Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Asymmetric Activation of *tropos* 2,2'-Biphenol with Cinchonine Generating a Remarkably Effective Catalyst for the Asymmetric Strecker Reaction of *N*-Ts Protected Aldimines and Ketoimines

Jun Wang, Xiaolei Hu, Jun Jiang, Shaohua Gou, Xiao Huang, Xiaohua Liu, Xiaoming Feng*

CONTENTS:

(A) General

^{1}H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts are reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Melting points (m.p.) were measured on electrothermal digital melting point apparatus and were uncorrected. Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel OD-H/AD-H/AS-H in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]_D^{20}$ (c: g/100 mL, in solvent). ESI-HRMS spectra were recorded on a commercial apparatus and methanol was used to dissolve the sample. *N*-Ts Imines were prepared according to the literature procedures.[1] TMSCN and Ti(O*i*Pr)$_4$ were commercially available and distilled before use. Cinchona alkaloids are commercially available and directly used without further purification. Toluene used in the catalytic reactions was distilled from sodium benzophenone ketyl. Substituted BIPOLs[2a-f] and BINOL[2g] were synthesized according to the literatures. The spectra and other data were consistent with the reported values.

(B) General procedure for the asymmetric catalytic Strecker reaction

Method 1 was used for optimizing reaction conditions and studying catalyst structure; method 2 was used to expand the substrate scope of *N*-Ts imines.

Method 1:

Under Ar atmosphere, Ti(O*i*Pr)$_4$ (1.0 M in toluene, 20 *u*L, 0.02 mmol) was added to a dry tube containing a suspension of cinchonine (5.9 mg, 0.02 mmol), biphenol (0.02 mmol) and 0.25 mL toluene. The mixture was stirred at 40^{o}C for 1 h to give a clear solution. After that, *N*-Ts benzaldimine (25.9 mg, 0.10 mmol) in 0.2 mL toluene was transferred to the catalyst preprared above at –20^{o}C. Then TMSCN (16.2 *u*L, 0.12 mmol) followed by *i*PrOH (2.4 M in toluene, 50 *u*L, 0.12 mmol) (if required) was added at the same temperature and allowed the content to stir until the imine was consumed. The residue was purified by silica gel column chromatography (petroleum ether/CH_2Cl_2/diethyl ether, 15/2/3, *V/V/V* for the aldimines; petroleum ether/ethyl acetate, 5/1, *V/V* for the ketoimines) to afford the corresponding *N*-Ts amino nitrile.

Method 2:

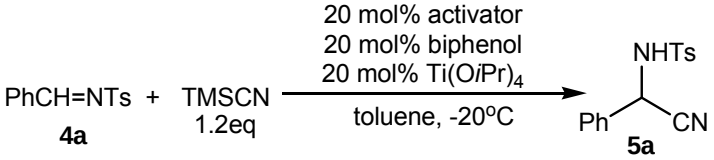
Step 1: Preparation of the catalyst (0.05 M in toluene):

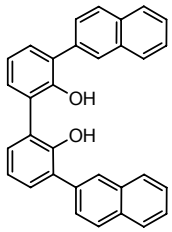
Under Ar atmosphere, Ti(O*i*Pr)$_4$ (1.0 M in toluene, 60 *u*L, 0.06 mmol) was added to a dry tube containing a suspension of cinchonine (15 mg, 0.05 mmol), bipenol **3h** (26.5 mg, 0.06 mmol) and toluene (0.6 mL). The mixture was stirred for 0.5-1.0 h at 40^{o}C and diluted to 1.0 mL with toluene to afford the catalyst solution (0.05 M in toluene).

Step 2: Manipulation of the asymmetric catalytic reaction:

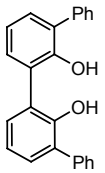
The catalyst (0.05 M in toluene, 100 *u*L, 0.005 mmol) prepared above was introduced to a dry reaction tube charged with *N*-Ts imine (0.1 mmol) and toluene (0.3 mL) under Ar atmosphere at –20^{o}C. Then TMSCN (2.4 M in toluene, 50 *u*L, 0.12 mmol) and *i*PrOH (2.4 M in toluene, 50 *u*L, 0.12 mmol) were added in turn with stirring. The reaction was monitored by TLC. When the imine was consumed, the residue was purified by silica gel column chromatography (petroleum ether/CH_2Cl_2/diethyl ether, 15/2/3, *V/V/V* for the aldimines; petroleum ether/ethyl acetate, 5/1, *V/V* for the ketoimines) to afford the desired corresponding *N*-Ts amino nitrile.

(C) The results of the asymmetric Strecker reaction employing some other amino alcohols and cinchona alkaloids as activators





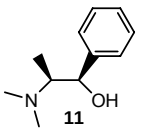
3h



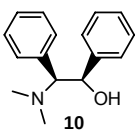
3g

Table 1. Asymmetric cyanation of **4a** using other activators.

entry	activator	biphenol	ee%
1	**10**	**3g**	4
2	**11**	**3g**	9
3	cinchonidine	**3h**	90(*R*)
4	quinine	**3h**	79(*R*)
5	quinidine	**3h**	93(*S*)



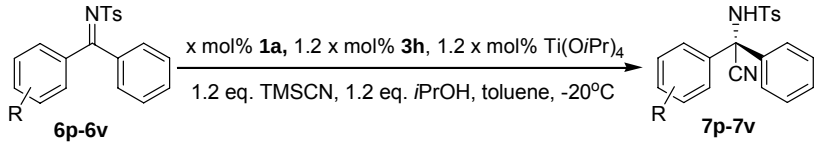
11



10

Other amino alcohols and cinchona alkaloids were tried to replace the cinchonine, but none of them exhibited better result (Table 1). However, cinchonidine gave the product in 90% ee with the opposite configuration, which made it possible to provide the (*R*)-enantiomer conveniently.

(D) The results of the cyanation of *N*-Ts unsymmetrical diarylketoimines



p: R = 2-F **t:** R = 3-Me
q: R = 2-Cl **u:** R = 4-Me
r: R = 2-Me **v:** R = 4-MeO
s: R = 3-Cl

Table 2. Asymmetric cyanation of *N*-Ts unsymmetrical diarylketoimines.

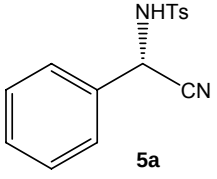
entry	ketoimine	x	time (h)	yield [%][b]	ee [%][c]
1	**6p**	5	45	26	76
2	**6p**	10	5	96	98
3	**6q**	10	45	95	97
4	**6r**	10	45	90	94
5[d]	**6r**	10	45	90	97
6	**6s**	10	11	>99	0
8	**6t**	10	8	>99	2
9	**6u**	10	8	>99	28
10	**6v**	10	8	>99	28

[a] Unless noted, reactions were carried out with imine (0.1 mmol), TMSCN (0.12 mmol), *i*PrOH (0.12 mmol) and toluene (0.5 mL) at –20°C. [b] Isolated yield. [c] Determined by HPLC. [d] 1.5 eq. TMSCN and 1.5 eq. *i*PrOH was used.

From Table 2 we can see that the activity and enantioselectivity varied considerably with the catalyst loading and the substituted position of substituent R. In the presence of 5 mol% catalyst, low reactivity and moderate enantioselectivity were observed in the cyanation of **6p** (entry 1). While excellent result could be obtained by increasing the catalyst loading to 10 mol% (entry 2). Also it is evident that *ortho*-substituted diarylketoimines were the most suitable substrates which could be transformed to the corresponding amino nitriles with excellent ee's and yields (entries 2-5). Whereas *meta*- and *para*-substituted benzophenone imines turned out poor ee's (entries 6-10).

(E) The analytical and spectral characterization data of optically active *N*-Ts amino nitriles

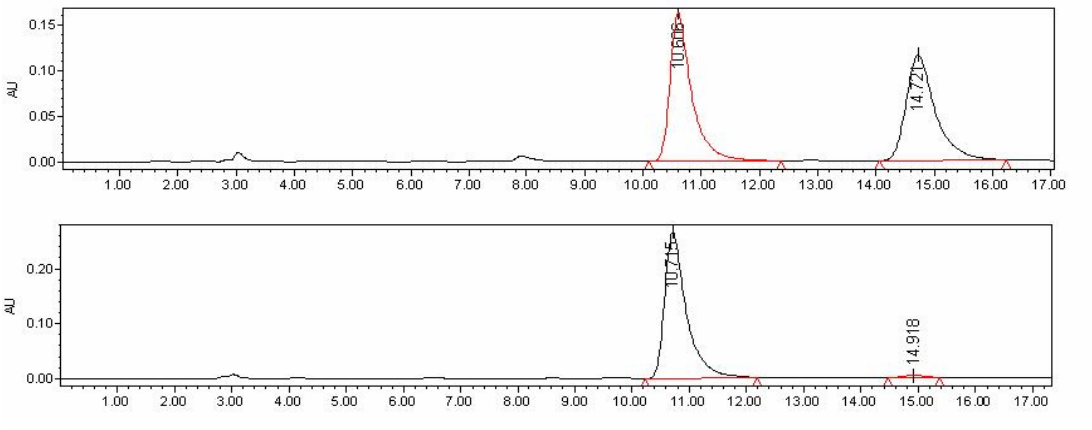
(*S*)-2-phenyl-2-(tosylamino)acetonitrile (5a)



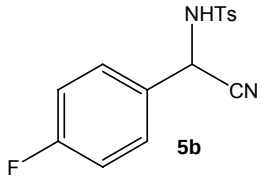
5a

white solid; m.p. 124-126°C; >99% yield, 97% ee. $[\alpha]_D^{20} = -53.5$ (c = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL AD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.6 min (major) and 14.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 2.45 (s, 3H), 5.34 (d, J = 8.8 Hz, 1H), 5.46 (d, J = 8.8 Hz, 1H), 7.35-7.81 (m, 9H)

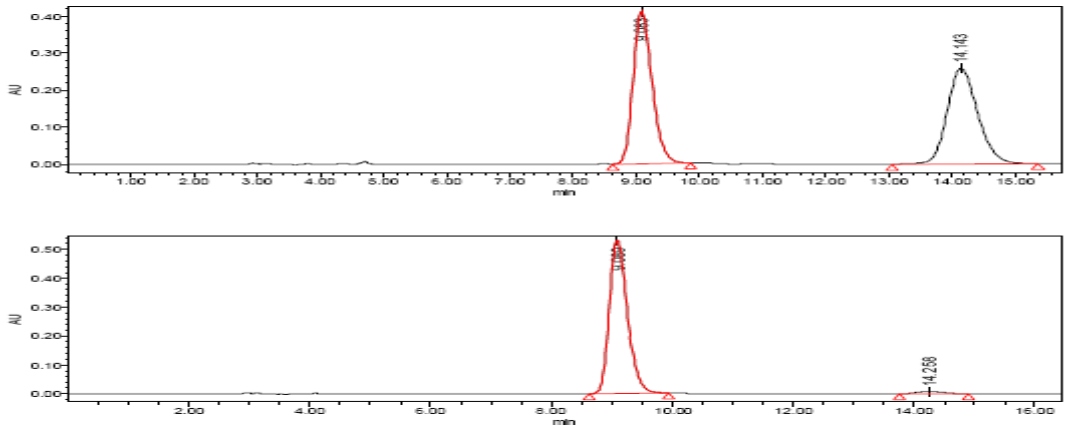
ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 21.7, 48.2, 116.3, 127.1, 127.4, 129.4, 129.9, 130.1, 132.1, 136.0, 144.8 ppm; HRMS (ESI-TOF) calcd for $C_{15}H_{13}N_2O_2S$ ([M-H$^+$]) = 285.0697, Found 285.0698.



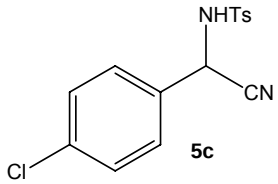
2-(4-fluorophenyl)-2-(tosylamino)acetonitrile (5b)



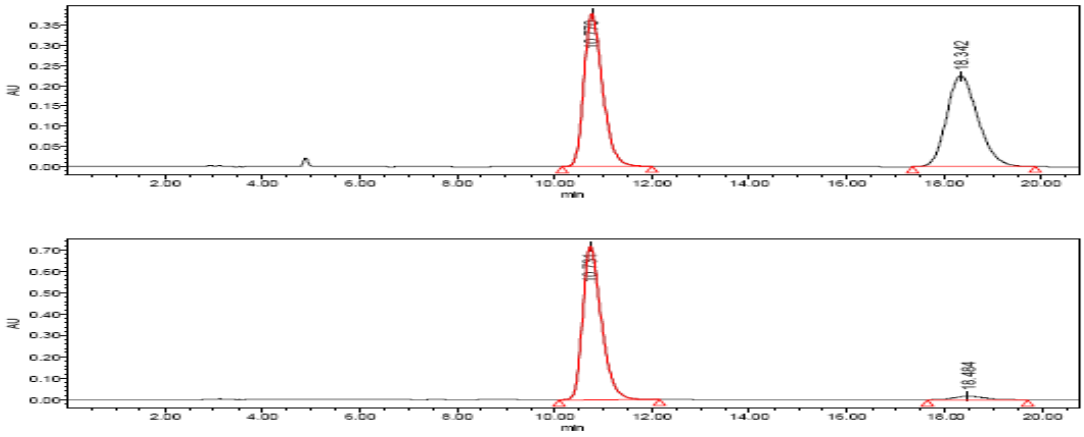
white solid; m.p. 100-104°C; >99% yield, 96% ee. $[\alpha]_D^{20}$ = –47.4 (c = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 9.1 min (major) and 14.1 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.45 (s, 3H), 5.43 (d, J = 9.2 Hz, 1H), 5.56 (d, J = 9.2 Hz, 1H), 7.04-7.78 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 47.6, 116.2, 116.3, 116.6, 127.3, 128.0, 128.0, 129.1, 129.2, 130.1, 135.8, 144.9, 162.1, 164.6 ppm; HRMS (ESI-TOF) calcd for $C_{15}H_{12}FN_2O_2S$ ([M-H$^+$]) = 303.0603, Found 303.0603.



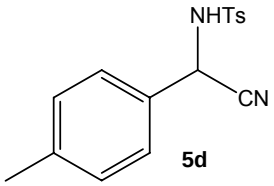
2-(4-chlorophenyl)-2-(tosylamino)acetonitrile (5c)



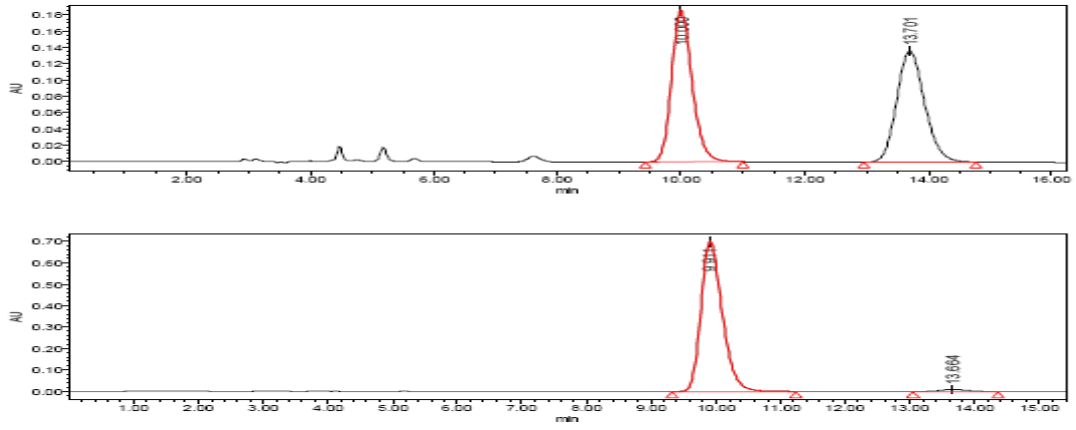
white solid; m.p. 113-115°C; 97% yield, 93% ee. $[\alpha]_D^{20}$ = –42.5 (c = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.8 min (major) and 18.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.45 (s, 3H), 5.42 (s, 1H), 5.61 (s, 1H), 7.33-7.76 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 47.6, 116.0, 127.3, 128.5, 129.6, 130.1, 130.6, 135.8, 136.0, 144.9 ppm; HRMS (ESI-TOF) calcd for $C_{15}H_{13}ClN_2O_2SNa$ ([M+Na$^+$]) = 343.0284, Found 343.0284.



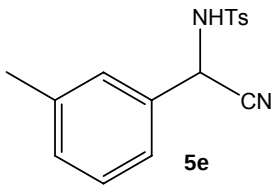
2-*p*-tolyl-2-(tosylamino)acetonitrile (5d)



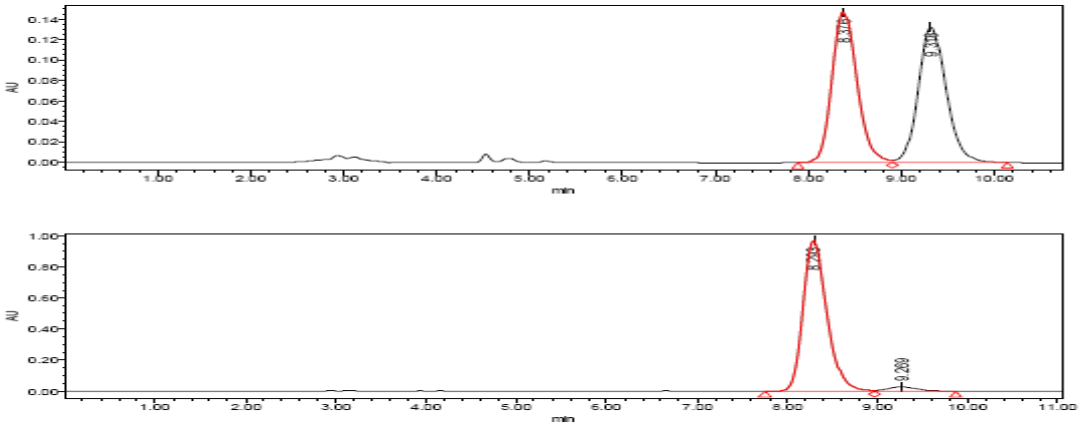
white solid; m.p. 120-121°C; >99% yield, 97% ee. $[\alpha]_D^{20} = -52.8$ (c = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.0 min (major) and 13.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.35 (s, 3H), 2.45 (s, 3H), 5.33 (d, J = 8.0 Hz, 1H), 5.40 (d, J = 8.0 Hz, 1H), 7.17-7.80 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.2, 21.7, 48.0, 116.5, 127.0, 127.4, 129.1, 130.0, 130.1, 136.0, 140.0, 144.7 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_2S$ ([M-H$^+$]) = 299.0853, Found 299.0854.



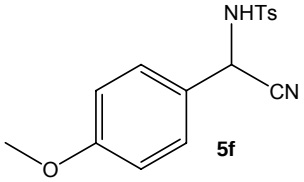
2-*m*-tolyl-2-(tosylamino)acetonitrile (5e)



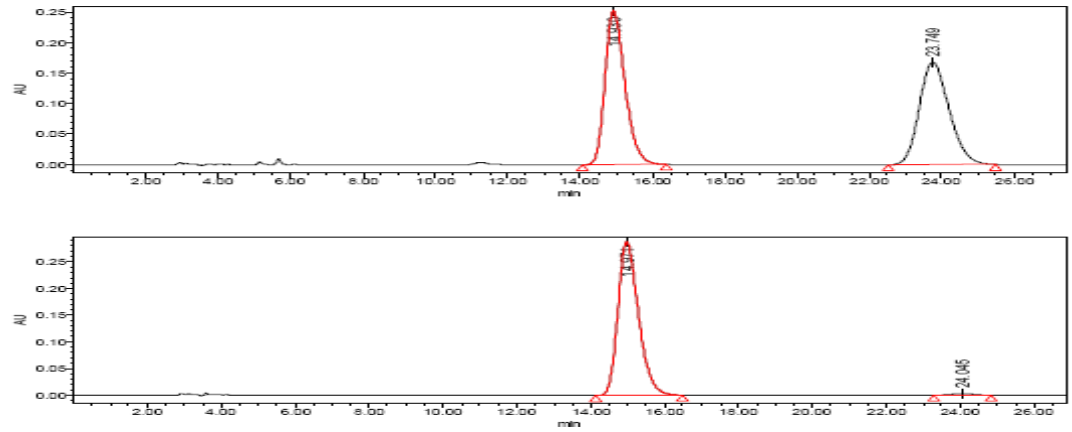
white solid; m.p. 101-103°C; >99% yield, 94% ee. $[\alpha]_D^{20} = -50.0$ (c = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.4 min (major) and 9.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.33 (s, 3H), 2.45 (s, 3H), 5.23-5.42 (m, 2H), 7.20-7.80 (m, 8H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.3, 21.7, 48.2, 116.4, 124.1, 127.4, 127.7, 129.3, 130.1, 130.6, 132.0, 136.0, 139.5, 144.7 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_2S$ ([M-H$^+$]) = 299.0853, Found 299.0854.



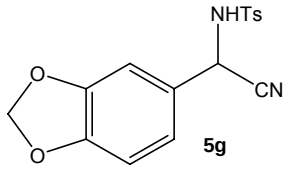
2-(4-methoxyphenyl)-2-(tosylamino)acetonitrile (5f)



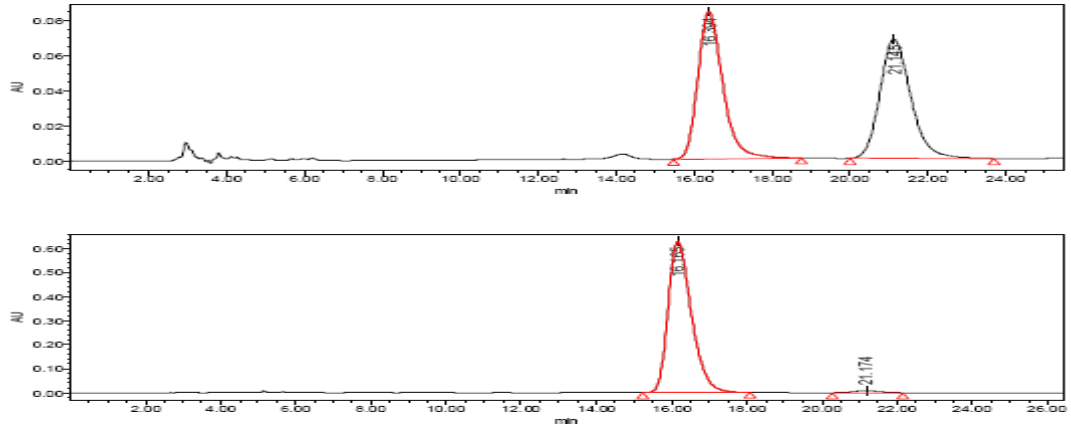
white solid; m.p. 100-101°C; >99% yield, 97% ee. $[\alpha]_D^{20}$ = –49.2 (*c* = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 14.9 min (major) and 23.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.45 (s, 3H), 3.80 (s, 3H), 5.38 (s, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 7.33 (t, *J* = 9.2 Hz, 4H), 7.78 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 47.7, 55.5, 114.7, 116.6, 124.0, 127.3, 128.6, 130.0, 136.0, 144.6, 160.6 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_3S$ ([M-H$^+$]) = 315.0803, Found 315.0803.



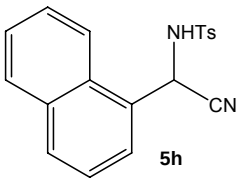
2-(benzo[*d*][1,3]dioxol-6-yl)-2-(tosylamino)acetonitrile (5g)



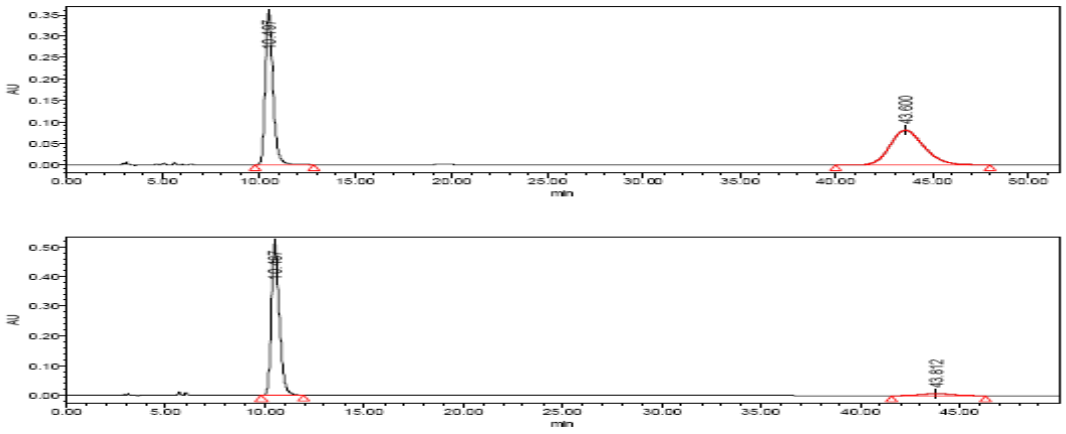
white solid; m.p. 124-126°C; >99% yield, 97% ee. $[\alpha]_D^{20}$ = –44.3 (*c* = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 16.4 min (major) and 21.1 min (minor); ^{1}H NMR (400 MHz, CD_3COCD_3, 25°C, TMS) δ = 2.44 (s, 3H), 2.93 (s, 1H), 5.65 (s, 1H), 6.05 (s, 2H), 6.85-6.97 (m, 3H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C, TMS) δ = 20.6, 47.5, 101.8, 107.4, 108.2, 117.2, 121.1, 127.1, 127.5, 129.7, 137.6, 143.8, 148.3, 148.5 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{13}N_2O_4S$ ([M-H$^+$]) = 329.0595, Found 329.0596.



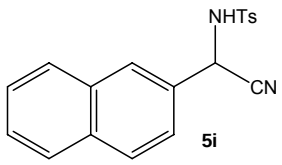
2-(1-naphthyl)-2-(tosylamino)acetonitrile (5h)



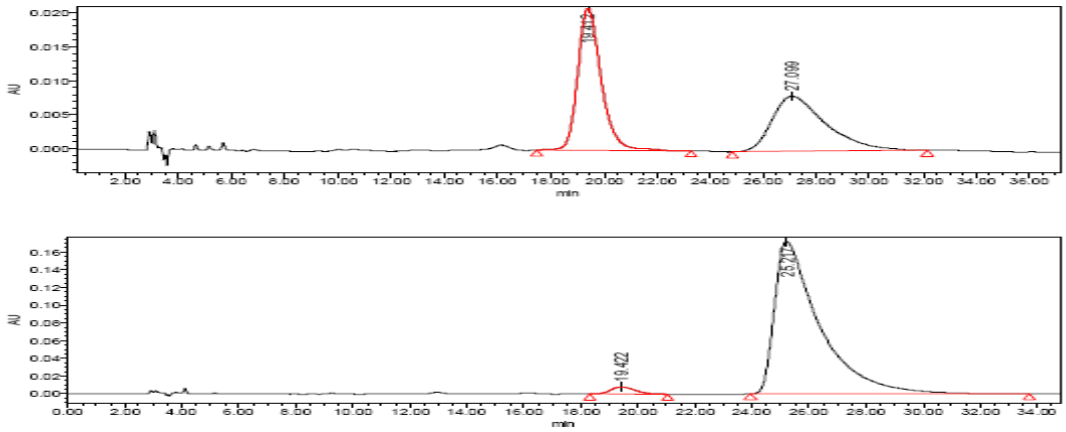
white solid; m.p. 115-116°C; 92% yield, 91% ee. $[\alpha]_D^{20} = -91.0$ (c = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.5 min (major) and 43.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.44 (s, 3H), 5.29 (s, 1H), 6.09 (d, J = 5.2 Hz, 1H), 7.29-8.03 (m, 11H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 46.4, 116.5, 122.4, 125.0, 126.6, 126.8, 127.0, 127.5, 127.9, 129.1, 129.6, 130.0, 131.3, 134.0, 135.8, 144.7 ppm; HRMS (ESI-TOF) calcd for $C_{19}H_{15}N_2O_2S$ ([M-H$^+$]) = 335.0853, Found 335.0853.



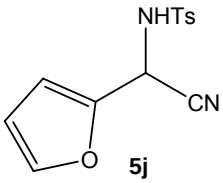
2-(2-naphthyl)-2-(tosylamino)acetonitrile (5i)



white solid; m.p. 138-140°C; 97% yield, 96% ee. $[\alpha]_D^{20} = -34.2$ (c = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 19.4 min (minor) and 27.1 min (major); ^{1}H NMR (400 MHz, CD_3COCD_3, 25°C, TMS) δ = 2.41 (s, 3H), 2.93 (s, 1H), 5.94 (s, 1H), 7.39-7.97 (m, 11H) ppm; ^{13}C NMR (100 MHz, CD_3COCD_3, 25°C, TMS) δ = 20.6, 48.0, 117.1, 124.4, 126.4, 126.9, 127.1, 127.2, 127.7, 128.1, 129.1, 129.7, 131.1, 133.0, 133.4, 137.6, 143.9 ppm; HRMS (ESI-TOF) calcd for $C_{19}H_{15}N_2O_2S$ ([M-H$^+$]) = 335.0853, Found 335.0854.

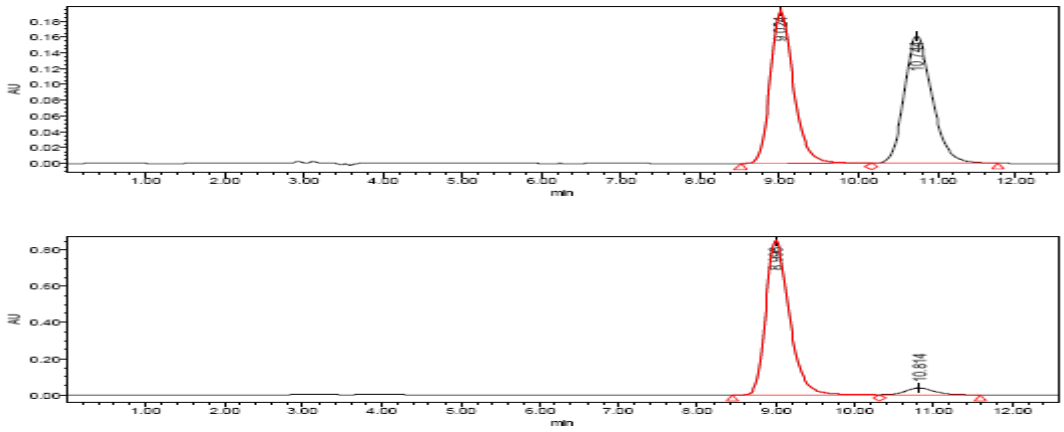


2-(2-furyl)-2-(tosylamino)acetonitrile (5j)

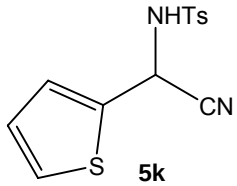


5j

white solid; m.p. 90-92°C; 93% yield, 90% ee. $[\alpha]_D^{20}$ = –23.6 (*c* = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 9.0 min (major) and 10.7 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.44 (s, 3H), 5.46 (d, *J* = 9.2 Hz, 1H), 5.53 (d, *J* = 9.2 Hz, 1H), 6.35 (s, 1H), 6.46 (d, *J* = 3.2, 1H), 7.34 (d, *J* = 8.0 Hz, 3H), 7.39 (s, 1H), 7.77 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 42.3, 110.5, 111.0, 114.7, 127.3, 130.0, 136.0, 144.0, 144.5, 144.8 ppm; HRMS (ESI-TOF) calcd for $C_{13}H_{11}N_2O_3S$ ([M-H$^+$]) = 275.0490, Found 275.0491.

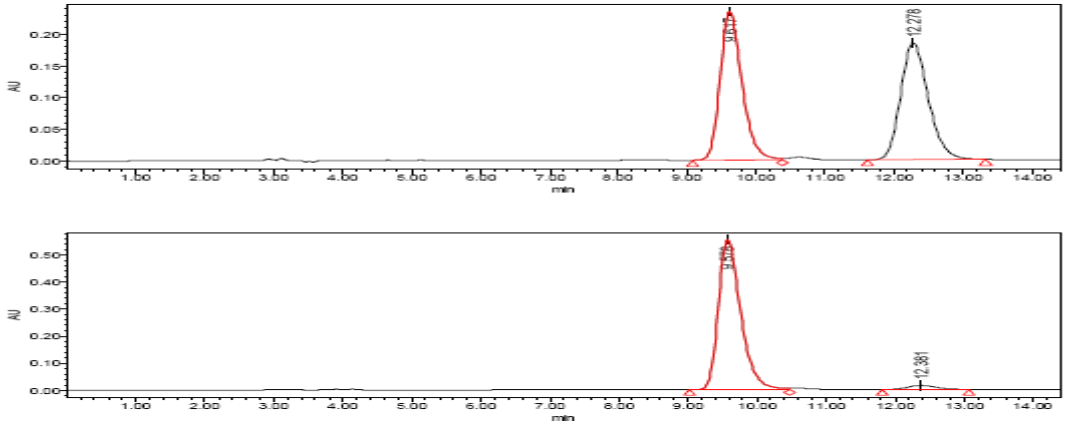


2-(2-thienyl)-2-(tosylamino)acetonitrile (5k)

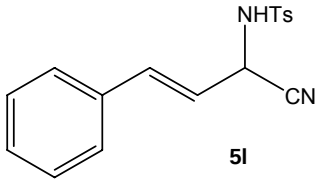


5k

white solid; m.p. 101-103°C; 94% yield, 94% ee. $[\alpha]_D^{20}$ = –59.6 (*c* = 0.14 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 9.6 min (major) and 12.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.44 (s, 3H), 5.58-5.64 (d, 2H), 6.96 (s, 1H), 7.19 (s, 1H), 7.35 (d, *J* = 6.4 Hz, 3H), 7.79 (d, *J* = 7.6 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 44.1, 115.8, 127.3, 127.4, 128.0, 128.2, 130.1, 134.6, 135.8, 144.9 ppm; HRMS (ESI-TOF) calcd for $C_{13}H_{11}N_2O_2S_2$ ([M-H$^+$]) = 291.0261, Found 291.0262.

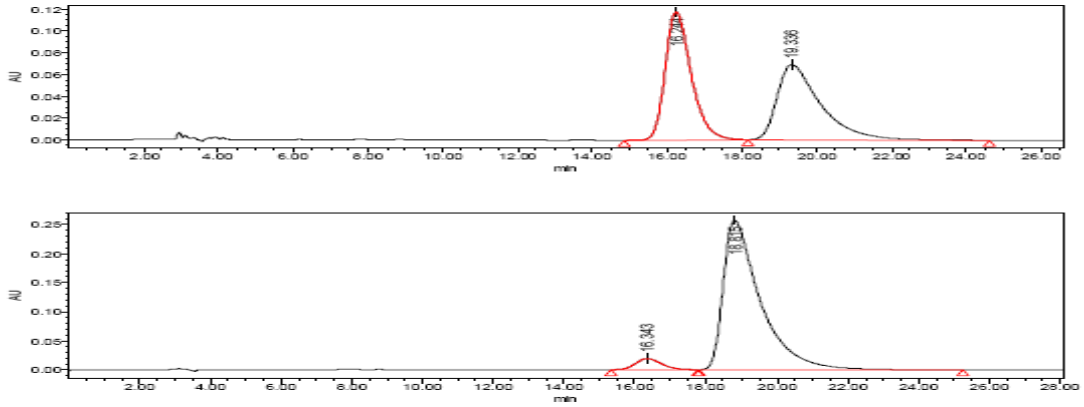


(E)-4-phenyl-2-(tosylamino)but-3-enenitrile (5l)

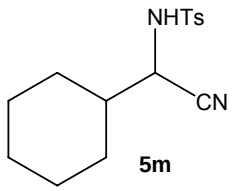


5l

white solid; m.p. 95-97°C; 96% yield, 91% ee. $[\alpha]_D^{20} = -46.4$ (c = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 25/75, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 16.2 min (minor) and 19.3 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.42 (s, 3H), 5.07 (t, 1H), 5.35 (d, J = 9.2 Hz, 1H), 5.99-6.04 (dd, J = 5.6, 16.0 Hz, 1H), 6.83 (d, J = 16.0 Hz, 1H), 7.32-7.81 (m, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 46.2, 115.7, 119.3, 127.1, 127.4, 128.9, 129.2, 130.1, 134.4, 135.8, 136.1, 144.8 ppm; HRMS (ESI-TOF) calcd for $C_{17}H_{15}N_2O_2S$ ([M-H$^+$]) = 311.0853, Found 311.0853.

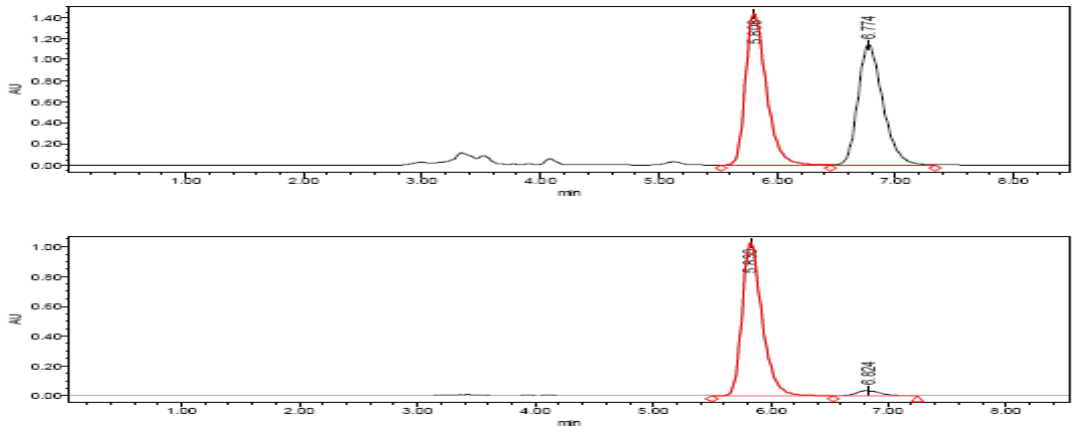


2-cyclohexyl-2-(tosylamino)acetonitrile (5m)

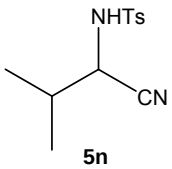


5m

white solid; m.p. 98-100°C; >99% yield, 92% ee. $[\alpha]_D^{20} = -29.1$ (c = 0.13 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 5.8 min (major) and 6.8 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.05-1.86 (m, 11H), 2.44 (s, 3H), 4.04 (dd, J = 6.4, 9.6 Hz, 1H), 5.47 (d, J = 9.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 25.3, 25.4, 25.6, 28.3, 28.8, 41.3, 49.8, 116.8, 127.2, 130.0, 136.0, 144.6 ppm; HRMS (ESI-TOF) calcd for $C_{15}H_{19}N_2O_2S$ ([M-H$^+$]) = 291.1166, Found 291.1167.

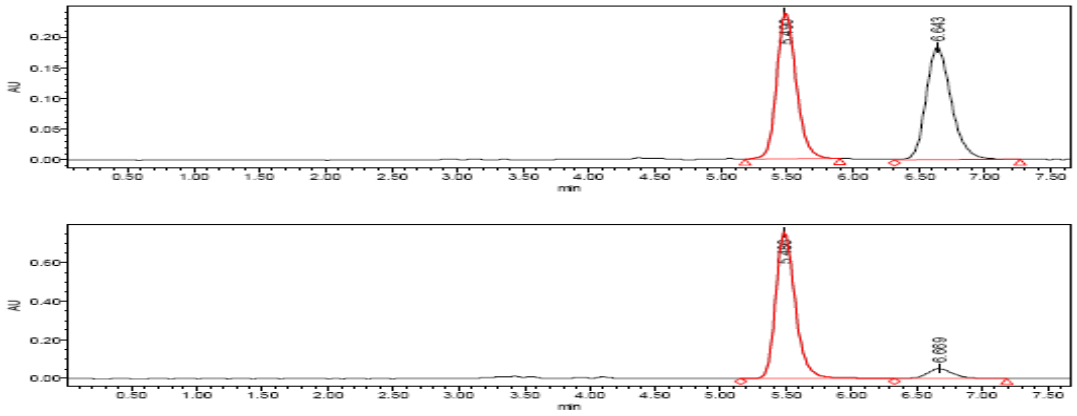


3-methyl-2-(tosylamino)butanenitrile (5n)

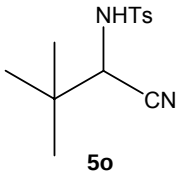


5n

white solid; m.p. 74-76°C; 96% yield, 84% ee. $[\alpha]_D^{20}$ = –38.2 (*c* = 0.19 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 5.5 min (major) and 6.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.04 (dd, *J* = 1.6, 6.8 Hz, 6H), 2.04 (q, *J* = 6.8 Hz, 1H), 2.44 (s, 3H), 4.04 (dd, *J* = 6.0, 10.0 Hz, 1H), 5.67 (d, *J* = 10.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 17.8, 18.4, 21.6, 32.4, 50.7, 116.7, 127.2, 130.1, 136.1, 144.6 ppm; HRMS (ESI-TOF) calcd for $C_{12}H_{16}N_2O_2SNa$ ([M+Na$^+$]) = 275.0830, Found 275.0830.

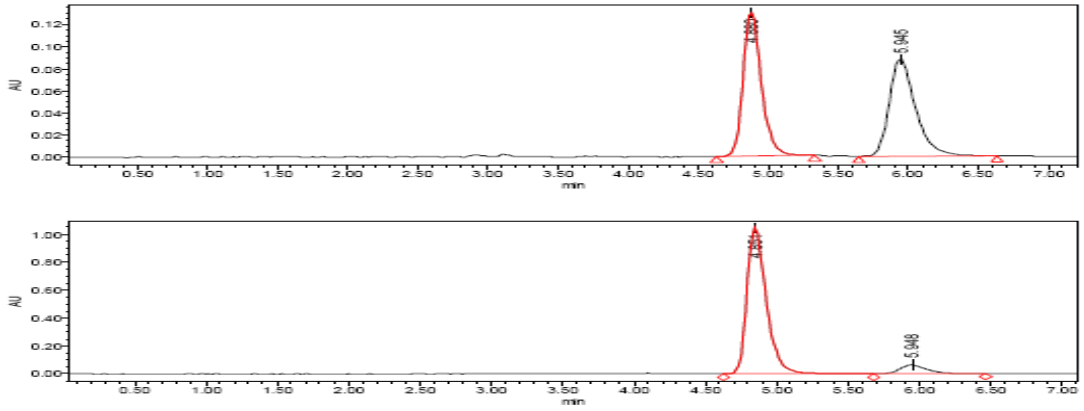


3,3-dimethyl-2-(tosylamino)butanenitrile (5o)

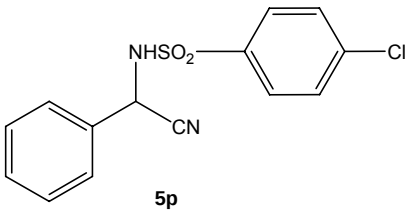


5o

white solid; m.p. 130-132°C; 98% yield, 84% ee. $[\alpha]_D^{20}$ = –43.4 (*c* = 0.12 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 4.9 min (major) and 5.9 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.06 (s, 9H), 2.45 (s, 3H), 3.88 (d, *J* = 10.8 Hz), 5.55 (br, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.7, 25.7, 35.3, 54.7, 116.7, 127.3, 130.1, 135.9, 144.6 ppm; HRMS (ESI-TOF) calcd for $C_{13}H_{17}N_2O_2S$ ([M-H$^+$]) = 265.1010, Found 265.1010.

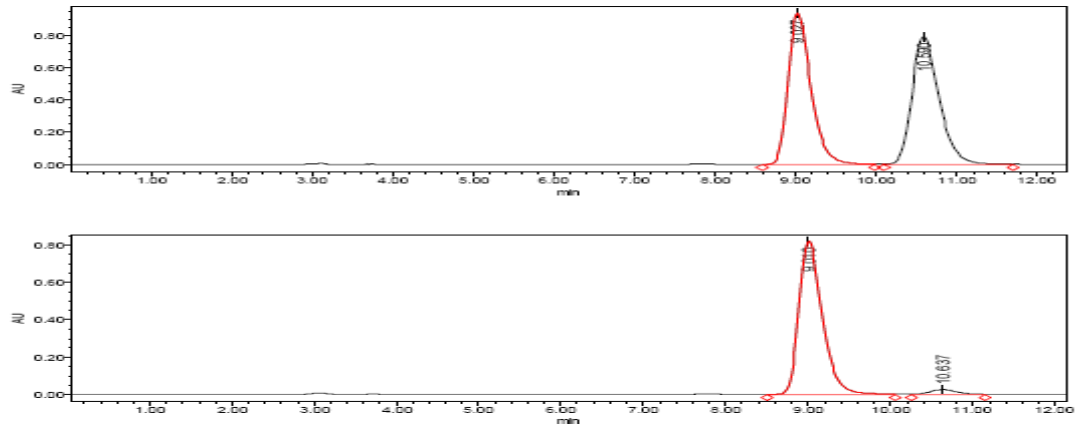


2-phenyl-2-(4-Clbenzenesulphonyl amino)acetonitrile (5p)

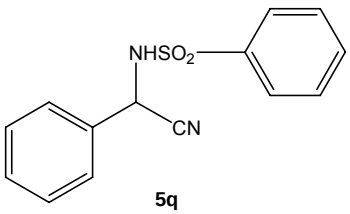


5p

white solid; m.p. 120-122°C; >99% yield, 94% ee. $[\alpha]_D^{25} = -54.7$ (c = 0.25 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 9.0 min (major) and 10.6 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 5.34 (s, 1H), 5.50 (s, 1H), 7.40-7.46 (m, 5H), 7.53 (d, J = 8.8 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 48.3, 116.1, 127.1, 128.7, 129.5, 129.8, 130.1, 131.8, 137.6, 140.3 ppm; HRMS (ESI-TOF) calcd for $C_{14}H_{11}ClN_2O_2SNa$ ([M+Na$^+$]) = 329.0127, Found 329.0129.

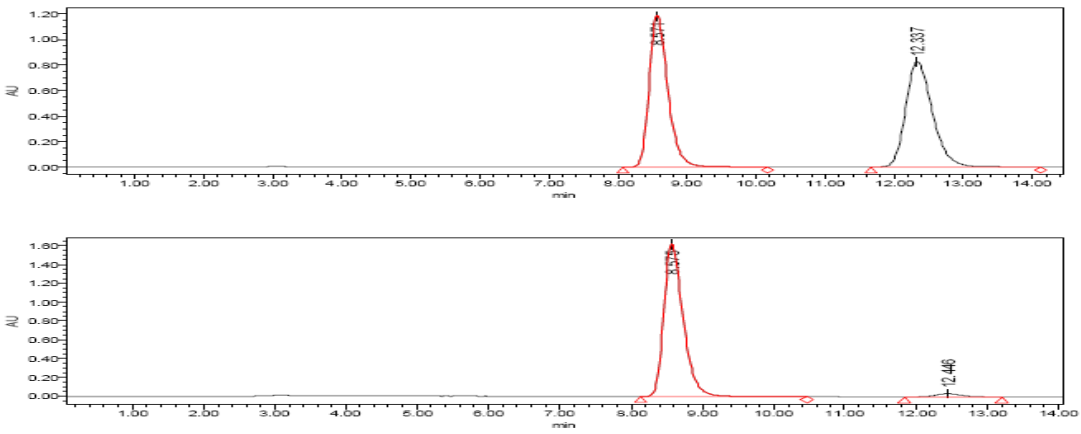


2-phenyl-2-(benzenesulphonyl amino)acetonitrile (5q)

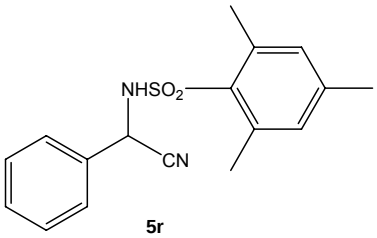


5q

white solid; m.p. 100-102°C; 94% yield, 94% ee. $[\alpha]_D^{25} = -51.4$ (c = 0.15 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.6 min (major) and 12.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 5.34-5.50 (m, 2H), 7.38-7.44 (m, 5H), 7.55-7.66 (m, 3H), 7.91-7.93 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 48.3, 116.3, 127.1, 127.3, 129.4, 129.5, 129.9, 132.1, 133.7, 139.1 ppm; HRMS (ESI-TOF) calcd for $C_{14}H_{12}N_2O_2S$ Na ([M+Na$^+$]) = 295.0517, Found 295.0520.

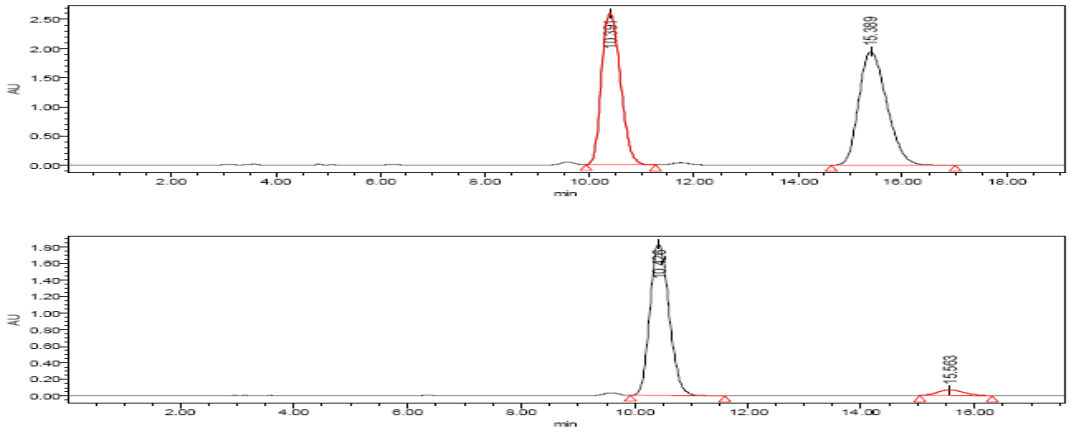


2-phenyl-2-(mesitylenesulphonyl amino)acetonitrile (5r)

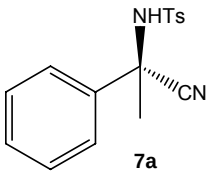


5r

colorless oil; 75% yield, 90% ee. $[\alpha]_D^{25} = -28.4$ (c = 0.44 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.4 min (major) and 15.4 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25^{o}C, TMS): δ = 2.33 (s, 3H), 2.66 (s, 6H), 5.13 (d, J = 8.4 Hz, 1H), 5.39 (d, J = 8.8 Hz, 1H), 7.01 (s, 2H), 7.40-7.46 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25^{o}C, TMS): δ = 21.1, 23.0, 47.9, 116.2, 127.2, 129.4, 129.9, 132.2, 132.3, 132.8, 139.4, 143.4 ppm; HRMS (ESI-TOF) calcd for $C_{17}H_{18}N_2O_2SNa$ ([M+Na$^+$]) = 337.0987, Found 337.0988.

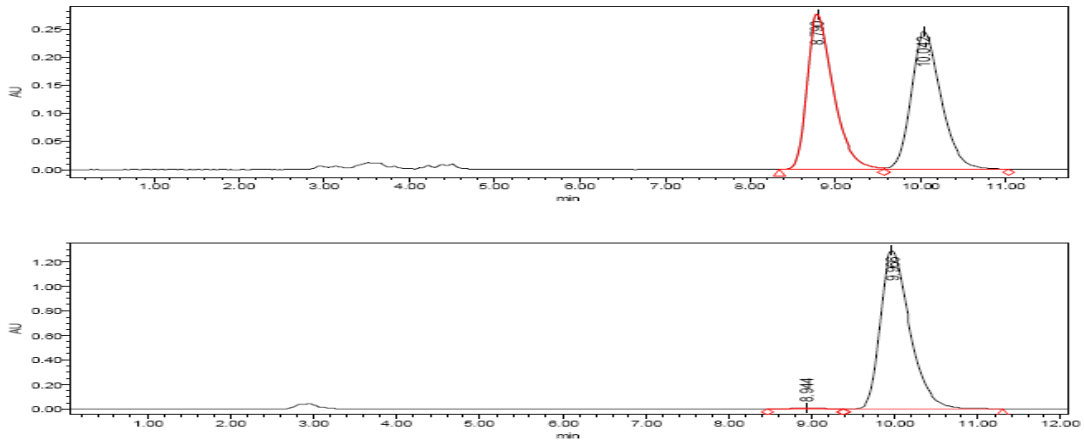


(*S*)-2-phenyl-2-(tosylamino)propanenitrile (7a)

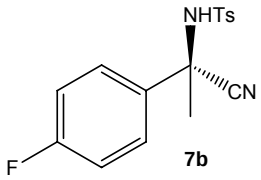


7a

white solid; m.p. 109-111^{o}C; >99% yield, >99% ee. $[\alpha]_D^{25} = -17.2$ (c = 0.25 in $CHCl_3$) [$[\alpha]_D^{25} = -13.4$ (c = 0.5 in CHCl $CHCl_3$, 85% ee, (*S*))].[1d] HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.8 min (minor) and 10.0 min (major); the NMR data were consistent with the reported values.

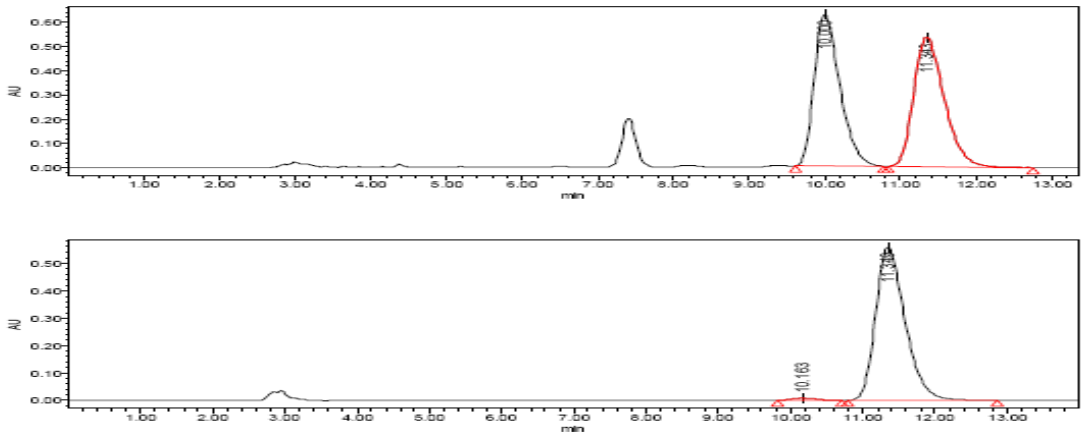


2-(4-fluorophenyl)-2-(tosylamino) propanenitrile (7b)

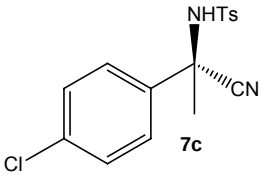


7b

white solid; m.p. 110-113°C; 90% yield, 98% ee. $[\alpha]_D^{25}$ = +1.9 (*c* = 0.43 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.0 min (minor) and 11.3 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.92 (s, 3H), 2.42 (s, 3H), 5.61 (s, 1H), 6.94-6.98 (m, 2H), 7.23-7.25 (d, *J* = 8.4, 2H), 7.42-7.46 (m, 2H), 7.55-7.57 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.6, 30.5, 56.0, 115.6, 115.8, 119.0, 127.4, 127.8, 127.9, 129.6, 132.8, 132.8, 137.1, 144.2, 161.7, 164.1 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}FN_2O_2SNa$ ([M+Na$^+$]) = 341.0736, Found 341.0738.

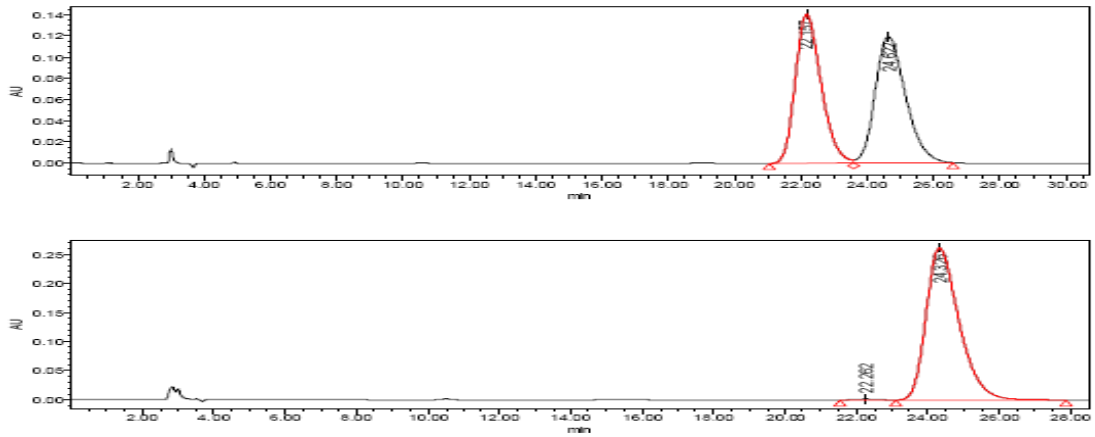


(*S*)-2-(4-chlorophenyl)-2-(tosylamino) propanenitrile (7c)

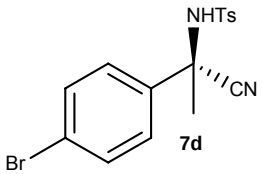


7c

white solid; m.p. 116-117°C; >99% yield, >99% ee. $[\alpha]_D^{25}$ = +6.1 (*c* = 0.20 in $CHCl_3$) [$[\alpha]_D^{25}$ = +6.92 (*c* = 0.52 in $CHCl_3$, 71% ee, (*S*))].[1d] HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 22.2 min (minor) and 24.6 min (major); the NMR data were consistent with the reported values.

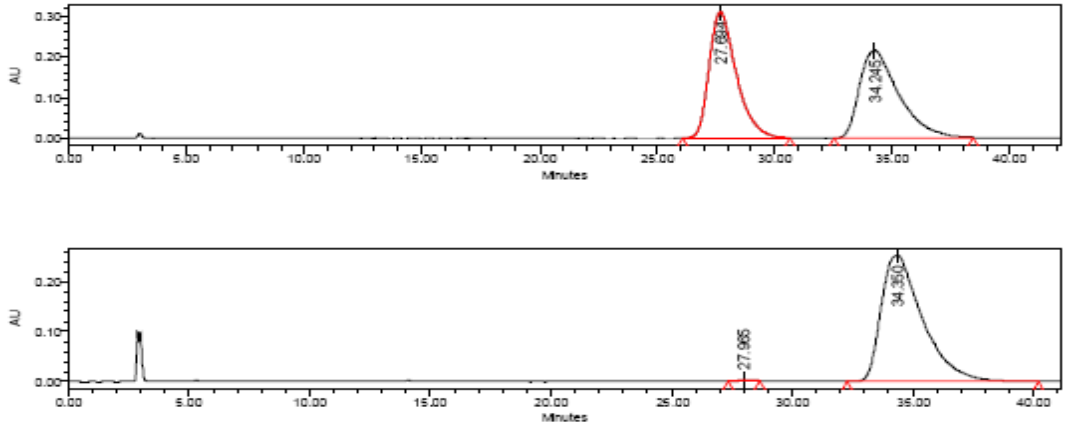


(*S*)-2-(4-bromophenyl)-2-(tosylamino) propanenitrile (7d)

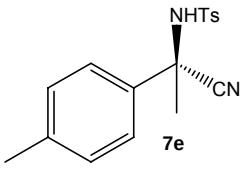


7d

white solid; m.p. 112-115°C; >99% yield, >99% ee. $[\alpha]_D^{25}$ = +11.3 (*c* = 0.33 in $CHCl_3$) [$[\alpha]_D^{25}$ = +9.29 (*c* = 0.56 in $CHCl_3$, 71% ee, (*S*))].[1d] HPLC (DAICEL CHIRALCEL AS-H, 2-propanol/*n*-hexane = 15/85, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 27.7 min (minor) and 34.2 min (major); the NMR data were consistent with the reported values.

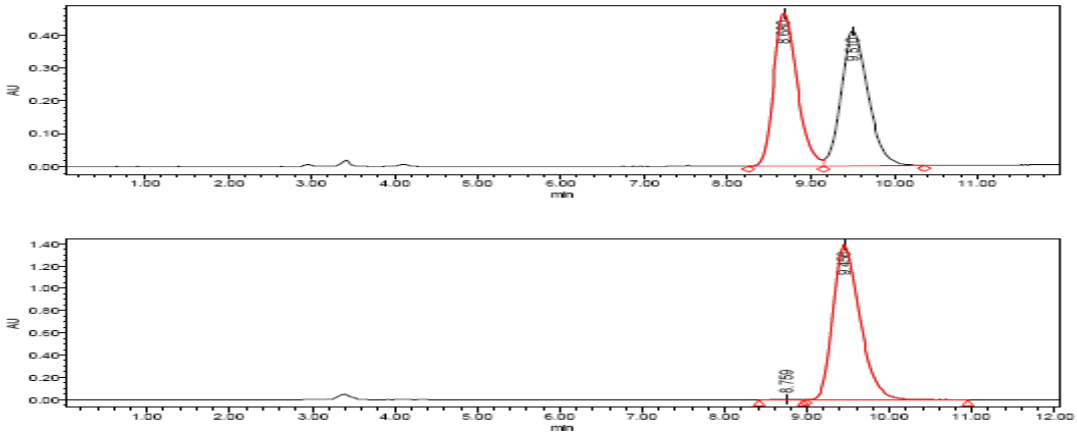


(*S*)-2-(4-methylphenyl)-2-(tosylamino) propanenitrile (7e)

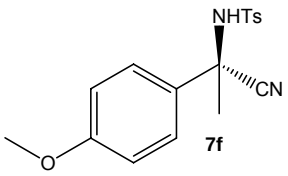


7e

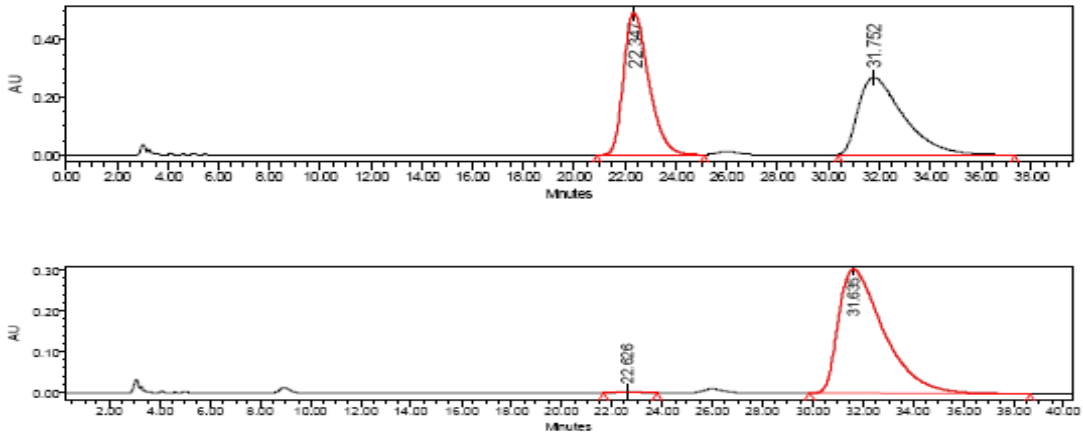
white solid; m.p. 94-97°C; >99% yield, >99% ee. $[\alpha]_D^{25}$ = –26.6 (*c* = 0.13 in $CHCl_3$) [$[\alpha]_D^{25}$ = –15.65 (*c* = 0.52 in $CHCl_3$), 61% ee, (*S*)].[1d] HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.7 min (minor) and 9.5 min (major); the NMR data were consistent with the reported values.



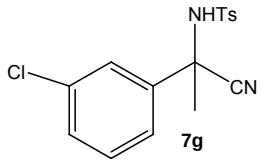
(*S*)-2-(4-methoxyphenyl)-2-(tosylamino) propanenitrile (7f)



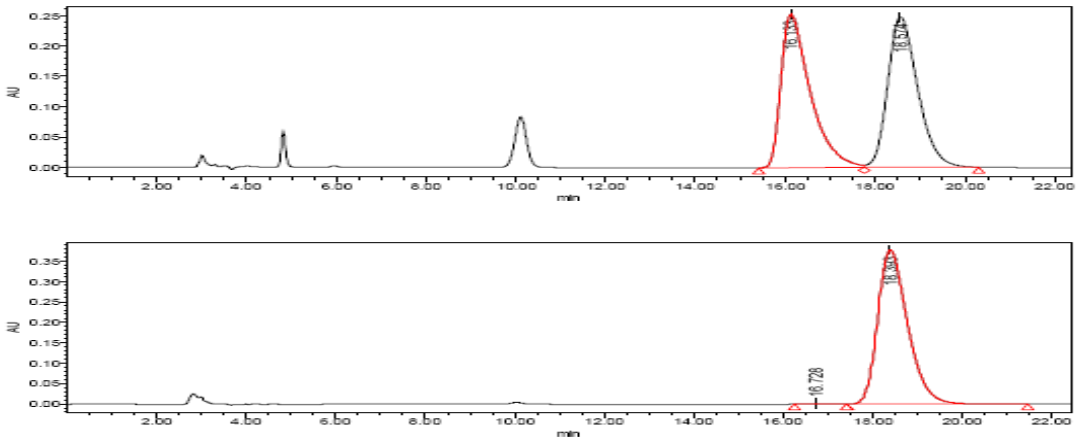
white solid; m.p. 94-96°C; 99% yield, >99% ee. $[\alpha]_D^{25} = -20.3$ (c = 0.12 in $CHCl_3$) [$[\alpha]_D^{25} = -11.96$ (c = 0.46 in $CHCl_3$, 76% ee, (*S*))].[1d] HPLC (DAICEL CHIRALCEL AS-H, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 22.3 min (minor) and 31.7 min (major); the NMR data were consistent with the reported values.



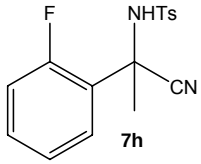
2-(3-chlorophenyl)-2-(tosylamino) propanenitrile (7g)



white solid; m.p. 112-114°C; >99% yield, >99% ee. $[\alpha]_D^{25} = -8.1$ (c = 0.30 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 16.1 min (minor) and 18.5 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.91 (s, 3H), 2.42 (s, 3H), 5.88 (s, 1H), 7.20-7.27 (m, 5H), 7.44-7.46 (m, 1H), 7.51-7.55 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.6, 30.7, 56.1, 118.8, 124.3, 126.0, 127.2, 129.3, 129.6, 130.0, 134.8, 136.9, 138.6, 144.3 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}ClN_2O_2SNa$ ([M+Na^+]) = 357.0441, Found 357.0441.

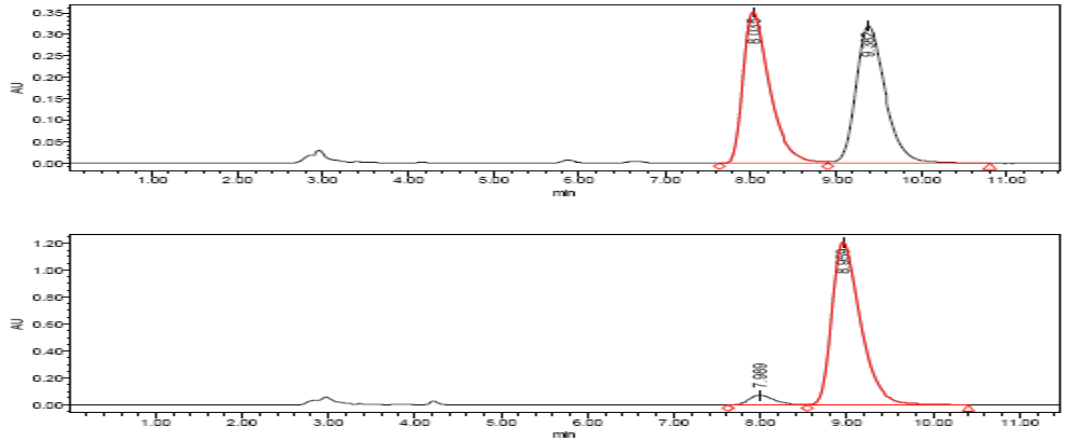


2-(2-fluorophenyl)-2-(tosylamino) propanenitrile (7h)

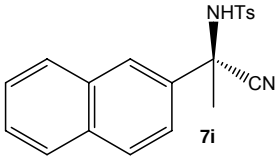


7h

white solid; m.p. 112-115°C; >99% yield, 90% ee. $[\alpha]_D^{25}$ = +12.9 (*c* = 0.27 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.0 min (minor) and 9.4 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 2.06 (s, 3H), 2.38 (s, 3H), 5.66 (s, 1H), 6.71-6.76 (m, 1H), 7.12-7.31 (m, 4H) 7.49 (d, *J* = 8.4, 2H), 7.70 (t, *J* = 8.0, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.5, 28.0, 28.0, 54.9, 116.6, 116.8, 118.2, 123.6, 123.6, 124.5, 124.5, 127.3, 128.7, 128.7, 129.3, 131.4, 131.5, 136.8, 143.8, 158.4, 160.9 ppm; HRMS (ESI-TOF) calcd for $C_{16}H_{15}FN_2O_2SNa$ ([M+Na$^+$]) = 341.0736, Found 341.0735.

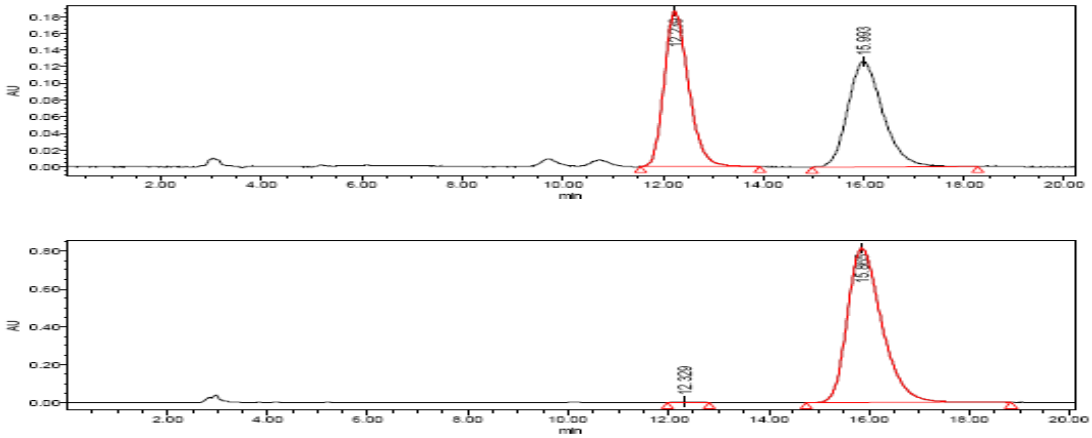


(*S*)-2-(2-naphthyl)-2-(tosylamino) propanenitrile (7i)

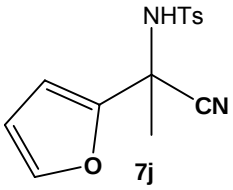


7i

pale yellow solid; m.p. 116-119°C; 90% yield, >99% ee. $[\alpha]_D^{25}$ = +8.5 (*c* = 0.34 in $CHCl_3$) [$[\alpha]_D^{25}$ = +7.0 (*c* = 0.6 in $CHCl_3$), 71% ee, (*S*)].[1d] HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 12.2 min (minor) and 15.9 min (major); the NMR data were consistent with the reported values.

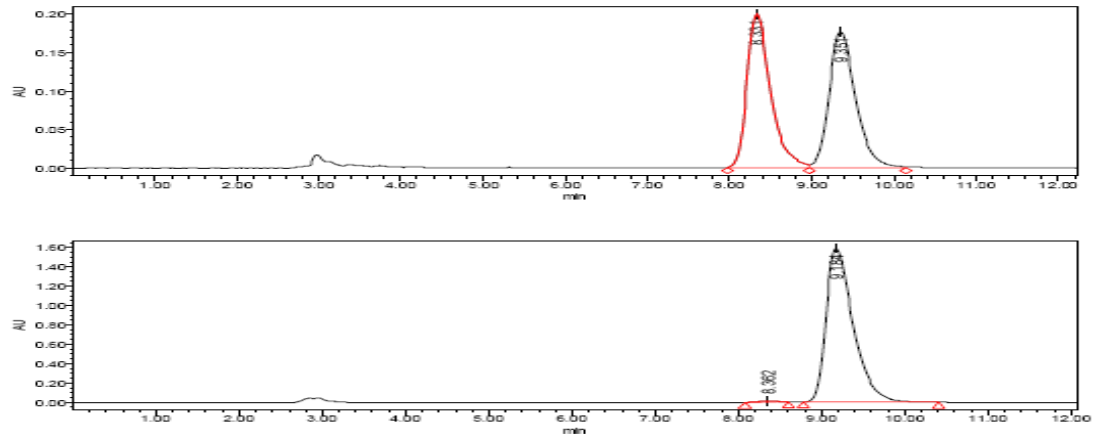


2-(2-furyl)-2-(tosylamino) propanenitrile (7j)

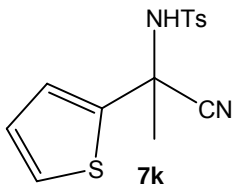


7j

white solid; m.p. 96-98°C; 97% yield, 99% ee. $[\alpha]_D^{25}$ = –31.2 (*c* = 0.24 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 8.3 min (minor) and 9.3 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 1.98 (s, 3H), 2.41 (s, 3H), 5.64 (s, 1H), 6.28 (m, 1H), 6.52 (d, *J* = 3.6), 7.18 (s, 1H), 7.25 (d, *J* = 8.0, 2H), 7.65 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 21.6, 26.5, 50.8, 109.9, 110.6, 117.8, 127.4, 129.6, 136.8, 143.8, 143.9, 147.7 ppm; HRMS (ESI-TOF) calcd for $C_{14}H_{14}N_2O_3SNa$ ([M+Na$^+$]) = 313.0623, Found 313.0625.

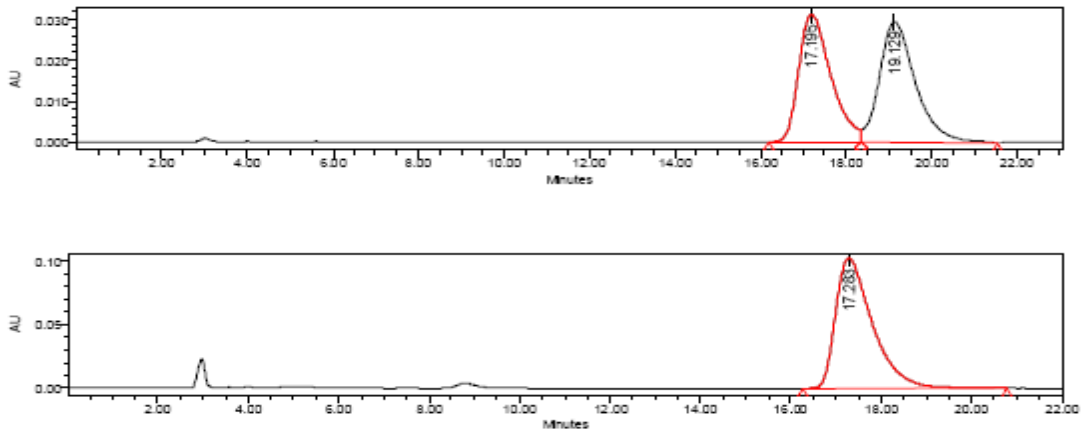


2-(2-thienyl)-2-(tosylamino) propanenitrile (7k)

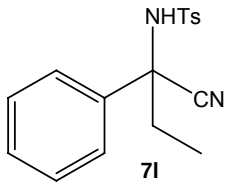


7k

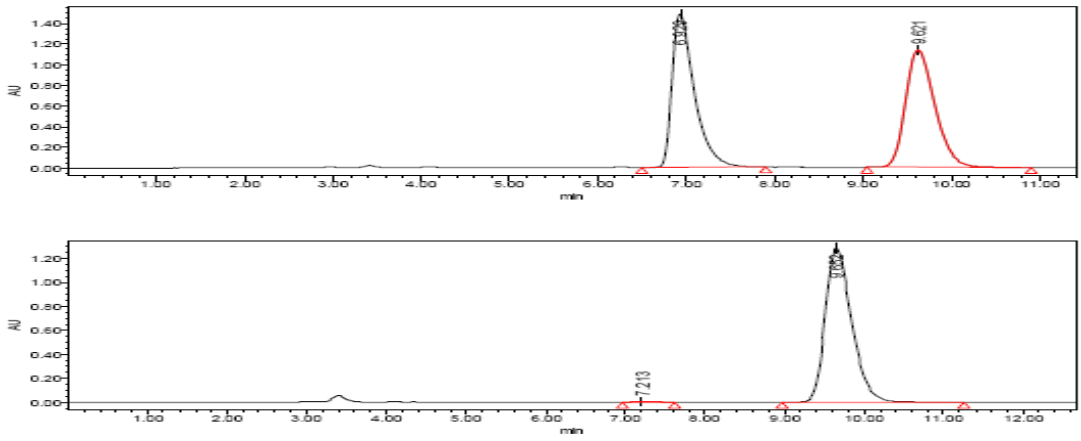
white solid; m.p. 90-91°C; 97% yield, >99% ee. $[\alpha]_D^{25}$ = –43.2 (*c* = 0.28 in $CHCl_3$). HPLC (DAICEL CHIRALCEL AS-H, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 17.2 min (major) and 19.1 min (minor); the NMR data were consistent with the reported values.



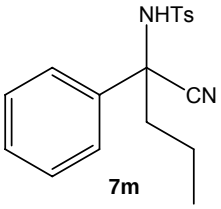
2-phenyl-2-(tosylamino)butanenitrile (7l)



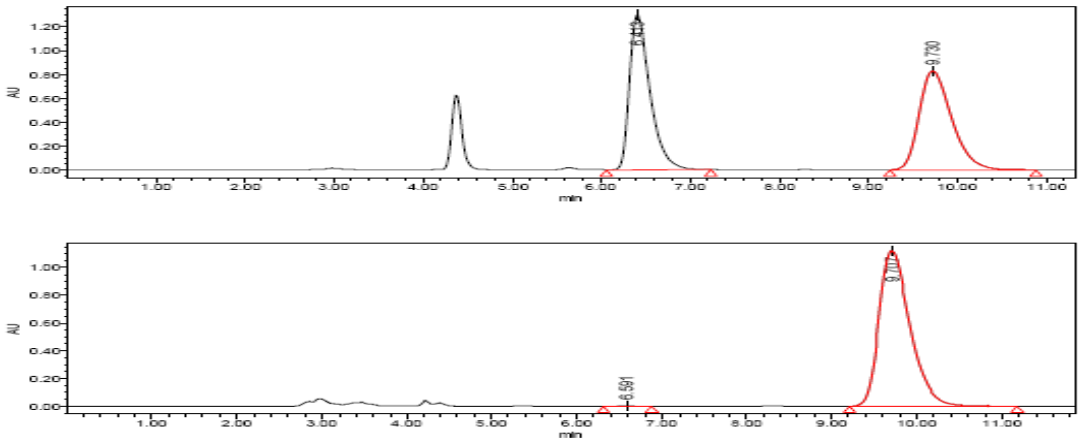
white solid; m.p. 112-114°C; >99% yield, >99% ee. $[\alpha]_D^{25}$ = +8.8 (*c* = 0.11 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 6.9 min (minor) and 9.6 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 0.86 (t, *J* = 7.2, 3H), 2.05 (m, 1H), 2.28 (m, 1H), 2.40 (s, 3H), 7.17 (d, *J* = 8.4, 2H), 7.22-7.40 (m, 5H), 7.50 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 8.6, 21.6, 36.1, 62.0, 118.2, 126.3, 127.3, 128.6, 128.9, 129.4, 135.1, 137.5, 143.7 ppm; HRMS (ESI-TOF) calcd for $C_{17}H_{18}N_2O_2SNa$ ([M+Na^+]) = 337.0987, Found 337.0981.



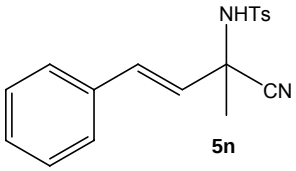
2-phenyl-2-(tosylamino)pentanenitrile (7m)



white solid; m.p. 92-95°C; 93% yield, >99% ee. $[\alpha]_D^{25}$ = +11.1 (*c* = 0.26 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 6.4 min (minor) and 9.7 min (major); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS) δ = 0.83 (t, *J* = 7.2, 3H), 1.01-1.09 (m, 1H), 1.40-1.48 (m, 1H), 1.93-2.00 (m, 1H), 2.15-2.22 (m, 1H), 2.40 (s, 3H), 7.17 (d, *J* = 8.0, 2H), 7.22-7.40 (m, 6H), 7.50 (d, *J* = 8.4, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS) δ = 13.4, 17.6, 21.6, 44.7, 61.1, 118.3, 126.2, 127.3, 128.6, 128.9, 129.4, 135.6, 137.5, 143.7 ppm; HRMS (ESI-TOF) calcd for $C_{18}H_{20}N_2O_2SNa$ ([M+Na^+]) = 351.1143, Found 351.1143.

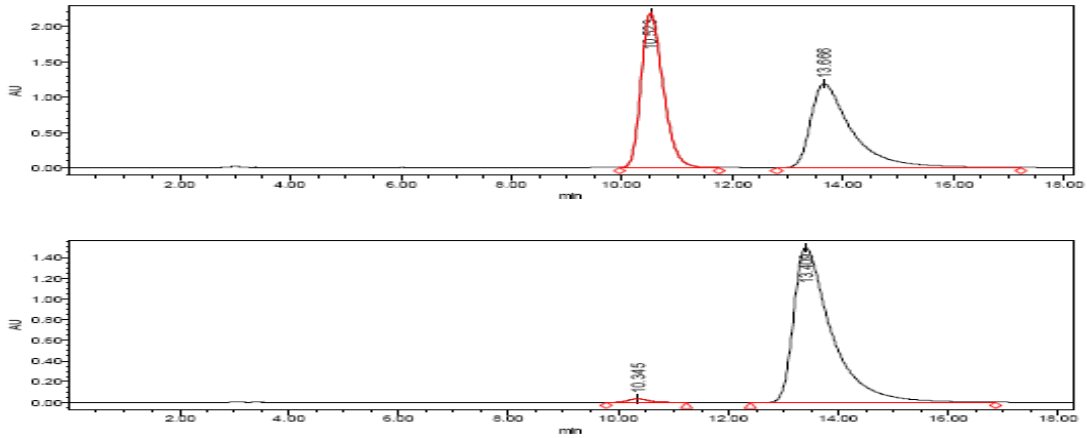


(*E*)-2-methyl-4-phenyl-2-(tosylamino)but-3-enenitrile (5n)

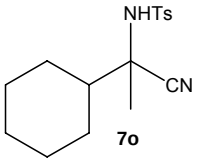


5n

white solid; m.p. 107-109°C; 97% yield, 98% ee. $[\alpha]_D^{25} = -118.8$ (c = 0.22 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 25/75, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.5 min (minor) and 13.6 min (major); the NMR data were consistent with the reported values.

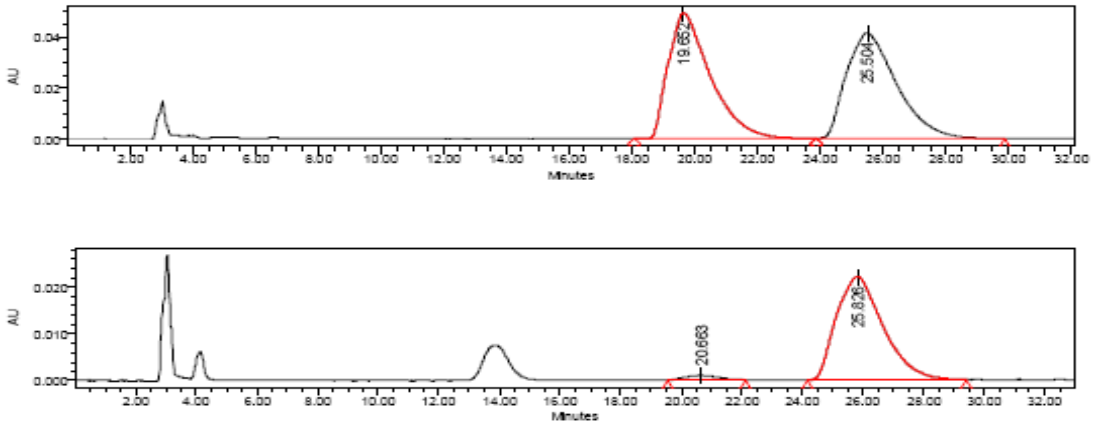


2-cyclohexyl-2-(tosylamino) propanenitrile (7o)

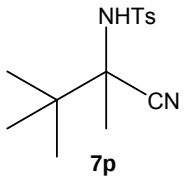


7o

white solid; m.p. 108-110°C; >99% yield, 94% ee. $[\alpha]_D^{25} = -25.8$ (c = 0.31 in $CHCl_3$). HPLC (DAICEL CHIRALCEL AS-H, 2-propanol/*n*-hexane = 15/85, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 19.6 min (minor) and 25.5 min (major); the NMR data were consistent with the reported values.

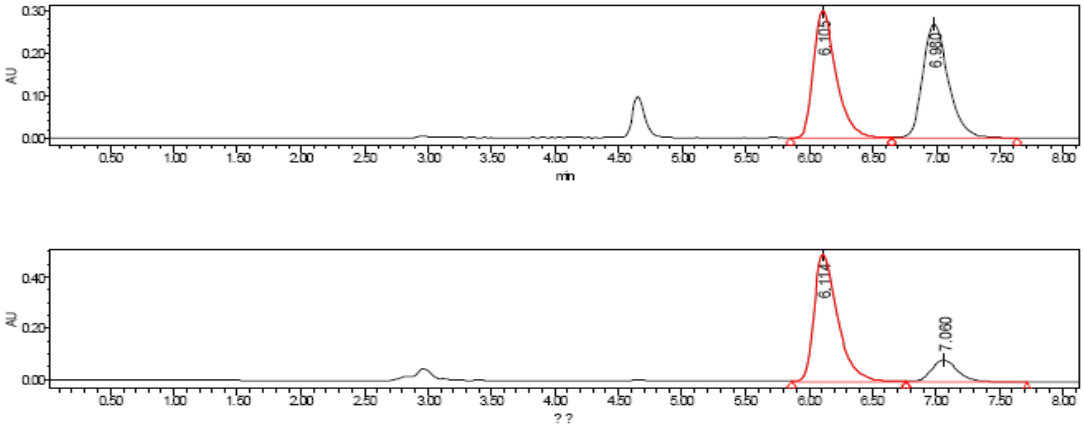


2,3,3-trimethyl-2-(tosylamino)butanenitrile (7p)

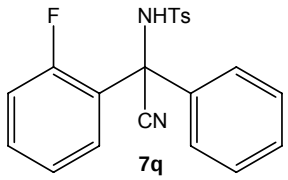


7p

white solid; m.p. 114-116°C; 98% yield, 69% ee. $[\alpha]_D^{25}$ = –22.6 (*c* = 0.25 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 6.1 min (major) and 7.0 min (minor); the NMR data were consistent with the reported values.

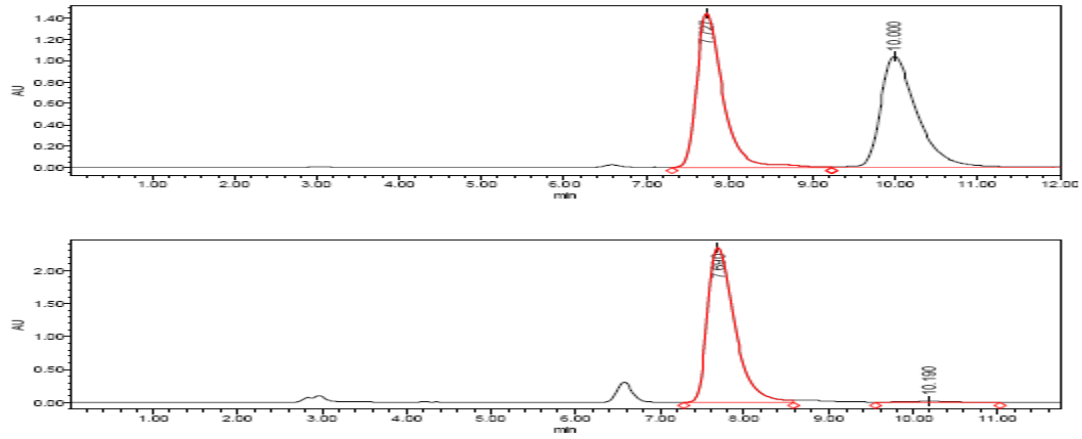


2-(2-fluorophenyl)-2-phenyl-2-(tosylamino)acetonitrile (7q)

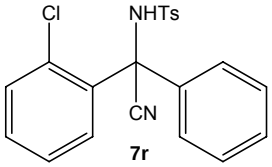


7q

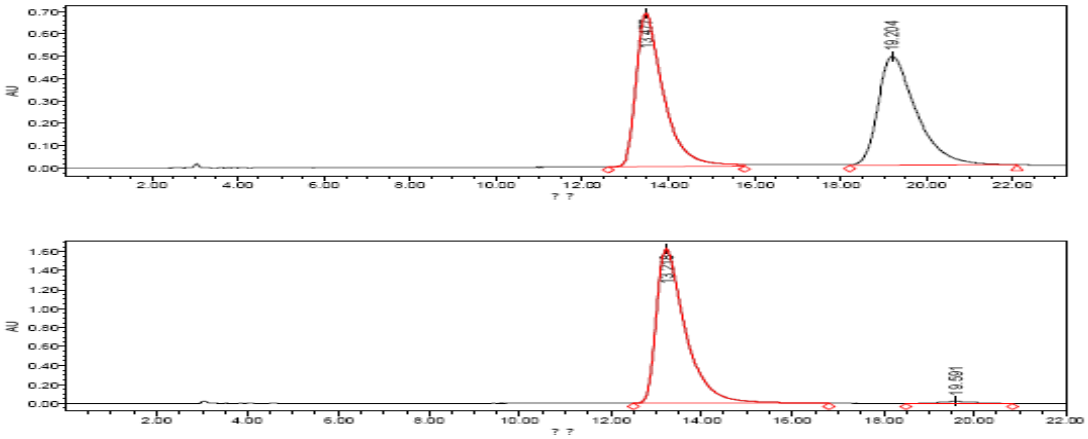
white solid; m.p. 102-104°C; 96% yield, 98% ee. $[\alpha]_D^{25}$ = –4.5 (*c* = 0.31 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 7.7 min (major) and 10.0 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 2.39 (s, 3H), 5.67 (s, 1H), 6.82-6.88 (m, 1H), 7.15-7.23 (m, 3H), 7.32-7.38 (m, 6H), 7.56-7.68 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 21.6, 60.9, 116.6, 116.8, 116.8, 116.8, 124.4, 124.5, 124.5, 126.6, 127.5, 129.1, 129.3, 129.4, 129.7, 131.7, 131.8, 136.6, 136.9, 143.9, 158.2, 160.7 ppm; HRMS (ESI-TOF) calcd for $C_{21}H_{17}FN_2O_2SNa$ ([M+Na$^+$]) = 403.0893, Found 403.0894.



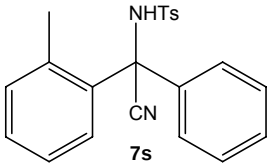
2-(2-chlorophenyl)-2-phenyl-2-(tosylamino)acetonitrile (7r)



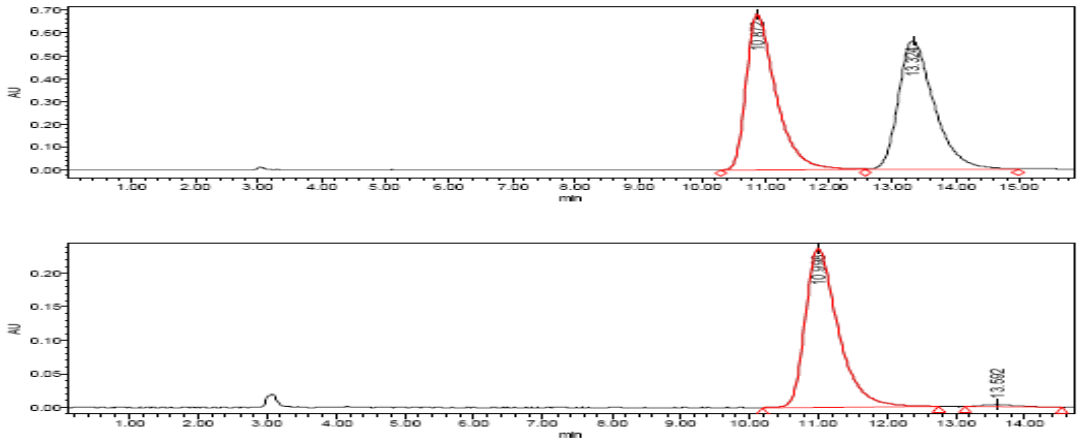
white solid; m.p. 96-98°C; 95% yield, 97% ee. $[\alpha]_D^{25} = -14.1$ (c = 0.37 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 13.4 min (major) and 19.2 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 2.38 (s, 3H), 5.97 (s, 1H), 7.14-7.19 (m, 3H), 7.29-7.38 (m, 7H), 7.57-7.59 (m, 2H), 7.87-7.89 (dd, J_1 = 3.2, J_2 = 8.0, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 21.5, 62.9, 116.6, 126.6, 127.2, 127.5, 129.2, 129.3, 129.5, 130.7, 130.8, 131.9, 132.4, 133.4, 136.8, 136.9, 143.8 ppm; HRMS (ESI-TOF) calcd for $C_{21}H_{17}ClN_2O_2SNa$ ([M+Na$^+$]) = 419.0597, Found 419.0597.



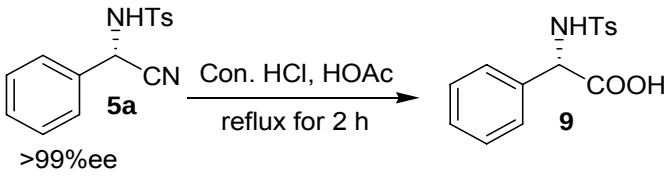
2-(2-methylphenyl)-2-phenyl-2-(tosylamino)acetonitrile (7s)



white solid; m.p. 70-72°C; 90% yield, 97% ee. $[\alpha]_D^{25} = -31.9$ (c = 0.41 in $CHCl_3$). HPLC (DAICEL CHIRALCEL OD-H, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 210 nm, retention time: 10.9 min (major) and 13.3 min (minor); ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 1.98 (s, 3H), 2.39 (s, 3H), 5.52 (s, 1H), 7.03-7.05 (m, 1H), 7.17 (d, J = 8.0, 2H), 7.26-7.33 (m, 7H), 7.53-7.63 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25°C, TMS): δ = 20.9, 21.6, 62.8, 117.9, 126.2, 127.2, 127.5, 128.2, 128.9, 129.3, 129.3, 129.6, 133.0, 134.6, 136.6, 136.8, 137.2, 143.8 ppm; HRMS (ESI-TOF) calcd for $C_{22}H_{20}N_2O_2SNa$ ([M+Na$^+$]) = 399.1143, Found 399.1144.



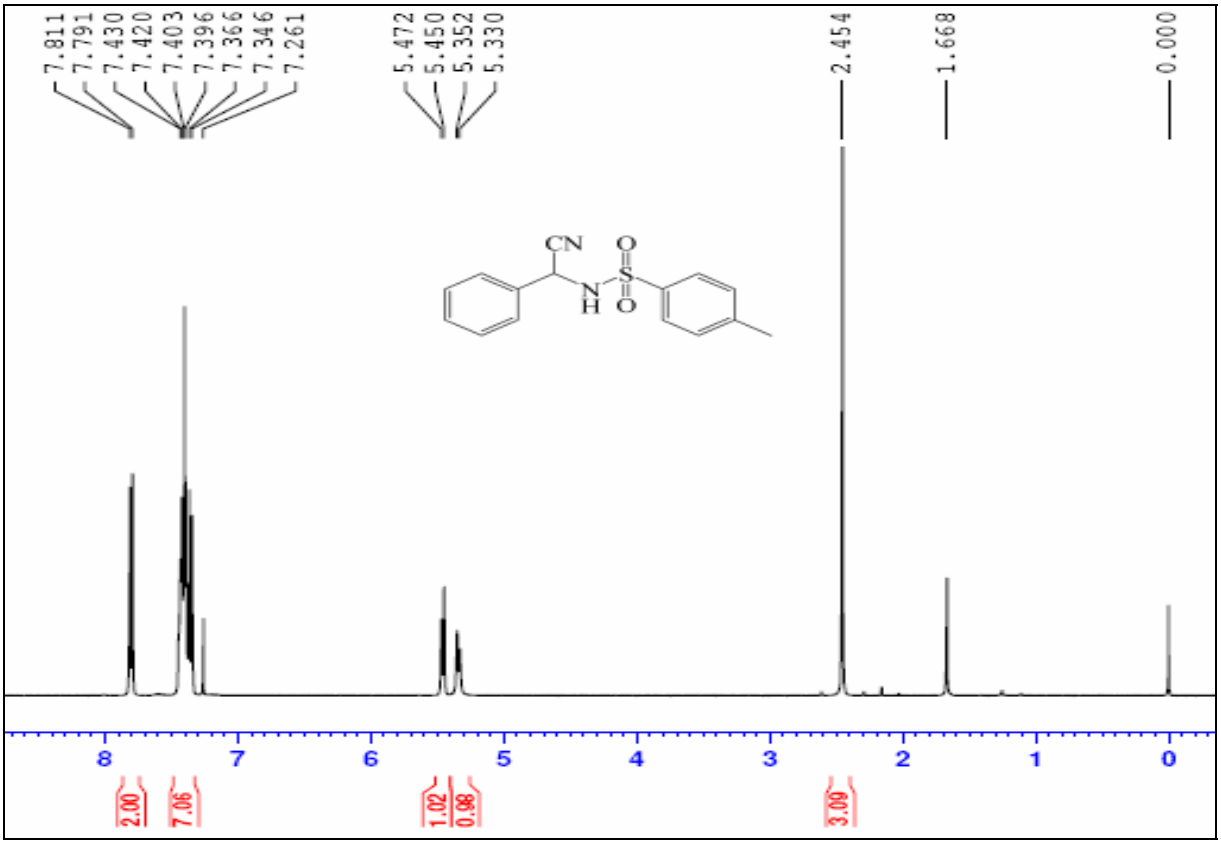
(F)Facile Converting the *N*-Ts Amino Nitrile to the Corresponding *N*-Ts Amino Acid and Assignment of the Absolute Configuration of 5a (the conditions were not optimized)

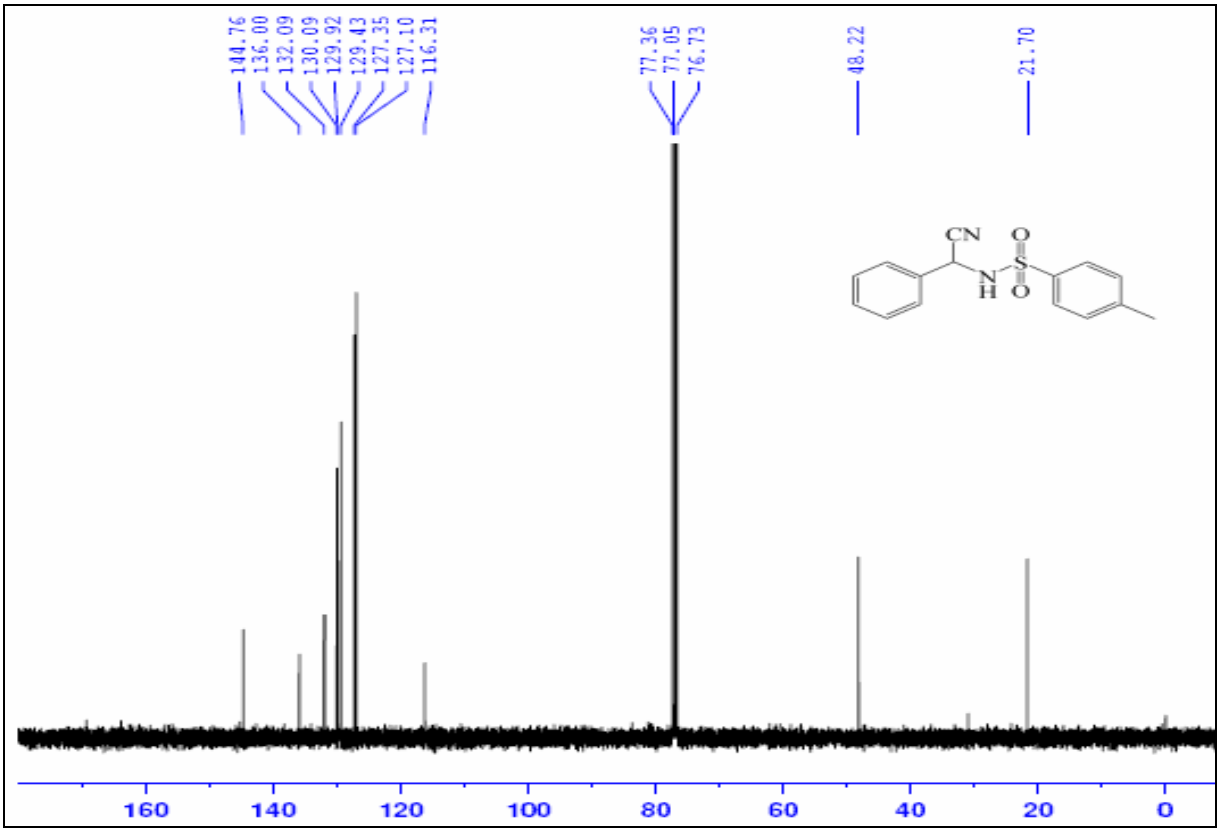


$[\alpha]_D^{20}$ = +109.2 (*c* = 0.21 in EtOH) (*S*)
[lit.[3]; $[\alpha]_D^{20}$ = +106.1 (*c* = 2.25 in EtOH, (*S*))]

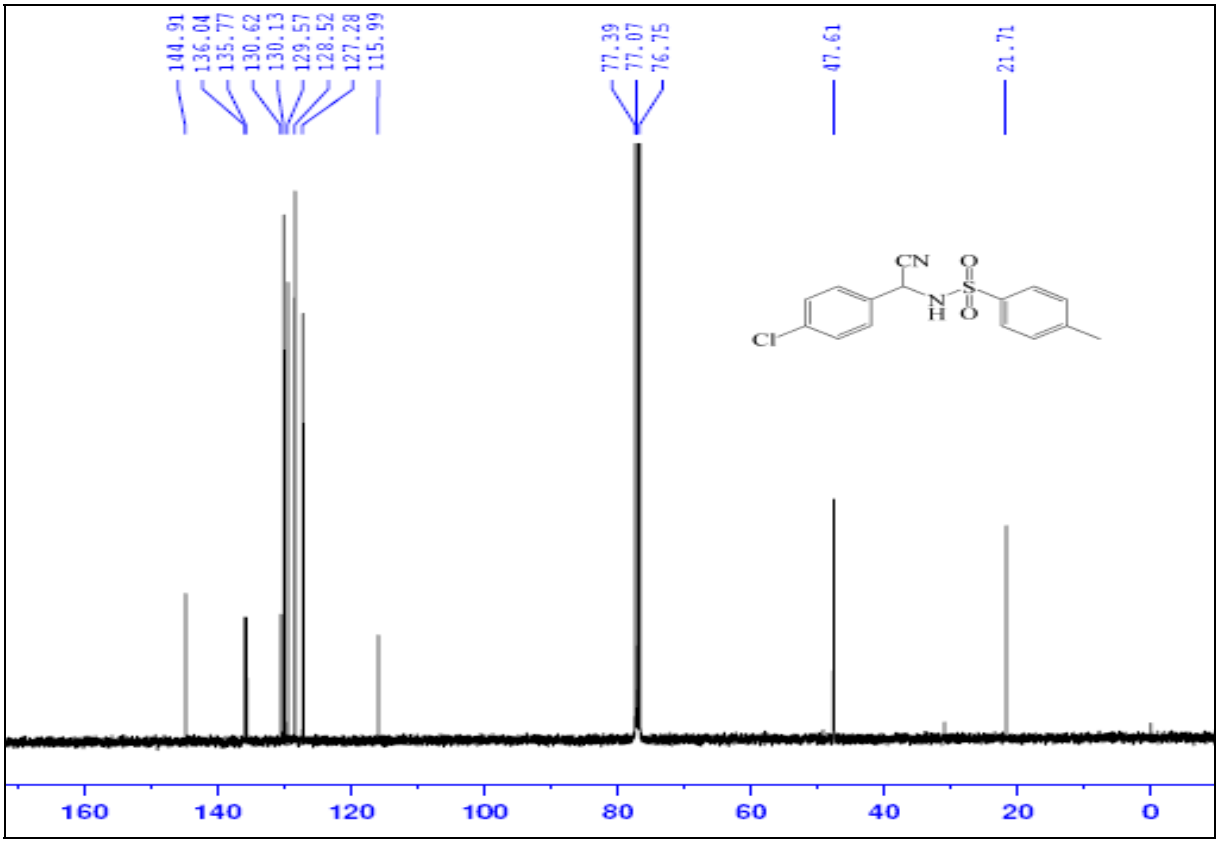
Recrystallization of the 97% ee of **5a** from ethyl acetate to afford the optically pure 2-phenyl-2-(tosylamino)acetonitrile (>99% ee); **5a** (48.0 mg, 0.168 mmol, >99% ee) placed in a round-bottom flask was treated with concentrated HCl (2 mL) and acetic acid (2 mL). The mixture was refluxed for 2 h with stirring. After that, water (5 mL) was added and cooled the mixture in the cool water bath for 15 min. Filtered out the precipitate, washed with water (5×1.5 mL) and dried to afford the pure 2-phenyl-2-(tosylamino)acetic acid **9** (37 mg, 0.121 mmol, 73% yield) without any loss of enantioselectivity; ^{1}H NMR (400 MHz, CD_3COCD_3, 25^{o}C, TMS) δ = 2.39 (s, 3H), 5.07 (s, 1H), 7.29-7.38 (m, 7H), 7.69 (d, *J* = 8.0 Hz, 2H) ppm. Absolute configuration was determined to be *S* based on the comparison of the optical rotation of **9** with the reported value; $[\alpha]_D^{20}$ = +109.2 (*c* = 0.21 in EtOH) [lit.[3]; $[\alpha]_D^{20}$ = +106.1 (*c* = 2.25 in EtOH, >99% ee (*S*))]

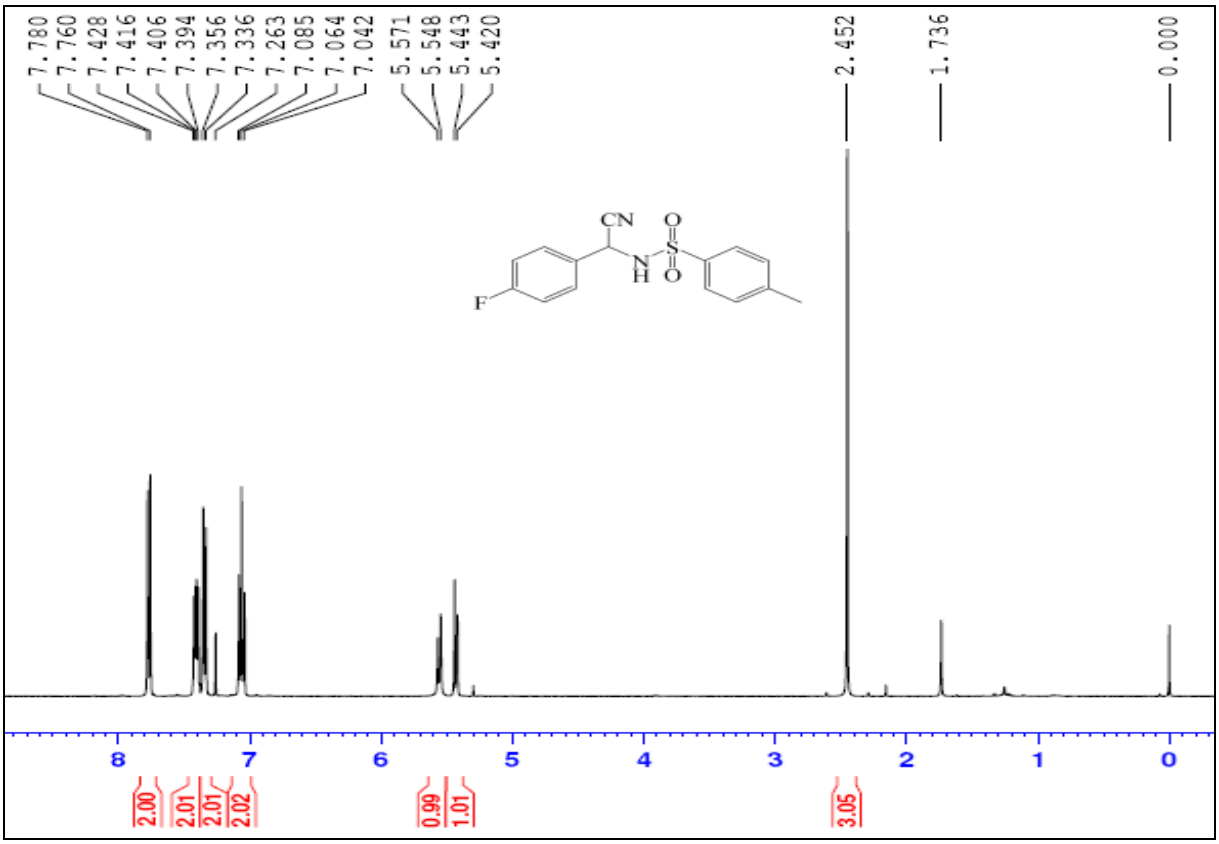
(G) Copies of NMR Spectra for the Products

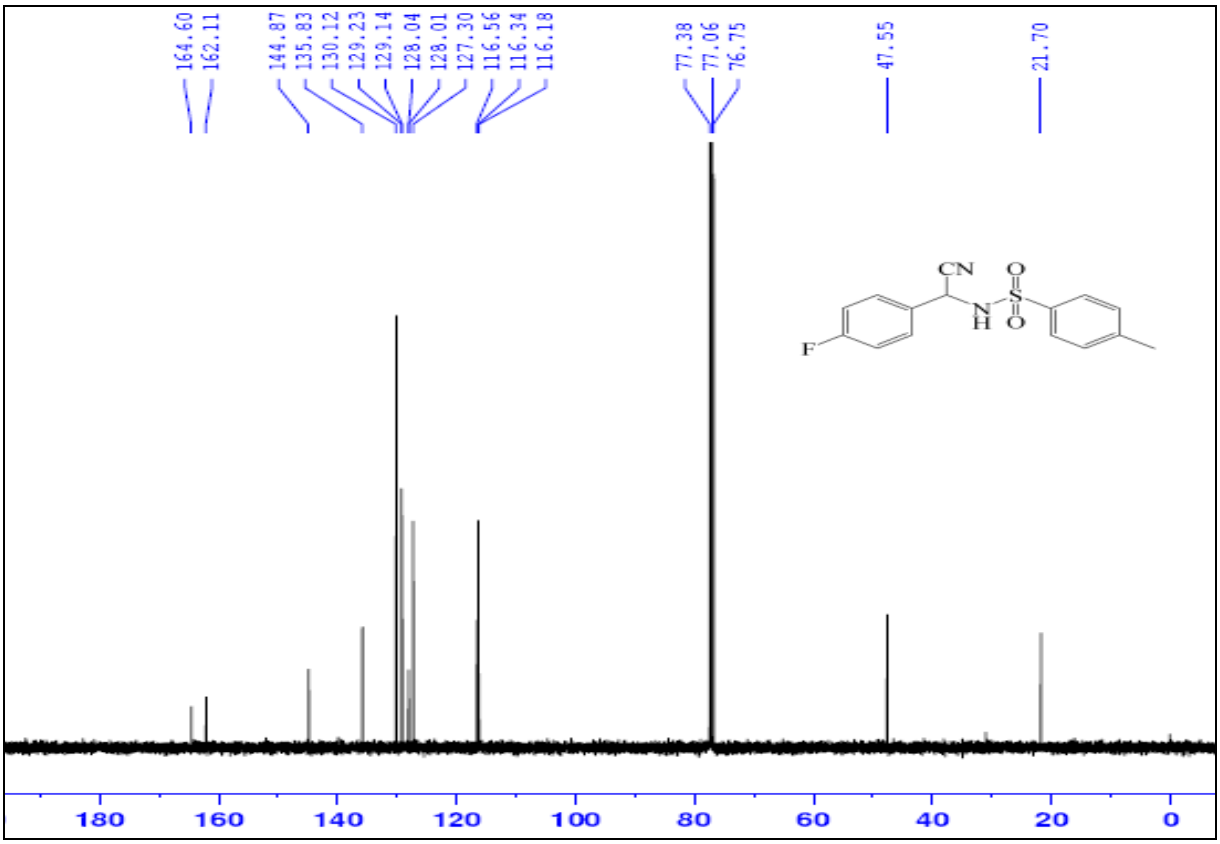


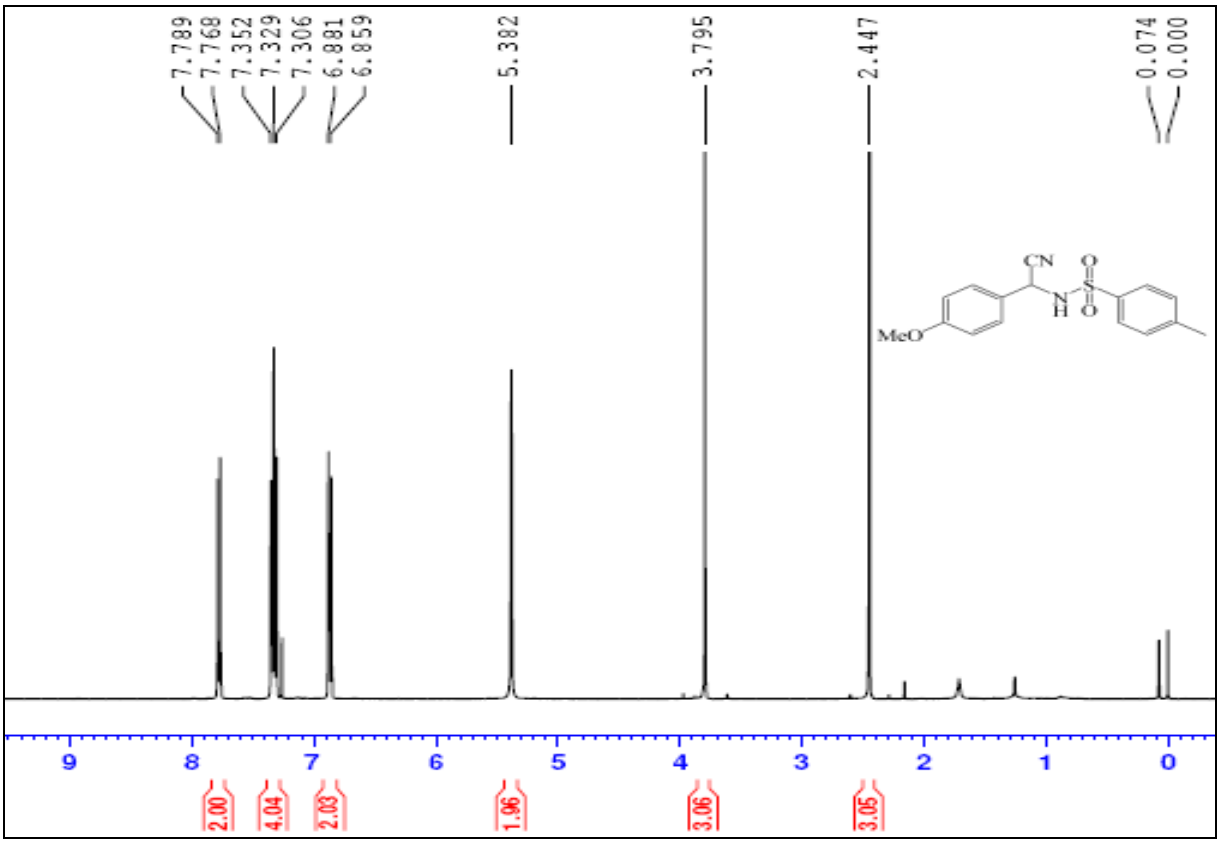


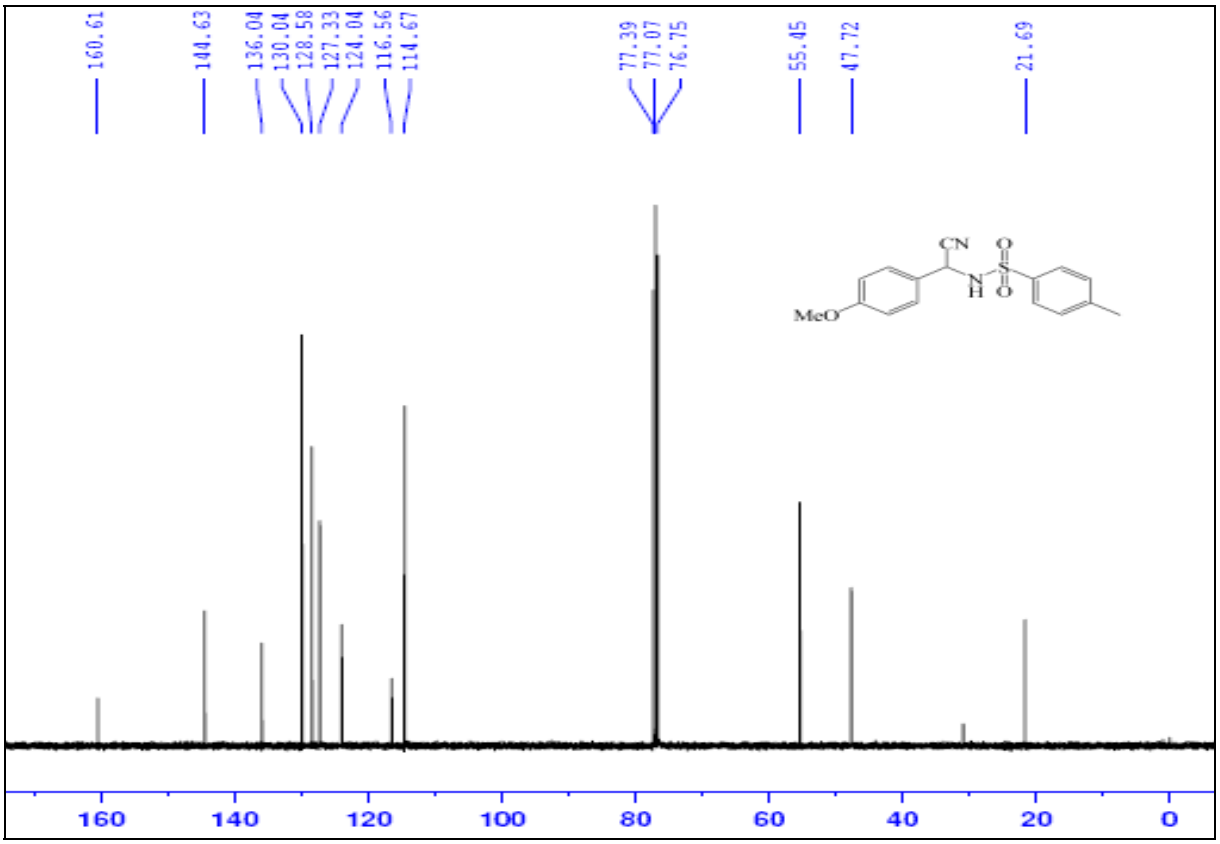

7.765
7.745
7.349
7.329
7.262
5.613
5.422
2.452
0.000
CN
O
S
N
H
O
O
Cl
9
8
7
6
5
4
3
2
1
0
2.00
6.03
0.83
1.03
3.05

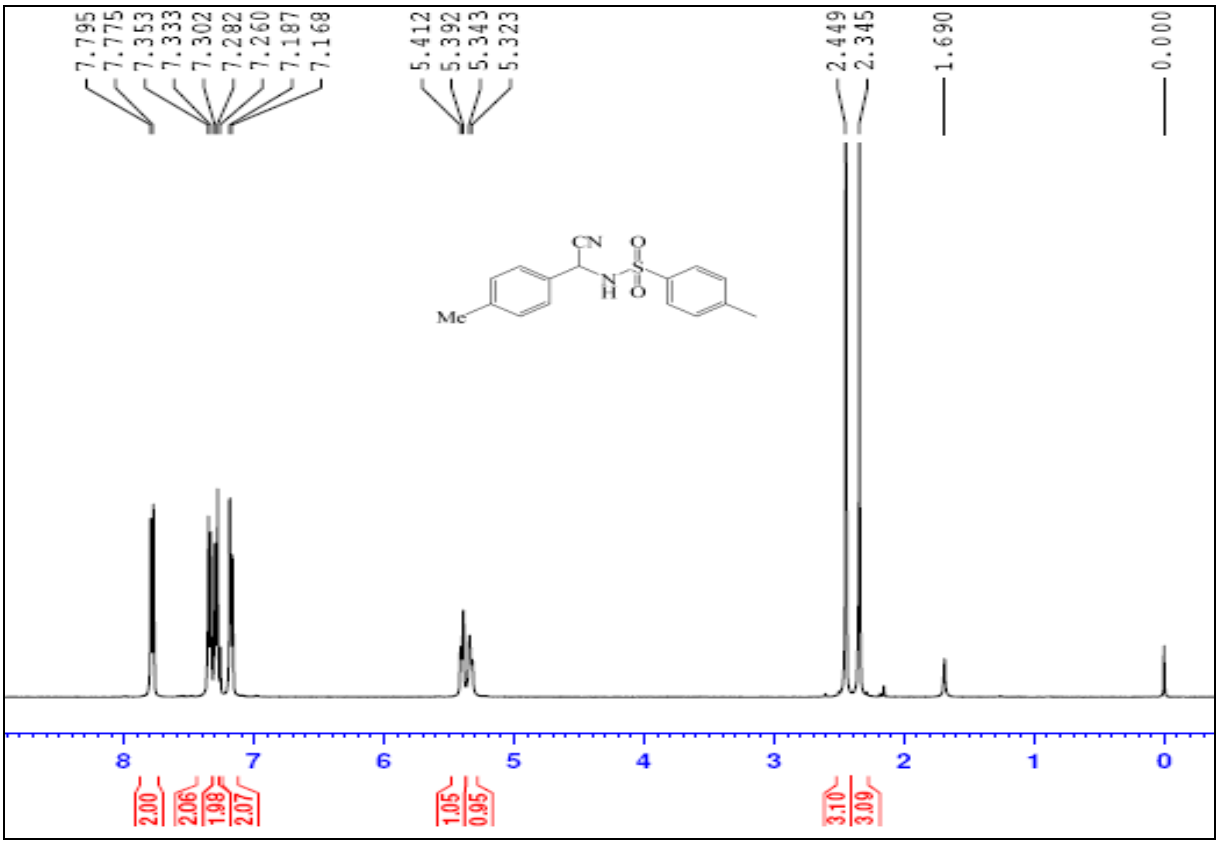

144.91
136.04
135.77
130.62
130.13
129.57
128.52
127.28
115.99
77.39
77.07
76.75
47.61
21.71
CN
O
S
N
H
O
O
Cl
160
140
120
100
80
60
40
20
0

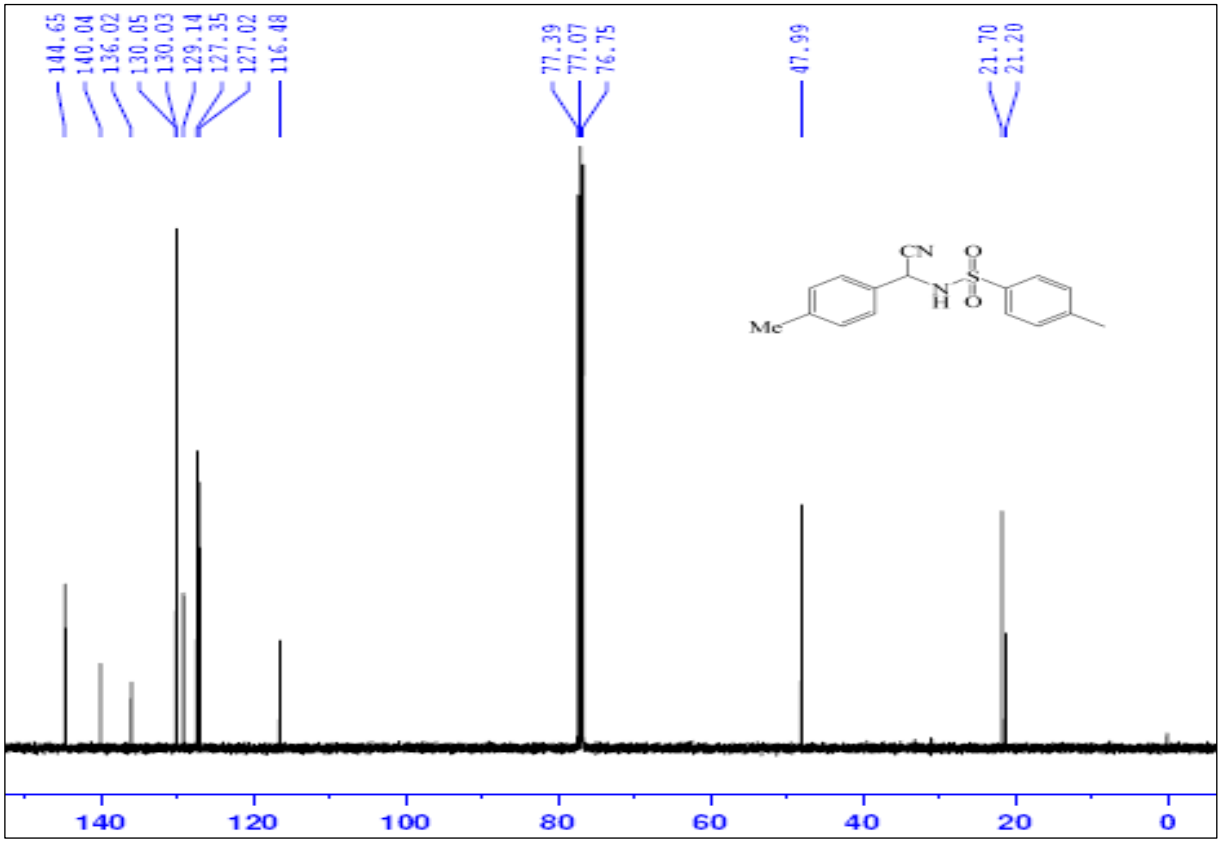

7.780
7.760
7.428
7.416
7.406
7.394
7.356
7.336
7.263
7.085
7.064
7.042
5.571
5.548
5.443
5.420
2.452
1.736
0.000
CN
O
S
N
H
O
F
8
7
6
5
4
3
2
1
0
2.00
2.01
2.01
2.02
0.99
1.01
3.05

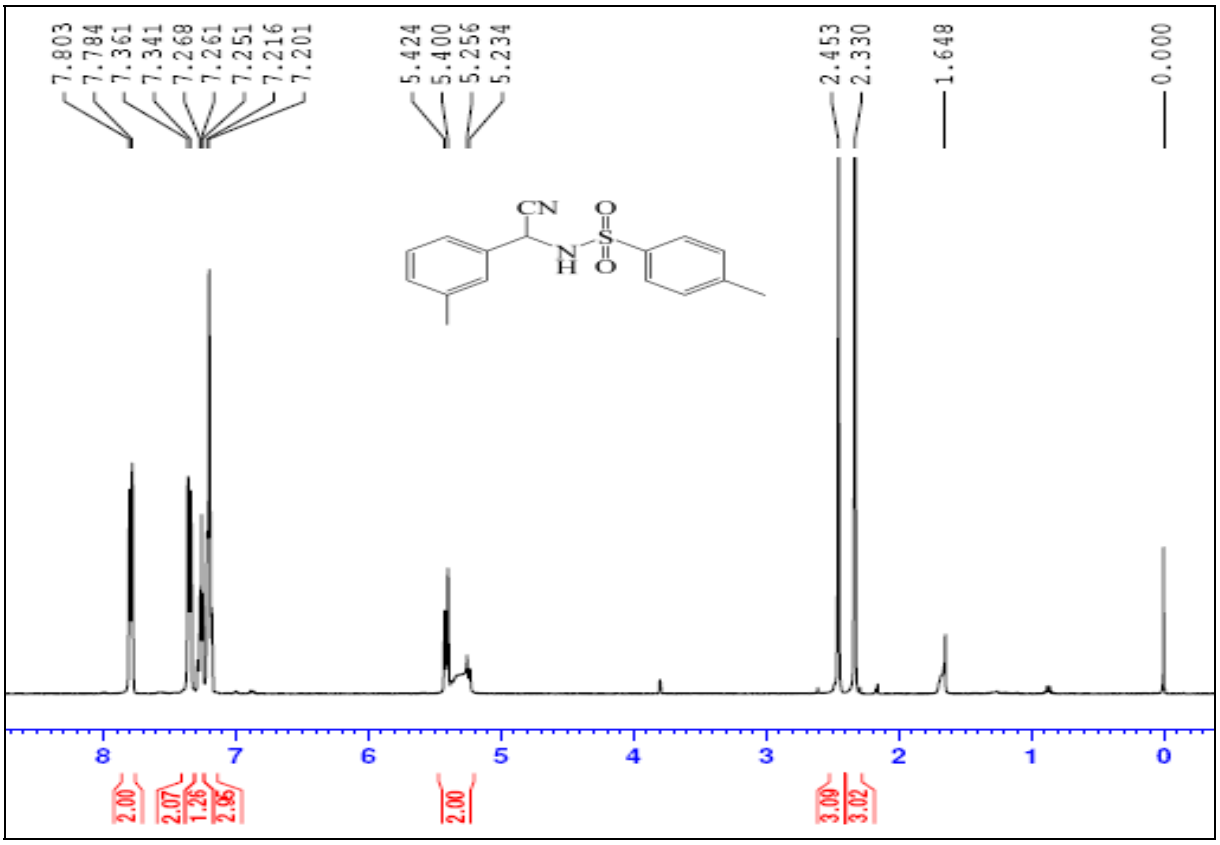

164.60
162.11
144.87
135.83
130.12
129.23
129.14
128.04
128.01
127.30
116.56
116.34
116.18
77.38
77.06
76.75
47.55
21.70
CN
O
S
N
H
O
F
180
160
140
120
100
80
60
40
20
0

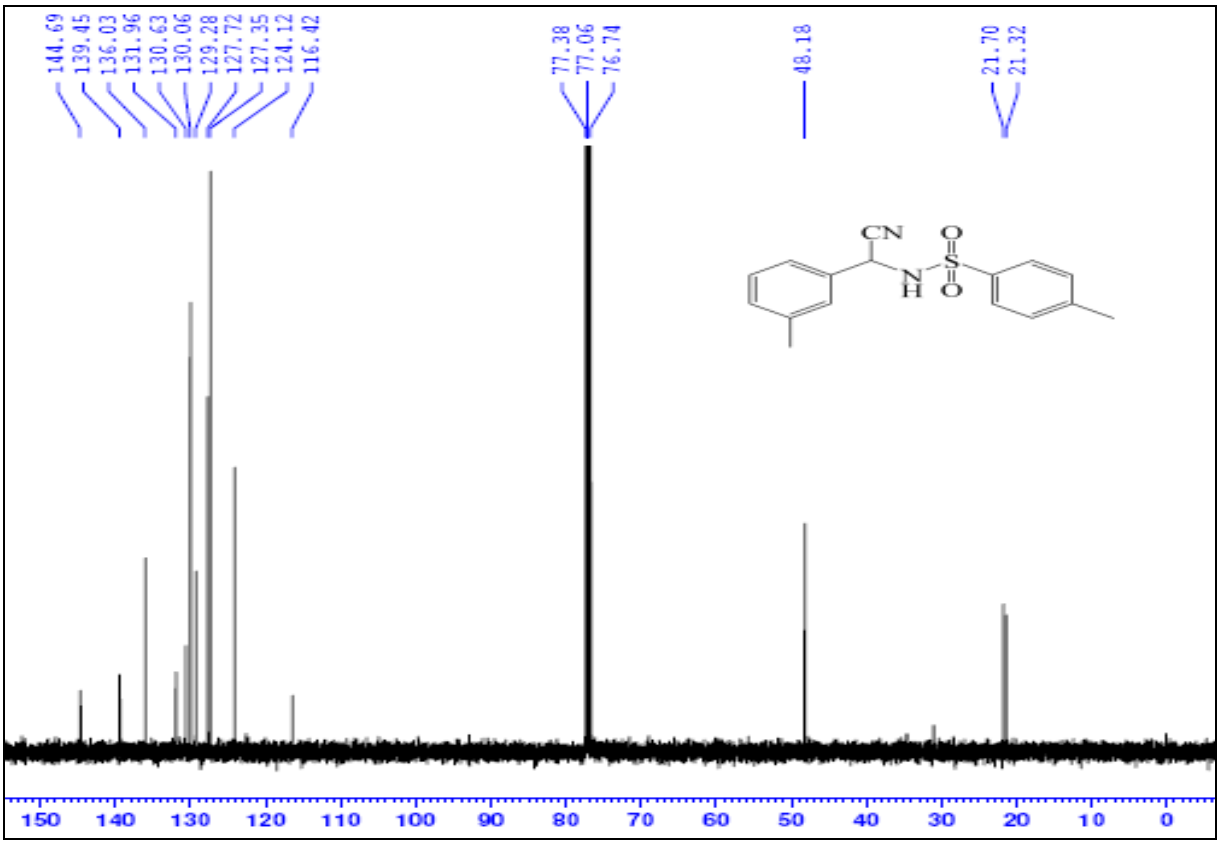

7.789
7.768
7.352
7.329
7.306
6.881
6.859
5.382
3.795
2.447
0.074
0.000
CN
N
H
O
O
O
MeO
9
8
7
6
5
4
3
2
1
0
2.00
4.04
2.03
1.96
3.06
3.05

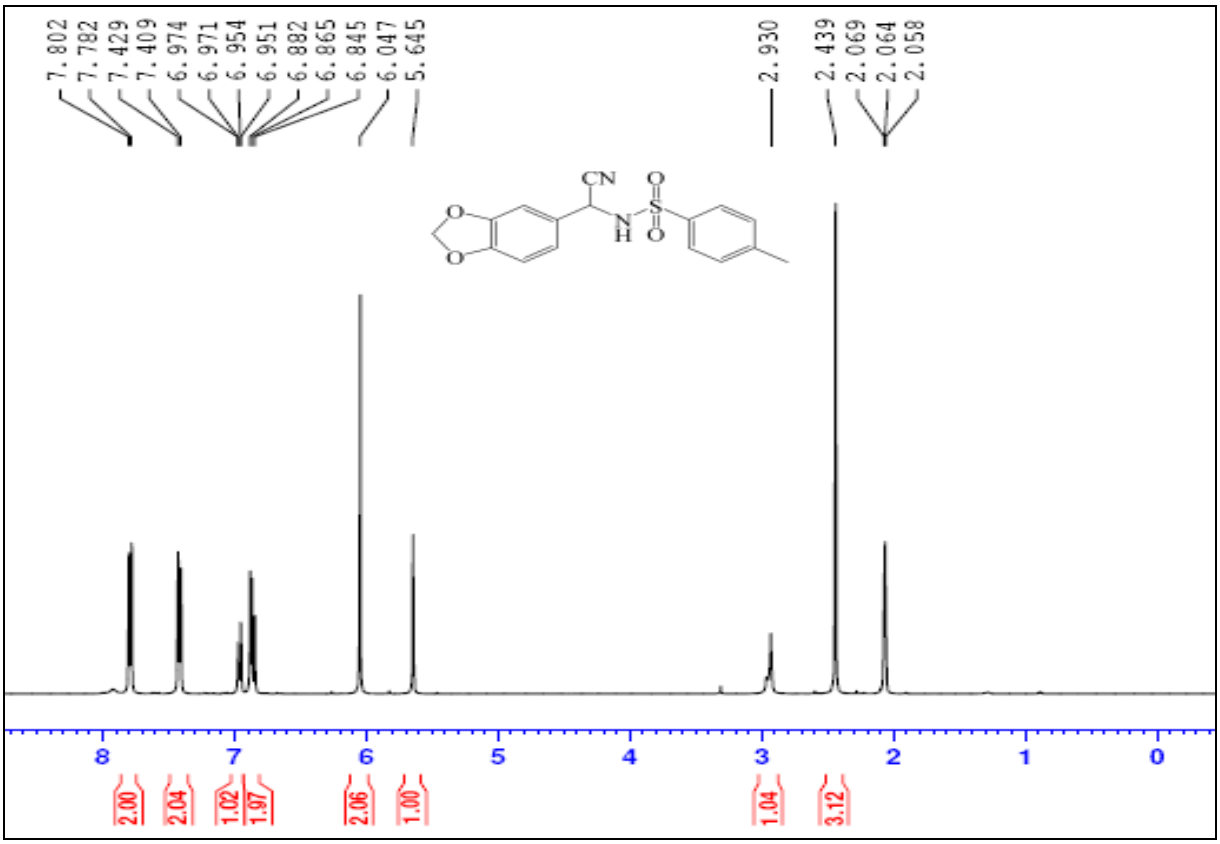

160.61
144.63
136.04
130.04
128.58
127.33
124.04
116.56
114.67
77.39
77.07
76.75
55.45
47.72
21.69
CN
N
H
O
O
O
MeO
160
140
120
100
80
60
40
20
0

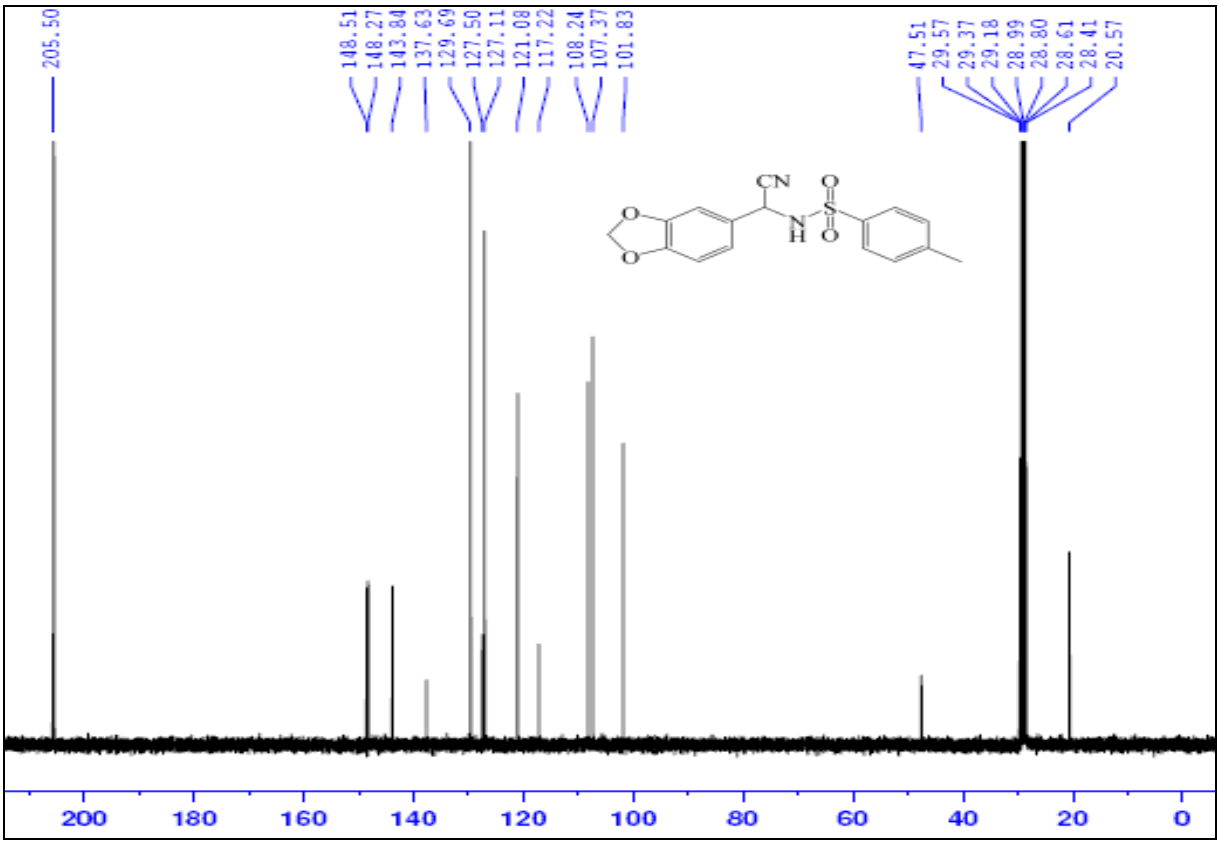

7.795
7.775
7.353
7.333
7.302
7.282
7.260
7.187
7.168
5.412
5.392
5.343
5.323
2.449
2.345
1.690
0.000
Cl
O
N
H
O
Me
8
7
6
5
4
3
2
1
0
2.00
2.06
1.98
2.07
1.05
0.95
3.10
3.09

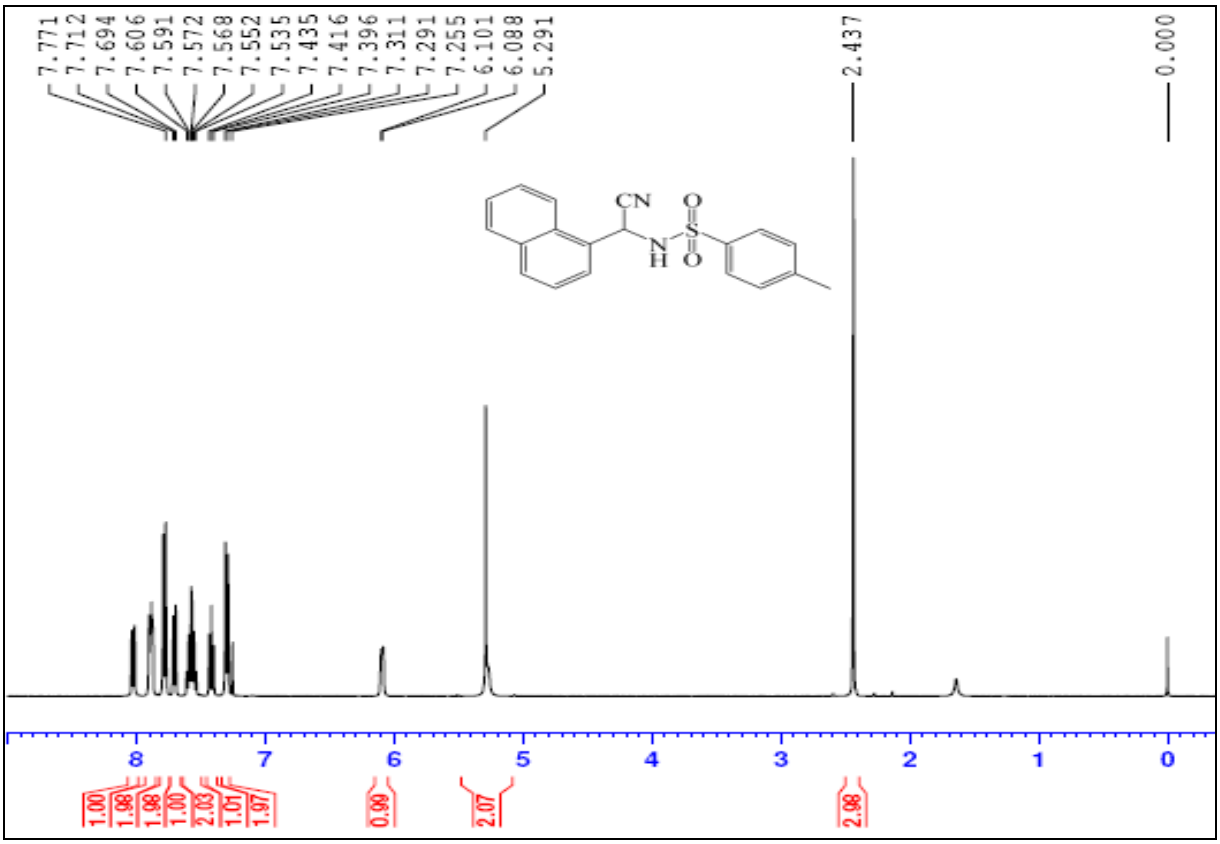

144.65
140.04
136.02
130.05
130.03
129.14
127.35
127.02
116.48
77.39
77.07
76.75
47.99
21.70
21.20
Cl
O
N
H
O
Me
140
120
100
80
60
40
20
0

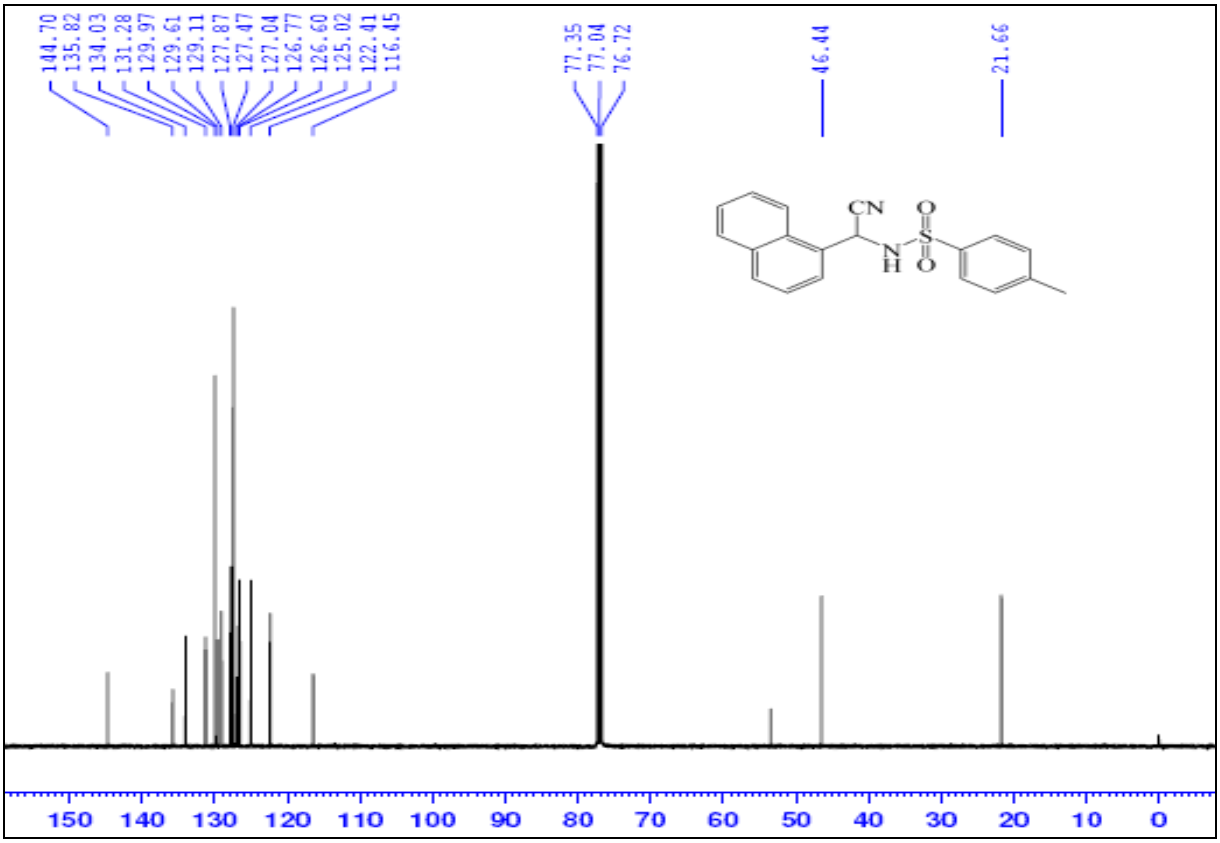

7.803
7.784
7.361
7.341
7.268
7.261
7.251
7.216
7.201
5.424
5.400
5.256
5.234
2.453
2.330
1.648
0.000
CN
O
S
N
H
O
8
7
6
5
4
3
2
1
0
2.00
2.07
1.26
2.00
3.09
3.02

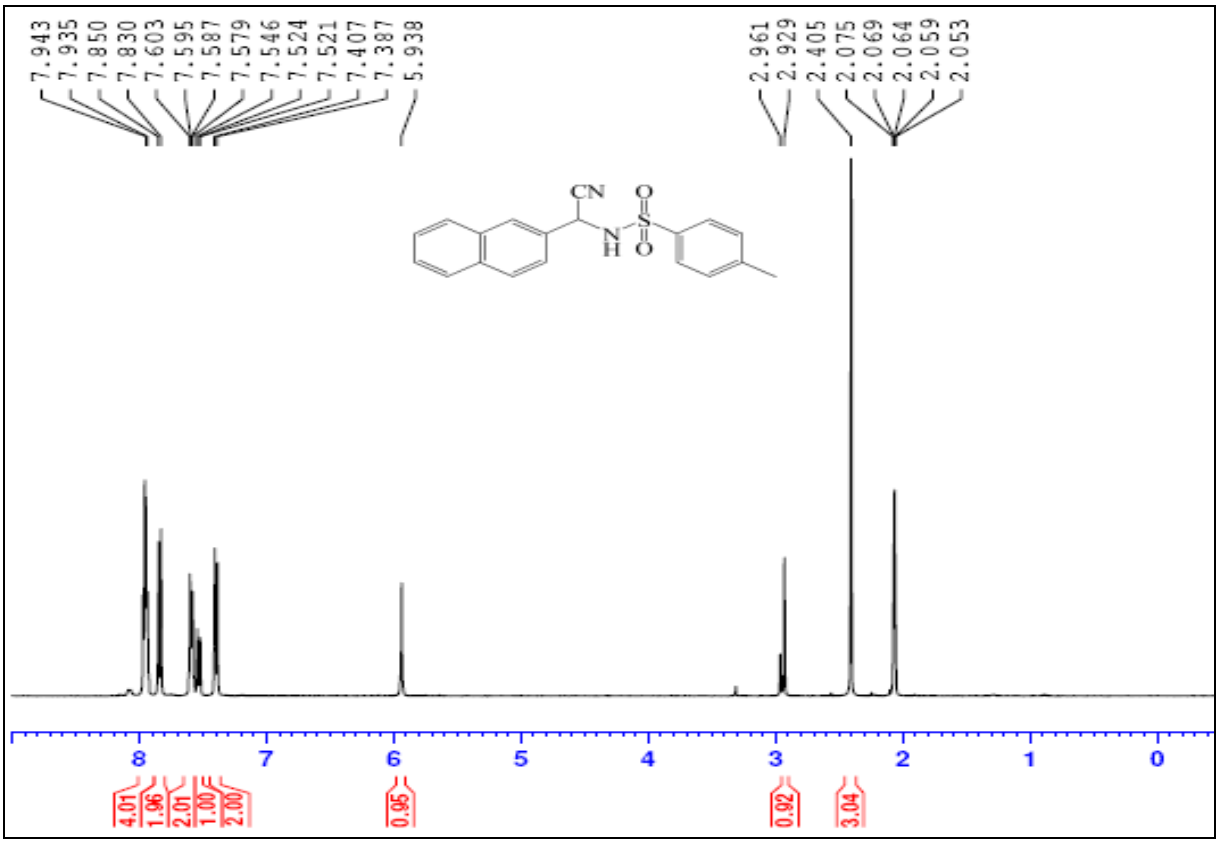

144.69
139.45
136.03
131.96
130.63
130.06
129.28
127.72
127.35
124.12
116.42
77.38
77.06
76.74
48.18
21.70
21.32
CN
O
S
N
H
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

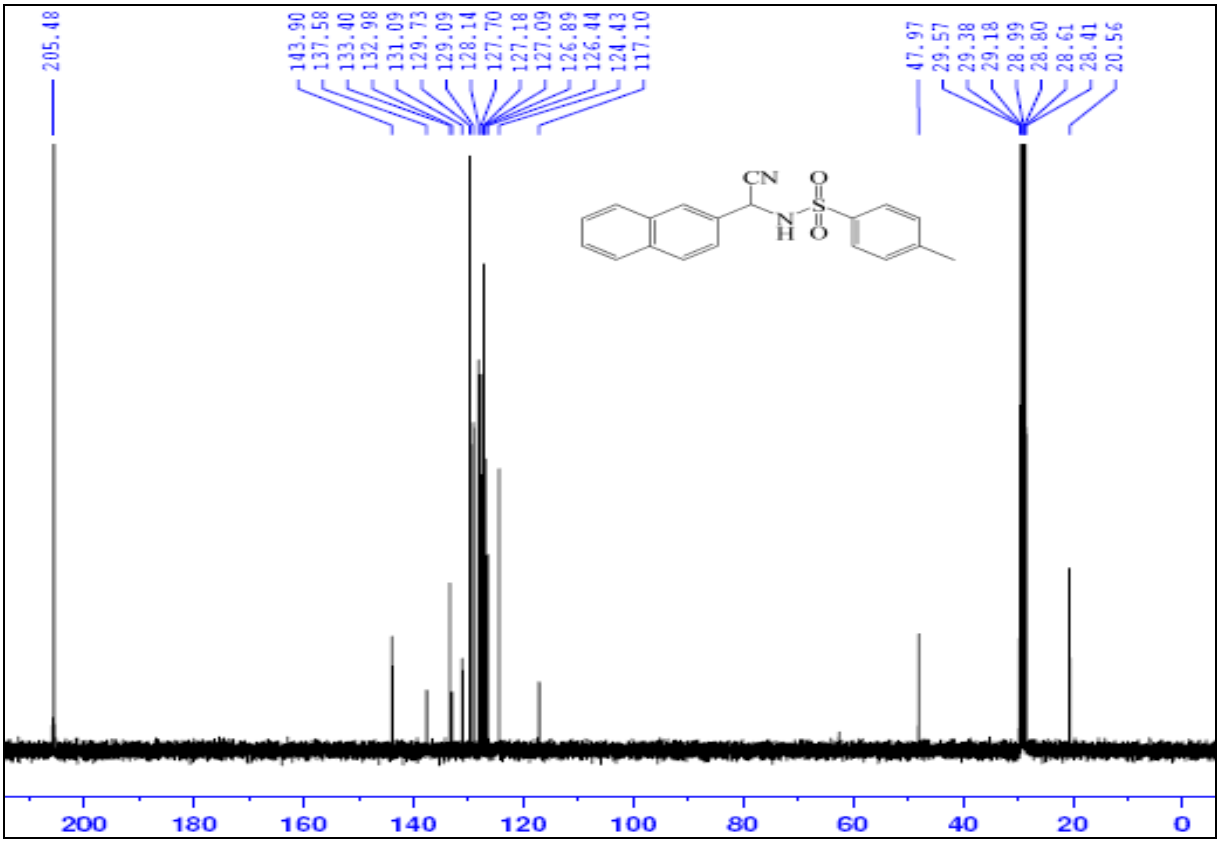

7.802
7.782
7.429
7.409
6.974
6.971
6.954
6.951
6.882
6.865
6.845
6.047
5.645
2.930
2.439
2.069
2.064
2.058
CN
O
N
H
S
O
O
O
8
7
6
5
4
3
2
1
0
2.00
2.04
1.02
1.97
2.06
1.00
1.04
3.12

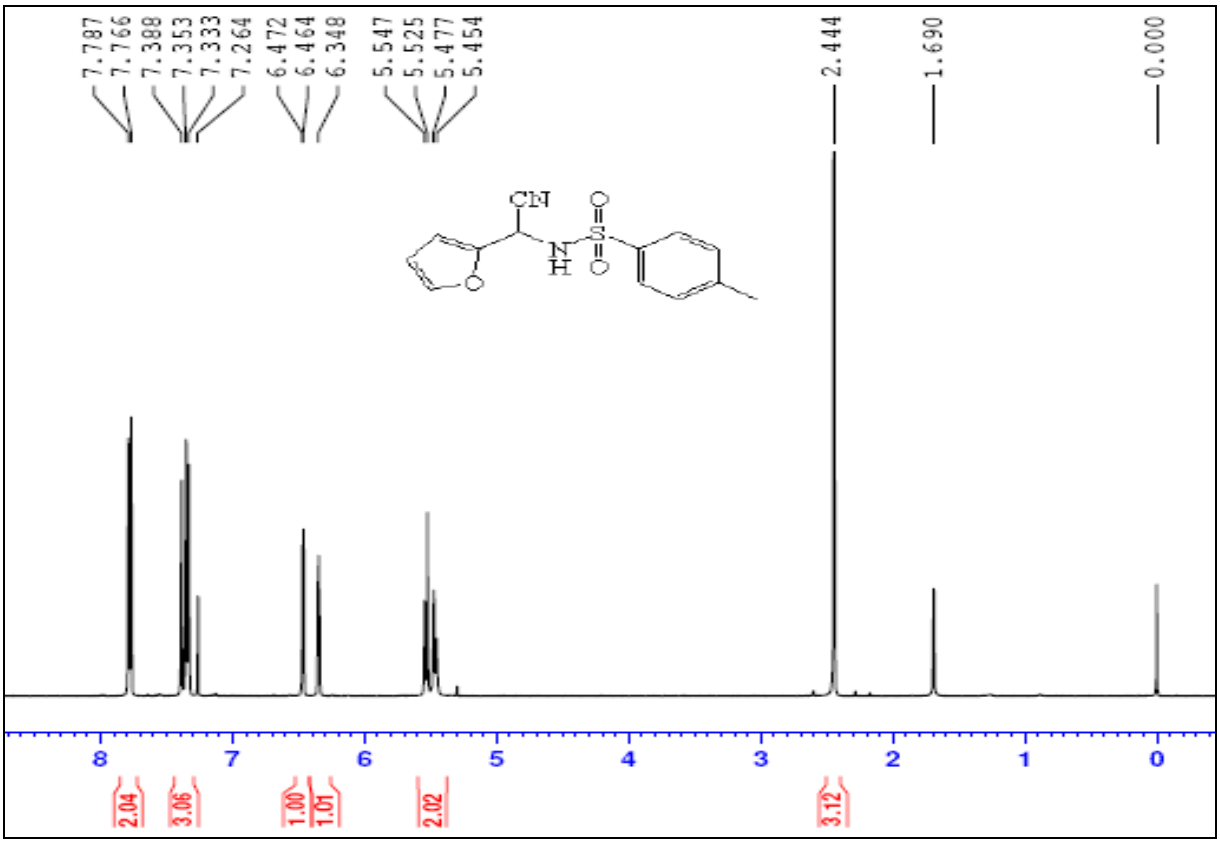

205.50
148.51
148.27
143.84
137.63
129.69
127.50
127.11
121.08
117.22
108.24
107.37
101.83
47.51
29.57
29.37
29.18
28.99
28.80
28.61
28.41
20.57
CN
O
N
H
S
O
O
O
200
180
160
140
120
100
80
60
40
20
0

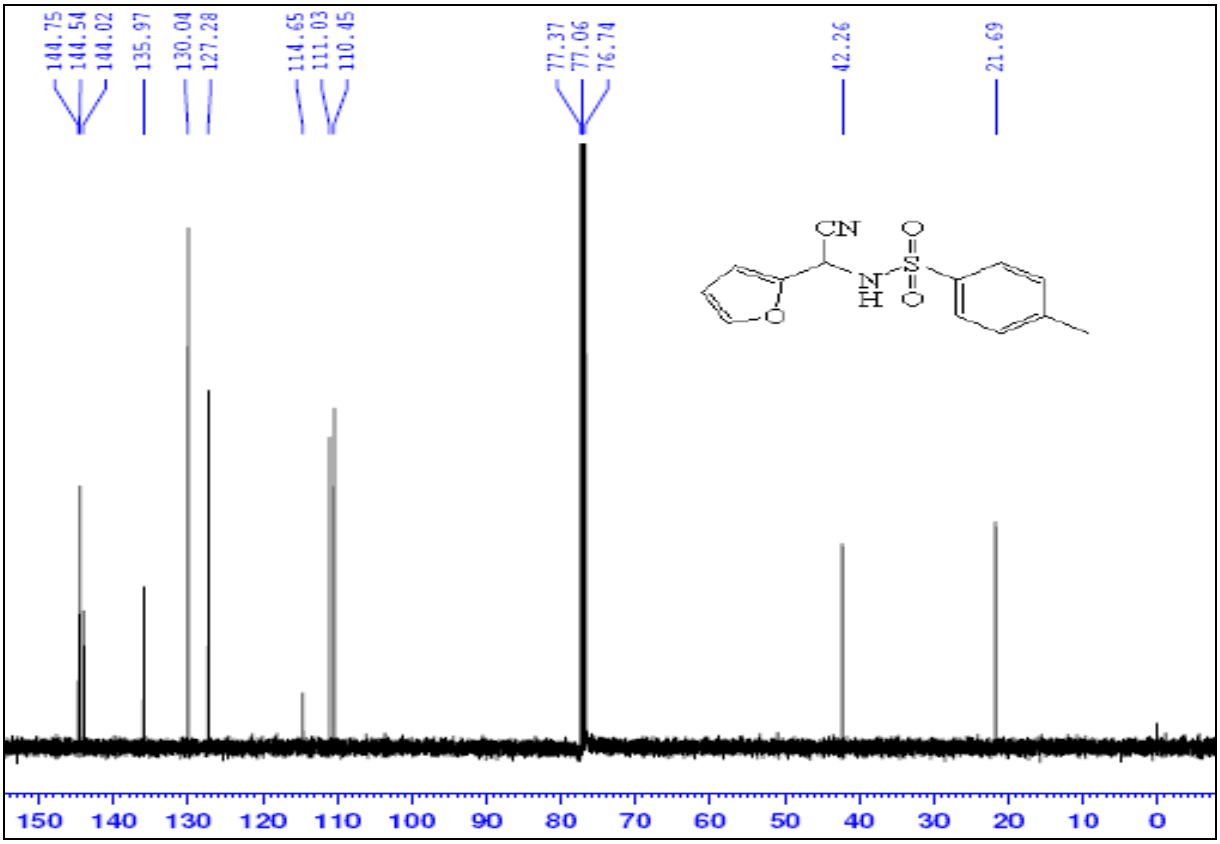

7.771
7.712
7.694
7.606
7.591
7.572
7.568
7.552
7.535
7.435
7.416
7.396
7.311
7.291
7.255
6.101
6.088
5.291
2.437
0.000
CN
O
S
N
H
O
8
7
6
5
4
3
2
1
0
1.00
1.98
1.98
1.00
2.03
1.01
1.97
0.99
2.07
2.98

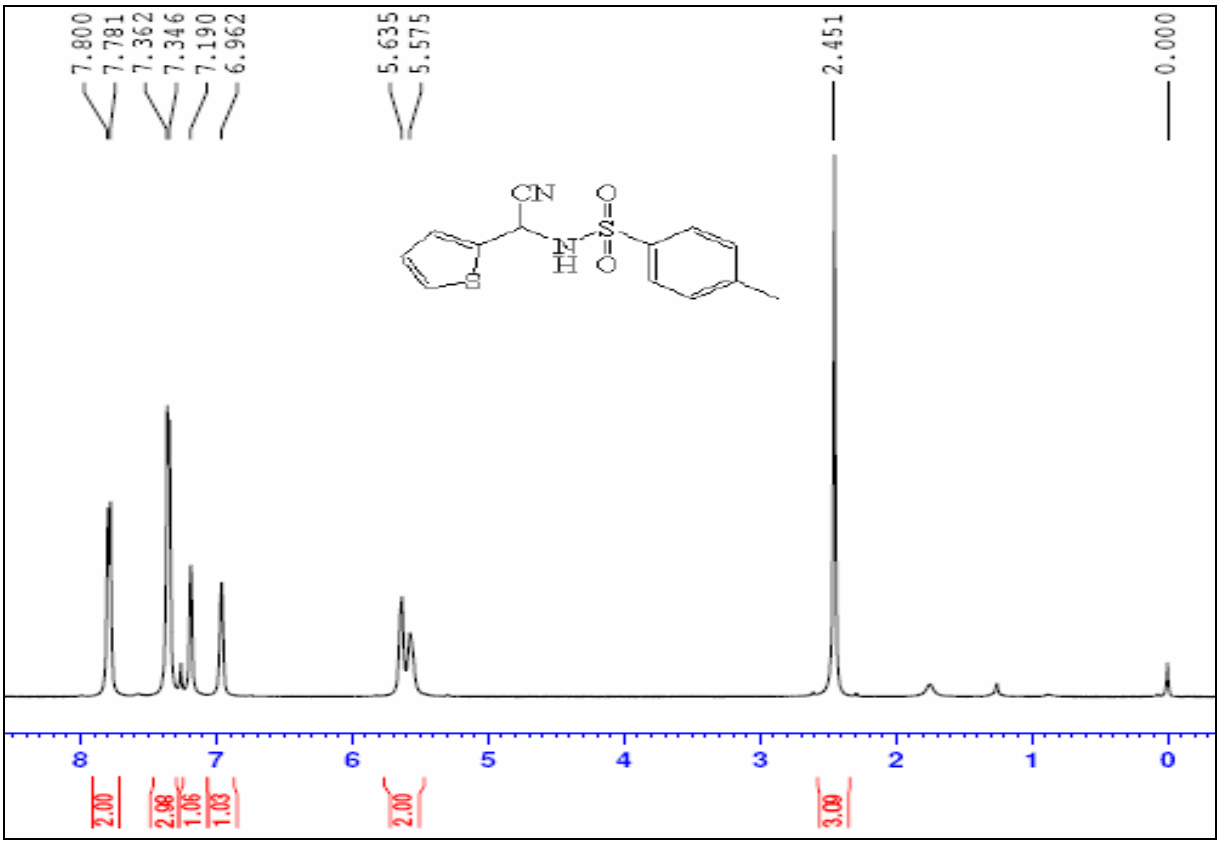

144.70
135.82
134.03
131.28
129.97
129.61
129.11
127.87
127.47
127.04
126.77
126.60
125.02
122.41
116.45
77.35
77.04
76.72
46.44
21.66
CN
O
S
N
H
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

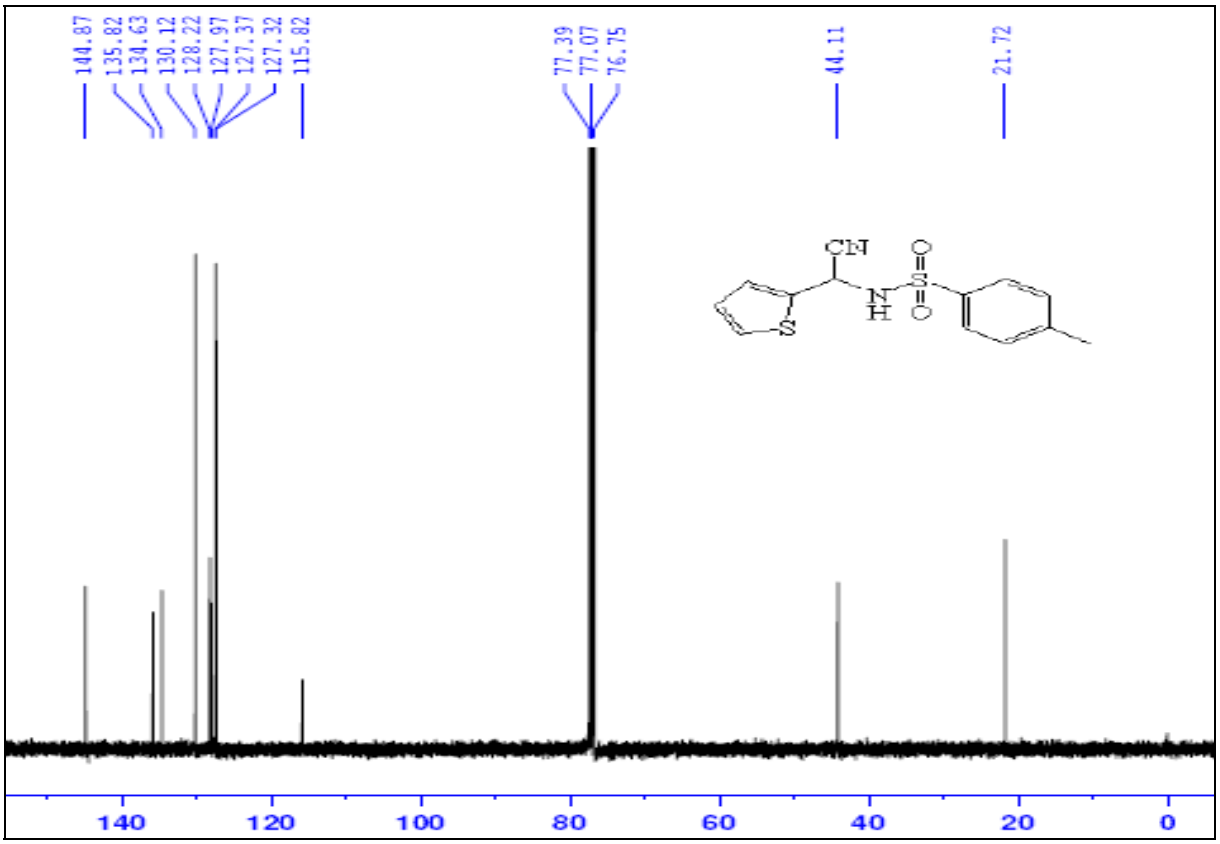

7.943
7.935
7.850
7.830
7.603
7.595
7.587
7.579
7.546
7.524
7.521
7.407
7.387
5.938
2.961
2.929
2.405
2.075
2.069
2.064
2.059
2.053
CN
O
S
N
H
O
8
7
6
5
4
3
2
1
0
4.01
1.96
2.01
1.00
2.00
0.95
0.92
3.04

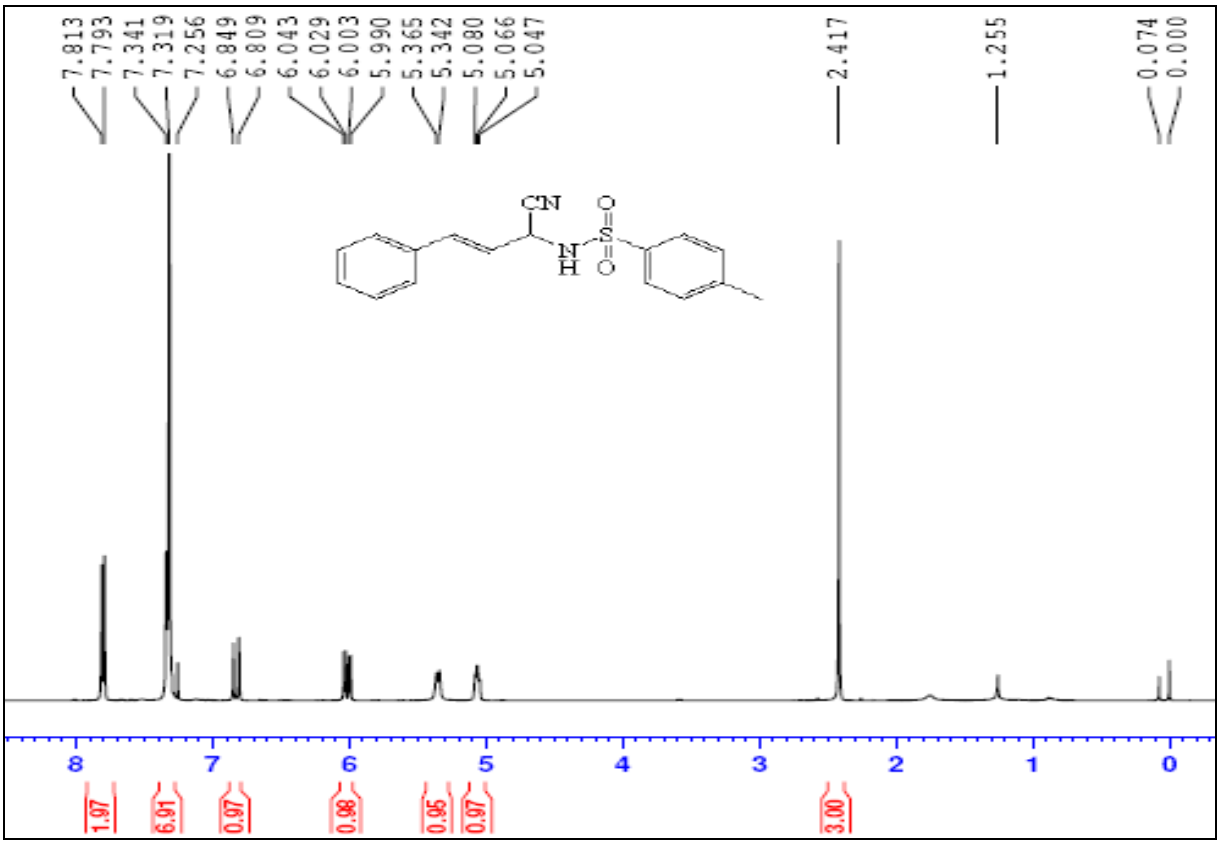

205.48
143.90
137.58
133.40
132.98
131.09
129.73
129.09
128.14
127.70
127.18
127.09
126.89
126.44
124.43
117.10
47.97
29.57
29.38
29.18
28.99
28.80
28.61
28.41
20.56
CN
O
S
N
H
O
200
180
160
140
120
100
80
60
40
20
0

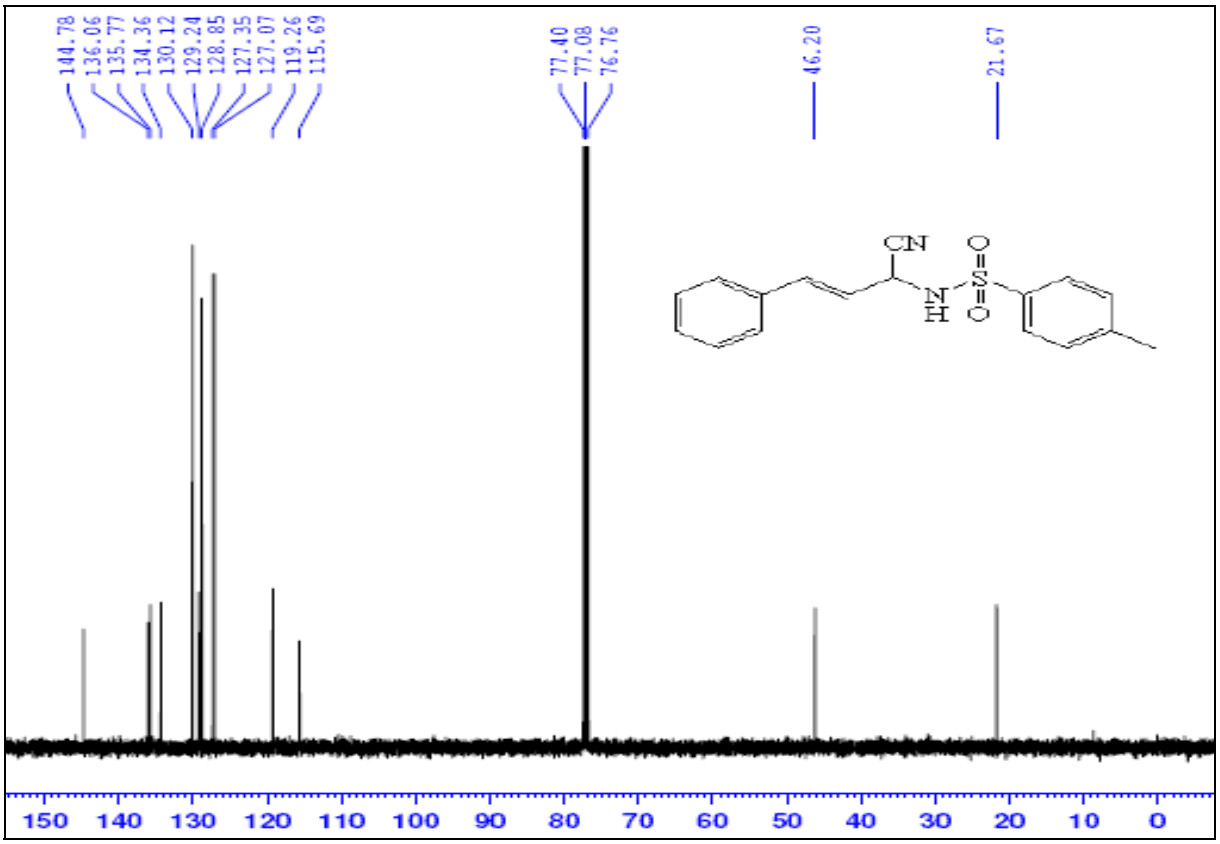

7.787
7.766
7.388
7.353
7.333
7.264
6.472
6.464
6.348
5.547
5.525
5.477
5.454
2.444
1.690
0.000
CN
HN
O=S=O
8
7
6
5
4
3
2
1
0
2.04
3.06
1.00
1.01
2.02
3.12

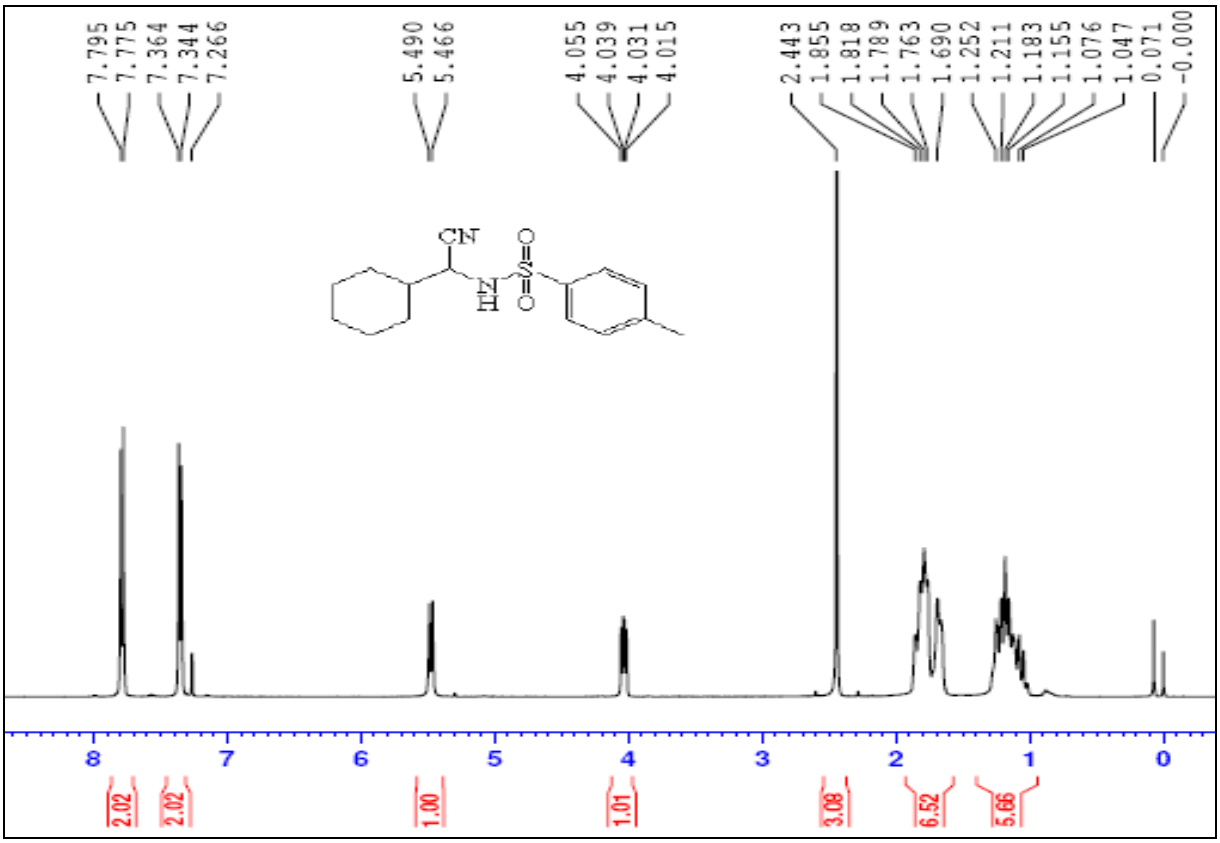

144.75
144.54
144.02
135.97
130.04
127.28
114.65
111.03
110.45
77.37
77.06
76.74
42.26
21.69
CN
HN
O=S=O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

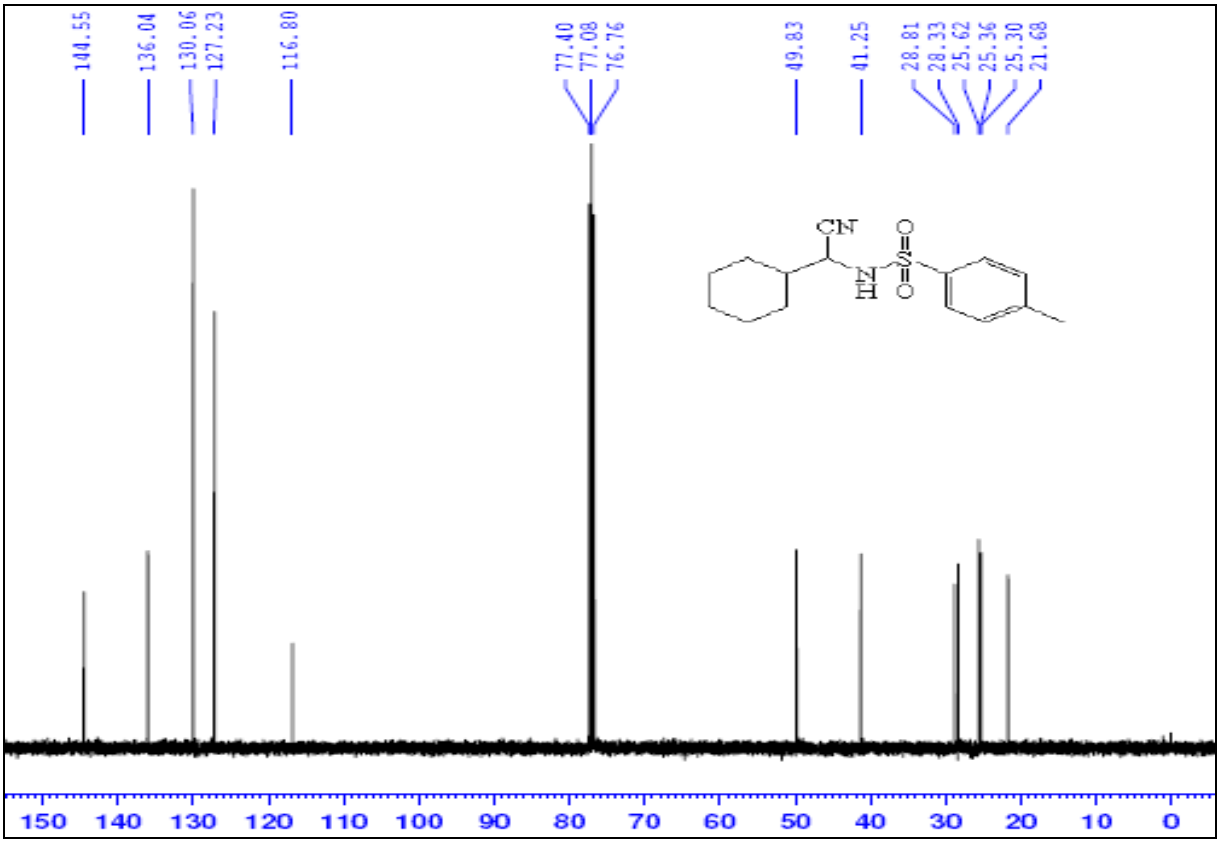

7.800
7.781
7.362
7.346
7.190
6.962
5.635
5.575
2.451
0.000
CN
O
S
O
H
N
O
8
7
6
5
4
3
2
1
0
2.00
2.98
1.06
1.03
2.00
3.09

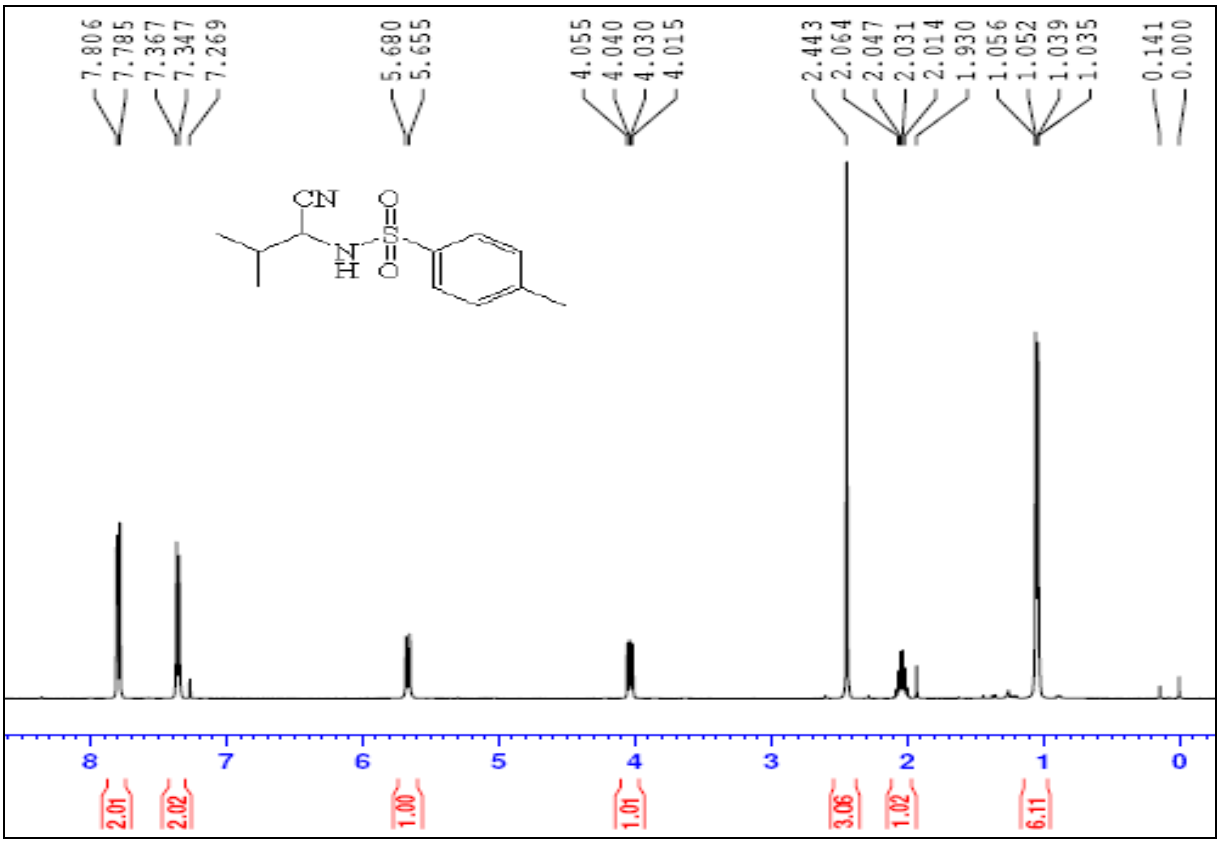

144.87
135.82
134.63
130.12
128.22
127.97
127.37
127.32
115.82
77.39
77.07
76.75
44.11
21.72
CN
O
S
O
H
N
O
140
120
100
80
60
40
20
0

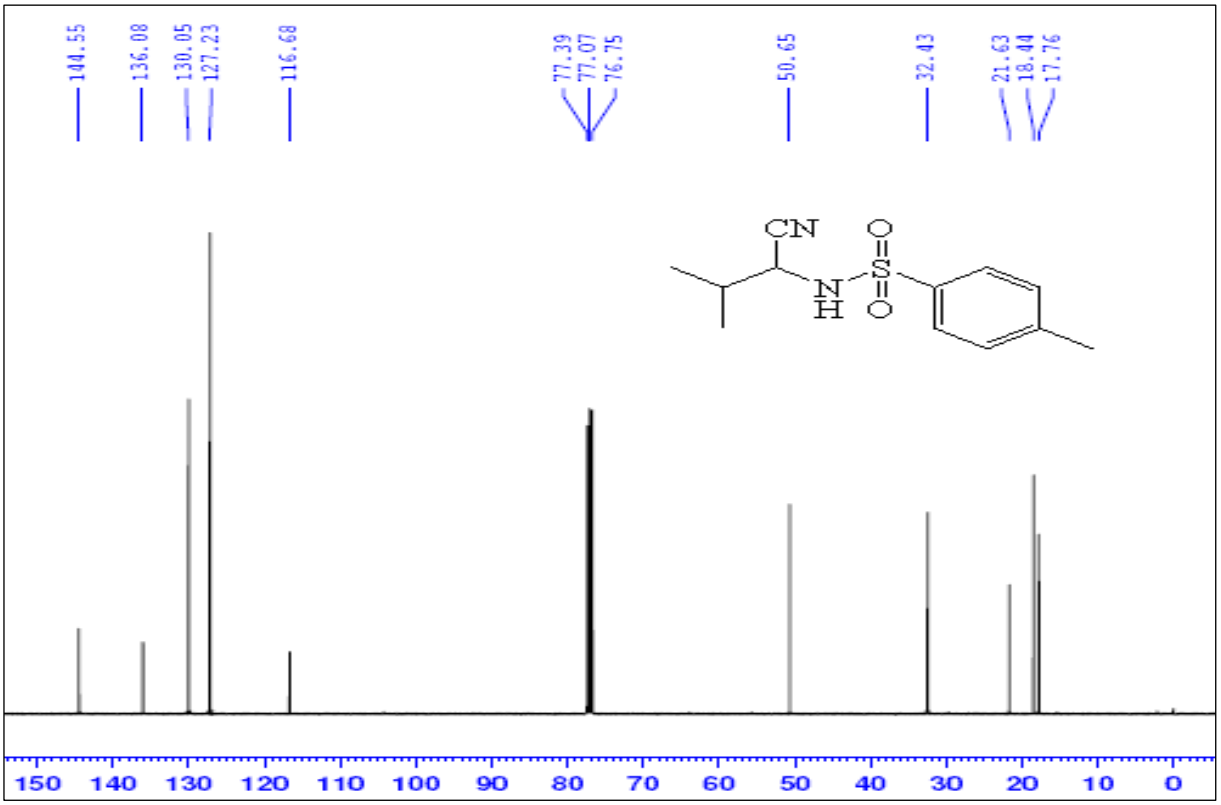

7.813
7.793
7.341
7.319
7.256
6.849
6.809
6.043
6.029
6.003
5.990
5.365
5.342
5.080
5.066
5.047
2.417
1.255
0.074
0.000
CN
N
H
O=S=O
8
7
6
5
4
3
2
1
0
1.97
6.91
0.97
0.98
0.95
0.97
3.00

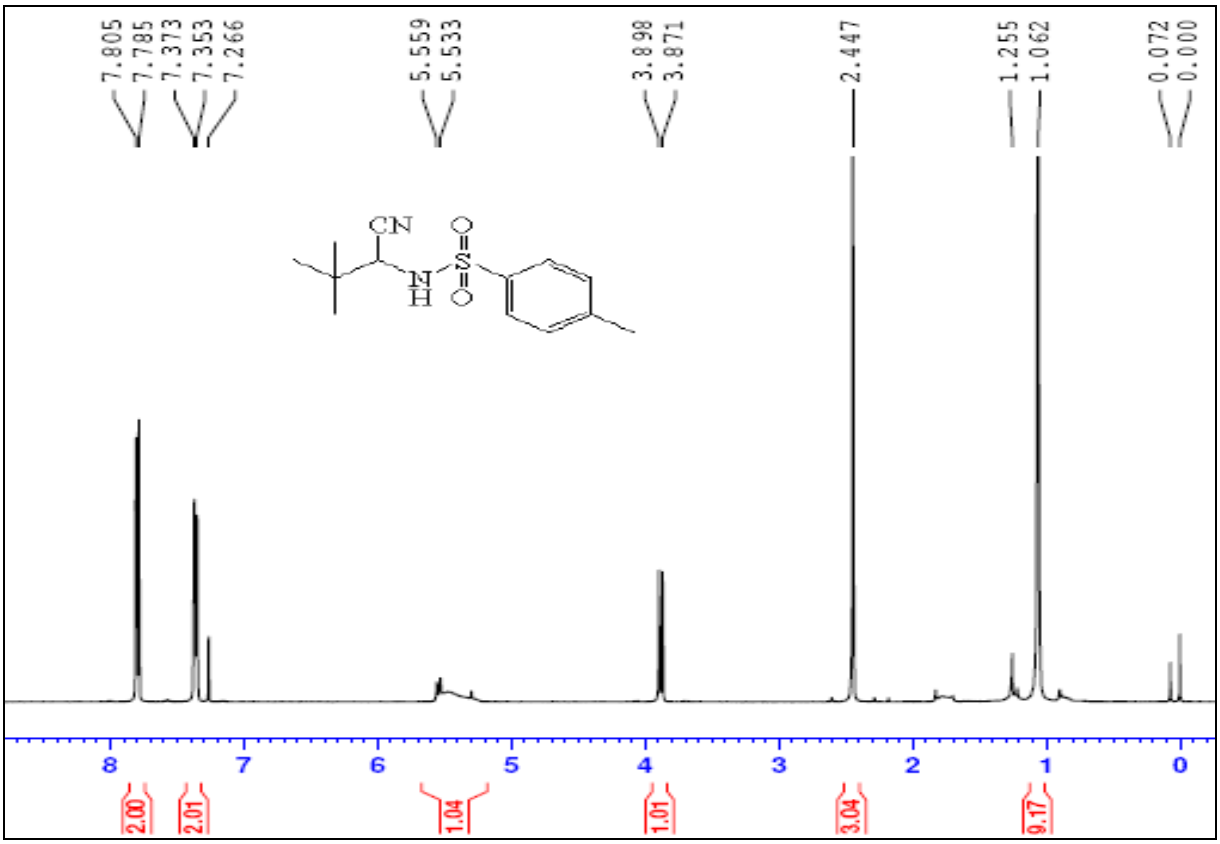

144.78
136.06
135.77
134.36
130.12
129.24
128.85
127.35
127.07
119.26
115.69
77.40
77.08
76.76
46.20
21.67
CN
N
H
O=S=O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

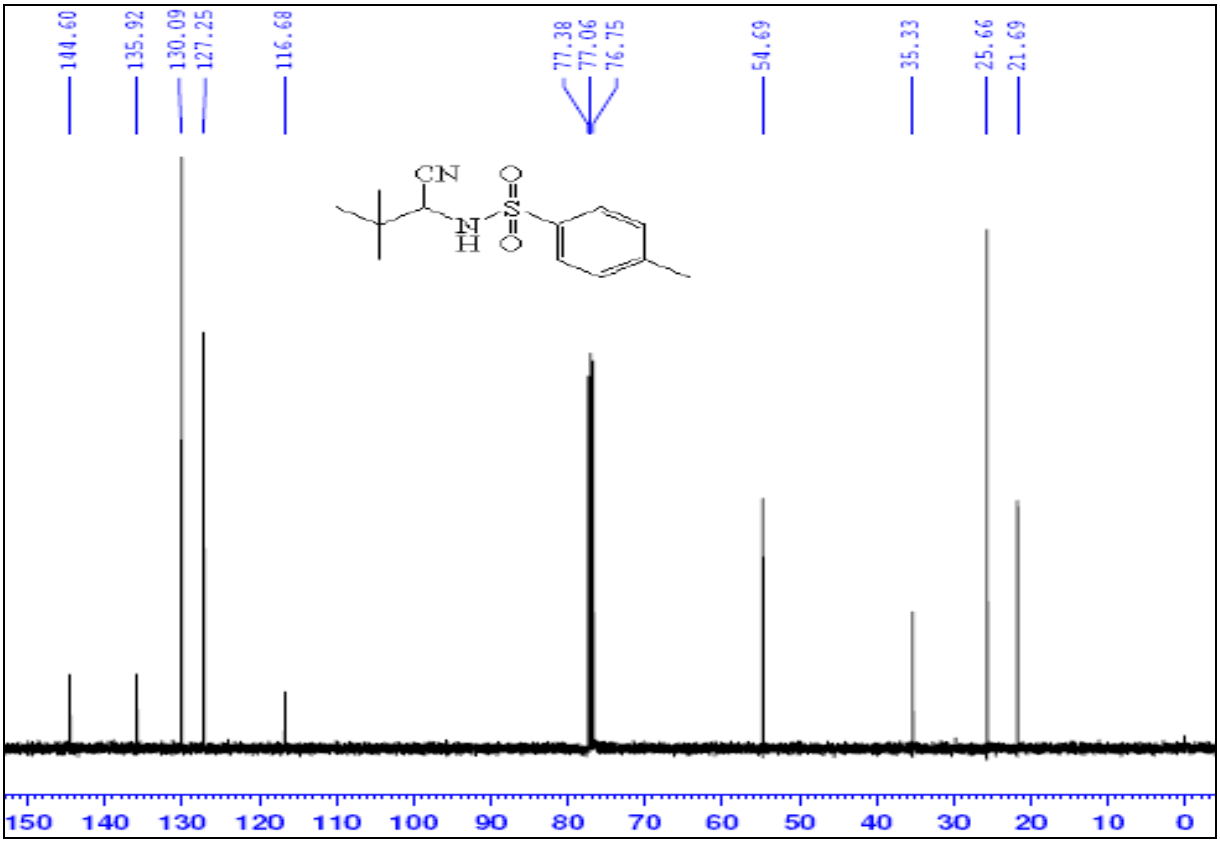

7.795
7.775
7.364
7.344
7.266
5.490
5.466
4.055
4.039
4.031
4.015
2.443
1.855
1.818
1.789
1.763
1.690
1.252
1.211
1.183
1.155
1.076
1.047
0.071
-0.000
CN
NH
O=S=O
8
7
6
5
4
3
2
1
0
2.02
2.02
1.00
1.01
3.08
6.52
5.66

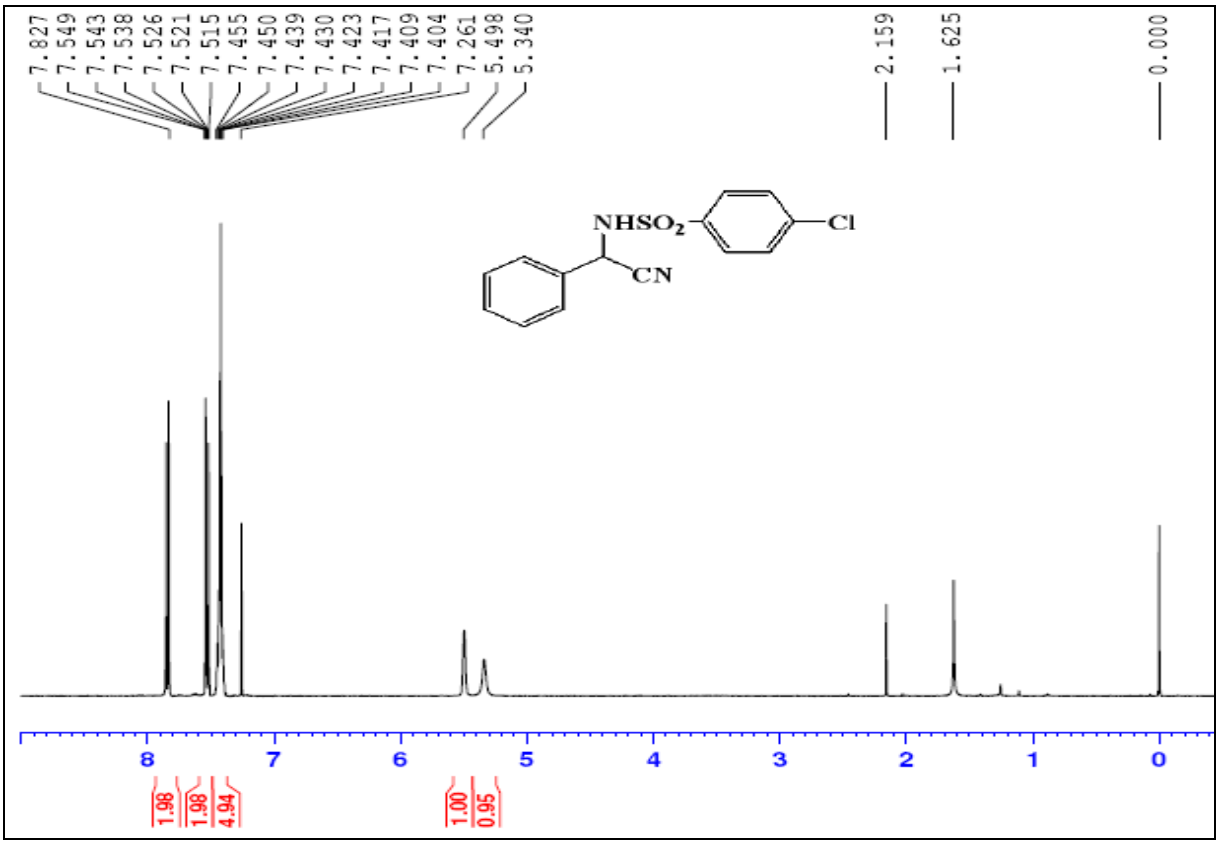

144.55
136.04
130.06
127.23
116.80
77.40
77.08
76.76
49.83
41.25
28.81
28.33
25.62
25.36
25.30
21.68
CN
NH
O=S=O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

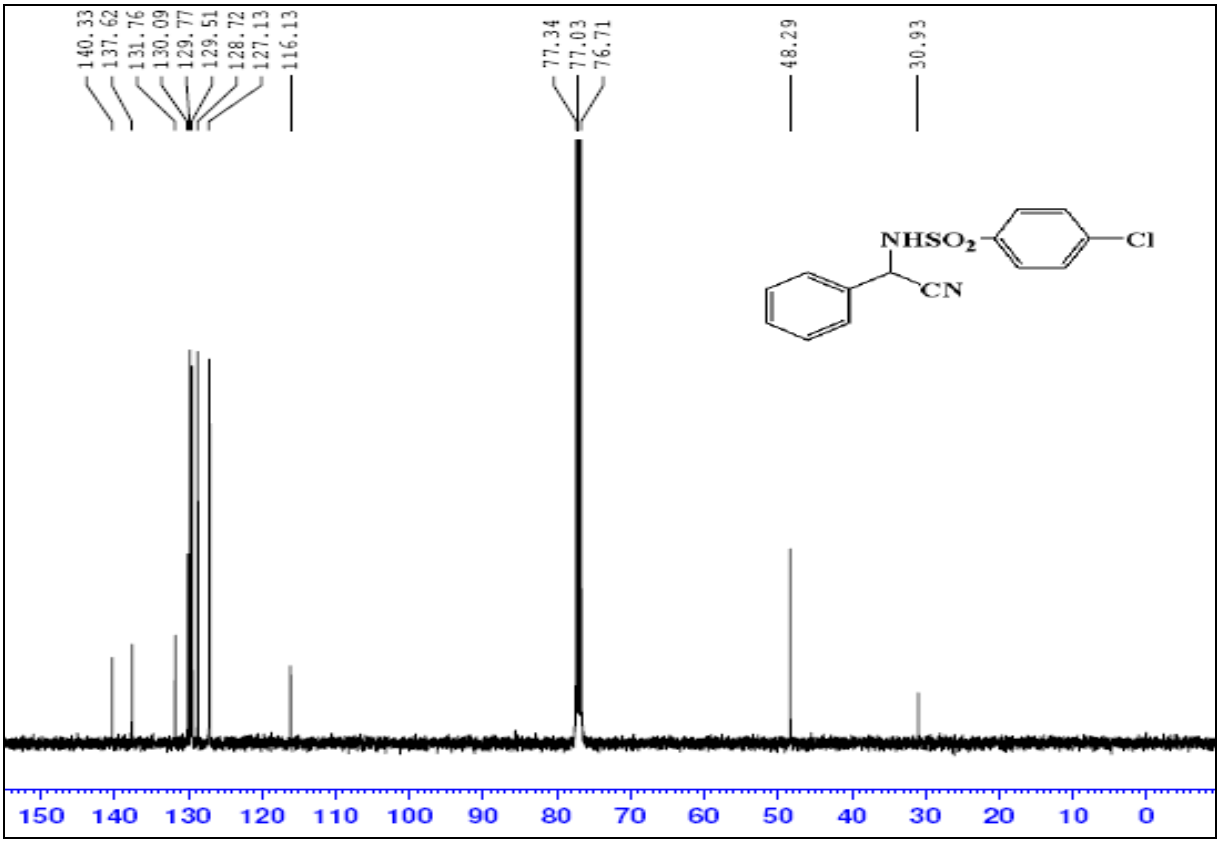

7.806
7.785
7.367
7.347
7.269
5.680
5.655
4.055
4.040
4.030
4.015
2.443
2.064
2.047
2.031
2.014
1.930
1.056
1.052
1.039
1.035
0.141
0.000
CN
O
S
O
N
H
O
8
7
6
5
4
3
2
1
0
2.01
2.02
1.00
1.01
3.06
1.02
6.11

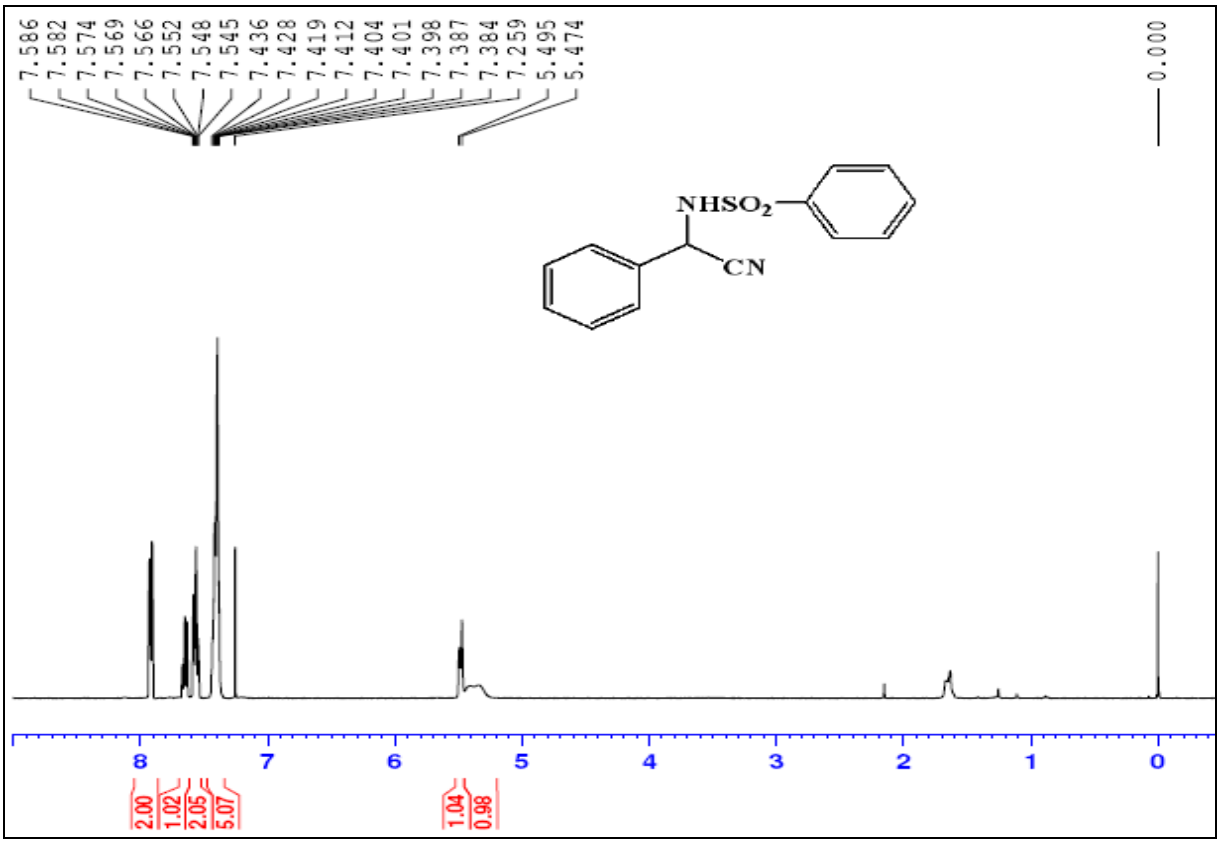

144.55
136.08
130.05
127.23
116.68
77.39
77.07
76.75
50.65
32.43
21.63
18.44
17.76
CN
O
S
O
N
H
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

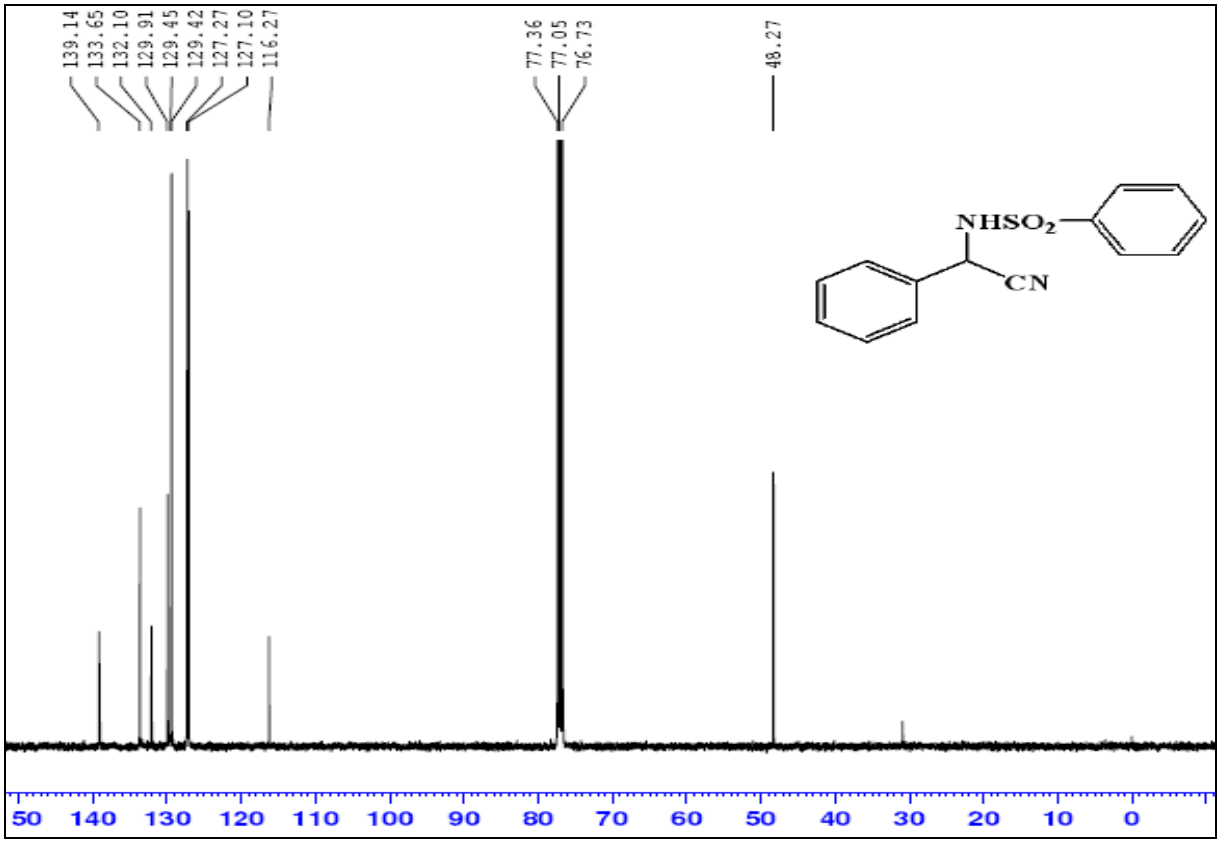

7.805
7.785
7.373
7.353
7.266
5.559
5.533
3.898
3.871
2.447
1.255
1.062
0.072
0.000
CN
H
N
O
S
O
8
7
6
5
4
3
2
1
0
2.00
2.01
1.04
1.01
3.04
9.17

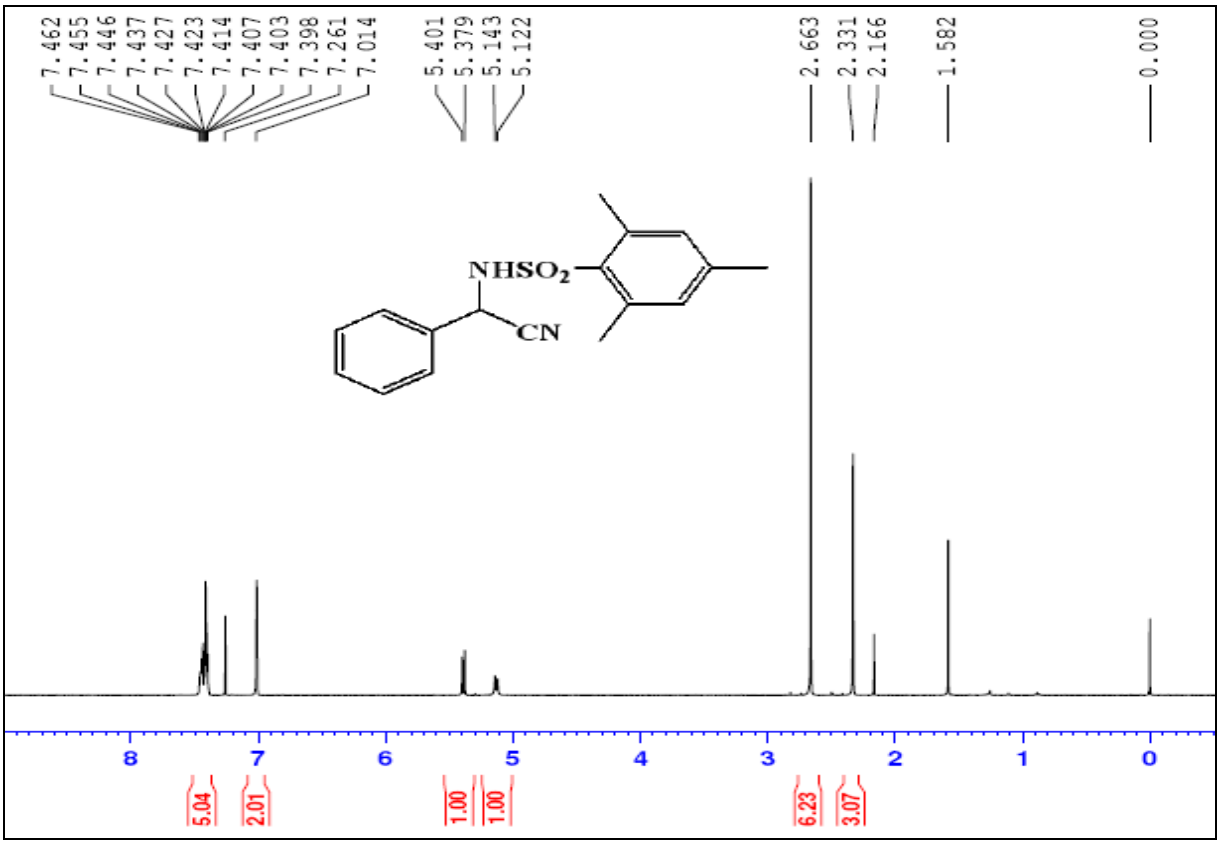

144.60
135.92
130.09
127.25
116.68
77.38
77.06
76.75
54.69
35.33
25.66
21.69
CN
H
N
O
S
O
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

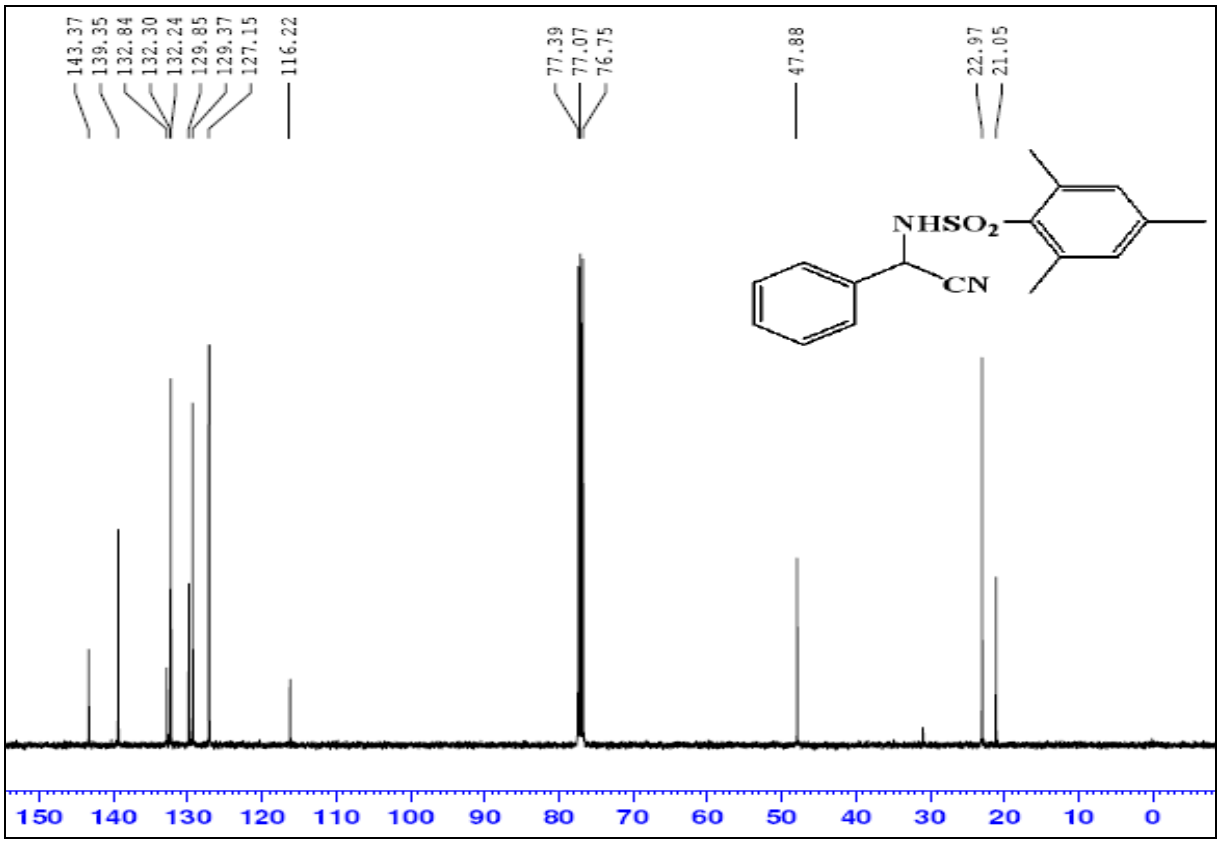

7.827
7.549
7.543
7.538
7.526
7.521
7.515
7.455
7.450
7.439
7.430
7.423
7.417
7.409
7.404
7.261
5.498
5.340
2.159
1.625
0.000
NHSO2
Cl
CN
8
7
6
5
4
3
2
1
0
1.98
1.98
4.94
1.00
0.95

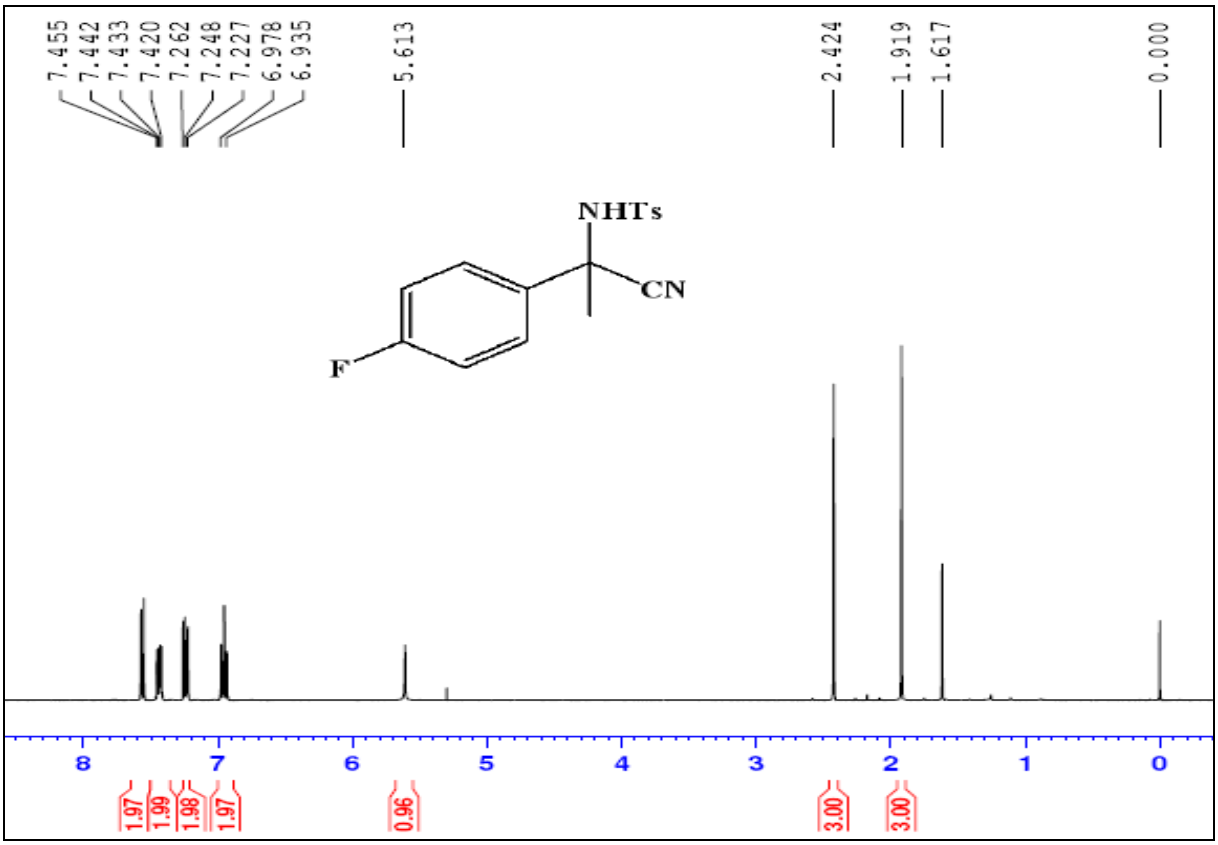

140.33
137.62
131.76
130.09
129.77
129.51
128.72
127.13
116.13
77.34
77.03
76.71
48.29
30.93
NHSO2
Cl
CN
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

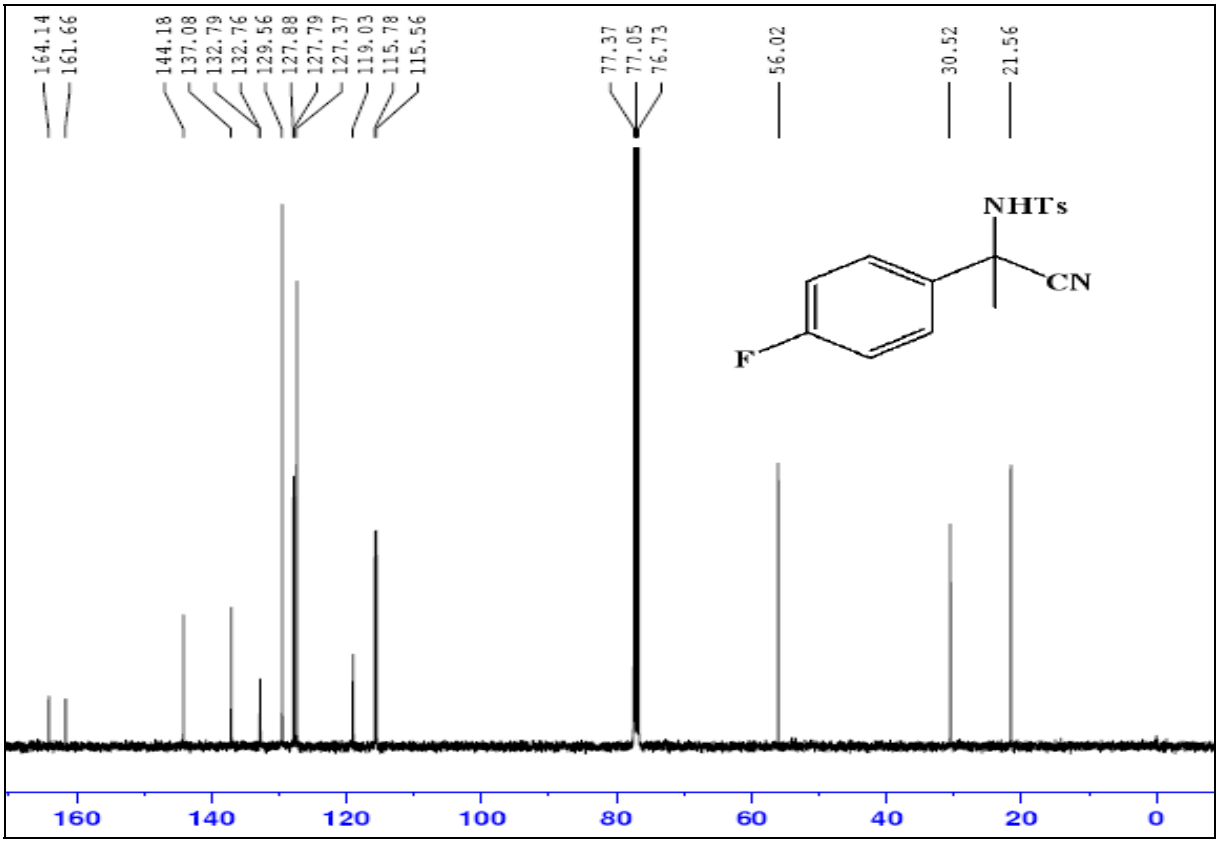

7.586
7.582
7.574
7.569
7.566
7.552
7.548
7.545
7.436
7.428
7.419
7.412
7.404
7.401
7.398
7.387
7.384
7.259
5.495
5.474
0.000
NHSO2
CN
8
7
6
5
4
3
2
1
0
2.00
1.02
2.05
5.07
1.04
0.98

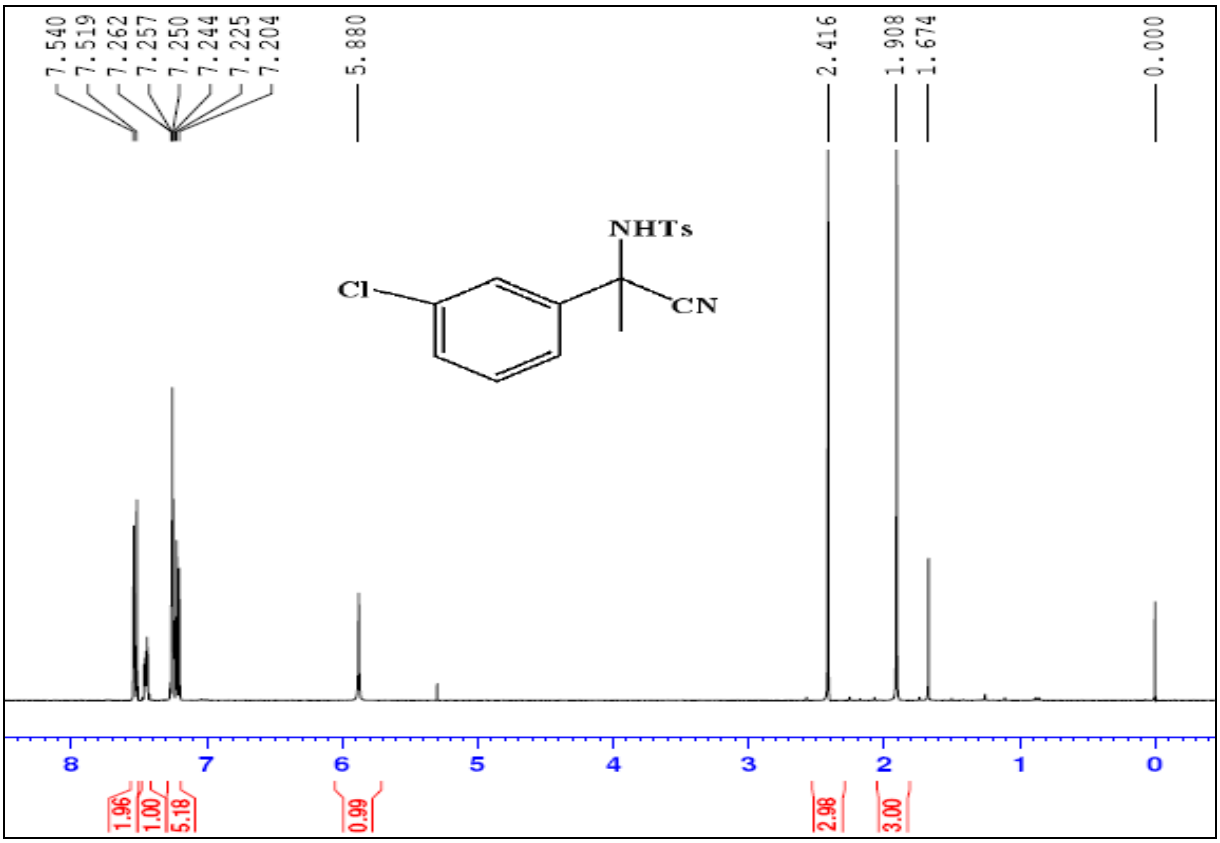

139.14
133.65
132.10
129.91
129.45
129.42
127.27
127.10
116.27
77.36
77.05
76.73
48.27
NHSO2
CN
50
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

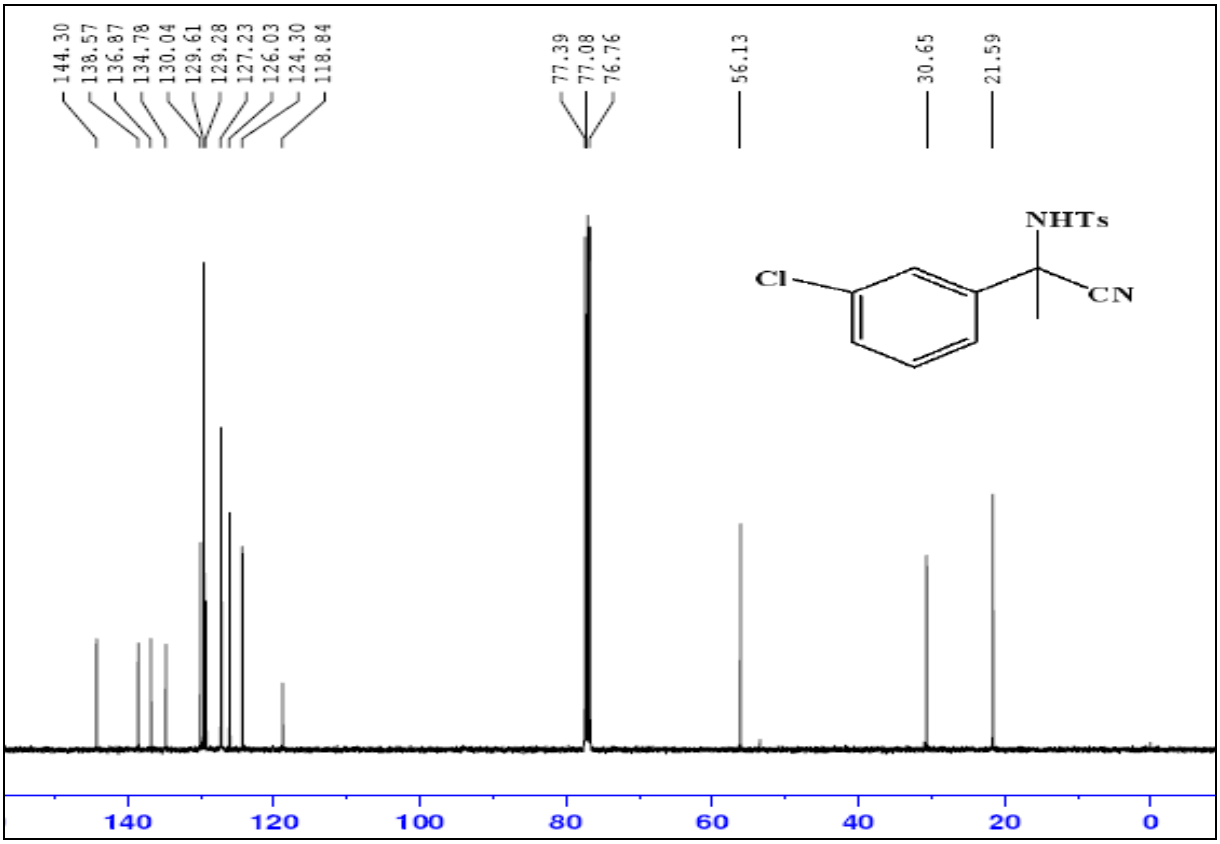

7.462
7.455
7.446
7.437
7.427
7.423
7.414
7.407
7.403
7.398
7.261
7.014
5.401
5.379
5.143
5.122
2.663
2.331
2.166
1.582
0.000
NHSO2
CN
8
7
6
5
4
3
2
1
0
5.04
2.01
1.00
1.00
6.23
3.07

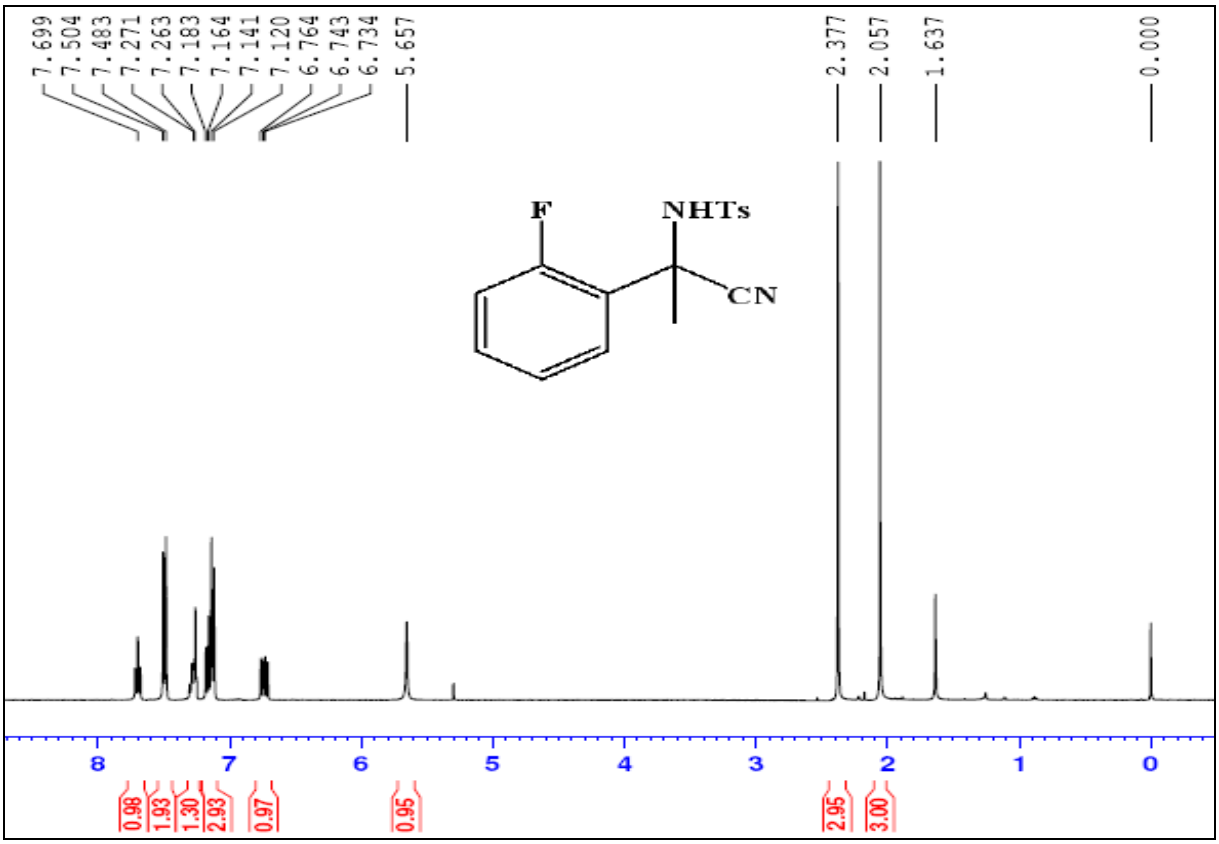

143.37
139.35
132.84
132.30
132.24
129.85
129.37
127.15
116.22
77.39
77.07
76.75
47.88
22.97
21.05
NHSO2
CN
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

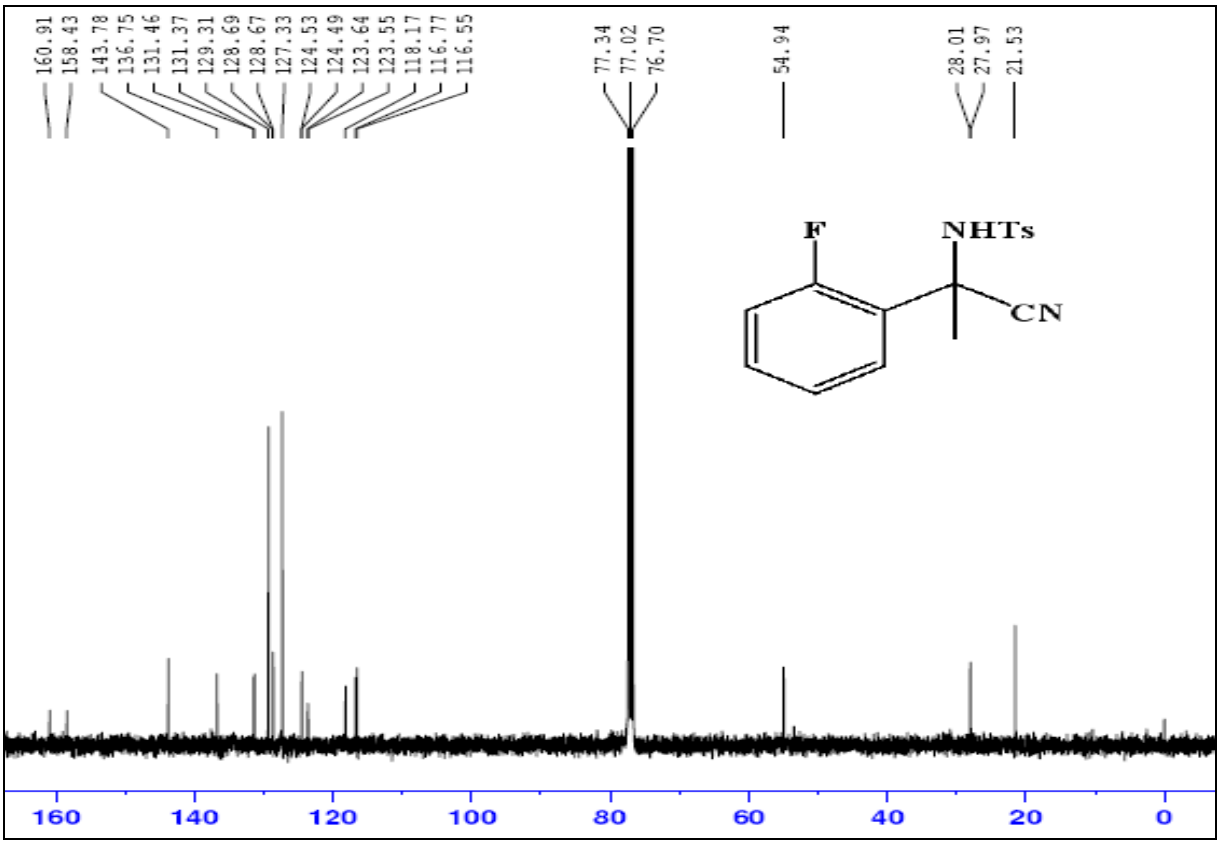

7.455
7.442
7.433
7.420
7.262
7.248
7.227
6.978
6.935
5.613
2.424
1.919
1.617
0.000
NHTs
CN
F
8
7
6
5
4
3
2
1
0
1.97
1.99
1.98
1.97
0.96
3.00
3.00

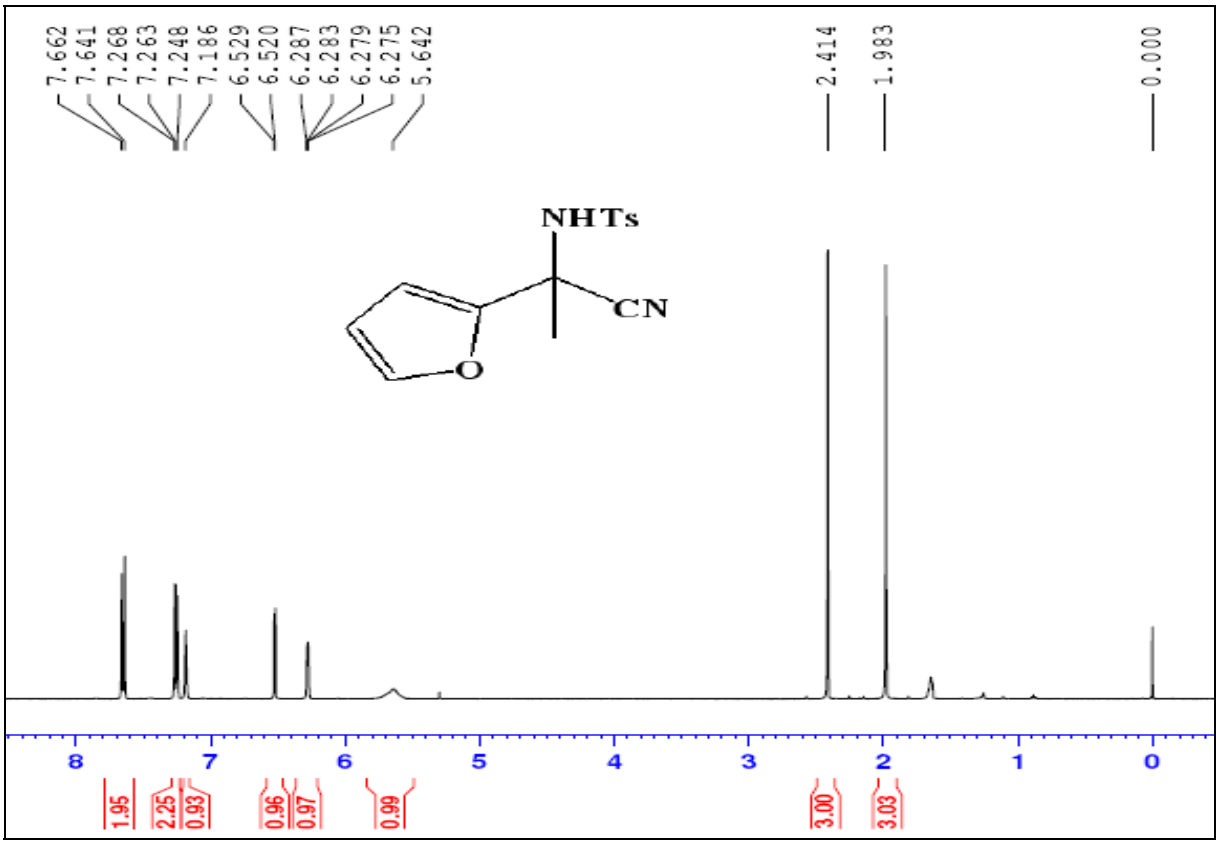

164.14
161.66
144.18
137.08
132.79
132.76
129.56
127.88
127.79
127.37
119.03
115.78
115.56
77.37
77.05
76.73
56.02
30.52
21.56
NHTs
CN
F
160
140
120
100
80
60
40
20
0

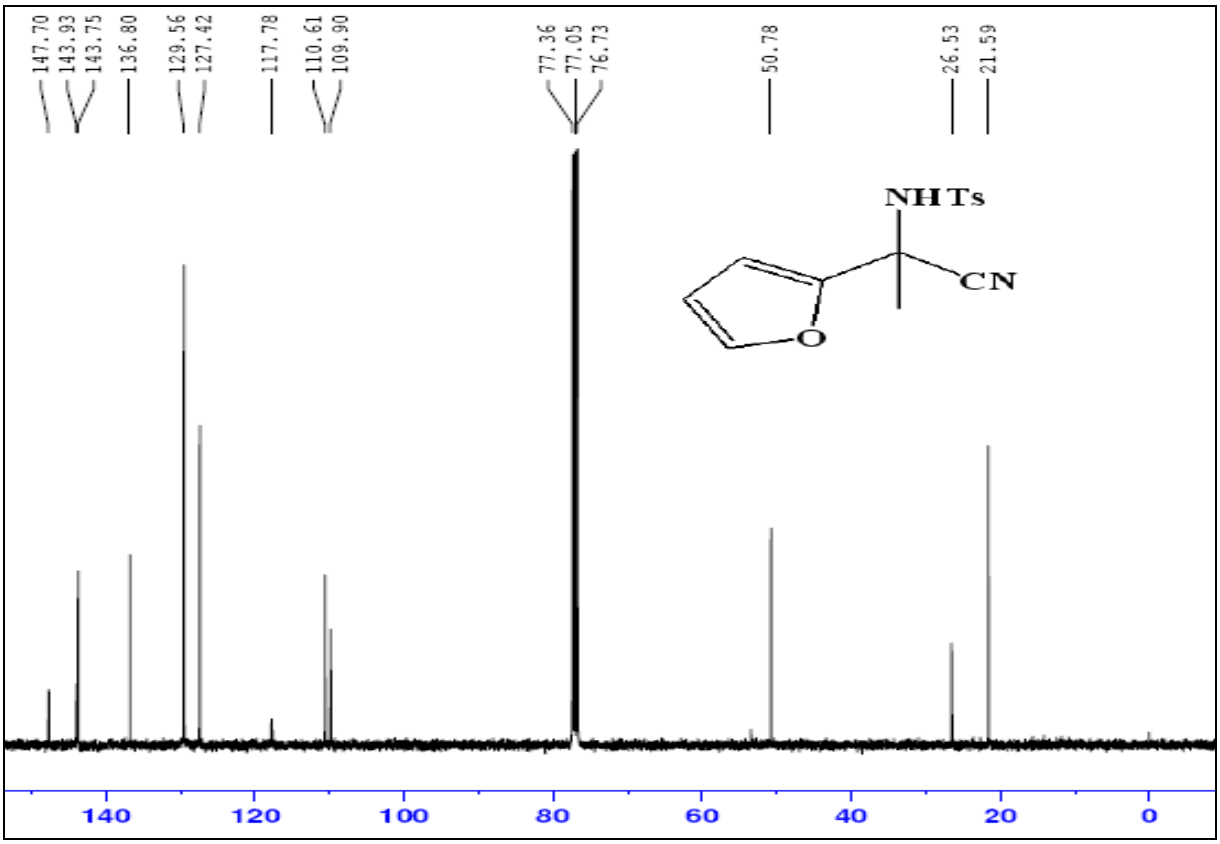

7.540
7.519
7.262
7.257
7.250
7.244
7.225
7.204
5.880
2.416
1.908
1.674
0.000
NHTs
Cl
CN
8
7
6
5
4
3
2
1
0
1.96
1.00
5.18
0.99
2.96
3.00

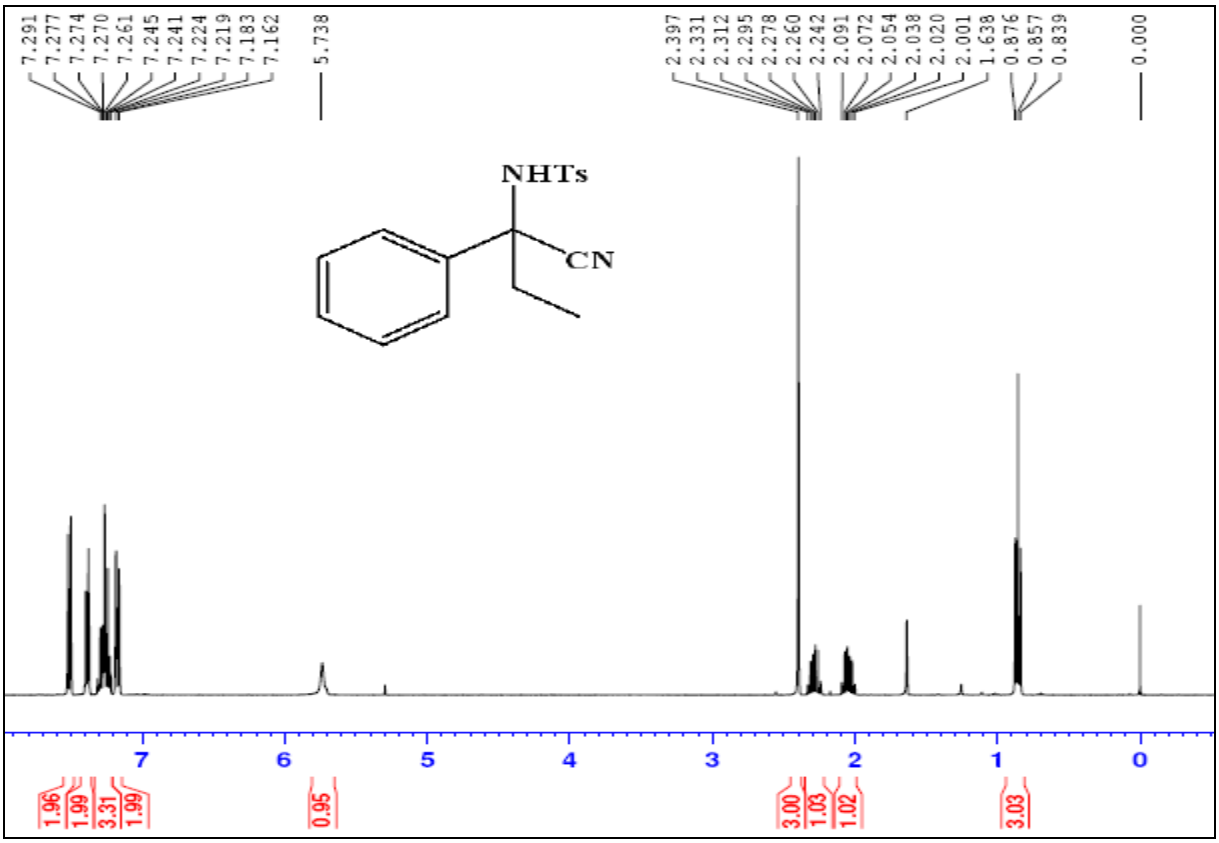

144.30
138.57
136.87
134.78
130.04
129.61
129.28
127.23
126.03
124.30
118.84
77.39
77.08
76.76
56.13
30.65
21.59
NHTs
Cl
CN
140
120
100
80
60
40
20
0

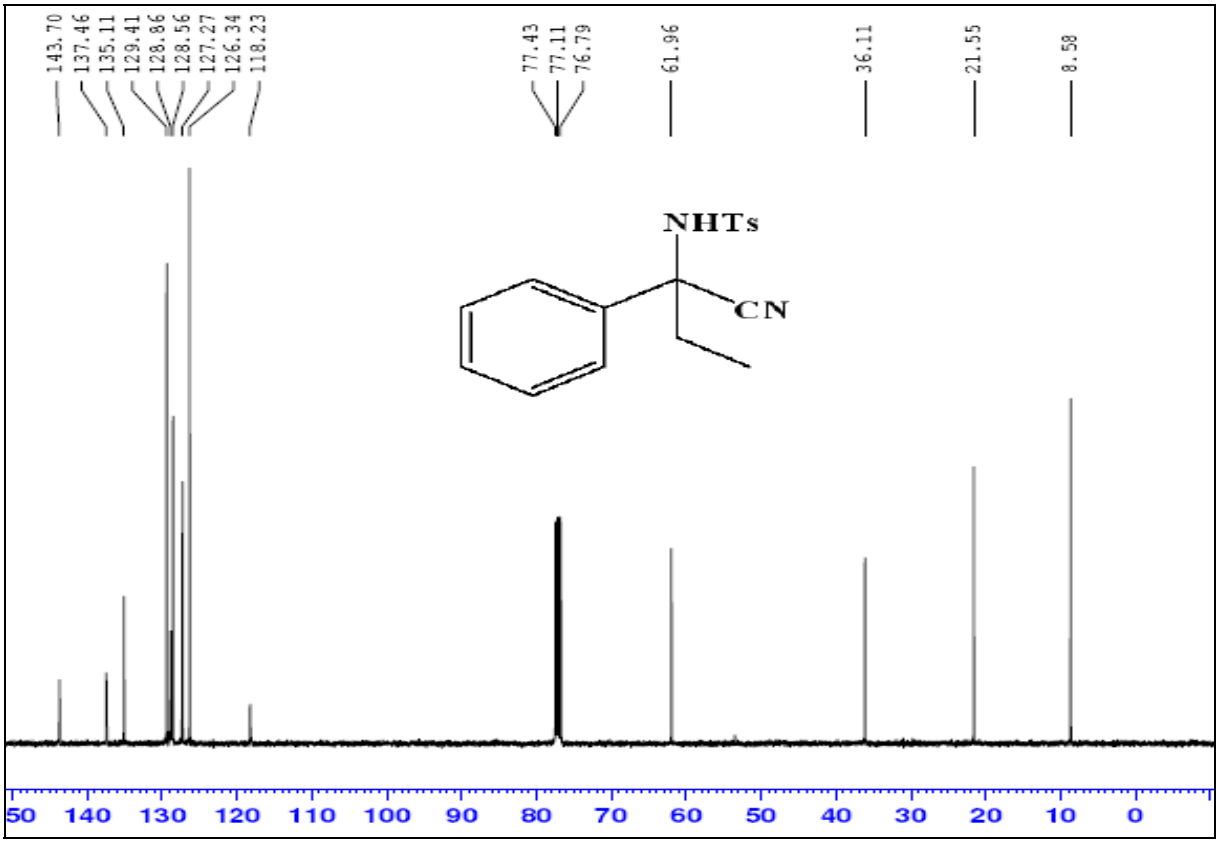

7.699
7.504
7.483
7.271
7.263
7.183
7.164
7.141
7.120
6.764
6.743
6.734
5.657
2.377
2.057
1.637
0.000
F
NHTs
CN
8
7
6
5
4
3
2
1
0
0.98
1.93
1.30
2.93
0.97
0.95
2.95
3.00

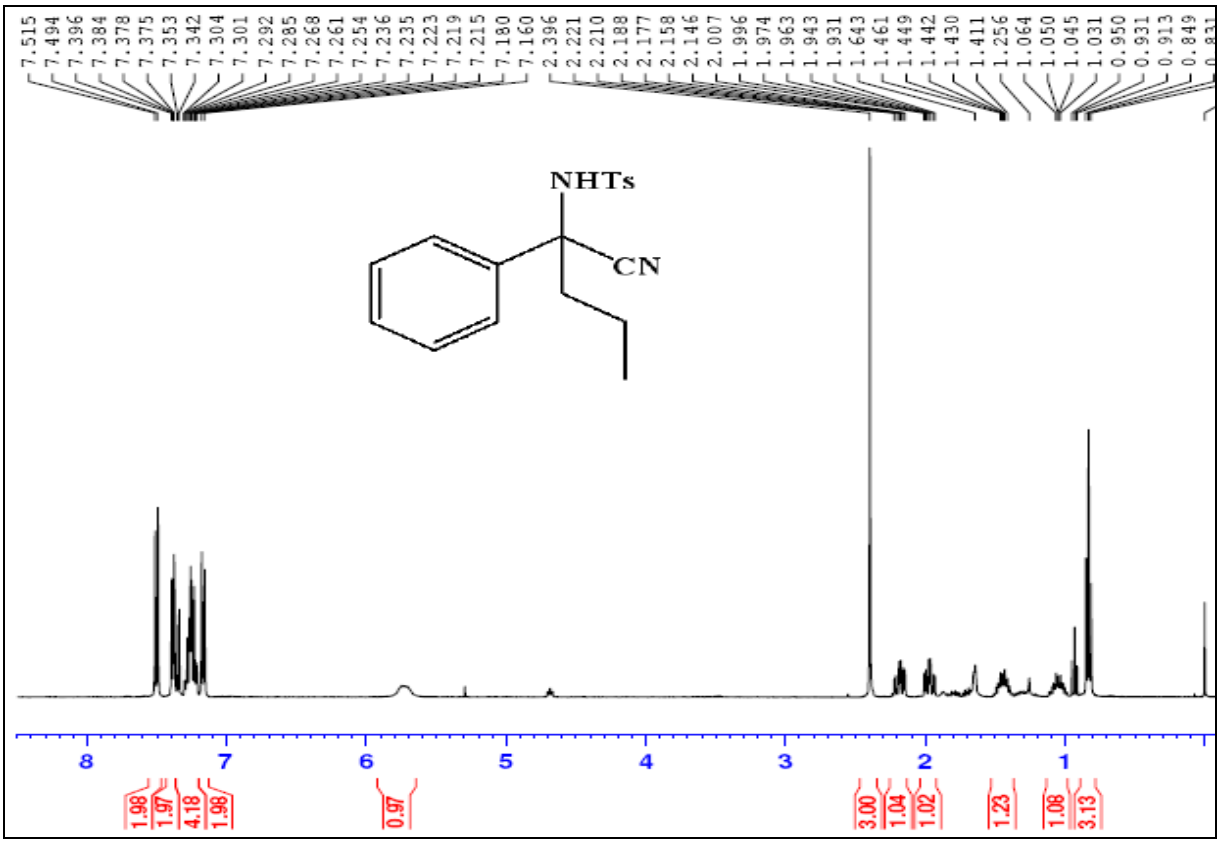

160.91
158.43
143.78
136.75
131.46
131.37
129.31
128.69
128.67
127.33
124.53
124.49
123.64
123.55
118.17
116.77
116.55
77.34
77.02
76.70
54.94
28.01
27.97
21.53
F
NHTs
CN
160
140
120
100
80
60
40
20
0

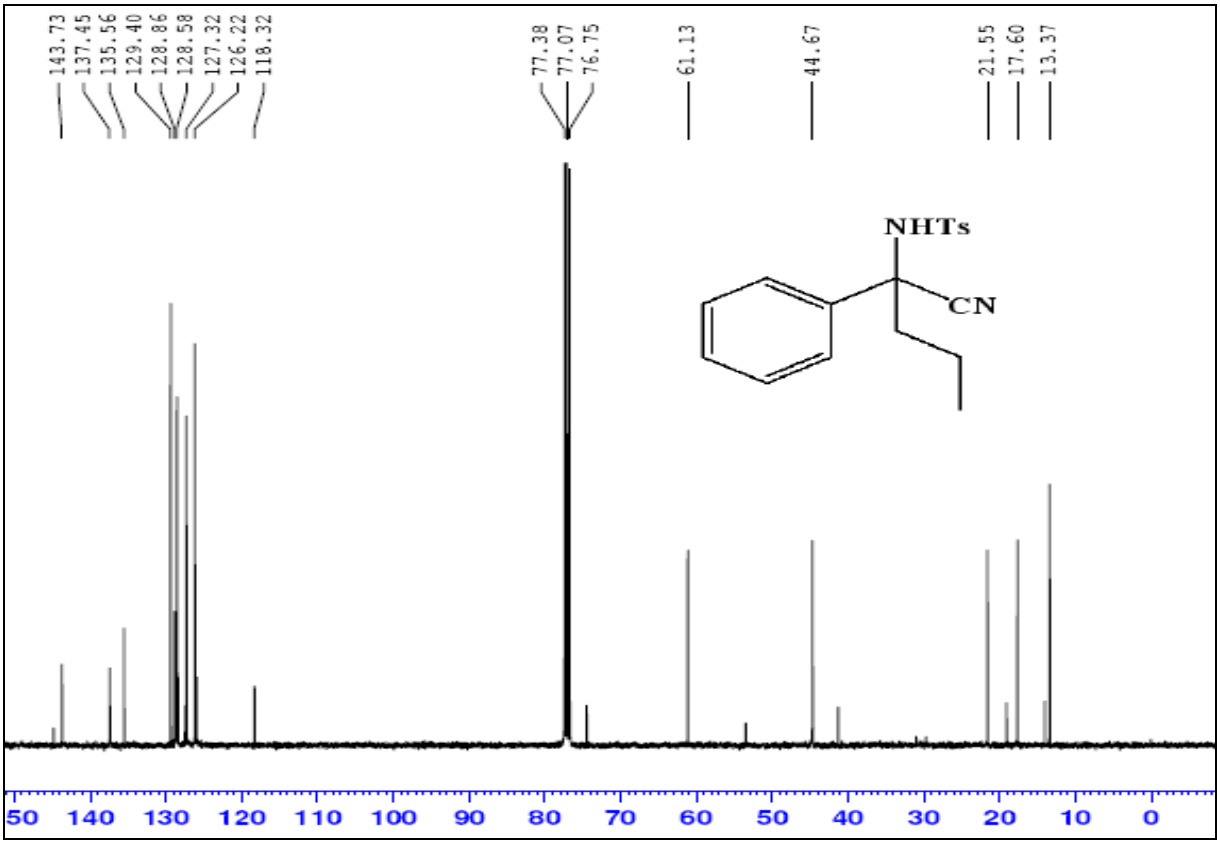

7.662
7.641
7.268
7.263
7.248
7.186
6.529
6.520
6.287
6.283
6.279
6.275
5.642
2.414
1.983
0.000
NHTs
CN
O
8
7
6
5
4
3
2
1
0
1.95
2.25
0.93
0.96
0.97
0.99
3.00
3.03

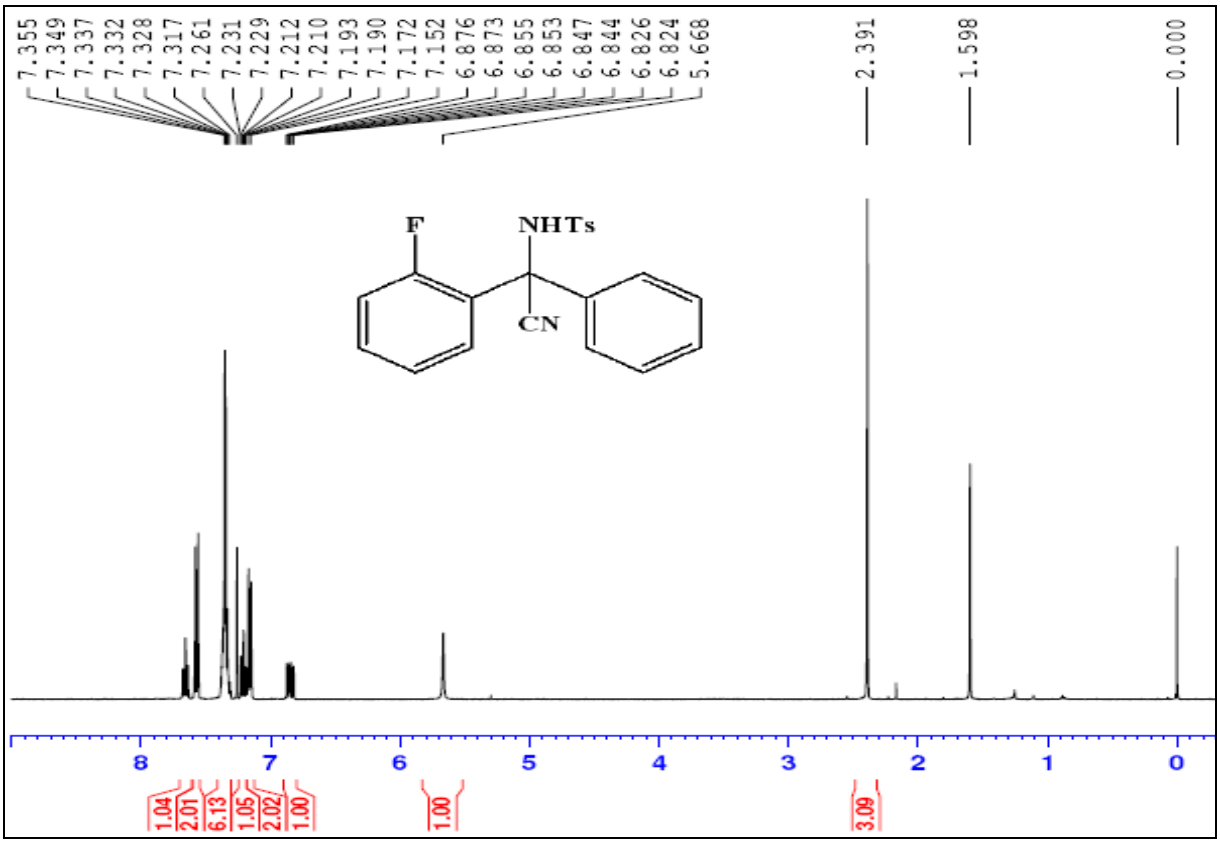

147.70
143.93
143.75
136.80
129.56
127.42
117.78
110.61
109.90
77.36
77.05
76.73
50.78
26.53
21.59
NHTs
CN
O
140
120
100
80
60
40
20
0

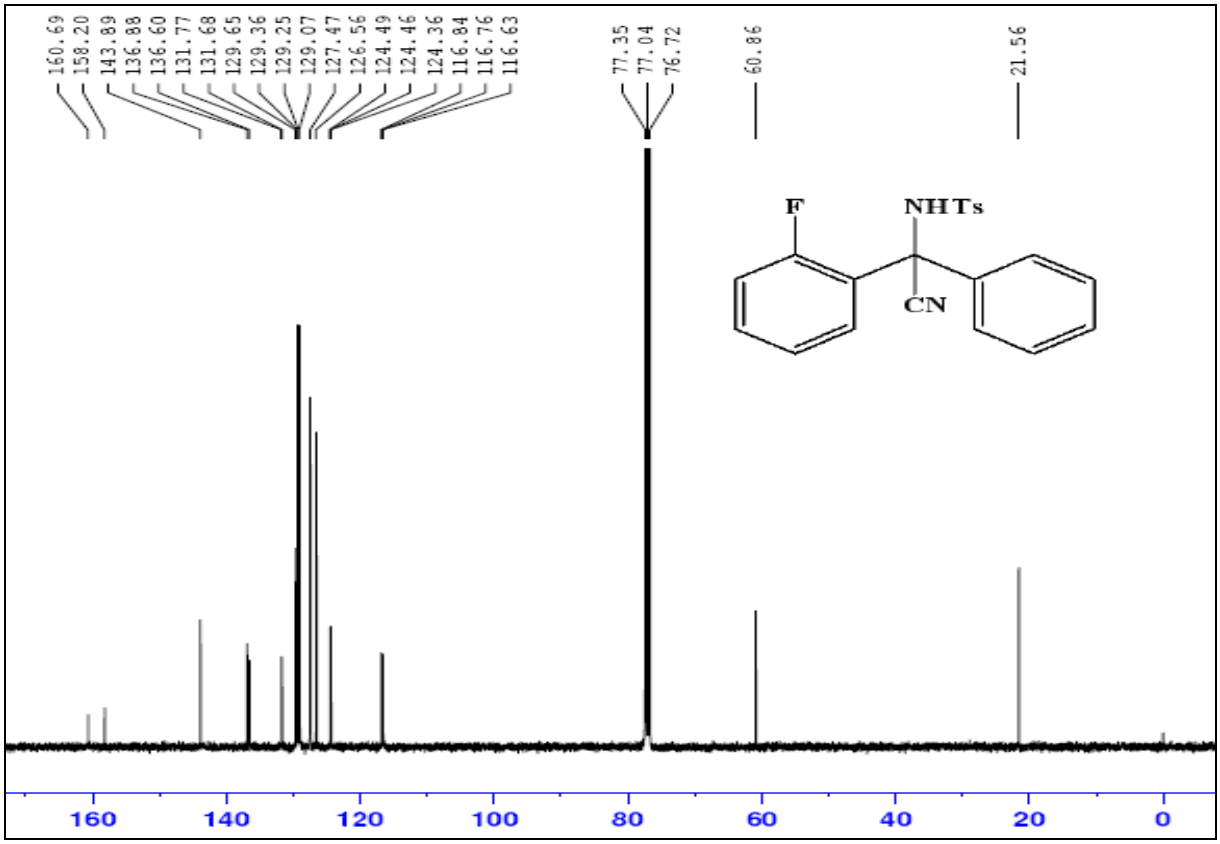

7.291
7.277
7.274
7.270
7.261
7.245
7.241
7.224
7.219
7.183
7.162
5.738
2.397
2.331
2.312
2.295
2.278
2.260
2.242
2.091
2.072
2.054
2.038
2.020
2.001
1.638
0.876
0.857
0.839
0.000
NHTs
CN
7
6
5
4
3
2
1
0
1.96
1.99
3.31
1.99
0.95
3.00
1.03
1.02
3.03

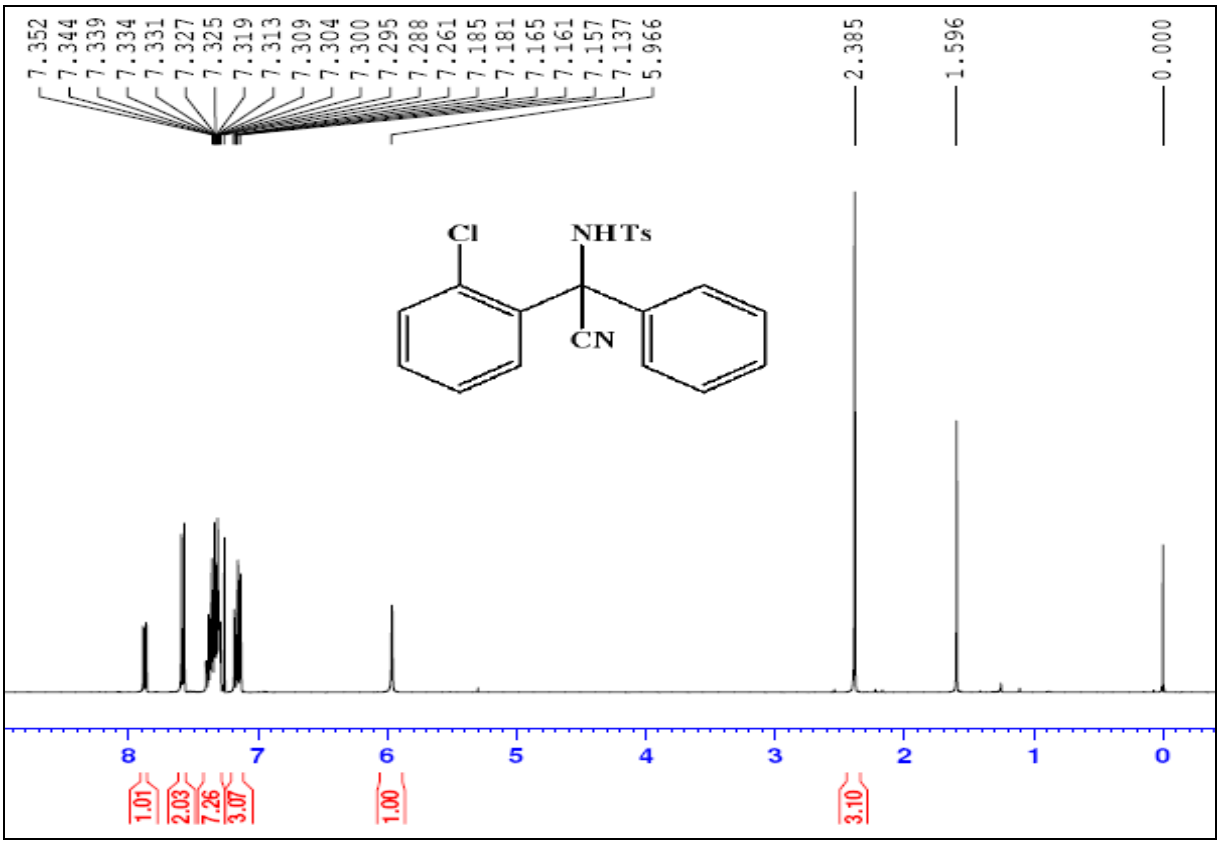

143.70
137.46
135.11
129.41
128.86
128.56
127.27
126.34
118.23
77.43
77.11
76.79
61.96
36.11
21.55
8.58
NHTs
CN
50
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

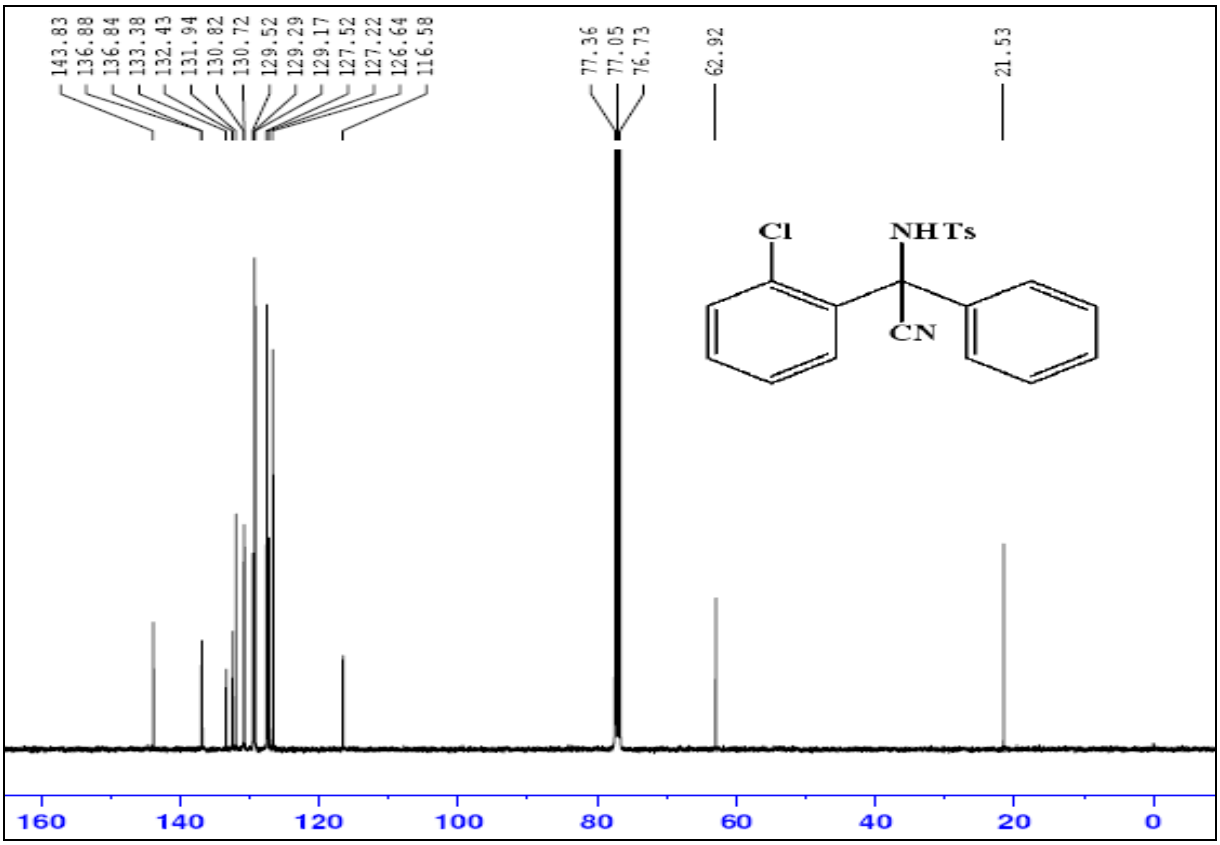

7.515
7.494
7.396
7.384
7.378
7.375
7.353
7.342
7.304
7.301
7.292
7.285
7.268
7.261
7.254
7.236
7.235
7.223
7.219
7.215
7.180
7.160
2.396
2.221
2.210
2.188
2.177
2.158
2.146
2.007
1.996
1.974
1.963
1.943
1.931
1.643
1.461
1.449
1.442
1.430
1.411
1.256
1.064
1.050
1.045
1.031
0.950
0.931
0.913
0.849
NHTs
CN
8
7
6
5
4
3
2
1
1.98
1.97
4.18
1.98
0.97
3.00
1.04
1.02
1.23
1.06
3.13

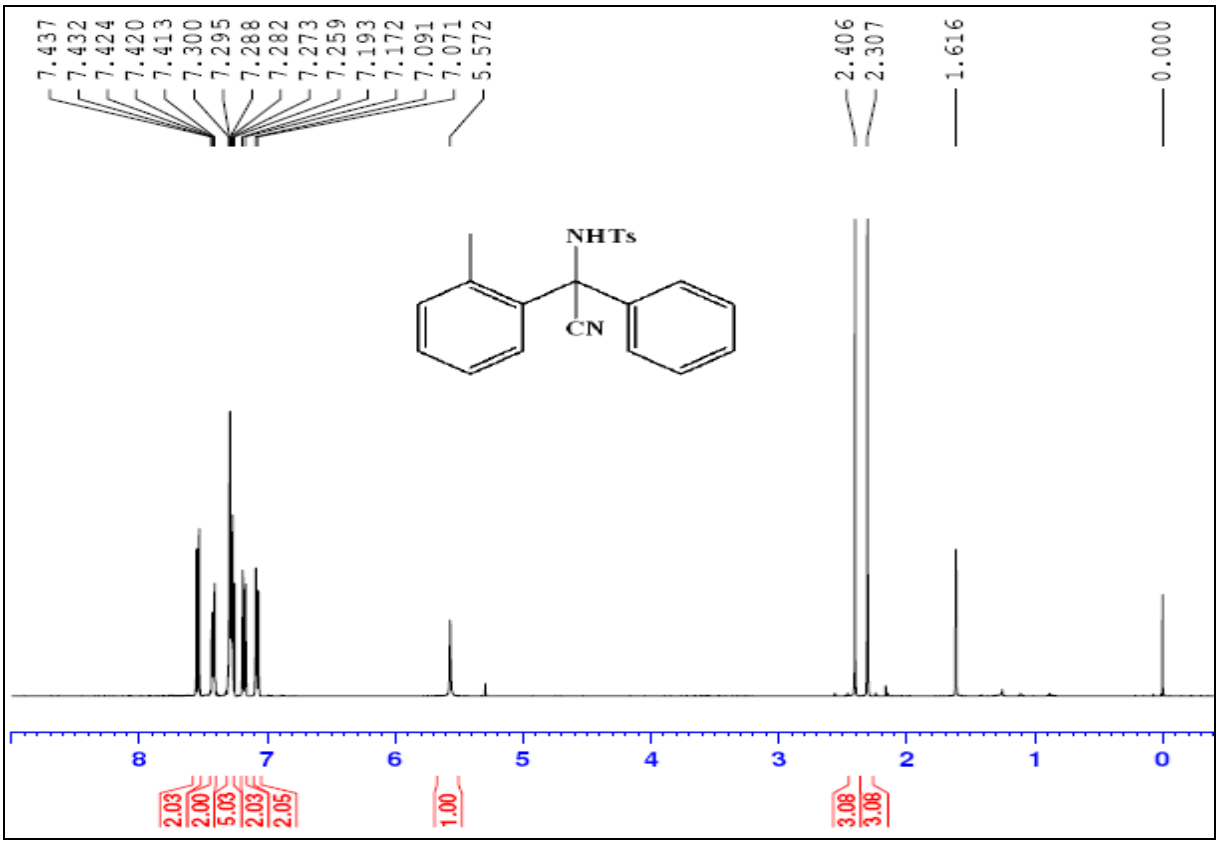

143.73
137.45
135.56
129.40
128.86
128.58
127.32
126.22
118.32
77.38
77.07
76.75
61.13
44.67
21.55
17.60
13.37
NHTs
CN
50
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

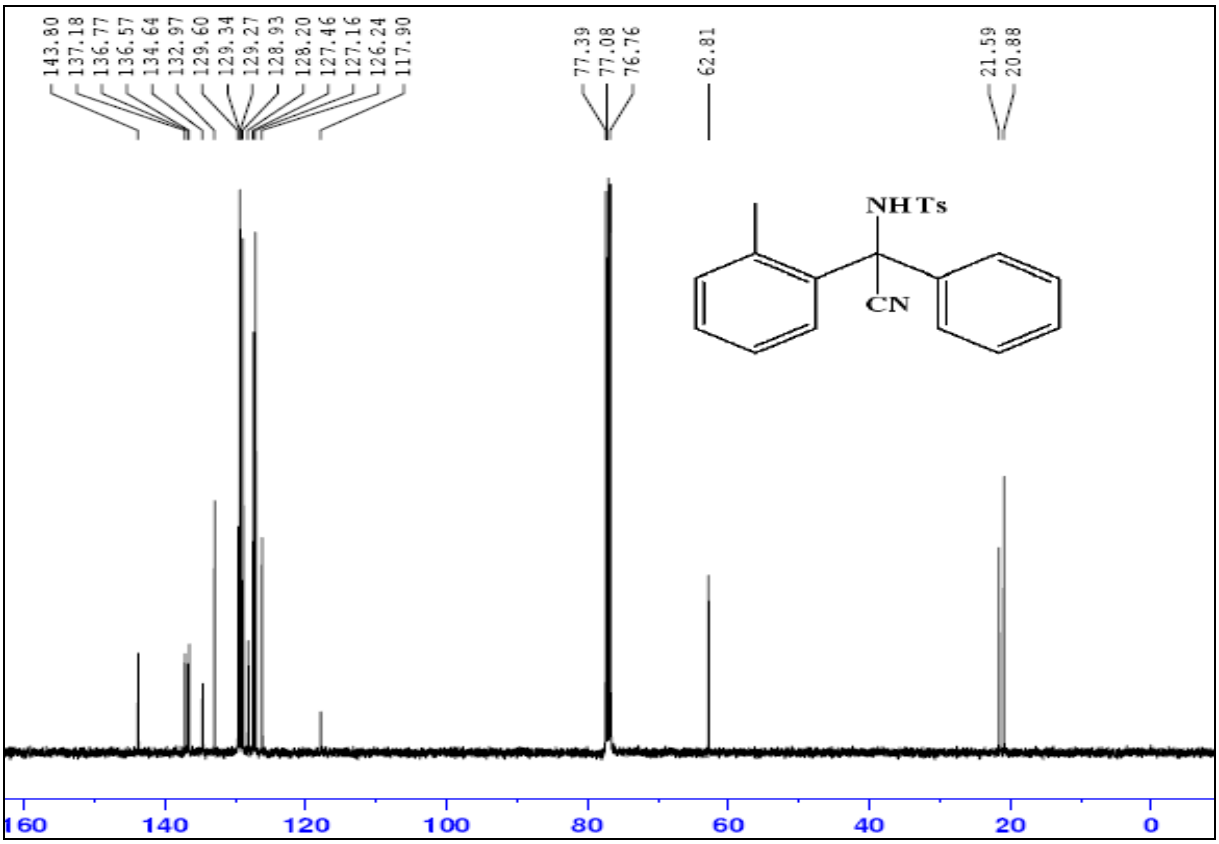

7.355
7.349
7.337
7.332
7.328
7.317
7.261
7.231
7.229
7.212
7.210
7.193
7.190
7.172
7.152
6.876
6.873
6.855
6.853
6.847
6.844
6.826
6.824
5.668
2.391
1.598
0.000
F
NHTs
CN
8
7
6
5
4
3
2
1
0
1.04
2.01
6.13
1.05
2.02
1.00
1.00
3.09


160.69
158.20
143.89
136.88
136.60
131.77
131.68
129.65
129.36
129.25
129.07
127.47
126.56
124.49
124.46
124.36
116.84
116.76
116.63
77.35
77.04
76.72
60.86
21.56
F
NHTs
CN
160
140
120
100
80
60
40
20
0


7.352
7.344
7.339
7.334
7.331
7.327
7.325
7.319
7.313
7.309
7.304
7.300
7.295
7.288
7.261
7.185
7.181
7.165
7.161
7.157
7.137
5.966
2.385
1.596
0.000
Cl
NHTs
CN
8
7
6
5
4
3
2
1
0
1.01
2.03
7.26
3.07
1.00
3.10


143.83
136.88
136.84
133.38
132.43
131.94
130.82
130.72
129.52
129.29
129.17
127.52
127.22
126.64
116.58
77.36
77.05
76.73
62.92
21.53
Cl
NHTs
CN
160
140
120
100
80
60
40
20
0


7.437
7.432
7.424
7.420
7.413
7.300
7.295
7.288
7.282
7.273
7.259
7.193
7.172
7.091
7.071
5.572
2.406
2.307
1.616
0.000
NHTs
CN
8
7
6
5
4
3
2
1
0
2.03
2.00
5.03
2.03
2.05
1.00
3.08
3.08


143.80
137.18
136.77
136.57
134.64
132.97
129.60
129.34
129.27
128.93
128.20
127.46
127.16
126.24
117.90
77.39
77.08
76.76
62.81
21.59
20.88
NHTs
CN
160
140
120
100
80
60
40
20
0

(H) References

[1] For the preparation of aldimines, see: a) W. B. Jennings, C. J. Lovely, *Tetrahedron* **1991**, *47*, 5561; b) F. Chemla, V. Hebbe, J-F. Normant, *Synthesis* **2000**, 75; c) T. Ooi, Y. Uematsu, K. Maruoka, *J. Am. Chem. Soc.* **2006**, *128*, 2548. For the preparation of ketoimines, see: d) X. Huang, J. L. Huang, Y. H. Wen, X. M. Feng, *Adv. Synth. Catal.* **2006**, *348*, 2579; e) R. N. Ram, A. A. Khan, *Synth. Comm.* **2001**, *31*, 841.

[2] a) D. R. Armstrong, C. Cameron, D. C. Nonhebel, P. G. Perkins, *J. Chem. Soc. Perkin Trans. II* **1983**, 587; b) T. Yamato, K. Hasegawa, Y. Saruwatari, L. K. Doamekpor, *Chem. Ber.* **1993**, *126*, 1435; c) M. Hirano, S. Yakabe, H. Chikamori, J. H. Clark, T. Morimoto, *J. Chem. Research (S)* **1998**, 770; d) R. Kadyrov, D. Heller, R. Selke, *Tetrahedron: Asymmetry* **1998**, *9*, 329; e) A. Alexakis, D. Polet, S. Rosset, S. March, *J. Org. Chem.* **2004**, *69*, 5660; f) R. E elkema, B. L. Feringa, *J. Am. Chem. Soc.* **2005**, *127*, 13480; g) T. R. Wu, L. Shen, J. M. Chong, *Org. Lett.* **2004**, *6*, 2701.

[3] G.-L. Li, G. Zhao, *Org. Lett.* **2006**, *8*, 633.