Palladium-catalyzed direct arylation of free NH_2 substituted thiophene derivatives

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General. All reactions were perfomed in Schlenck tubes under argon. DMAc analytical grade was not distilled before use. Potassium acetate 99+ was used. Commercial aryl bromides and thiophene derivatives were used without purification. ^{1}H (300 MHz), ^{13}C (75 MHz) spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CDCl_3$ (^{1}H: 7.26 and ^{13}C: 77.0). Flash chromatography was performed on silica gel (230-400 mesh).

General procedure

As a typical experiment, the reaction of 4-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) at 120 °C during 20 h in DMAc (3 mL) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) under argon affords the corresponding product methyl 3-amino-4-methyl-5-(4-trifluoromethylphenyl)-thiophene-2-carboxylate **1a** after extraction with dichloromethane, evaporation and filtration on silica gel (pentane/ether) in 82% (0.258 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (d, J = 8.5 Hz, 2H), 7.55 (d, J = 8.5 Hz, 2H), 5.50 (s, 2H), 3.85 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 153.3, 141.8, 137.7, 130.3 (q, J = 32.6 Hz), 129.3, 125.7 (q, J = 271.6 Hz), 125.6 (q, J = 3.8 Hz), 124.3, 100.3, 51.3, 11.7; elemental analysis: calcd (%) for $C_{14}H_{12}F_3NO_2S$ (315.31): C 53.33, H 3.84; found: C 53.40, H 3.70.

4-Methyl-2,5-bis-(4-trifluoromethylphenyl)-thiophen-3-ylamine (1b)

The reaction of 4-(trifluoromethyl)bromobenzene (0.675 g, 2 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.171 g, 1 mmol), KOH (0.084, 1.5 mmol) and KOAc (0.147 g, 1.5 mmol) the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 150 °C during 20 h affords the corresponding product **1b** in 70% (0.281 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.60 (m, 6H), 7.58 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 2H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.4, 138.1, 135.8, 129.5 (q, *J* = 32.2 Hz), 129.2, 128.1 (q, *J* = 32.2 Hz), 127.4, 126.4, 126.0 (q, *J* = 3.8 Hz), 125.6 (q, *J* = 3.8 Hz), 124.1 (q, *J* = 271.6 Hz), 124.0 (q, *J* = 271.6 Hz), 114.2, 12.6; elemental analysis: calcd (%) for $C_{19}H_{13}F_6NS$ (401.37): C 56.86, H 3.26; found: C 56.89, H 3.34.

4-Methyl-5-(4-trifluoromethylphenyl)-thiophen-3-ylamine (1c)

Methyl 3-amino-4-methyl-5-(4-trifluoromethylphenyl)-thiophene-2-carboxylate **1a** (0.315 g, 1 mmol) and KOH (0.067 g, 1.2 mmol) were stirred at 100°C during 15 h in a mixture EtOH/H_2O (3/1 mL). After addition of an HCl solution to reach pH 7, the solution was washed with saturated aq. $NaHCO_3$. After extraction with dichloromethane, evaporation and filtration on silica gel, **1c** was obtained in 78% (0.201 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 6.26 (s, 1H), 3.51 (s, 2H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.7, 138.9, 136.1, 129.3 (q, *J* = 32.2 Hz), 129.1, 125.8, 125.4 (q, *J* = 3.6 Hz), 122.4 (q, *J* = 271.6 Hz), 99.8, 11.2; elemental analysis: calcd (%) for $C_{12}H_{10}F_3NS$ (257.28): C 56.02, H 3.92; found: C 56.10, H 3.98.

4-Methyl-2-(4-trifluoromethylphenyl)-thiophen-3-ylamine (1d)

The reaction of 4-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), 3-amino-4-methylthiophene (0.228 g, 2 mmol) and KOAc (0.196 g, 2 mmol) at 150 °C during 20 h in DMAc (3 mL) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) under argon affords the corresponding product **1d** in 77% (0.198g) yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67-7.61 (m, 4H), 6.90 (s, 1H), 3.74 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 140.6, 139.4, 129.9, 128.0 (q, *J* = 32.2 Hz), 127.2, 122.4 (q, *J* = 271.6 Hz), 125.9 (q, *J* = 3.6 Hz), 120.4, 114.4, 13.8; elemental analysis: calcd (%) for $C_{12}H_{10}F_3NS$ (257.28): C 56.02, H 3.92; found: C 56.14, H 3.80.

4,4'-Bis-(trifluoromethyl)biphenyl (1e)

This side-product was detected using GC/MS.

Methyl 3-amino-5-(4-formylphenyl)-4-methylthiophene-2-carboxylate (2)

The reaction of 4-bromobenzaldehyde (0.185 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **2** in 87% (0.239 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 10.04 (s, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.60 (d, *J* = 8.5 Hz, 2H), 5.50 (s, 2H), 3.84 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.5, 164.9, 153.3, 141.9, 140.1, 135.7, 129.9, 129.5, 124.5, 100.5, 51.3, 11.9; elemental analysis: calcd (%) for $C_{14}H_{13}NO_3S$ (275.32): C 61.07, H 4.76; found: C 61.01, H 4.87.

Methyl 3-amino-4-methyl-5-(4-propionylphenyl)-thiophene-2-carboxylate (3)

The reaction of 4-bromopropiophenone (0.213 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120°C affords the corresponding product **3** in 86% (0.261 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H), 5.51 (s, 2H), 3.80 (s, 3H), 2.98 (q, *J* = 7.2 Hz, 2H), 2.07 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.9, 164.8, 153.3, 142.2, 138.3, 136.2, 128.9, 128.1, 124.1, 100.0, 51.1, 31.7, 11.8, 8.1; elemental analysis: calcd (%) for $C_{16}H_{17}NO_3S$ (303.38): C 63.34, H 5.65; found: C 63.21, H 5.71.

Methyl 3-amino-5-(4-cyanophenyl)-4-methylthiophene-2-carboxylate (4)

The reaction of 4-bromobenzonitrile (0.182 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **4** in 87% (0.237 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 5.51 (s, 2H), 3.83 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 153.2, 141.0, 138.6, 132.3, 129.5, 124.6, 118.4, 111.8, 100.6, 51.3, 11.8; elemental analysis: calcd (%) for $C_{14}H_{12}N_2O_2S$ (272.32): C 61.75, H 4.44; found: C 61.71, H 4.28.

Methyl 3-amino-4-methyl-5-(4-nitrophenyl)-thiophene-2-carboxylate (5)

The reaction of 4-bromonitrobenzene (0.202 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **5** in 83% (0.242 g) isolated

yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.5 Hz, 2H), 5.51 (s, 2H), 3.85 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.8, 153.2, 147.3, 140.6, 129.7, 129.6, 124.9, 123.8, 100.9, 51.4, 11.9; elemental analysis: calcd (%) for $C_{13}H_{12}N_2O_4S$ (292.31): C 53.43, H 4.14; found: C 53.50, H 4.20.

Methyl 3-amino-5-(4-fluorophenyl)-4-methyl-thiophene-2-carboxylate (6)

The reaction of 4-bromofluorobenzene (0.175 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **6** in 89% (0.236 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (dd, *J* = 8.5, 5.4 Hz, 2H), 7.10 (t, *J* = 8.5 Hz, 2H), 5.44 (s, 2H), 3.83 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.0, 162.7 (d, *J* = 249 Hz), 153.3, 142.7, 130.7 (d, *J* = 8.2 Hz), 129.9, 123.4, 115.6 (d, *J* = 22.0 Hz), 99.3, 55.1, 11.6; elemental analysis: calcd (%) for $C_{13}H_{12}FNO_2S$ (265.30): C 58.85, H 4.56; found: C 58.80, H 4.44.

Methyl 3-amino-4-methyl-5-*p*-tolylthiophene-2-carboxylate (7)

The reaction of 4-bromotoluene (0.171 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **7** in 81% (0.212 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 5.53 (s, 2H), 3.86 (s, 3H), 2.41 (s, 3H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 153.4, 144.0, 138.2, 131.0, 129.2, 128.7, 123.0, 99.0, 51.0, 21.1, 11.6; elemental analysis: calcd (%) for $C_{14}H_{15}NO_2S$ (261.34): C 64.34, H 5.79; found: C 64.48, H 5.87.

Methyl 3-amino-5-(4-methoxyphenyl)-4-methyl-thiophene-2-carboxylate (8)

The reaction of 4-bromoanisole (0.187 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **8** in 58% (0.161 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.6 Hz, 2H), 5.44 (s, 2H), 3.90 (s, 3H), 3.81 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.0, 164.8, 153.3, 142.2, 138.4, 129.7, 128.8, 124.1, 100.0, 52.1, 51.1, 11.8; elemental analysis: calcd (%) for $C_{14}H_{15}NO_3S$ (277.34): C 60.63, H 5.45; found: C 60.74, H 5.50.

Methyl 3-amino-4-methyl-5-(3-trifluoromethylphenyl)-thiophene-2-carboxylate (9)

The reaction of 3-(trifluoromethyl)bromobenzene (0.225 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **9** in 92% (0.290 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.68 (s, 1H), 7.65-7.50 (m, 3H), 5.50 (s, 2H), 3.85 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 153.3, 141.8, 134.8, 132.2, 131.1 (q, *J* = 32.0 Hz), 129.2, 125.7 (q, *J* = 4.8 Hz), 124.9 (q, *J* = 4.8 Hz), 124.2, 123.6 (q, *J* = 272.0 Hz), 100.0, 51.2, 11.7; elemental analysis: calcd (%) for $C_{14}H_{12}F_3NO_2S$ (315.31): C 53.33, H 3.84; found: C 53.40, H 3.70.

Methyl 3-amino-4-methyl-5-naphthalen-2-ylthiophene-2-carboxylate (10)

The reaction of 2-bromonaphthalene (0.207 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **10** in 80% (0.238 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92-7.86 (m, 4H), 7.57-7.53 (m, 3H), 5.56 (s, 2H), 3.89 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 153.5, 143.7, 132.9, 132.7, 131.2, 128.1, 128.0, 127.9, 127.5, 126.5, 126.4, 126.3, 99.5, 51.1, 11.7; elemental analysis: calcd (%) for $C_{17}H_{15}NO_2S$ (397.37): C 68.66, H 5.08; found: C 68.51, H 5.14.

Methyl 3-amino-5-(2-methoxycarbonylphenyl)-4-methylthiophene-2-carboxylate (11)

The reaction of methyl 2-bromobenzoate (0.215 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **11** in 87% (0.266 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.2 Hz, 1H), 7.55-7.40 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 5.50 (s, 2H), 3.78 (s, 3H), 3.70 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 165.1, 152.7, 142.4, 134.1, 131.5, 131.4, 131.3, 130.1, 128.6, 125.1, 99.6, 52.3, 51.1, 11.3; elemental analysis: calcd (%) for $C_{15}H_{15}NO_4S$ (305.35): C 59.00, H 4.95; found: C 58.87, H 5.00.

Methyl 3-amino-5-(2-cyanophenyl)-4-methylthiophene-2-carboxylate (12)

The reaction of 2-bromobenzonitrile (0.182 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)(dppb)$ (12.2

mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **12** in 90% (0.245 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.5 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.53-7.43 (m, 2H), 5.51 (s, 2H), 3.82 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 152.7, 138.4, 137.4, 133.2, 132.6, 131.2, 128.8, 126.6, 117.5, 113.1, 100.9, 51.2, 12.0; elemental analysis: calcd (%) for $C_{14}H_{12}N_2O_2S$ (272.32): C 61.75, H 4.44; found: C 61.87, H 4.51.

Methyl 3-amino-4-methyl-5-pyridin-3-ylthiophene-2-carboxylate (13)

The reaction of 3-bromopyridine (0.158 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **13** in 77% (0.191 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.61 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.35 (dd, J = 7.8, 4.8 Hz, 1H), 5.53 (s, 2H), 3.81 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.8, 153.2, 149.3, 149.1, 139.5, 136.1, 124.5, 123.5, 123.4, 100.2, 51.2, 11.3; elemental analysis: calcd (%) for $C_{12}H_{12}N_2O_2S$ (248.30): C 58.05, H 4.87; found: C 58.14, H 4.67.

Methyl 3-amino-4-methyl-5-pyridin-4-ylthiophene-2-carboxylate (14)

The reaction of 4-bromopyridine hydrochloride (0.194 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.294 g, 3 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **14** in 89% (0.221 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (m, 2H), 7.32 (d, *J* = 4.4 Hz, 2H), 5.53 (s, 2H), 3.82 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 153.3, 150.0, 141.7, 140.0, 124.9, 123.2, 100.6, 51.3, 11.8; elemental analysis: calcd (%) for $C_{12}H_{12}N_2O_2S$ (248.30): C 58.05, H 4.87; found: C 58.01, H 4.84.

Methyl 3-amino-4-methyl-5-quinolin-3-ylthiophene-2-carboxylate (15)

The reaction of 3-bromoquinoline (0.208 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C affords the corresponding product **15** in 70% (0.209 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.14 (s, 1H), 8.11 (d, *J* = 8.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.71 (t, *J* = 7.1 Hz, 1H), 7.54 (t, *J* = 7.1 Hz, 1H), 5.56 (s, 2H), 3.83 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.8, 153.3, 150.1, 147.4, 139.6, 135.4, 130.0, 129.2, 127.9, 127.3, 127.2, 127.1,

124.7, 100.3, 51.2, 11.8; elemental analysis: calcd (%) for $C_{16}H_{14}N_2O_2S$ (298.36): C 64.41, H 4.73; found: C 64.31, H 4.68.

4-Methyl-2-*p*-tolylthiophen-3-ylamine (16a)

The reaction of 4-bromotoluene (0.171 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol), KOH (0.084, 1.5 mmol) and KOAc (0.147 g, 1.5 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 150 °C during 20 h affords the corresponding product **16a** in 64% (0.130 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 6.82 (s, 1H), 3.62 (s, 2H), 2.93 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.2, 136.1, 131.9, 129.7, 127.6, 118.7, 116.4, 21.1, 14.0; elemental analysis: calcd (%) for $C_{12}H_{13}NS$ (203.30): C 70.89, H 6.45; found: C 71.01, H 6.30.

4-Methyl-2-pyridin-3-ylthiophen-3-ylamine (17a)

The reaction of 3-bromopyridine (0.158 g, 1 mmol), methyl 3-amino-4-methylthiophene-2-carboxylate (0.342 g, 2 mmol), KOH (0.084, 1.5 mmol) and KOAc (0.147 g, 1.5 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 150 °C during 20 h affords the corresponding product **17a** in 66% (0.125 g) isolated yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.79 (s, 1H), 8.47-8.40 (m, 1H), 7.79 (d, *J* = 6.2 Hz, 1H), 7.32-7.25 (m, 1H), 6.88 (s, 1H), 3.75 (s, 2H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.1, 146.8, 140.6, 134.3, 131.1, 129.7, 123.5, 120.2, 111.7, 13.7; elemental analysis: calcd (%) for $C_{10}H_{10}N_2S$ (190.27): C 63.13, H 5.30; found: C 63.00, H 5.30.

4-Methyl-5-pyridin-3-yl-thiophen-3-ylamine (17b)

Methyl 3-amino-4-methyl-5-pyridin-3-ylthiophene-2-carboxylate **13** (0.248 g, 1 mmol) and KOH (0.067 g, 1.2 mmol) were stirred at 100 °C during 15 h in a mixture EtOH/H_2O (3/1 mL). After addition of an HCl solution to reach pH 7, the solution was washed with saturated aq. $NaHCO_3$. After extraction with dichloromethane, evaporation and filtration on silica gel, **17b** was obtained in 75% (0.142 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.69 (s, 1H), 8.57-8.55 (m, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.34 (dd, *J* = 8.2, 4.7, 1H), 6.27 (s, 1H), 2.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.6, 148.2, 144.7, 139.7, 136.2, 126.1, 123.3, 120.0, 99.8, 12.1; elemental analysis: calcd (%) for $C_{10}H_{10}N_2S$ (190.27): C 63.13, H 5.30; found: C 63.05, H 5.28.

4-Methyl-5-pyridin-3-yl-2-*p*-tolylthiophen-3-ylamine (18)

The reaction of 4-bromotoluene (0.171 g, 1 mmol), 4-methyl-5-pyridin-3-yl-thiophen-3-ylamine **17b** (0.342 g, 2 mmol) and KOAc (0.196 g, 2 mmol) at 150 °C during 20 h in DMAc (3 mL) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) under argon affords the corresponding product **18** in 75% (0.210 g) yield.

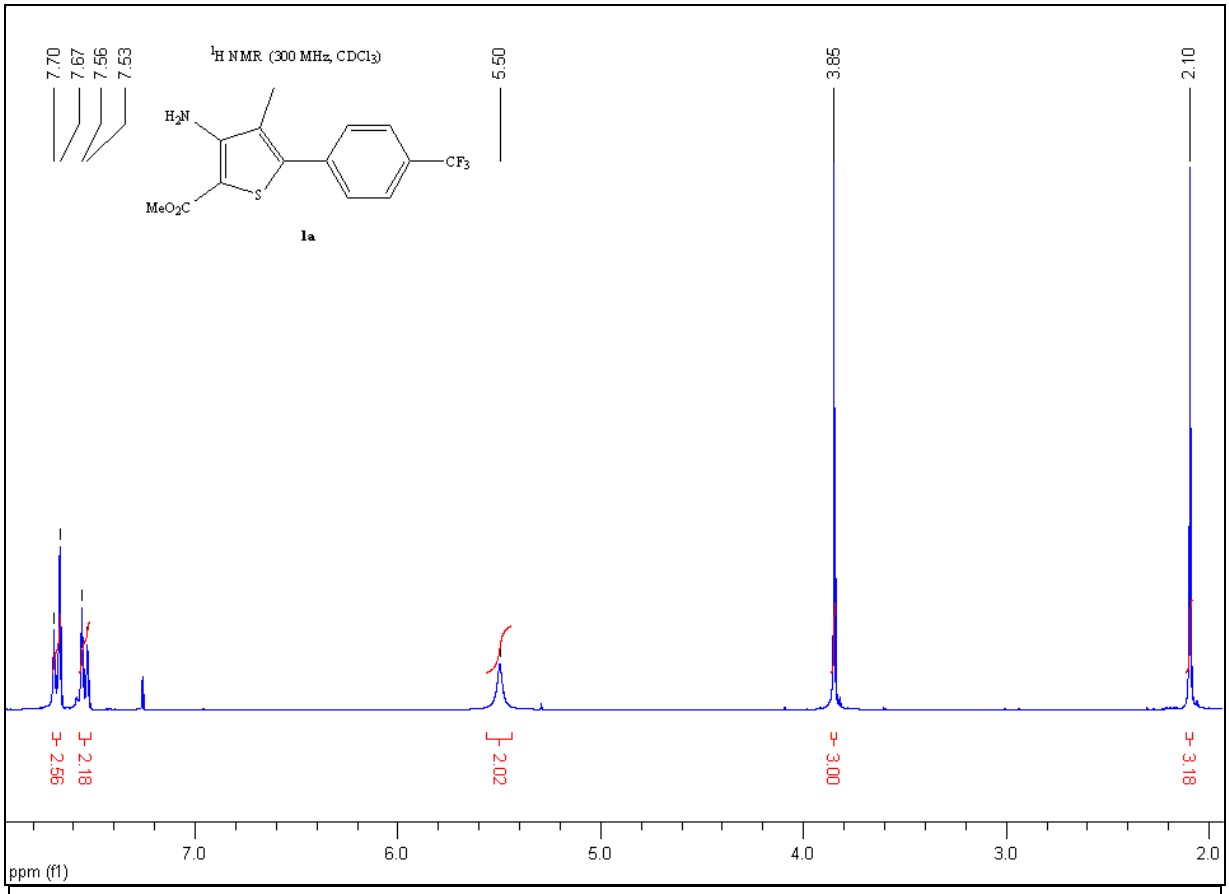
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.84 (s, 1H), 8.48-8.47 (m, 1H), 7.84 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.38-7.30 (m, 3H), 7.26-7.22 (m, 2H), 2.40 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.3, 146.9, 141.2, 137.8, 137.6, 134.7, 131.5, 131.1, 129.3, 128.9, 125.2, 123.8, 110.5, 21.2, 12.6; elemental analysis: calcd (%) for $C_{17}H_{16}N_2S$ (280.39): C 72.82, H 5.75; found: C 72.76, H 5.71.

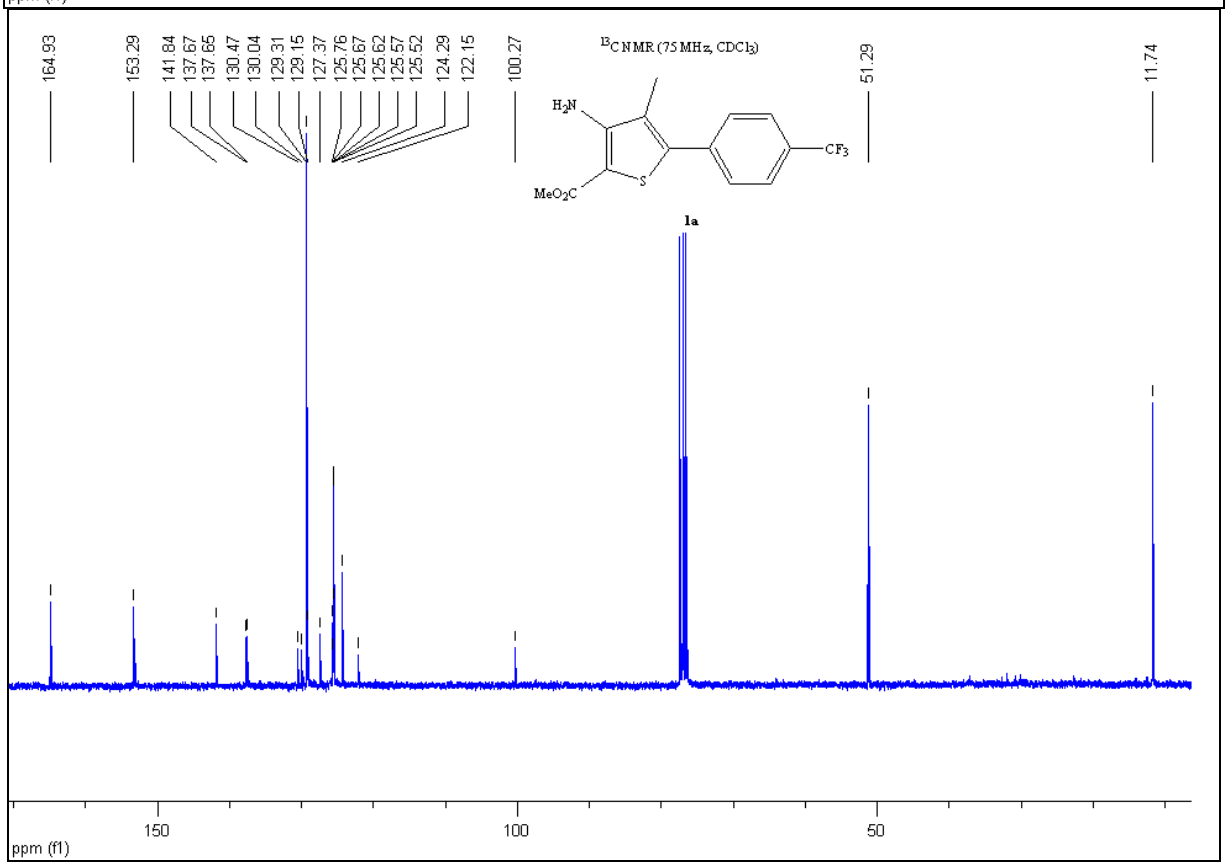
Methyl 3-amino-5-naphthalen-1-yl-thiophene-2-carboxylate (19a) and methyl 3-amino-4-naphthalen-1-yl-thiophene-2-carboxylate (19b)

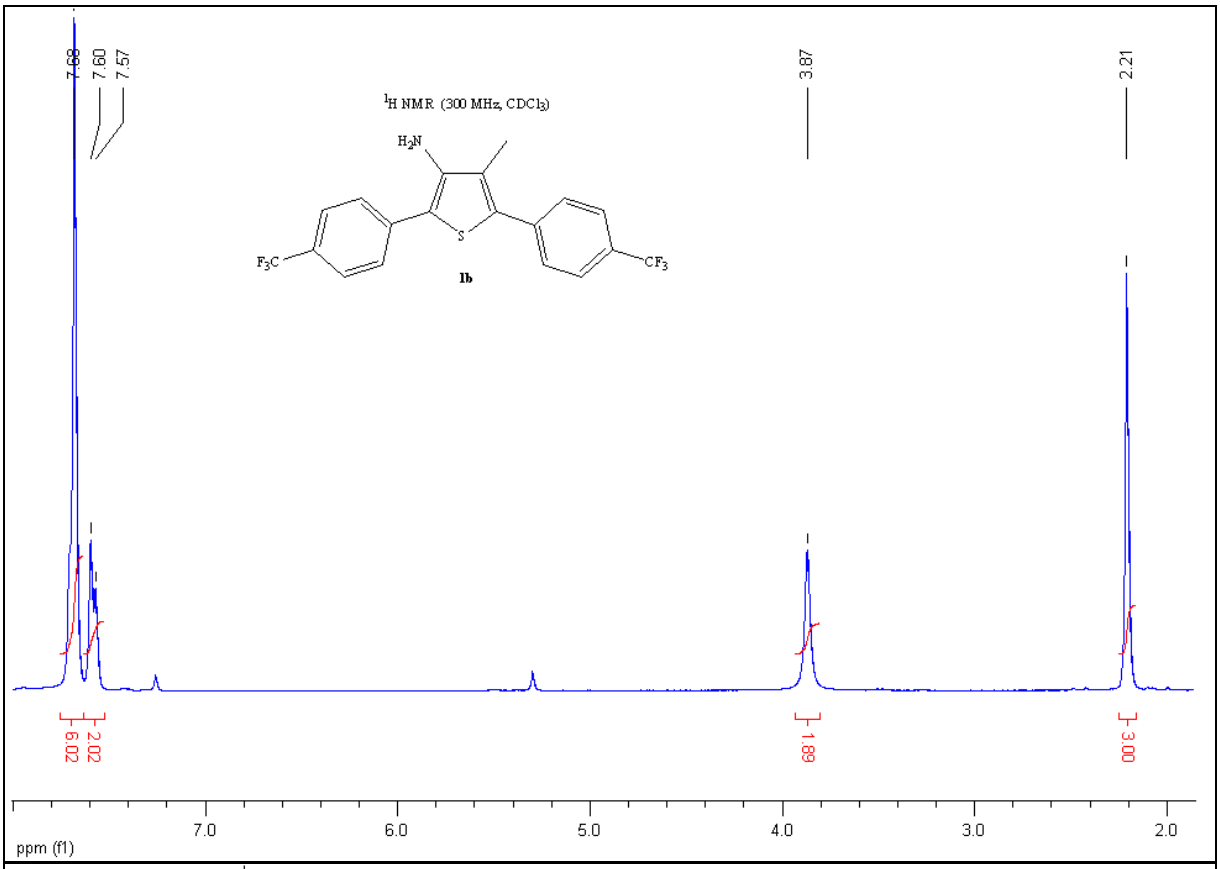
The reaction of 1-bromonaphthalene (0.207 g, 1 mmol), methyl 3-aminothiophene-2-carboxylate (0.314 g, 2 mmol) and KOAc (0.196 g, 2 mmol) in the presence of $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) in DMAc at 120 °C during 20 h affords the corresponding products **19a** in 52% (0.147 g) and **19b** in 12% (0.034 g) isolated yields.

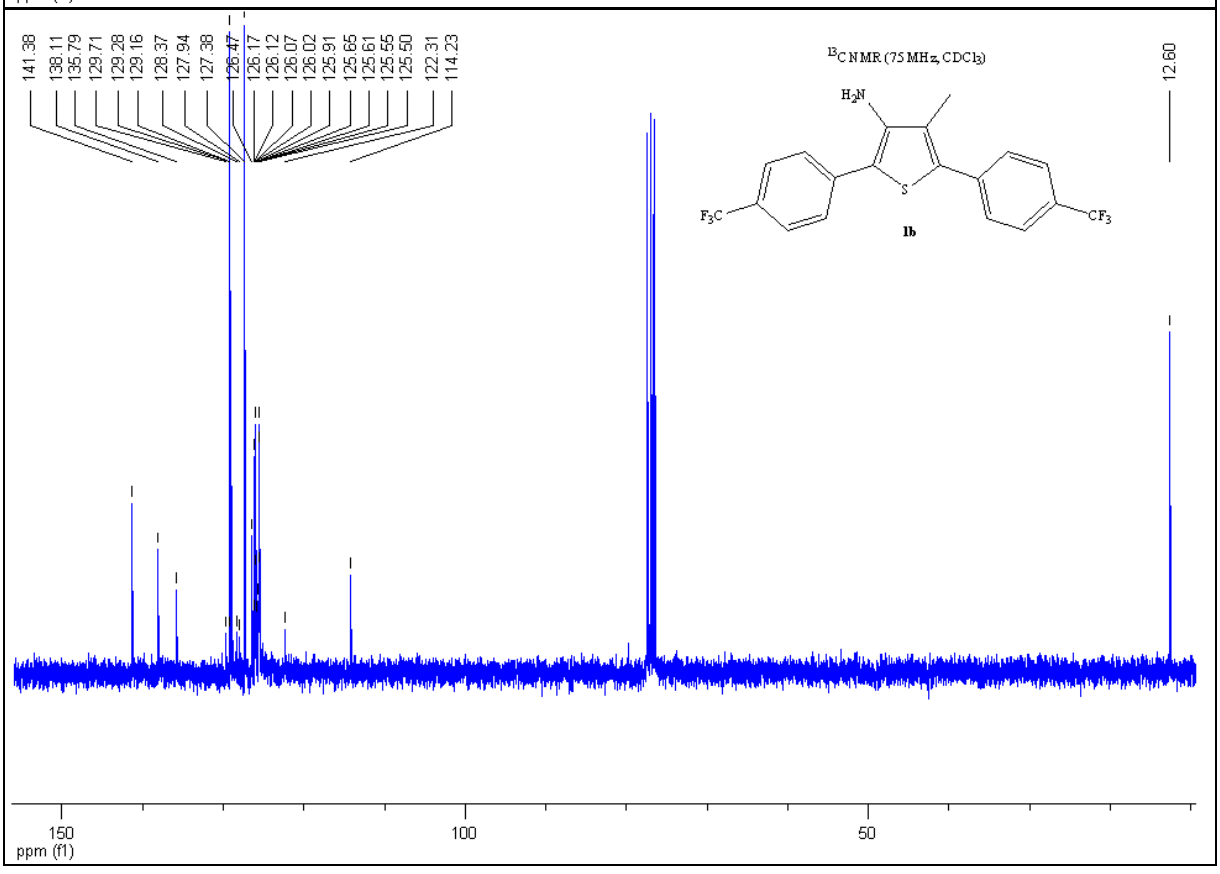
19a: ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24-8.22 (m, 1H), 7.89-7.87 (m, 2H), 7.57-7.45 (m, 4H), 6.70 (s, 1H), 5.54 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.9, 153.6, 147.5, 133.7, 131.5, 131.2, 129.2, 128.4, 127.7, 126.7, 126.2, 125.3, 125.1, 120.1, 101.3, 51.2. elemental analysis: calcd (%) for $C_{16}H_{13}N_2O_2S$ (283.35): C 67.82, H 4.62; found: C 67.70, H 4.52.

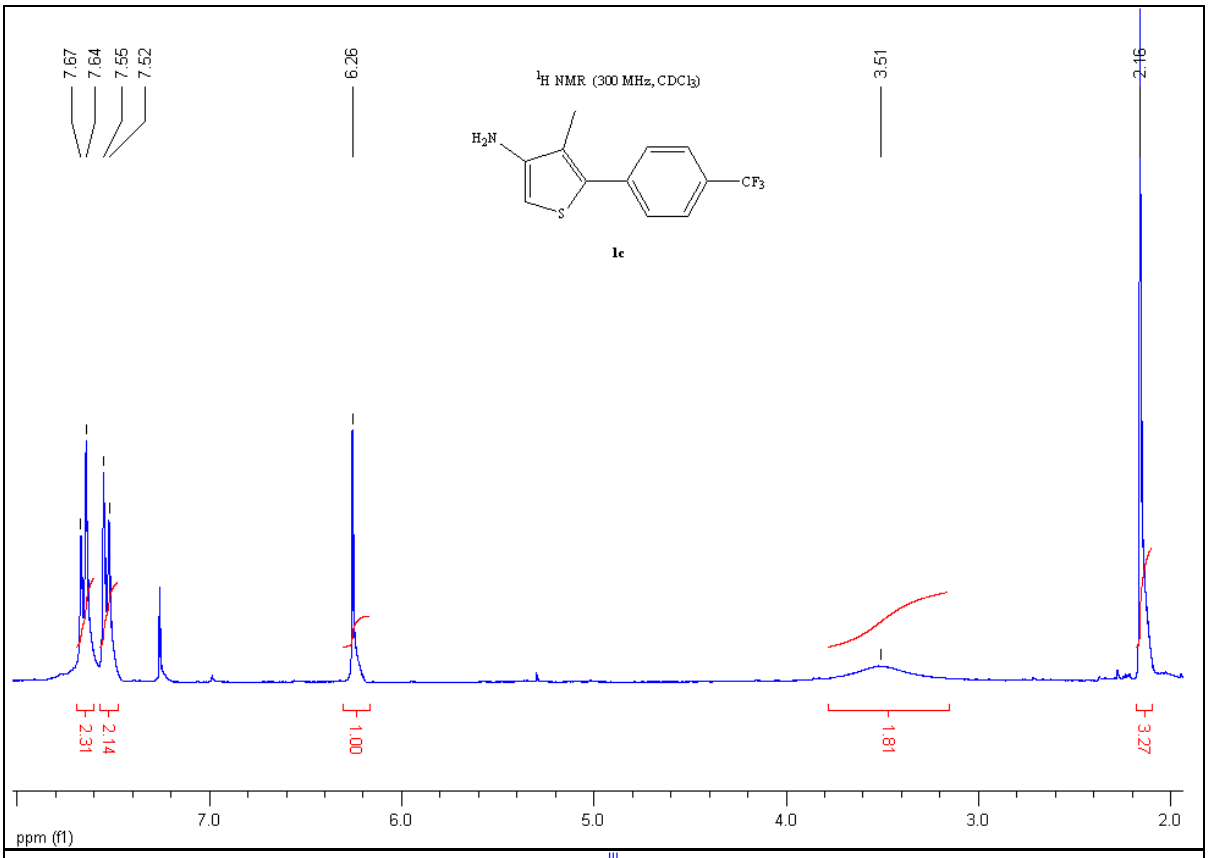
19b: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94-7.88 (m, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.54-7.44 (m, 4H), 7.31 (s, 1H), 5.35 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 152.3, 133.8, 131.7, 131.6, 131.5, 130.1, 128.9, 128.4, 127.9, 126.6, 126.3, 125.6, 125.5, 100.7, 51.3. elemental analysis: calcd (%) for $C_{16}H_{13}N_2O_2S$ (283.35): C 67.82, H 4.62; found: C 67.97, H 4.70.

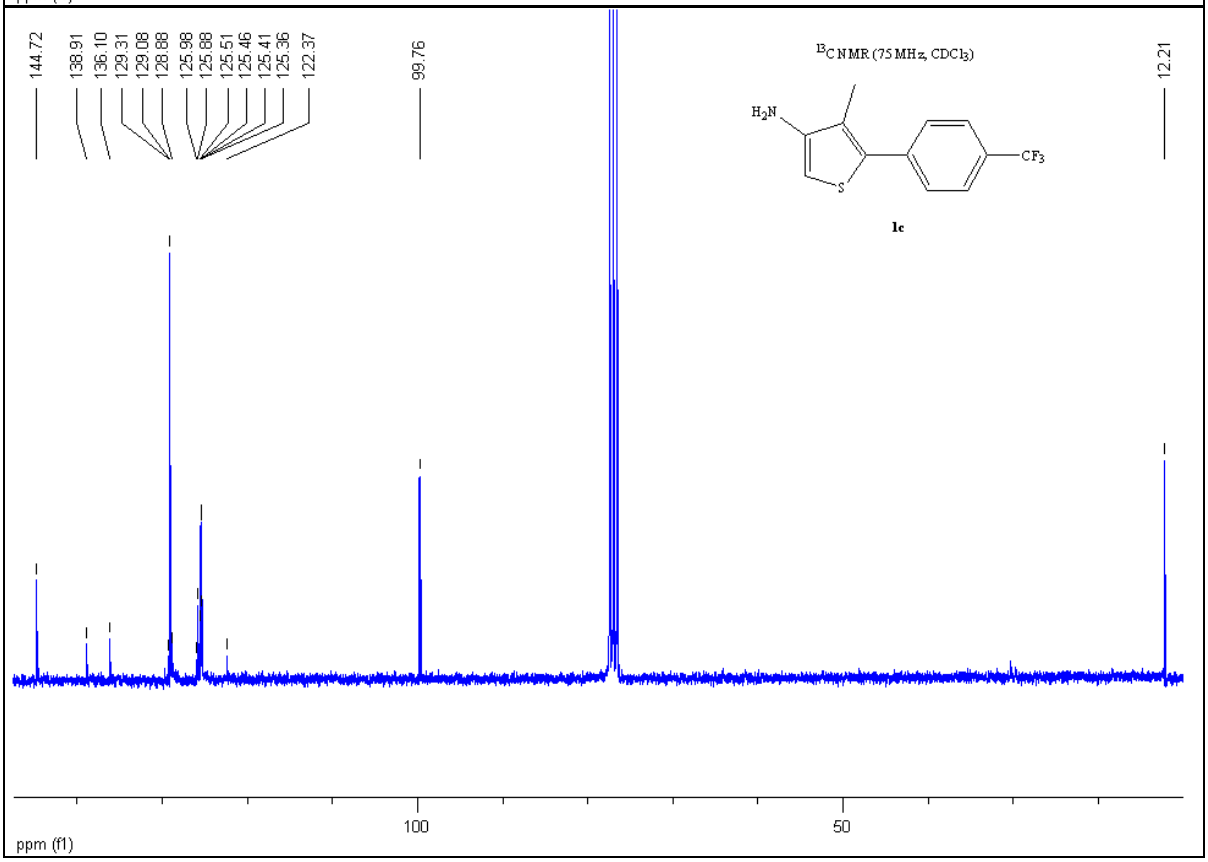

7.70
7.67
7.56
7.53
^{1}H NMR (300 MHz, CDCl$_3$)
5.50
3.85
2.10
H_2N
CF_3
MeO_2C
S
1a
2.56
2.18
2.02
3.00
3.18
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

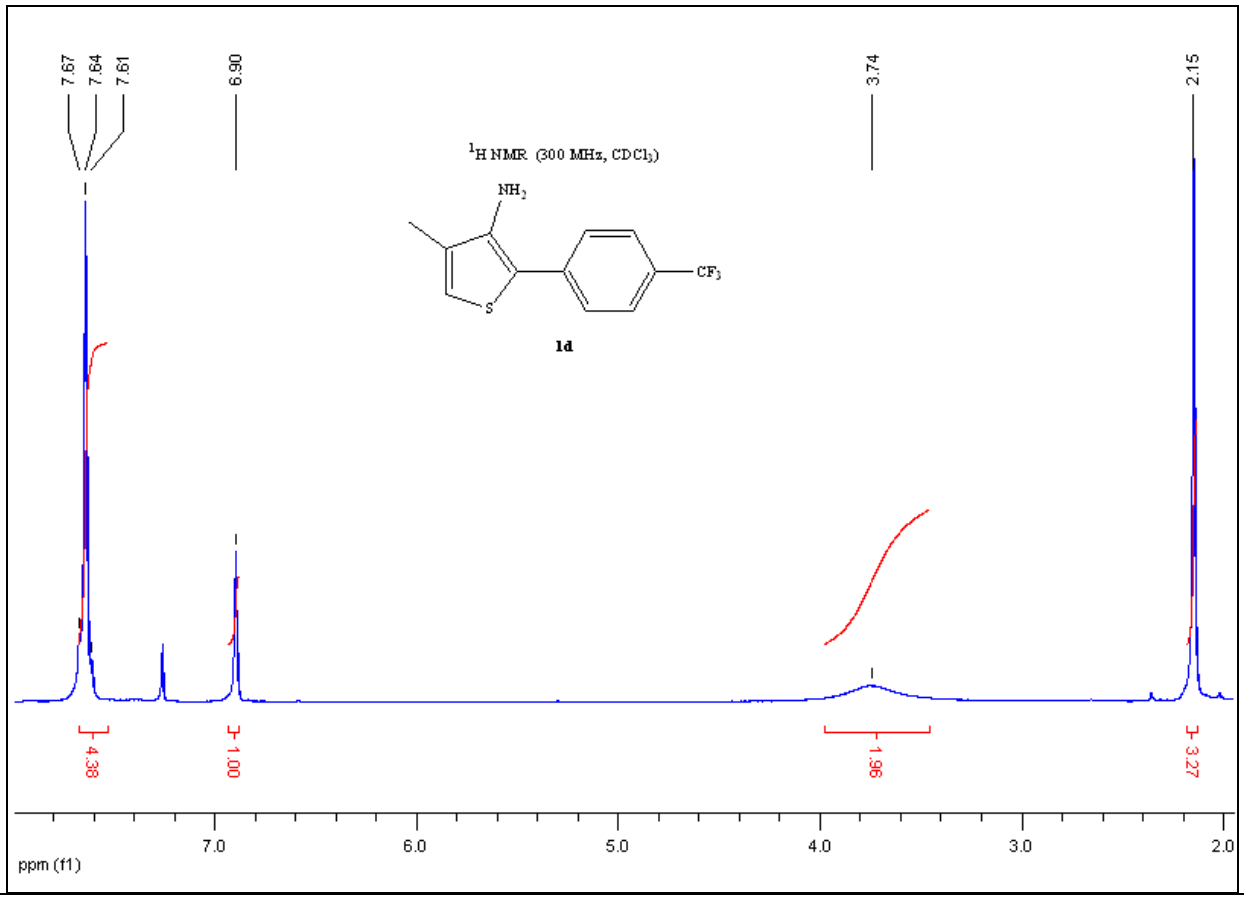

164.93
153.29
141.84
137.67
137.65
130.47
130.04
129.31
129.15
127.37
125.76
125.67
125.62
125.57
125.52
124.29
122.15
100.27
^{13}C NMR (75 MHz, CDCl$_3$)
51.29
11.74
H_2N
CF_3
MeO_2C
S
1a
150
100
50
ppm (f1)

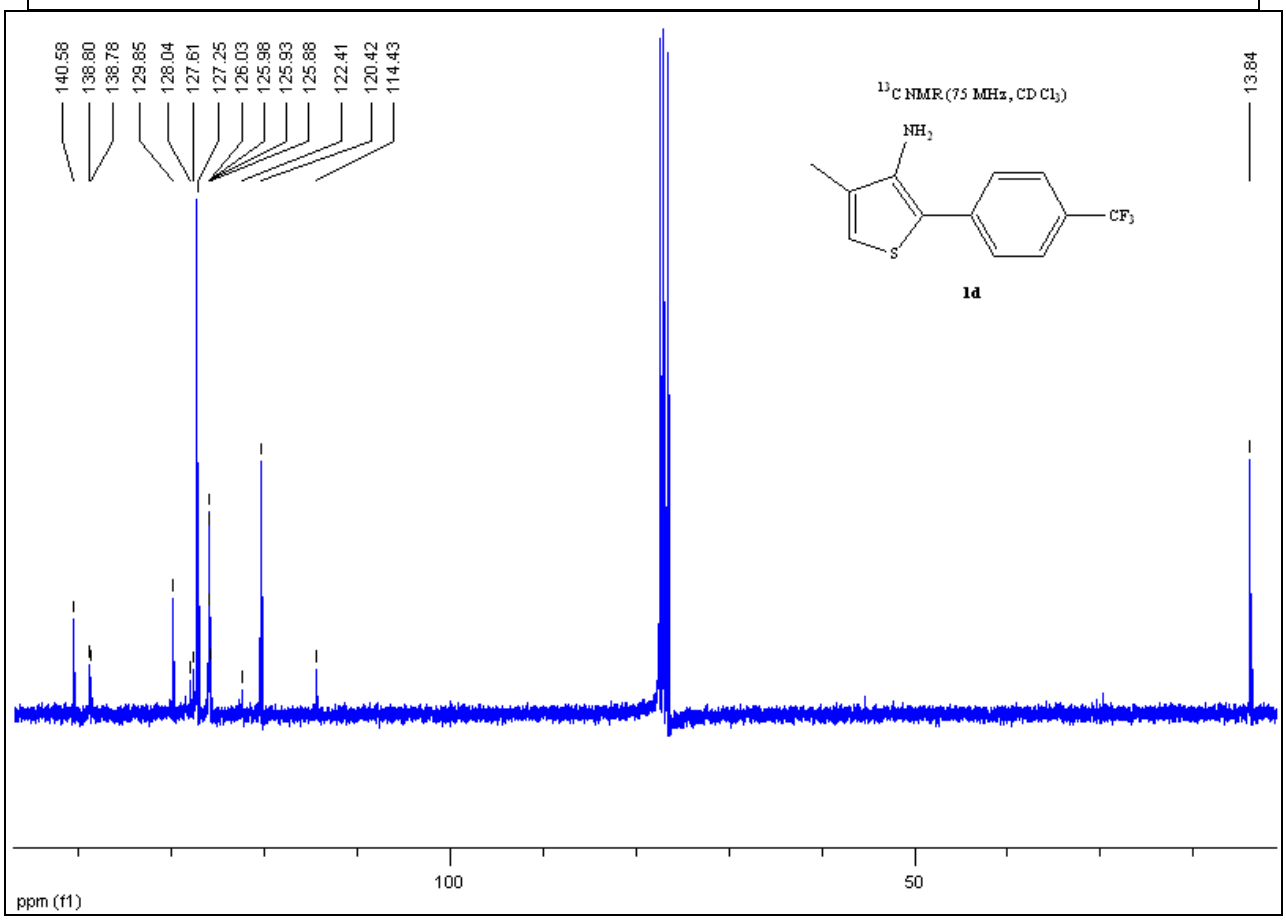

7.68
7.60
7.57
3.87
2.21
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
S
F_3C
CF_3
1b
9.02
2.02
1.89
3.00
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

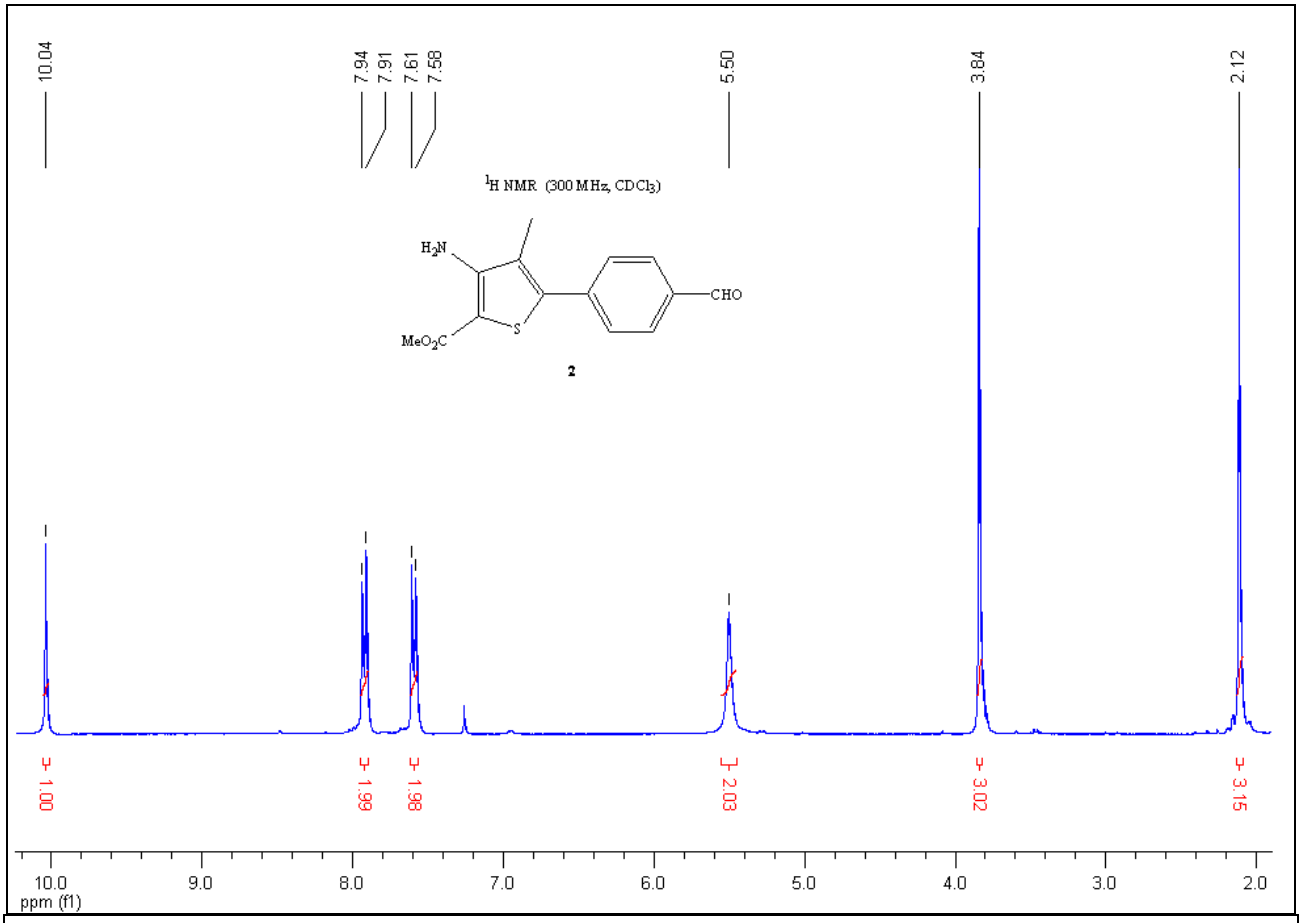

141.38
138.11
135.79
129.71
129.28
129.16
128.37
127.94
127.38
126.47
126.17
126.12
126.07
126.02
125.91
125.65
125.61
125.55
125.50
122.31
114.23
^{13}C NMR (75 MHz, CDCl$_3$)
12.60
H_2N
S
F_3C
CF_3
1b
150
100
50
ppm (f1)

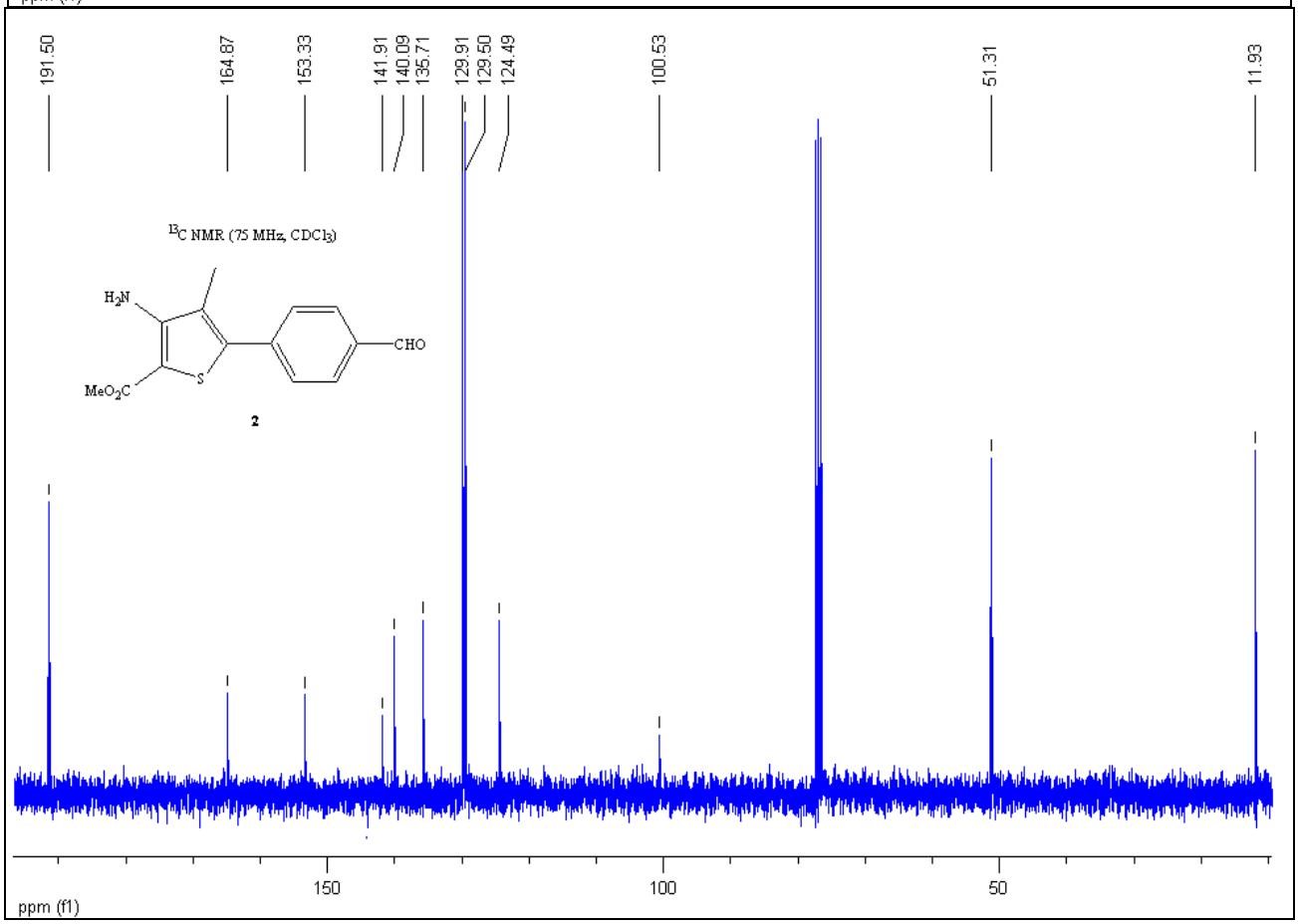

7.67
7.64
7.55
7.52
6.26
3.51
2.46
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
CF_3
S
1c
2.31
2.14
1.00
1.81
3.27
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

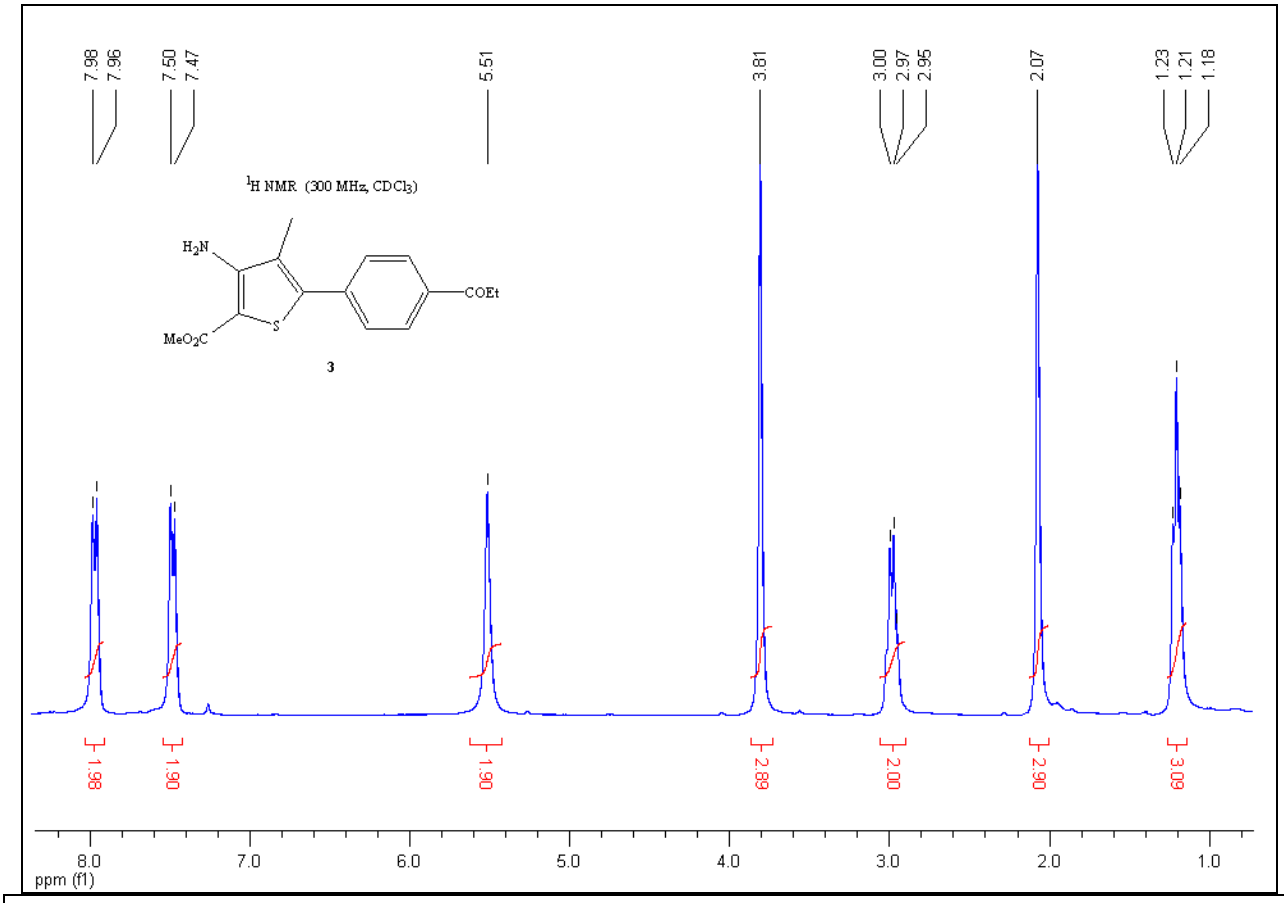

144.72
138.91
136.10
129.31
129.08
128.88
125.98
125.88
125.51
125.46
125.41
125.36
122.37
99.76
^{13}C NMR (75 MHz, CDCl$_3$)
12.21
H_2N
CF_3
S
1c
100
50
ppm (f1)

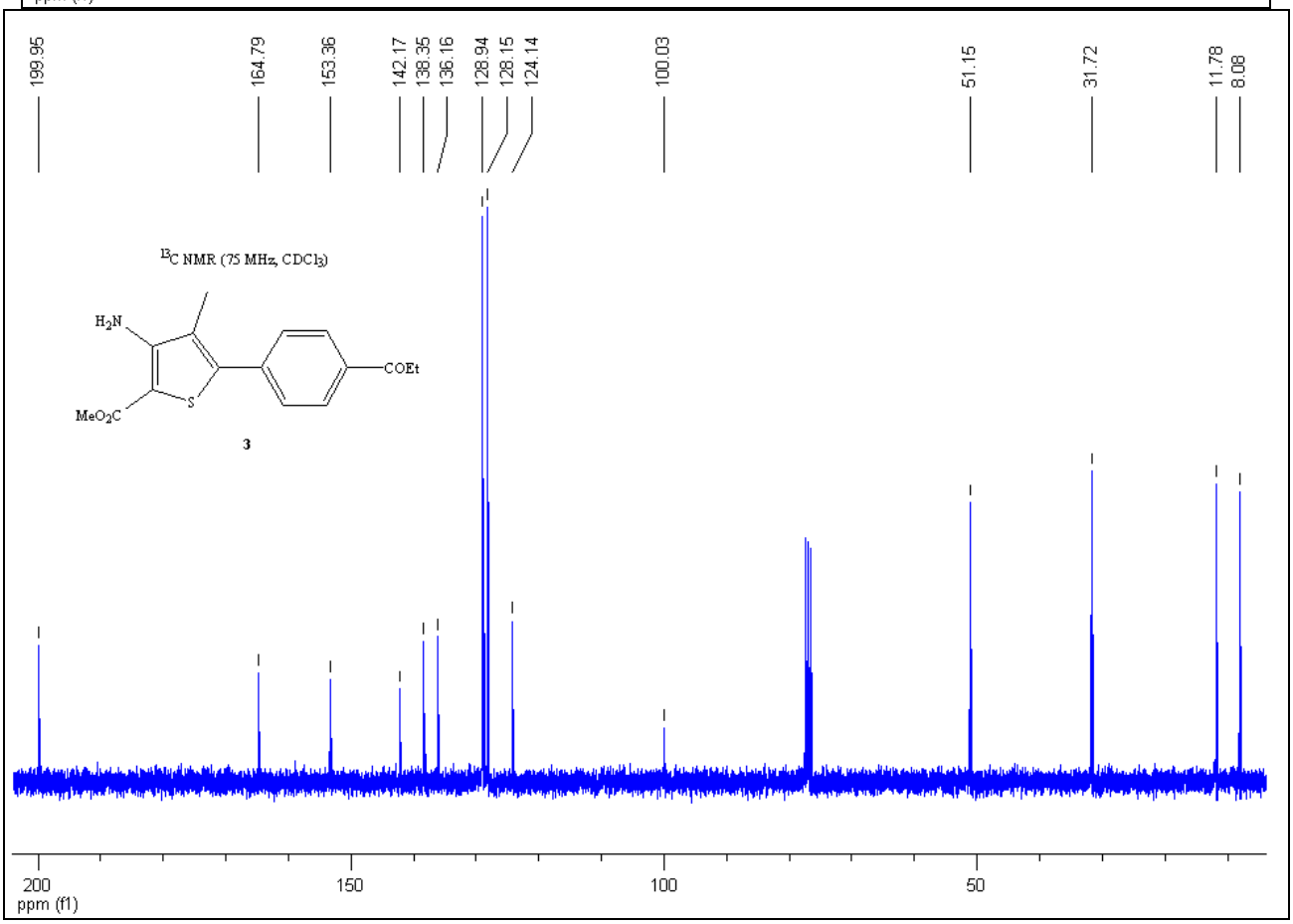

7.67
7.64
7.61
6.90
3.74
2.15
^{1}H NMR (300 MHz, CDCl$_3$)
NH$_2$
CF$_3$
S
1d
4.38
1.00
1.96
3.27
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

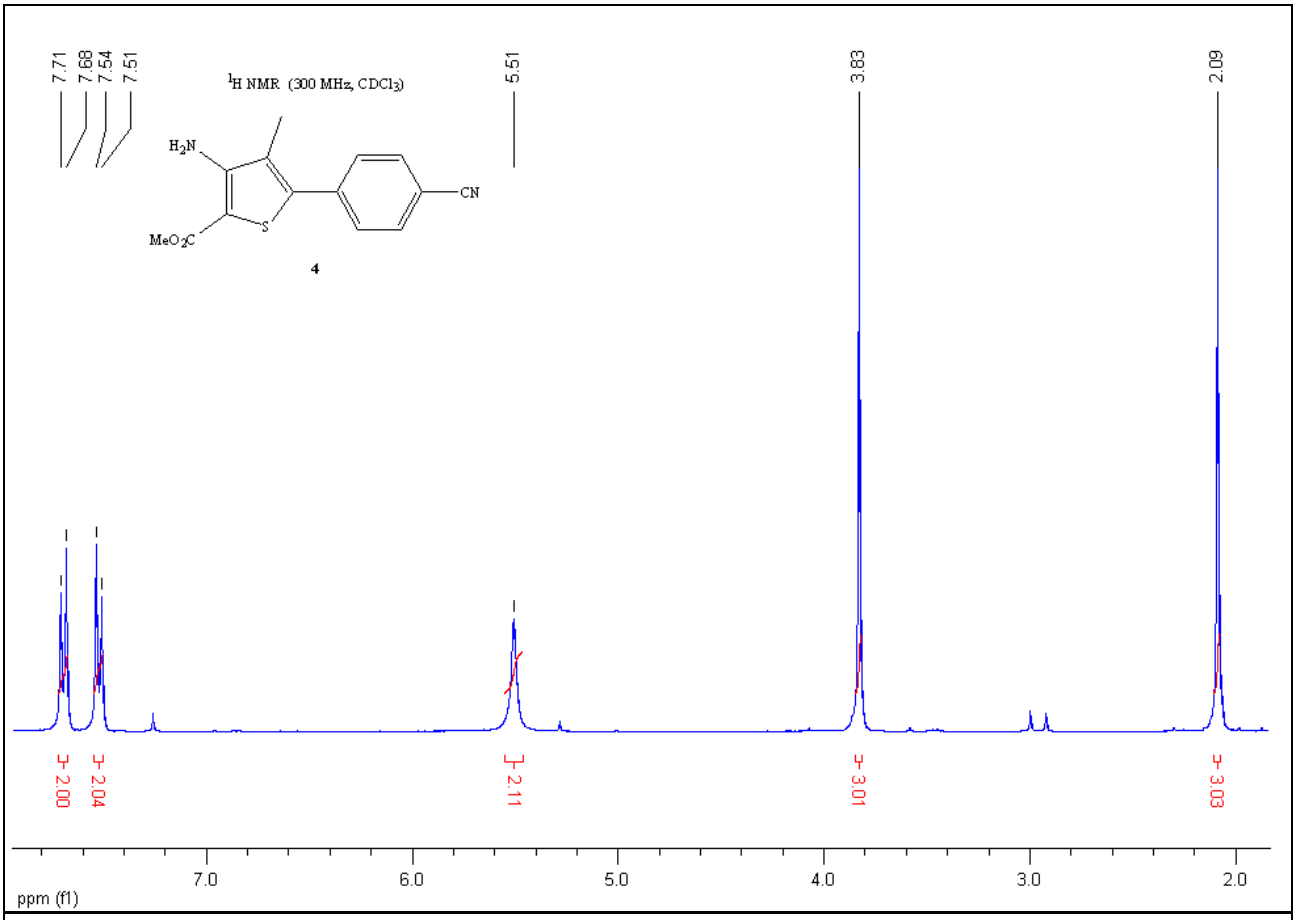

140.58
138.80
138.78
129.85
128.04
127.61
127.25
126.03
125.98
125.93
125.88
122.41
120.42
114.43
13.84
^{13}C NMR (75 MHz, CDCl$_3$)
NH$_2$
CF$_3$
S
1d
100
50
ppm (f1)

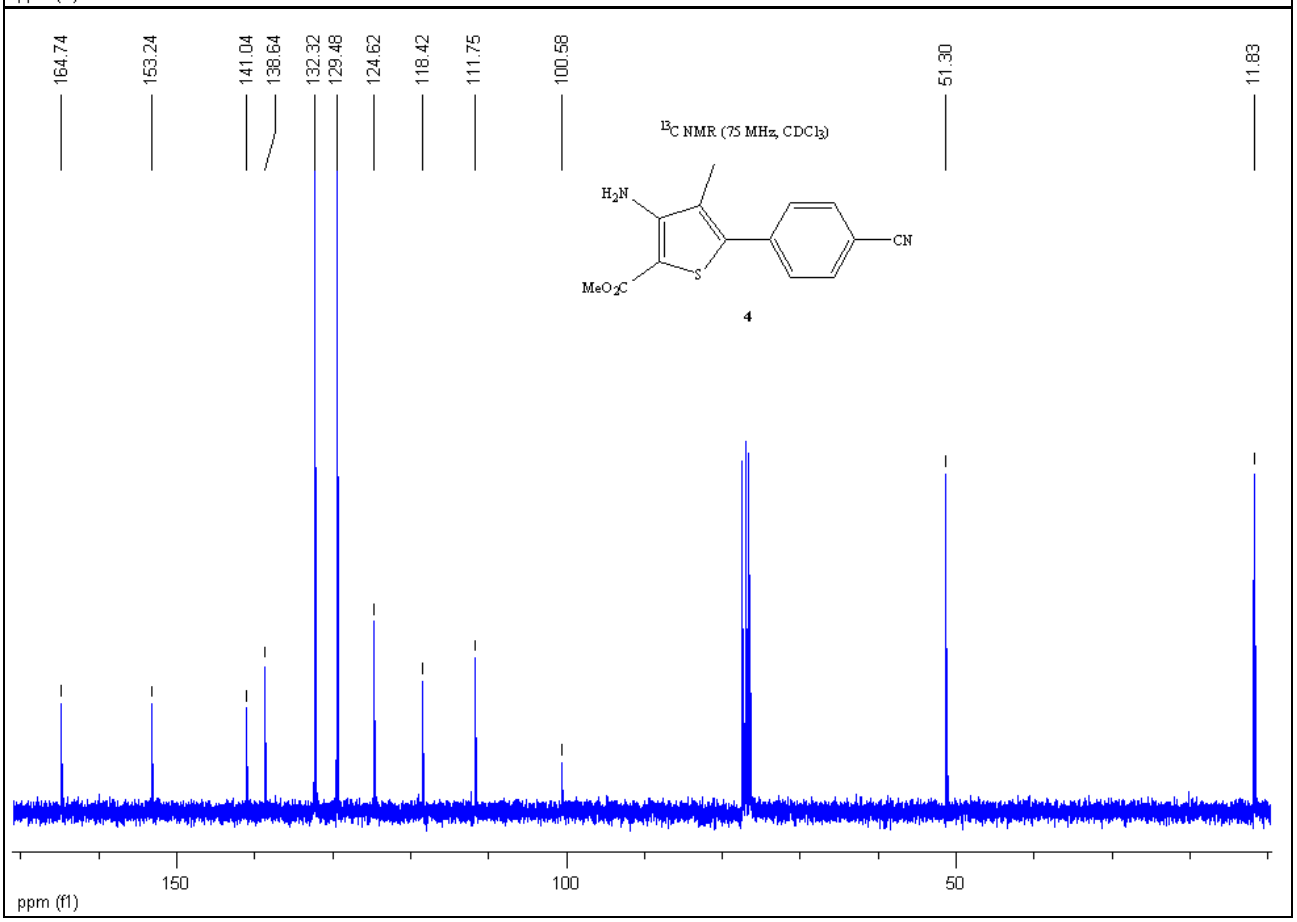

10.04
7.94
7.91
7.61
7.58
5.50
3.84
2.12
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
CHO
MeO_2C
S
2
1.00
1.99
1.98
2.03
3.02
3.15
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

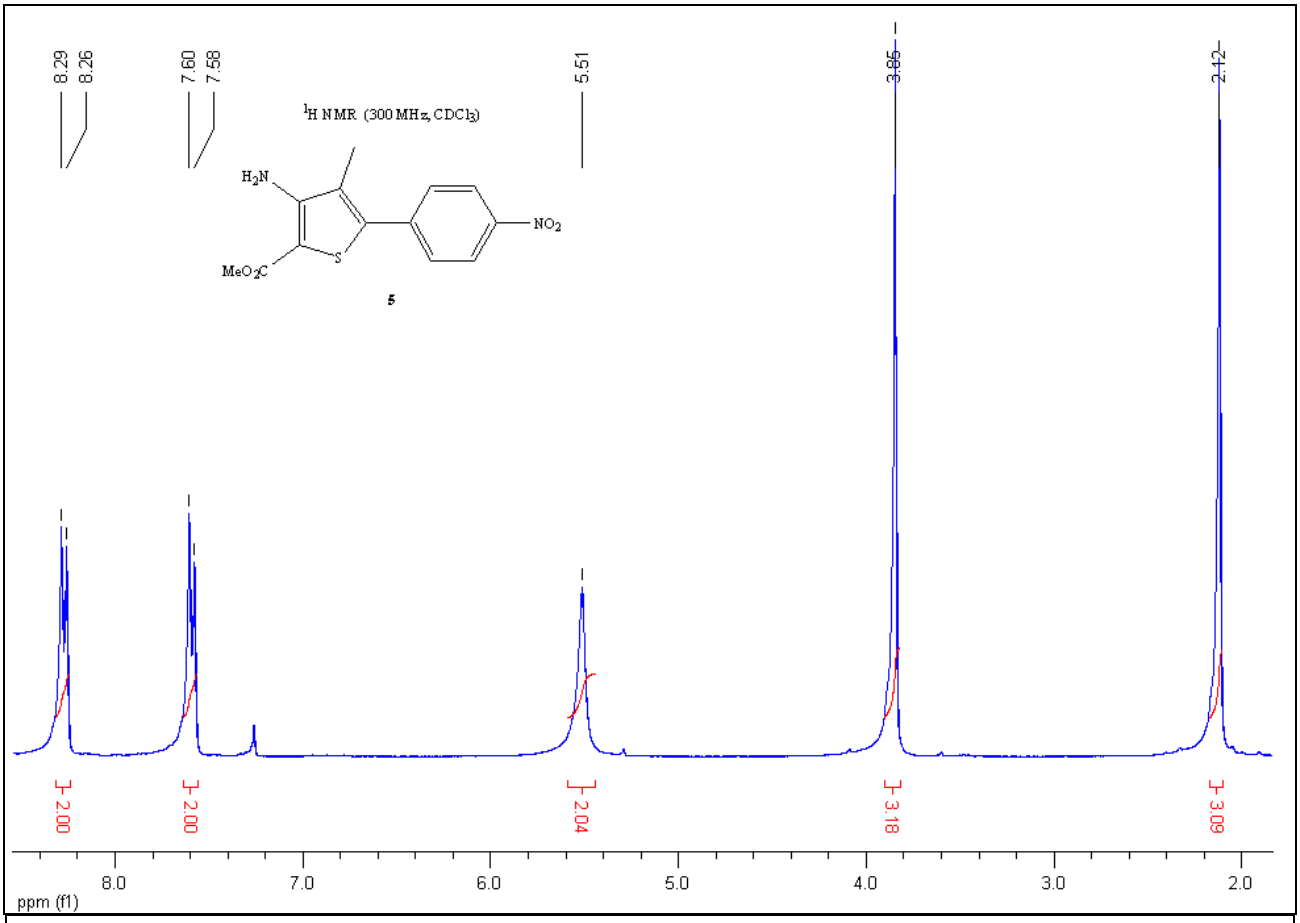

191.50
164.87
153.33
141.91
140.09
135.71
129.91
129.50
124.49
100.53
51.31
11.93
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
CHO
MeO_2C
S
2
150
100
50
ppm (f1)

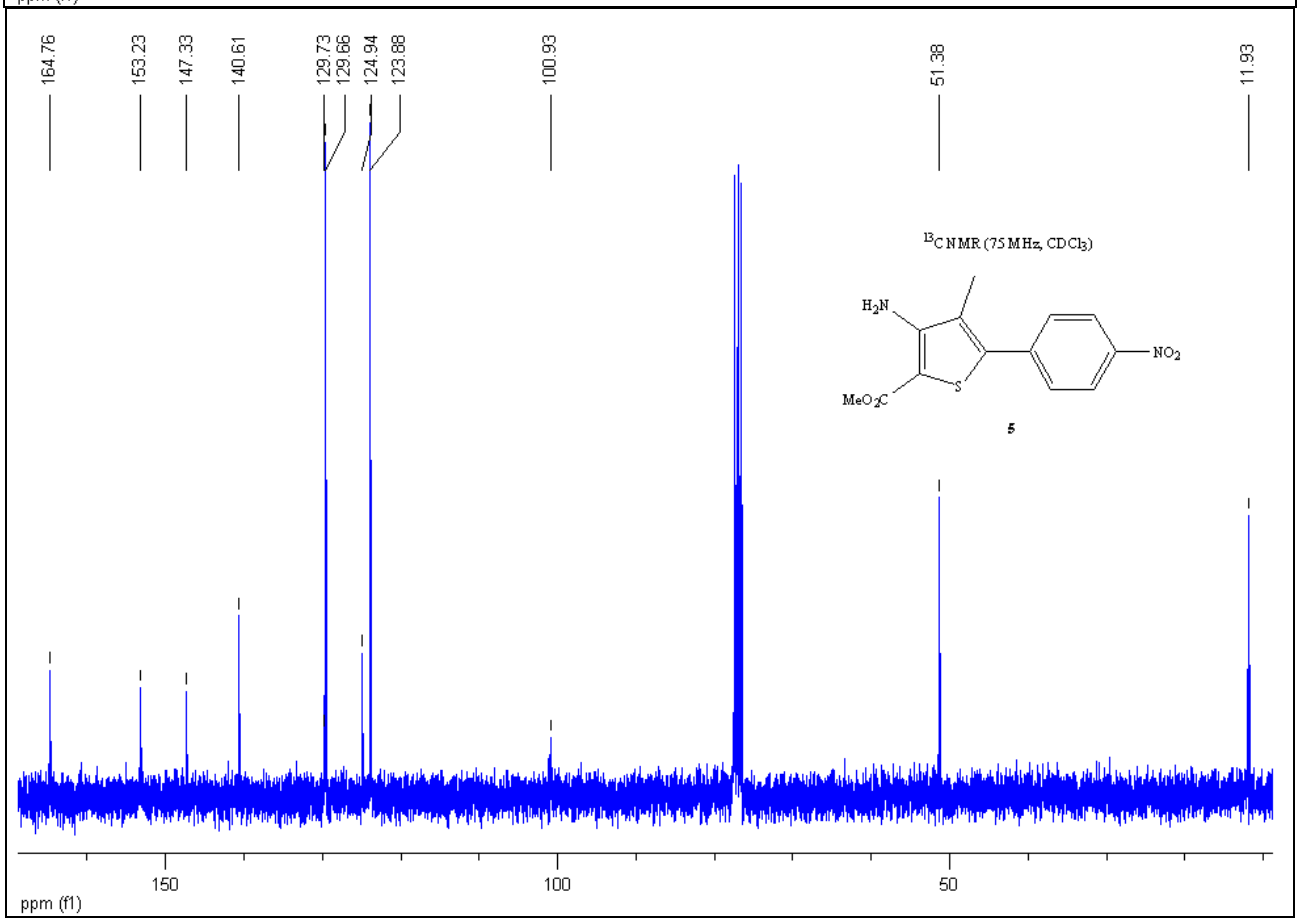

7.98
7.96
7.50
7.47
5.51
3.81
3.00
2.97
2.95
2.07
1.23
1.21
1.18
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
COEt
MeO_2C
S
3
1.98
1.60
1.90
2.89
2.00
2.90
3.09
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)

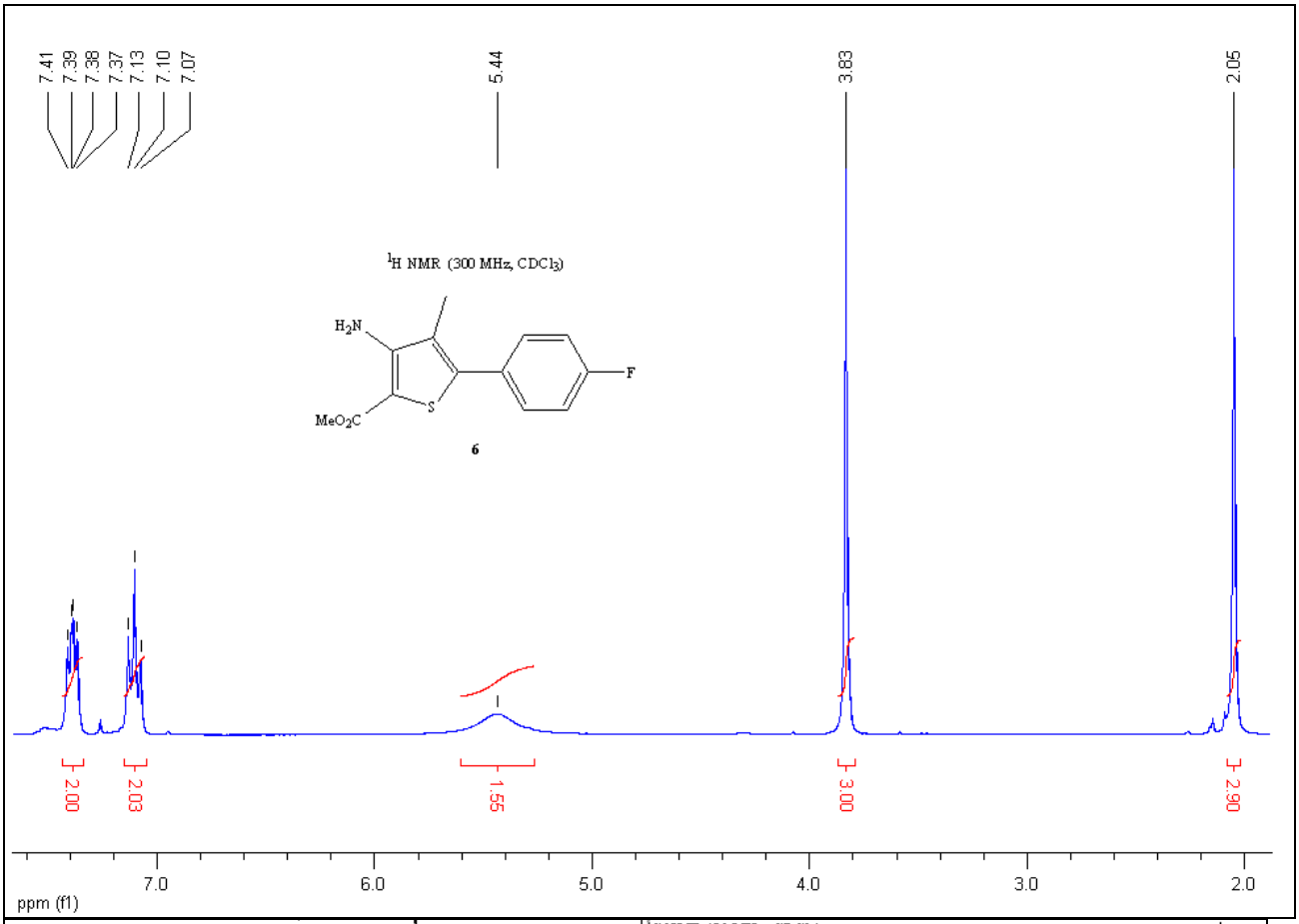

199.95
164.79
153.36
142.17
138.35
136.16
128.94
128.15
124.14
100.03
51.15
31.72
11.78
8.08
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
COEt
MeO_2C
S
3
200
150
100
50
ppm (f1)

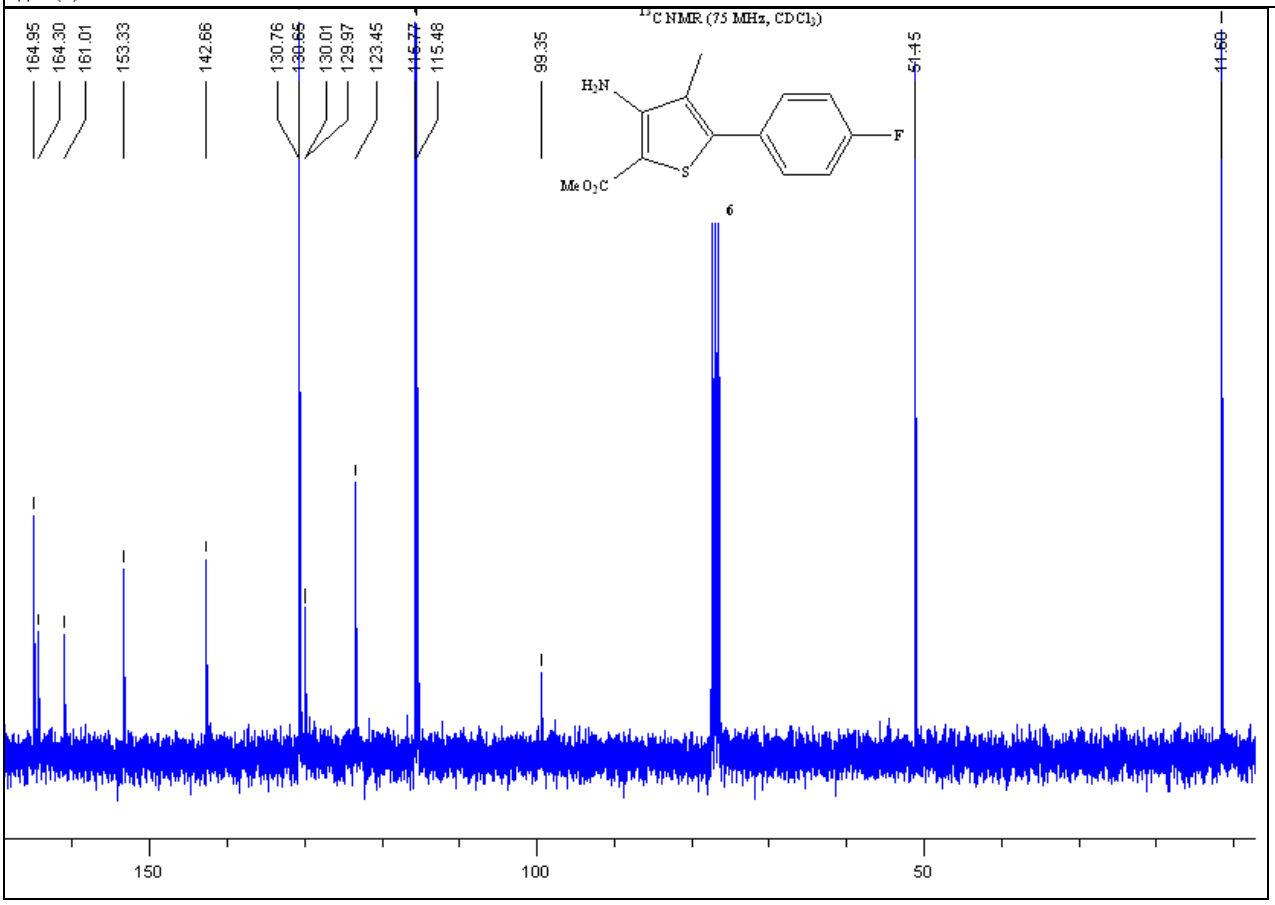

7.71
7.68
7.54
7.51
^{1}H NMR (300 MHz, CDCl$_3$)
5.51
3.83
2.09
H_2N
CN
MeO_2C
S
4
2.00
2.04
2.11
3.01
3.03
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

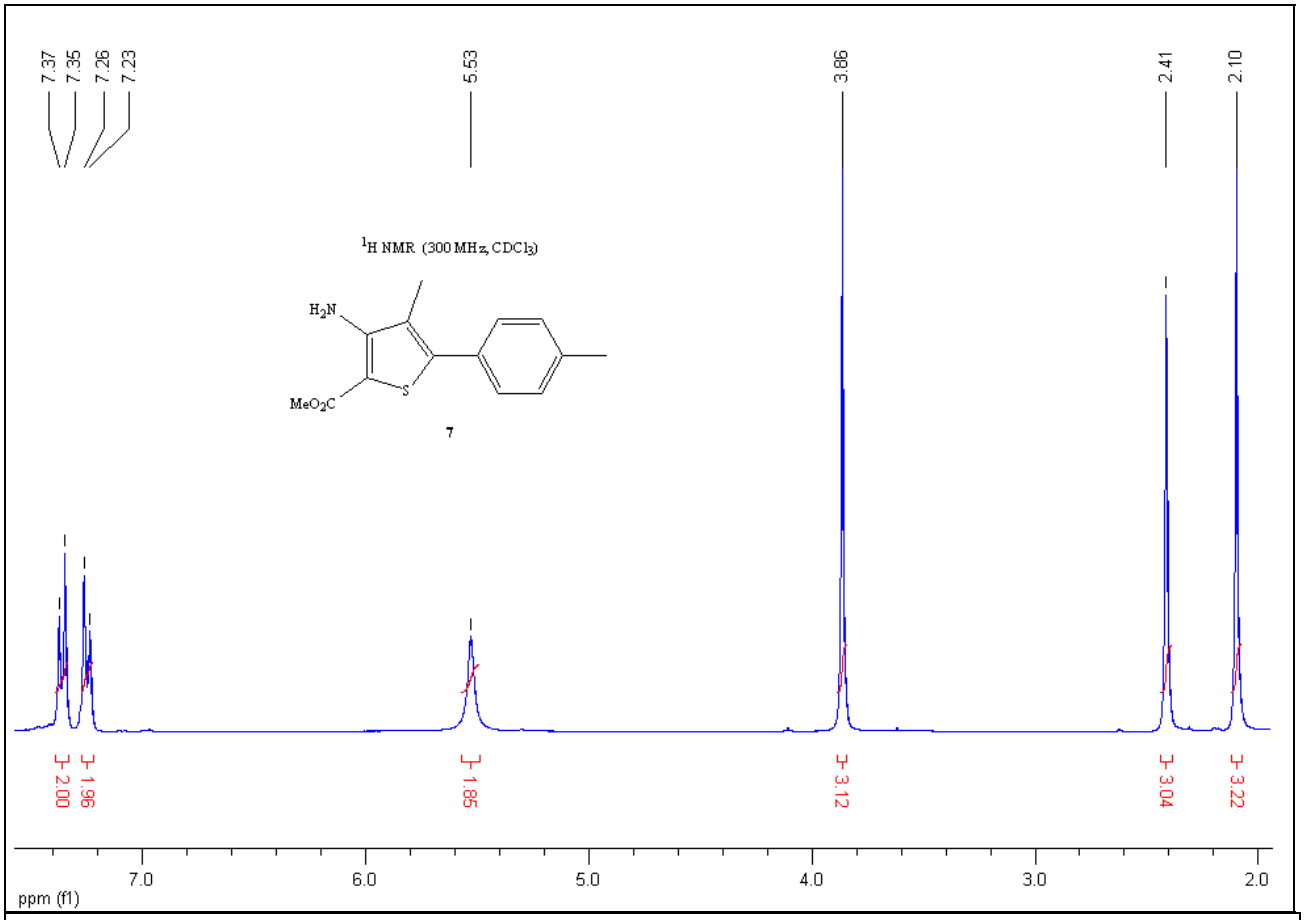

164.74
153.24
141.04
138.64
132.32
129.48
124.62
118.42
111.75
100.58
51.30
11.83
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
CN
MeO_2C
S
4
150
100
50
ppm (f1)

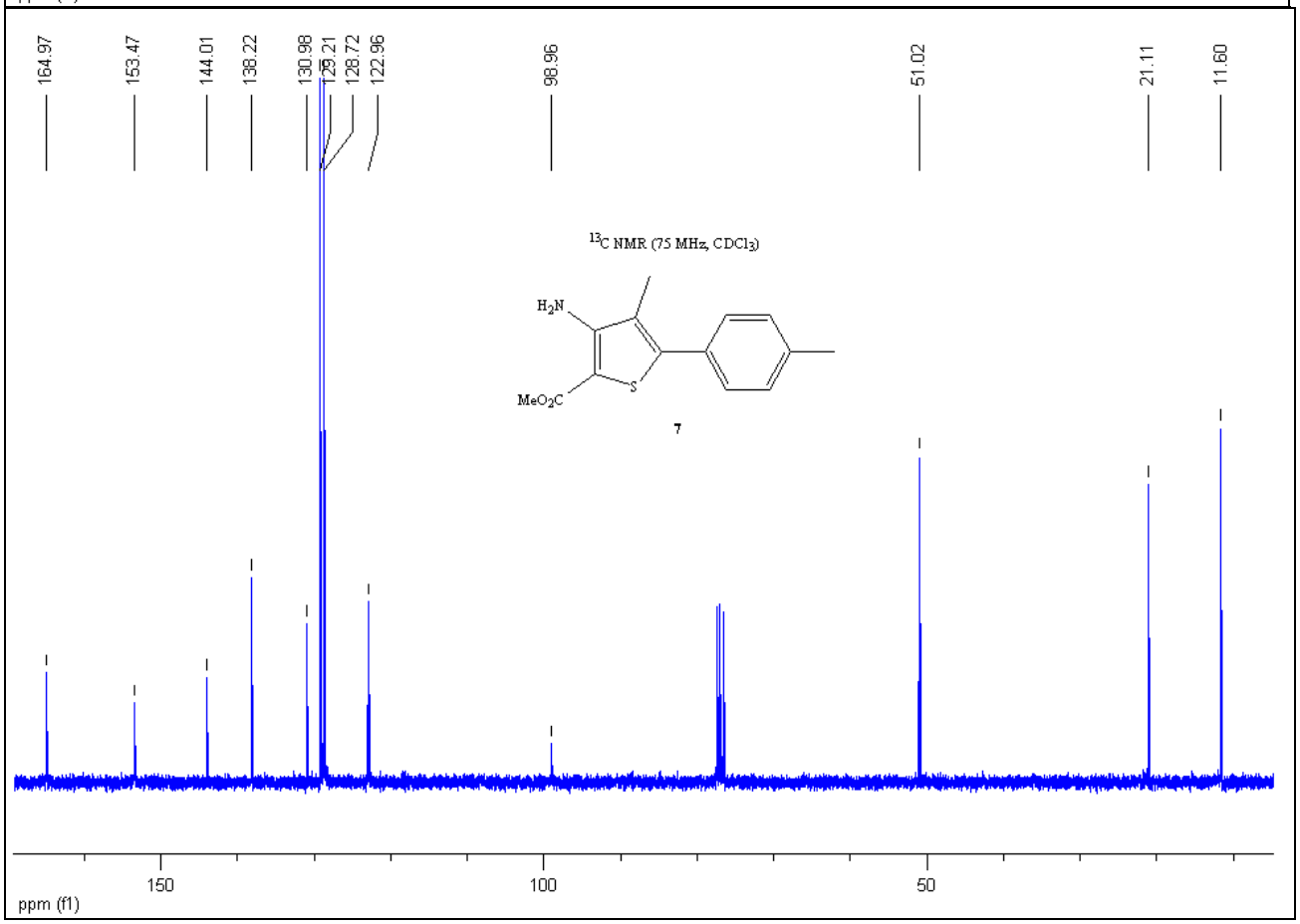

8.29
8.26
7.60
7.58
5.51
3.85
2.12
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
NO_2
MeO_2C
S
5
2.00
2.00
2.04
3.18
3.09
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

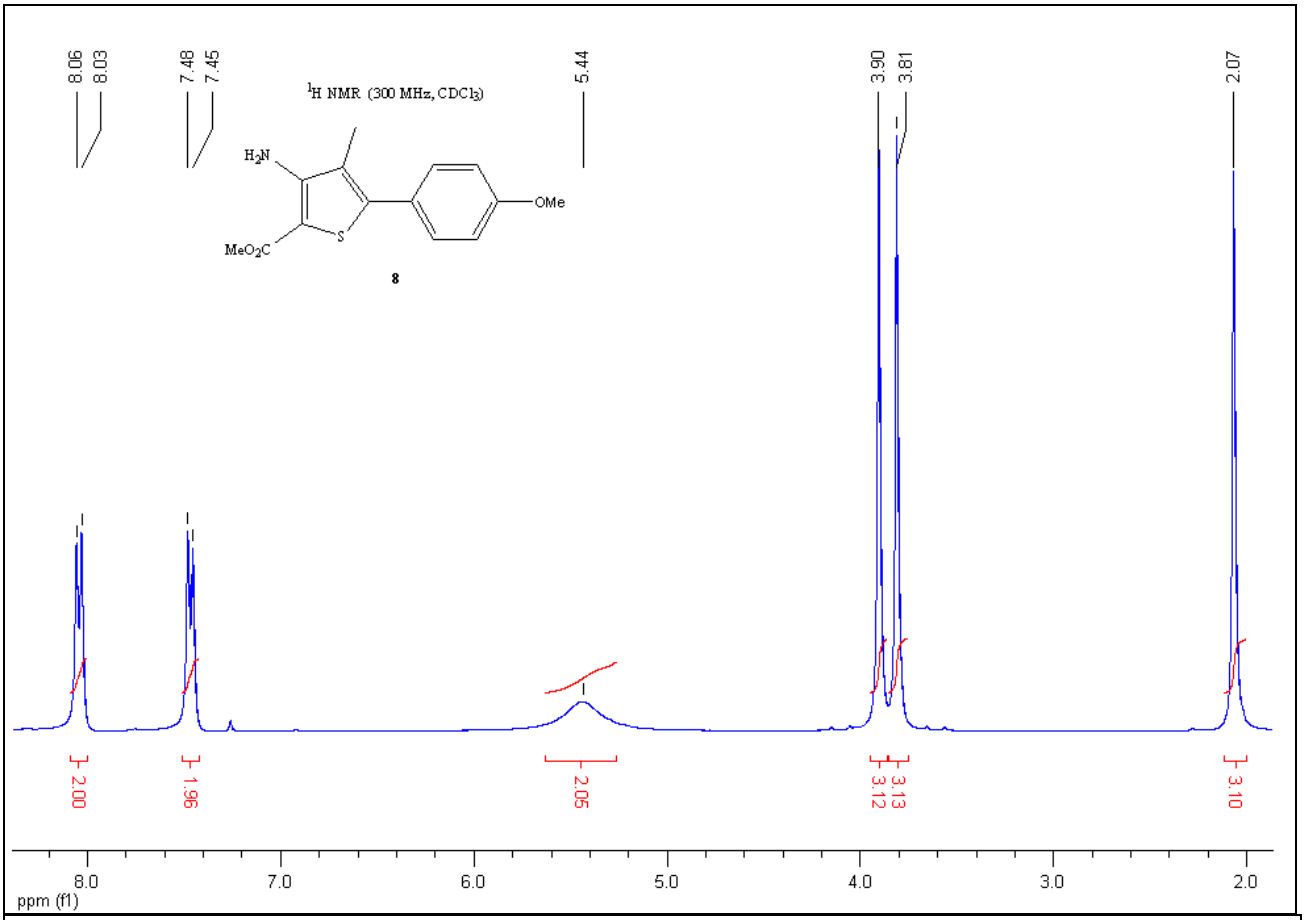

164.76
153.23
147.33
140.61
129.73
129.66
124.94
123.88
100.93
51.38
11.93
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
NO_2
MeO_2C
S
5
150
100
50
ppm (f1)

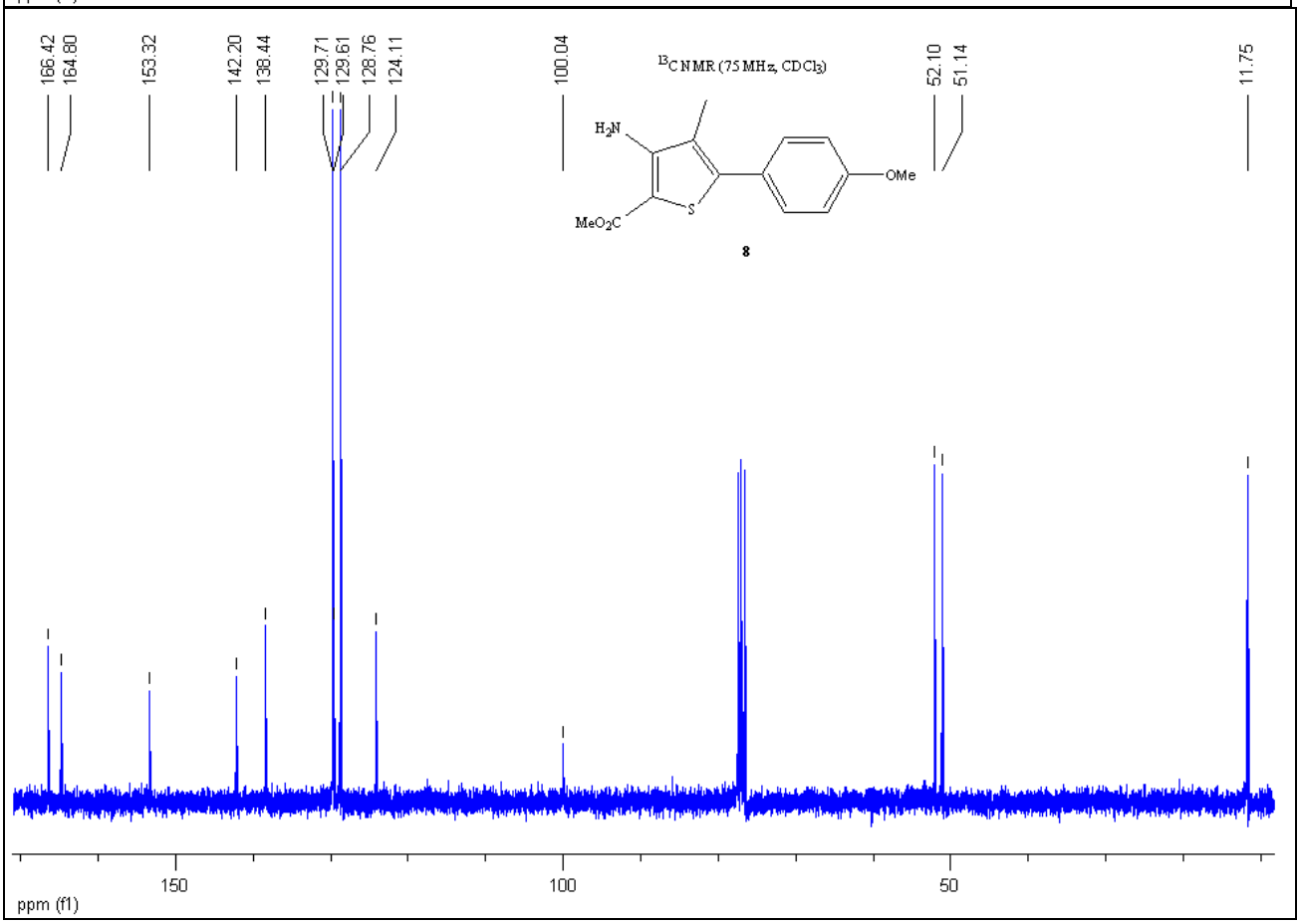

7.41
7.39
7.38
7.37
7.13
7.10
7.07
5.44
3.83
2.05
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
F
MeO_2C
S
6
2.00
2.03
1.55
3.00
2.90
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

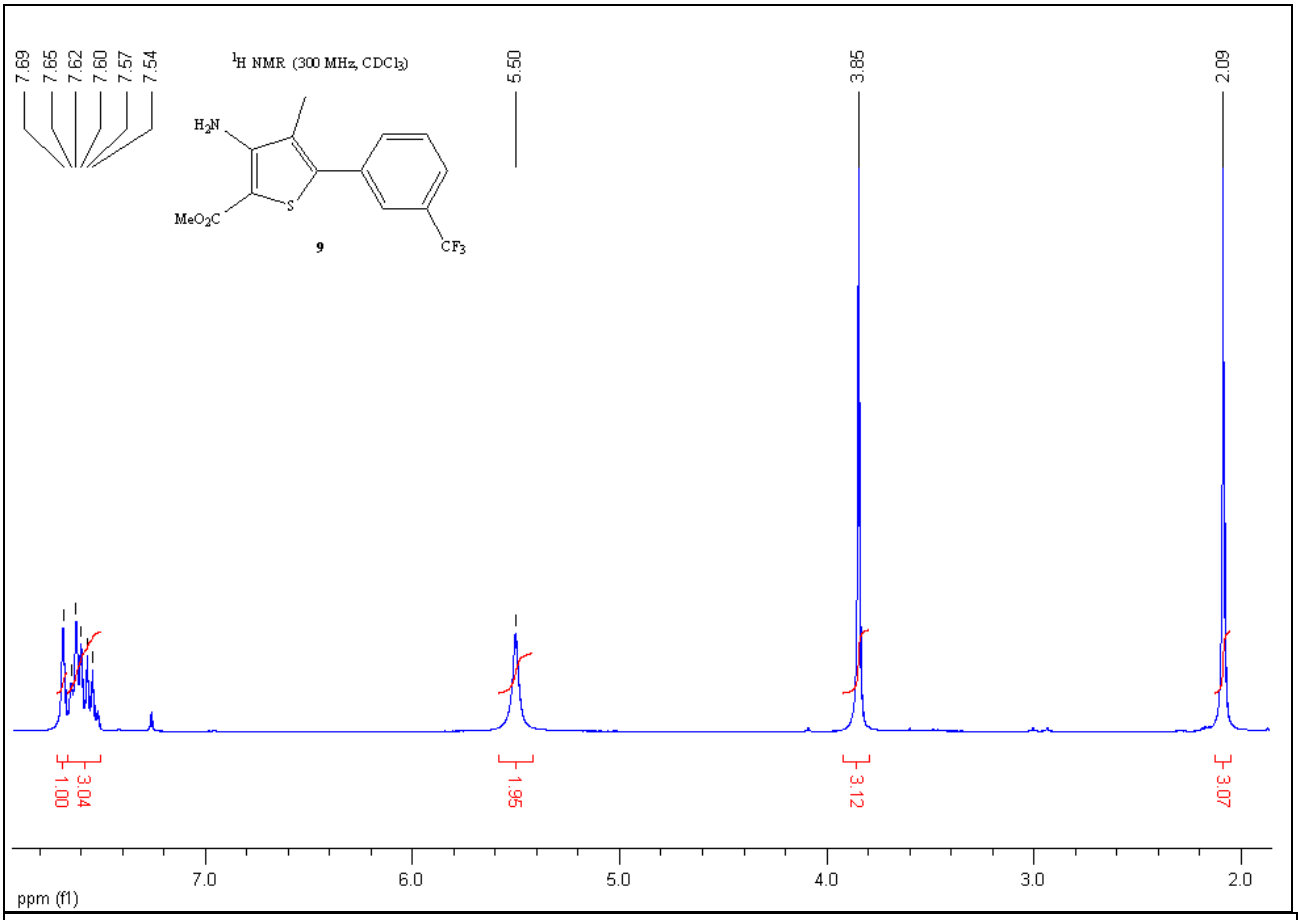

164.95
164.30
161.01
153.33
142.66
130.76
130.65
130.01
129.97
123.45
115.77
115.48
99.35
51.45
11.60
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
F
$Me\,O_2C$
S
6
150
100
50

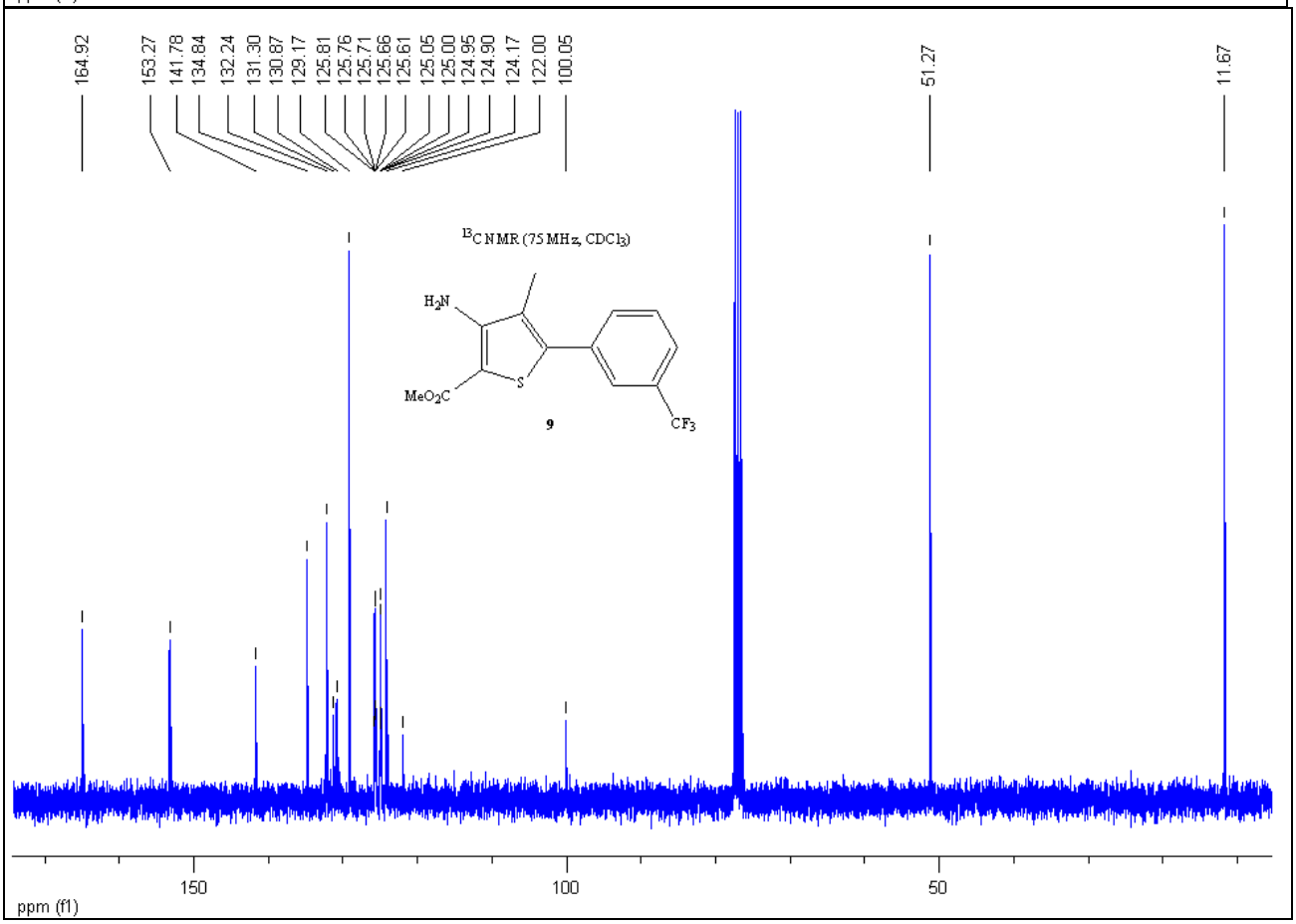

7.37
7.35
7.26
7.23
5.53
3.86
2.41
2.10
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
7
2.00
1.96
1.85
3.12
3.04
3.22
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

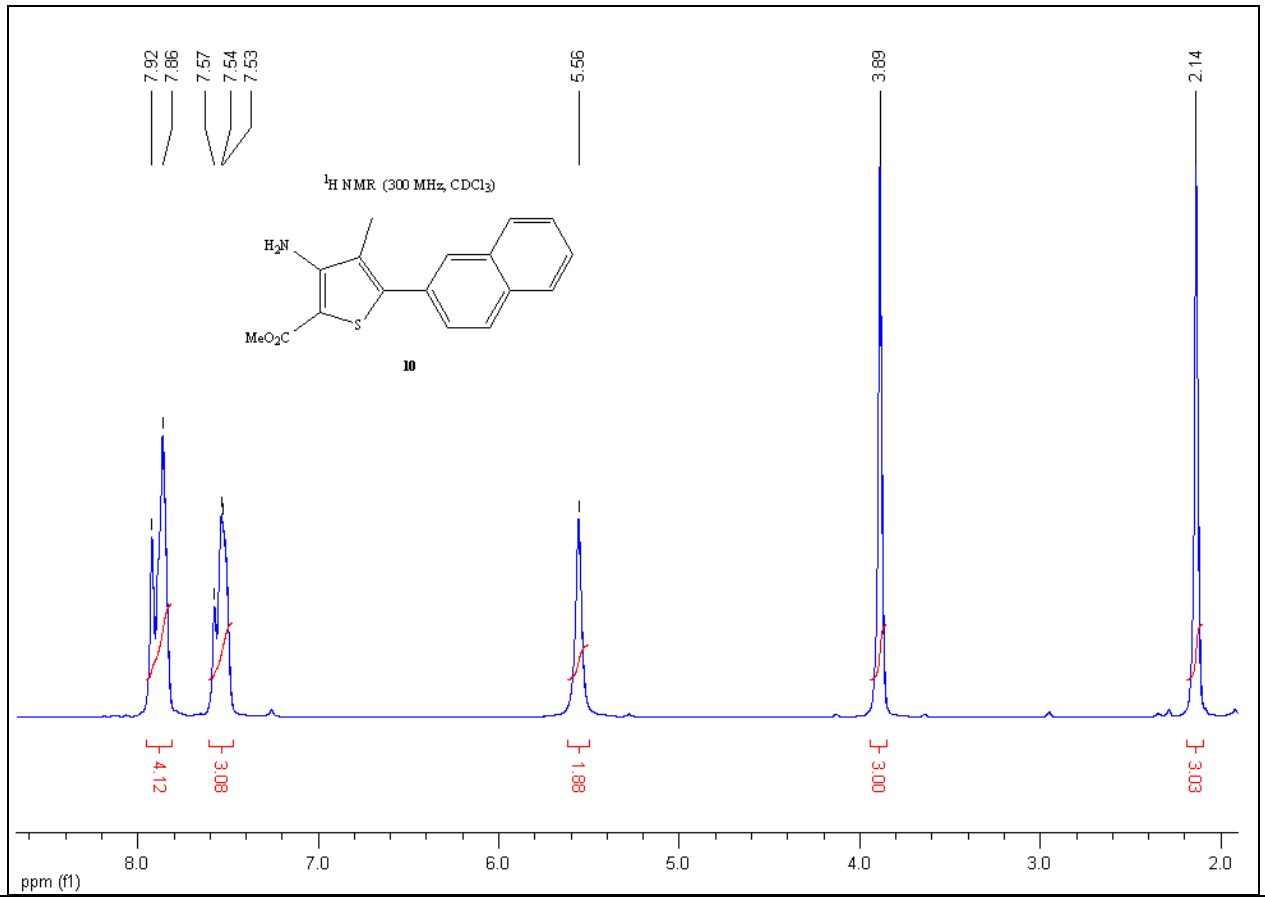

164.97
153.47
144.01
138.22
130.98
129.21
128.72
122.96
98.96
51.02
21.11
11.60
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
7
150
100
50
ppm (f1)

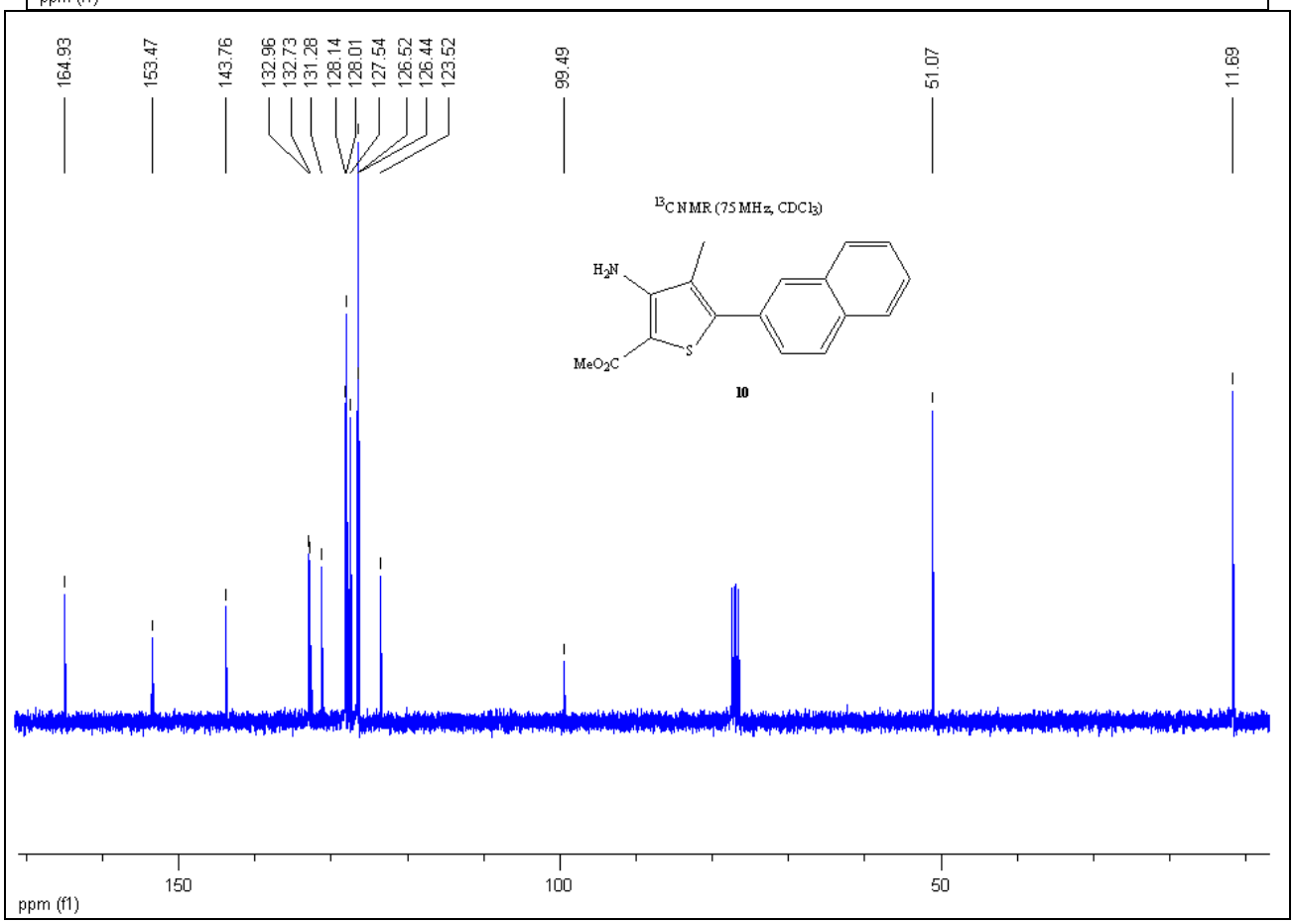

8.06
8.03
7.48
7.45
5.44
3.90
3.81
2.07
^{1}H NMR (300 MHz, CDCl$_3$)
H$_2$N
OMe
MeO$_2$C
S
8
2.00
1.96
2.05
3.13
3.12
3.10
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

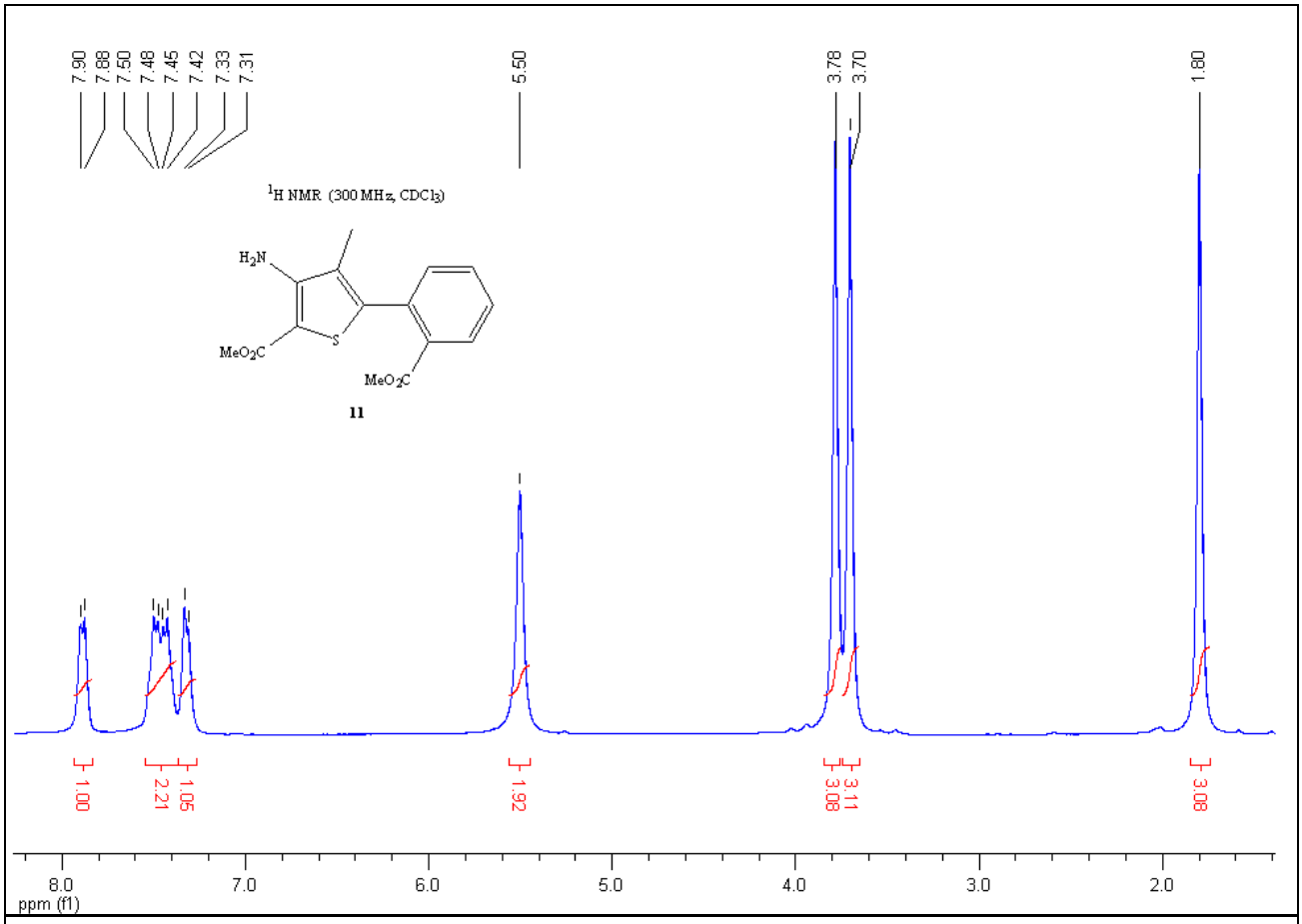

166.42
164.80
153.32
142.20
138.44
129.71
129.61
128.76
124.11
100.04
^{13}C NMR (75 MHz, CDCl$_3$)
52.10
51.14
11.75
H$_2$N
OMe
MeO$_2$C
S
8
150
100
50
ppm (f1)

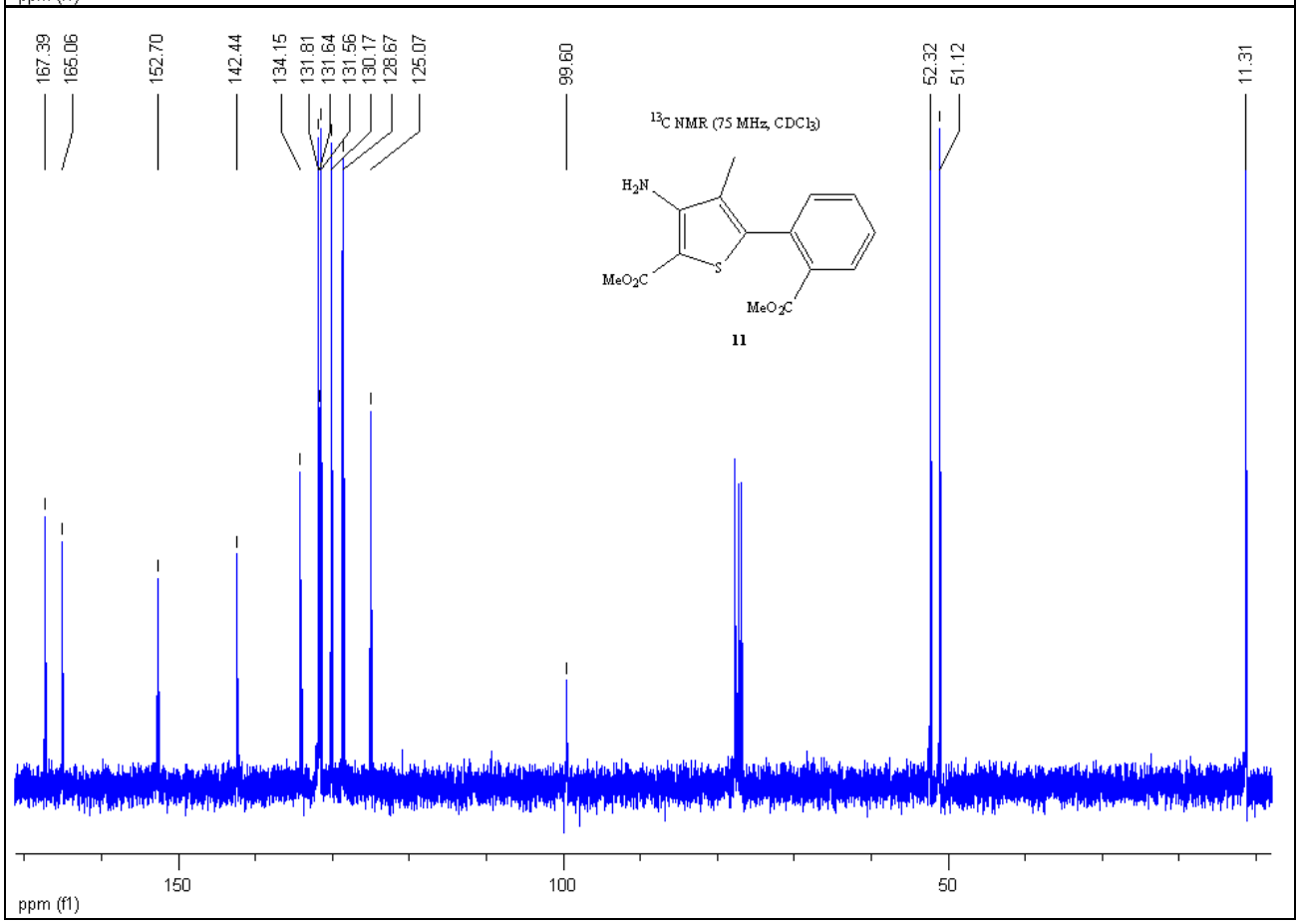

7.69
7.65
7.62
7.60
7.57
7.54
^{1}H NMR (300 MHz, CDCl$_3$)
5.50
3.85
2.09
H_2N
MeO_2C
S
CF_3
9
1.00
3.04
1.95
3.12
3.07
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

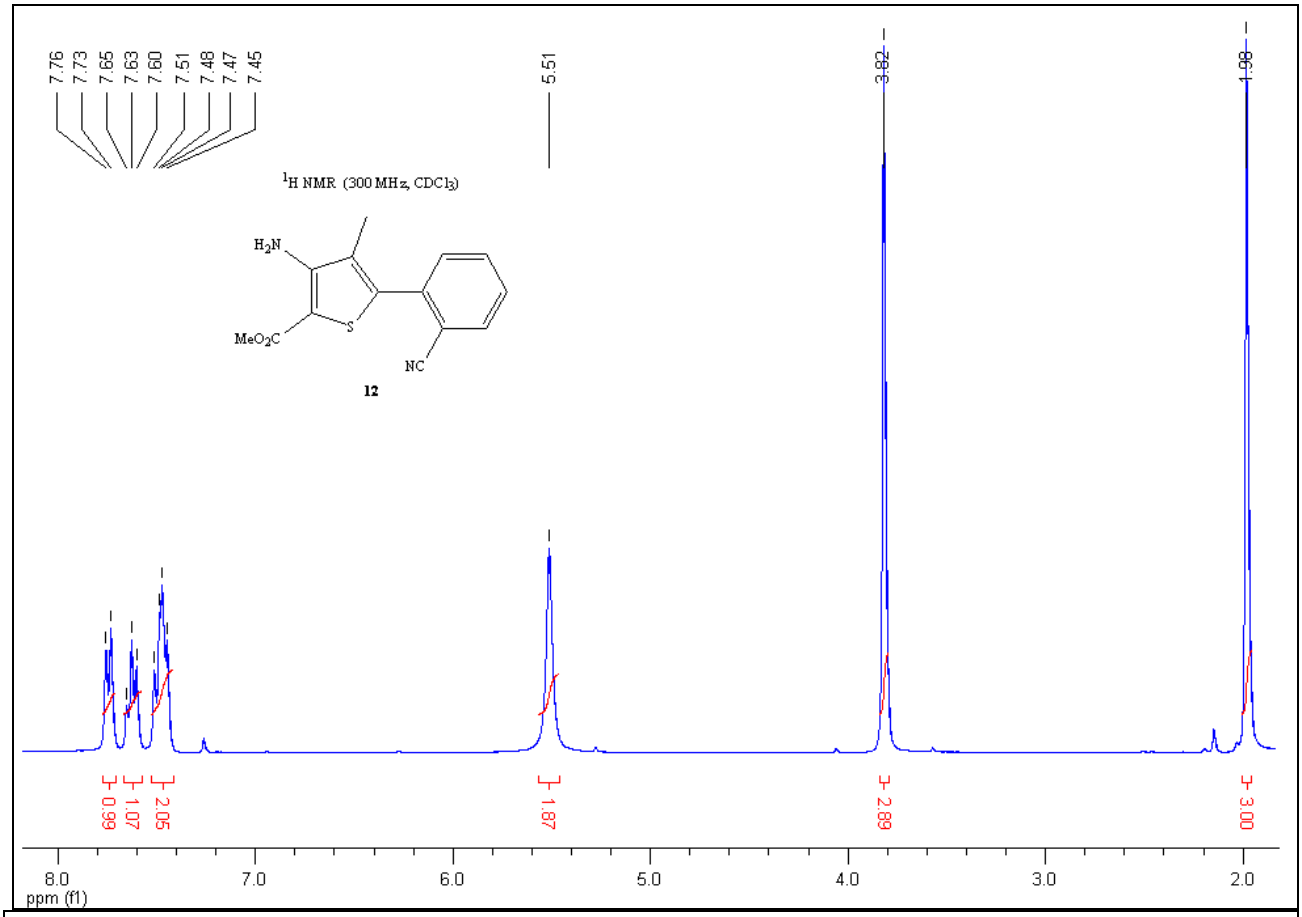

164.92
153.27
141.78
134.84
132.24
131.30
130.87
129.17
125.81
125.76
125.71
125.66
125.61
125.05
125.00
124.95
124.90
124.17
122.00
100.05
51.27
11.67
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
CF_3
9
150
100
50
ppm (f1)

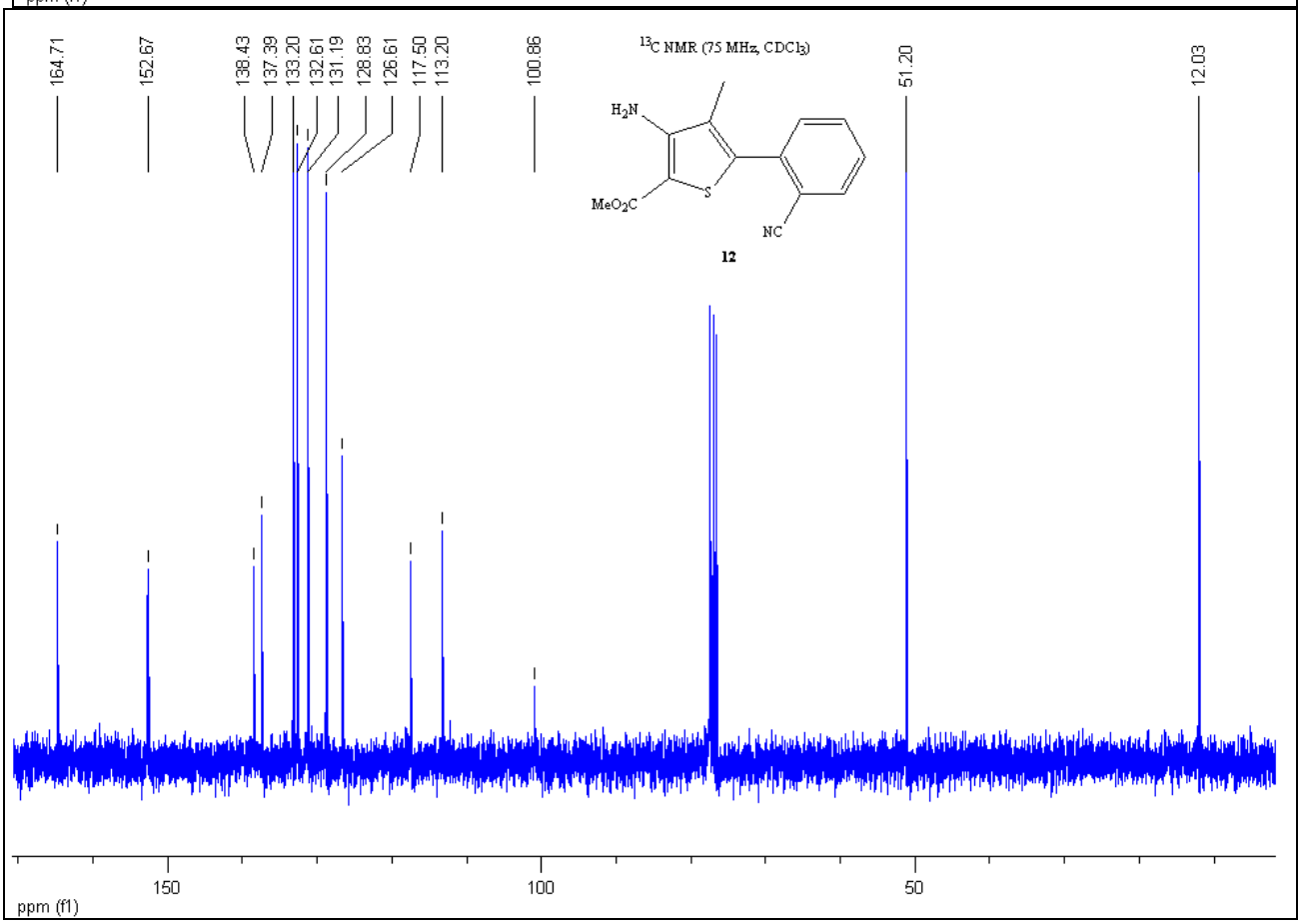

7.92
7.86
7.57
7.54
7.53
5.56
3.89
2.14
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
10
4.12
3.08
1.88
3.00
3.03
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

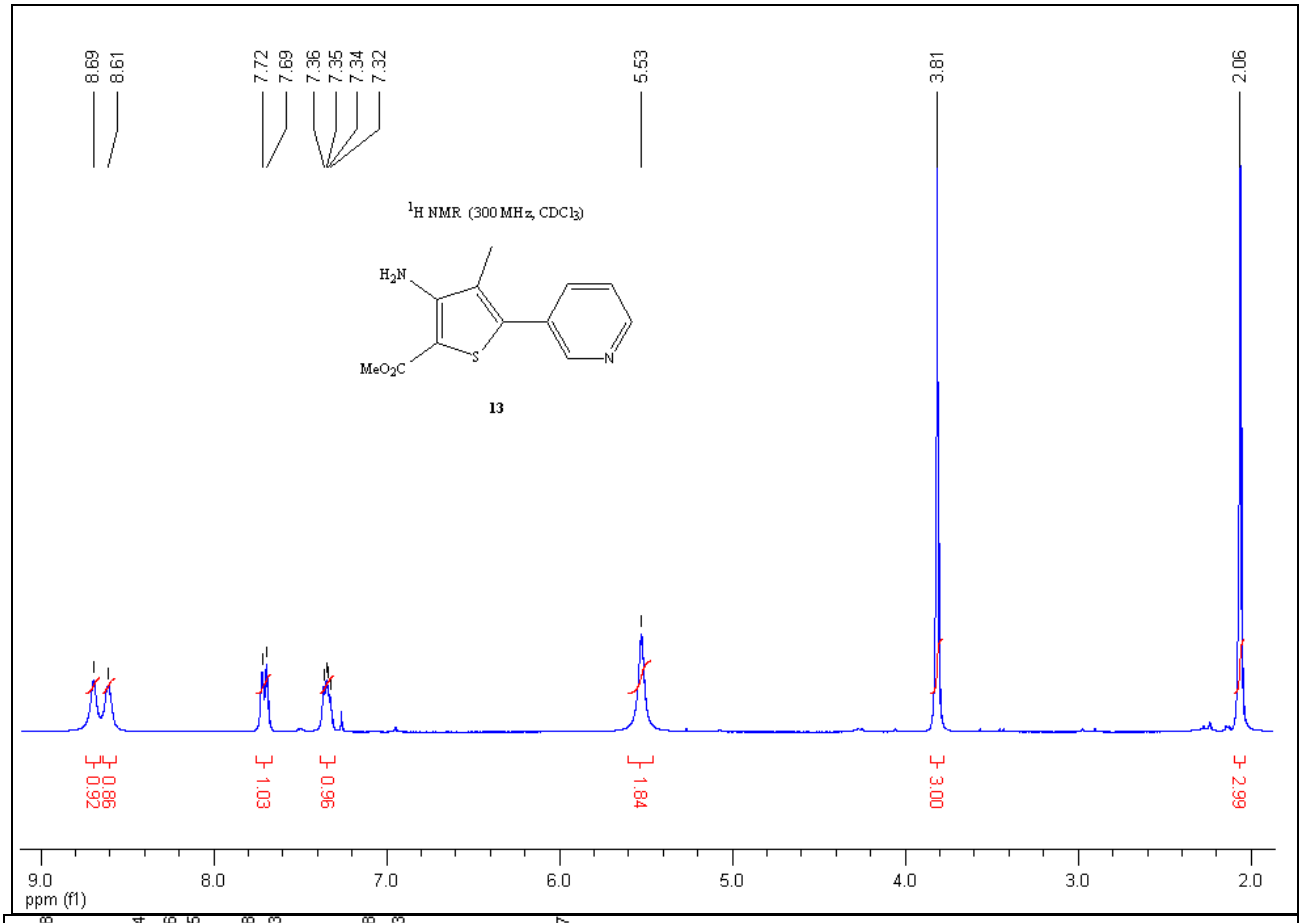

164.93
153.47
143.76
132.96
132.73
131.28
128.14
128.01
127.54
126.52
126.44
123.52
99.49
51.07
11.69
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
10
150
100
50
ppm (f1)

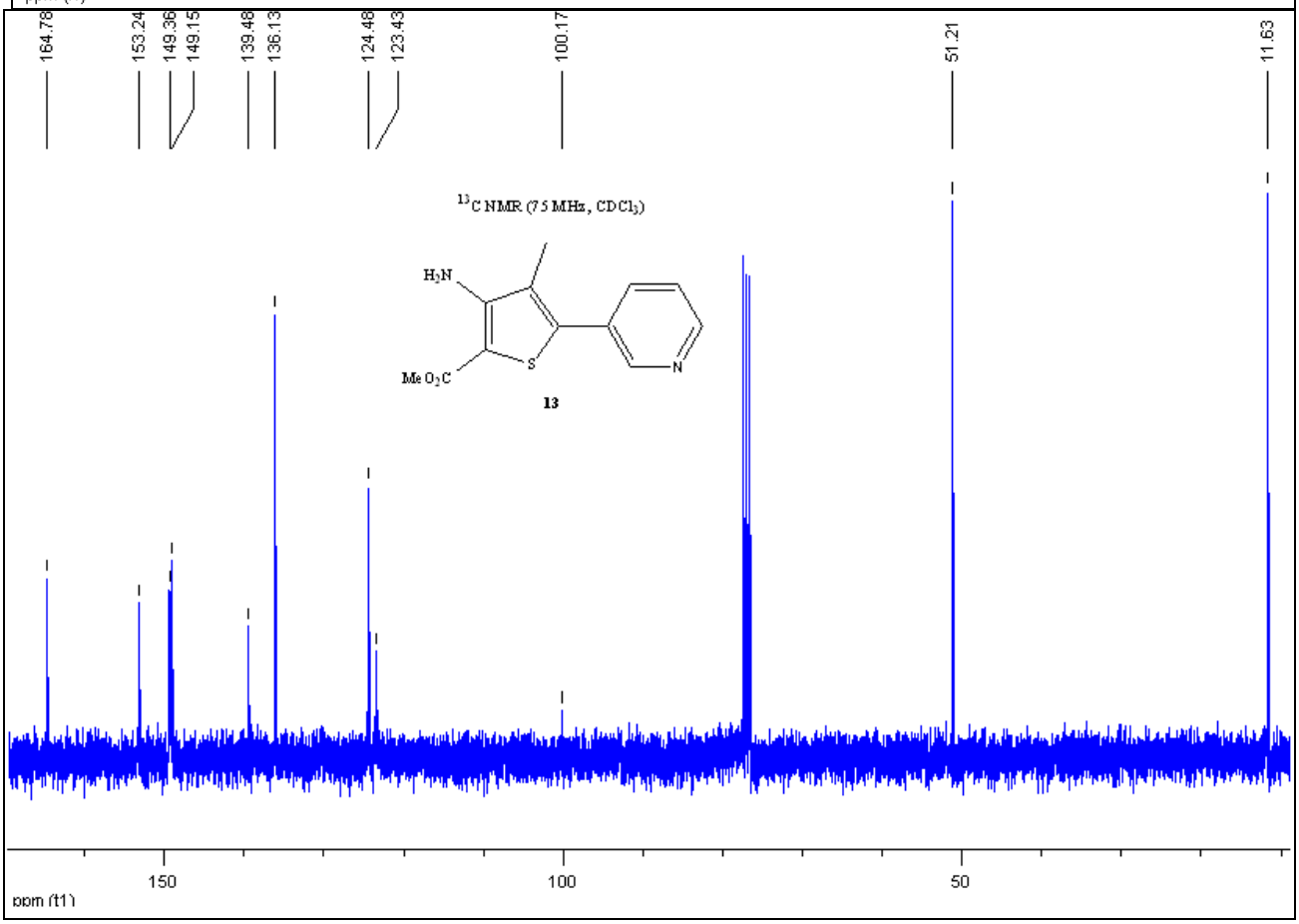

7.90
7.88
7.50
7.48
7.45
7.42
7.33
7.31
5.50
3.78
3.70
1.80
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
MeO_2C
11
1.00
2.21
1.05
1.92
3.11
3.08
3.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

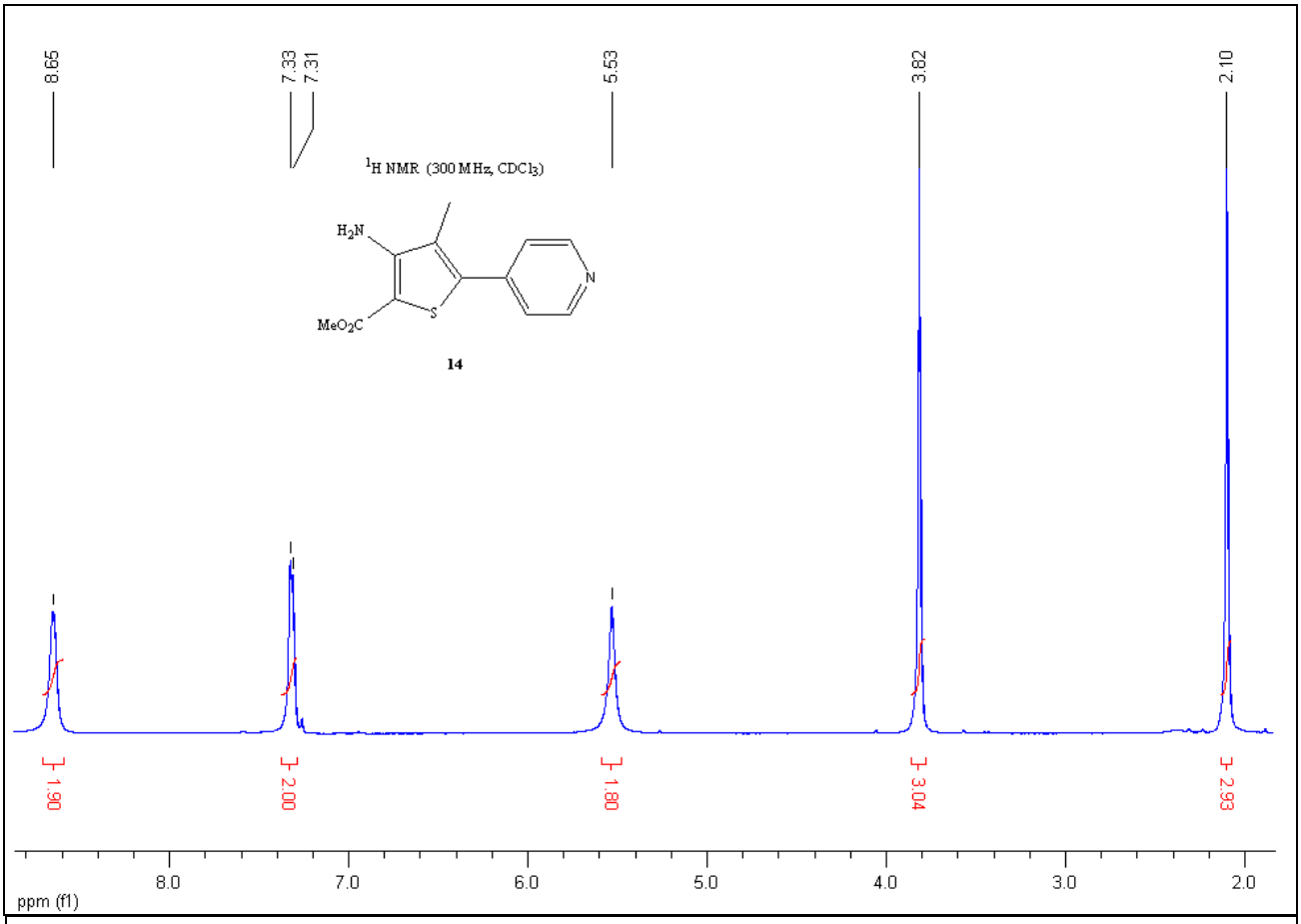

167.39
165.06
152.70
142.44
134.15
131.81
131.64
131.56
130.17
128.67
125.07
99.60
52.32
51.12
11.31
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
MeO_2C
11
150
100
50
ppm (f1)

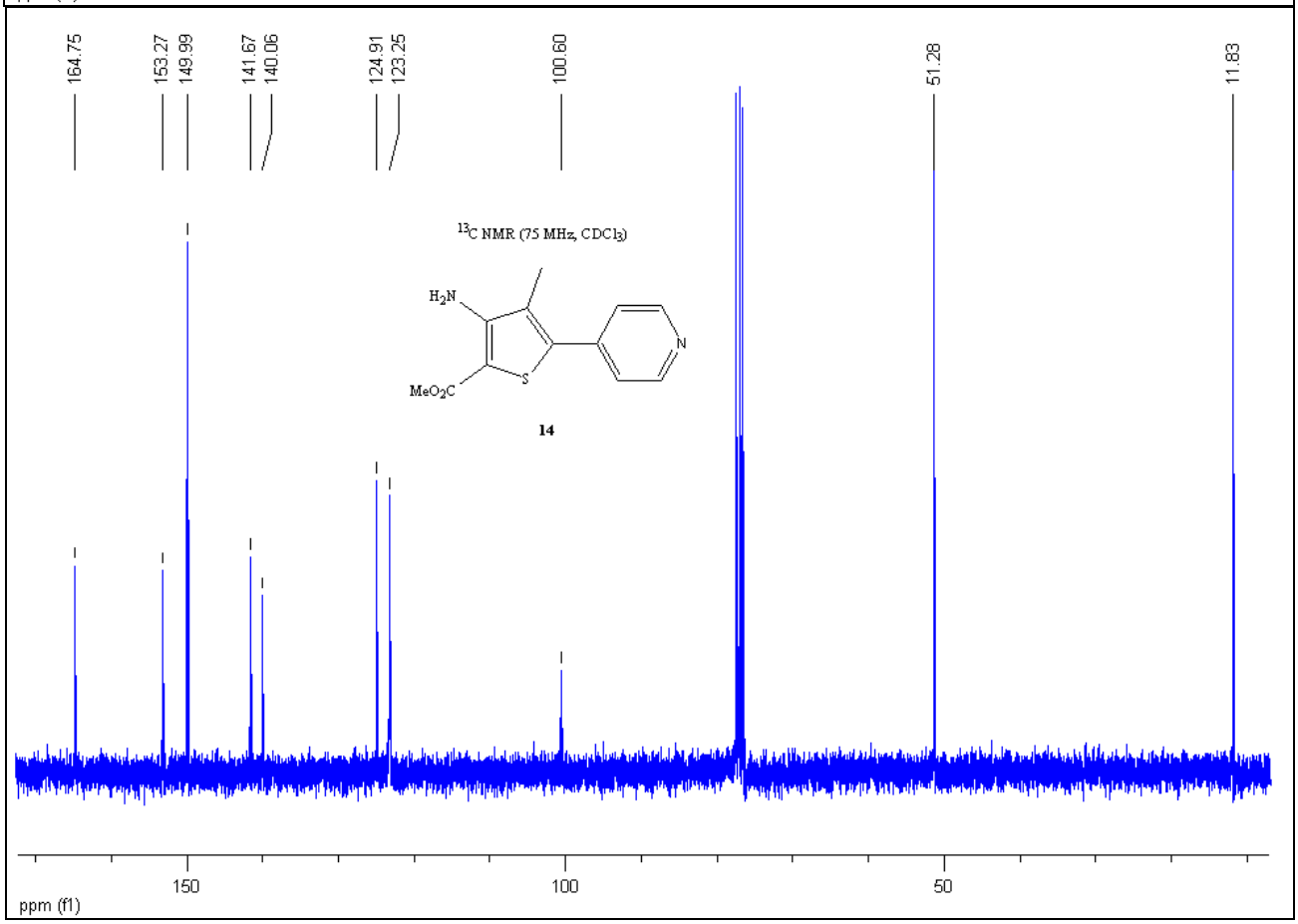

7.76
7.73
7.65
7.63
7.60
7.51
7.48
7.47
7.45
5.51
3.82
1.98
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
NC
12
0.99
1.07
2.05
1.87
2.89
3.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

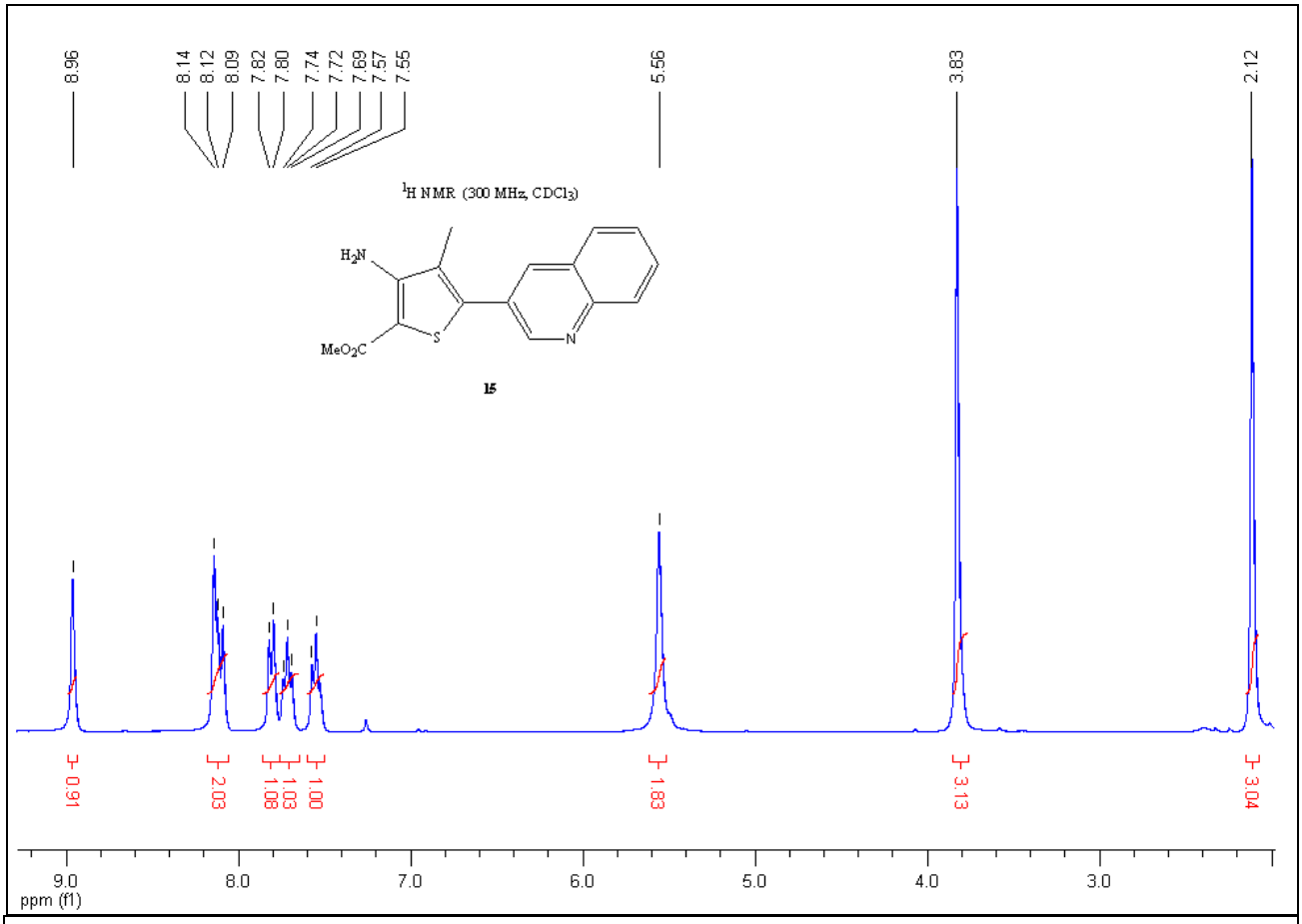

164.71
152.67
138.43
137.39
133.20
132.61
131.19
128.83
126.61
117.50
113.20
100.86
^{13}C NMR (75 MHz, CDCl$_3$)
51.20
12.03
H_2N
MeO_2C
S
NC
12
150
100
50
ppm (f1)

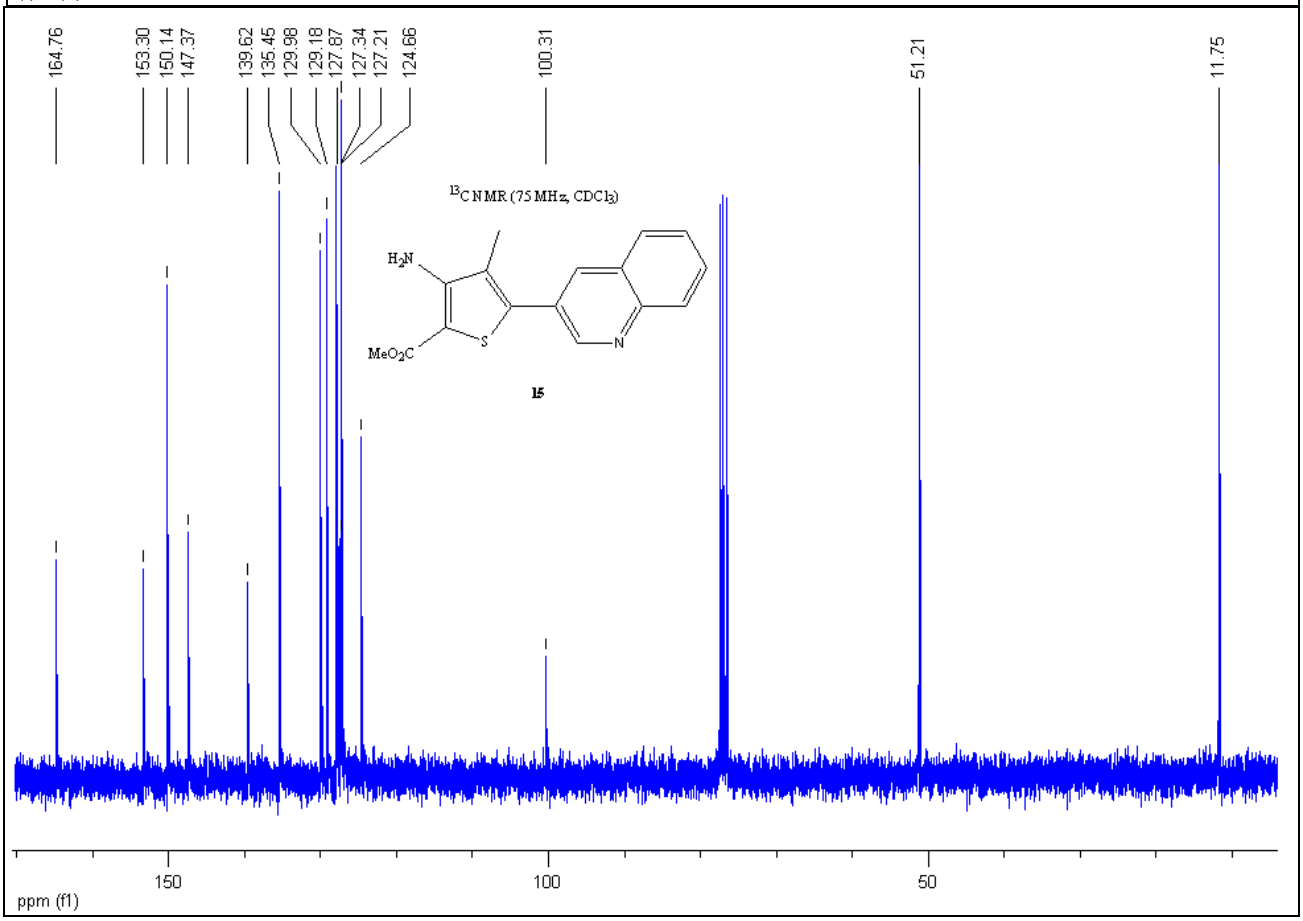

8.69
8.61
7.72
7.69
7.36
7.35
7.34
7.32
5.53
3.81
2.06
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
N
13
0.92
0.80
1.03
0.96
1.84
3.00
2.99
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

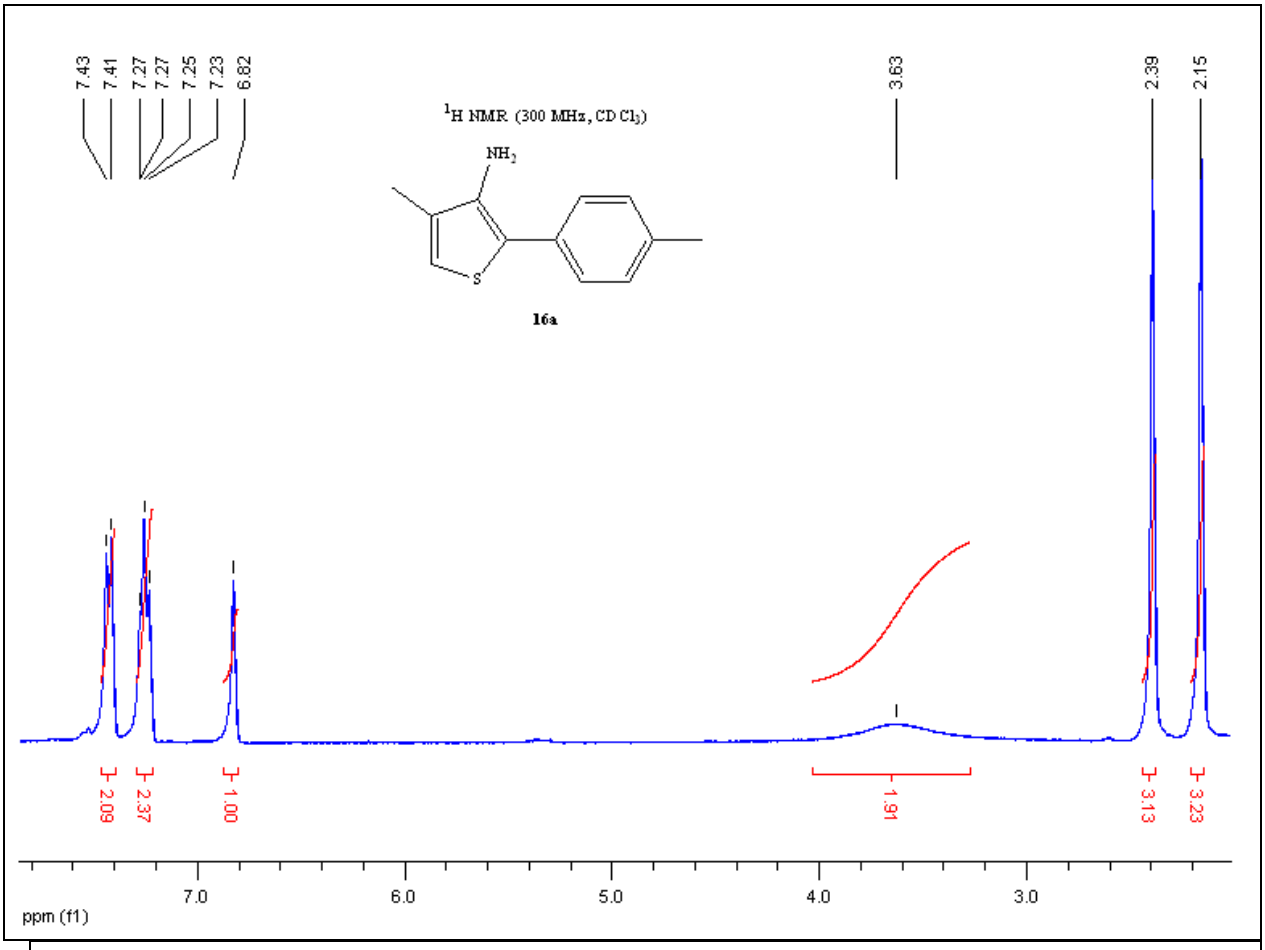

164.78
153.24
149.36
149.15
139.48
136.13
124.48
123.43
100.17
51.21
11.63
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
$Me O_2C$
S
N
13
150
100
50
ppm (f1)

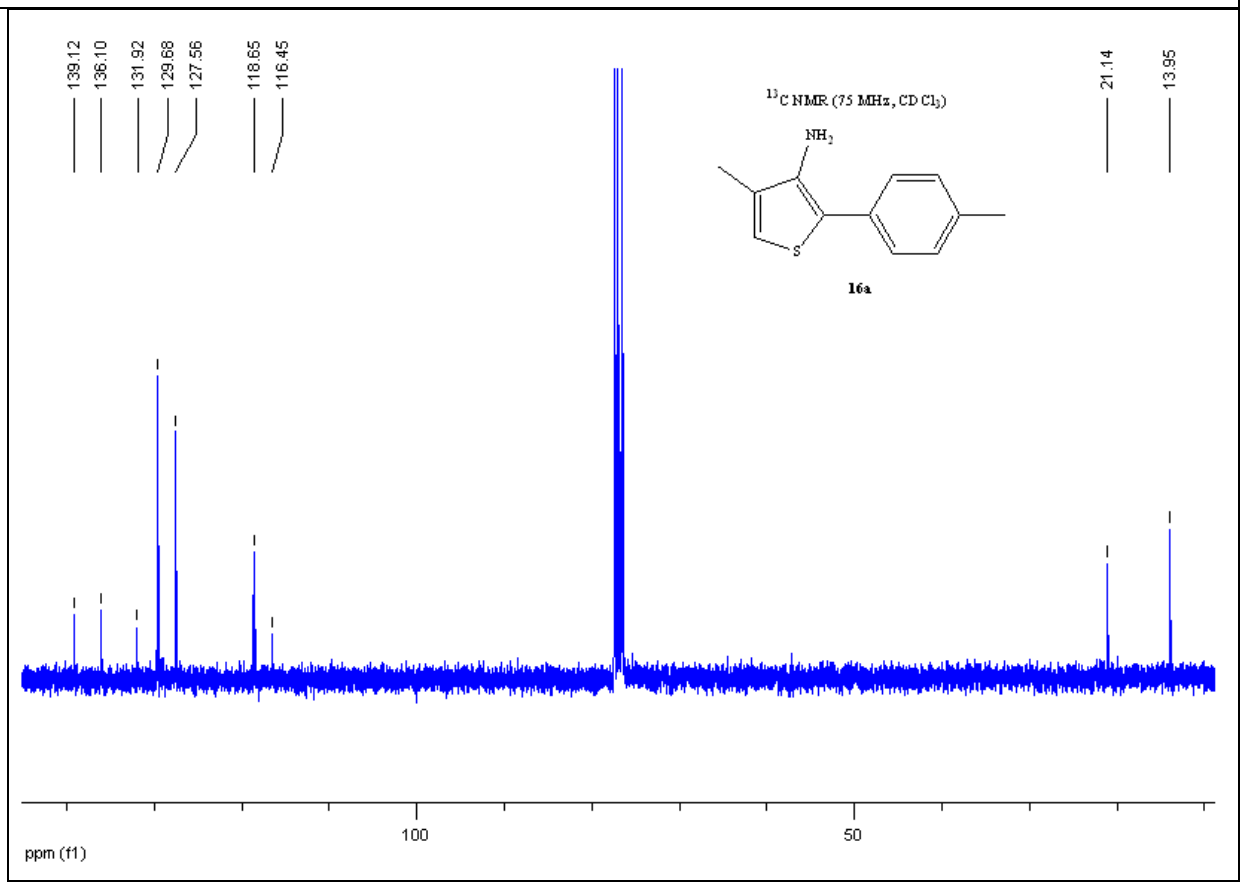

8.65
7.33
7.31
5.53
3.82
2.10
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
N
14
1.90
2.00
1.80
3.04
2.93
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

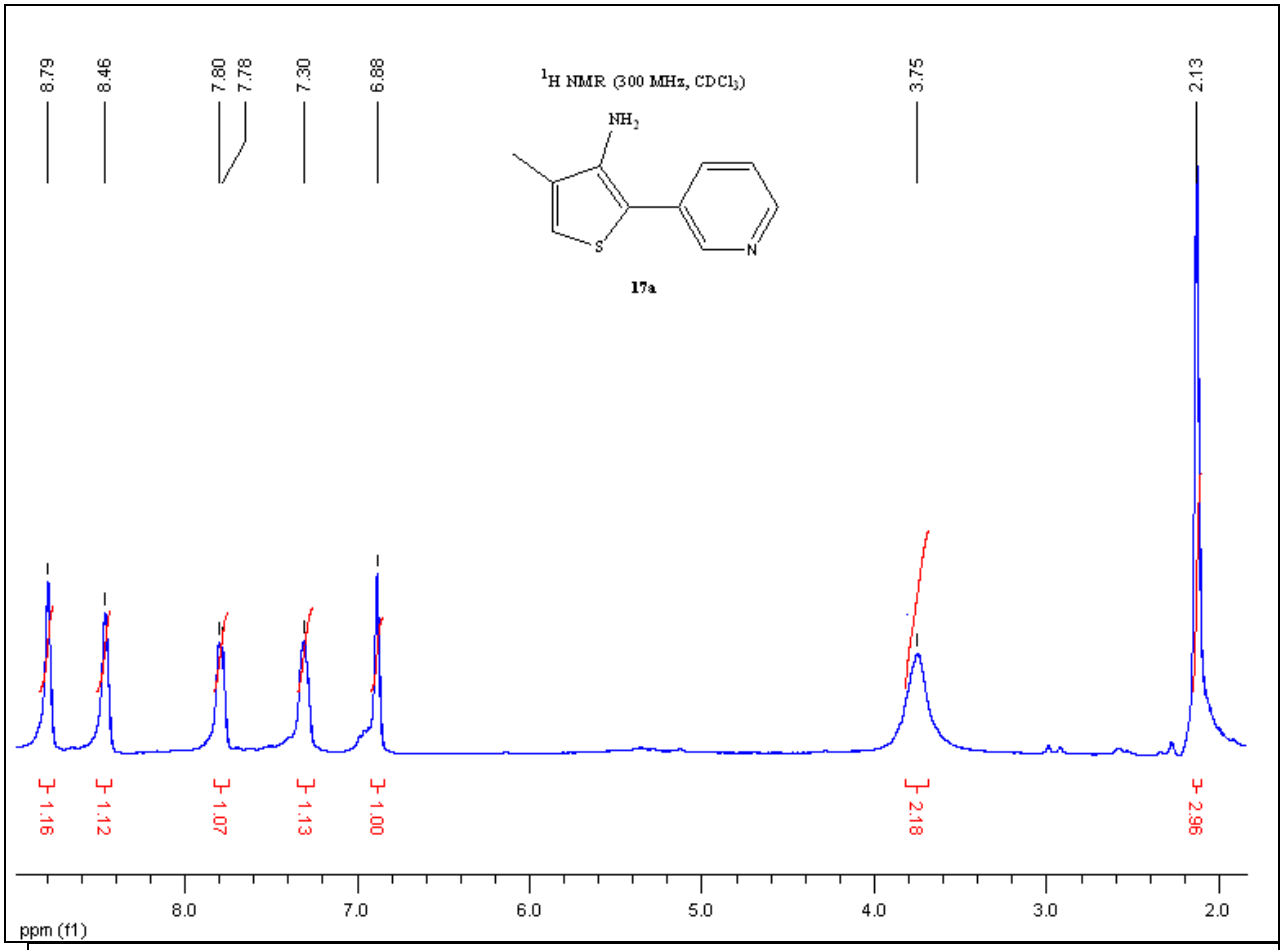

164.75
153.27
149.99
141.67
140.06
124.91
123.25
100.60
51.28
11.83
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
N
14
150
100
50
ppm (f1)

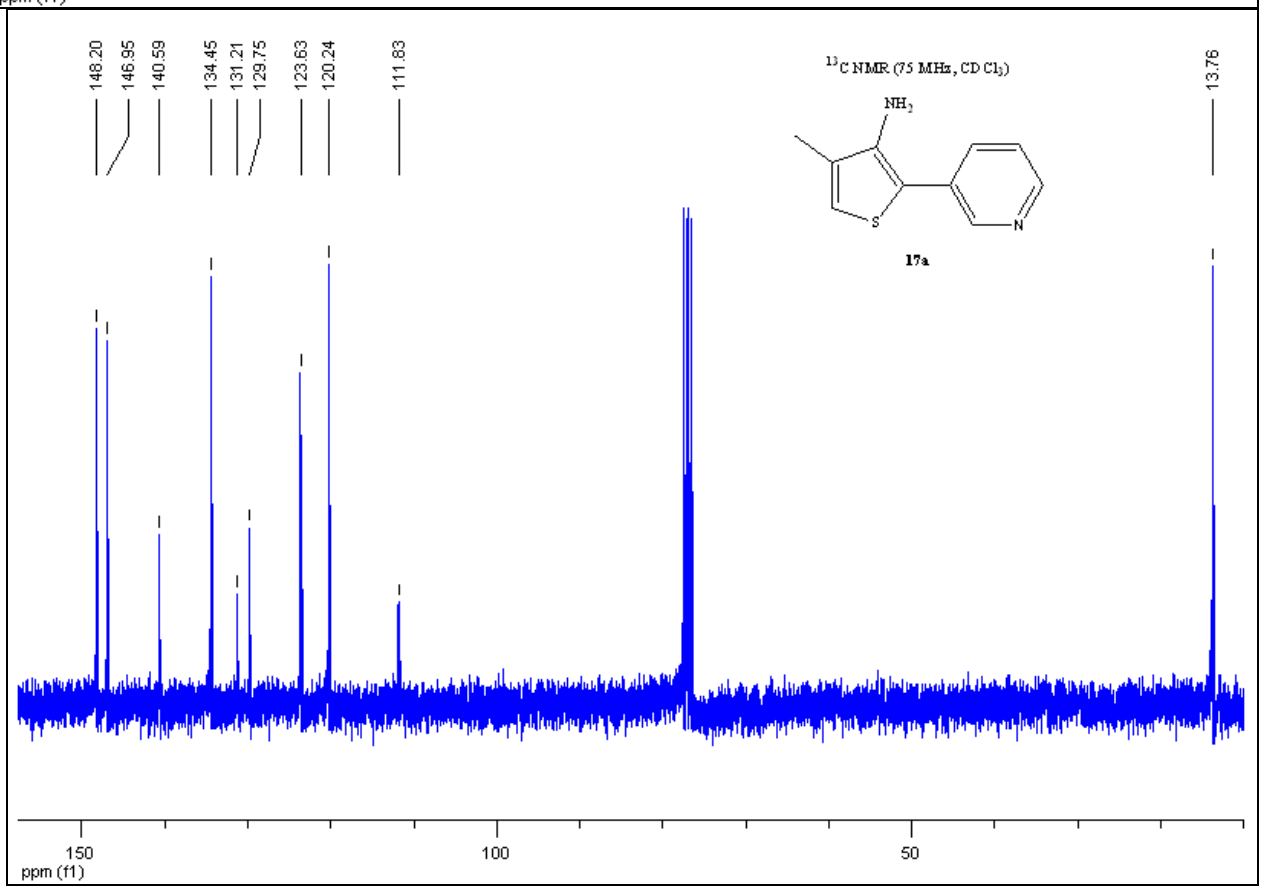

8.96
8.14
8.12
8.09
7.82
7.80
7.74
7.72
7.69
7.57
7.55
5.56
3.83
2.12
^{1}H NMR (300 MHz, CDCl$_3$)
H_2N
MeO_2C
S
N
15
0.91
2.03
1.08
1.03
1.00
1.83
3.13
3.04
9.0
8.0
7.0
6.0
5.0
4.0
3.0
ppm (f1)

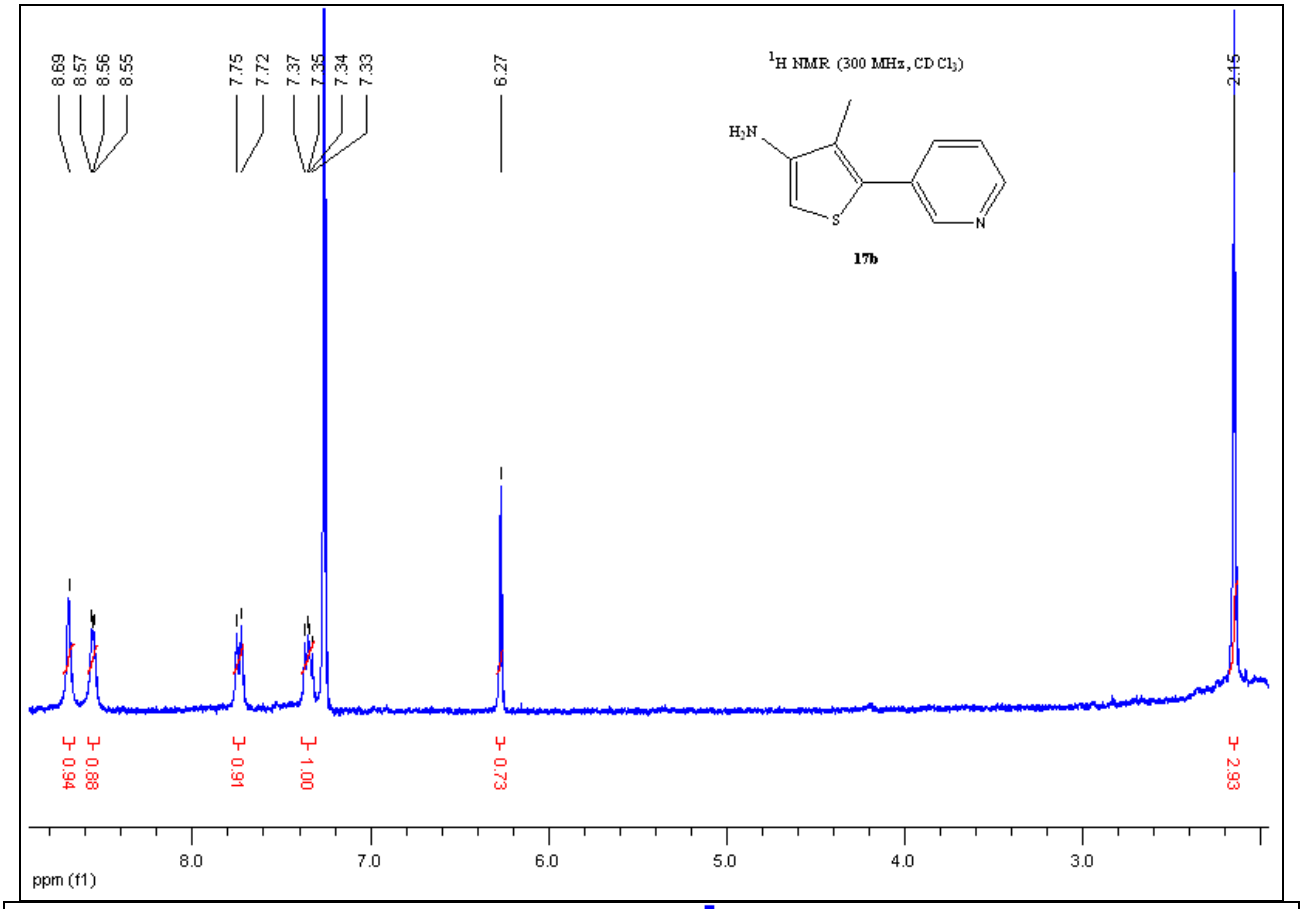

164.76
153.30
150.14
147.37
139.62
135.45
129.98
129.18
127.87
127.34
127.21
124.66
100.31
51.21
11.75
^{13}C NMR (75 MHz, CDCl$_3$)
H_2N
MeO_2C
S
N
15
150
100
50
ppm (f1)

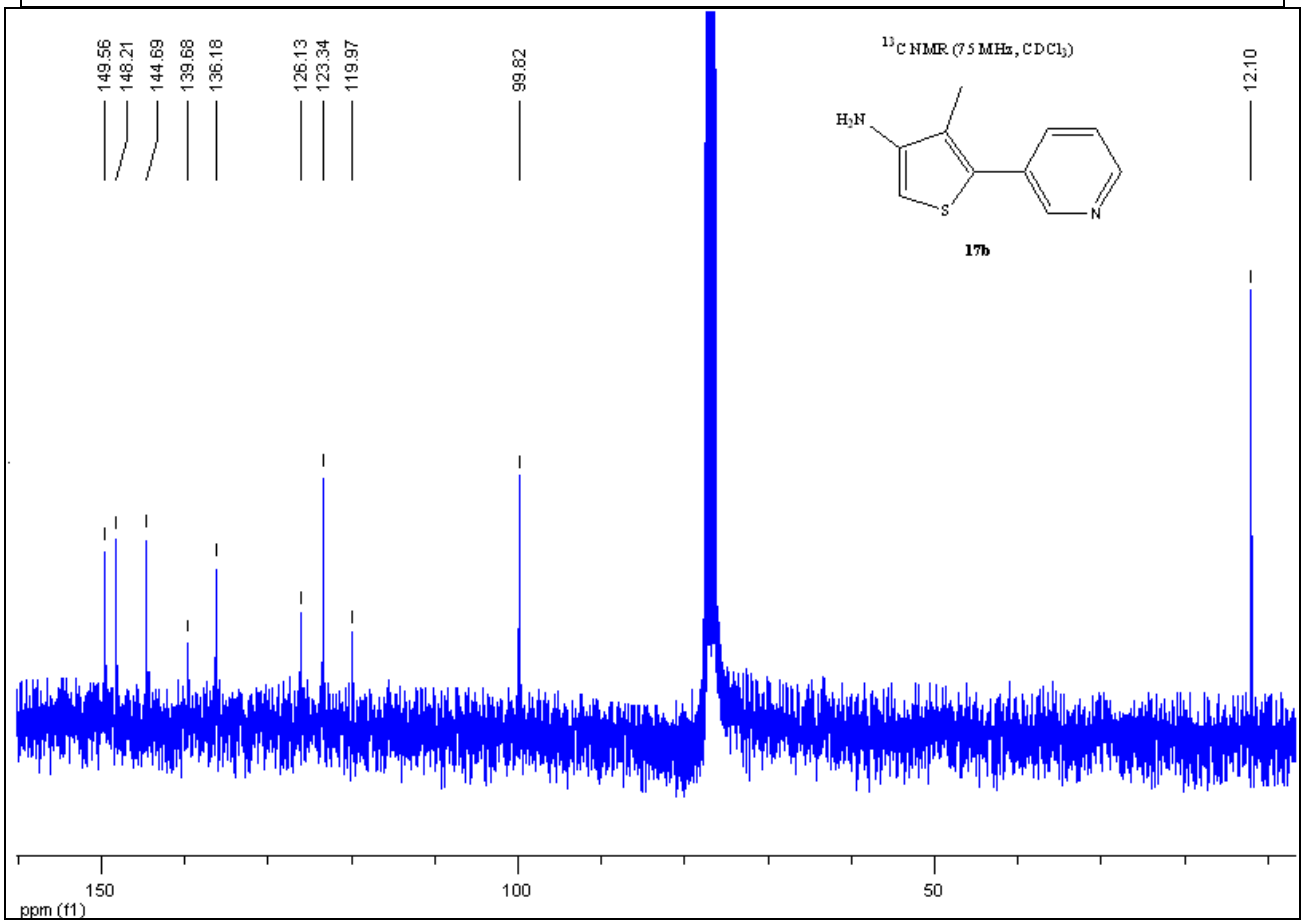

7.43
7.41
7.27
7.27
7.25
7.23
6.82
3.63
2.39
2.15
^{1}H NMR (300 MHz, CD Cl$_3$)
NH$_2$
S
16a
2.09
2.37
1.00
1.91
3.13
3.23
7.0
6.0
5.0
4.0
3.0
ppm (f1)

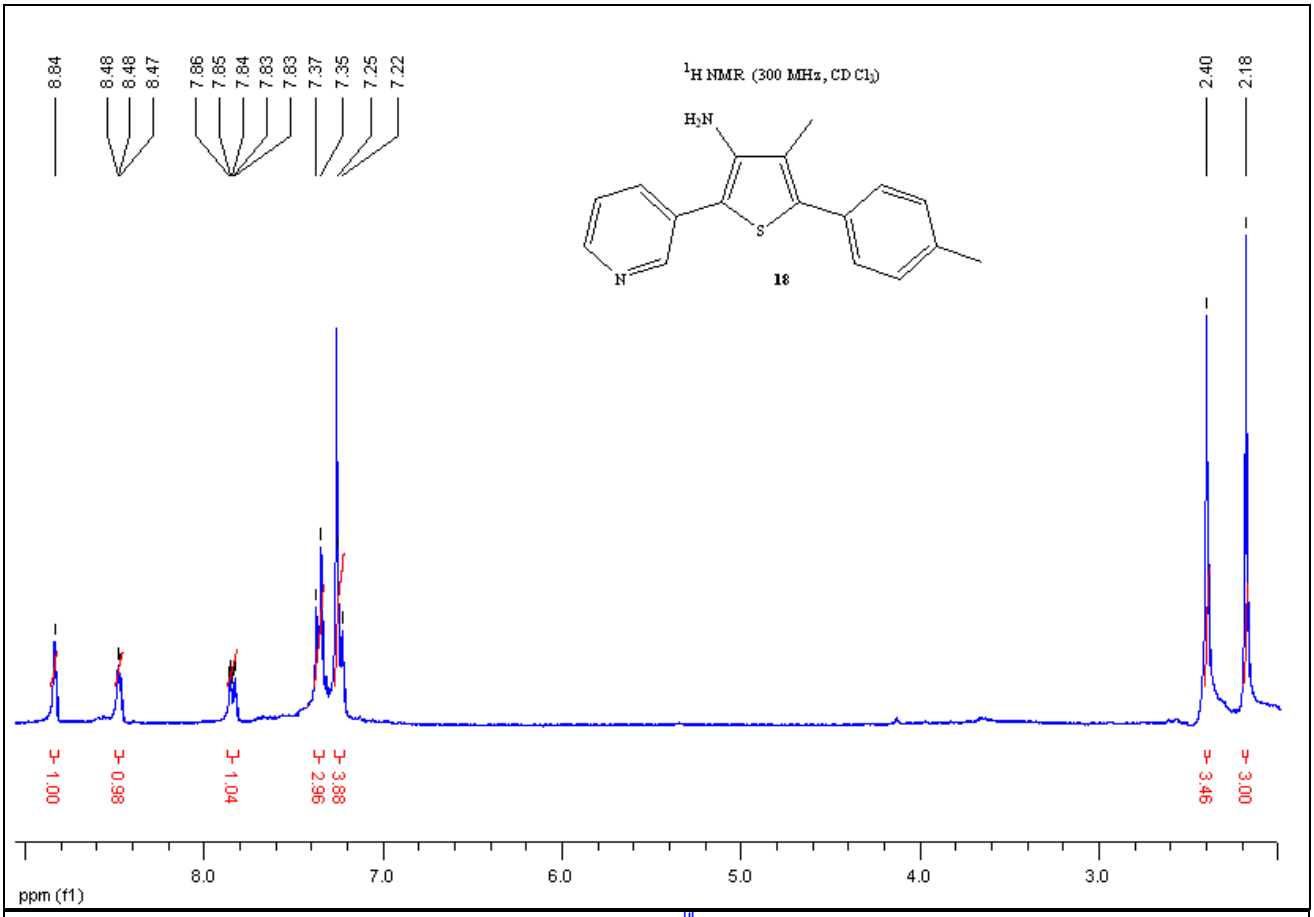

139.12
136.10
131.92
129.68
127.56
118.65
116.45
21.14
13.95
^{13}C NMR (75 MHz, CD Cl$_3$)
NH$_2$
S
16a
100
50
ppm (f1)


8.79
8.46
7.80
7.78
7.30
6.88
3.75
2.13
^{1}H NMR (300 MHz, CDCl$_3$)
NH$_2$
S
N
17a
1.16
1.12
1.07
1.13
1.00
2.18
2.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)


148.20
146.95
140.59
134.45
131.21
129.75
123.63
120.24
111.83
13.76
^{13}C NMR (75 MHz, CDCl$_3$)
NH$_2$
S
N
17a
150
100
50
ppm (f1)

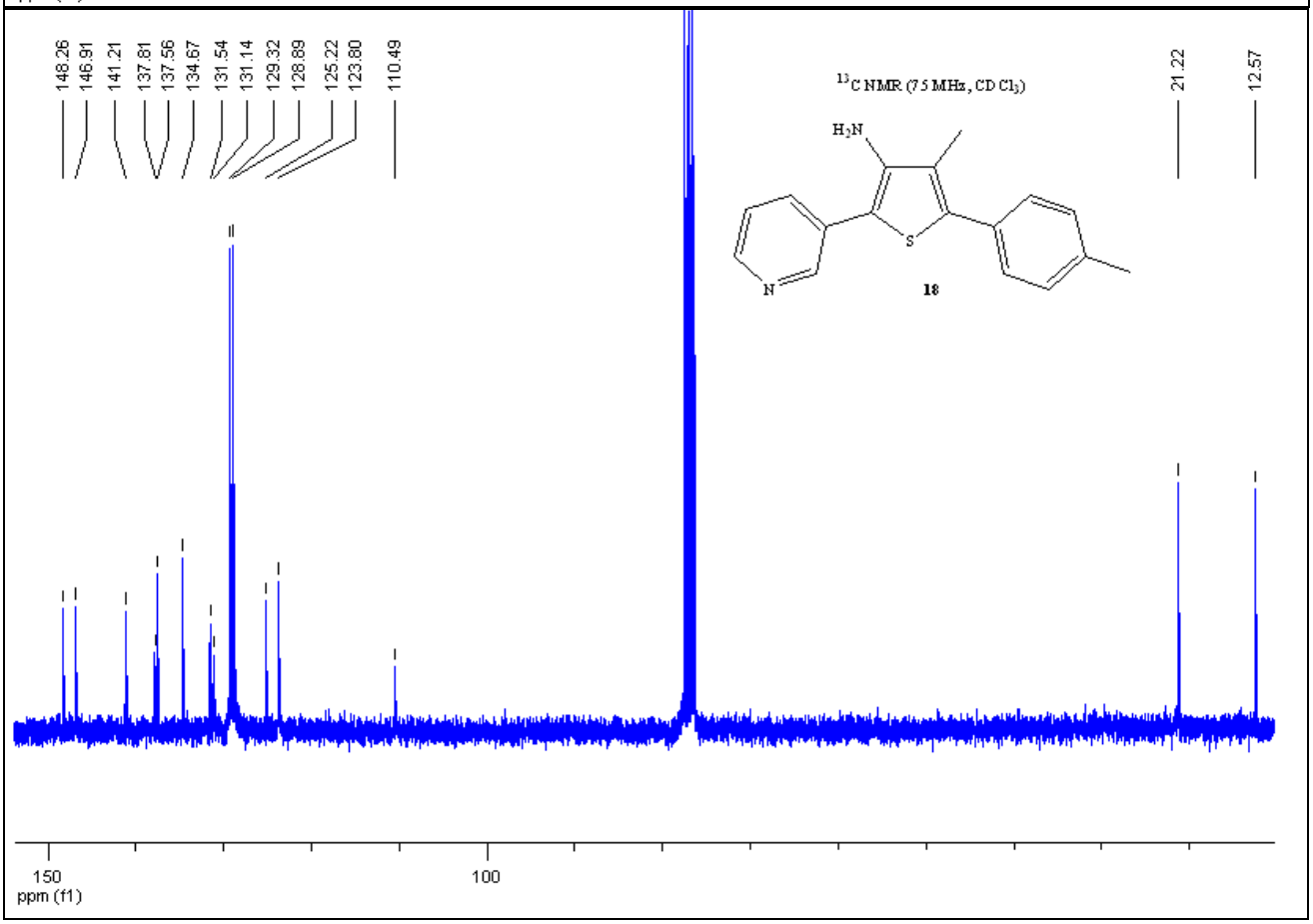

8.69
8.57
8.56
8.55
7.75
7.72
7.37
7.35
7.34
7.33
6.27
2.45
^{1}H NMR (300 MHz, CDCl$_3$)
H$_2$N
S
N
17b
3- 0.94
3- 0.88
3- 0.91
3- 1.00
3- 0.73
3- 2.83
8.0
7.0
6.0
5.0
4.0
3.0
ppm (f1)


149.56
148.21
144.69
139.68
136.18
126.13
123.34
119.97
99.82
12.10
^{13}C NMR (75 MHz, CDCl$_3$)
H$_2$N
S
N
17b
150
100
50
ppm (f1)



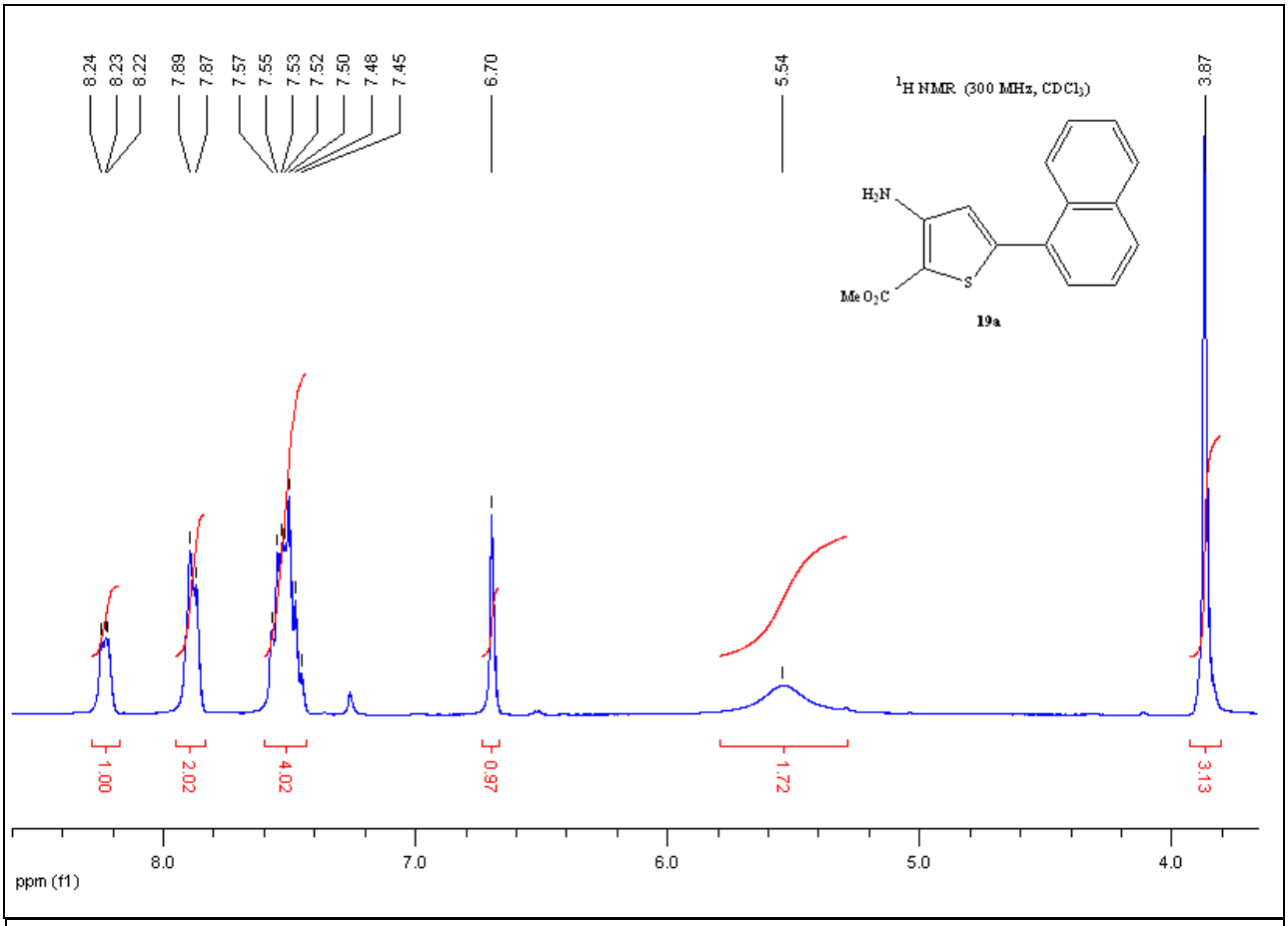
^{1}H NMR (300 MHz, $CDCl_3$)

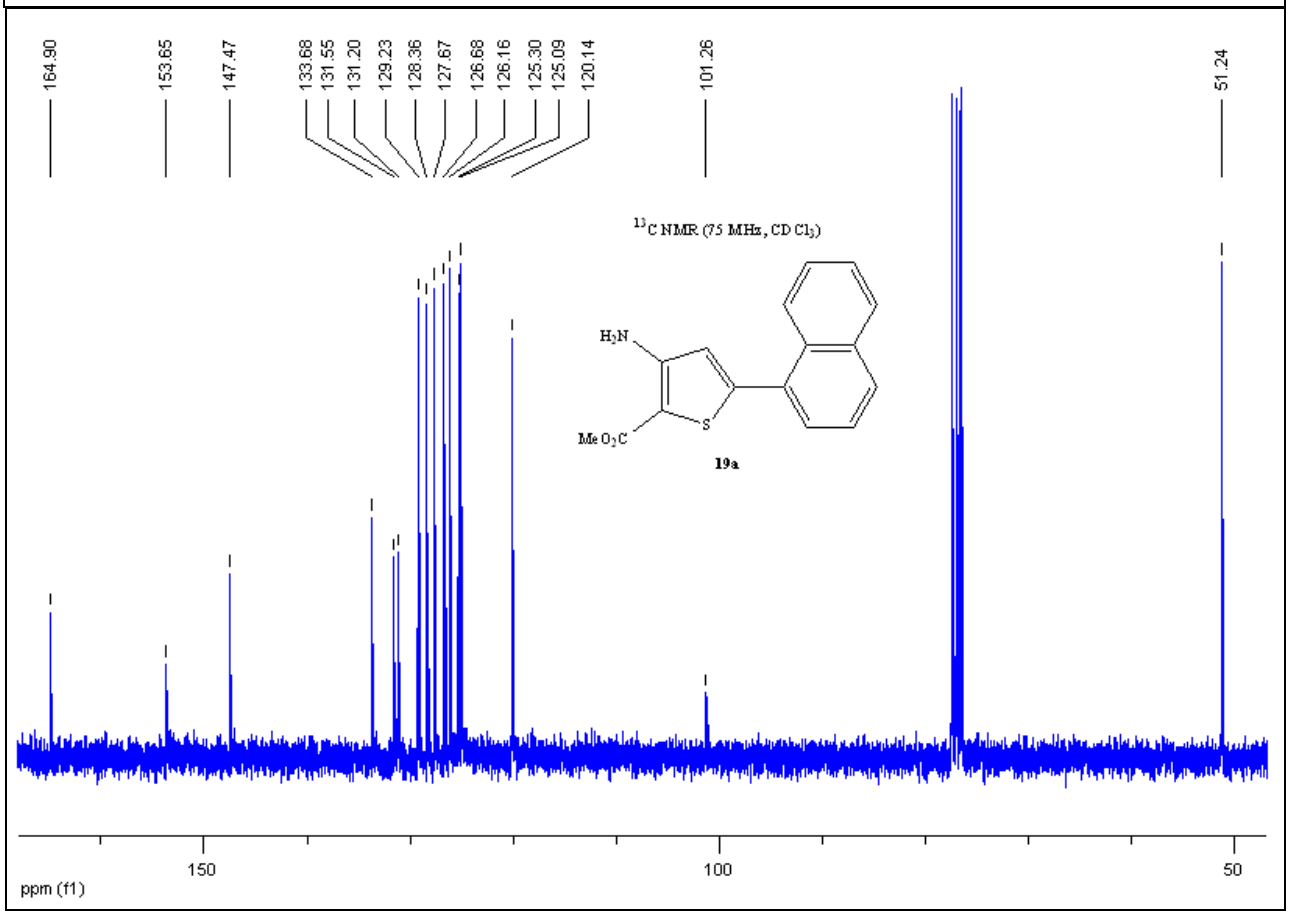
18

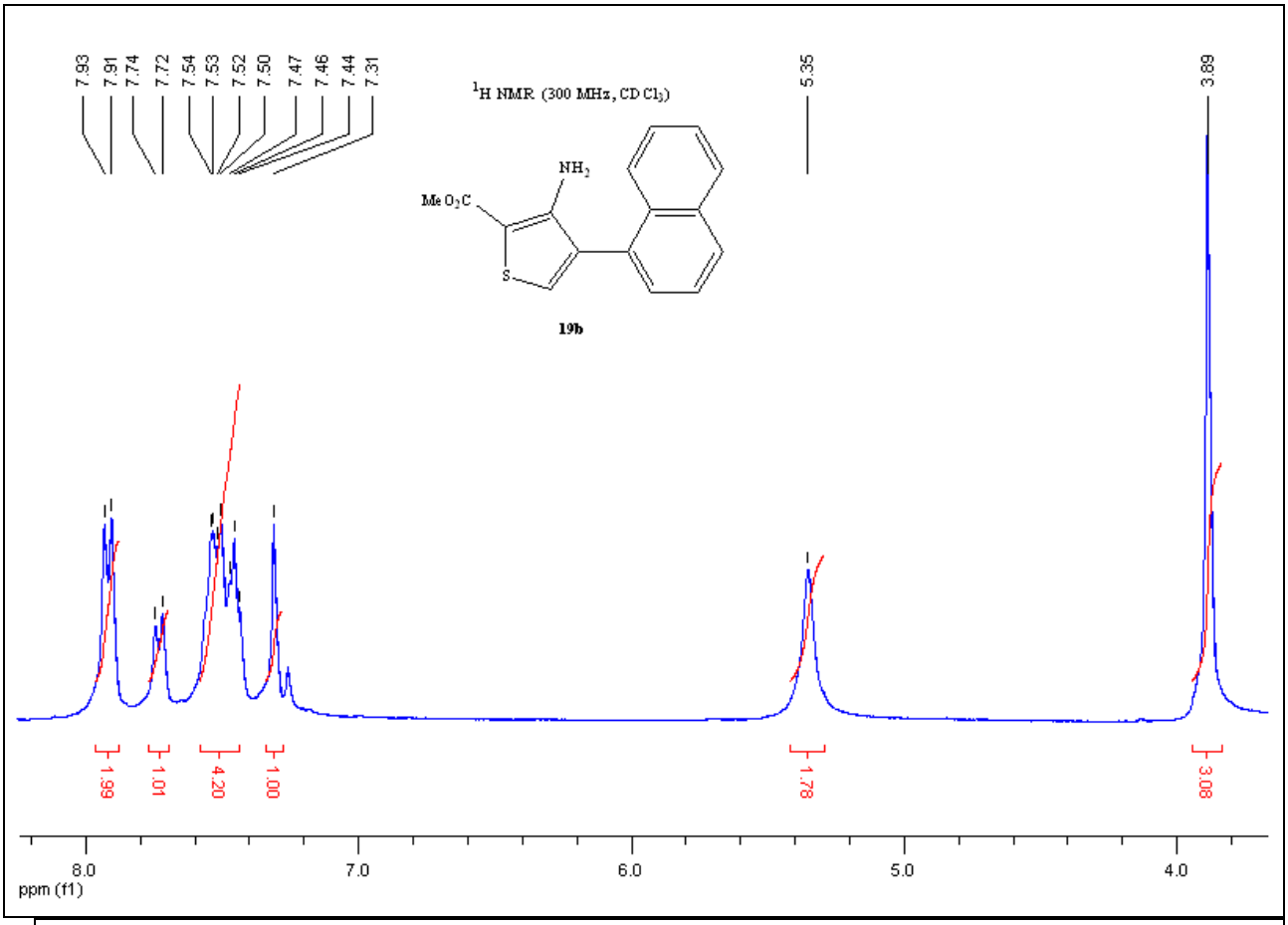


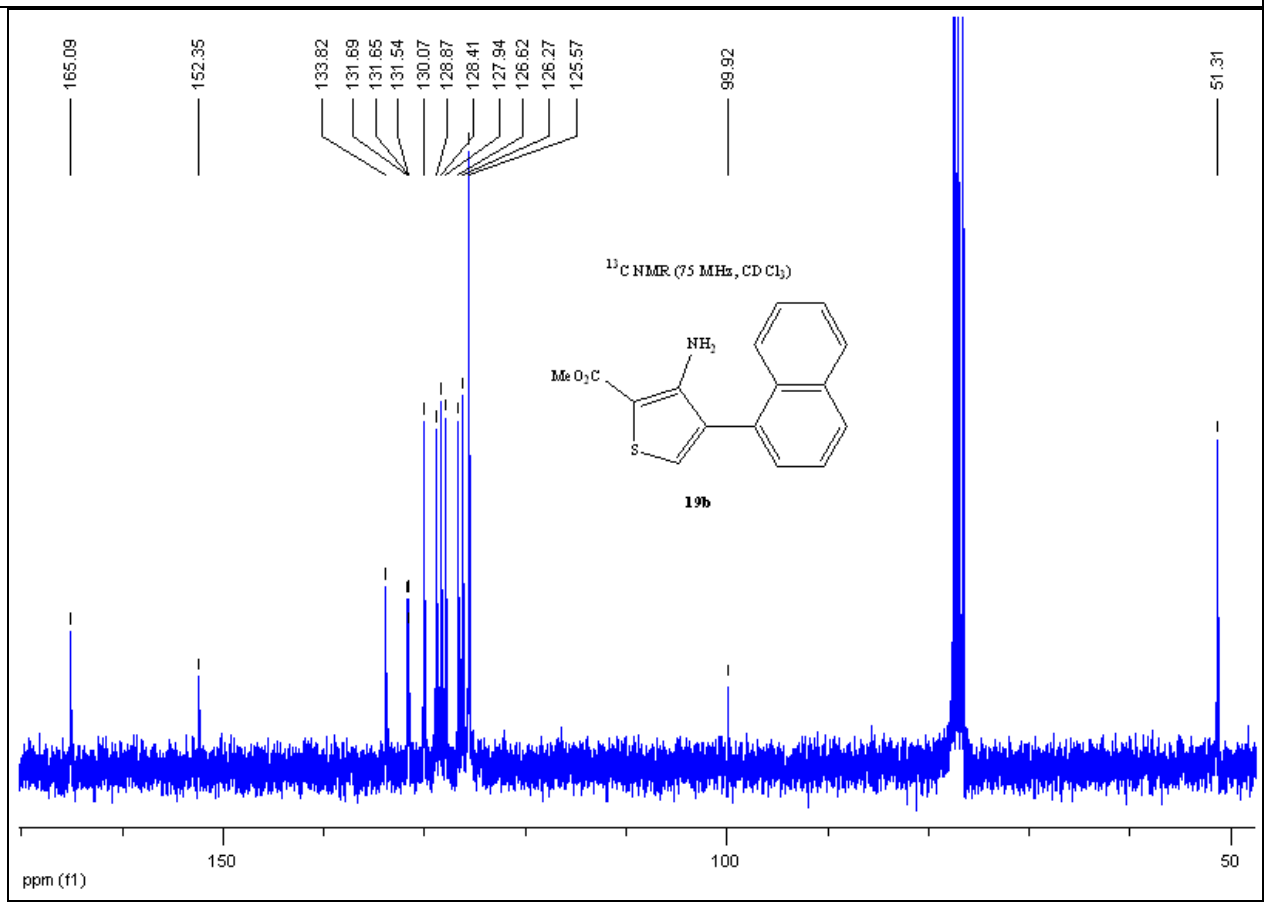
^{13}C NMR (75 MHz, $CDCl_3$)

18


8.24
8.23
8.22
7.89
7.87
7.57
7.55
7.53
7.52
7.50
7.48
7.45
6.70
5.54
3.87
^{1}H NMR (300 MHz, CDCl$_3$)
H$_2$N
MeO$_2$C
S
19a
1.00
2.02
4.02
0.97
1.72
3.13
8.0
7.0
6.0
5.0
4.0
ppm (f1)


164.90
153.65
147.47
133.68
131.55
131.20
129.23
128.36
127.67
126.68
126.16
125.30
125.09
120.14
101.26
51.24
^{13}C NMR (75 MHz, CDCl$_3$)
H$_2$N
MeO$_2$C
S
19a
150
100
50
ppm (f1)


7.93
7.91
7.74
7.72
7.54
7.53
7.52
7.50
7.47
7.46
7.44
7.31
5.35
3.89
^{1}H NMR (300 MHz, CD Cl$_3$)
NH$_2$
Me O$_2$C
S
19b
1.99
1.01
4.20
1.00
1.78
3.08
8.0
7.0
6.0
5.0
4.0
ppm (f1)


165.09
152.35
133.82
131.69
131.65
131.54
130.07
128.87
128.41
127.94
126.62
126.27
125.57
99.92
51.31
^{13}C NMR (75 MHz, CD Cl$_3$)
NH$_2$
Me O$_2$C
S
19b
150
100
50
ppm (f1)