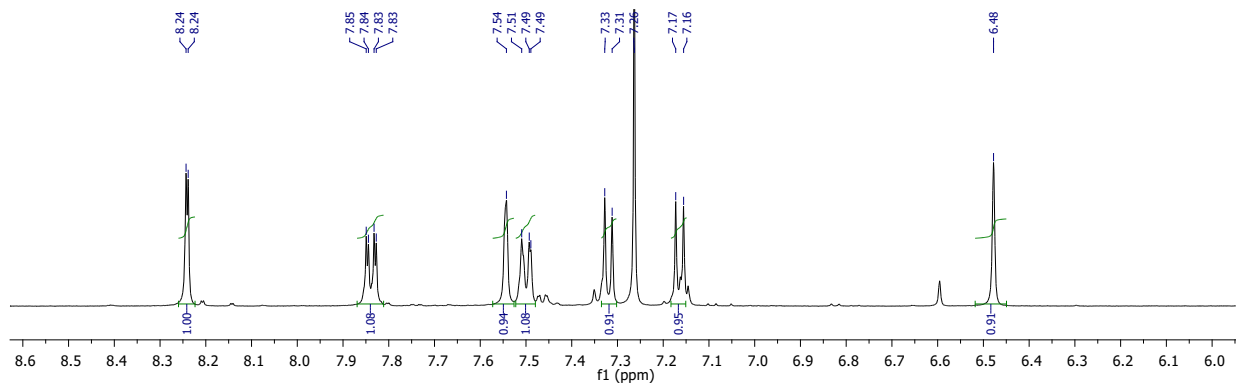
Representative spectral data



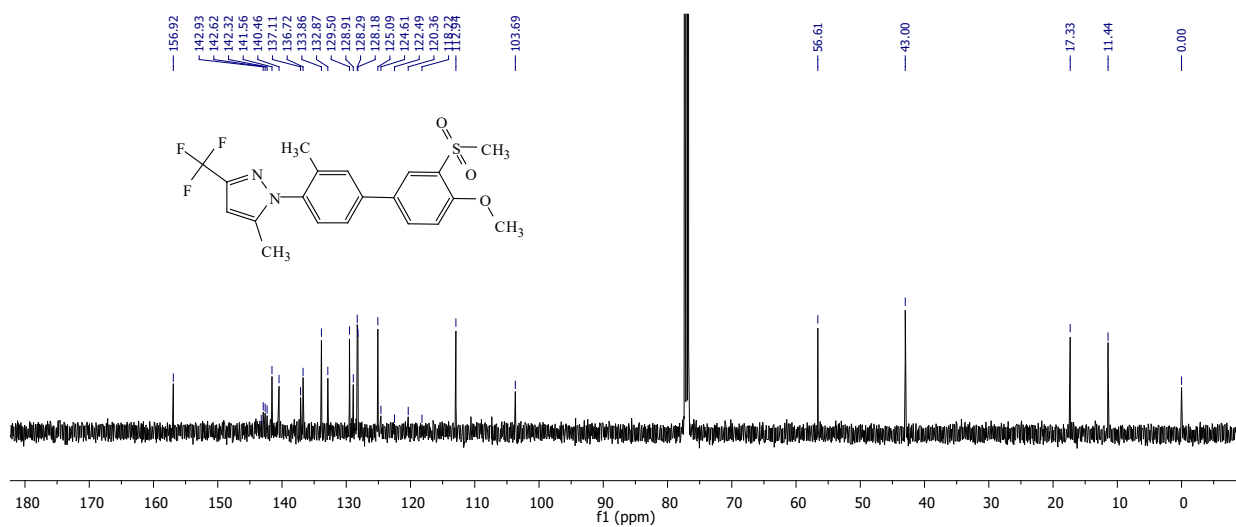
¹H NMR spectrum (500 MHz, CDCl₃) of 1-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1*H*-pyrazole (**5a**)



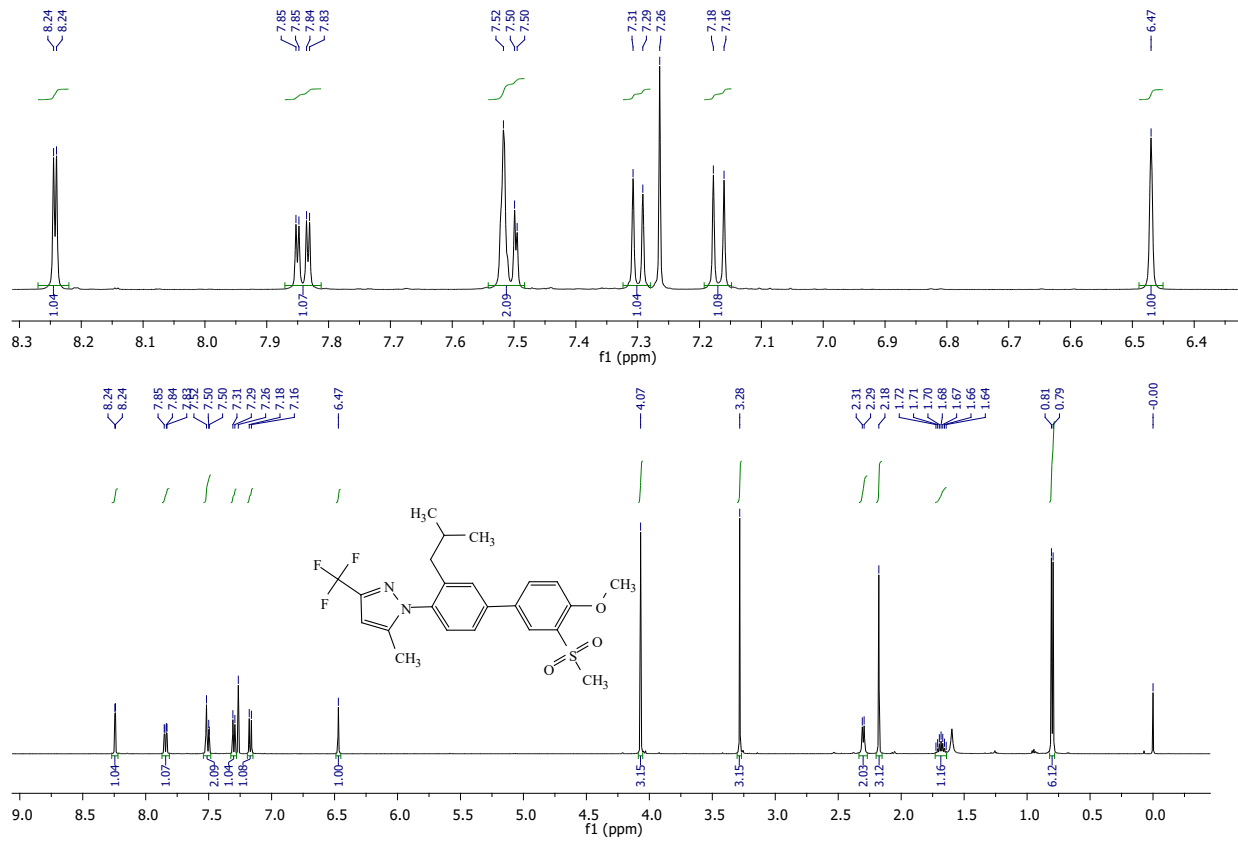
^{13}C NMR spectrum (126 MHz, CDCl_3) of 1-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5a**)



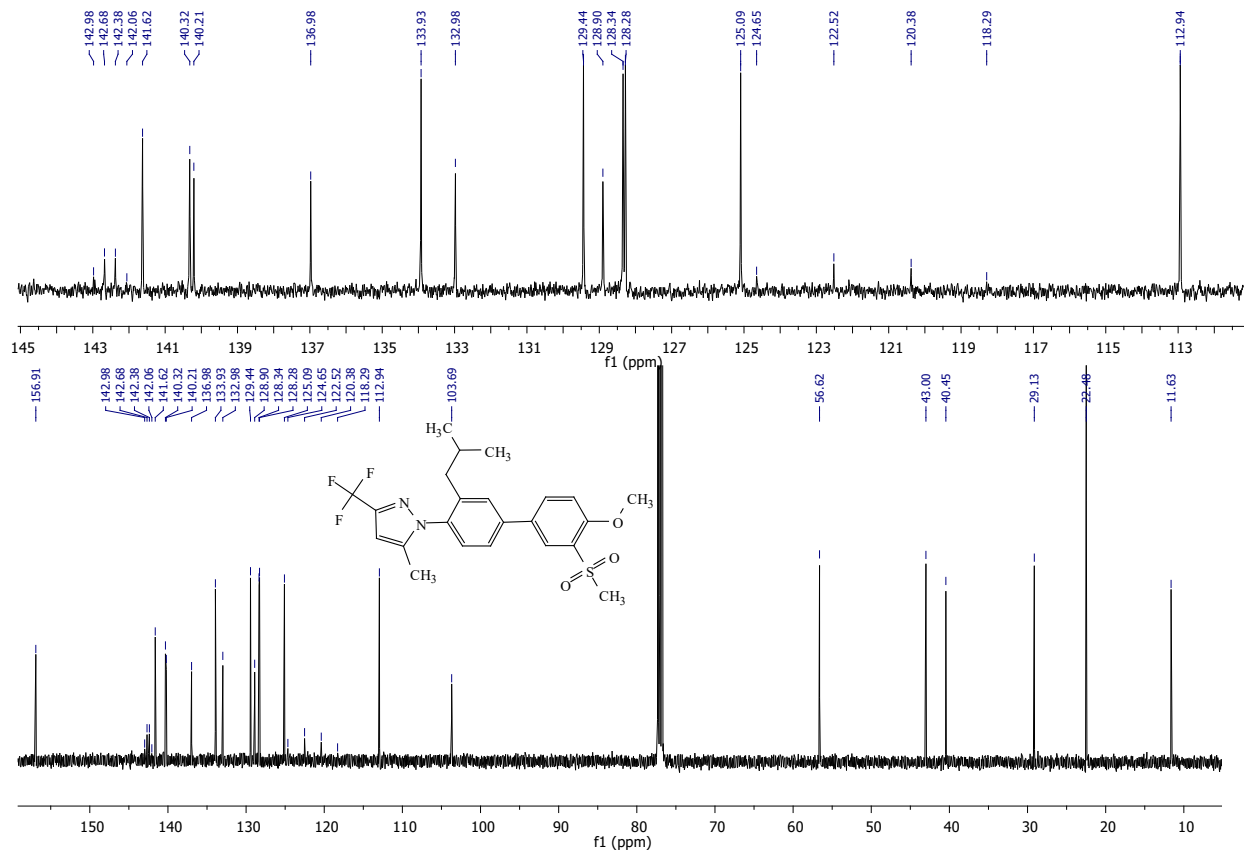
^1H NMR spectrum (500 MHz, CDCl_3) of 1-(4'-methoxy-3-methyl-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5b**)



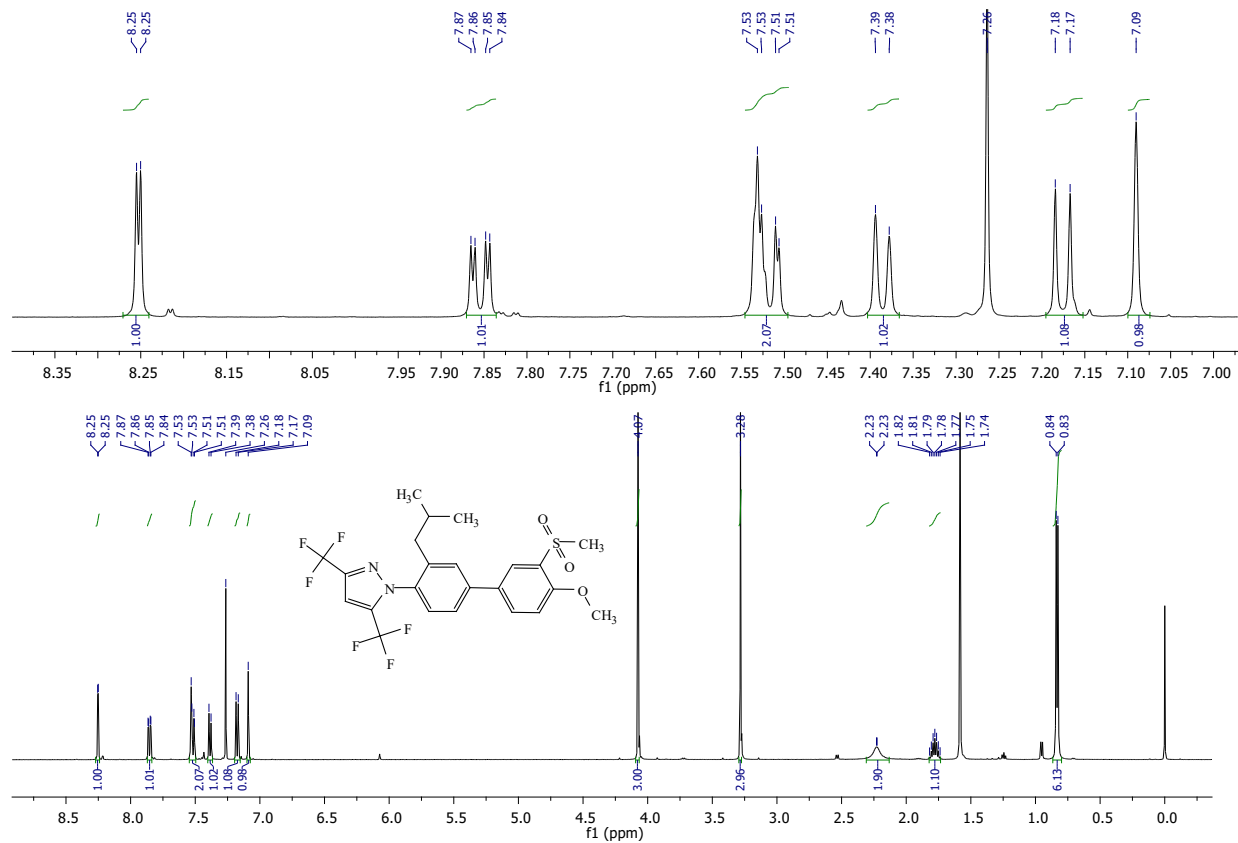
^{13}C NMR spectrum (126 MHz, CDCl_3) of 1-(4'-methoxy-3-methyl-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5b**)



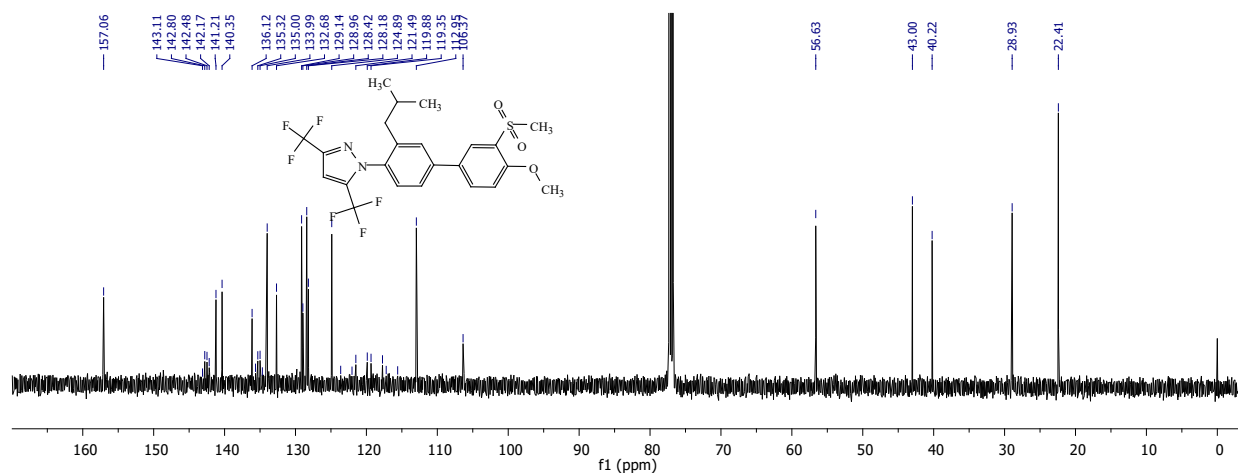
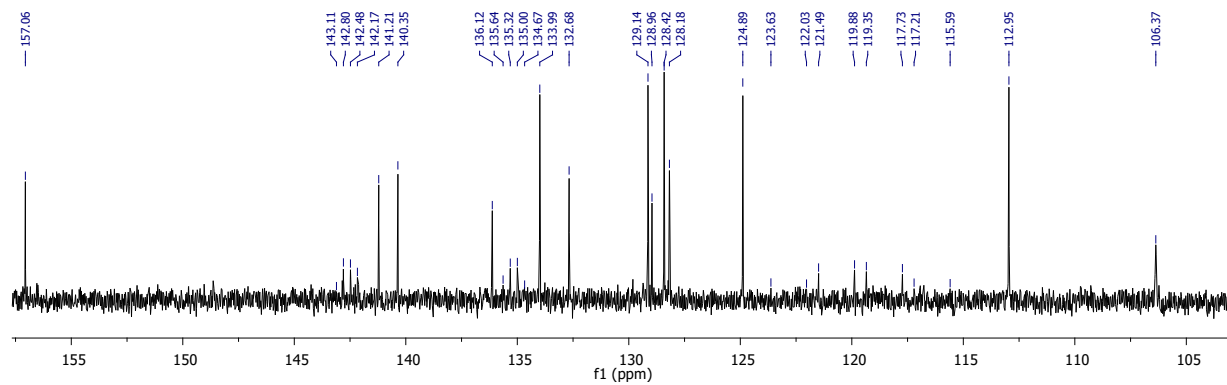
¹H NMR spectrum (500 MHz, CDCl₃) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1*H*-pyrazole (**5c**)



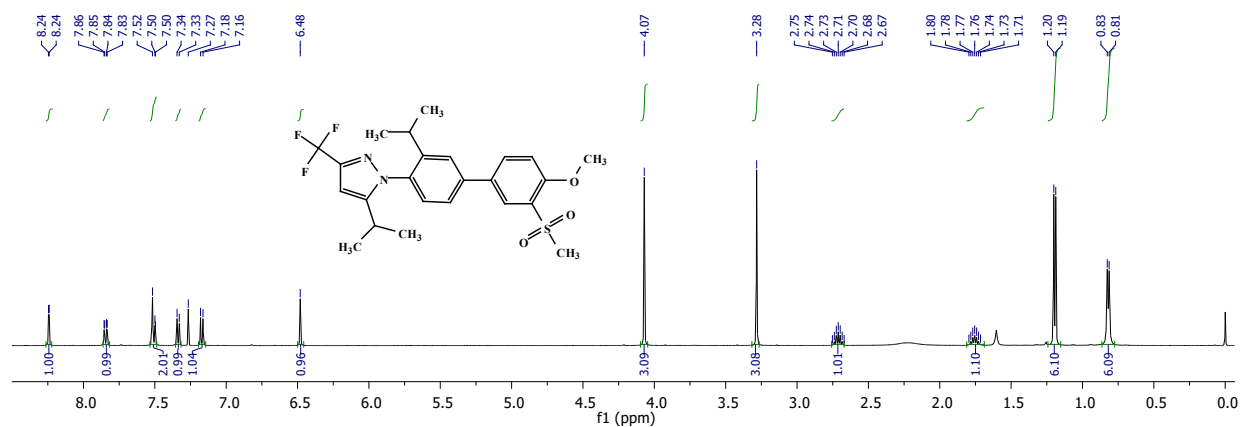
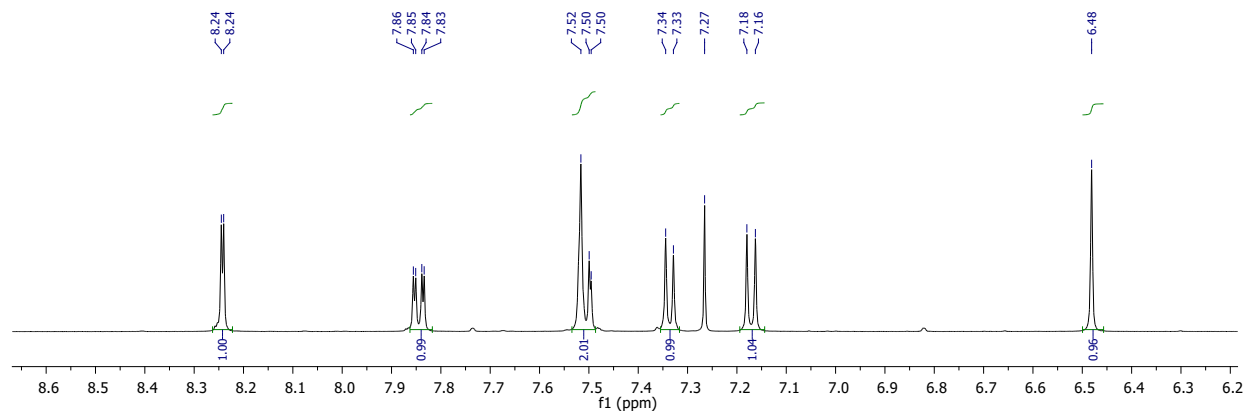
¹³C NMR spectrum (126 MHz, CDCl₃) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1*H*-pyrazole (**5c**)



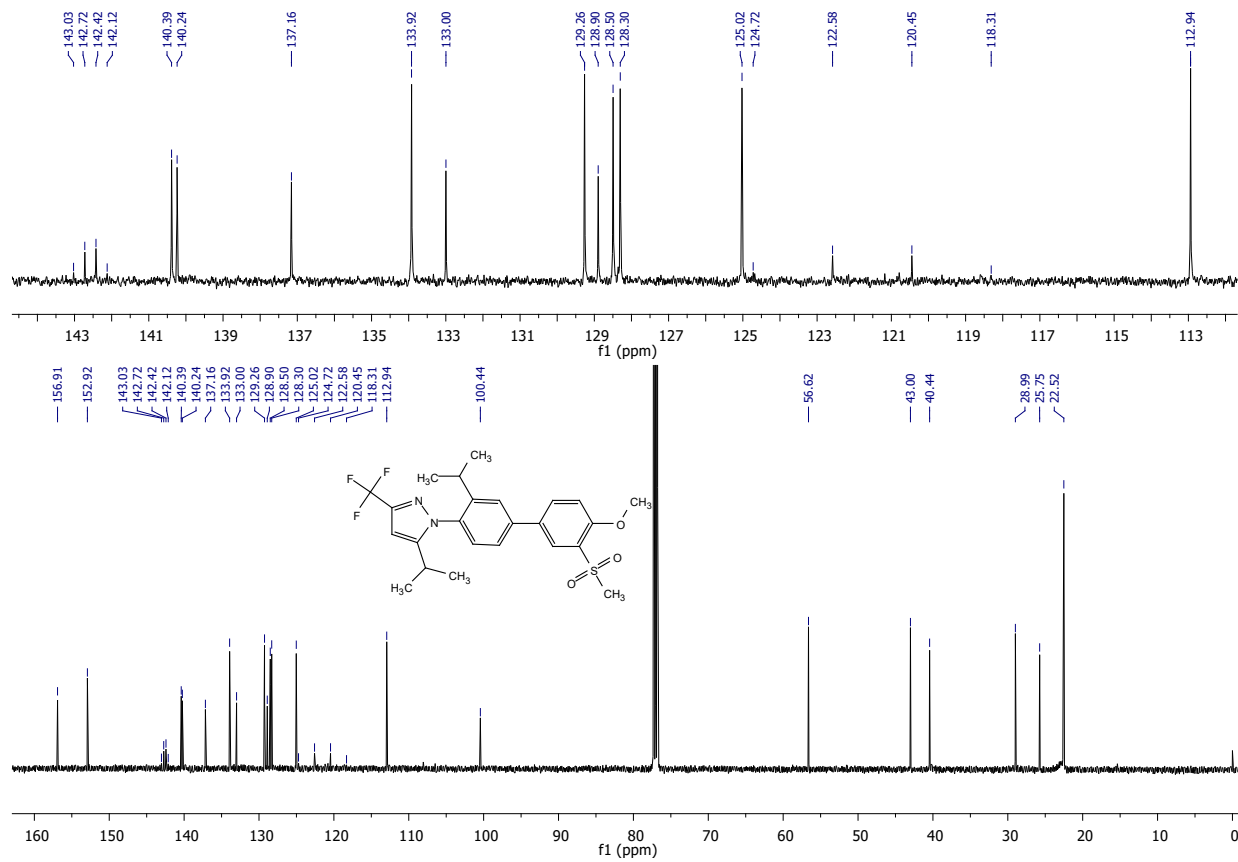
¹H NMR spectrum (500 MHz, CDCl₃) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3,5-bis(trifluoromethyl)-1*H*-pyrazole (**5d**)



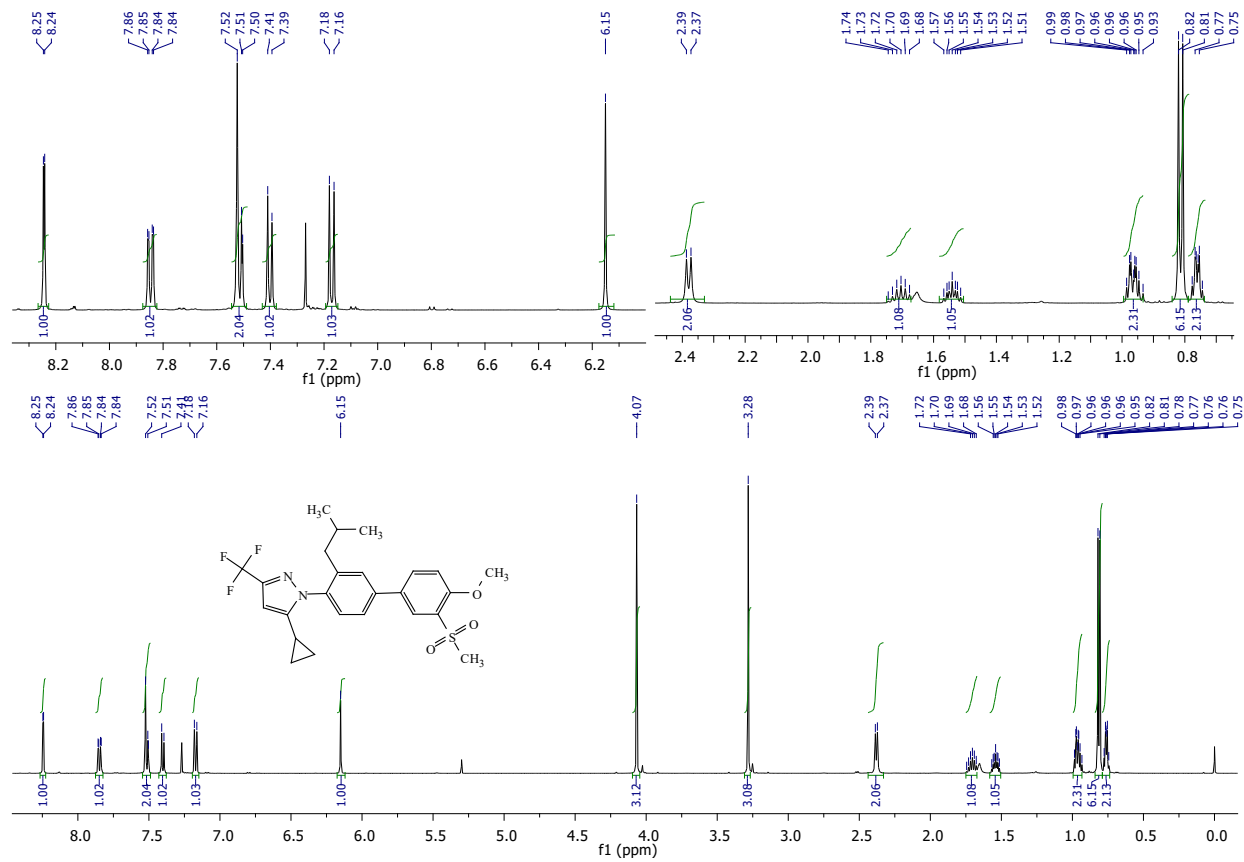
¹³C NMR spectrum (126 MHz, CDCl₃) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3,5-bis(trifluoromethyl)-1*H*-pyrazole (**5d**)



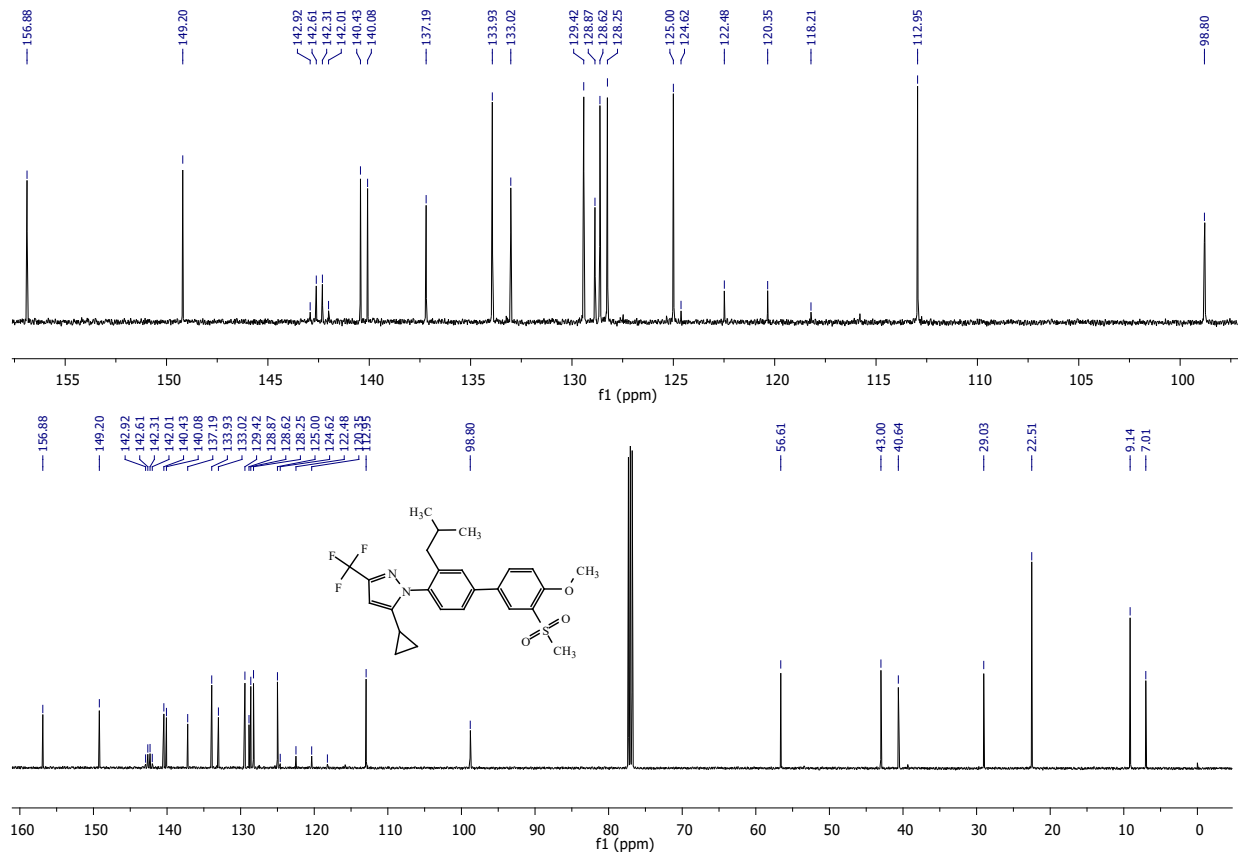
^1H NMR spectrum (500 MHz, CDCl_3) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-isopropyl-3-(trifluoromethyl)-1*H*-pyrazole (**5e**)



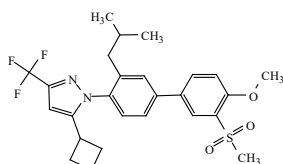
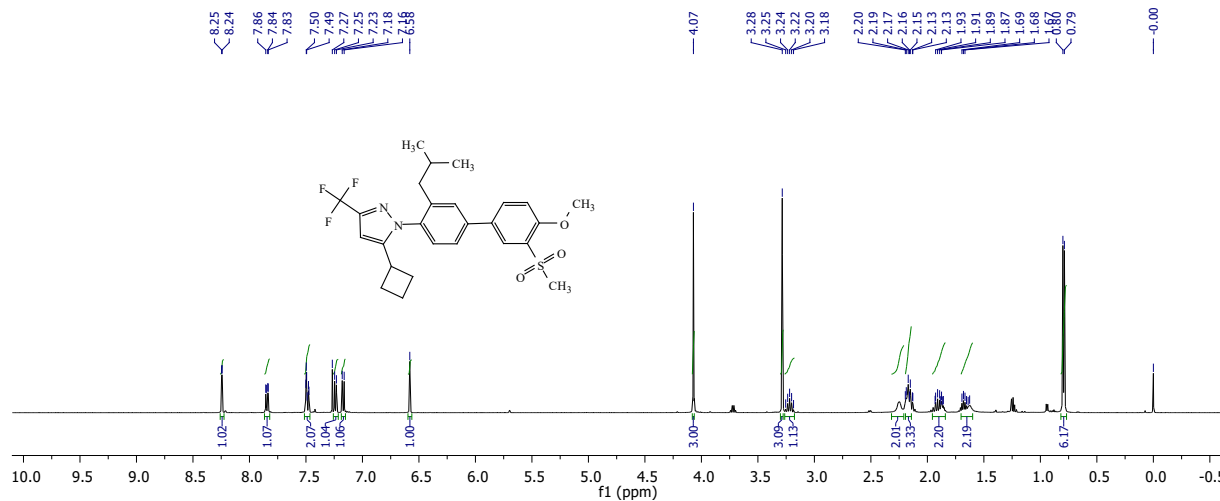
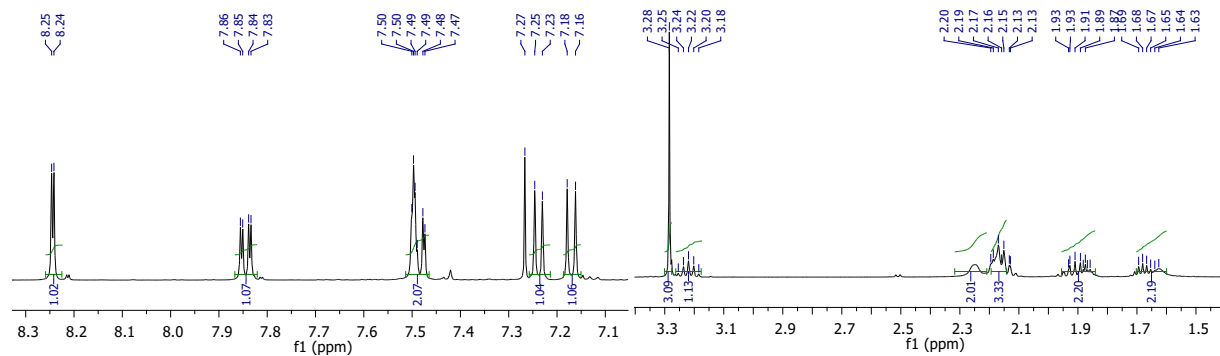
¹³C NMR spectrum (126 MHz, CDCl₃) of 1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-isopropyl-3-(trifluoromethyl)-1*H*-pyrazole (**5e**)



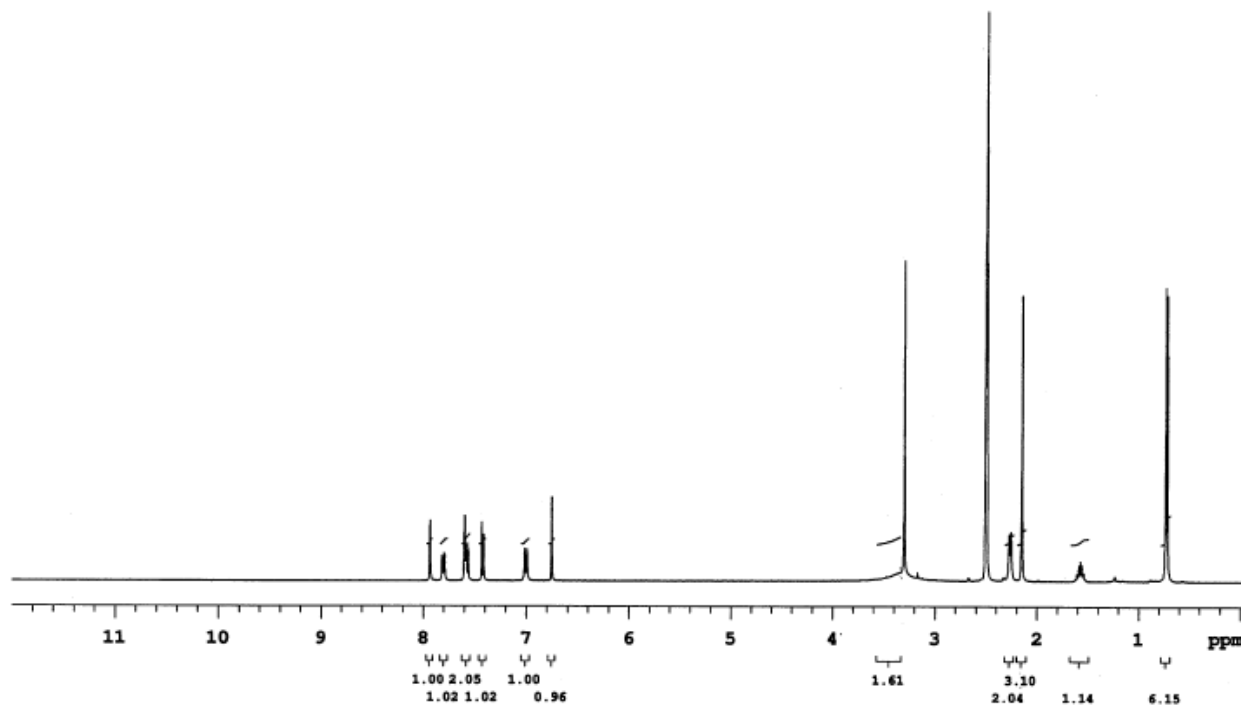
¹H NMR spectrum (500 MHz, CDCl₃) of 5-cyclopropyl-1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**5f**)



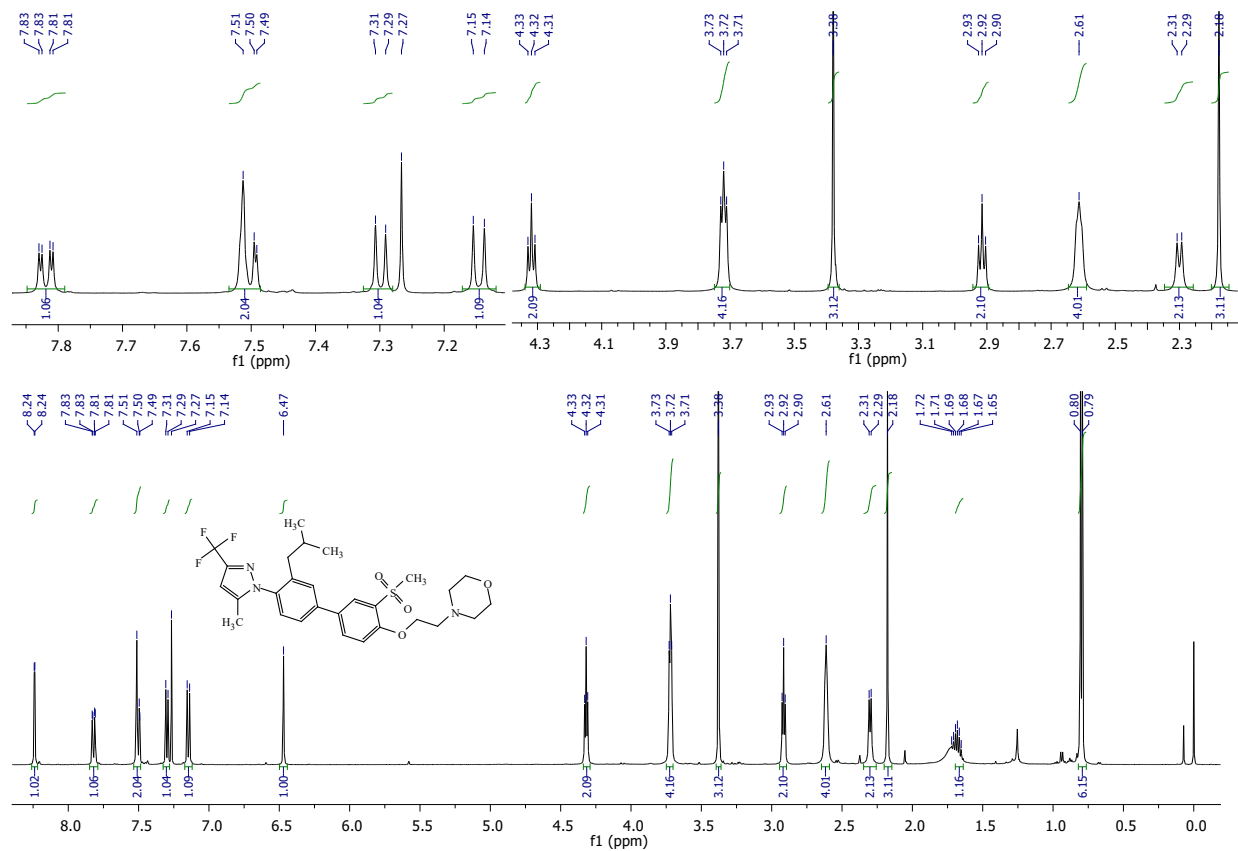
¹³C NMR spectrum (126 MHz, CDCl₃) of 5-cyclopropyl-1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**5f**)



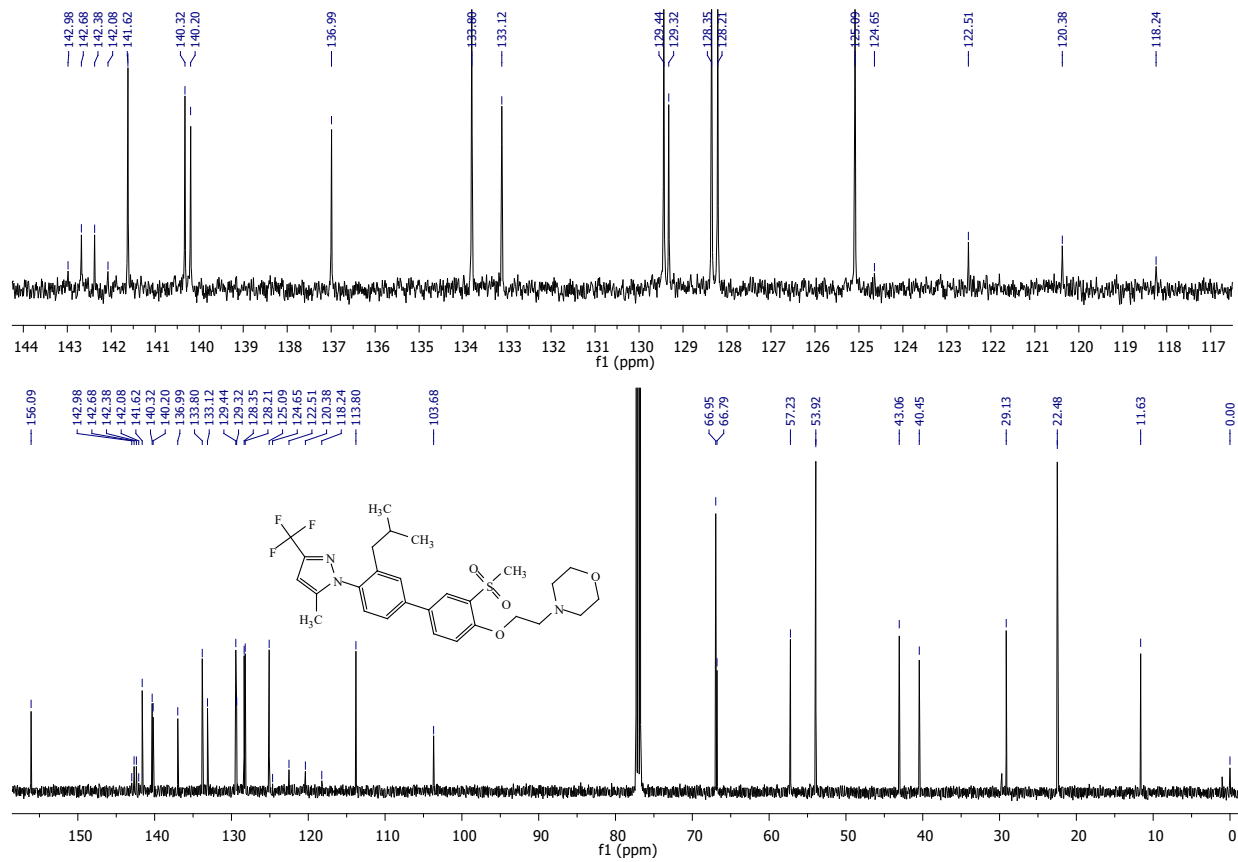
^1H NMR spectrum (500 MHz, CDCl_3) of 5-cyclobutyl-1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**5g**)



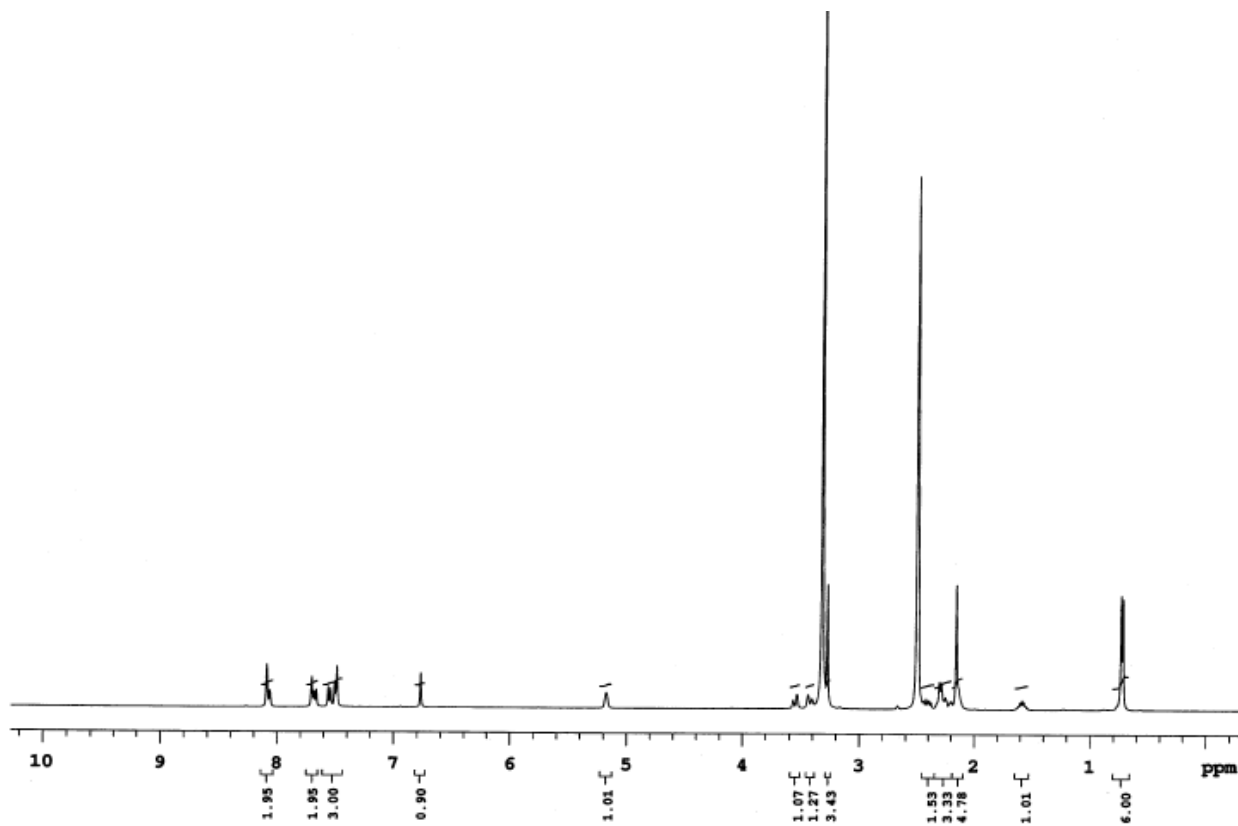
^1H NMR spectrum (400 MHz, $\text{DMSO-}d_6$) of 3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**6a**)



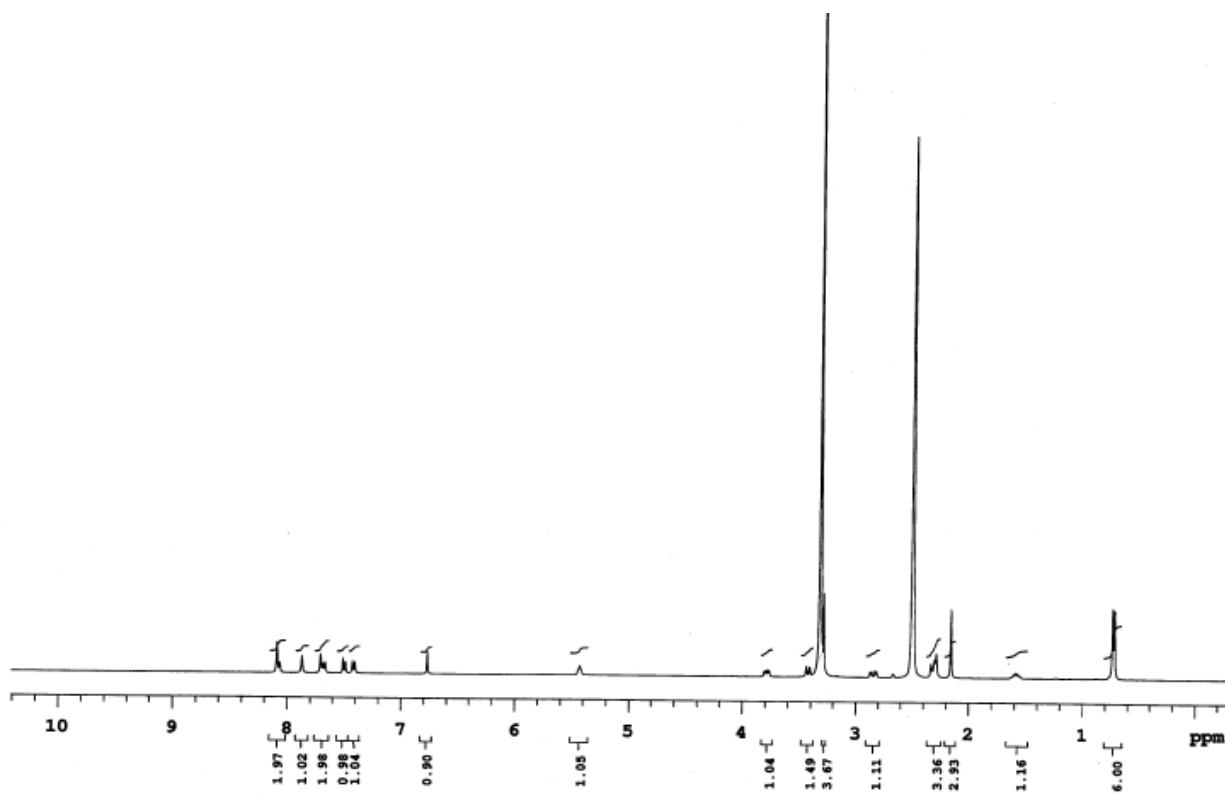
¹H NMR spectrum (500 MHz, CDCl₃) of 4-(2-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)ethyl)morpholine (**6b**)



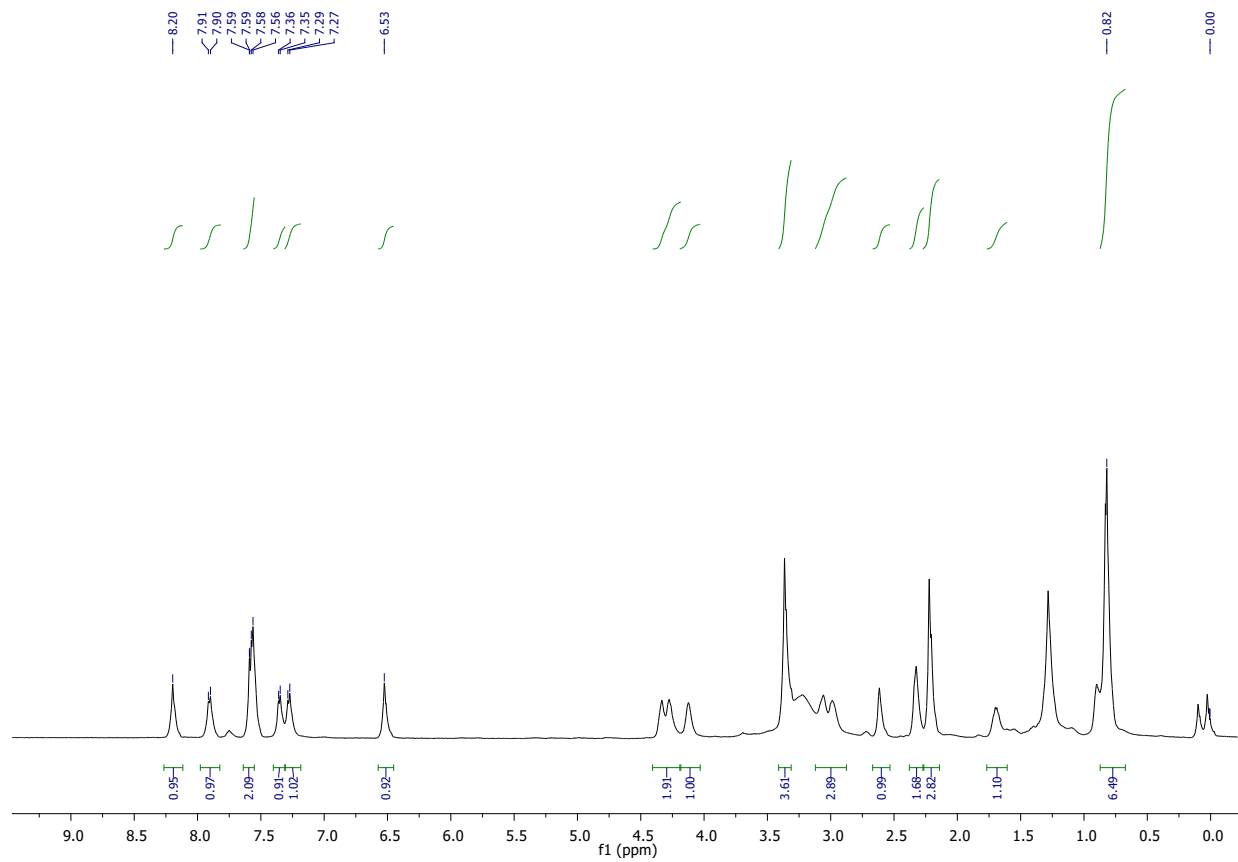
¹³C NMR spectrum (126 MHz, CDCl₃) of 4-(2-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)ethyl)morpholine (**6b**)



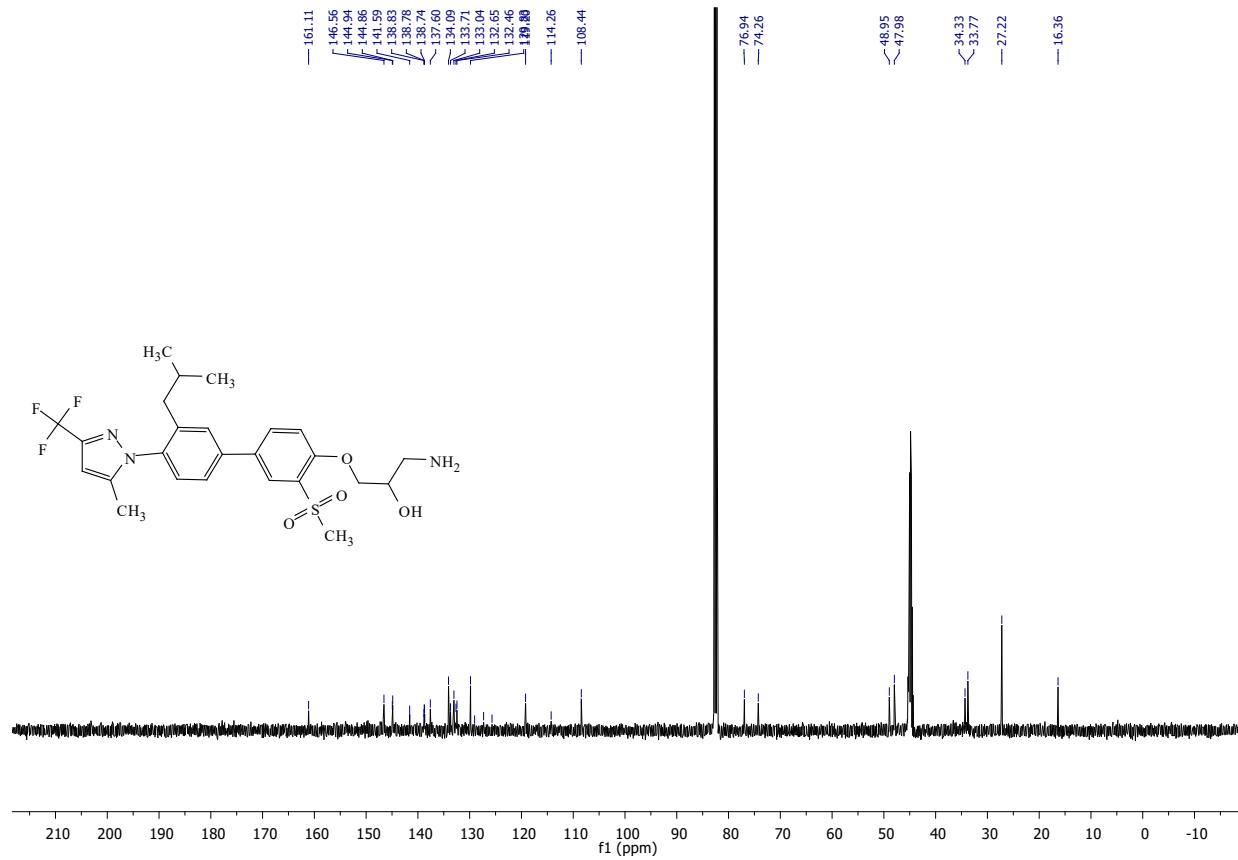
¹H NMR spectrum (400 MHz, DMSO-*d*₆) of 5-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)piperidin-2-one, (**6c**)



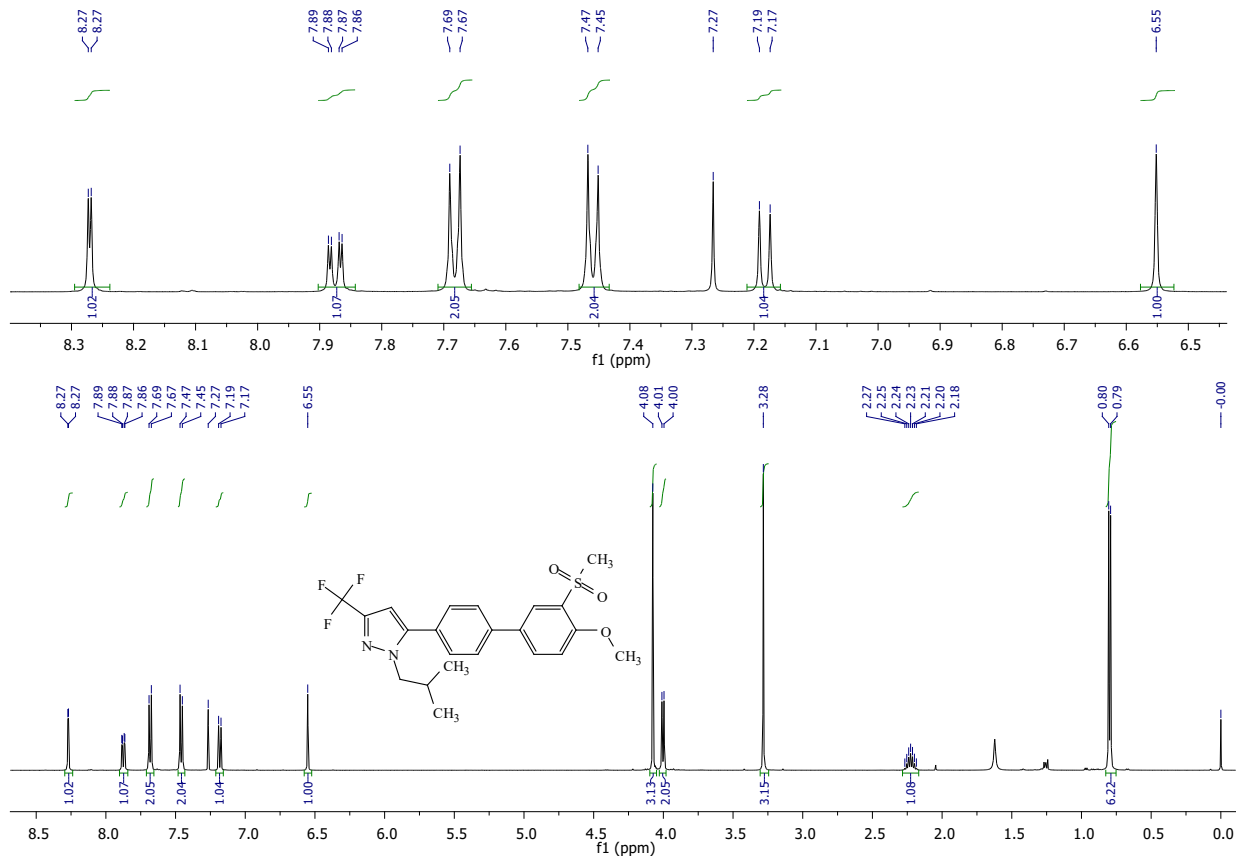
¹H NMR spectrum (400 MHz, DMSO-*d*₆) of 4-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)pyrrolidin-2-one (**6d**)

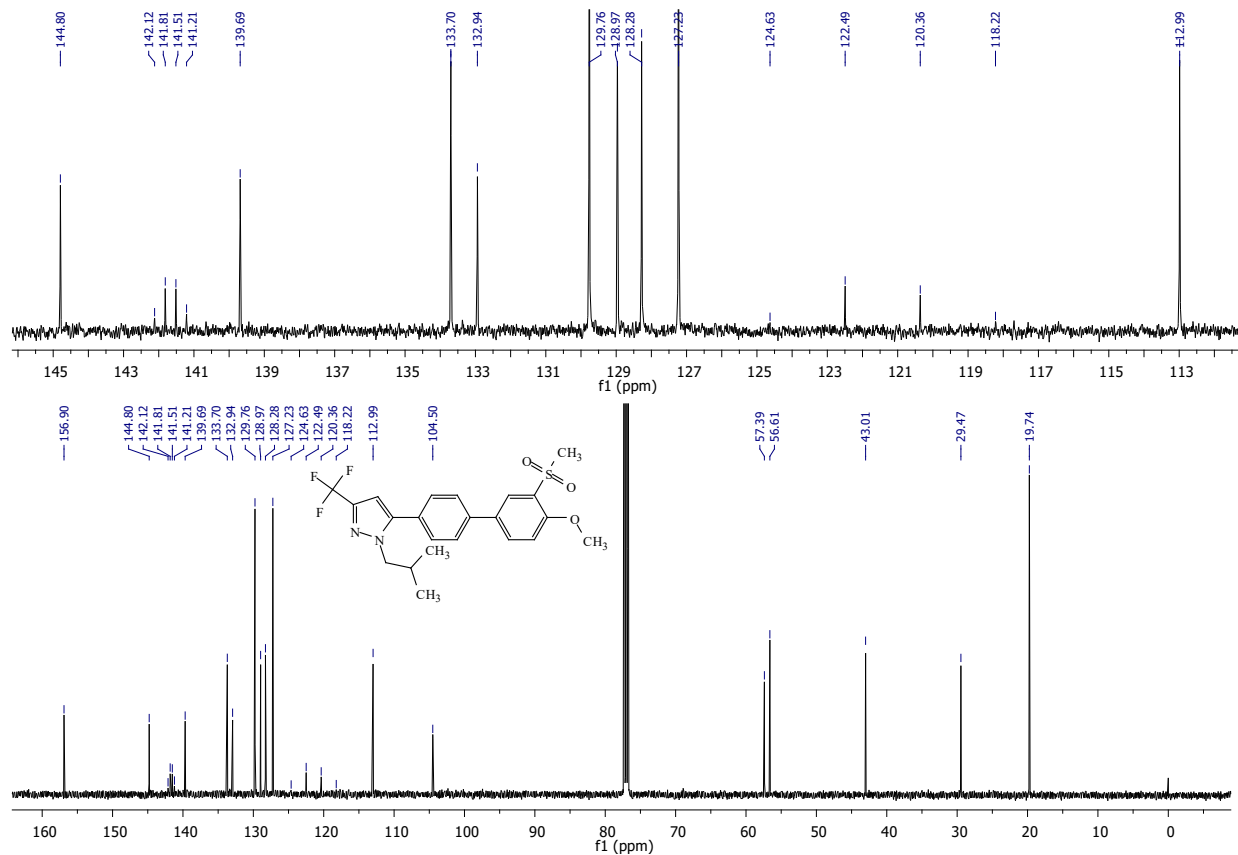


¹H NMR spectrum (500 MHz, CDCl₃) of 1-amino-3-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (**6e**)

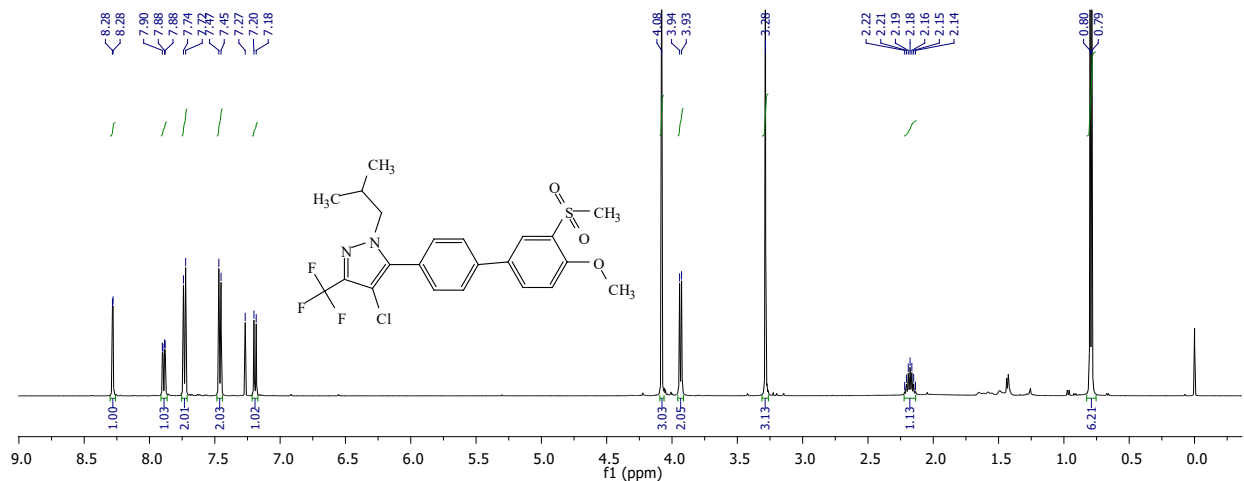
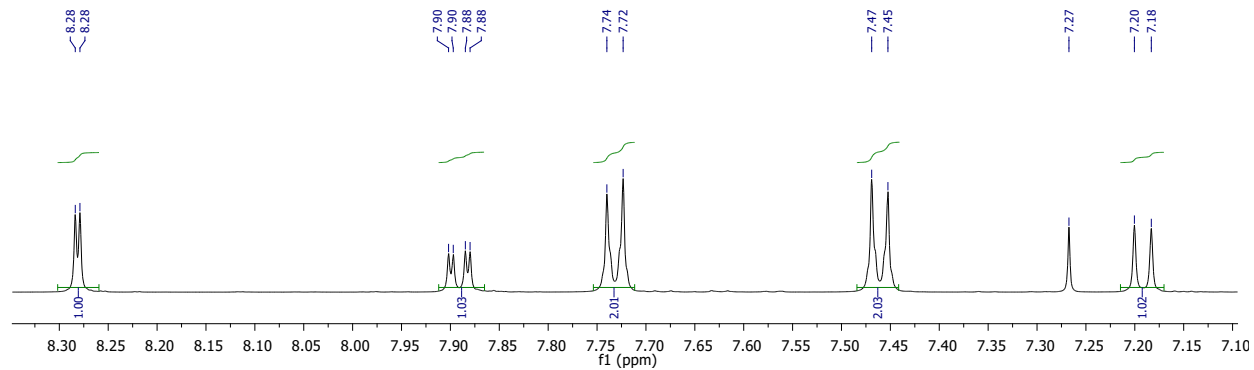


¹³C NMR spectrum (126 MHz, CDCl₃) of 1-amino-3-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (6e)

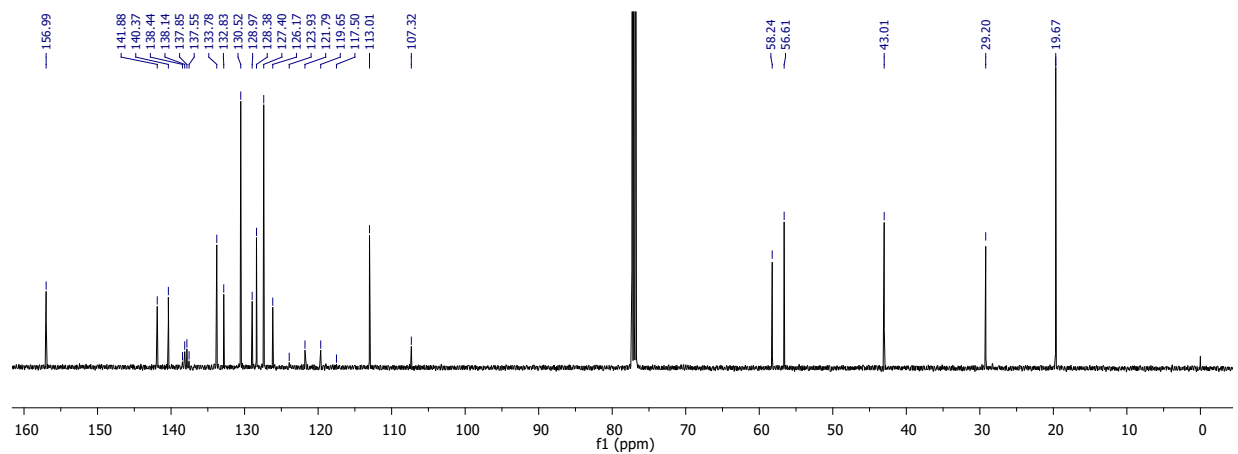
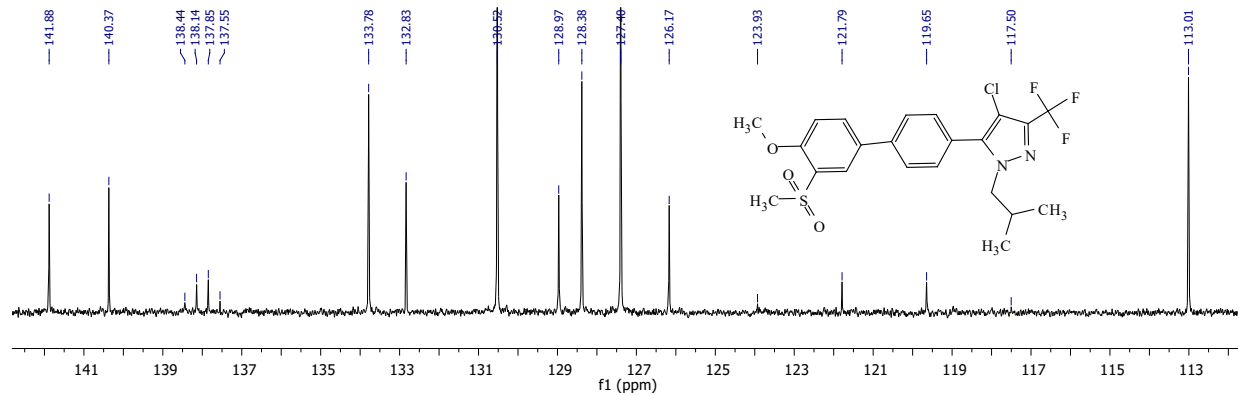




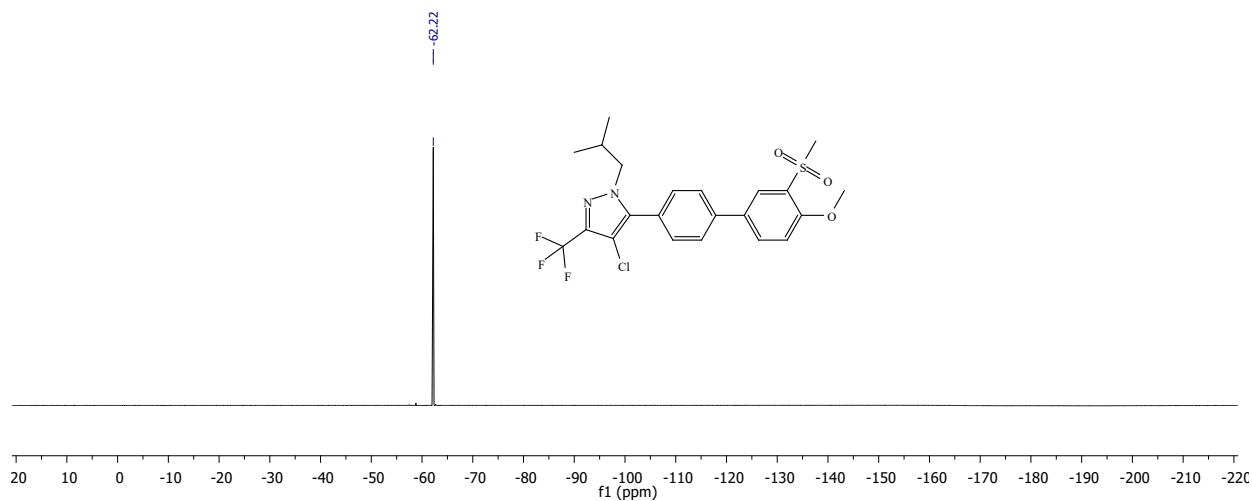
¹³C NMR spectrum (126 MHz, CDCl₃) of 1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**9a**)



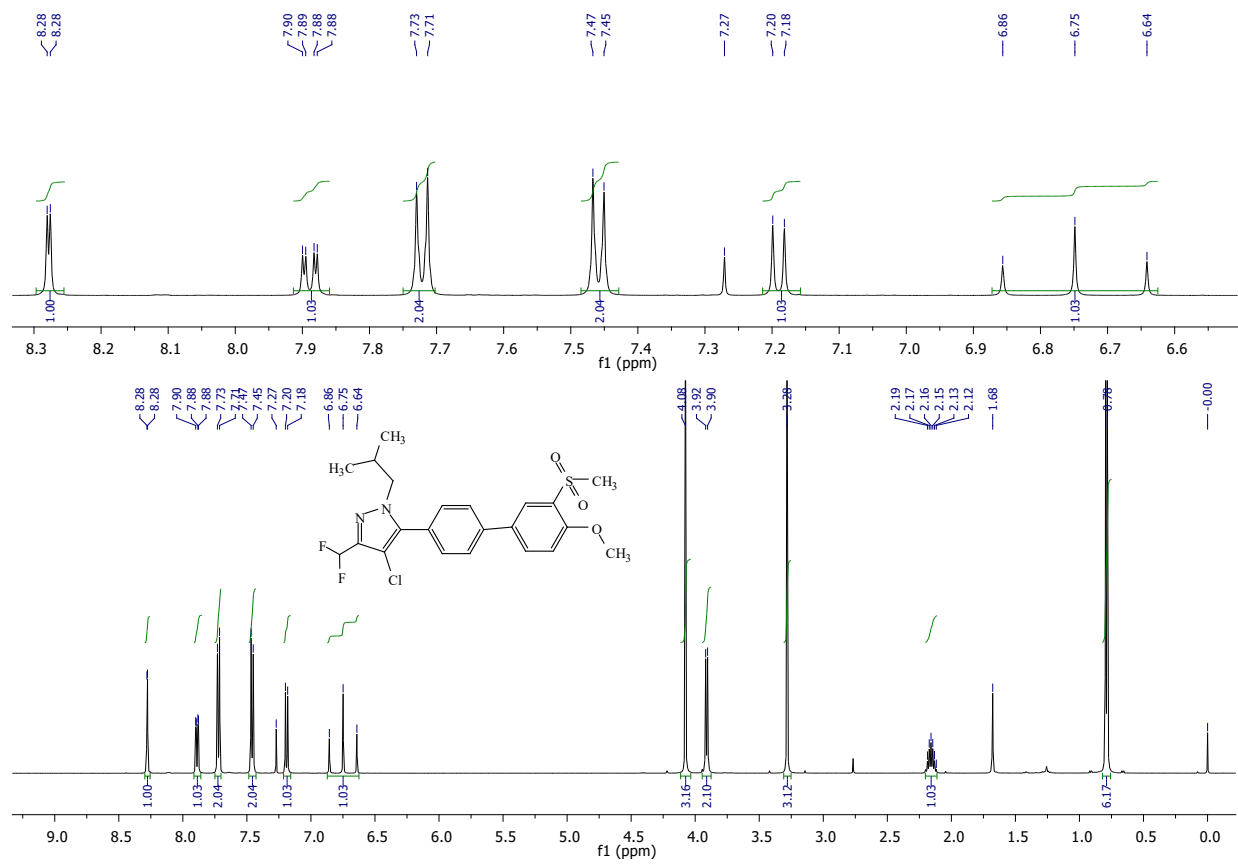
¹H NMR spectrum (500 MHz, CDCl₃) of 4-chloro-1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**9b**)

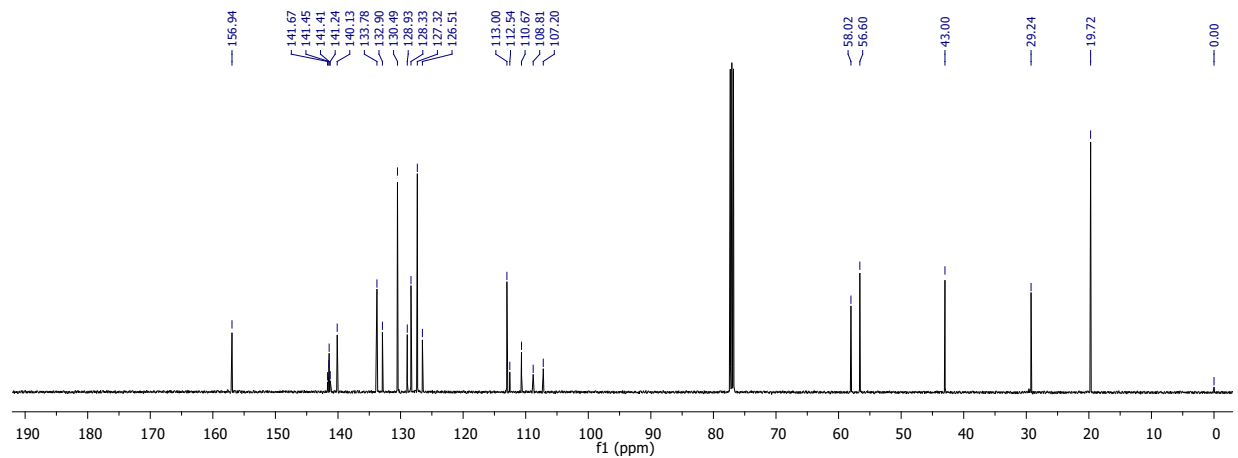
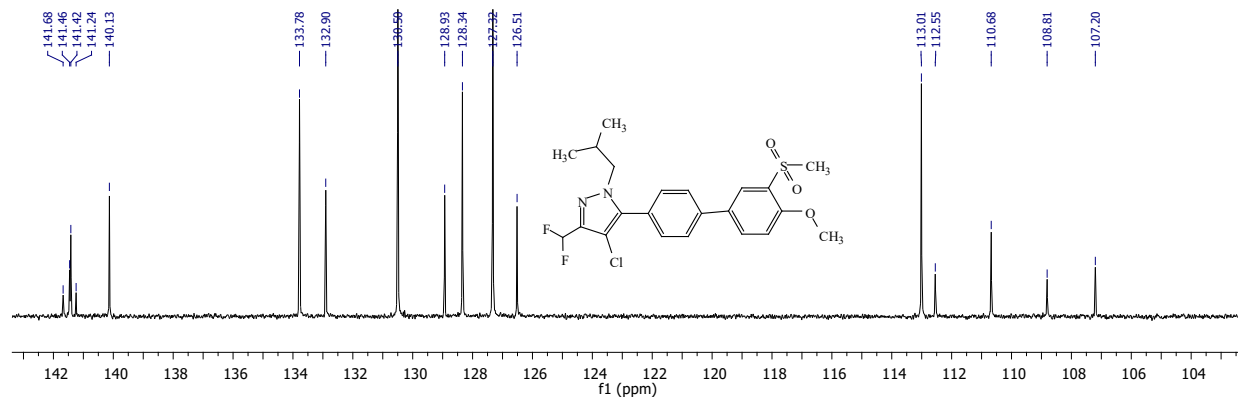


^{13}C NMR spectrum (126 MHz, CDCl_3) of 4-chloro-1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**9b**)

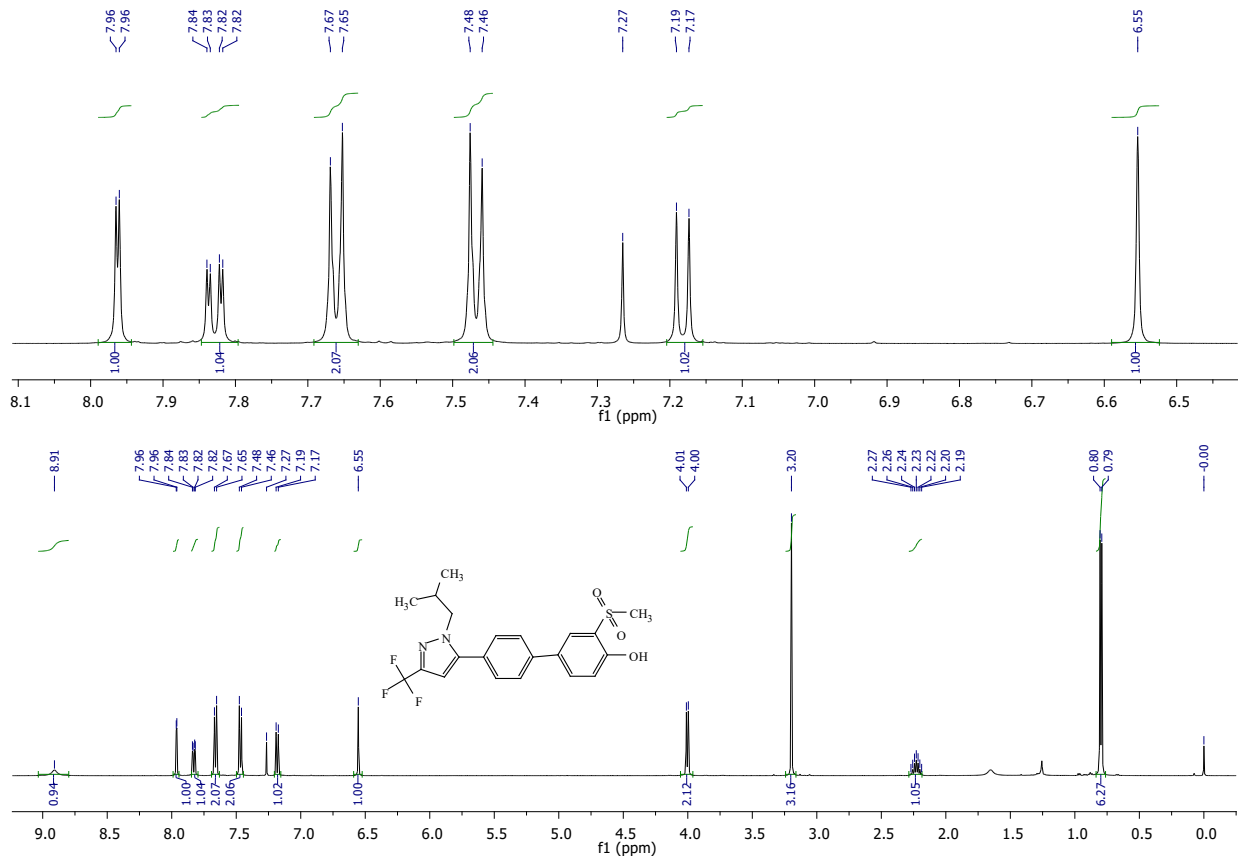


^{19}F NMR spectrum (500 MHz, CDCl_3) of 4-chloro-1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**9b**)

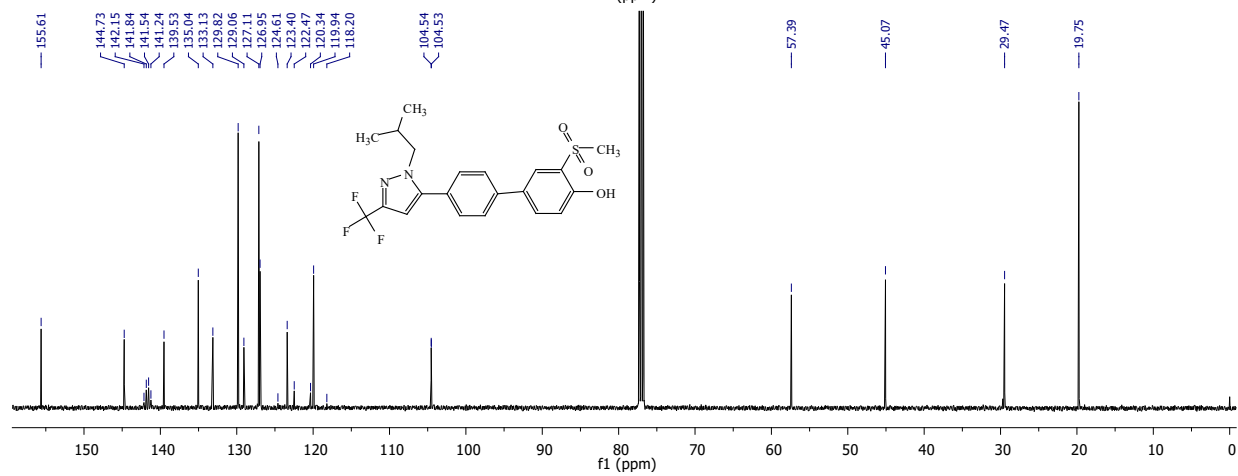
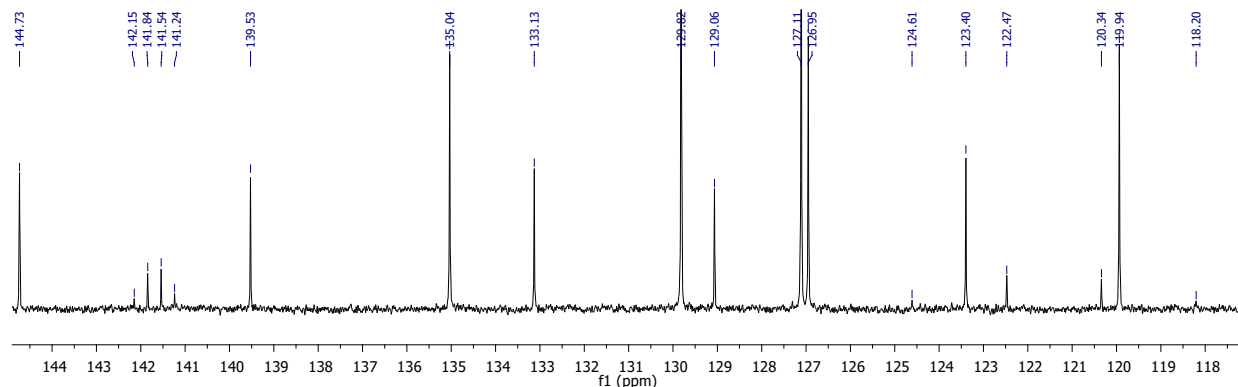




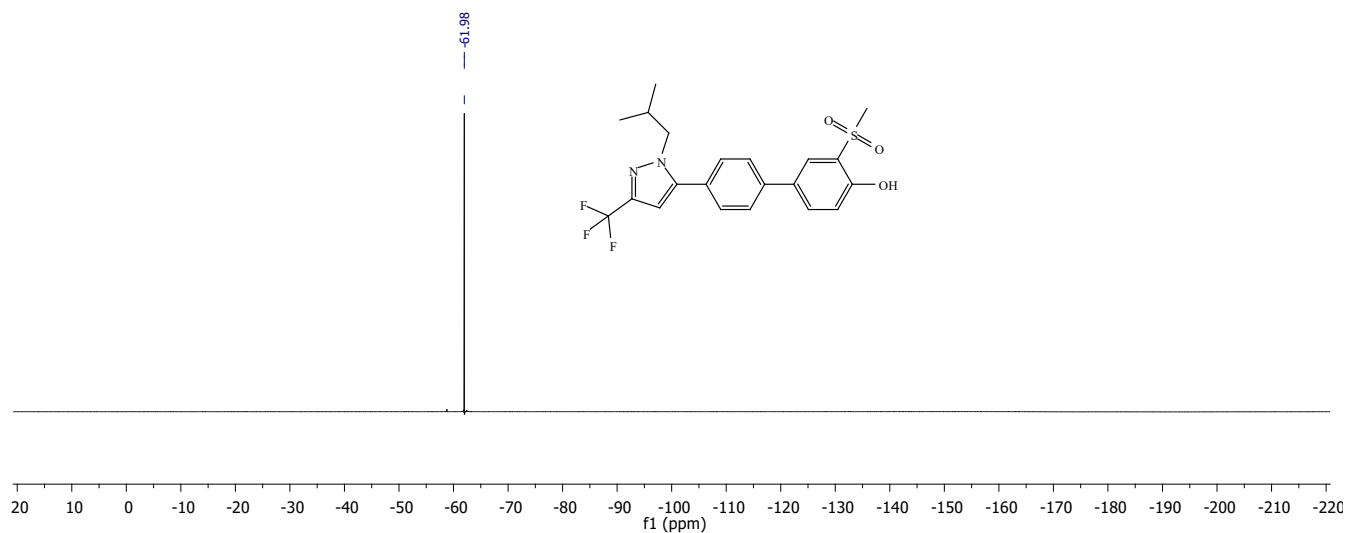
^{13}C NMR spectrum (126 MHz, CDCl_3) of 4-chloro-3-(difluoromethyl)-1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-1H-pyrazole (**9c**)



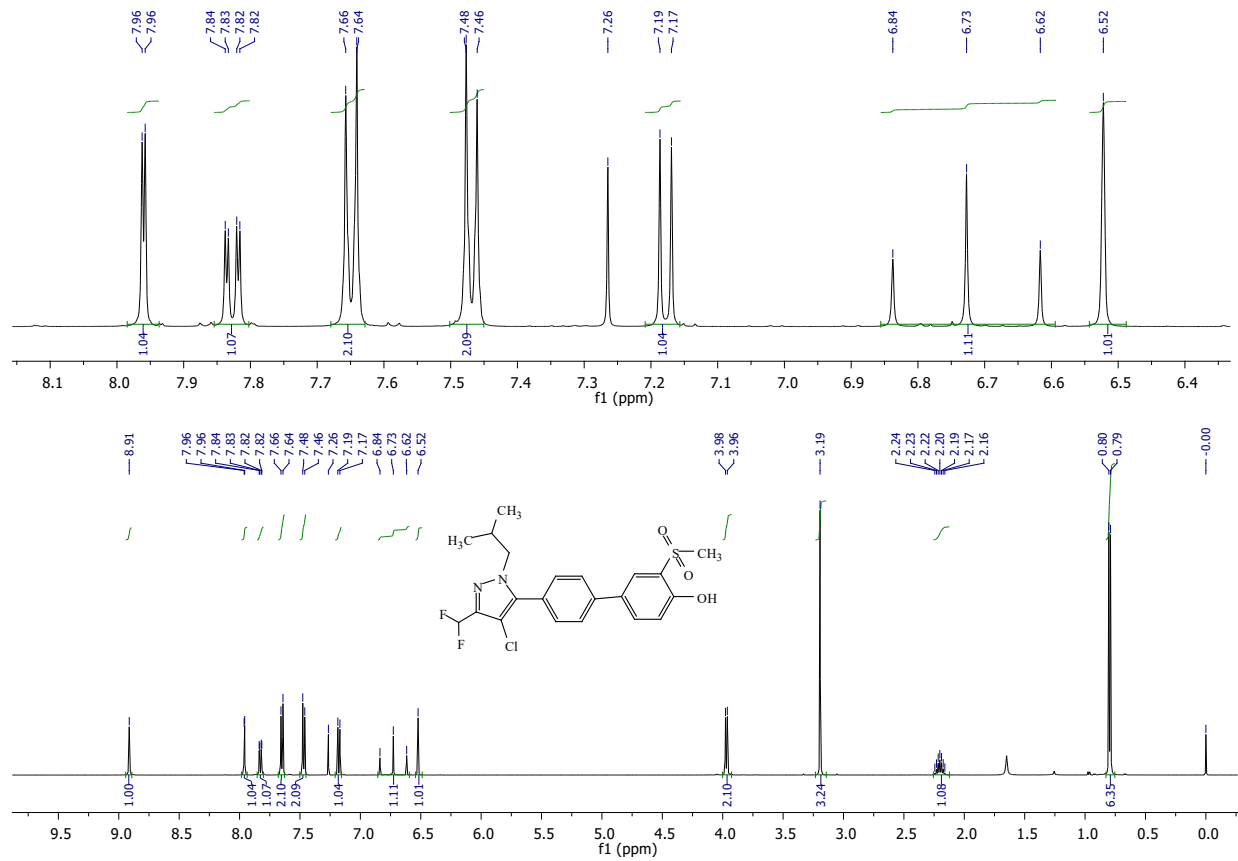
¹H NMR spectrum (500 MHz, CDCl₃) of 4'-(1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10a**)



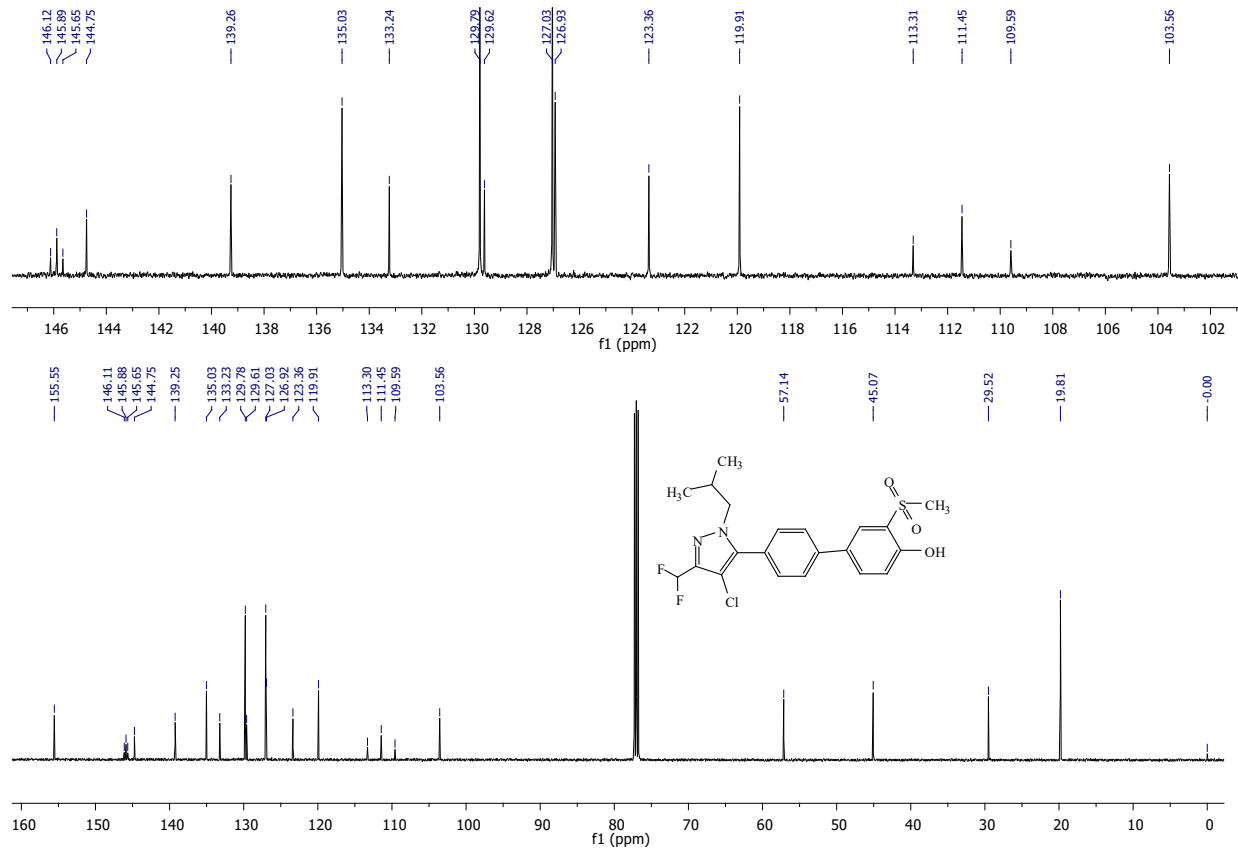
^{13}C NMR spectrum (126 MHz, CDCl_3) of 4'-(1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10a**)



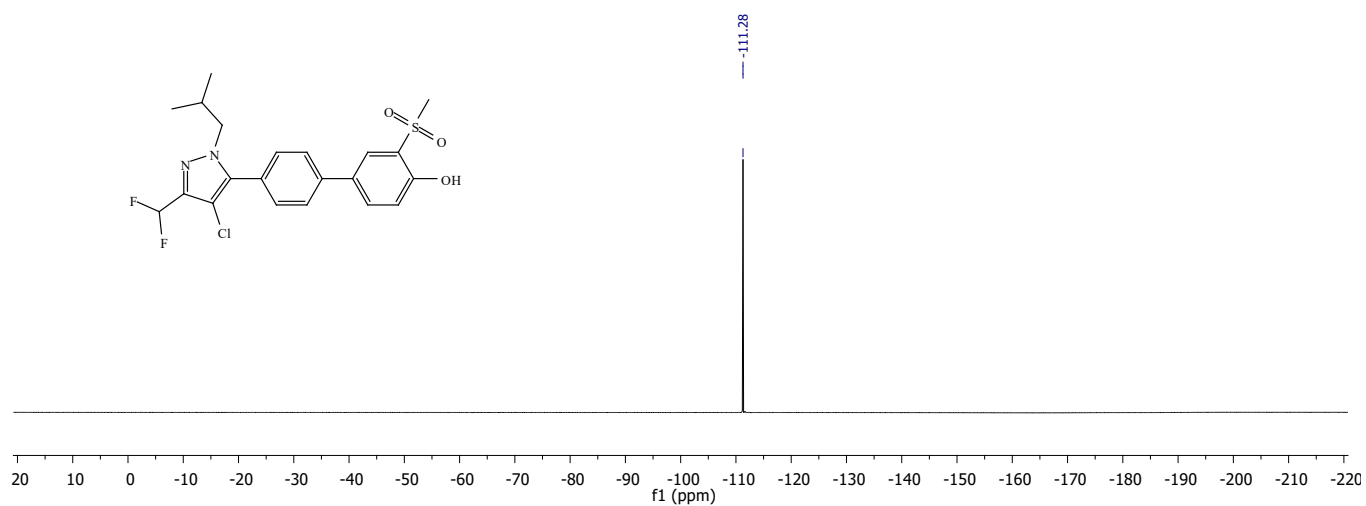
^{19}F NMR spectrum (500 MHz, CDCl_3) of 4'-(1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10a**)



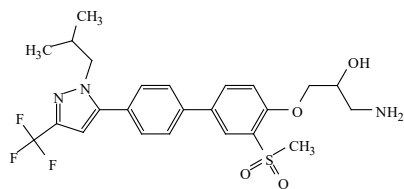
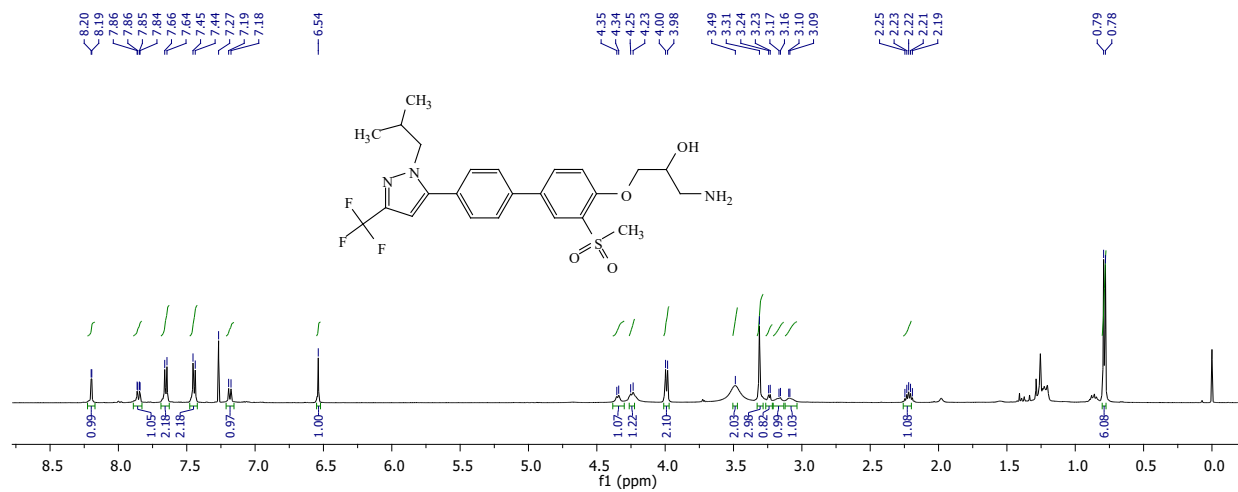
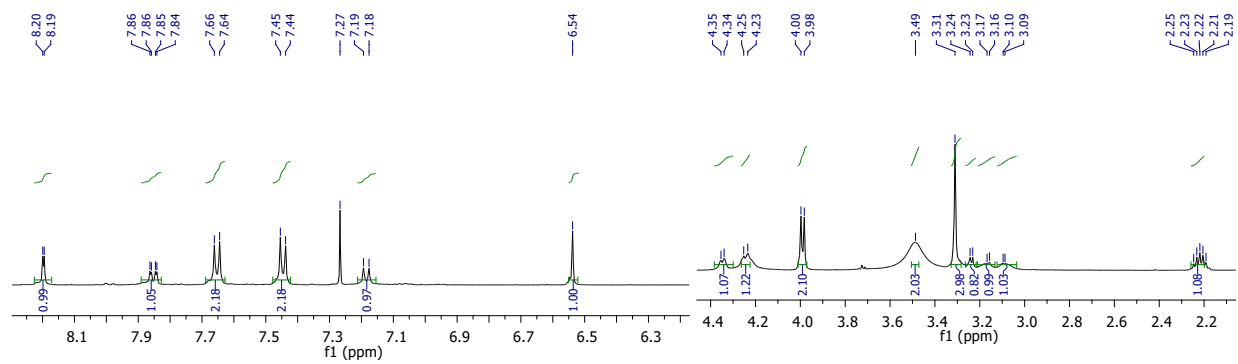
^1H NMR spectrum (500 MHz, CDCl_3) of 4'-(4-chloro-3-(difluoromethyl)-1-isobutyl-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10c**)



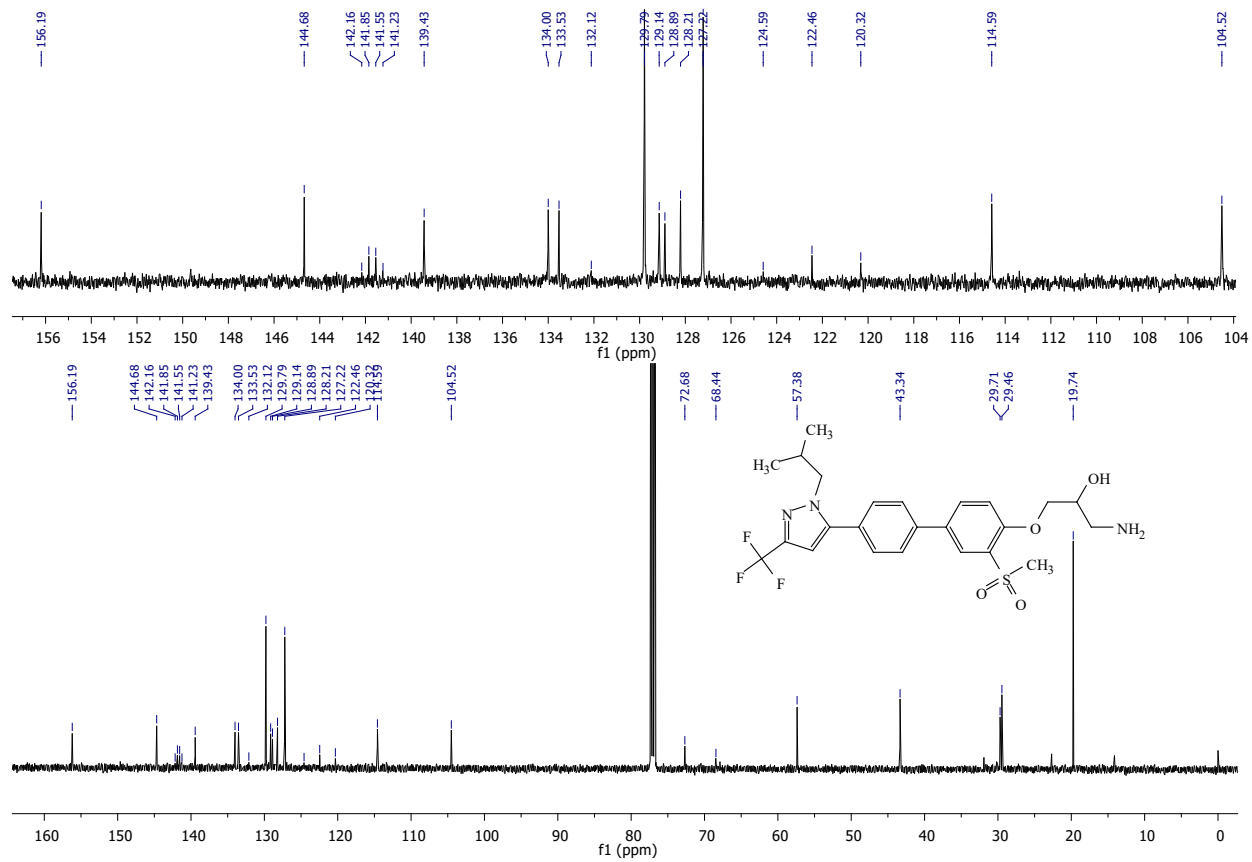
^{13}C NMR spectrum (126 MHz, CDCl_3) of 4'-(4-chloro-3-(difluoromethyl)-1-isobutyl)-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10c**)



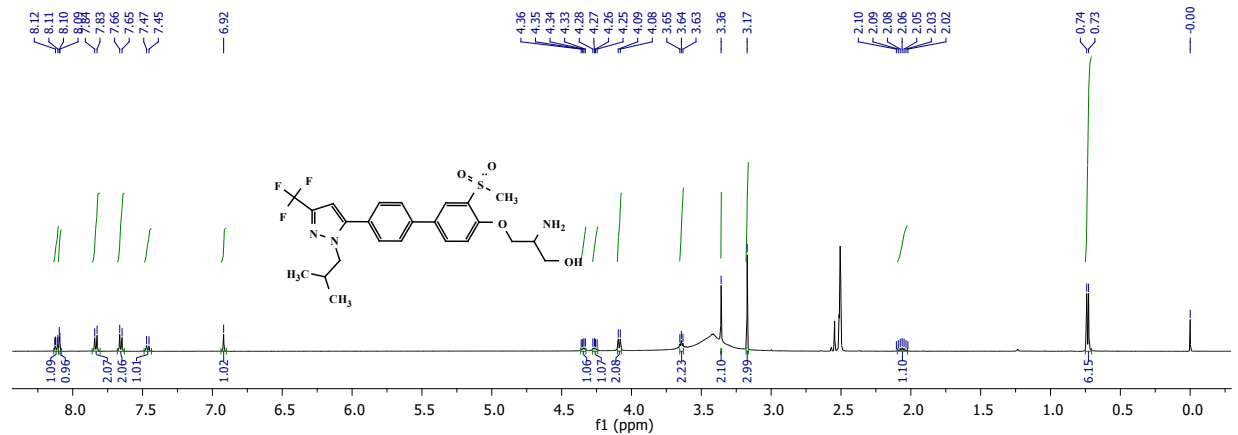
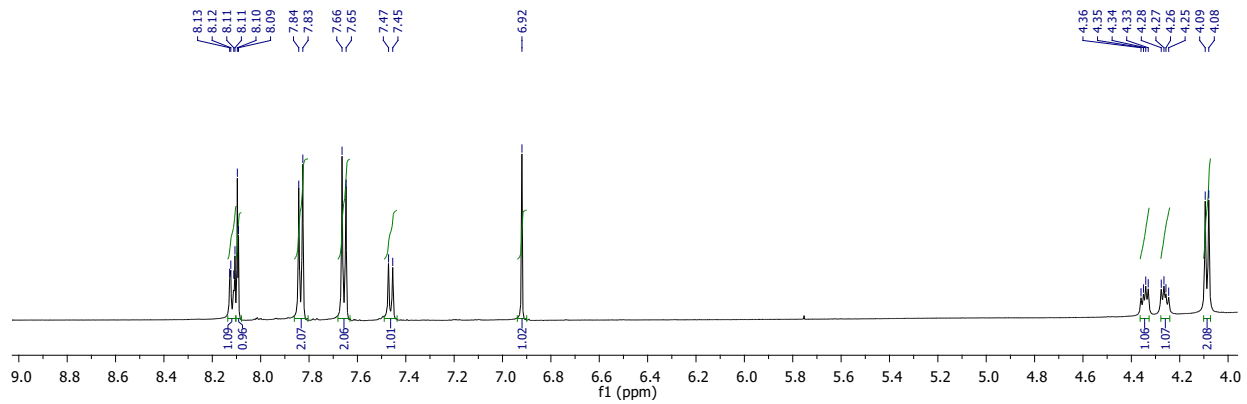
^{19}F NMR spectrum (500 MHz, CDCl_3) of 4'-(4-chloro-3-(difluoromethyl)-1-isobutyl)-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10c**)



^1H NMR spectrum (500 MHz, CDCl_3) of 1-amino-3-((4'-(1-isobutyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (**11a**)



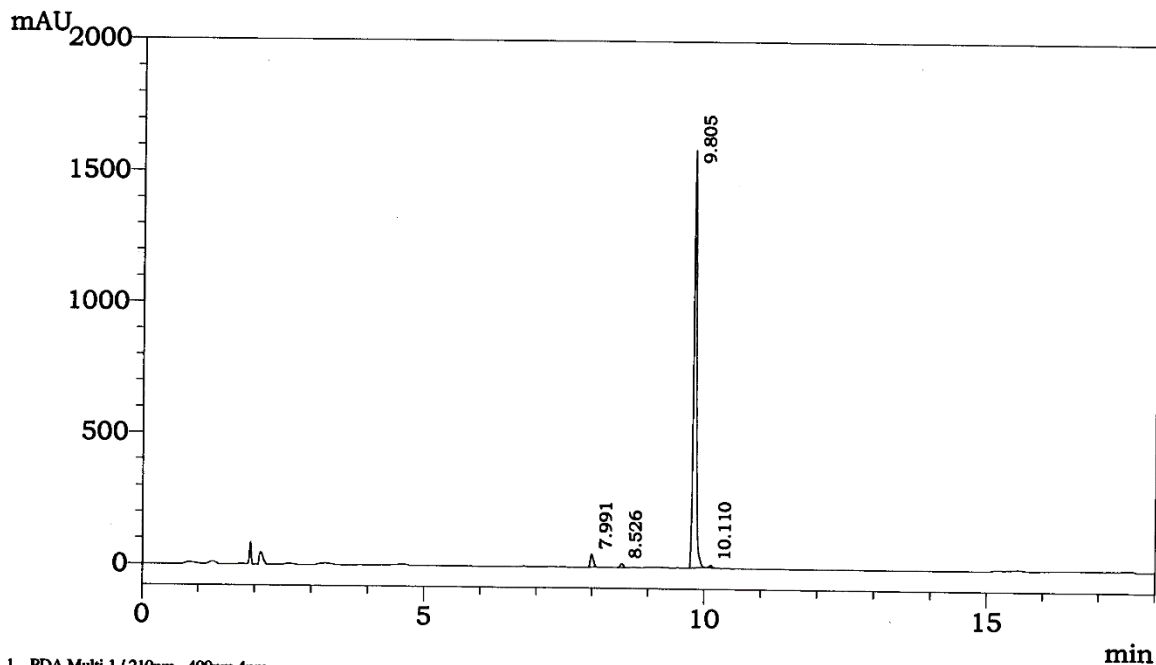
¹³C NMR spectrum (126 MHz, CDCl₃) of 1-amino-3-((4'-(1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (**11a**)



2-amino-3-((4'-(1-isobutyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-1-ol (**11b**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0μL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

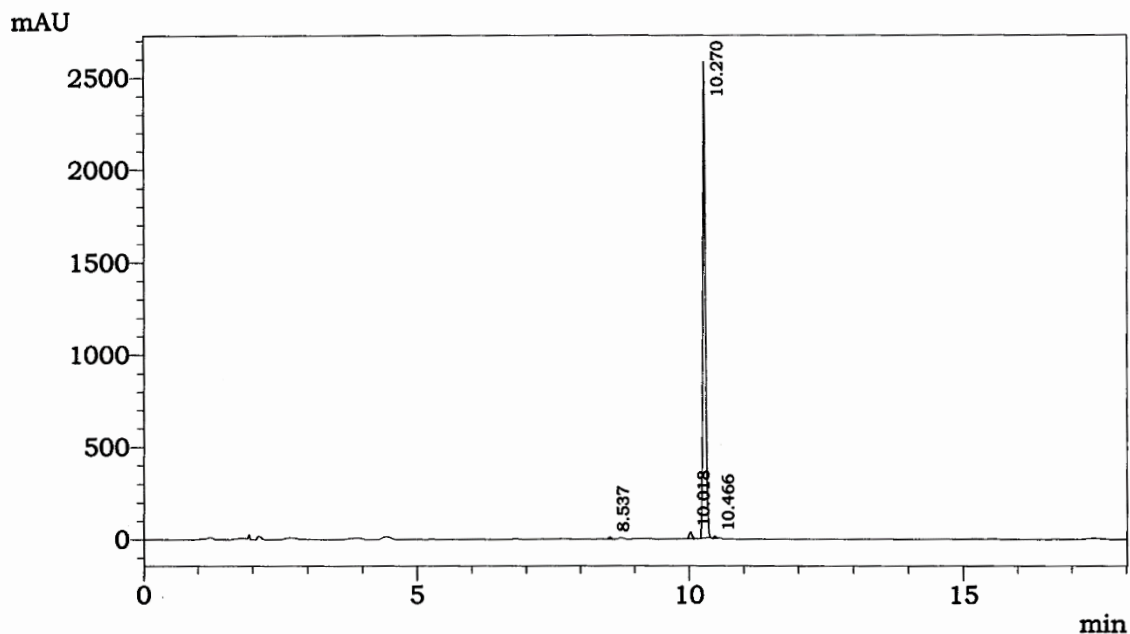
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	7.991	171253	2.798	0.99999
2	8.526	50072	0.818	0.99999
3	9.805	5868283	95.877	0.98761
4	10.110	31059	0.507	0.99999
Total		6120668	100.000	

HPLC chromatogram of 1-(4'-Methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1H-pyrazole (**5a**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

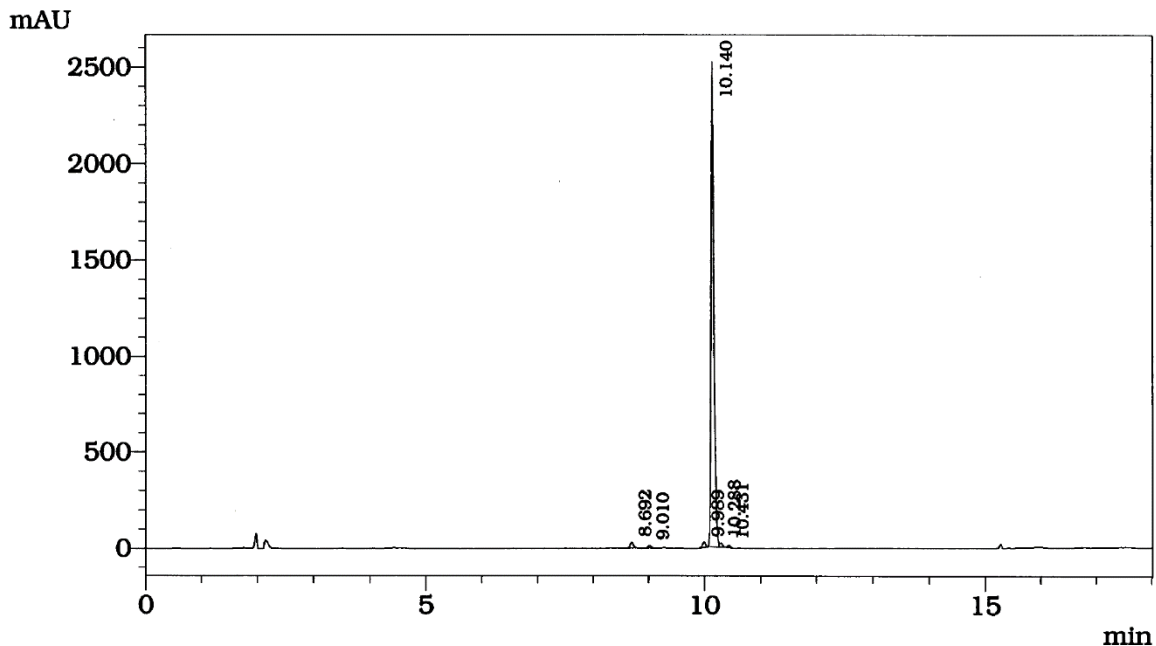
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	8.537	32158	0.373	0.99997
2	10.018	122602	1.423	0.98036
3	10.270	8433977	97.866	0.96113
4	10.466	29150	0.338	0.80651
Total		8617888	100.000	

HPLC chromatogram of 1-(4'-Methoxy-3-methyl-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1*H*-pyrazole (**5b**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

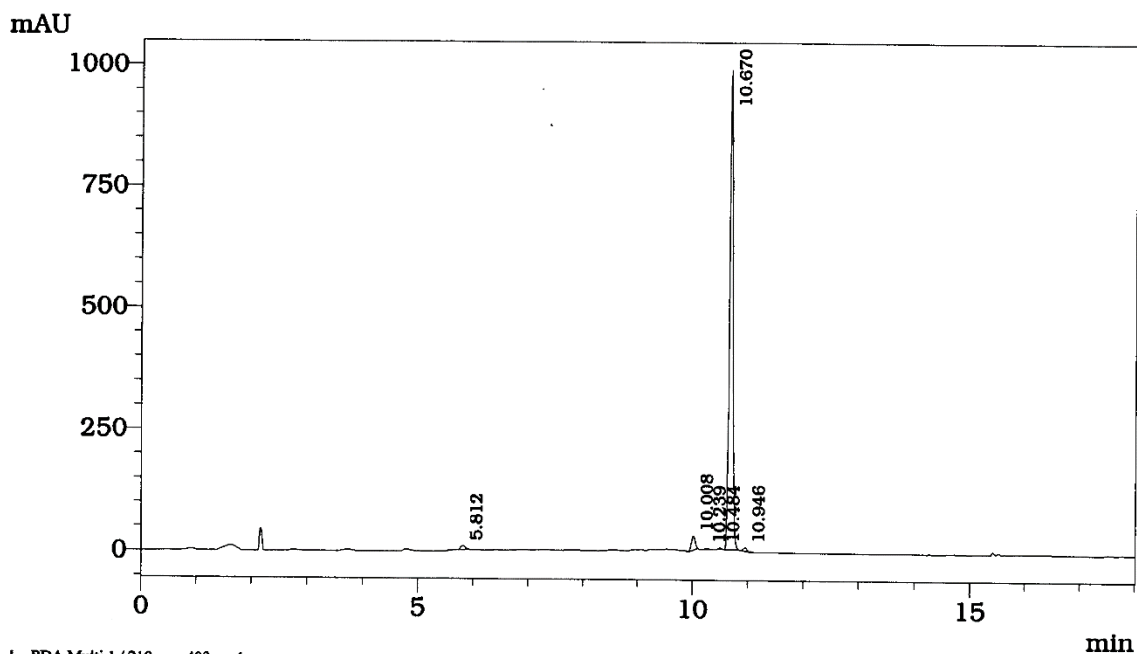
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	8.692	110311	1.195	1.00000
2	9.010	46352	0.502	0.99999
3	9.989	99204	1.074	0.68321
4	10.140	8869703	96.048	0.99989
5	10.288	71056	0.769	0.98312
6	10.431	38068	0.412	0.99986
Total		9234694	100.000	

HPLC chromatogram of 1-(3-Isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-methyl-3-(trifluoromethyl)-1*H*-pyrazole, (5c).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

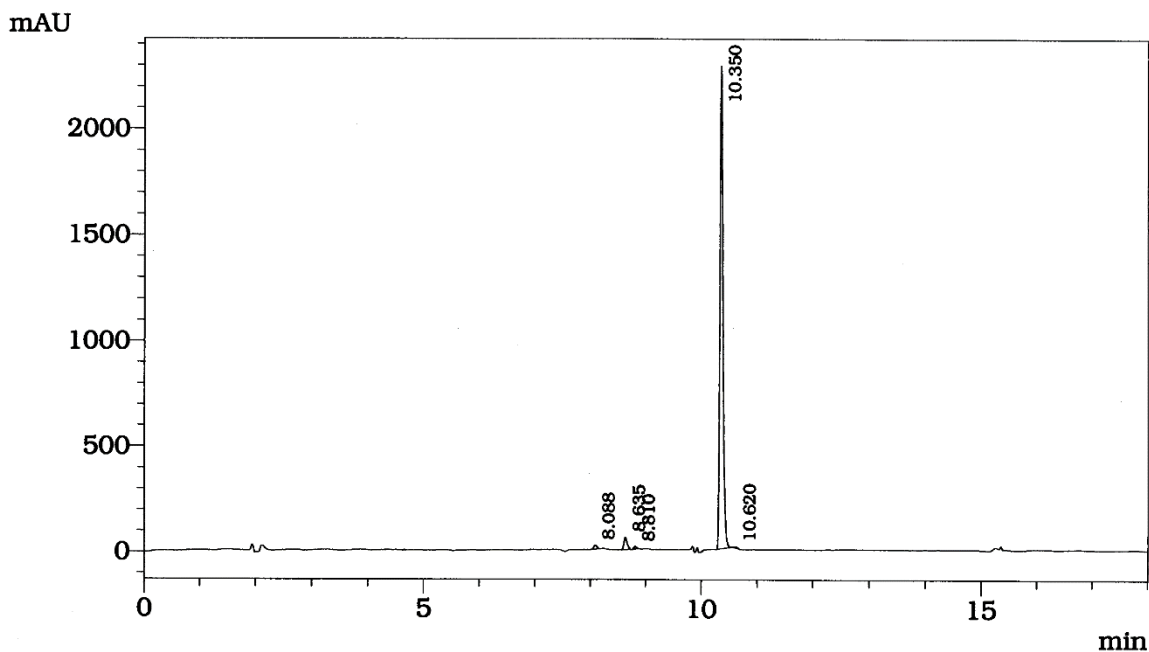
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	5.812	35591	0.786	1.00000
2	10.008	127243	2.810	0.99999
3	10.239	10044	0.222	1.00000
4	10.484	7575	0.167	0.99999
5	10.670	4319693	95.391	1.00000
6	10.946	28284	0.625	0.99997
Total		4528429	100.000	

HPLC chromatogram of 1-(3-Isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-5-isopropyl-3-(trifluoromethyl)-1*H*-pyrazole, (**5e**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

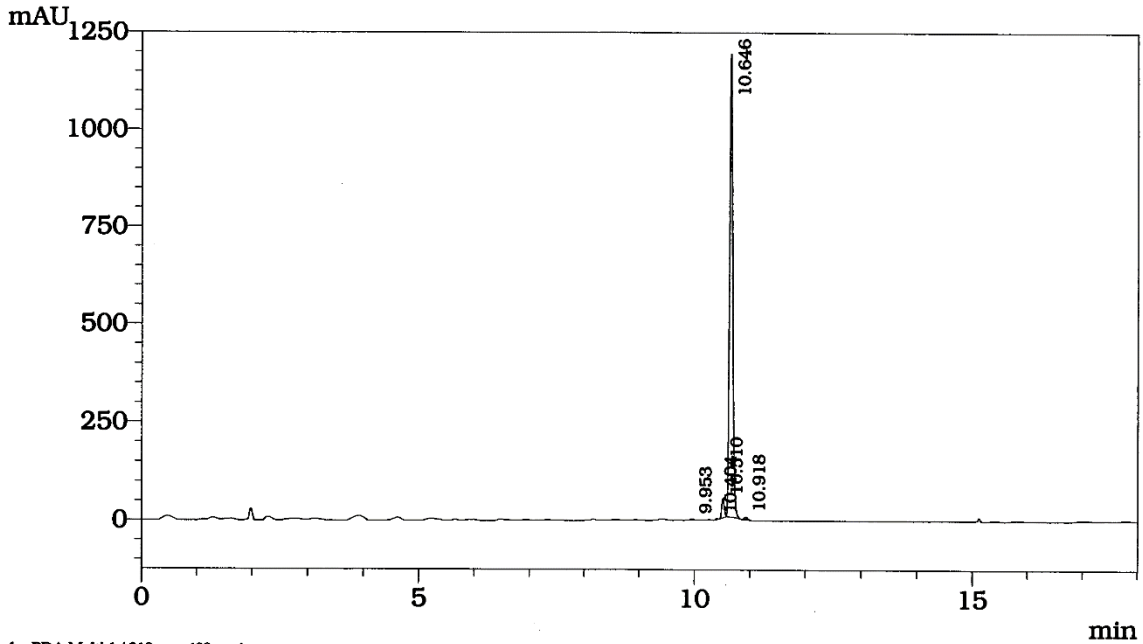
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	8.088	76943	0.855	0.99995
2	8.635	219997	2.445	1.00000
3	8.810	42374	0.471	1.00000
4	10.350	8644767	96.076	1.00000
5	10.620	13805	0.153	0.99483
Total		8997886	100.000	

HPLC chromatogram of 5-Cyclopropyl-1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole, (**5f**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

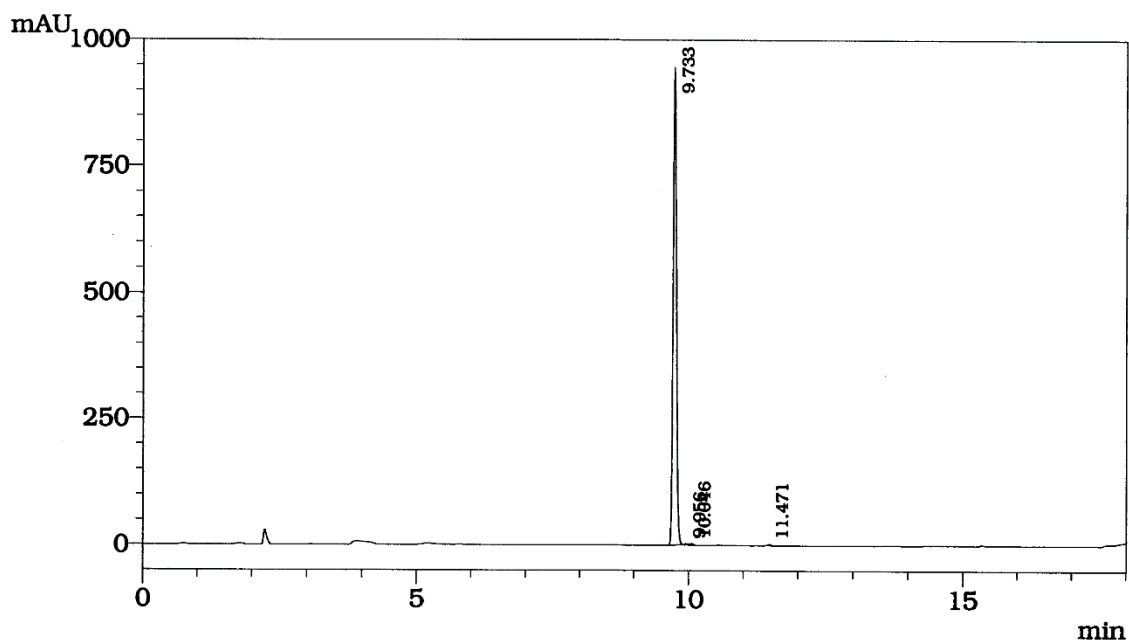
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	9.953	7777	0.164	1.00000
2	10.404	6660	0.140	0.99989
3	10.510	166533	3.505	0.99760
4	10.646	4547119	95.705	1.00000
5	10.918	23084	0.486	0.99999
Total		4751173	100.000	

HPLC chromatogram of 5-Cyclobutyl-1-(3-isobutyl-4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1*H*-pyrazole (**5g**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

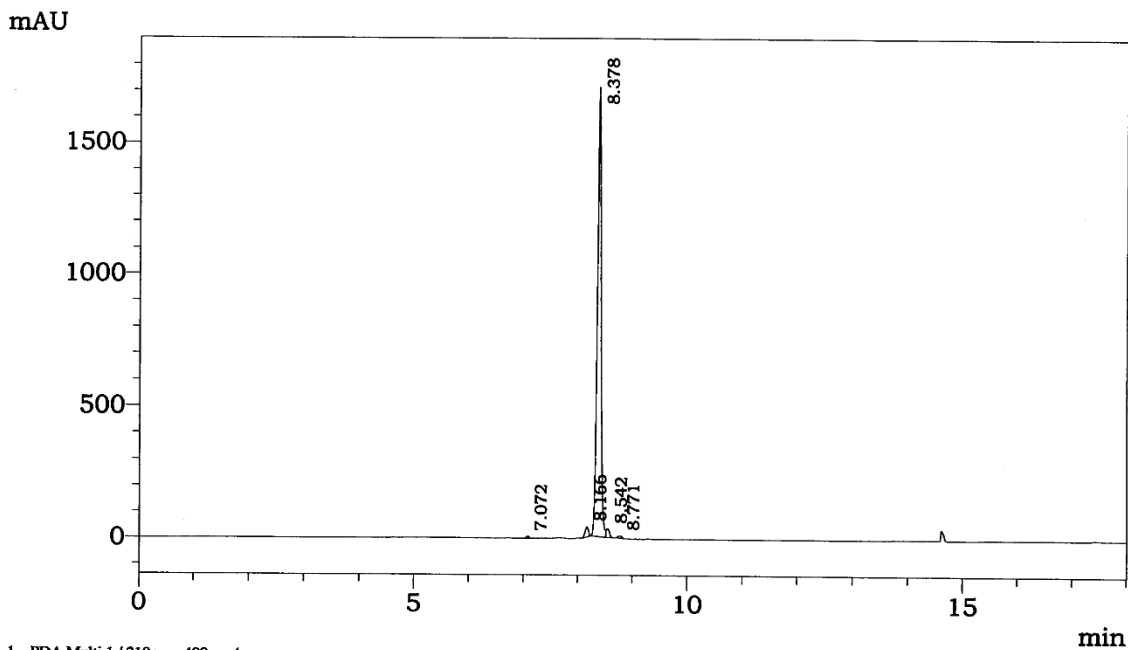
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	9.733	3923559	99.310	1.00000
2	9.956	9507	0.241	0.87776
3	10.046	10395	0.263	0.32045
4	11.471	7342	0.186	0.99994
Total		3950803	100.000	

HPLC chromatogram of 3'-Isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**6a**).

Method:- HPLC_X-Bridge(NH3)
 Column : X-Bridge C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% NH3 in water
 Inj Volume; 5.0μL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial 98% B to 15 % B in 6 minute, hold till 8 min,
 at 9.0 min B conc is 0 % hold up to 12 min., at 14 min B conc. 98% hold

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

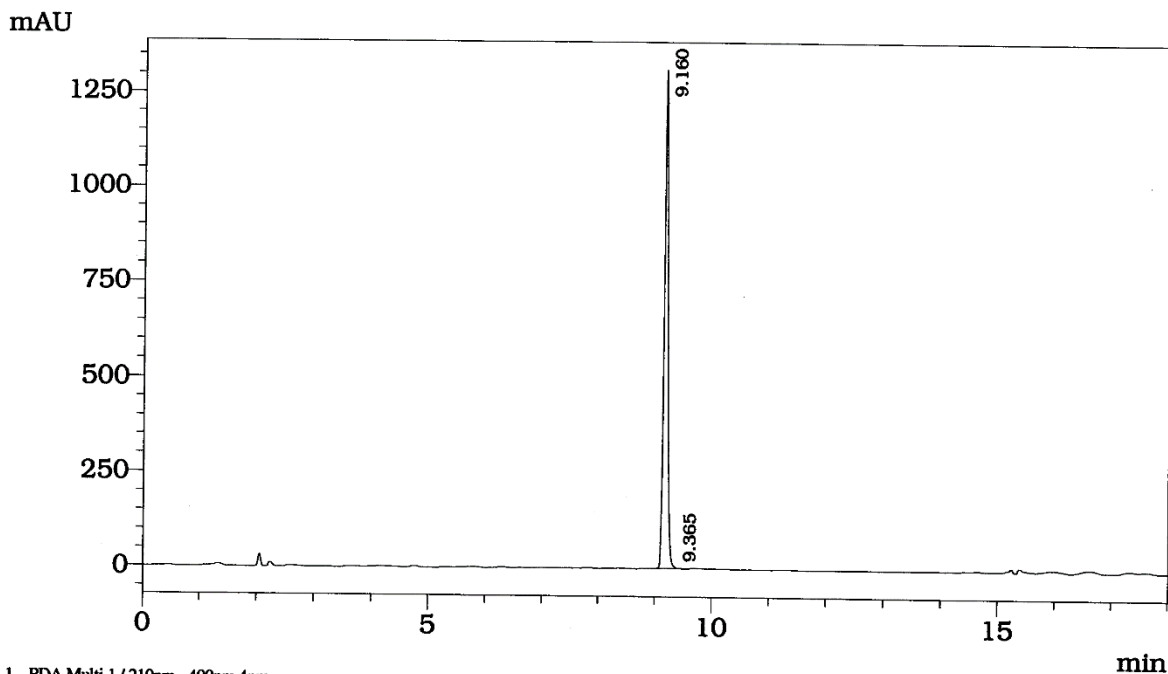
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	7.072	27628	0.319	0.99994
2	8.166	164373	1.895	1.00000
3	8.378	8303200	95.736	1.00000
4	8.542	132102	1.523	0.99998
5	8.771	45754	0.528	0.99998
Total		8673057	100.000	

HPLC chromatogram of 4-(2-((3'-Isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)ethyl)morpholine (**6b**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA.Multi 1/210nm - 400nm 4nm

PeakTable

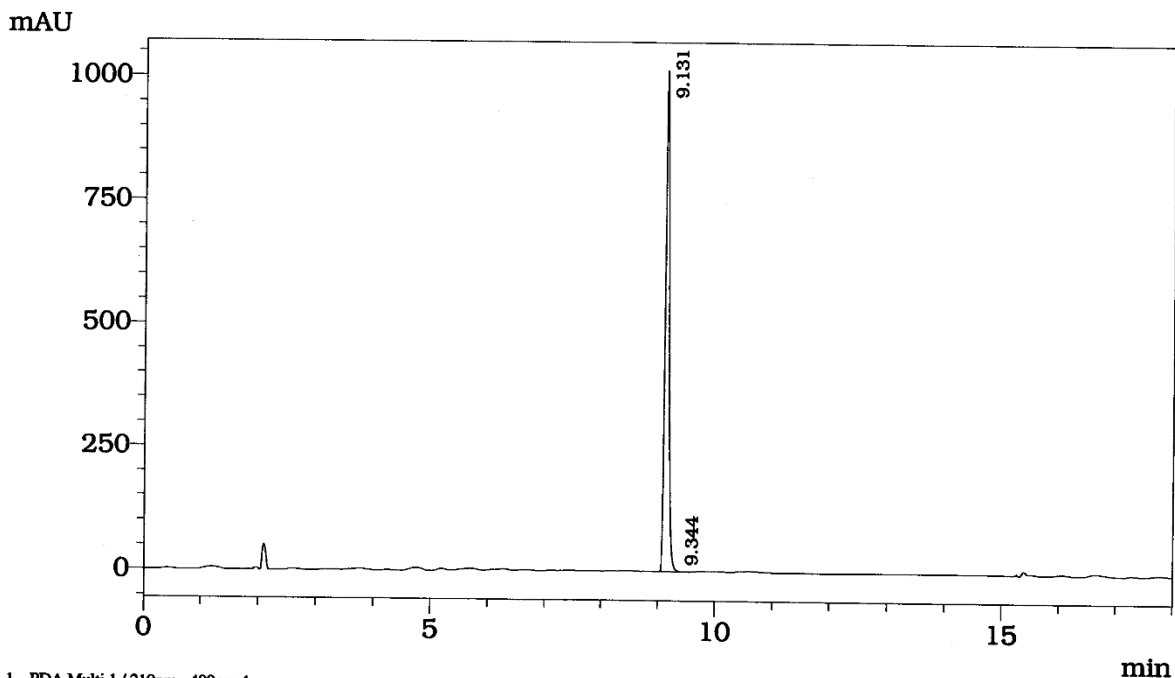
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	9.160	6209957	99.936	1.00000
2	9.365	3988	0.064	0.99955
Total		6213945	100.000	

HPLC chromatogram of 5-((3'-Isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)piperidin-2-one (**6c**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

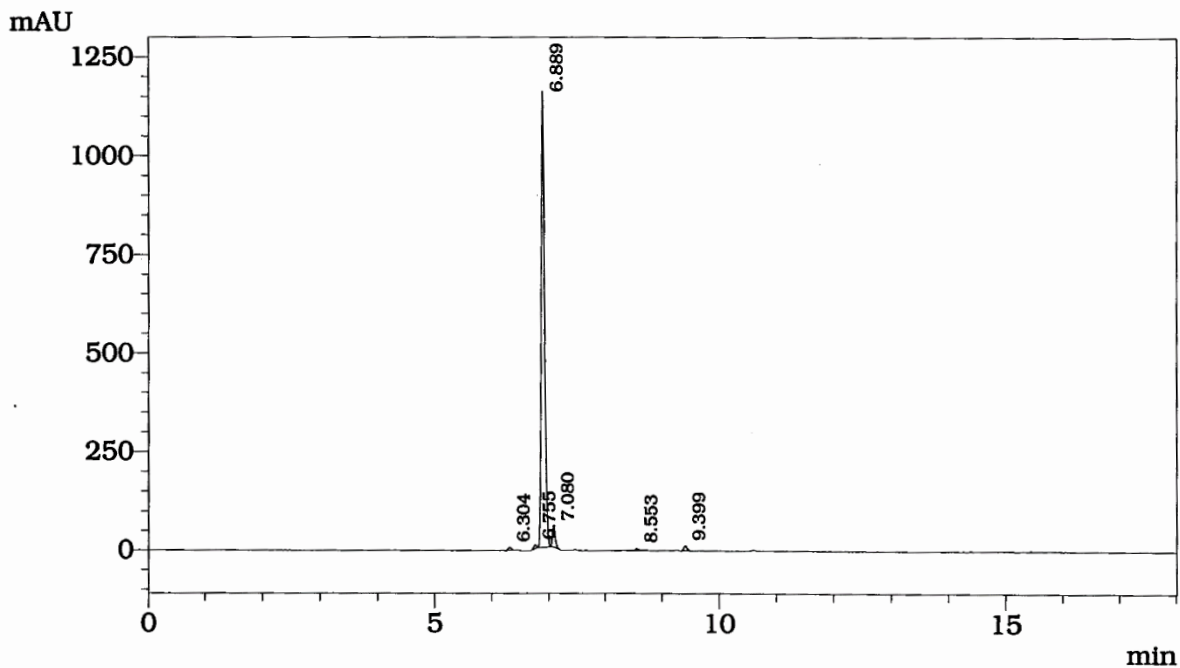
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	9.131	4843445	99.920	1.00000
2	9.344	3854	0.080	0.99696
Total		4847299	100.000	

HPLC chromatogram of 4-((3'-Isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)pyrrolidin-2-one (**6d**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

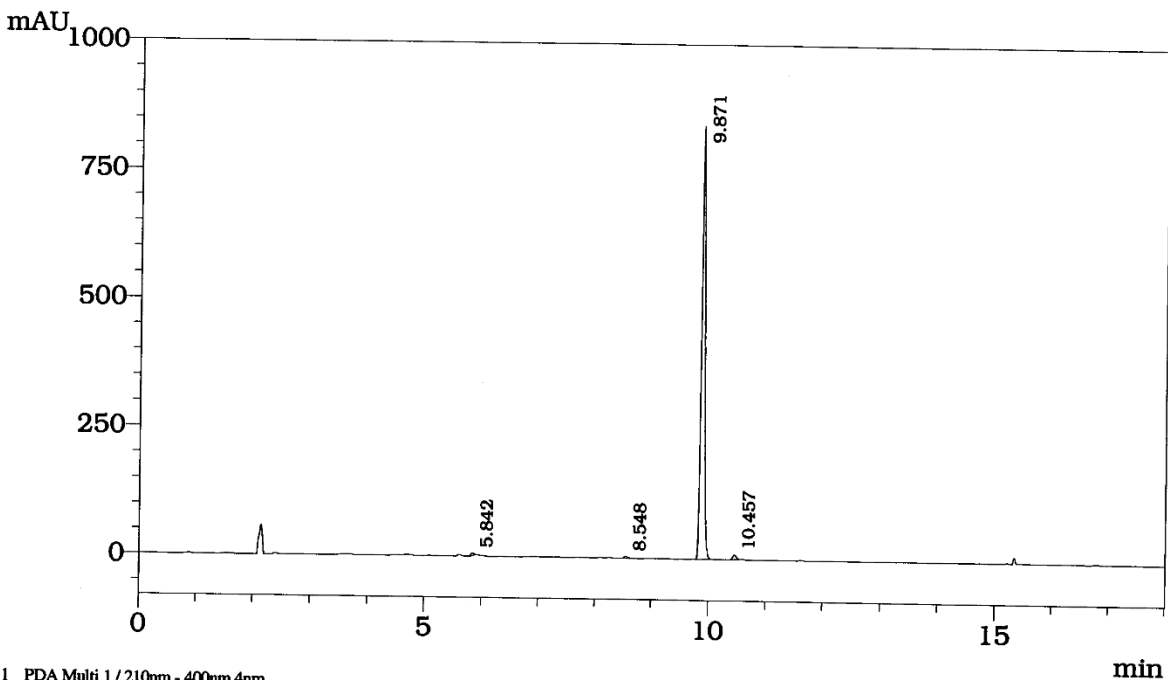
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	6.304	27040	0.542	0.99983
2	6.755	32442	0.651	0.99983
3	6.889	4683632	93.932	1.00000
4	7.080	178949	3.589	1.00000
5	8.553	17014	0.341	1.00000
6	9.399	47091	0.944	0.99997
Total		4986168	100.000	

HPLC chromatogram of 1-Amino-3-((3'-isobutyl-4'-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (**6e**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

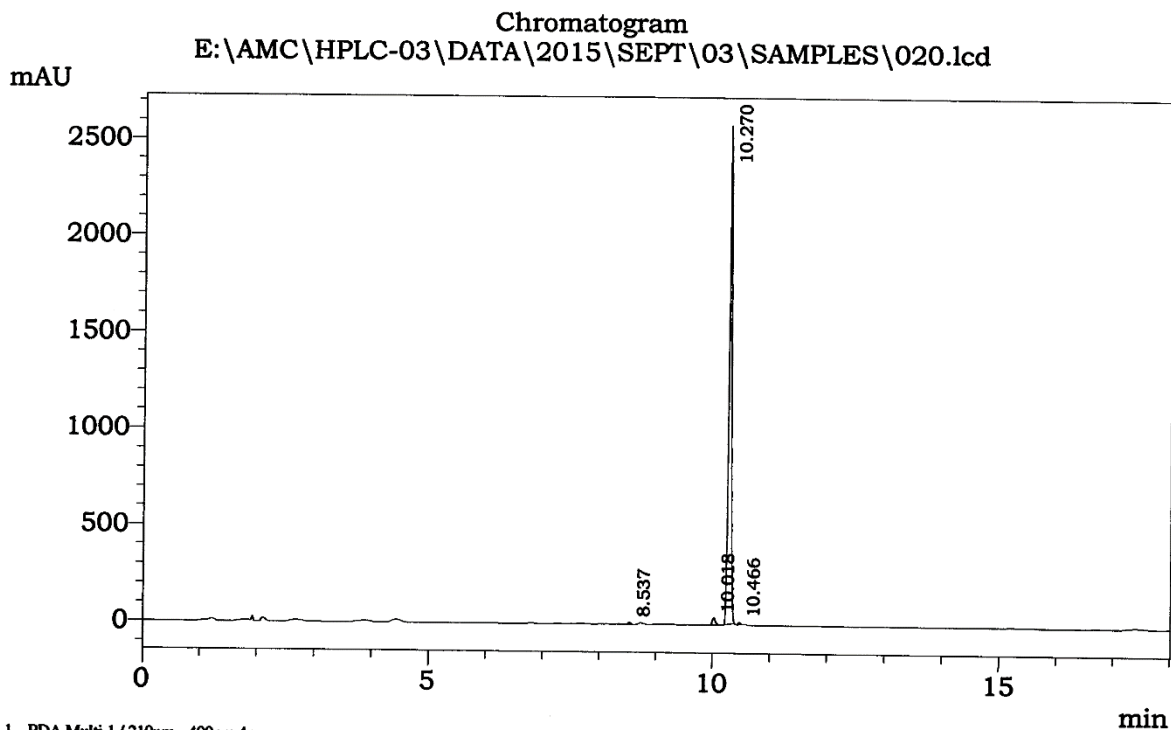
PeakTable

PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	5.842	19844	0.533	0.99997
2	8.548	17084	0.458	0.99997
3	9.871	3647546	97.884	1.00000
4	10.457	41938	1.125	0.99991
Total		3726412	100.000	

HPLC chromatogram of 1-Isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-3-(trifluoromethyl)-1H-pyrazole (**9a**).

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min



PeakTable

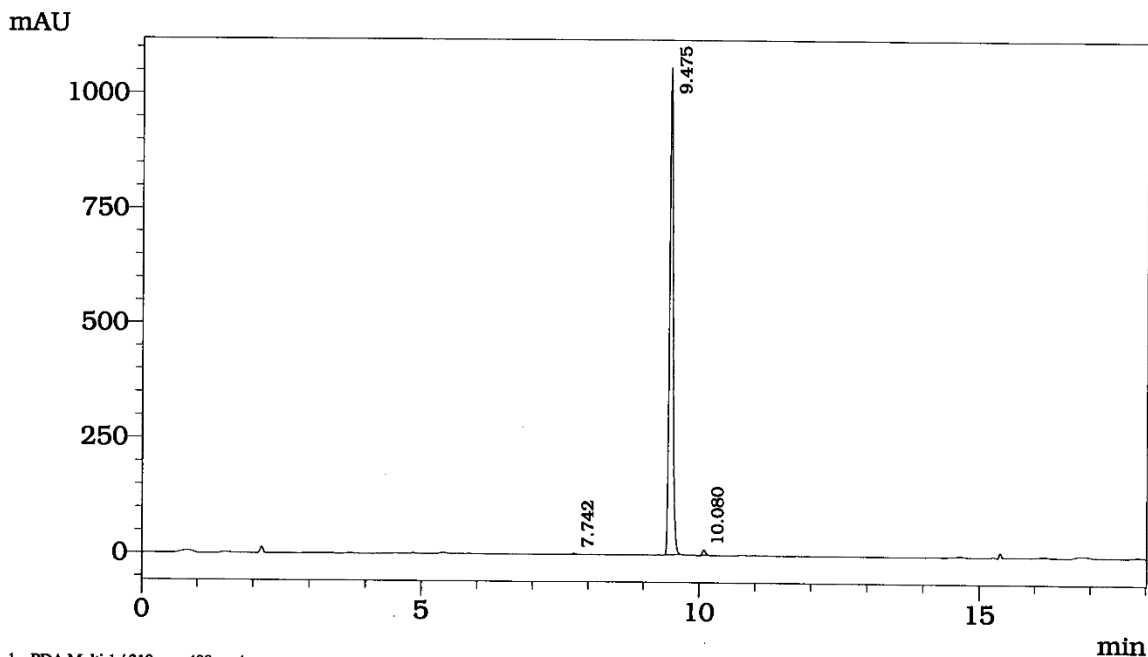
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	8.537	32158	0.373	0.99997
2	10.018	122602	1.423	0.98036
3	10.270	8433977	97.866	0.96113
4	10.466	29150	0.338	0.80651
Total		8617888	100.000	

HPLC chromatogram of 4-Chloro-3-(difluoromethyl)-1-isobutyl-5-(4'-methoxy-3'-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)-1*H*-pyrazole (**9c**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

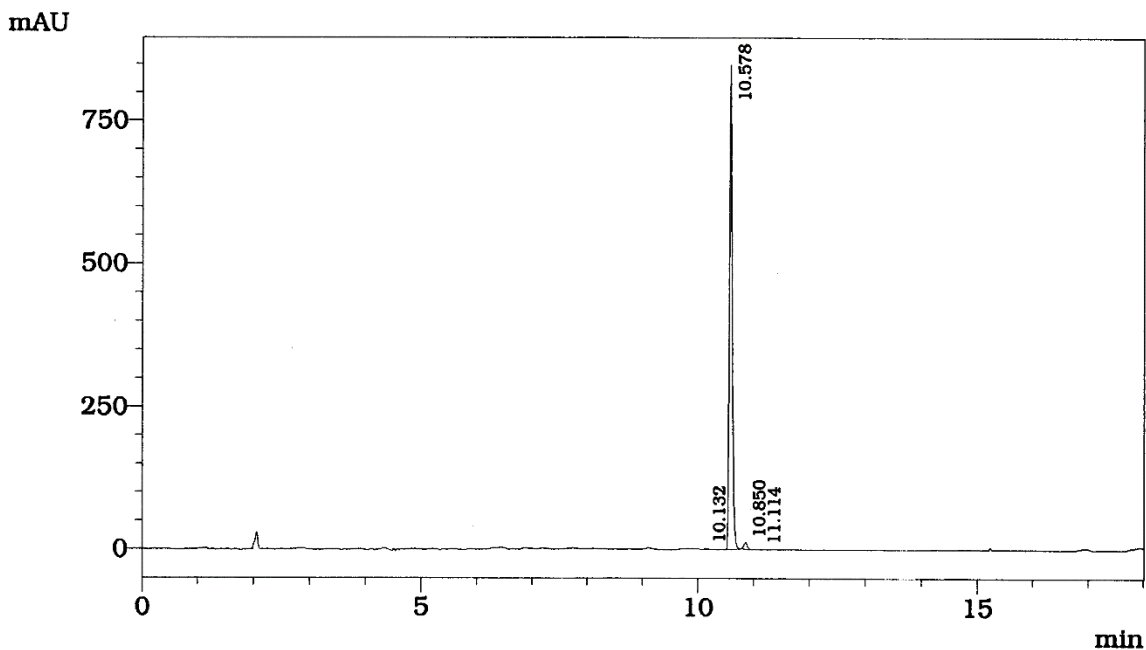
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	7.742	9242	0.191	0.99999
2	9.475	4772508	98.840	1.00000
3	10.080	46761	0.968	1.00000
Total		4828511	100.000	

HPLC chromatogram of 4'-(1-Isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol (**10a**)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 5% Phase A + 0.1% Formic acid + water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

PDA Ch1 210nm - 400nm 4nm

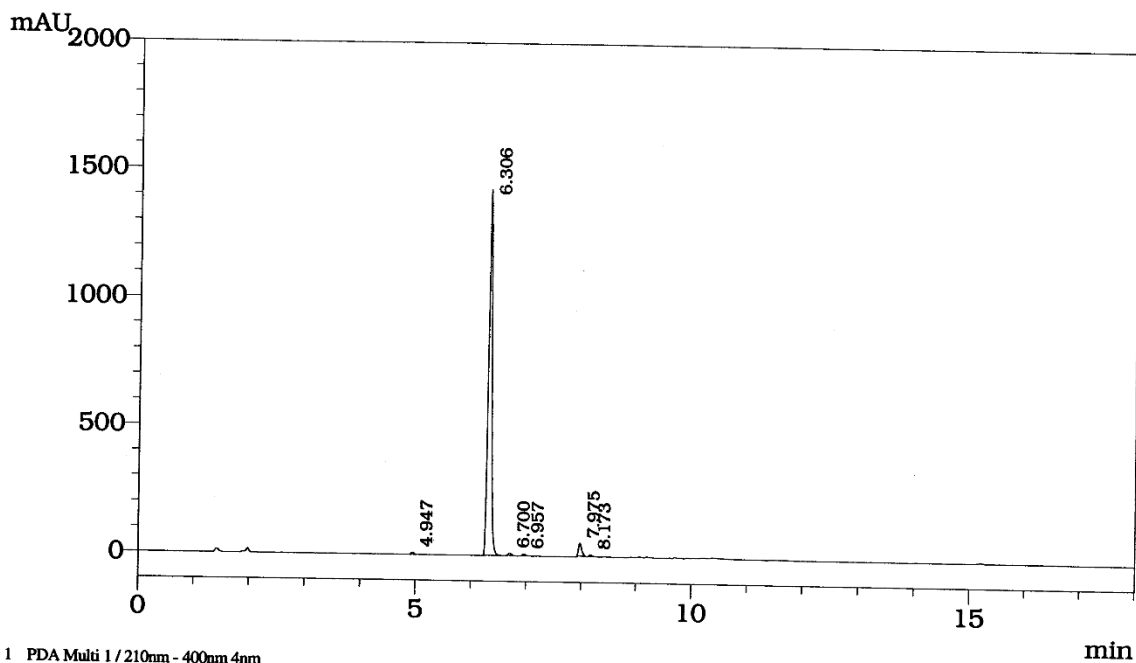
Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	10.132	3182	0.105	Cannot be calculated
2	10.578	2975452	98.436	1.00000
3	10.850	42366	1.402	0.99992
4	11.114	1729	0.057	Cannot be calculated
Total		3022730	100.000	

HPLC chromatogram of 4'-(4-Chloro-1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-ol, (**10b**)

HPLC chromatogram of (10c)

Method:- HPLC_X-Select(Formic acid)
 Column : X-Select CSH C18 (4.6*150) mm 3.5u
 Mobile Phase: A - Acetonitrile
 B - 0.1% Formic acid+5% Acetonitrile in water
 Inj Volume; 5.0µL,
 Flow Rate: 1.0. mL/minute
 Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
 hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable

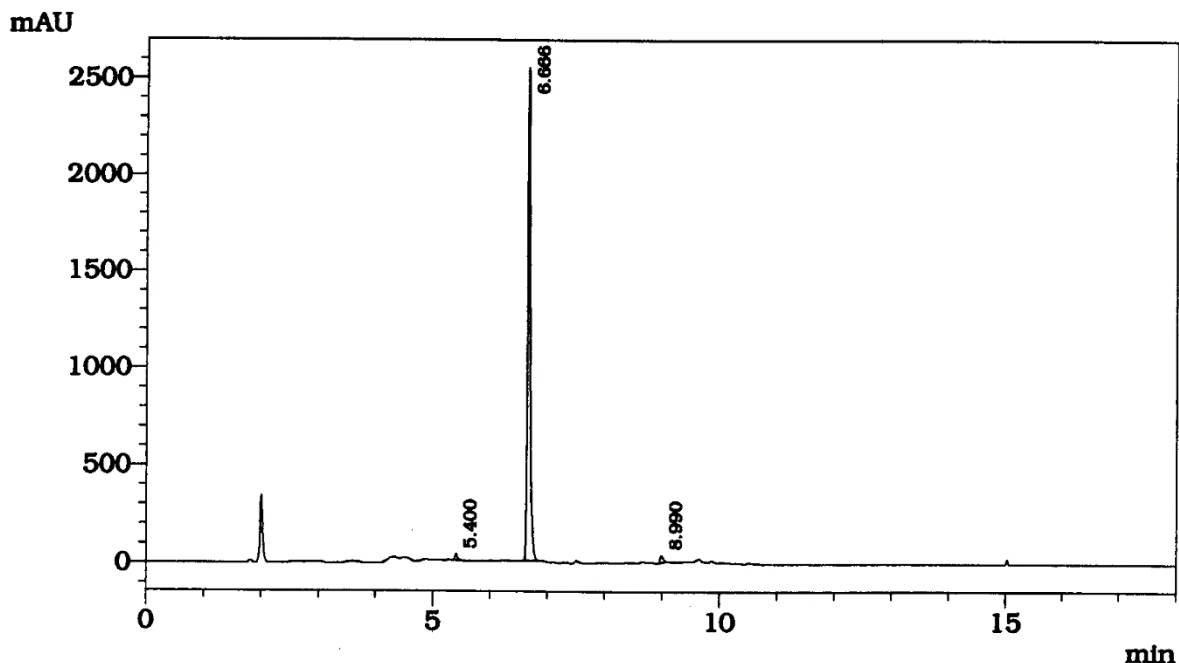
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	4.947	27535	0.432	0.99999
2	6.306	6075243	95.315	1.00000
3	6.700	33311	0.523	0.99990
4	6.957	19225	0.302	0.99982
5	7.975	200952	3.153	1.00000
6	8.173	17615	0.276	0.99981
Total		6373881	100.000	

HPLC chromatogram of 1-Amino-3-((4'-(1-isobutyl-3-(trifluoromethyl)-1H-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-2-ol (**11a**).

Method:- HPLC_X-Select(Formic acid)
Column : X-Select CSH C18 (4.6*150) mm 3.5u
Mobile Phase: A - Acetonitrile
B - 0.1% Formic acid+5% Acetonitrile in water
Inj Volume; 5.0µL,
Flow Rate: 1.0. mL/minute
Gradient program: Initial hold 95% B for 1 min., 95% B to 0 % B in 8 minute,
hold till 12 min, at 15.0 min B conc is 95 % up to 18 min

Chromatogram



1 PDA Multi 1 / 210nm - 400nm 4nm

PeakTable
PDA Ch1 210nm - 400nm 4nm

Peak#	Ret. Time	Area	Area %	Peak Purity Index
1	5.400	91238	1.095	0.99999
2	6.666	8105251	97.256	0.99891
3	8.990	137484	1.650	0.97315
Total		8333974	100.000	

HPLC chromatogram of 2-amino-3-((4'-(1-isobutyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl)-3-(methylsulfonyl)-[1,1'-biphenyl]-4-yl)oxy)propan-1-ol (**11b**)