Electronic Supplementary Material (ESI) for RSC Advances.

Potentially antibreast cancer enamidines *via* azide-alkyne-amine coupling and their molecular docking studies

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Supporting Information

1. General Information

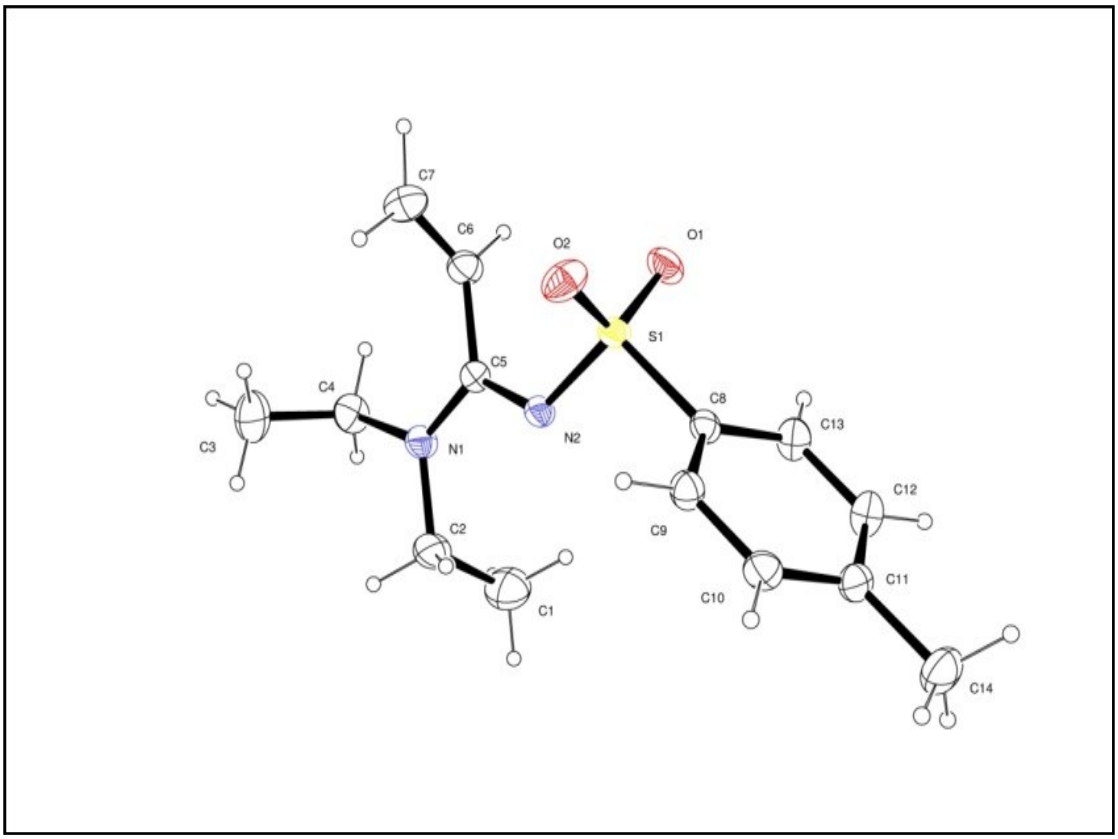
1.1 Materials

Unless otherwise stated, all commercial reagents and solvents were used without additional purification. Analytical thin layer chromatography (TLC) was performed on Merck precoated silica gel 60F 254 plates. All other chemicals were obtained from local suppliers or synthesized according to the literature procedures.

1.2 Methods

The visualization on TLC was achieved by the use of UV light (254 nm). Column chromatography was undertaken on silica gel (60-120 mesh). ^{1}H NMR was recorded on 300 MHz spectrometer. Chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane (TMS). The following abbreviations were used to describe peak patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constant, *J*, was reported in Hertz unit (Hz). ^{13}C NMR was recorded on 75 MHz spectrometer and was fully decoupled by broad band decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-d.

2. Crystallographic Data:



ORTEP Drawing of Compound 4a

Table 1.Crystal data and structure refinement for 4a

Identification code	**4a**
Empirical formula	$C_{14}\ H_{20}\ N_2\ O_2\ S$
Formula weight	280.38
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	monoclinic, space group $P2^{1/n}$
Unit cell dimensions	a = 6.605 A alpha = 90 deg.

	b = 13.973 A beta = 94.04 deg.
	c = 16.200 A gamma = 90 deg.
Volume	1491.4 A^3
Z, Calculated density	4, 1.249 Mg/m^3
Absorption coefficient	0.217 mm^-1
F(000)	600
Crystal size	0.20 x 0.20 x 0.15 mm
Theta range for data collection	2.52 to 24.99 deg.
Limiting indices	-7<=h<=7, -16<=k<=16, -19<=l<=19
Reflections collected / unique	12478 / 2615 [R(int) = 0.0183]
Completeness to theta = 24.99	99.7 %
Max. and min. transmission	0.9682 and 0.9579
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2615 / 3 / 184
Goodness-of-fit on F^2	1.041
Final R indices [I>2sigma(I)]	R1 = 0.0474, wR2 = 0.1303
R indices (all data)	R1 = 0.0536, wR2 = 0.1395
Largest diff. peak and hole	0.574 and -0.303 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropicdisplacement parameters (A^2 x 10^3) for 0231_200.U(eq) is defined as one third of the trace of the orthogonalizedUij tensor

	xy	z	U(eq)	
C(1)	4754(6)	4330(3)	10948(2)	101(1)
C(2)	2866(5)	3961(2)	10538(2)	73(1)
C(3)	-628(5)	2581(3)	11113(2)	88(1)
C(4)	1618(4)	2544(2)	11304(2)	62(1)
C(5)	3623(3)	2352(2)	10076(1)	42(1)
C(6)	3559(4)	1294(2)	10203(2)	59(1)
C(7)	2161(6)	742(2)	9914(2)	85(1)
C(8)	7067(3)	3053(2)	8348(1)	42(1)
C(9)	6130(4)	3656(2)	7758(2)	51(1)
C(10)	7234(4)	4371(2)	7411(2)	55(1)
C(11)	9282(4)	4489(2)	7631(1)	52(1)
C(12)	10191(4)	3873(2)	8212(2)	61(1)
C(13)	9099(4)	3157(2)	8570(2)	56(1)
C(14)	10486(5)	5265(2)	7241(2)	78(1)
N(1)	2747(3)	2909(1)	10614(1)	53(1)
N(2)	4555(3)	2764(1)	9481(1)	45(1)
O(1)	7096(3)	1469(1)	9178(1)	65(1)
O(2)	4207(3)	1784(1)	8181(1)	71(1)
S(1)	5660(1)	2142(1)	8803(1)	44(1)

Table 3.Bond lengths [A] and angles [deg] for 4a

C(1)-C(2)	1.464(5)
C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600
C(1)-H(1C)	0.9600
C(2)-N(1)	1.478(3)
C(2)-H(2A)	0.9700
C(2)-H(2B)	0.9700
C(3)-C(4)	1.495(4)
C(3)-H(3A)	0.9600
C(3)-H(3B)	0.9600
C(3)-H(3C)	0.9600
C(4)-N(1)	1.478(3)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-N(2)	1.312(3)
C(5)-N(1)	1.330(3)
C(5)-C(6)	1.494(3)
C(6)-C(7)	1.267(4)
C(6)-H(6)	1.060(18)
C(7)-H(7')	1.082(19)
C(7)-H(7")	1.076(19)
C(8)-C(13)	1.373(3)
C(8)-C(9)	1.386(3)
C(8)-S(1)	1.768(2)
C(9)-C(10)	1.380(3)
C(9)-H(9)	0.9300
C(10)-C(11)	1.384(3)
C(10)-H(10)	0.9300
C(11)-C(12)	1.381(4)

C(11)-C(14)	1.510(3)
C(12)-C(13)	1.384(4)
C(12)-H(12)	0.9300
C(13)-H(13)	0.9300
C(14)-H(14A)	0.9600
C(14)-H(14B)	0.9600
C(14)-H(14C)	0.9600
N(2)-S(1)	1.6143(18)
O(1)-S(1)	1.4391(18)
O(2)-S(1)	1.4324(18)
C(2)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
C(2)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
C(1)-C(2)-N(1)	111.2(3)
C(1)-C(2)-H(2A)	109.4
N(1)-C(2)-H(2A)	109.4
C(1)-C(2)-H(2B)	109.4
N(1)-C(2)-H(2B)	109.4
H(2A)-C(2)-H(2B)	108
C(4)-C(3)-H(3A)	109.5
C(4)-C(3)-H(3B)	109.5
H(3A)-C(3)-H(3B)	109.5
C(4)-C(3)-H(3C)	109.5
H(3A)-C(3)-H(3C)	109.5
H(3B)-C(3)-H(3C)	109.5
N(1)-C(4)-C(3)	112.2(2)
N(1)-C(4)-H(4A)	109.2
C(3)-C(4)-H(4A)	109.2

N(1)-C(4)-H(4B)	109.2
C(3)-C(4)-H(4B)	109.2
H(4A)-C(4)-H(4B)	107.9
N(2)-C(5)-N(1)	118.2(2)
N(2)-C(5)-C(6)	123.7(2)
N(1)-C(5)-C(6)	118.1(2)
C(7)-C(6)-C(5)	125.4(3)
C(7)-C(6)-H(6)	108.6(19)
C(5)-C(6)-H(6)	126.0(19)
C(6)-C(7)-H(7')	121(2)
C(6)-C(7)-H(7'')	110(3)
H(7')-C(7)-H(7'')	129(4)
C(13)-C(8)-C(9)	119.8(2)
C(13)-C(8)-S(1)	120.01(17)
C(9)-C(8)-S(1)	120.20(17)
C(10)-C(9)-C(8)	119.9(2)
C(10)-C(9)-H(9)	120.1
C(8)-C(9)-H(9)	120.1
C(9)-C(10)-C(11)	121.1(2)
C(9)-C(10)-H(10)	119.5
C(11)-C(10)-H(10)	119.5
C(12)-C(11)-C(10)	118.1(2)
C(12)-C(11)-C(14)	121.1(2)
C(10)-C(11)-C(14)	120.8(2)
C(11)-C(12)-C(13)	121.4(2)
C(11)-C(12)-H(12)	119.3
C(13)-C(12)-H(12)	119.3
C(8)-C(13)-C(12)	119.7(2)
C(8)-C(13)-H(13)	120.1
C(12)-C(13)-H(13)	120.1
C(11)-C(14)-H(14A)	109.5

C(11)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(11)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(5)-N(1)-C(2)	120.0(2)
C(5)-N(1)-C(4)	124.0(2)
C(2)-N(1)-C(4)	116.0(2)
C(5)-N(2)-S(1)	121.44(16)
O(2)-S(1)-O(1)	117.19(13)
O(2)-S(1)-N(2)	110.76(11)
O(1)-S(1)-N(2)	112.38(10)
O(2)-S(1)-C(8)	107.67(11)
O(1)-S(1)-C(8)	107.25(10)
N(2)-S(1)-C(8)	99.97(10)

Symmetry transformations used to generate equivalent atoms:

Table 4.Anisotropic displacement parameters (A^2 x 10^3) for 4a. The anisotropic displacement factor exponent takes the form: -2 pi^2 [h^2 a*^2 U11 +...+ 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
C(1)	115(3)	85(2)	105(3)	-25(2)	15(2)	-11(2)
C(2)	88(2)	58(2)	79(2)	-14(1)	40(2)	0(2)
C(3)	71(2)	120(3)	75(2)	16(2)	29(2)	-3(2)
C(4)	74(2)	73(2)	41(1)	3(1)	19(1)	3(1)
C(5)	43(1)	43(1)	40(1)	1(1)	3(1)	2(1)
C(6)	70(2)	47(1)	61(2)	9(1)	18(1)	3(1)
C(7)	96(2)	51(2)	108(3)	8(2)	17(2)	-9(2)
C(8)	45(1)	44(1)	37(1)	-2(1)	11(1)	4(1)
C(9)	46(1)	56(1)	53(1)	6(1)	4(1)	4(1)
C(10)	64(2)	53(1)	51(1)	12(1)	8(1)	9(1)
C(11)	61(1)	54(1)	43(1)	-3(1)	18(1)	-4(1)
C(12)	47(1)	80(2)	57(1)	7(1)	6(1)	-7(1)
C(13)	48(1)	68(2)	50(1)	14(1)	1(1)	4(1)
C(14)	88(2)	74(2)	76(2)	11(2)	26(2)	-17(2)
N(1)	61(1)	49(1)	51(1)	-2(1)	21(1)	2(1)
N(2)	49(1)	39(1)	47(1)	0(1)	15(1)	3(1)
O(1)	72(1)	49(1)	76(1)	15(1)	27(1)	20(1)
O(2)	88(1)	68(1)	55(1)	-11(1)	5(1)	-28(1)
S(1)	53(1)	37(1)	44(1)	-3(1)	12(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for 4a

	x	y	z	U(eq)
H(1A)	4795	5013	10887	151
H(1B)	5891	4050	10699	151
H(1C)	4813	4169	11525	151
H(2A)	2794	4136	9958	88
H(2B)	1718	4249	10786	88
H(3A)	-1301	2336	11575	132
H(3B)	-987	2199	10632	132
H(3C)	-1039	3231	11009	132
H(4A)	1971	2922	11795	74
H(4B)	2022	1887	11421	74
H(9)	4760	3579	7597	62
H(10)	6591	4781	7023	67
H(12)	11567	3940	8365	73
H(13)	9740	2749	8959	67
H(14A)	9612	5619	6853	117
H(14B)	11565	4981	6959	117
H(14C)	11047	5690	7663	117
H(7')	2240(60)	-21(15)	10030(20)	125(13)
H(7'')	990(60)	1140(30)	9570(30)	180(20)
H(6)	4660(40)	880(20)	10551(19)	97(11)

Table 6.Torsion angles [deg] for 4a

N(2)-C(5)-C(6)-C(7)	-93.6(4)
N(1)-C(5)-C(6)-C(7)	88.9(4)
C(13)-C(8)-C(9)-C(10)	-1.4(4)
S(1)-C(8)-C(9)-C(10)	179.36(18)
C(8)-C(9)-C(10)-C(11)	1.1(4)
C(9)-C(10)-C(11)-C(12)	-0.2(4)
C(9)-C(10)-C(11)-C(14)	179.2(2)
C(10)-C(11)-C(12)-C(13)	-0.3(4)
C(14)-C(11)-C(12)-C(13)	-179.7(3)
C(9)-C(8)-C(13)-C(12)	0.9(4)
S(1)-C(8)-C(13)-C(12)	-179.9(2)
C(11)-C(12)-C(13)-C(8)	-0.1(4)
N(2)-C(5)-N(1)-C(2)	-0.9(3)
C(6)-C(5)-N(1)-C(2)	176.8(3)
N(2)-C(5)-N(1)-C(4)	178.9(2)
C(6)-C(5)-N(1)-C(4)	-3.4(3)
C(1)-C(2)-N(1)-C(5)	-84.7(3)
C(1)-C(2)-N(1)-C(4)	95.4(3)
C(3)-C(4)-N(1)-C(5)	-100.8(3)
C(3)-C(4)-N(1)-C(2)	79.0(4)
N(1)-C(5)-N(2)-S(1)	179.91(17)
C(6)-C(5)-N(2)-S(1)	2.4(3)
C(5)-N(2)-S(1)-O(2)	79.3(2)
C(5)-N(2)-S(1)-O(1)	-53.8(2)
C(5)-N(2)-S(1)-C(8)	-167.31(18)
C(13)-C(8)-S(1)-O(2)	-143.6(2)
C(9)-C(8)-S(1)-O(2)	35.6(2)
C(13)-C(8)-S(1)-O(1)	-16.6(2)
C(9)-C(8)-S(1)-O(1)	162.59(18)

C(13)-C(8)-S(1)-N(2)	100.7(2)
C(9)-C(8)-S(1)-N(2)	-80.1(2)

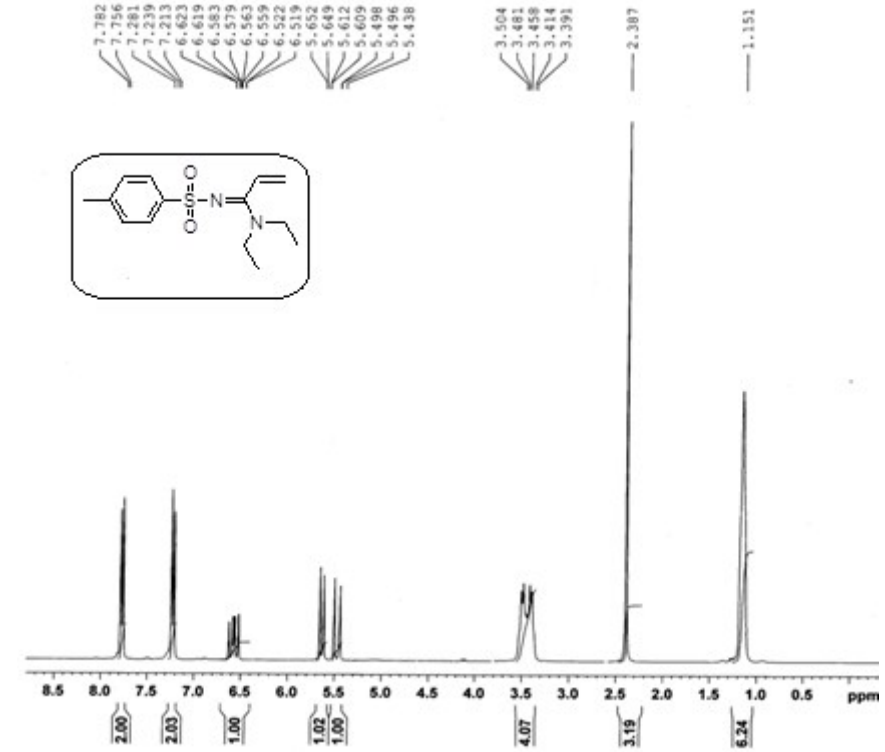
Symmetry transformations used to generate equivalent atoms

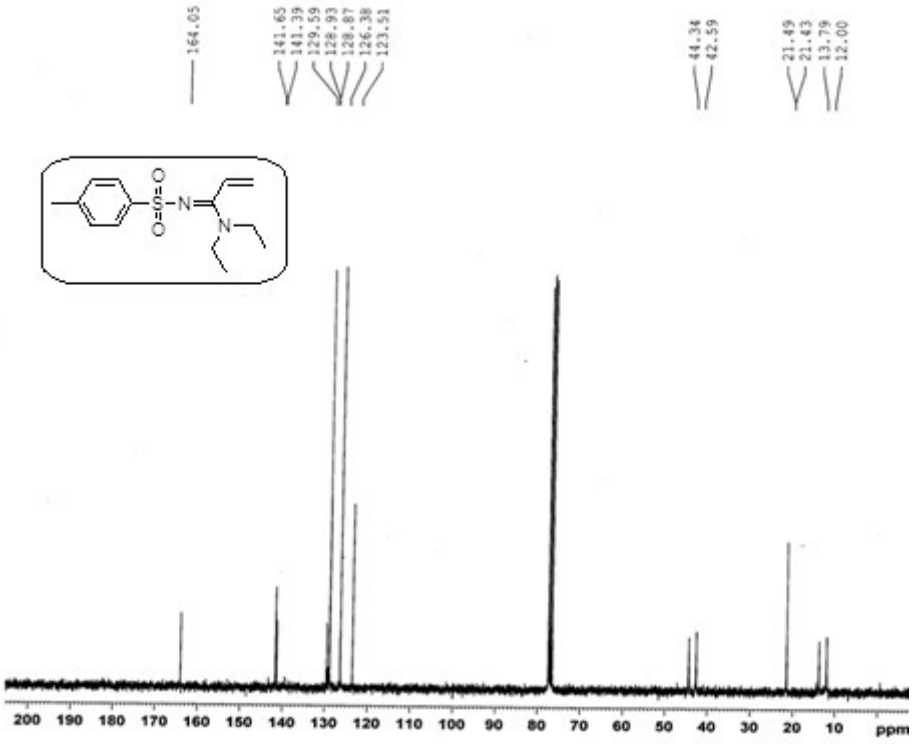
Table 7.Hydrogen bonds for4a [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

3. ^{1}H and ^{13}C NMR spectra of enamidines obtained in this study

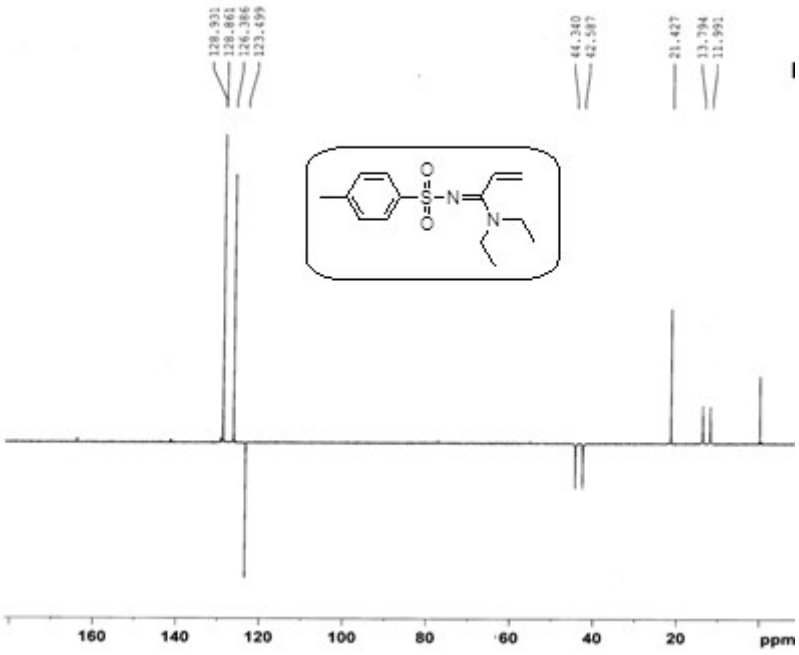
***N*,*N*-Diethyl-*N*'-[(4-methylphenyl)sulfonyl]prop-2-enamidamide**
(Table 2, entry 4a)



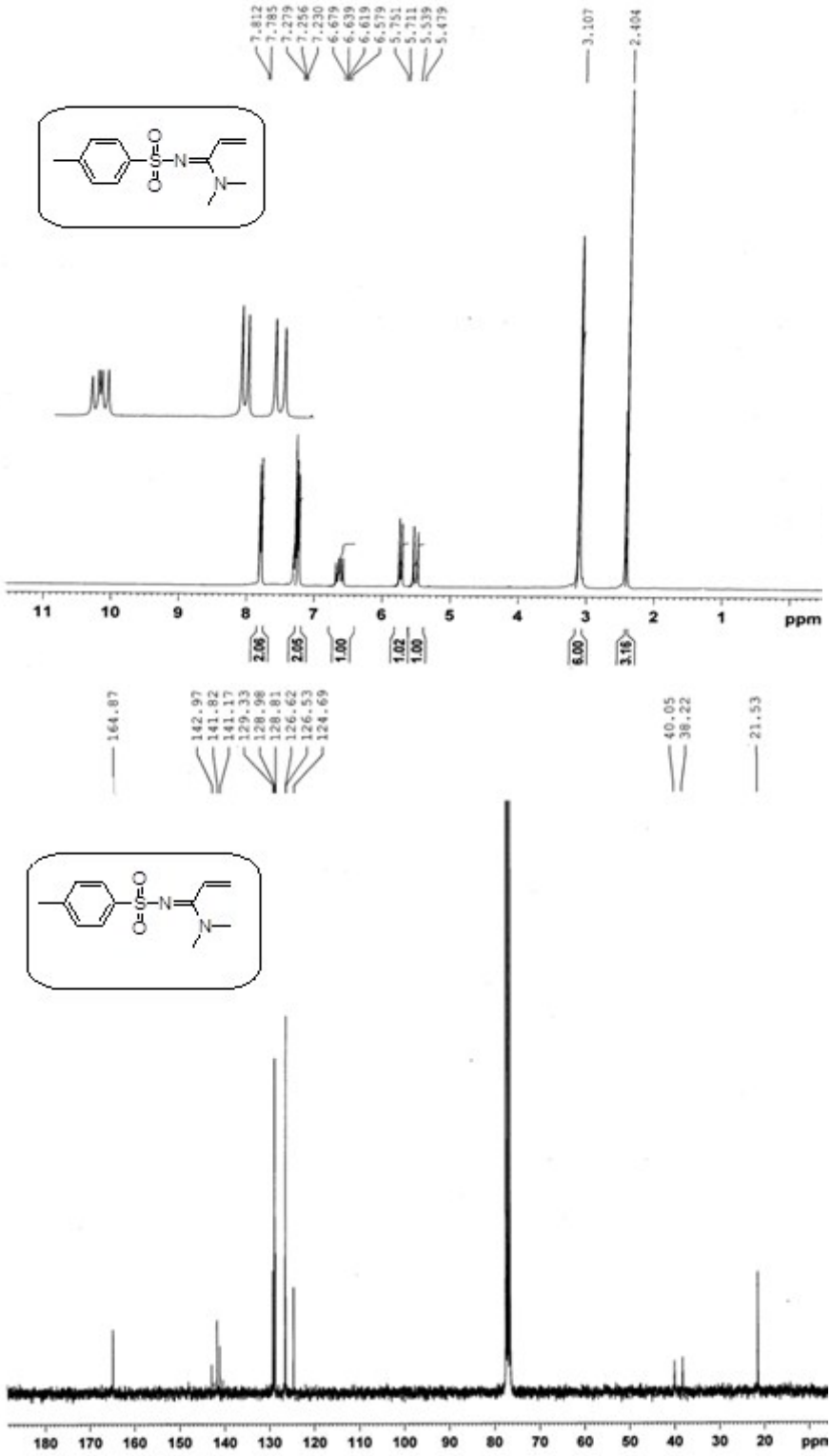


DEPT spectrum of *N*,*N*-diethyl-*N*'-[(4-methylphenyl)sulfonyl]prop-2-enimidamide

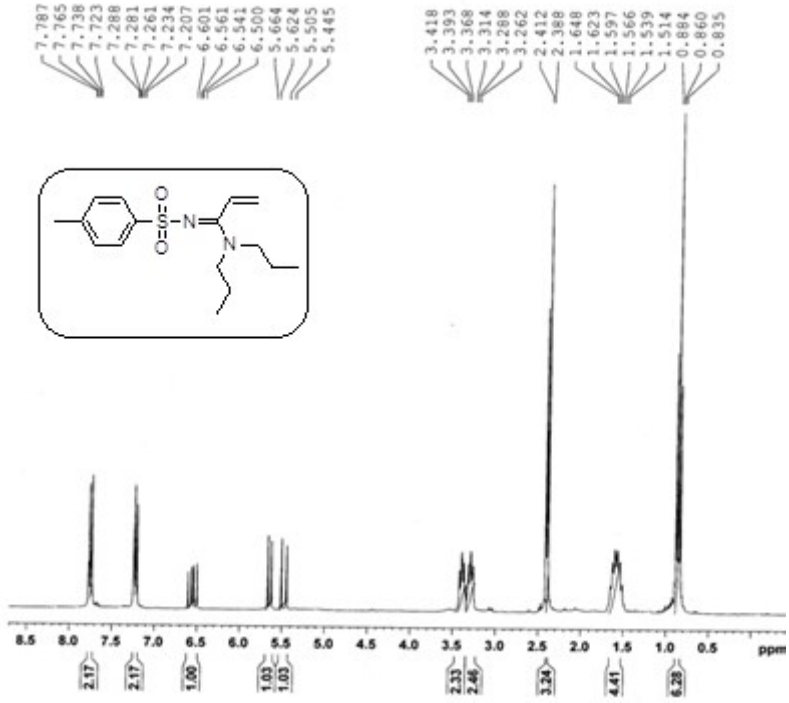
(Table 2, entry 4a)

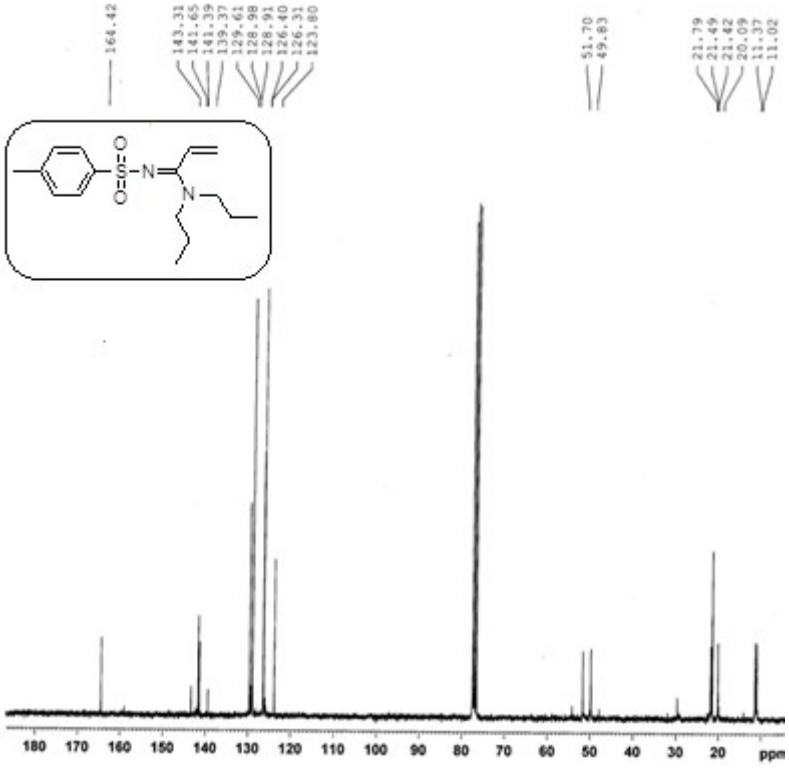


***N*,*N*-Dimethyl-*N*'-[(4-methylphenyl)sulfonyl]prop-2-enamidamide**
(Table 2, entry 4b)

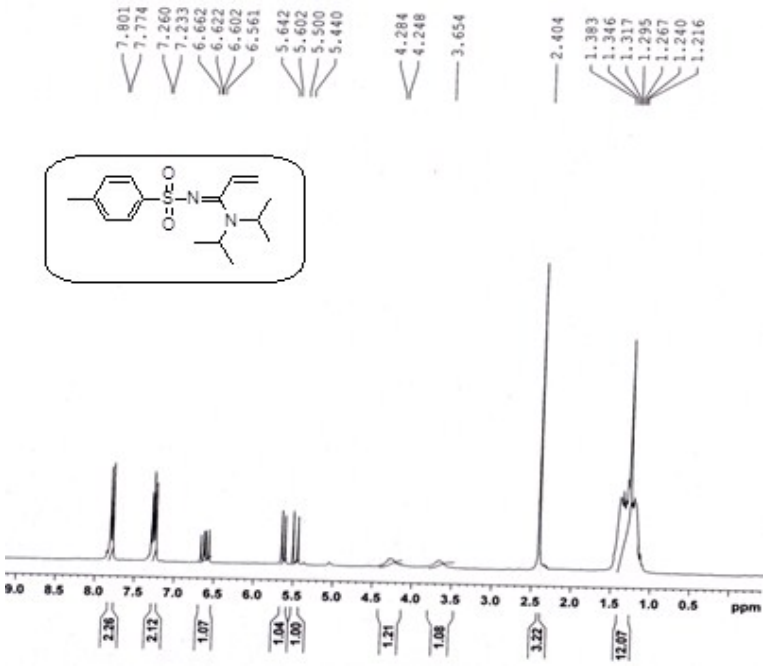


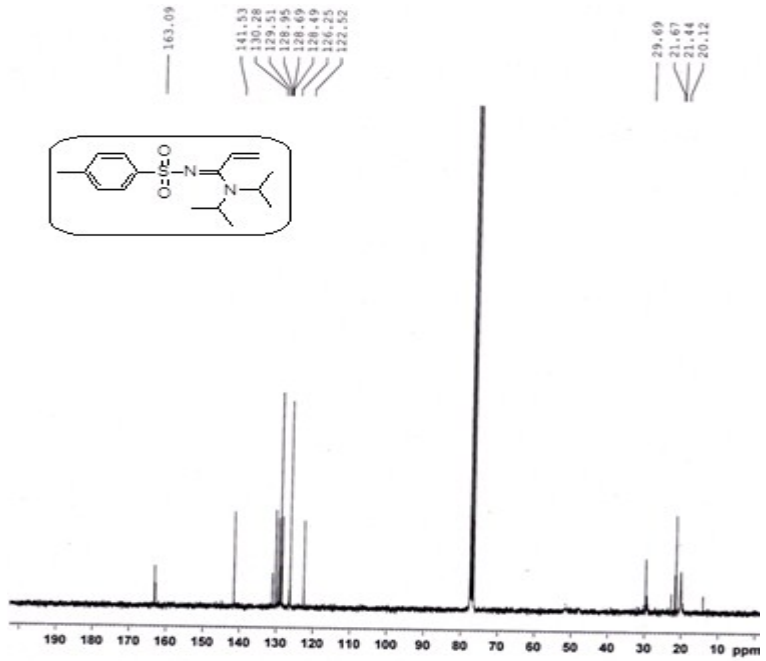
_N_'-[(4-Methylphenyl)sulfonyl]-_N_,_N_-dipropylprop-2-enamidamide
(Table 2, entry 4c)



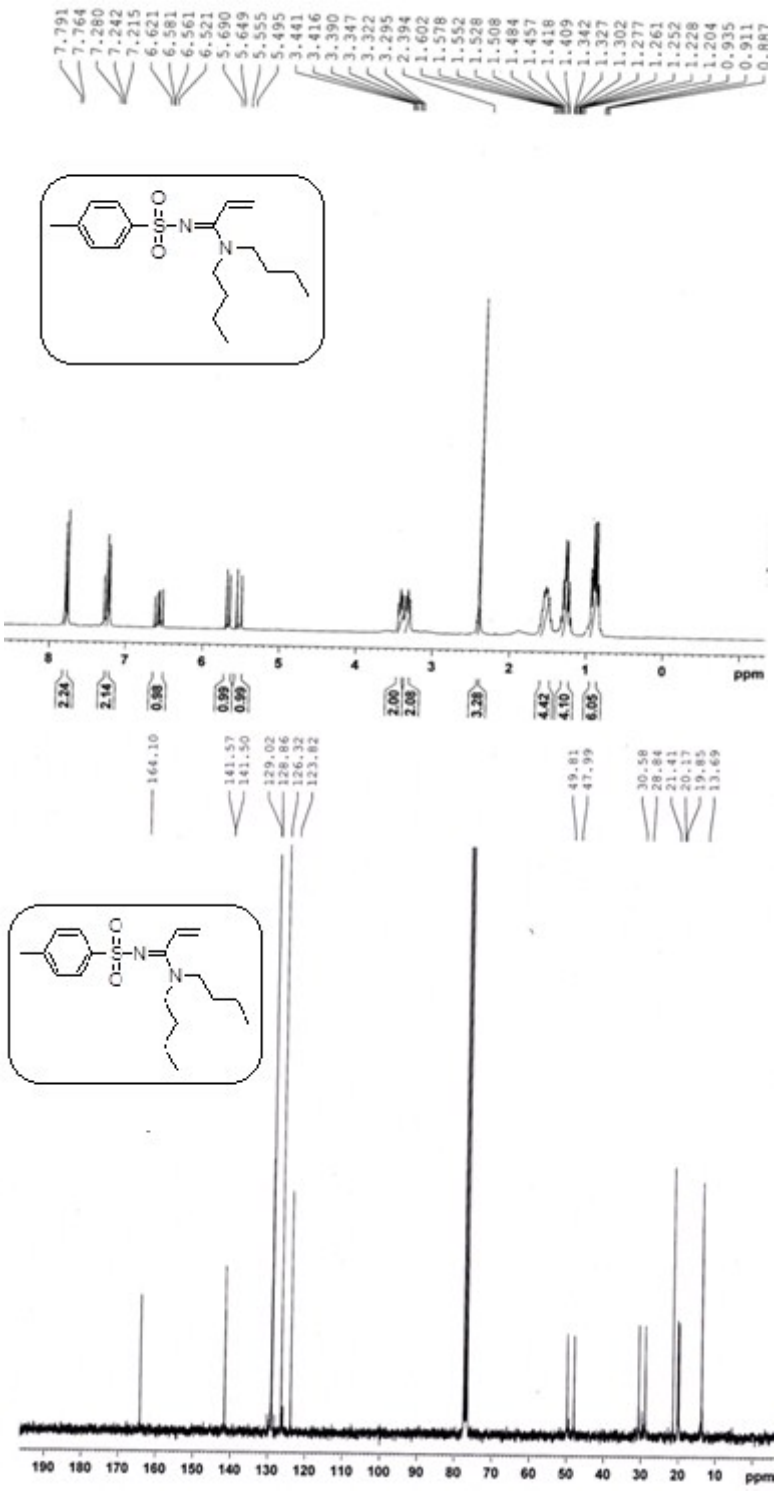


_N,N_-Diisopropyl-_N′_-[(4-methylphenyl)sulfonyl]prop-2-enamidamide
(Table 2, entry 4d)

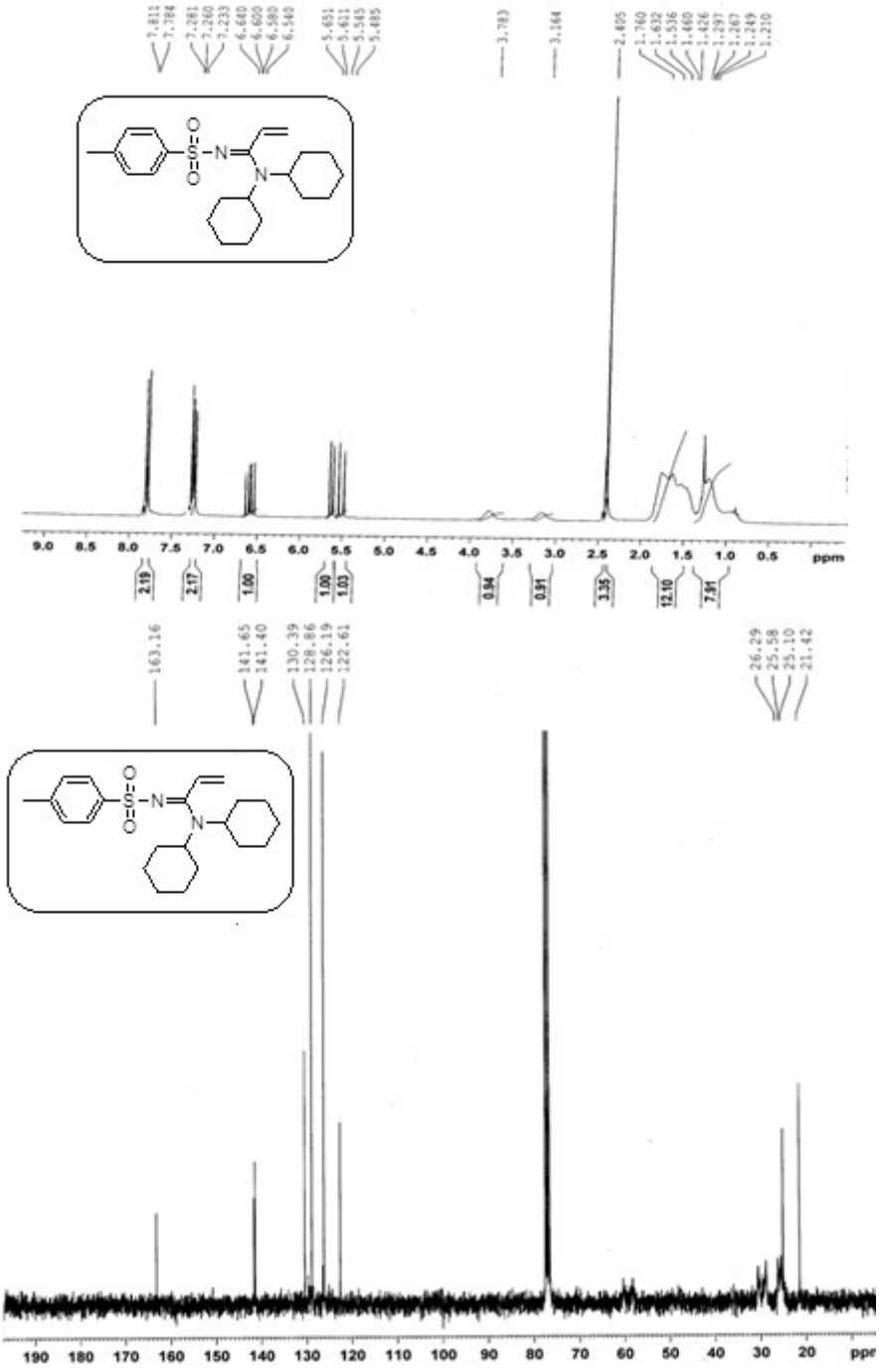




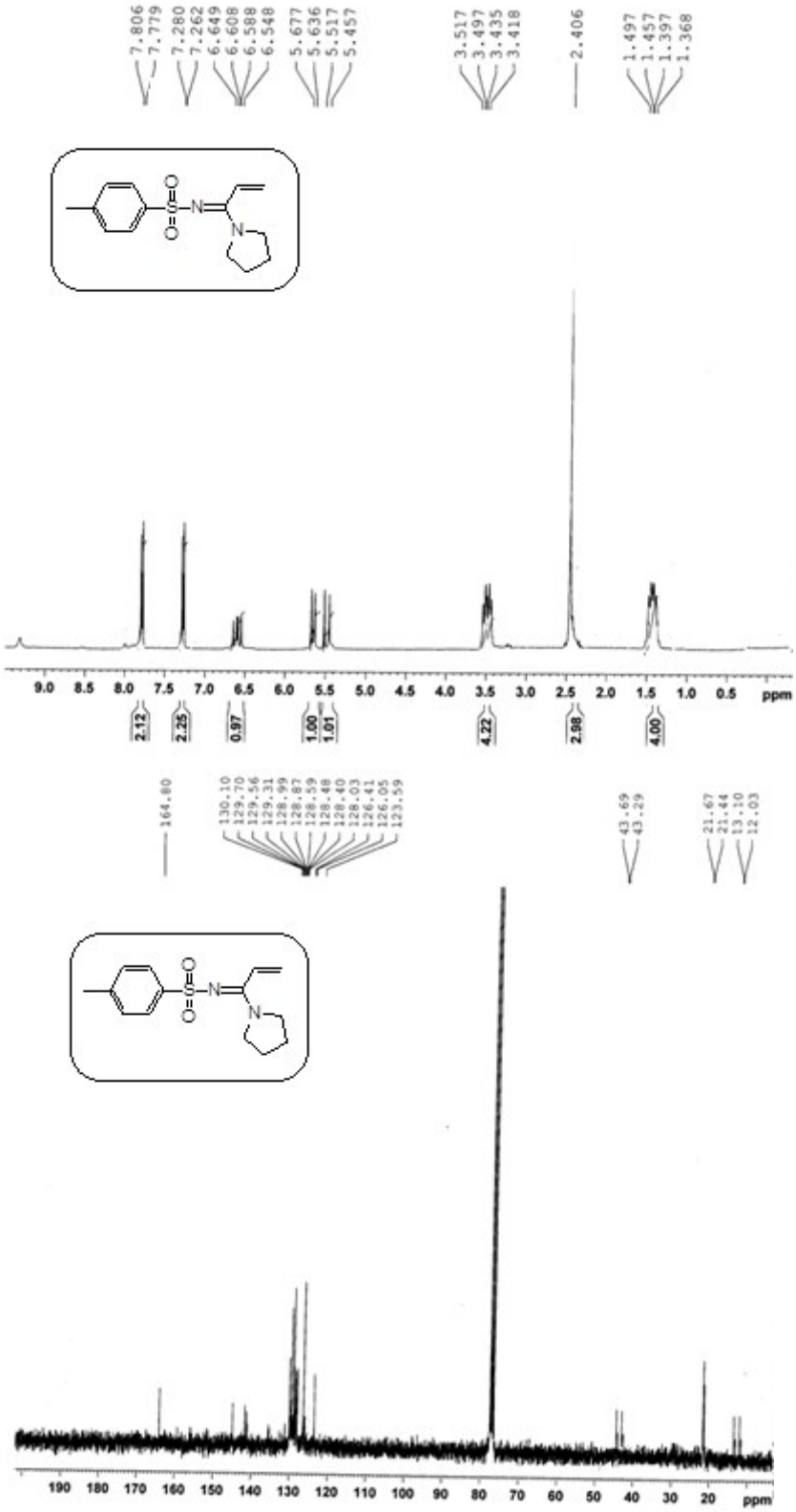
_N_'-[(4-Methylphenyl)sulfonyl]-_N_,_N_-di(n-butyl)prop-2-enamidamide
(Table 2, entry 4e)



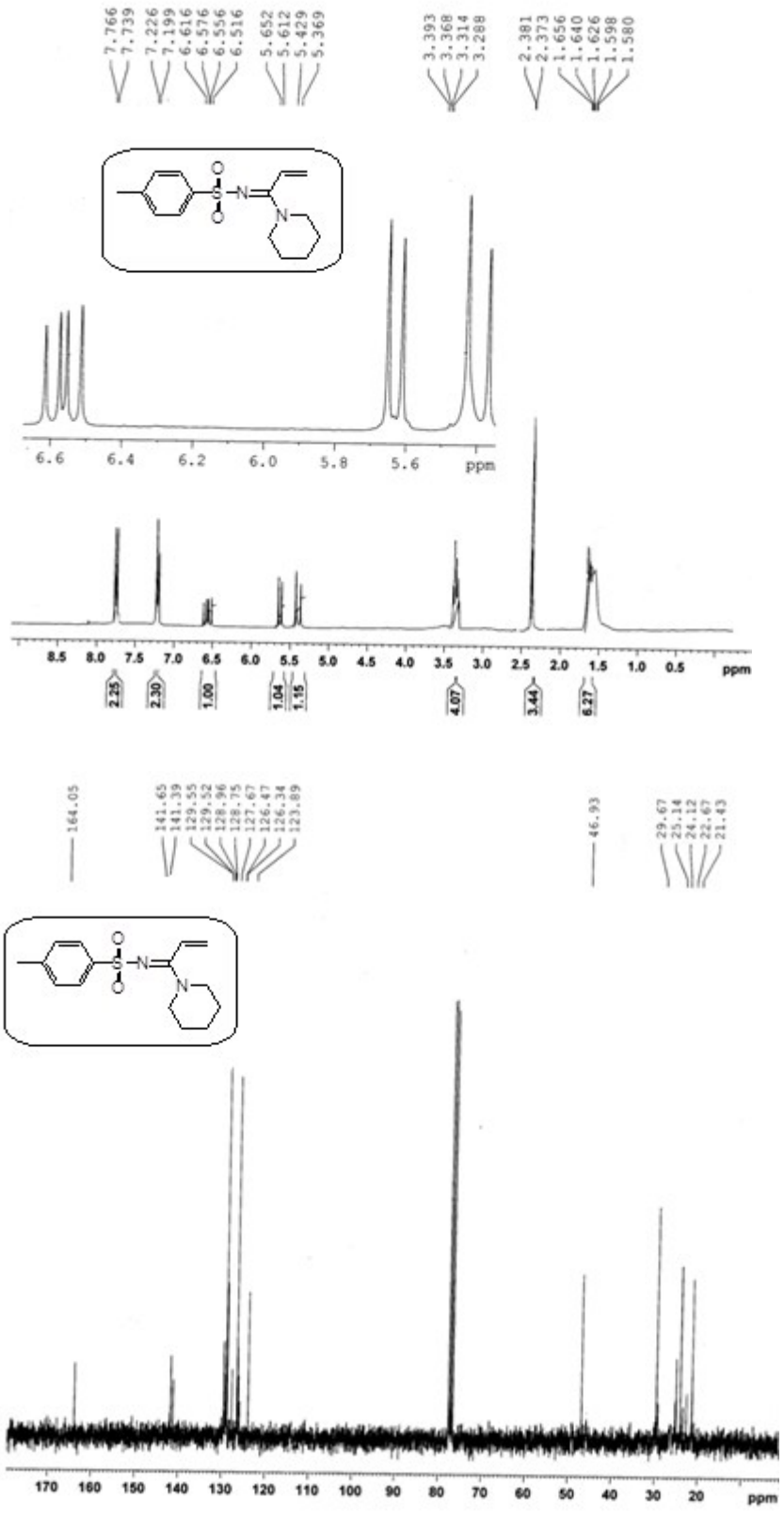
_N_'-[(4-Methylphenyl)sulfonyl]-_N_,_N_-di(cyclohexyl)prop-2-enamidamide
(Table 2, entry 4f)



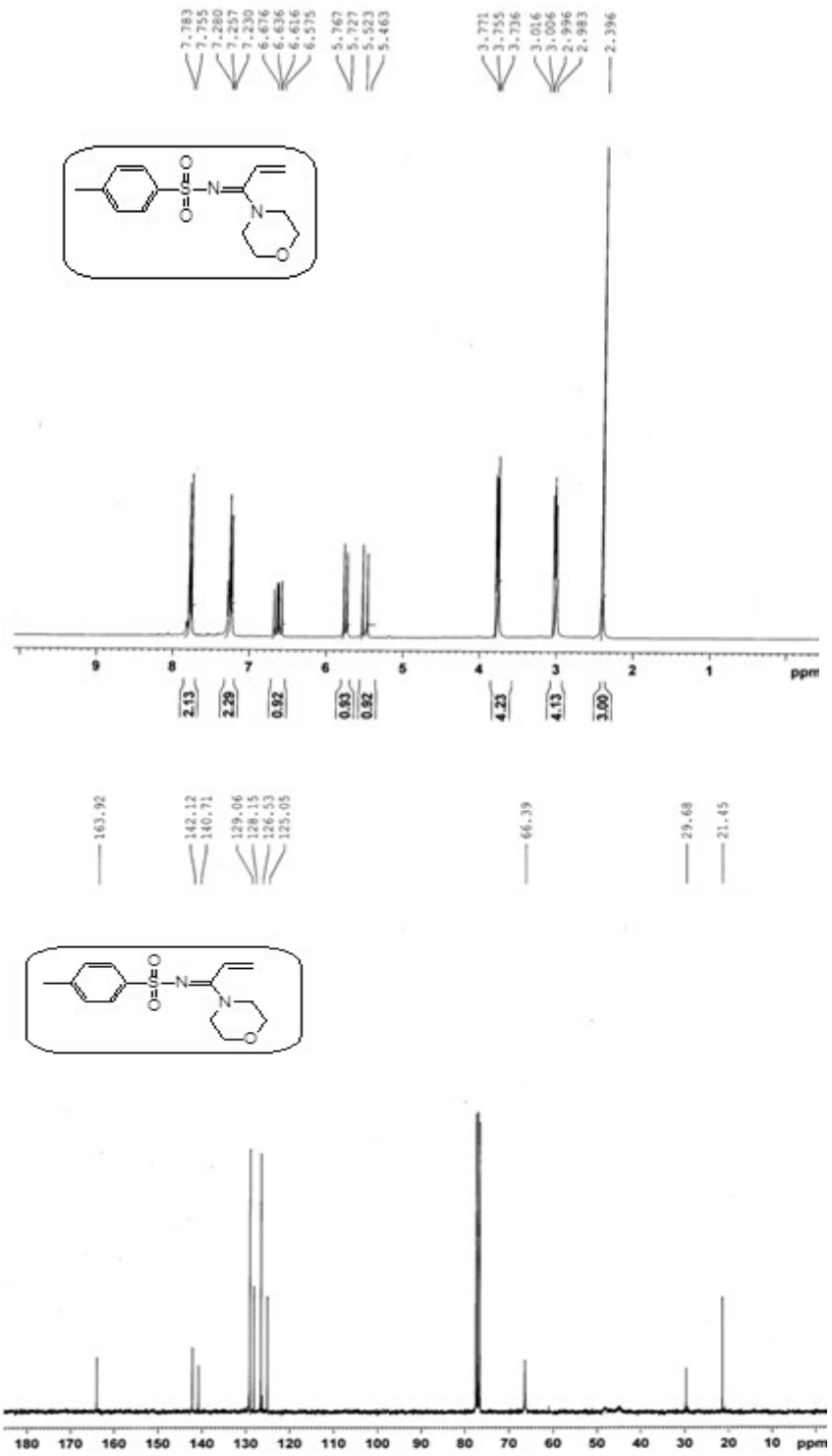
4-Methyl-*N*-(1-pyrrolidin-1-ylprop-2-en-1-ylidene)benzenesulfonamide
(Table 2, entry 4g)



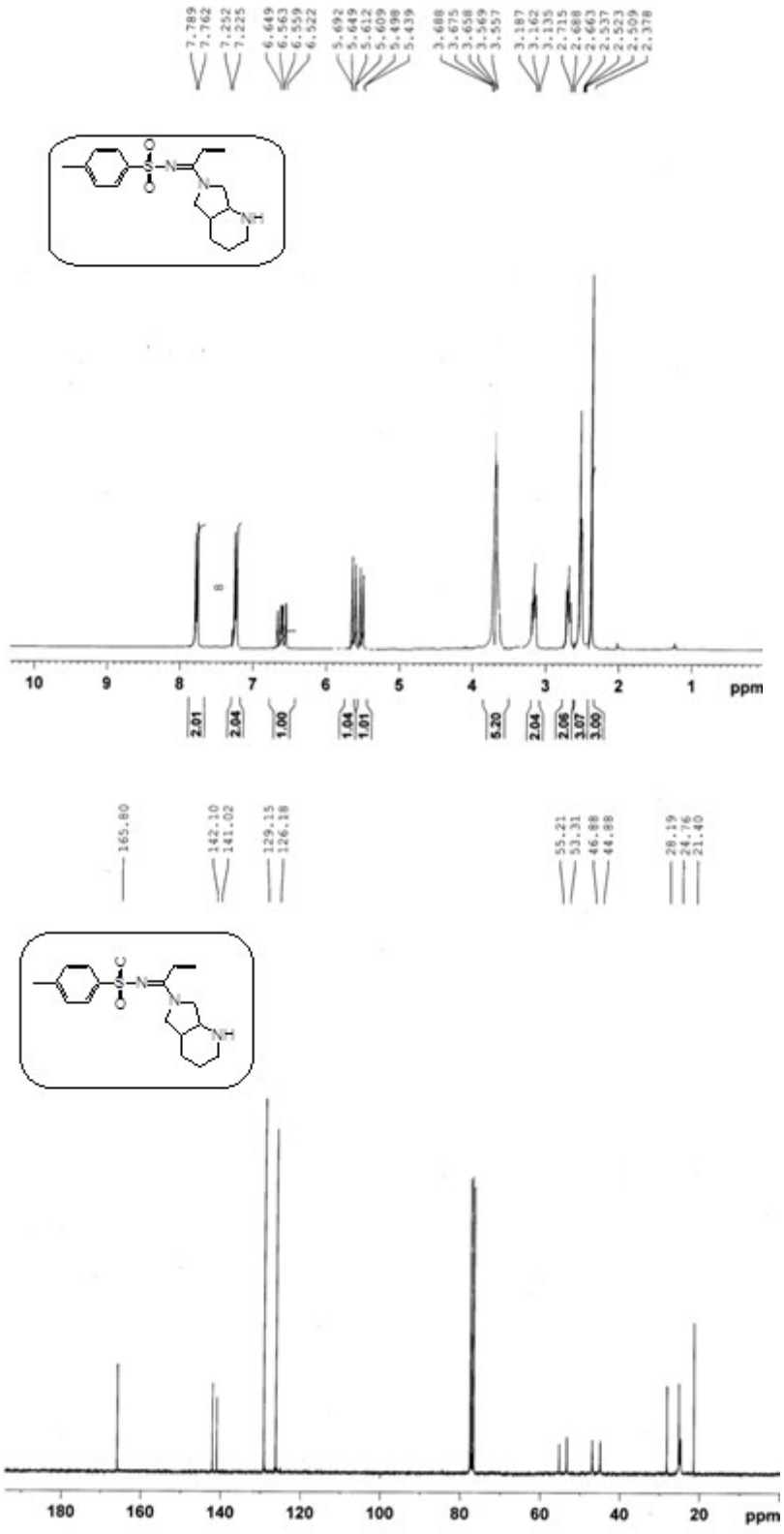
4-Methyl-*N*-(1-piperidin-1-ylprop-2-en-1-ylidene)benzenesulfonamide
(Table 2, entry 4h)



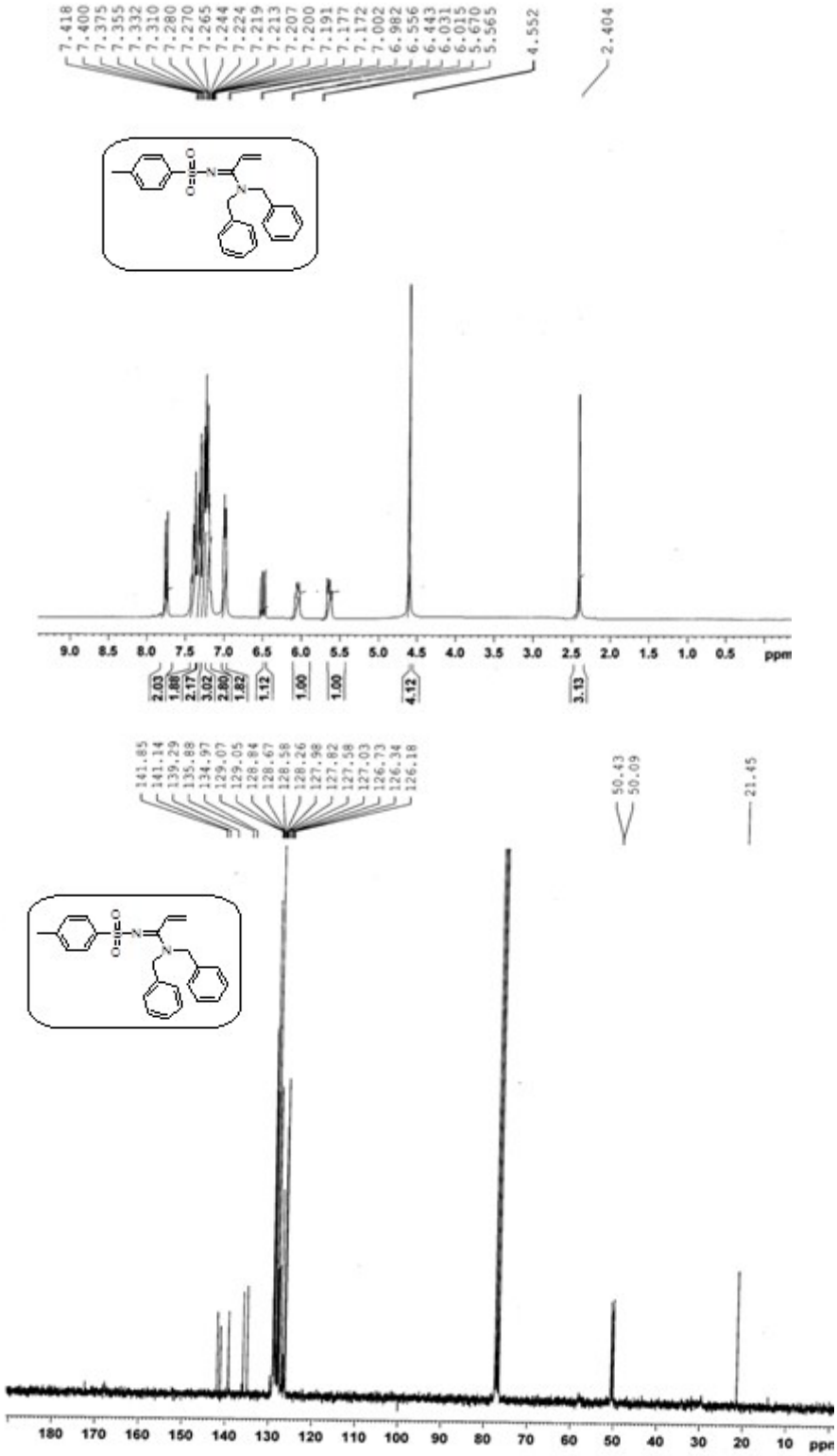
4-Methyl-*N*-(1-morpholin-4-ylprop-2-en-1-ylidene)benzenesulfonamide
(Table 2, entry 4i)



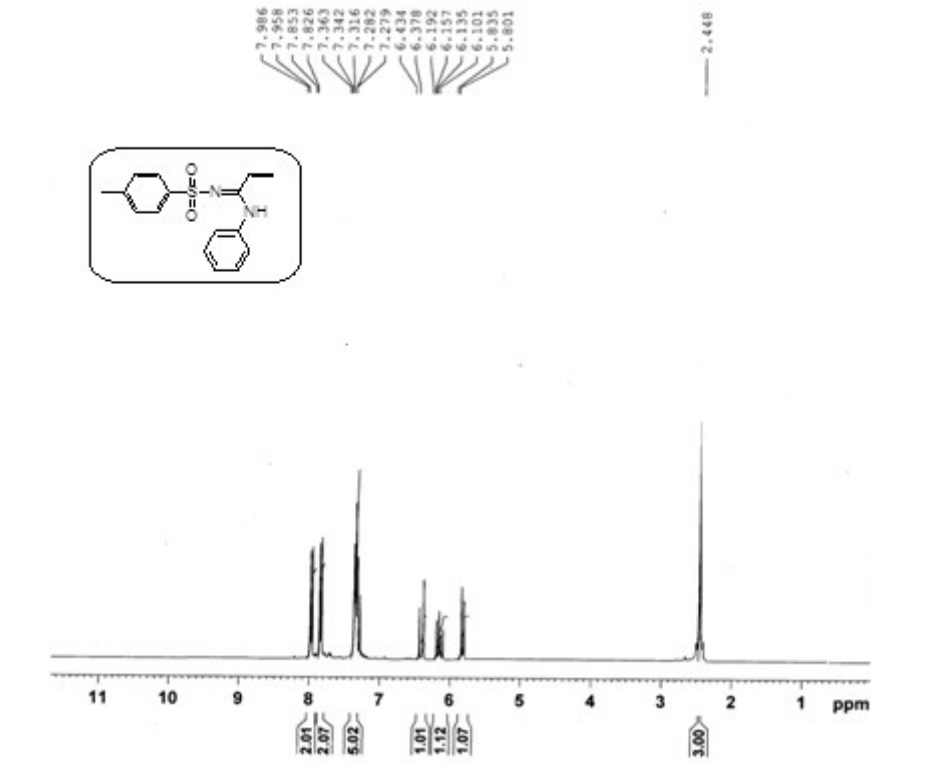
4-Methyl-*N*-[1-(octahydro-6*H*-pyrrolo[3,4-*b*]pyridin-6-yl)prop-2-en-1-ylidene]benzenesulfonamide(Table 2, entry 4j)

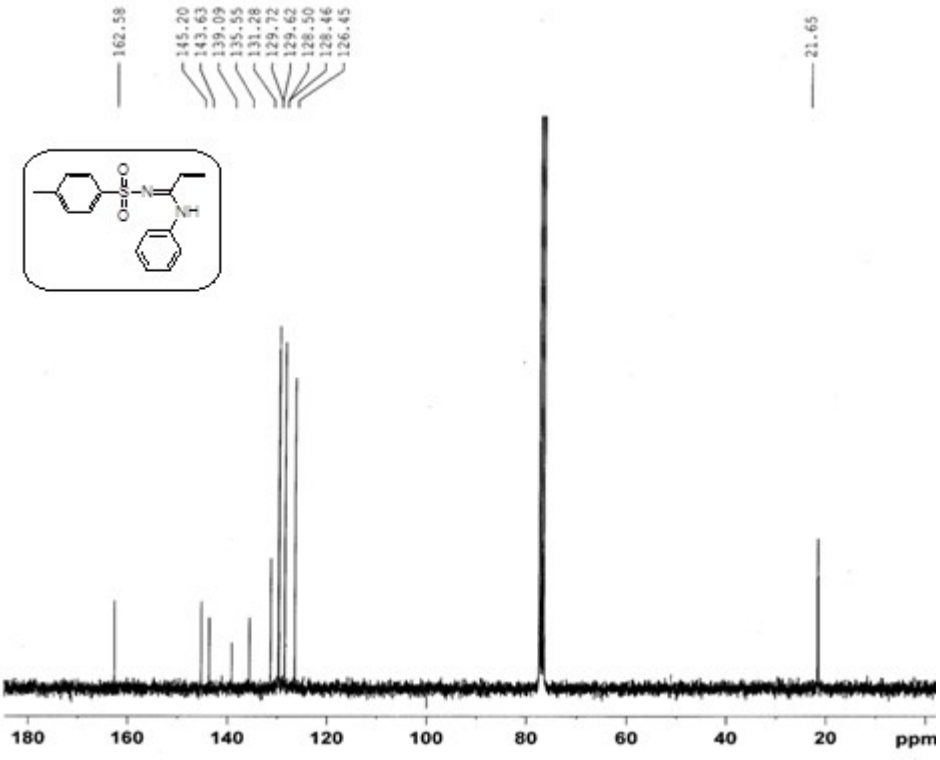


_N_'-[(4-Methylphenyl)sulfonyl]-_N_,_N_-dibenzylprop-2-enamidamide
(Table 2, entry 4k)



_N_'-[(4-Methylphenyl)sulfonyl]-_N_-phenylprop-2-enamidamide
(Table 2, entry 4l)





***N*-(2-Methoxyphenyl)-*N*'-[(4-methylphenyl)sulfonyl]prop-2-enamidamide**
(Table 2, entry 4m)