Synthesis and evaluation of new 2-aminothiophenes against *Mycobacterium tuberculosis*

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COSY of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27)**[1]

HMQC of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27)**[1]

^{1}H-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(28)**

^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(28)**

COSY of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(28)**

HMQC of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(28)**

^{1}H-NMR of compound 6-(t*ert*-butyl) 3-ethyl 2-(perfluorobenzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(29)**

^{13}C-NMR of compound 6-(t*ert*-butyl) 3-ethyl 2-(perfluorobenzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(29)**

^{1}H-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30)**

^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30)**

COSY of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30)**

^{1}H-NMR of compound ethyl 2-acetamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(31)**[6]

^{13}C-NMR of compound ethyl 2-acetamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(31)**[6]

^{1}H-NMR of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32)**

^{13}C-NMR of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32)**

COSY of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32)**

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^{13}C-NMR of compound ethyl 6-ethyl-2-(perfluorobenzamido)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(33)**

^{1}H-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34)**

^{13}C-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34)**

COSY of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34)**

^{1}H-NMR of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35)**

^{13}C-NMR of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35)**

COSY of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35)**

HMQC of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35)**

^{1}H-NMR of compound Ethyl 2-acetamido-4,5,6,7-tetrahydrobenzo[*b*] thiophene-3-carboxylate (**36**)[7]

^{13}C-NMR of compound ethyl 2-acetamido-4,5,6,7-tetrahydrobenzo[*b*] thiophene-3-carboxylate (**36**)[7]

^{1}H-NMR of compound ethyl-2-benzamido-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**37**)[8]

^{13}C-NMR of compound ethyl-2-benzamido-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**37**)[8]

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^{13}C-NMR of compound ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (**55**)[9]

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^{1}H-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-5-phenylthiophene-3-carboxylate (**57**)

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^{1}H-NMR of compound 2-Amino-6-((benzyloxy)carbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**40**)

^{13}C-NMR of compound 2-Amino-6-((benzyloxy)carbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**40**)

^{1}H-NMR of compound 2-Amino-6-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**41**)[10]

^{13}C-NMR of compound 2-amino-6-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**41**)[10]

^{1}H-NMR of compound 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**42**)

^{13}C-NMR of compound 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**42**)

^{1}H-NMR of compound 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**43**)[11]

^{13}C-NMR of compound 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**43**)[11]

^{1}H-NMR of compound 2-Amino-5-phenylthiophene-3-carboxylic acid (**58**)[12]

^{13}C-NMR of compound 2-Amino-5-phenylthiophene-3-carboxylic acid (**58**)[12]

^{1}H-NMR of compound 2-amino-*N*-butyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**44**)

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^{1}H-NMR of compound 2-amino-*N*-benzyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**45**)

^{13}C-NMR of compound 2-amino-*N*-benzyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**45**)

^{1}H-NMR of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46**)

^{13}C-NMR of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46**)

COSY of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46**)

^{1}H-NMR of compound 2-amino-6-ethyl-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**47**)

^{13}C-NMR of compound 2-amino-6-ethyl-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**47**)

^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**48**)

^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**48**)

^{1}H-NMR of compound 2-amino-*N*-butyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**49**)

^{13}C-NMR of compound 2-amino-*N*-butyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**49**)

^{1}H-NMR of compound 2-amino-*N*-benzyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**50**[13])

^{13}C-NMR of compound 2-amino-*N*-benzyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**50**[13])

^{1}H-NMR of compound 2-amino-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**51)**

^{13}C-NMR of compound 2-amino-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**51)**

^{1}H-NMR of compound 2-amino-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**52**)

^{13}C-NMR of compound 2-amino-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**52**)

^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**53**)

^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**53**)

^{1}H-NMR of compound 2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (**59**)[14]

^{13}C-NMR of compound 2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (**59**)[14]

^{1}H-NMR of compound 2-amino-*N*-benzyl-5-phenylthiophene-3-carboxamide (**60**)

^{13}C-NMR of compound 2-amino-*N*-benzyl-5-phenylthiophene-3-carboxamide (**60**)

^{1}H-NMR of compound 2-amino-*N*-(4-methylbenzyl)-5-phenylthiophene-3-carboxamide (**61**)

^{13}C-NMR of compound 2-amino-*N*-(4-methylbenzyl)-5-phenylthiophene-3-carboxamide (**61**)

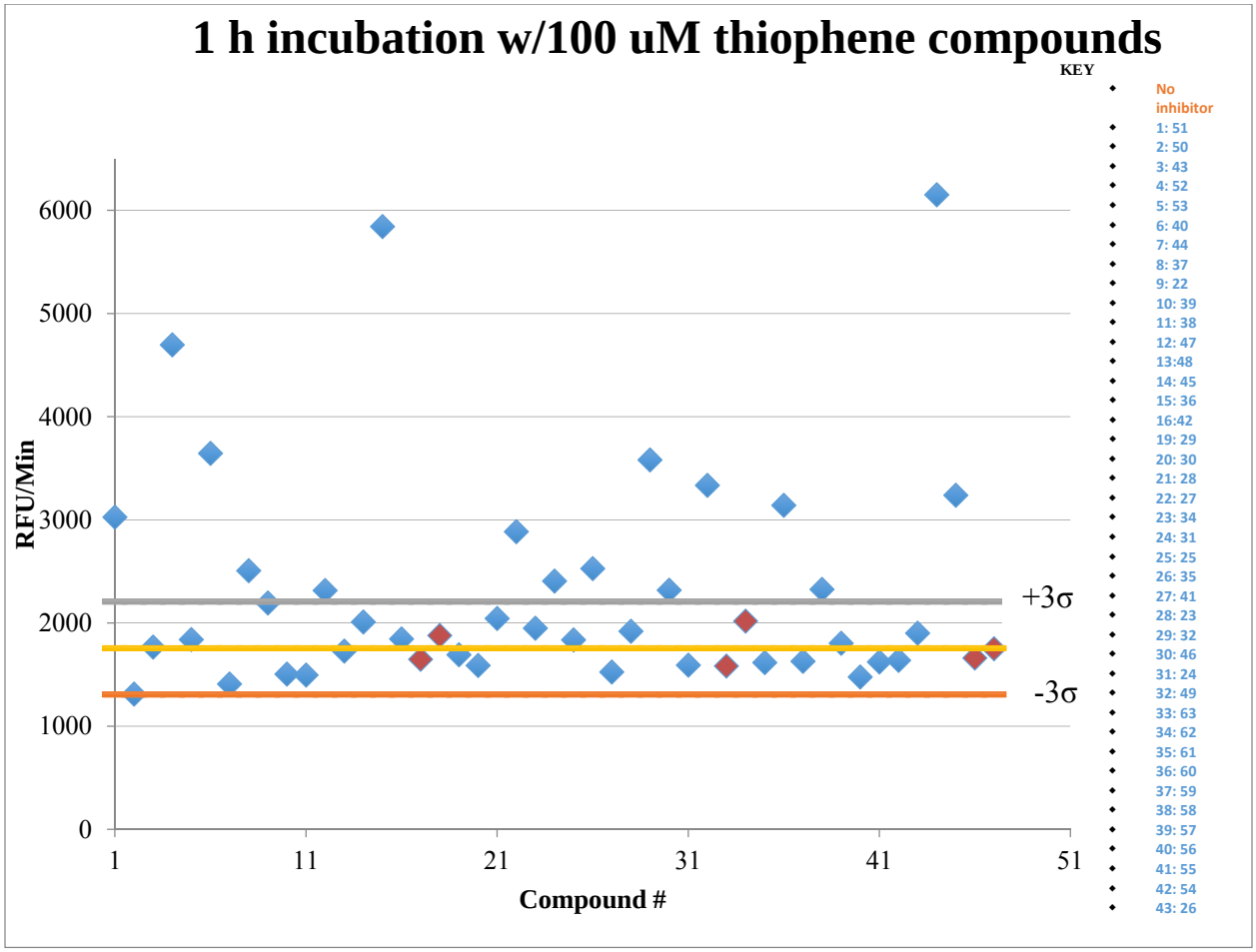
^{1}H-NMR of compound 2-Amino-*N*-(2-methoxybenzyl)-5-phenylthiophene-3-carboxamide (**62**)

^{13}C-NMR of compound 2-Amino-*N*-(2-methoxybenzyl)-5-phenylthiophene-3-carboxamide (**62**)

^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-5-phenylthiophene-3-carboxamide (**63**)

^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-5-phenylthiophene-3-carboxamide (**63**)

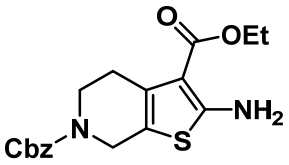
SI-Figure 1. HTS of thiophene library against Ag85C



- Average is of the 6 uninhibited reactions.
- ±3σ determined from that average.
- RFU/Min should decrease for inhibition of Ag85C.
- No compounds displayed activity below -3σ.
- -3σ would represent compounds with approximately 25% inhibition.

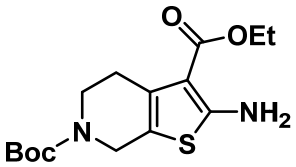
Experimental for known compounds

6-Benzyl 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (22)[1]



Yield: 86% (1.36 g); silica gel TLC R_f = 0.51 (40 % ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.38 (m, 4H, H-19, 20, 22, 23), 7.33 (m, 1H, H-21), 6.02 (s, 2H, H-17), 5.17 (s, 2H, H-8), 4.44 (s, 2H, H-6), 4.26 (q, 2H, 2H, $J_{13,14}$ 6Hz, H-13), 3.71 (s, 2H, H-10), 2.83 (m, 2H, H-5), 1.34 (t, 3H, $J_{14,13}$ 6Hz, H-14); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 165.79 (C-2), 162.34 (C-110, 155.27 (C-15), 136.67 (C-18), 131.66 (C-9), 130 (C-22, 20), 128.10 (C-19,23), 128 (C-21), 113.13 (C-4), 105.22 (C-5), 67.33 (C-17), 56.65 9C-13), 50.92 (C-8), 42.68 (C-6), 41.20 (C-5), 14.45 (C-14); mass spectrum (ESI), *m/z* = 383.10 $(M+23)^+$ $C_{18}H_{20}N_2O_4S$ requires 383.10 $(M+23)^+$.

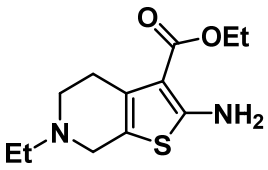
6-(*Tert*-butyl) 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(*5H*)-dicarboxylate (23)[2]



Yield: 63% (4.2 g); silica gel TLC R_f = 0.49 (40% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 4.36 (s, 2H, H-9), 4.27 (q, 2H, $J_{16,17}$ 6Hz, H-16), 3.62 (t, 2H, $J_{2,3}$ 6Hz, H-2), 2.81 (t, 2H, $J_{3,2}$ 6Hz, H-3), 1.49 (s, 9H, H-13, 20, 21), 1.35 (t, 3H, $J_{16,17}$ 6Hz, H-17); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.54 (C-2), 163.44 (C-11), 153.88 (C-13), 130.80 (C-4, 9), 102.61 (C-3), 79.08 (C-

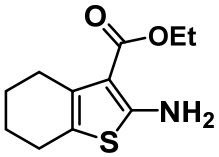
15), 42.48 (C-8), 41.45 (C-6), 28.07 (C-20, 19, 16), 14.11 (C-5); mass spectrum (ESI), *m/z* = 349.1 $(M+23)^+$ $C_{15}H_{22}N_2O_4S$ requires 349.11 $(M+23)^+$.

Ethyl 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (24) [3]



Yield: 86% (140.0 mg); silica gel TLC R_f = 0.2 (10 % methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 5.96 (s, 2H, H-10), 4.25 (q, 2H, $^3J_{15,16}$ 7.2 Hz, H-15), 3.43 (s, 2H, H-8), 2.84 (t, 2H, $^3J_{5,6}$ 8 Hz, H-5), 2.72 (t, 2H, $^3J_{6,5}$ 8 Hz, H-6), 2.58 (q, 2H, $^3J_{13,14}$ 7.2 Hz, H-13), 1.33 (t, 3H, $^3J_{16,15}$ 7.2 Hz, H-16), 1.17 (t, 3H, $^3J_{14,13}$ 7.2 H-14); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 165.96 (C-2), 162.01 (C-11), 131.14 (C-4), 114.82 (C-9), 105.36 (C-3), 59.41 (C-15), 51.57 (C-12), 51.09 (C-8), 50.23 (C-6), 27.43 (C-5), 14.43 (C-16), 12.58 (C-14); mass spectrum (ESI), *m/z* = 277.09 $(M+23)^+$ $C_{12}H_{18}N_2O_2S$ requires 277.10 $(M+23)^+$.

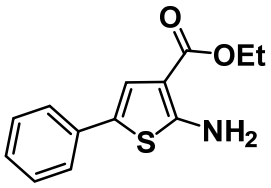
Ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (25)[4]



Yield: 59% (140.0 mg); silica gel TLC R_f = 0.53 (10 % ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 5.94 (s, 12H, H-10), 4.26 (q, 2H, $^3J_{13,14}$ 7.2 Hz, H-13), 2.71 (t, 2H, $^3J_{8,7}$ 5.01 Hz, H-8), 2.51 (t, 2H, $^3J_{5,6}$ 5.01 Hz, H-5), 1.80-1.73 (m, 4H, 2 × CH_2, H-6,7), 1.34 (t, 3H, $^3J_{14,13}$ 7.2 H-14); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.13 (C-2), 161.63 (C-11), 132.46 (C-4), 117.63 (C-9),

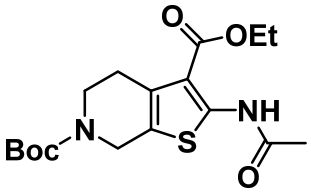
105.76 (C-3), 59.36 (C-13), 26.93 (C-8), 24.52 (C-5), 23.23 (C-7), 22.81 (C-6), 14.46 (C-14); mass spectrum (ESI), *m/z* = 248.07 $(M+23)^+$ $C_{11}H_{15}NO_2S$ requires 248.07 $(M+23)^+$.

Ethyl 2-amino-5-phenylthiophene-3-carboxylate (26)[5]



Yield: 12.5 g, 61% (140.0 mg); silica gel TLC R_f = 0.53 (30 % ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.44 (m, 2H, H-12, 16), 7.32 (t, 2H, $J_{13,14}$ 6.0 Hz, H-13, 15), 7.25 (s, 1H, H-4), 7.21 (s, 1H, H-14), 4.30 (q, 2H, $J_{9,10}$ 6Hz H-9), 1.37 (t, 3H, $J_{10,9}$ 6Hz H-10); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 165.54 (C-2), 161.73 (C-7), 129.24 (C-5), 128.97 (C-13, 15, 11), 1226.79 (C-14), 124.89 (C-12, 16), 121.40 (C-3), 60.09 (C-9), 14.72 (C-10); mass spectrum (ESI), *m/z* = 270.05 $(M+23)^+$ $C_{13}H_{13}NO_2S$ requires 270.06 $(M+23)^+$.

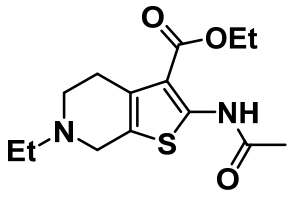
6-(*Tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (27)[1]



Yield: 41% (92.6 mg); silica gel TLC R_f = 0.67 (7 % methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 11.25 (s, 1H, H-10), 4.50 (s, 2H, H-8), 4.35 (q, 2H, $^3J_{15,16}$ 7.15 Hz, H-15), 3.65 (t, 2H,

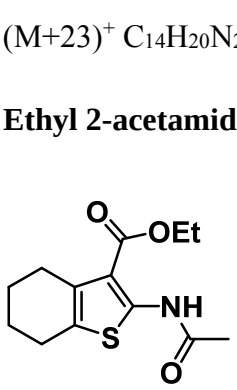
$^{3}J_{6,5}$ 5.67 Hz, H-6), 2.88 (t, $^{3}J_{5,6}$ 4.97 Hz, H-5), 2.28 (s, 3H, H-21), 1.49 (s, 9H, H-20,24,25), 1.40 (t, 3H, $^{3}J_{15,16}$ 7.15 Hz, H-16); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 167.11 (C-2), 166.28 (C-11), 154.64 (C-17), 148.44 (C-13), 129.72 (C-4), 123.33 (C-9), 110.82 (C-3), 80.15 (C-19), 60.75 (C-15), 42.63 (C-8), 40.98 (C-6), 26.45 (C-25, 24, 20), 26.55 (C-5), 23.68 (C-21), 14.31 (C-16); mass spectrum (ESI), *m/z* = 391.13 $(M+23)^+$ $C_{17}H_{24}N_2O_5S$ requires 391.13 $(M+23)^+$.

Ethyl 2-acetamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (31)[6]



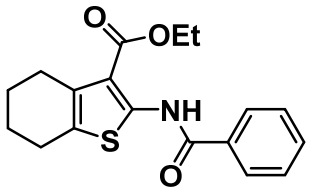
Yield: 33% (78.0 mg); silica gel TLC R_f = 0.30 (10 % methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 11.22 (s, 1H, H-10), 4.34 (q, 2H, $^{3}J_{17,18}$ 7.15 Hz, H-17), 3.59 (s, 2H, H-8), 2.92 (t, 2H, $^{3}J_{5,6}$ 5.50 Hz, H-5), 2.79 (t, 2H, H-6), 2.65 (q, 2H, $^{3}J_{15,16}$ 6.97 Hz, H-15), 2.27 (s, 3H, H-19), 1.38 (t, 3H, $^{3}J_{18,17}$ 6.97 Hz, H-18), 1.20 (t, 3H, $^{3}J_{16,15}$ 7.15 Hz, H-16); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 167.13 (C-2), 166.50 (C-11), 148.27 (C-13), 129.39 (C-4), 128.36 (C-9), 110.90 (C-3), 60.72 (C-17), 51.66 (C-15), 51.01 (C-8), 50.24 (C-6), 26.87 (C-5), 23.82 (C-19), 14.43 (C-18), 50.24 (C-6), 26.87 (C-5), 23.82 (C-19), 14.43 (C-18), 12.53 (C-16); mass spectrum (ESI), *m/z* = 319.10 $(M+23)^+$ $C_{14}H_{20}N_2O_3S$ requires 319.10 $(M+23)^+$.

Ethyl 2-acetamido-4,5,6,7-tetrahydrobenzo[*b*] thiophene-3-carboxylate (36)[7]



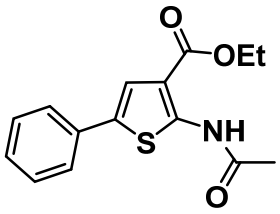
Yield: 59% (140.0 mg); silica gel TLC R_f = 0.41 (7 % methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 11.23 (s, 1H, H-10), 4.29 (q, 2H, $^3J_{15,16}$ 7.14 Hz, H-15), 2.73 (t, 2H, $^3J_{8,7}$ 5.94 H-8), 2.60 (t, 2H, $^3J_{5,6}$ 5.76 Hz, H-5), 2.23 (s, 3H, H-17), 1.78-1.73 (m, 4H, 2 CH_2, H-6, 7), 1.36 (t, 3H, $^3J_{16,15}$ 7.14, H-16); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.88 (C-2), 166.66 (C-11), 147.65 (C-13), 130.65 (C-4), 126.59 (C-9), 111.23 (C-3), 60.46 (C-15), 26.39 (C-8), 24.36 (C-5), 23.74 (C-17), 23.00 (C-7), 22.88 (C-6), 14.34 (C-16); mass spectrum (ESI), *m/z* = 290.08 $(M+23)^+$ $C_{13}H_{17}NO_3S$ requires 290.08 $(M+23)^+$.

Ethyl-2-benzamido-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (37)[8]



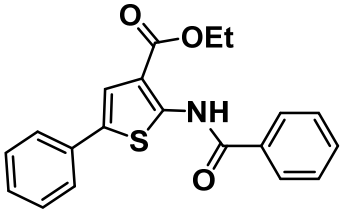
Yield: 57.2% (167.0 mg); silica gel TLC R_f = 0.62 (7% methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 12.32 (s, 1H, H-10), 8.01 (m, 2H, H-18, 22), 7.56 (m, 1H, H-20), 7.50 (m, 2H, H-19, 21), 4.35 (q, 2H, $^3J_{15,16}$ 7.14 Hz, H-15), 2.78 (t, 2H, $^3J_{8,7}$ 6.0 Hz, H-8), 2.67 (t, 2H, $^3J_{5,6}$ 5.82 Hz, H-5), 1.83-1.76 (m, 4H, H-6, 7), 1.39 (t, 3H, $^3J_{16,15}$ 7.14, H-16); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 167.06 (C-2), 163.39 (C-11), 148.08 (C-13), 132.53 (C-17), 132.45 (C-20), 131.08 (C-4), 128.94 (C-19, 21), 127.47 (C-18, 22), 127.06 (C-9), 111.97 (C-3), 60.65 (C-15), 26.45 (C-8), 24.46 (C-5), 23.03 (C-7), 22.89 (C-6), 14.39 (C-16); mass spectrum (ESI), *m/z* = 352.09 $(M+23)^+$ $C_{18}H_{19}NO_3S$ requires 352.10 $(M+23)^+$.

Ethyl 2-acetamido-5-phenylthiophene-3-carboxylate (54)[9]



Yield: 58% (136.7 mg); silica gel TLC R_f = 0.6 (30% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 11.01 (s, 1H, H-6), 7.60 (dd, 2H, $^3J_{18/14,17/15}$ 8.44 Hz, $^3J_{18/14,16}$ 1.28 Hz, H-18, 14), 7.41 (s, 1H, H-4), 7.39-7.37 (m, 2H, H-15, 17), 7.30-7.27 (s, 2H, H-16), 4.38 (q, 2H, $^3J_{11,12}$ 7.15 Hz, H-11), 2.31 (s, 3H, H-19), 1.42 (t, 3H, $^3J_{12,11}$ 7.15 Hz,); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 148.20 (C-9), 133.86 (C-13), 133.75 (C-5), 129.07 (C-14, 18), 127.55 (C-16), 125.60 (C-17, 15), 119.14 (C-4), 113.48 (C-3), 60.98 (C-11), 23.71 (C-19), 14.51 (C-12); mass spectrum (ESI), m/z = 312.06 $(M+H)^+$ $C_{15}H_{15}NO_3S$ requires 312.06 $(M+23)^+$.

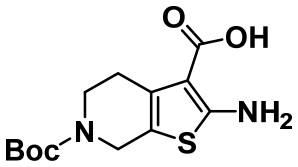
Ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (55)[9]



Yield: 98% (280 mg); silica gel TLC R_f = 0.66 (30% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 12.06 (s, 1H, H-6), 8.06 (dd, 2H, $^3J_{24/20,23/21}$ 8.44 Hz, $^3J_{24/20,22}$ 1.47 Hz, H-24, 20), 7.65 (dd, 2H, $^3J_{18/14,15/17}$ 8.44 Hz, $^3J_{18/14,16}$ 1.28 Hz, H-18, 14), 7.62 (d, $^3J_{22,23/21}$ 7.34 Hz, H-22), 7.56 (m, 2H, H-21, 23), 7.41 (m, 2H, H-15, 17), 7.30 (m, 1H, H-16), 4.44 (q, 2H, $^3J_{11,12}$ 7.15 Hz, H-11), 1.47 (t, 3H, $^3J_{12,11}$ 7.15 Hz, H-12); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.16 (C-2), 163.74 (C-7), 148.68 (C-9), 134.13 (C-19), 133.91 (C-13), 132.93 (C-22), 132.16 (C-5), 129.19 (C-17, 15), 129.13 (C-23, 21), 127.68 (C-24, 20), 127.64 (C-16), 125.65 (C-14, 18), 119.44 (C-4), 114.23 (C-

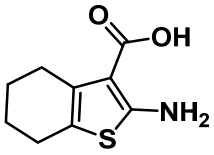
3), 61.15 (C-11), 14.58 (C-12); mass spectrum (ESI), *m/z* = 374.08 $(M+23)^+$ $C_{20}H_{17}NO_3S$ requires 374.0827 $(M+23)^+$.

2-Amino-6-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (41)[10]



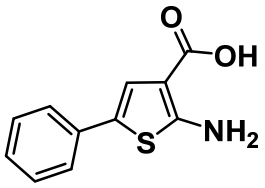
Yield: 59% (140.0 mg); silica gel TLC R_f = 0.54 (7 % methanol in CH_2Cl_2); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 11.95 (s, 1H, H-12), 7.29 (s, 2H, H-13), 4.24 (s, 2H, H-8), 3.49 (t, 2H, $J_{6,5}$ 6Hz, H-6), 2.64 (t, 2H, $J_{5,6}$ 6Hz, H-5), 1.14 (s, 9H, H-10); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.54 (C-2), 163.44 (C-11), 153.88 (C-13), 130.80 (C-4, 9), 102.61 (C-3), 79.08 (C-15), 42.48 (C-8), 41.45 (C-6), 28.07 (C-20, 19, 16), 14.11 (C-5); mass spectrum (ESI), *m/z* = 321.07 $(M+23)^+$ $C_{13}H_{18}N_2O_4S$ requires 321.08 $(M+23)^+$.

2-Amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (43)[11]



Yield: 44.4% (1.163g); silica gel TLC R_f = 0.11 (30% ethy lacetate in hexanes); ^{1}H-NMR (600 MHz, DMSO-d6): δ 11.73 (s, 1H, H-12), 7.17 (s, 2H, H-10), 2.57 (m, 2H, H-8), 2.40 (m, 2H, H-5), 2.67 (m, 2H, H-7), 1.63 (m, 2H, H-6)); ^{13}C-NMR (150 MHz, DMSO-d6): δ 167.27 (C-2), 163.24 (C-11), 132.25 (C-9), 115.50 (C-4), 103.59 (C-3), 26.97 (C-8), 24.38 (C-5), 23.35 (C-7), 22.86 (C-6); mass spectrum (ESI), *m/z* = 220.24 $(M+23)^+$ $C_8H_{11}N_2OS$ requires 220.04 $(M+23)^+$.

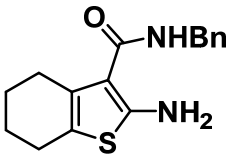
2-Amino-5-phenylthiophene-3-carboxylic acid (58)[12]



58

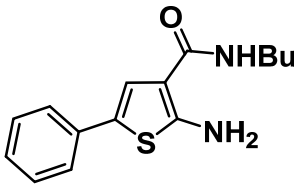
Yield: 83% (4.3 g); silica gel TLC R_f = 0.21 (30% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 12.05 (s, 1H, H-8), 7.43 (m, 4H, H-6, 10, 14), 7.32 (m, 2H, H-11, 13), 7.17 (m, 1H, H-12); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.10 (C-7), 163.24 (C-2), 133.88 (C-9), 128.97 (C-11, 13), 128.09 (C-12), 123.90 (C-10, 14), 121.79 (C -3), 121.72 (C-5), 105 (C-4); mass spectrum (ESI), *m/z* = 242.03 $(M+23)^+$ $C_{11}H_9NO_2S$ requires 242.02 $(M+23)^+$.

2-Amino-*N*-benzyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (50)[13]



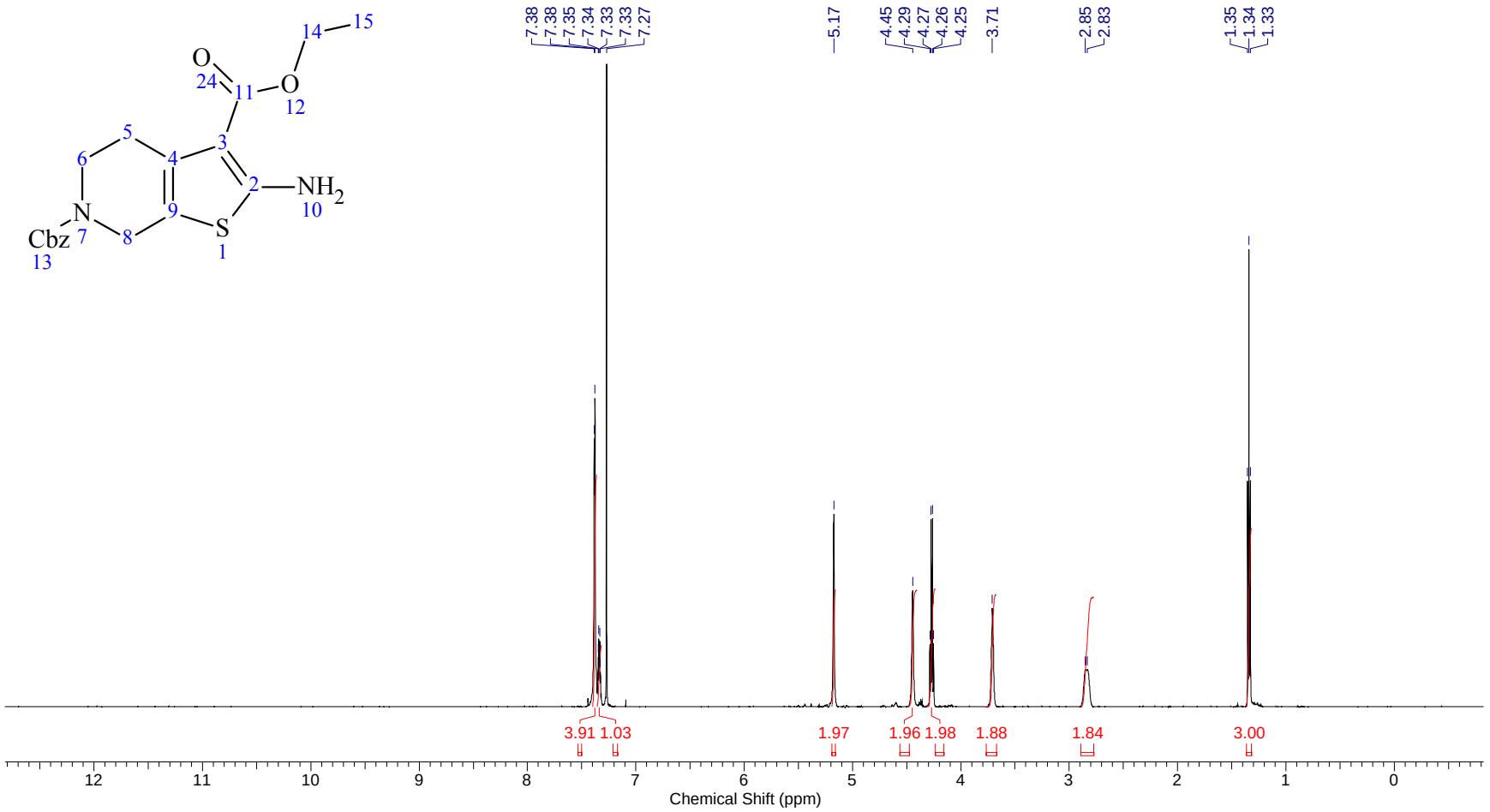
Yield: 22.08% (70.0 mg); silica gel TLC R_f = 0.33 (30% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.35-7.33 (m, 5H, H-16, 17, 18, 19, 20), 6.00 (s, 2H, H-10), 4.59 (d, 2H, $^3J_{14,15}$ 5.58 Hz, H-14), 2.60-2.59 (m, 2H, H-8), 2.55-2.54 (m, 2H, H-5), 1.78 (m, 4H, H-6,7) ; ^{13}C-NMR (150 MHz, $CDCl_3$): δ 166.43 (C-2), 158.66 (C-11), 138.75 (C-9), 128.80 (C-15), 128.74 (C-17, 19), 127.54 (C-16, 20), 127.36 (C-18), 119.31 (C-4), 108.88 (C-3), 43.25 (C-14), 27.24 (C-8), 24.56 (C-5), 22.93 (C-7), 22.85 (C-6); mass spectrum (ESI), *m/z* = 309.10 $(M+23)^+$ $C_{16}H_{18}N_2OS$ requires 309.10 $(M+23)^+$.

2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (59)[14]

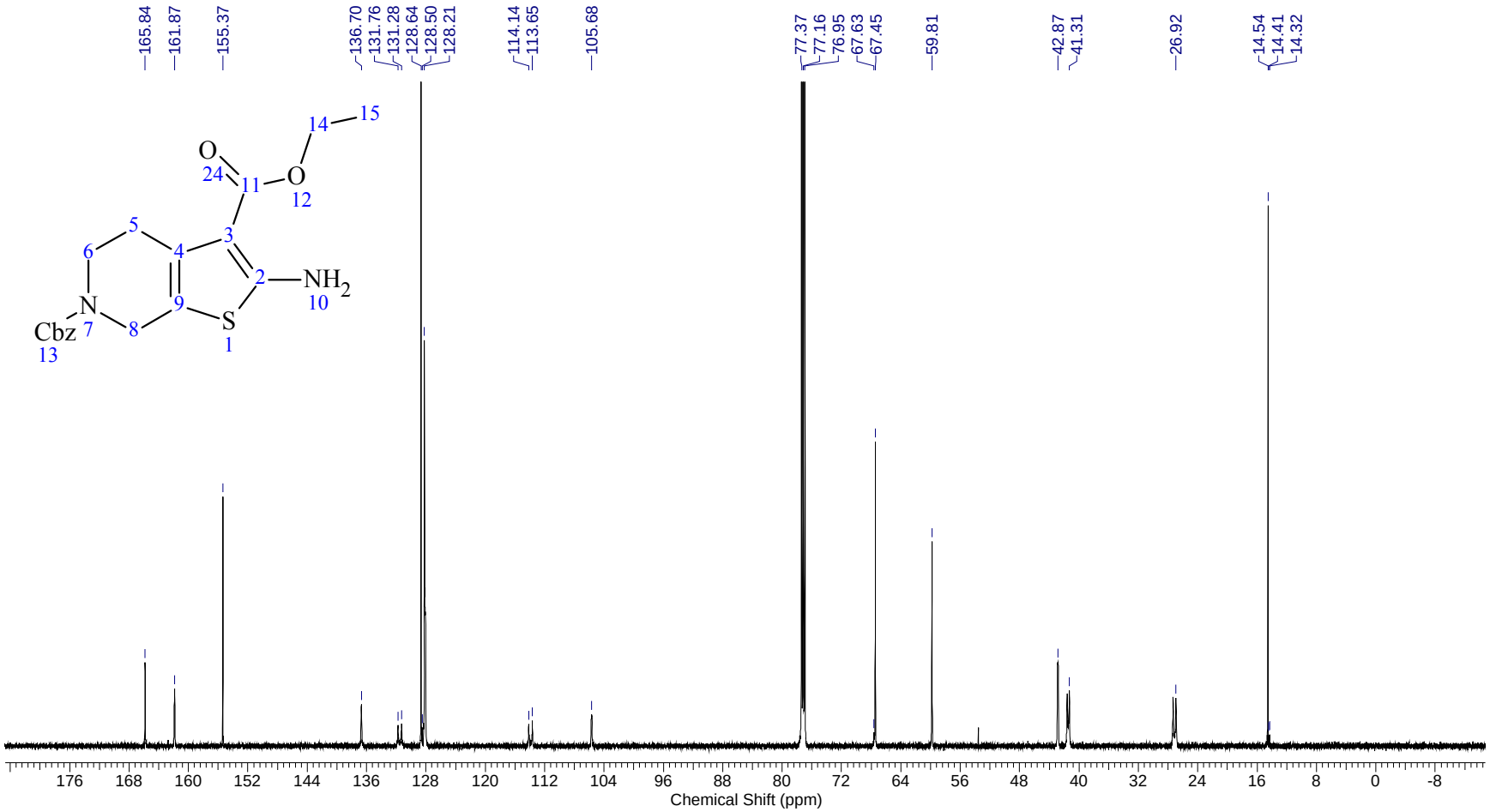


Yield: 61% (152.2 mg); silica gel TLC R_f = 0.36 (30% ethyl acetate in hexanes); ^{1}H-NMR (600 MHz, $CDCl_3$): δ 7.43 (d, 2H, $^3J_{10/14,11/13}$ 7.34 Hz, H-10, 14), 7.32 (m, 2H, H-11, 13), 7.21 (m, 1H, H-12), 7.00 (s, 1H, H-4) 5.87 (s, 1H, H-15), 3.40 (t, $^3J_{16,17}$ 6.97 Hz, H-16), 1.59 (quin, 2H, $^3J_{17,18/16}$ 7.34 Hz, H-17), 1.42 (sex, 2H, $^3J_{18,17/19}$ 7.70 Hz, H-18), 0.96 (t, $^3J_{19,18}$ 7.34 Hz, H-19); ^{13}C-NMR (150 MHz, $CDCl_3$): δ 165.81 (C-7), 158.64 (C-2), 133.94 (C-5), 128.99 (C-11, 13), 126.90 (C-12), 126.50 (C-9), 124.84 (C-14, 10), 118.13 (C-4), 111.02 (C-3), 39.22 (C-16), 32.09 (C-17), 20.34 (C-18), 13.96 (C-19); mass spectrum (ESI), *m/z* = 297.10 $(M+23)^+$ $C_{15}H_{18}N_2OS$ requires 297.1038 $(M+23)^+$.

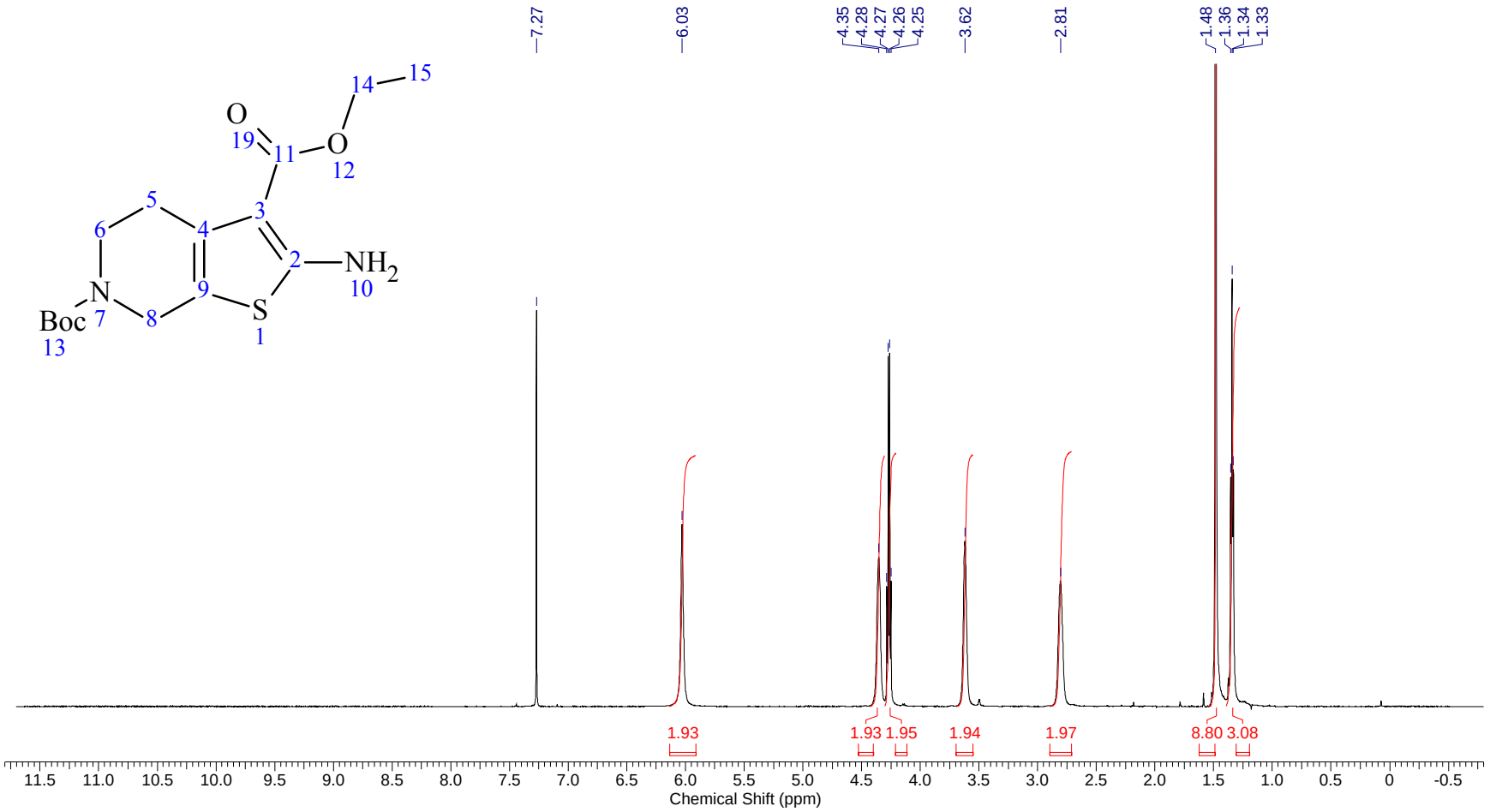
^{1}H-NMR of compound 6-benzyl 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (**22,** $CDCl_3$)[1]



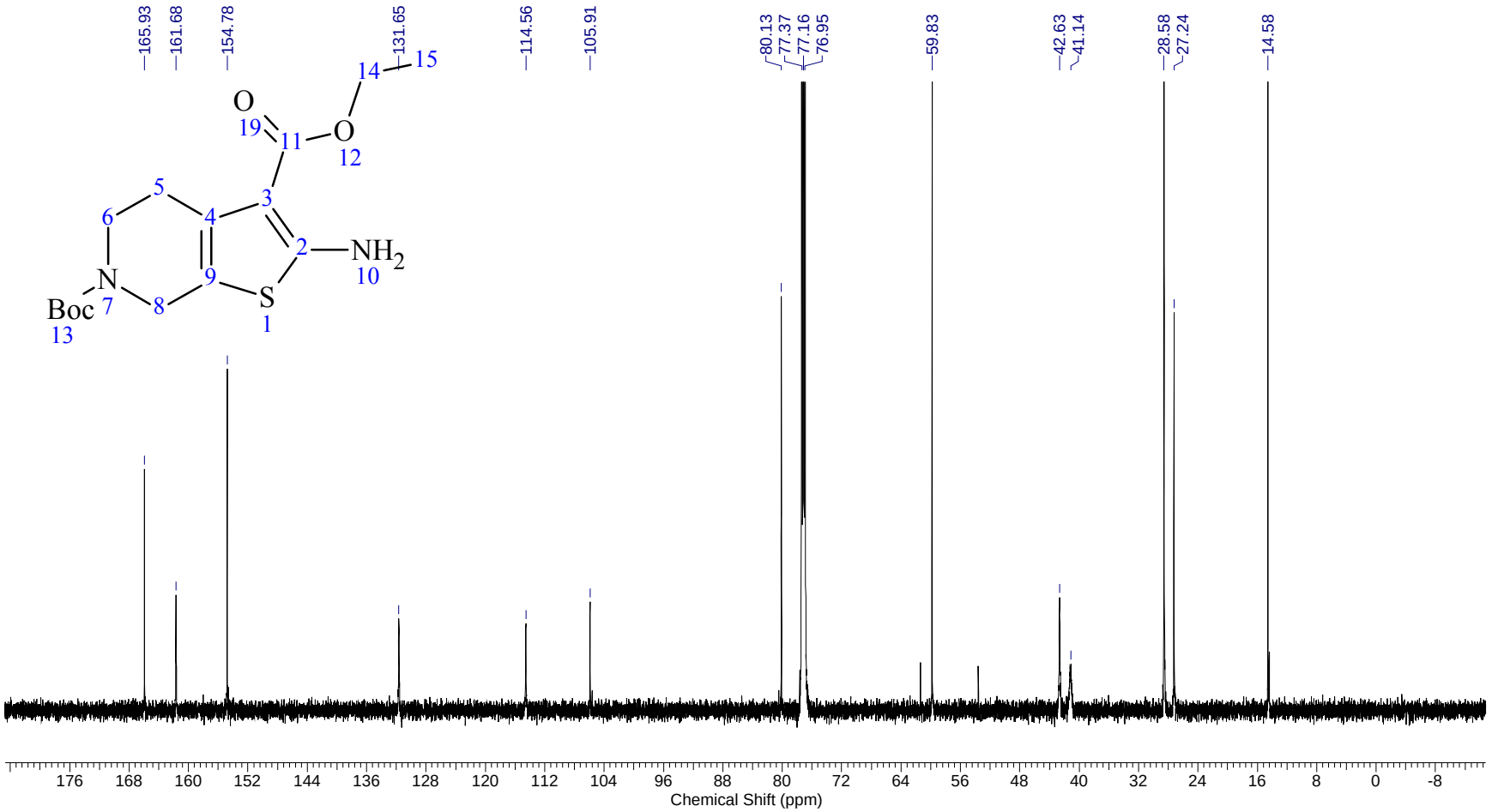
^{13}C-NMR of compound 6-benzyl 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(22,** $CDCl_3$**)**[1]



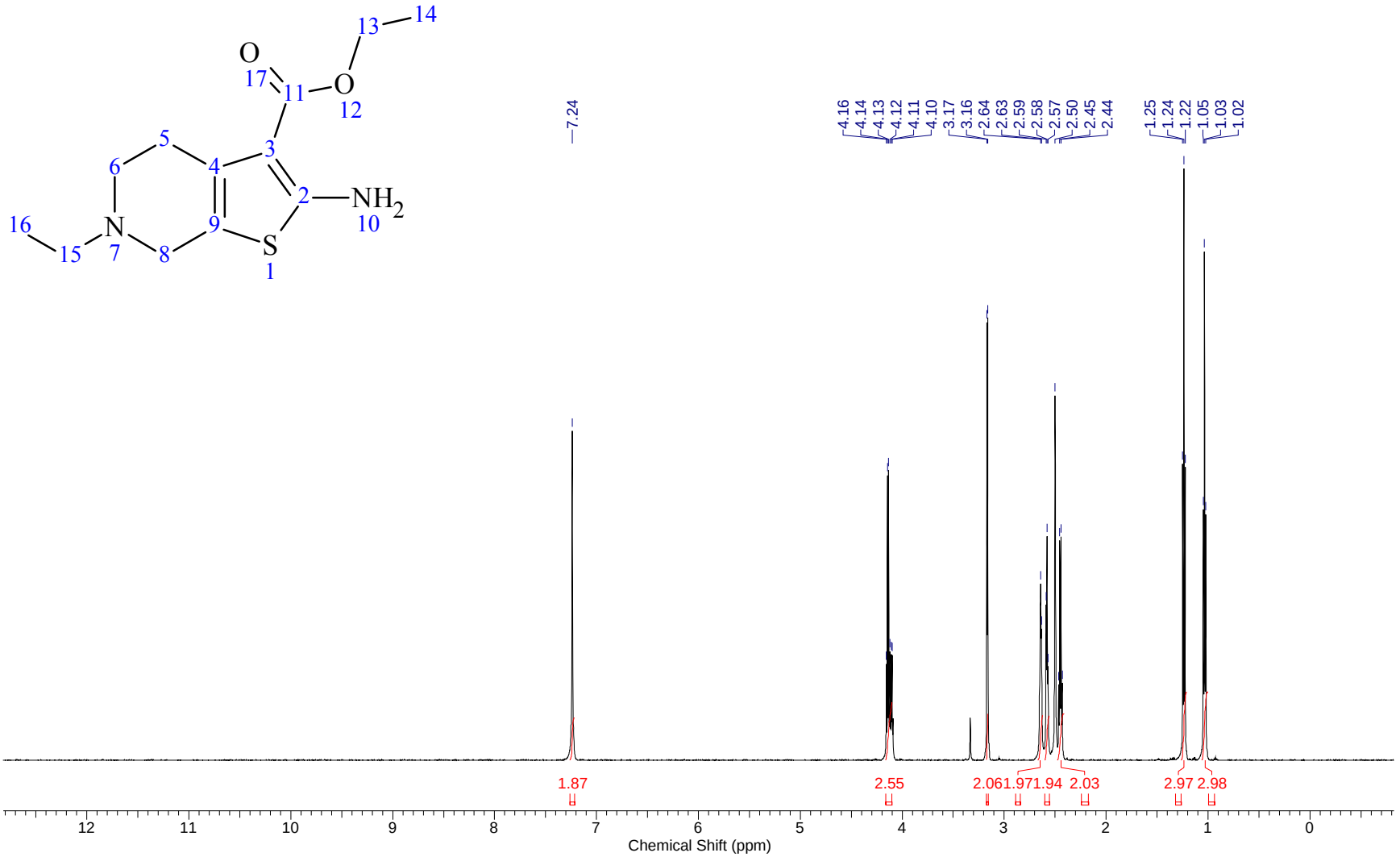
^{1}H-NMR of compound 6-(t*ert*-butyl) 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(*5H*)-dicarboxylate **(23**, $CDCl_3$**)**[2]



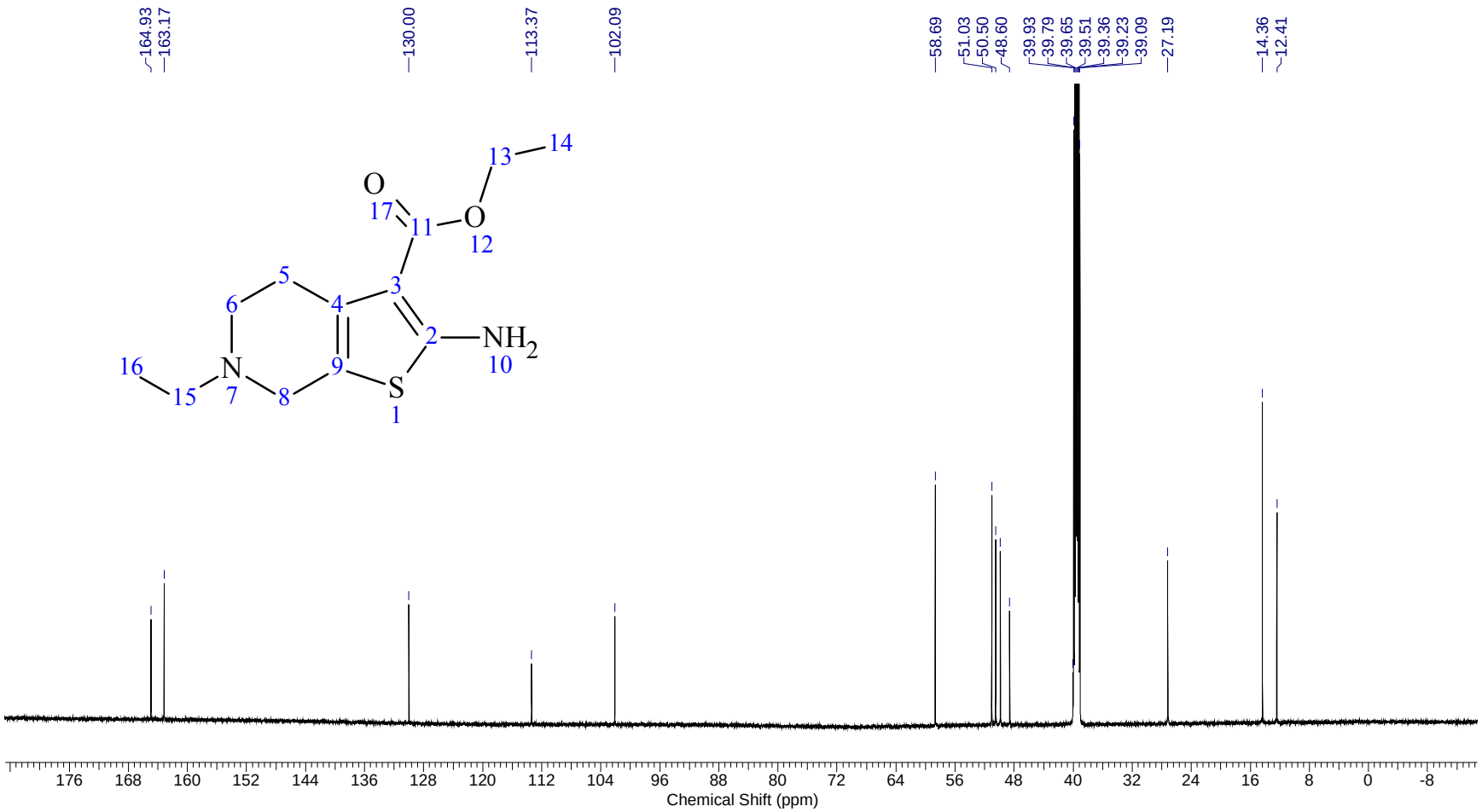
^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-amino-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(*5H*)-dicarboxylate **(23,** $CDCl_3$**)**[2]



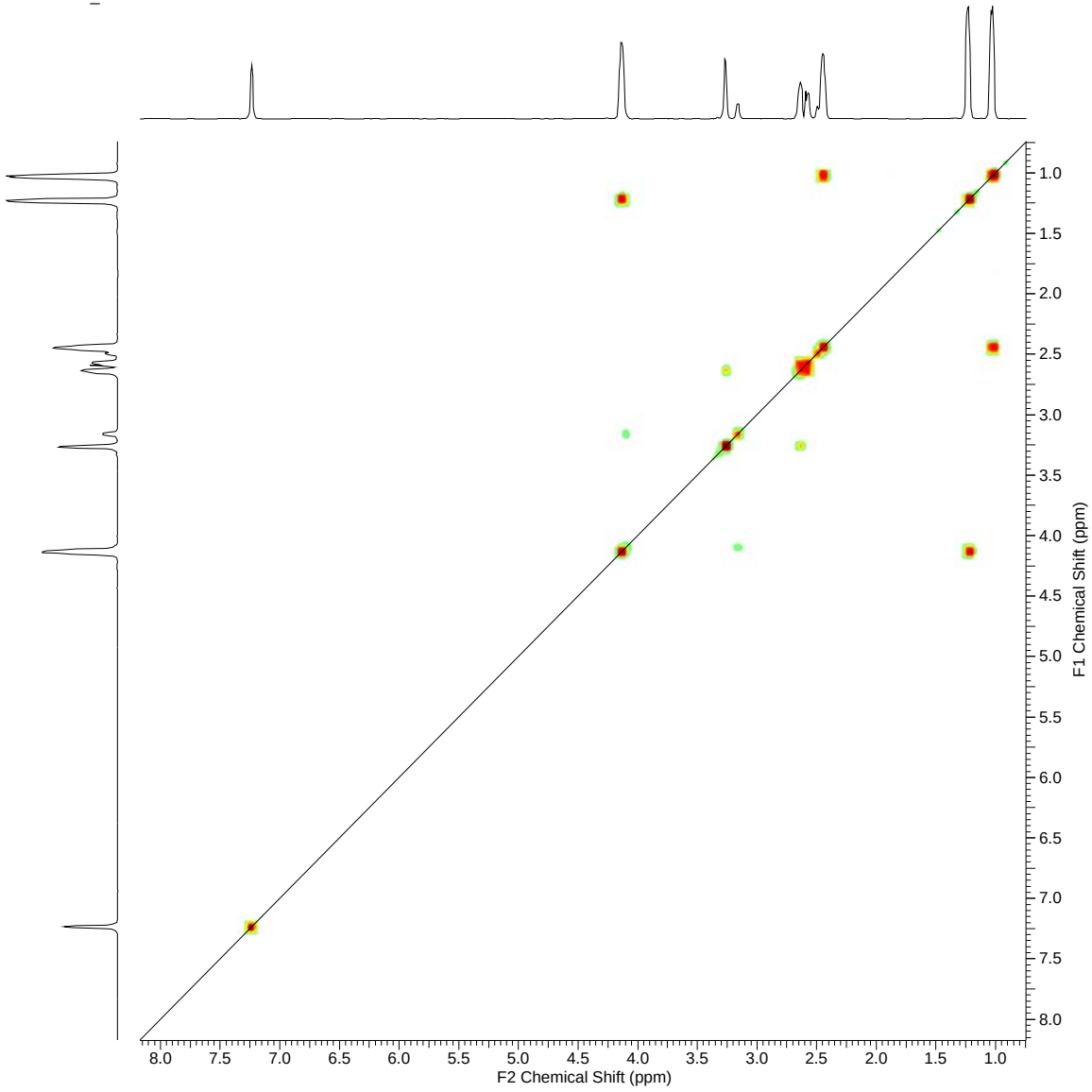
[1]H-NMR of compound ethyl 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (**24**, $(CD_3)_2SO$)[3]

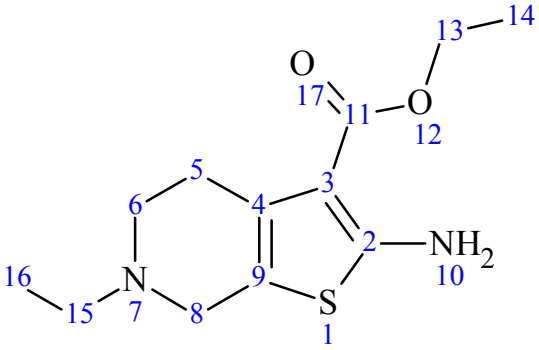


^{13}C-NMR of compound ethyl 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate (**24**, $(CD_3)_2SO$)[3]

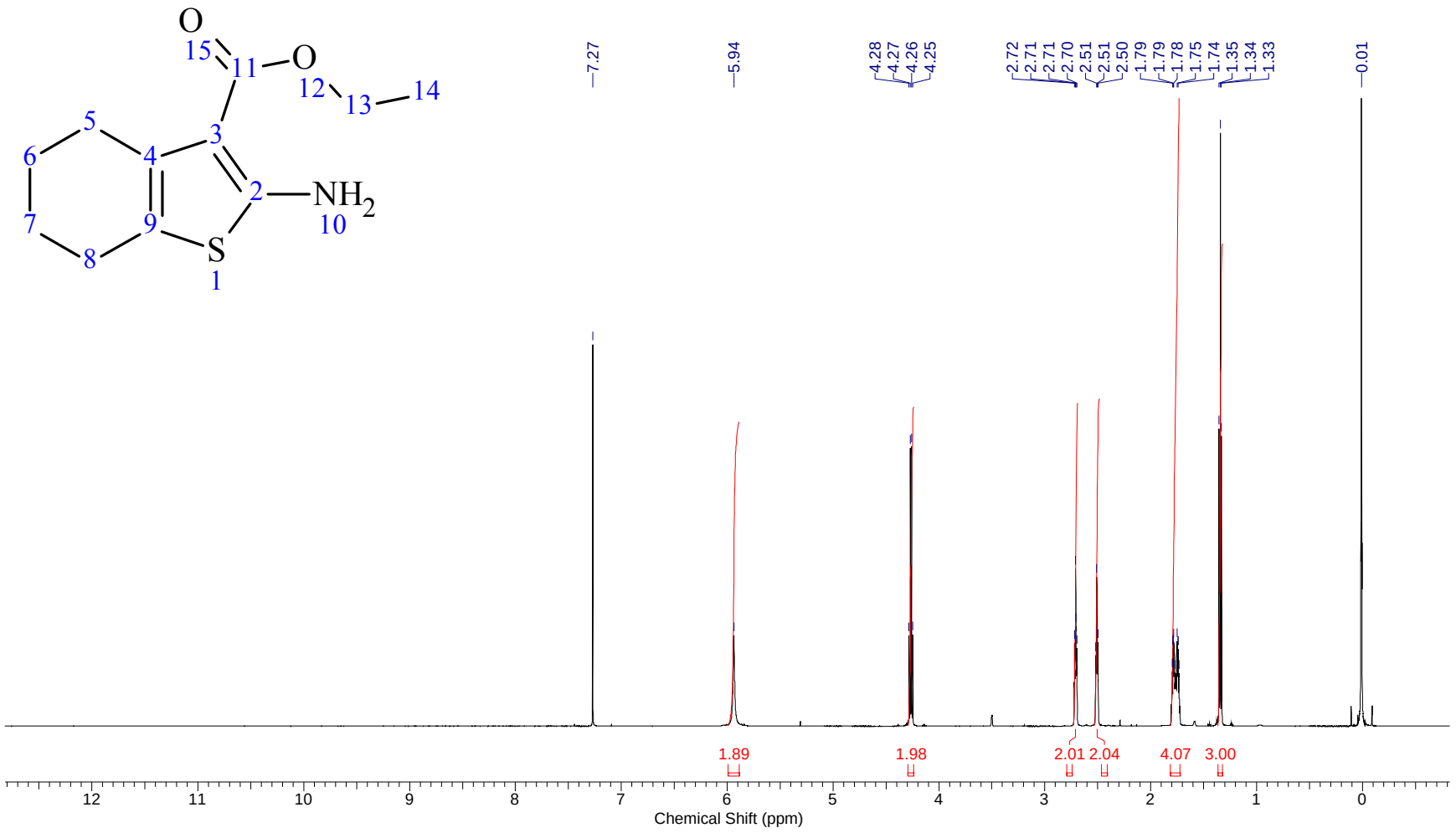


COSY of compound ethyl 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(24,** $(CD_3)_2SO$**)**[3]

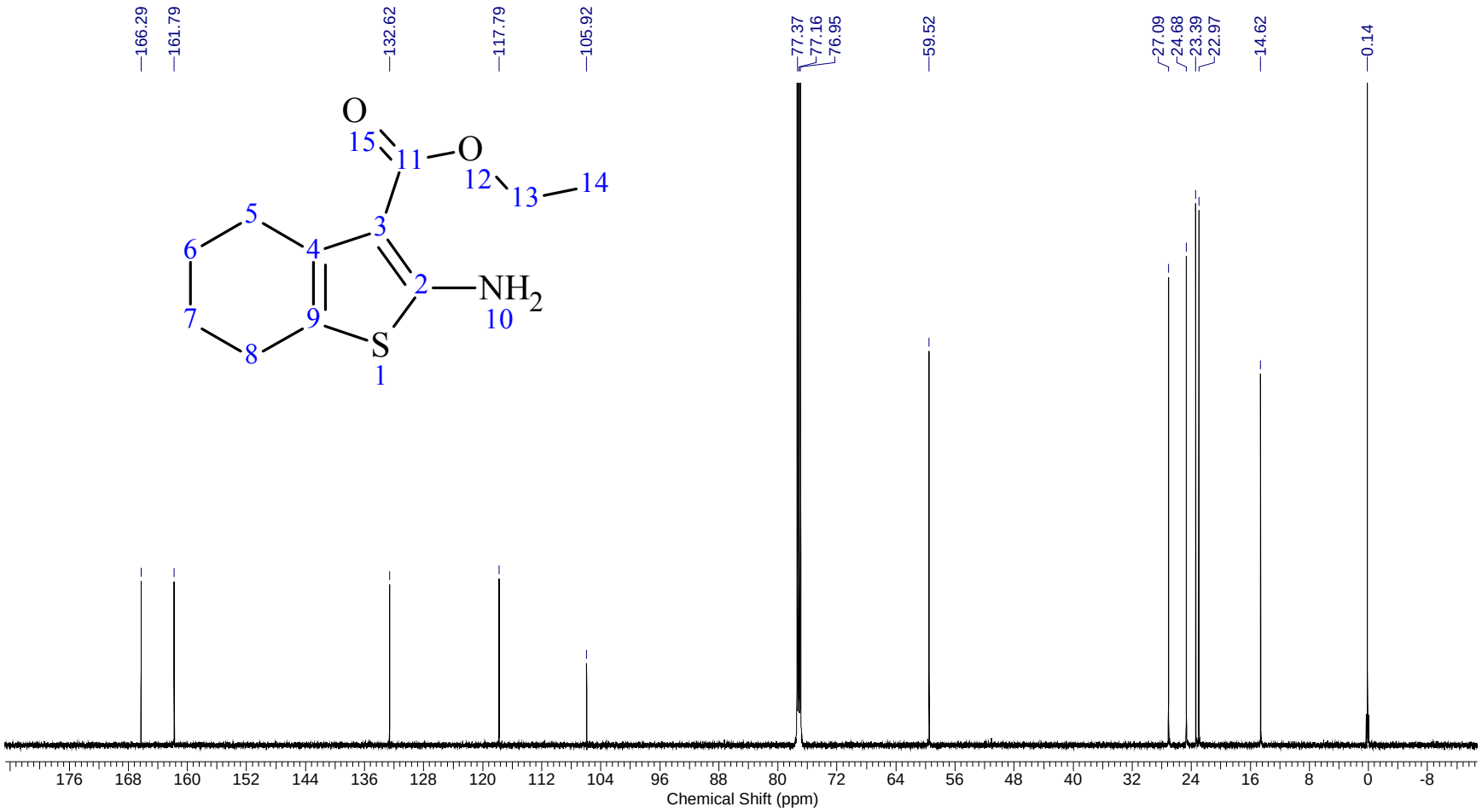




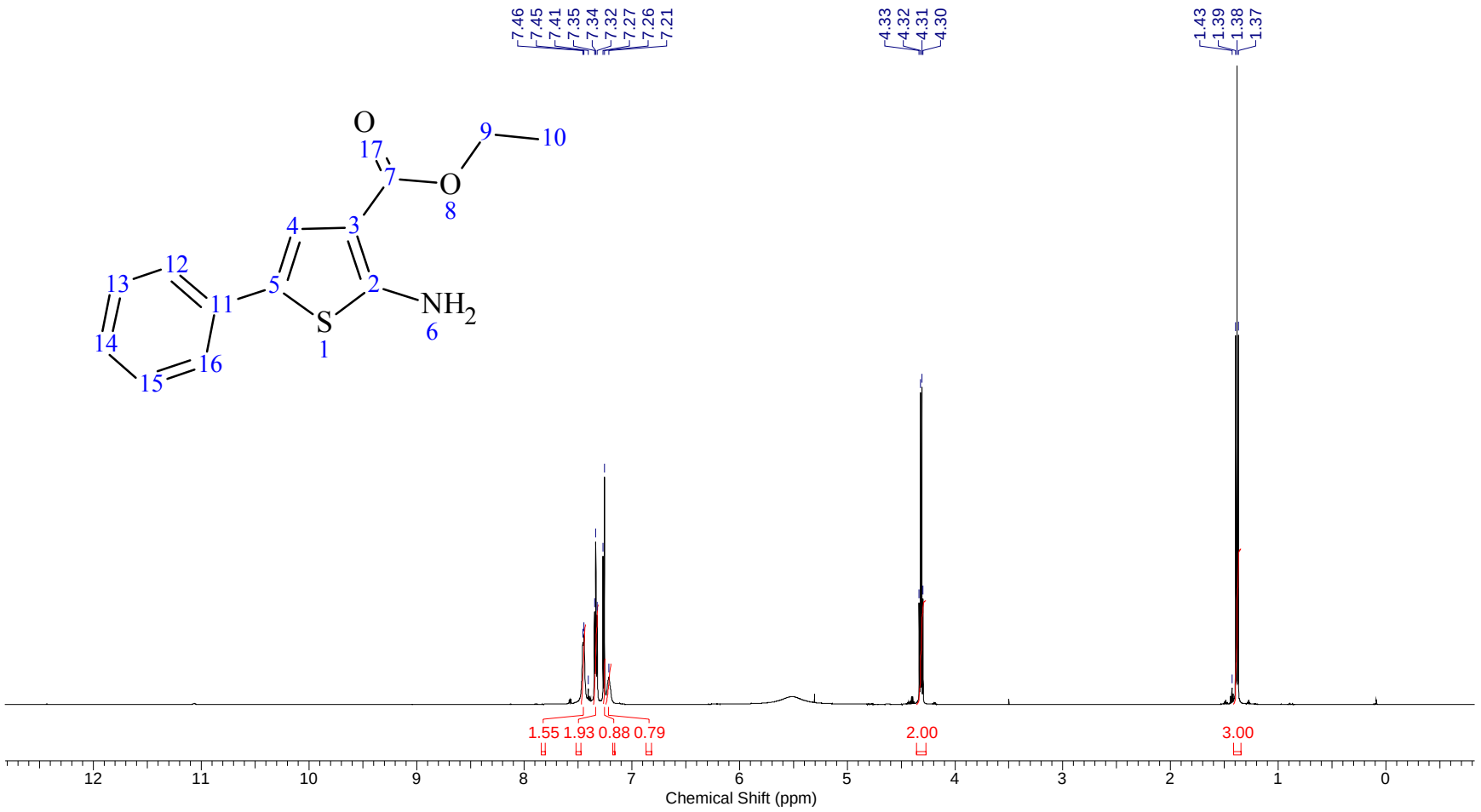
^{1}H-NMR of compound ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**25**, $CDCl_3$)[4]



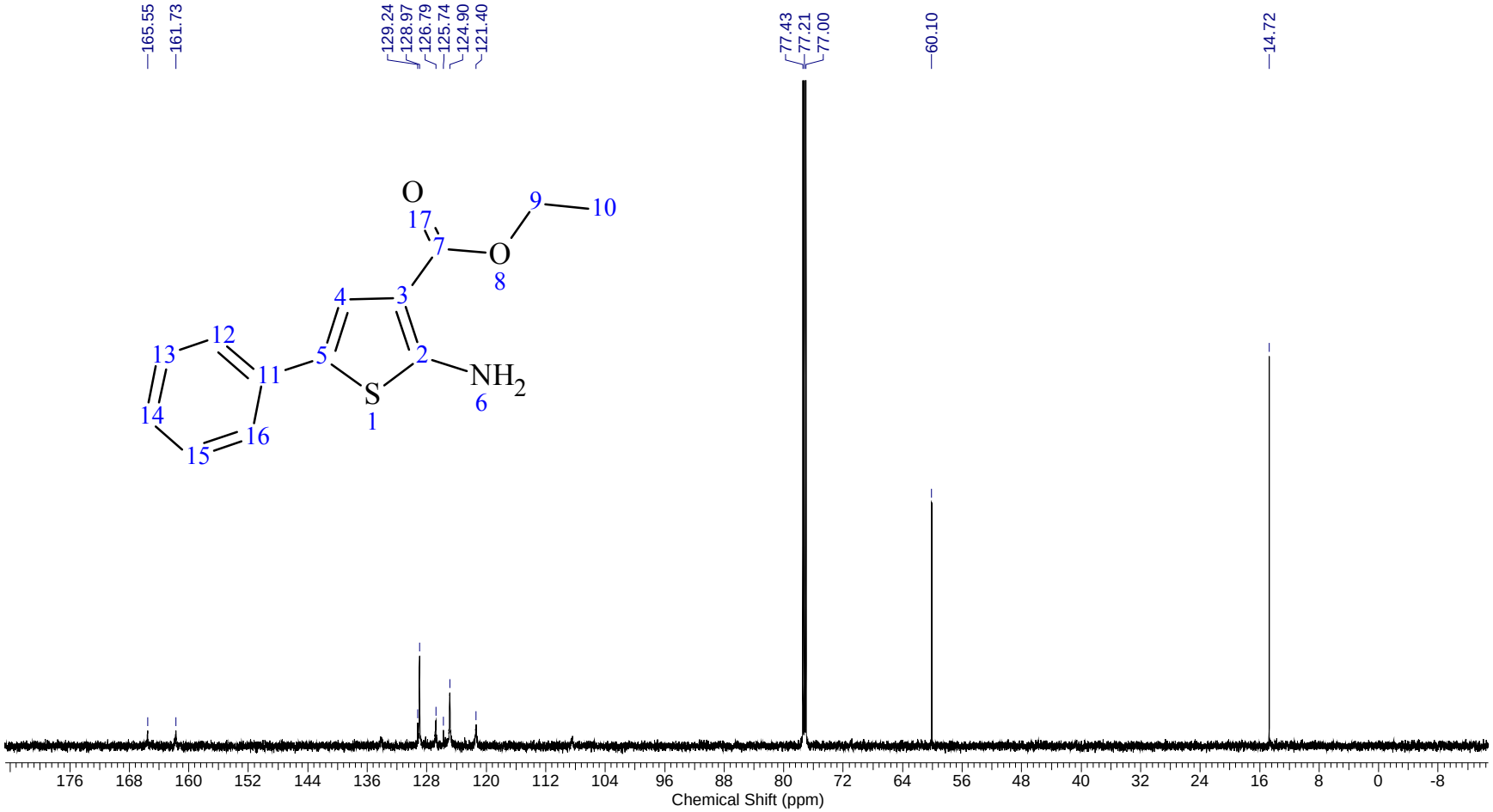
^{13}C-NMR of compound ethyl 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate **(25,** $CDCl_3$**)**[4]



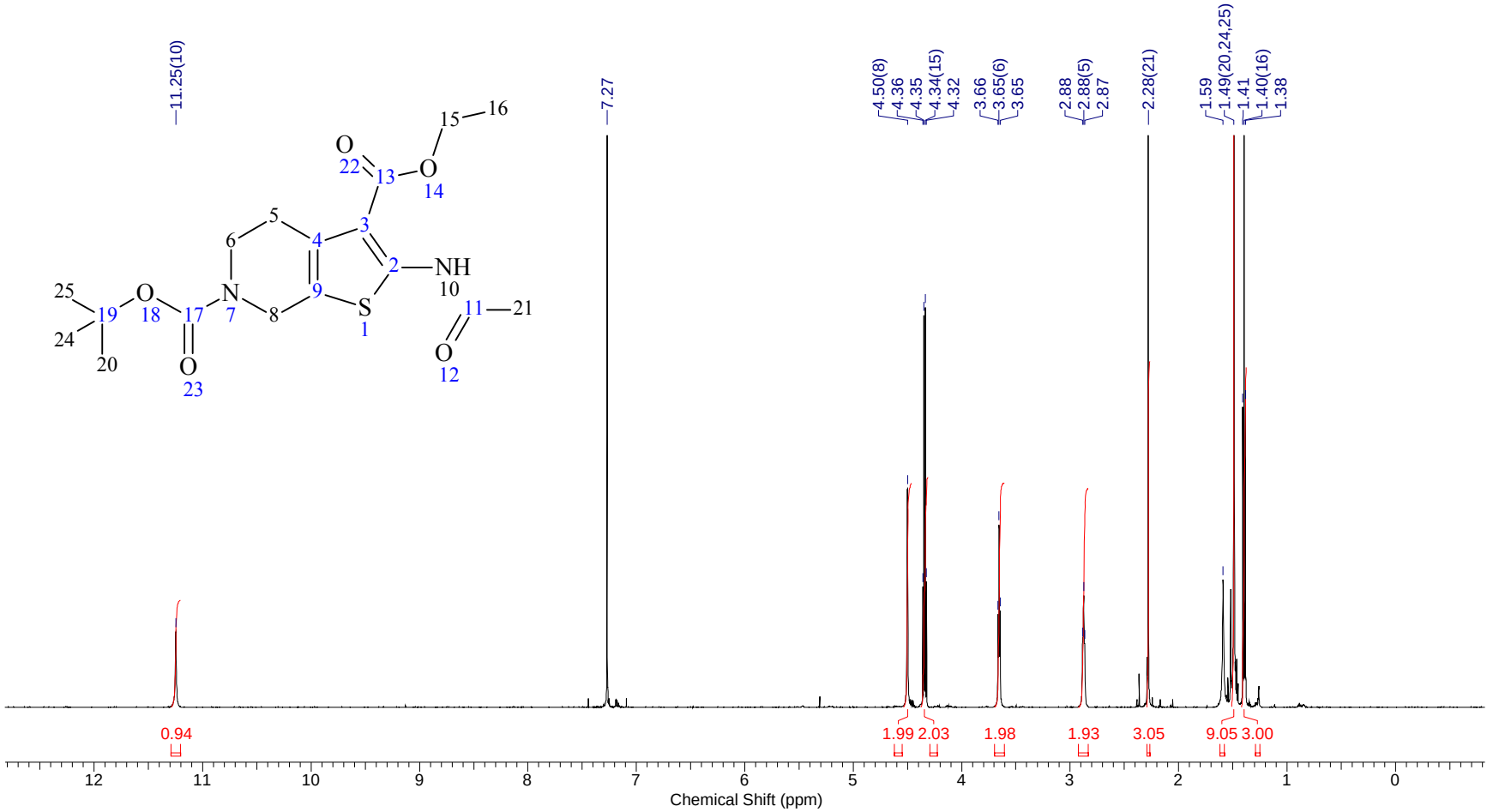
^{1}H-NMR of compound ethyl 2-amino-5-phenylthiophene-3-carboxylate **(26**, $CDCl_3$**)**[5]



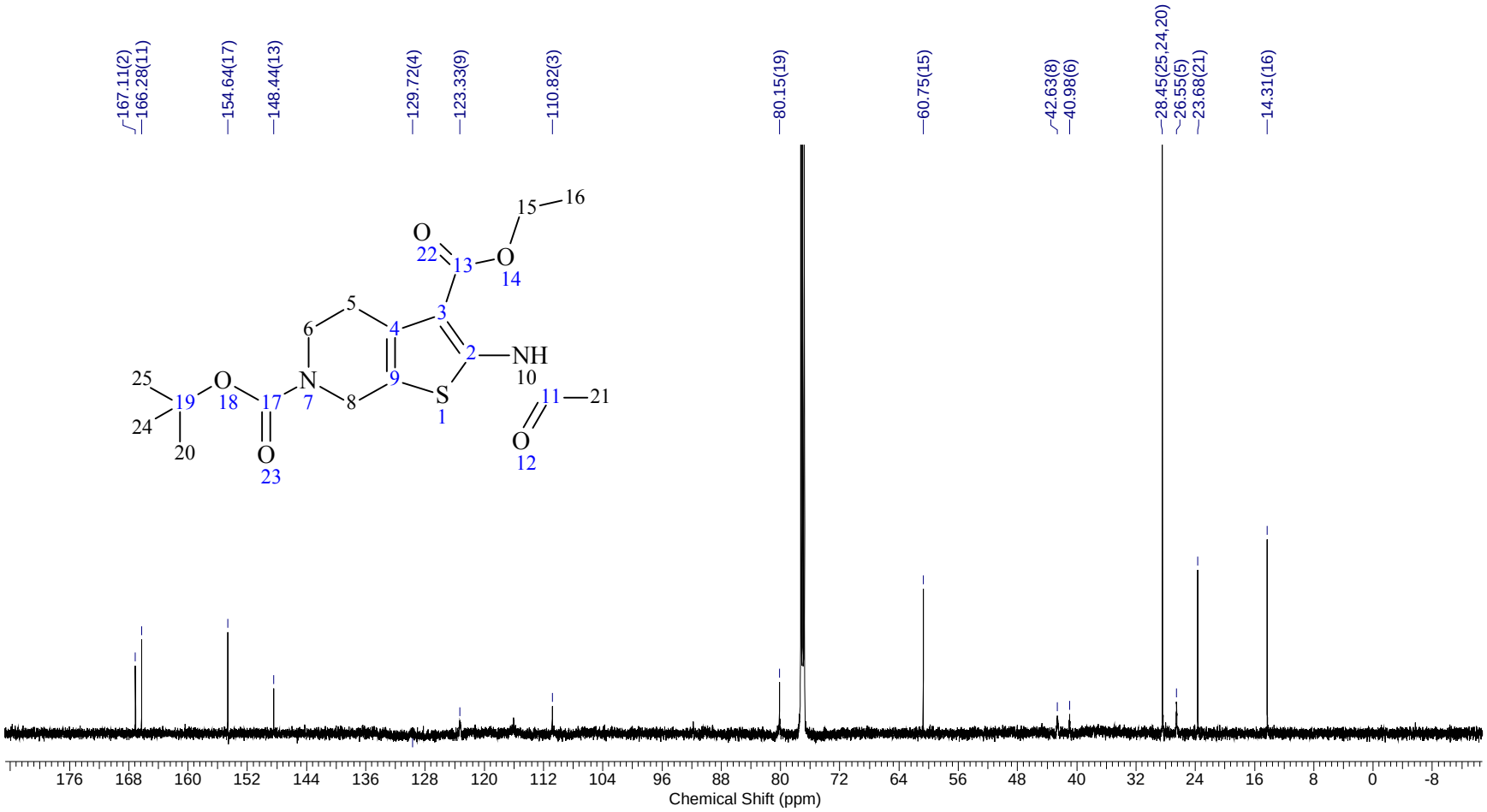
^{13}C-NMR of compound ethyl 2-amino-5-phenylthiophene-3-carboxylate **(26,** $CDCl_3$**)**[5]



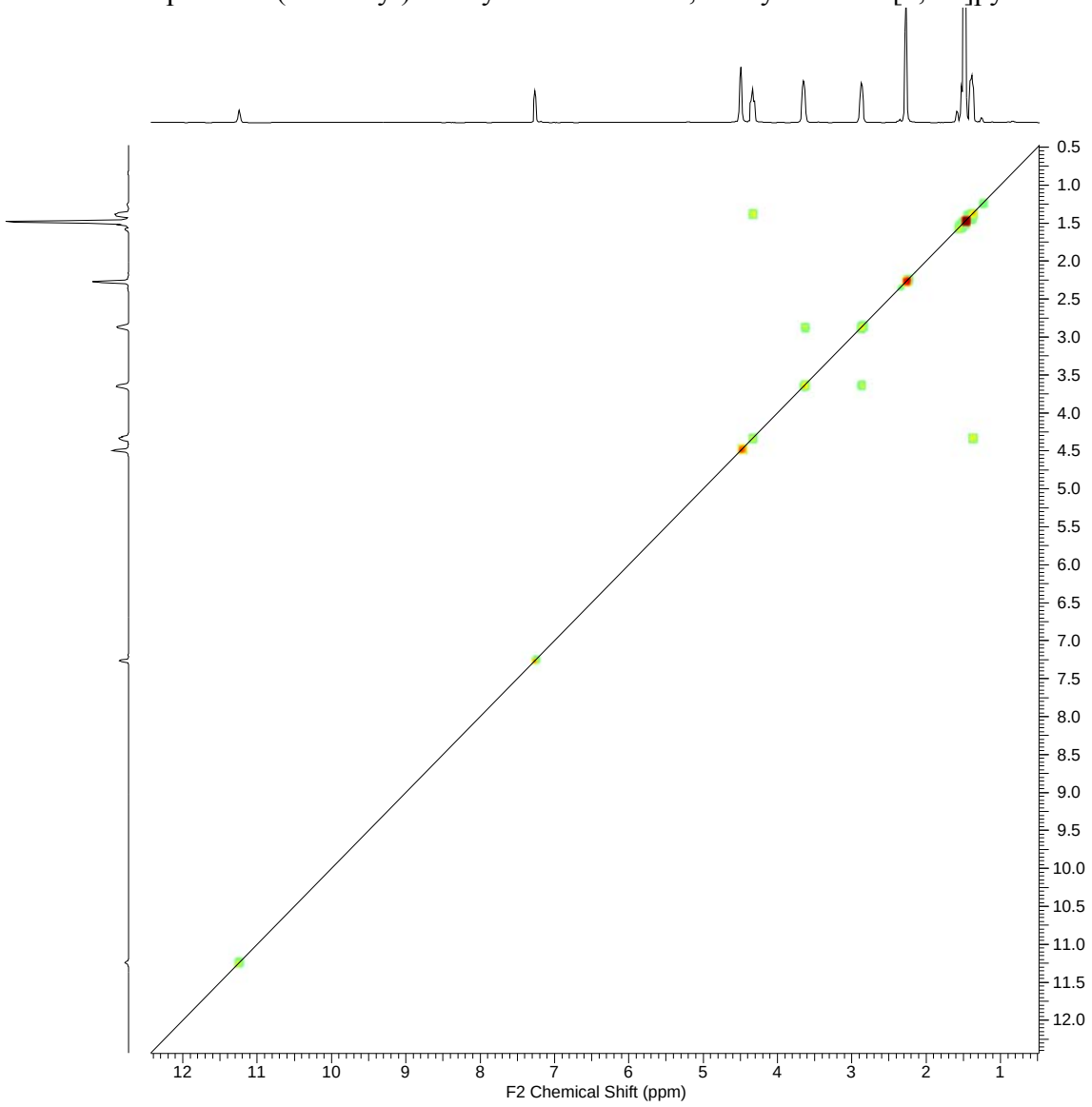
[1]H-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27,** $CDCl_3$**)**[1]

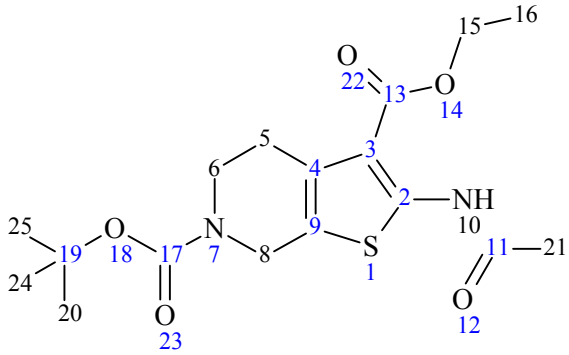


^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27**, $CDCl_3$**)**[1]

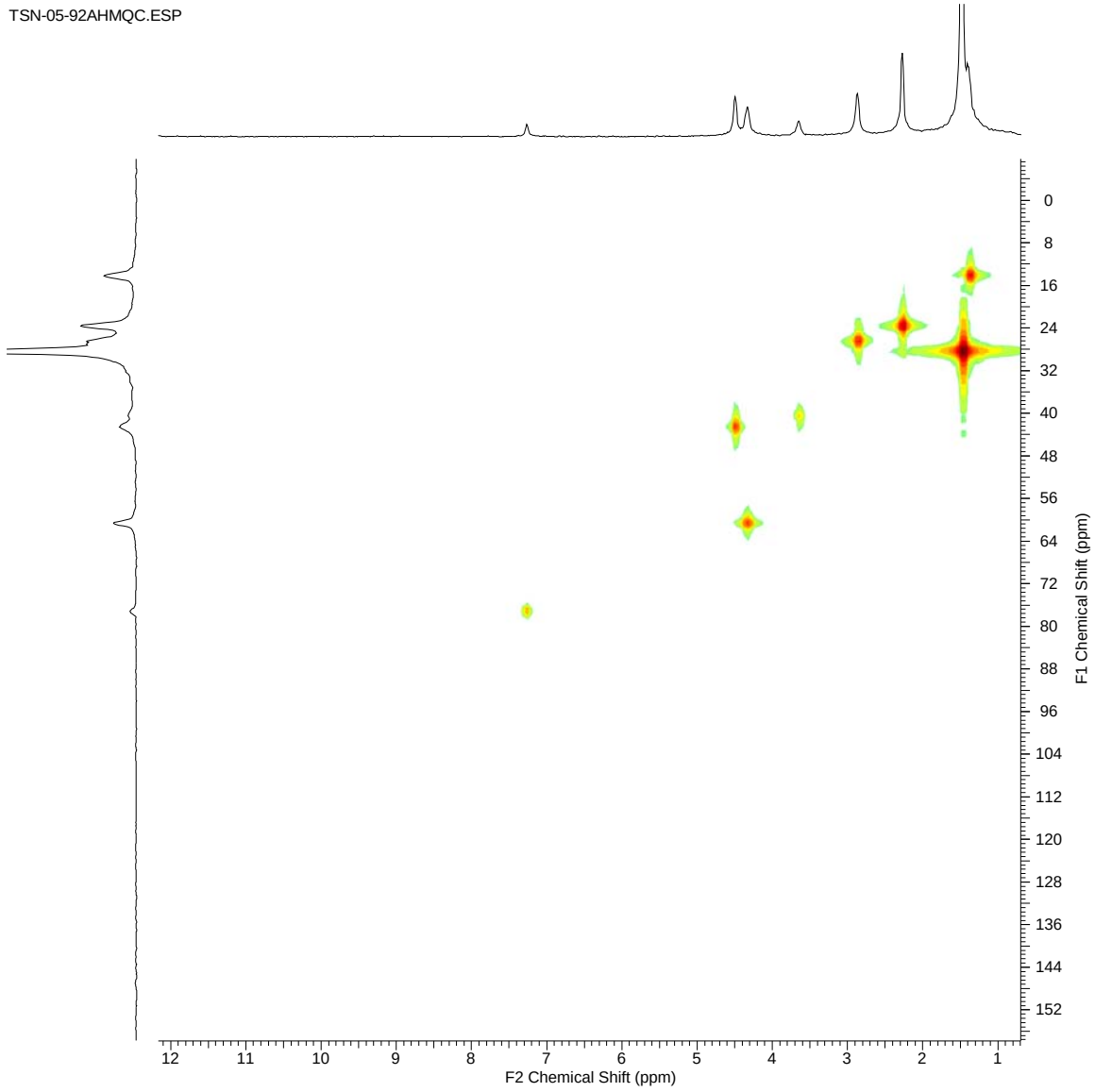


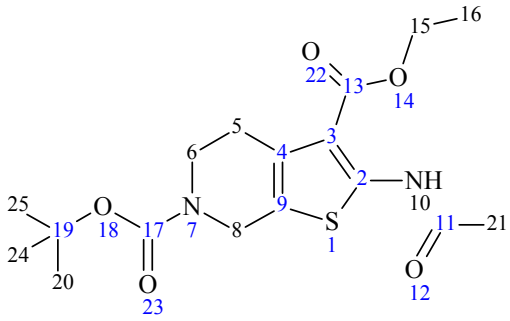
COSY of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27,** $CDCl_3$**)**[1]



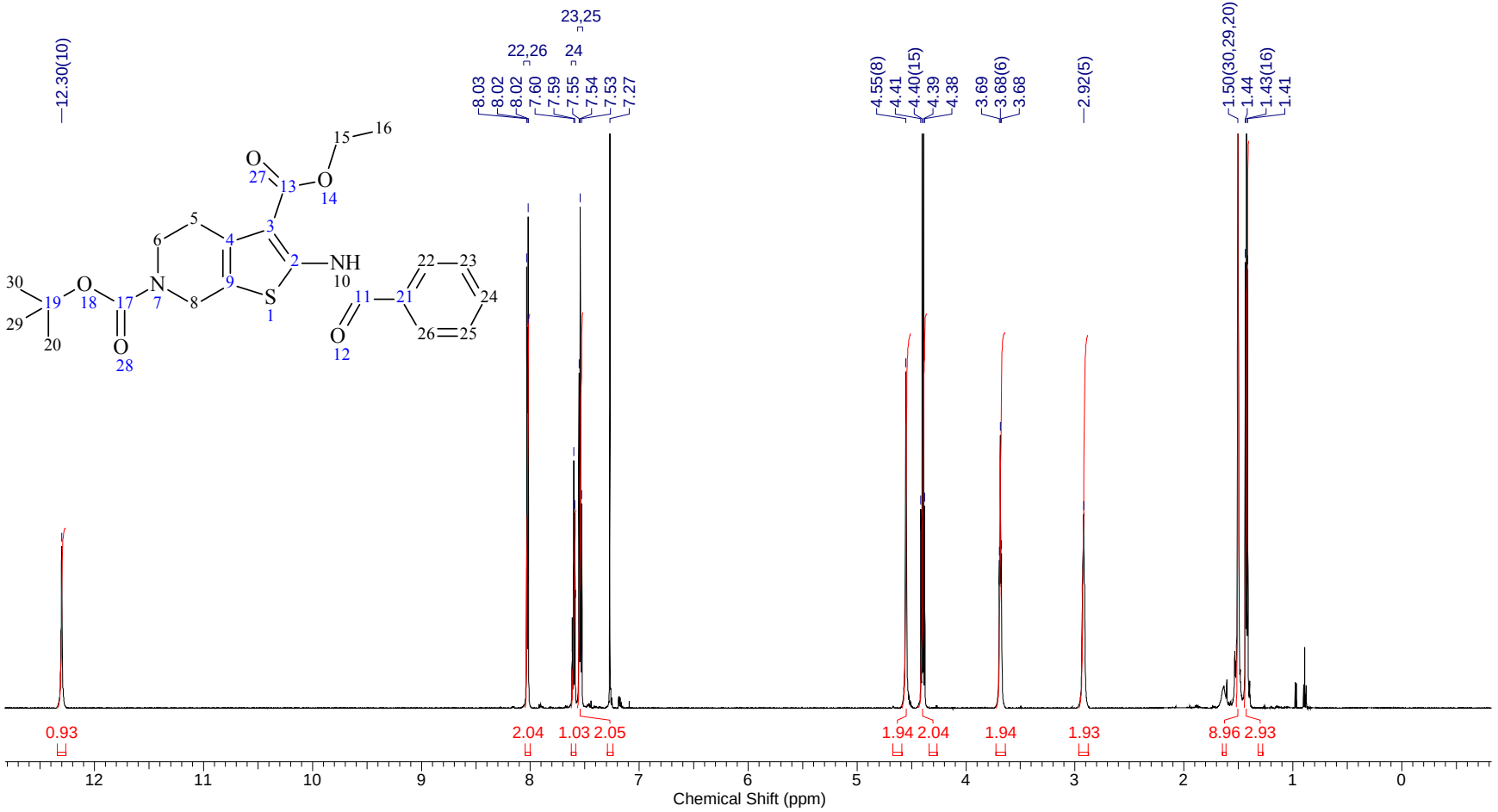


HMQC of compound 6-(*tert*-butyl) 3-ethyl 2-acetamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(27**, $CDCl_3$**)**[1]

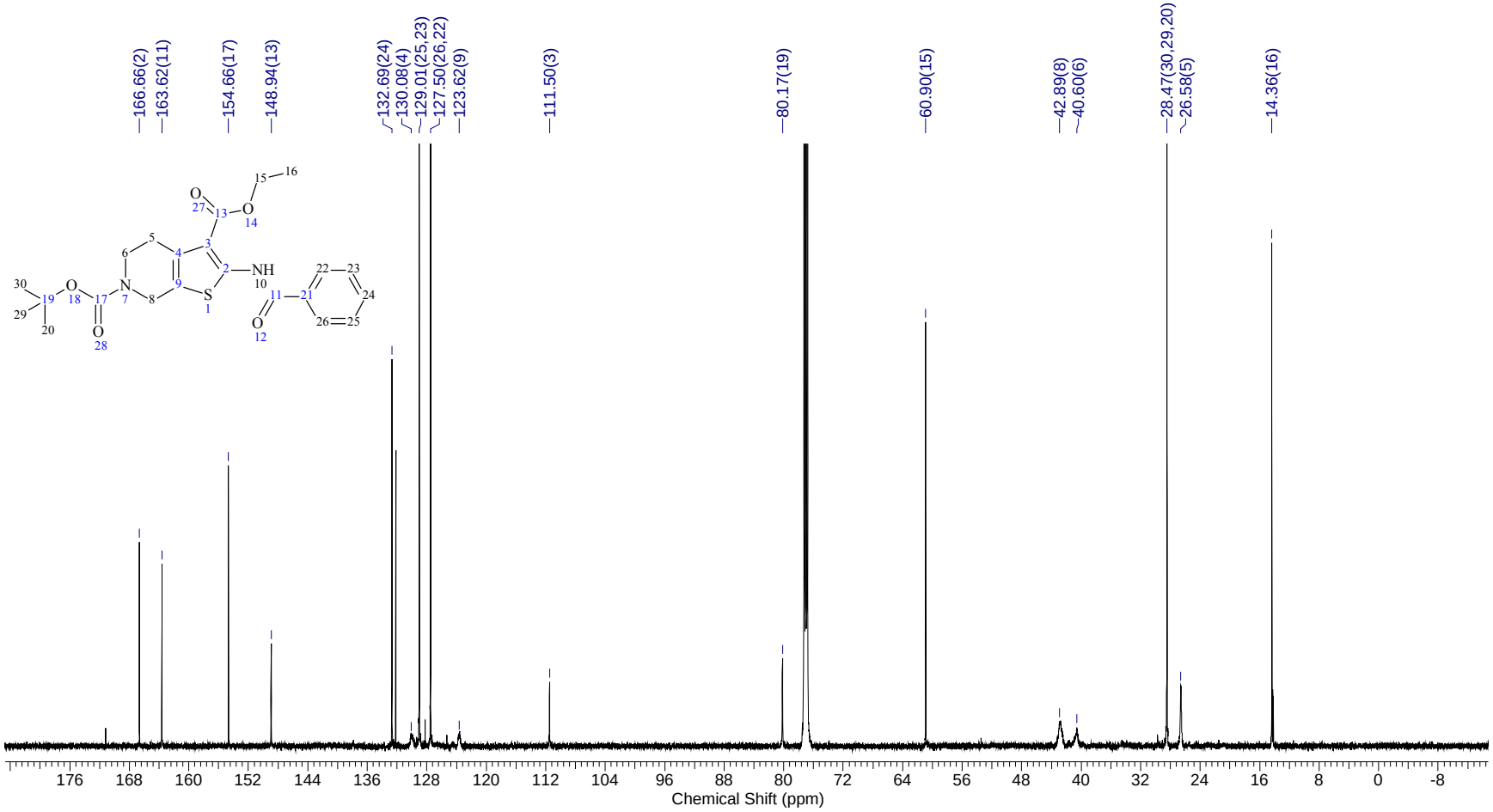




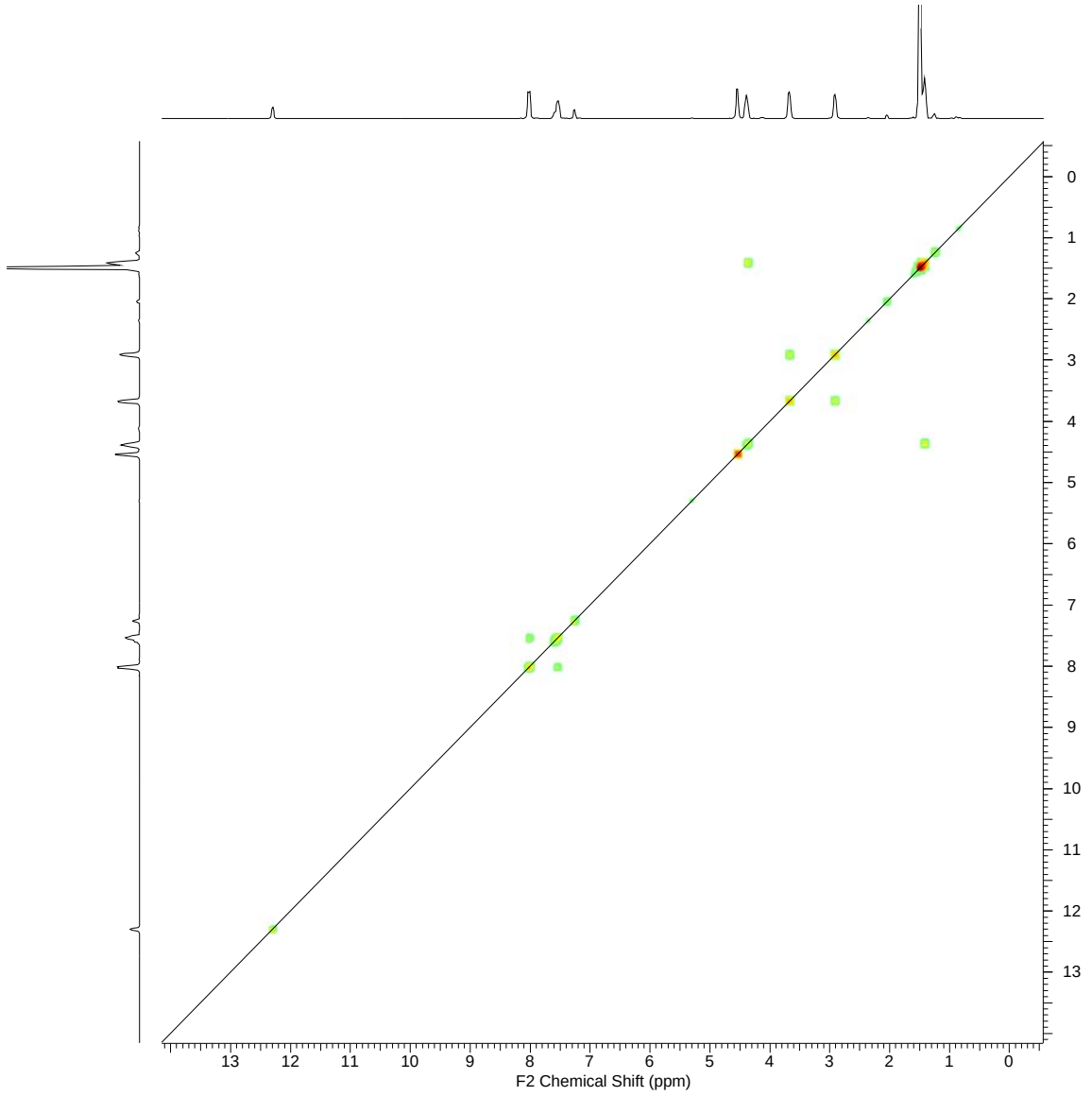
^{1}H-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (**28**, $CDCl_3$)

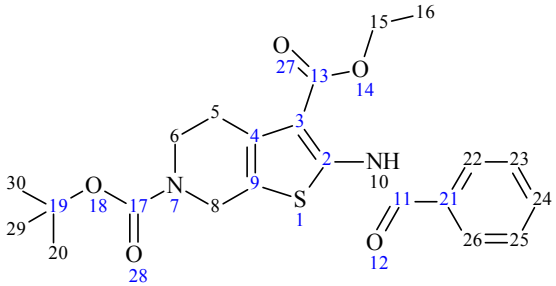


^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (**28**, $CDCl_3$)

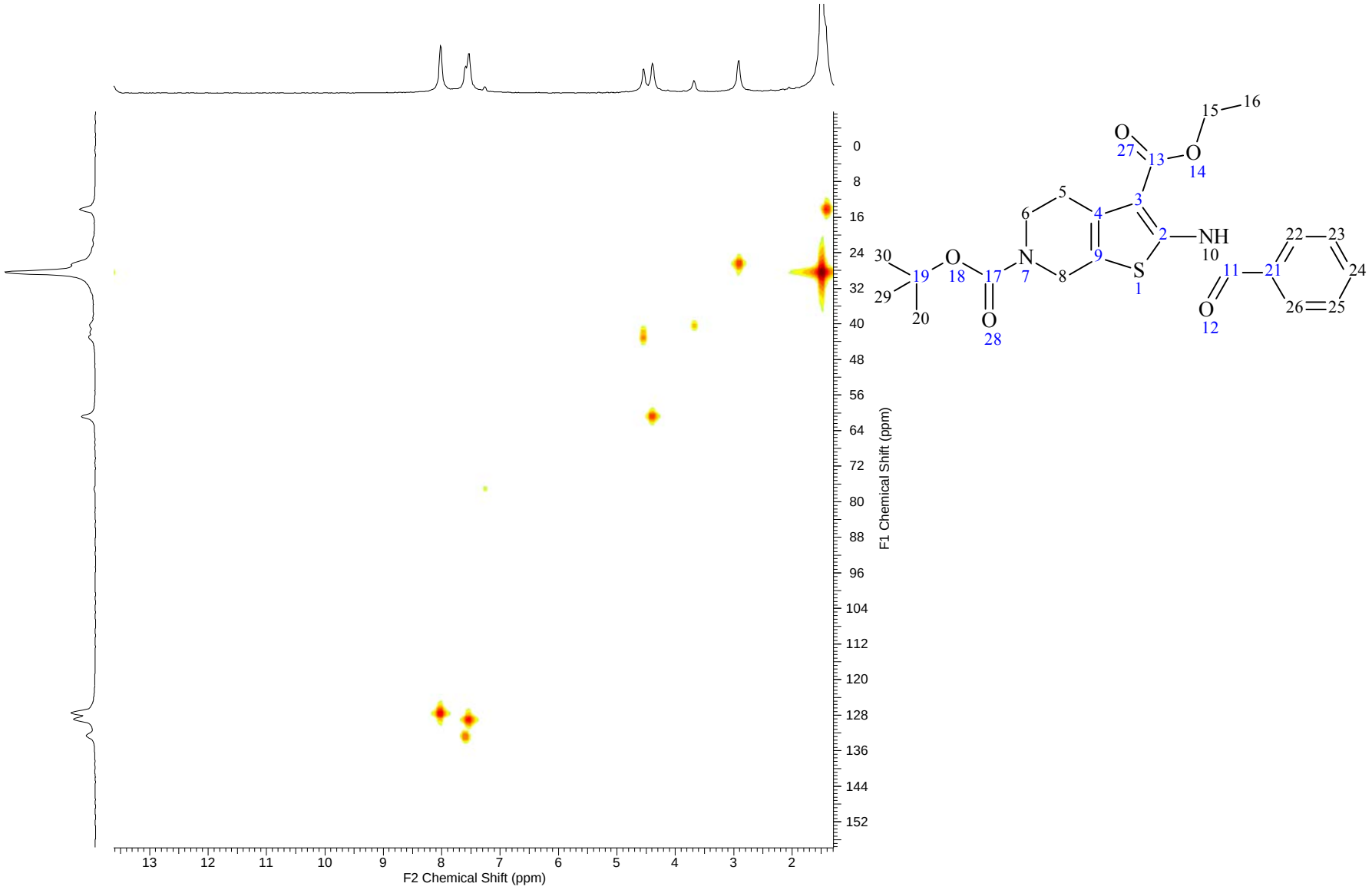


COSY of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate (**28**, $CDCl_3$)

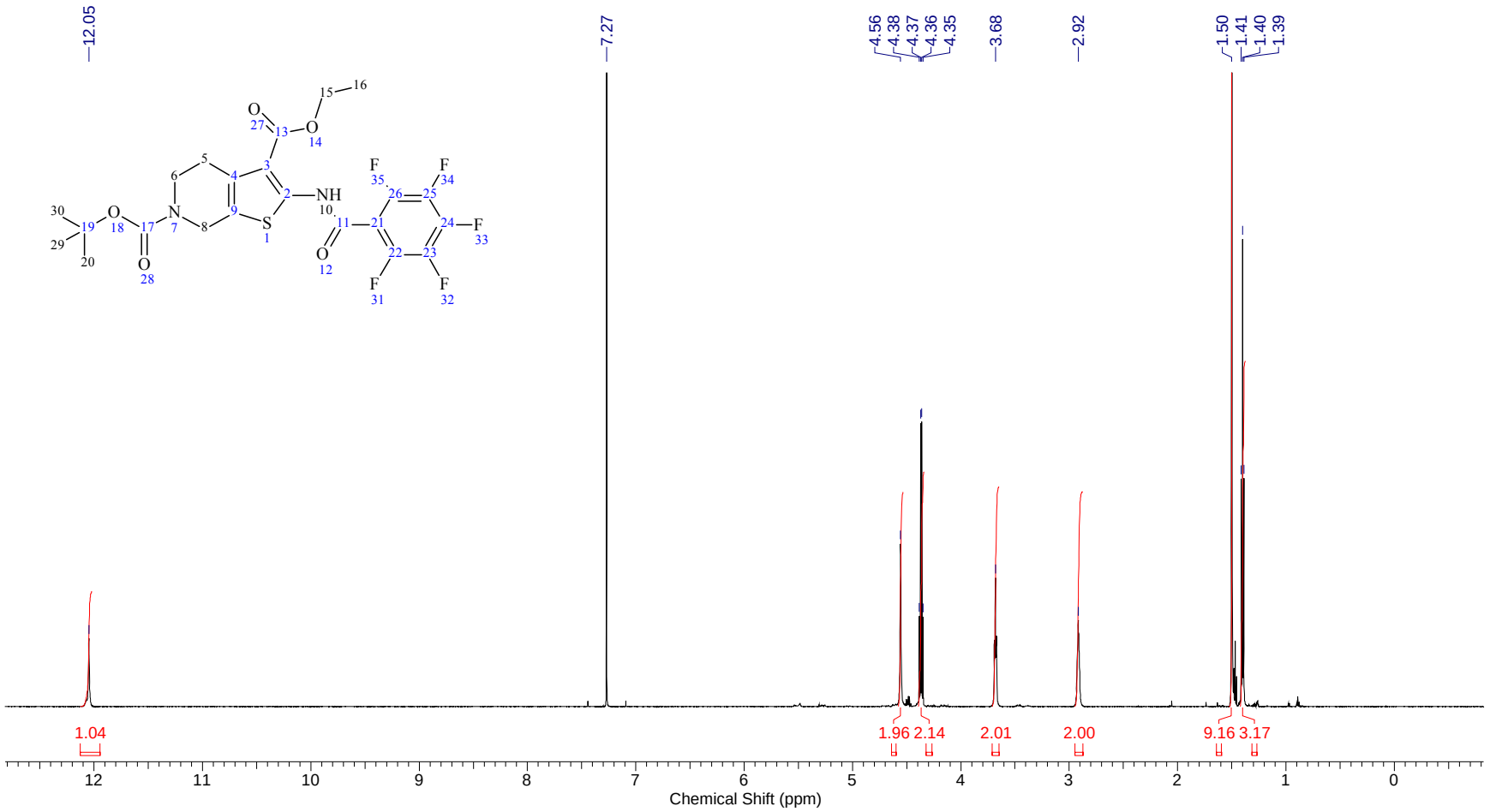




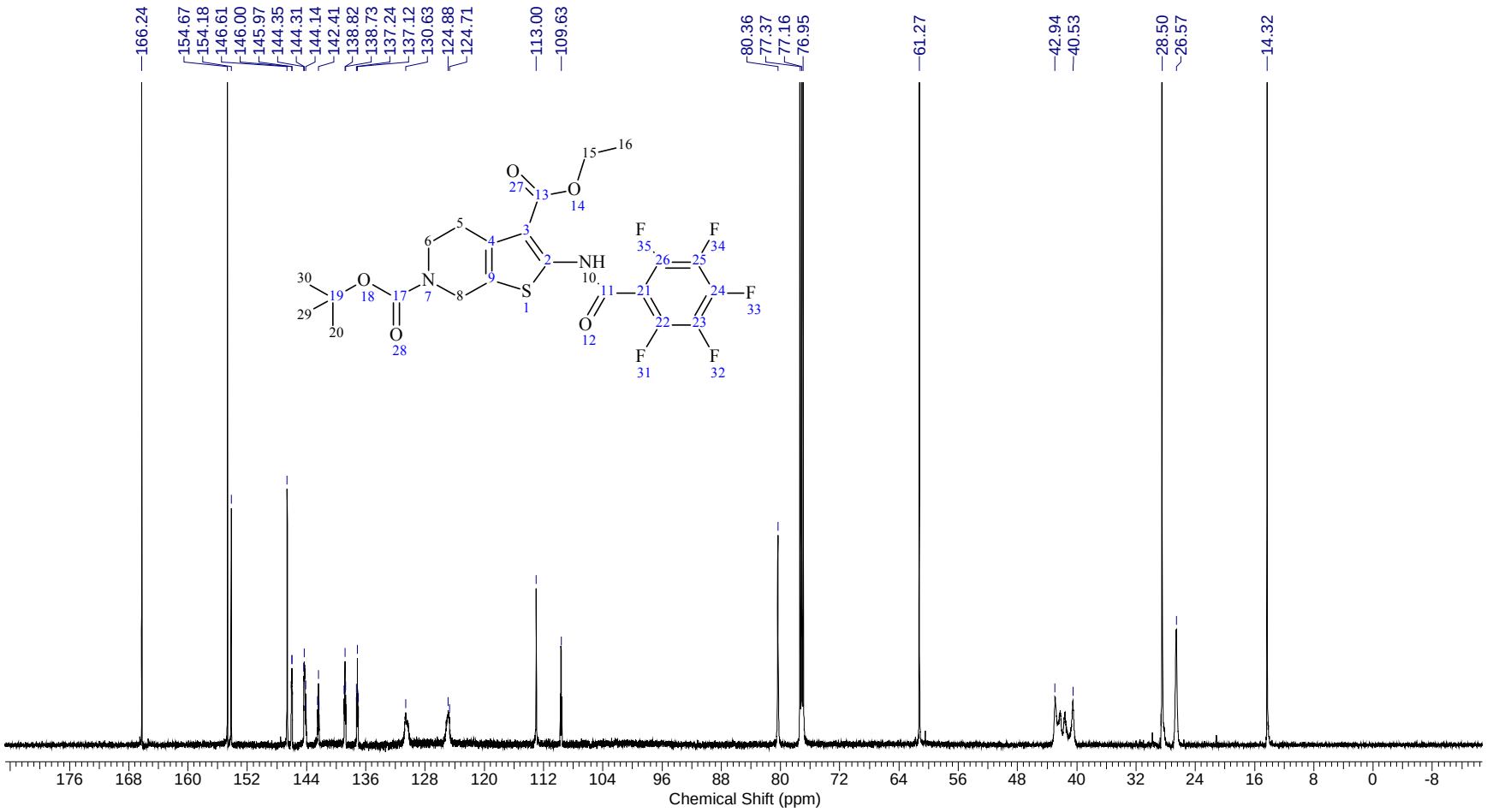
HMQC of compound 6-(*tert*-butyl) 3-ethyl 2-benzamido-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(28**, $CDCl_3$**)**



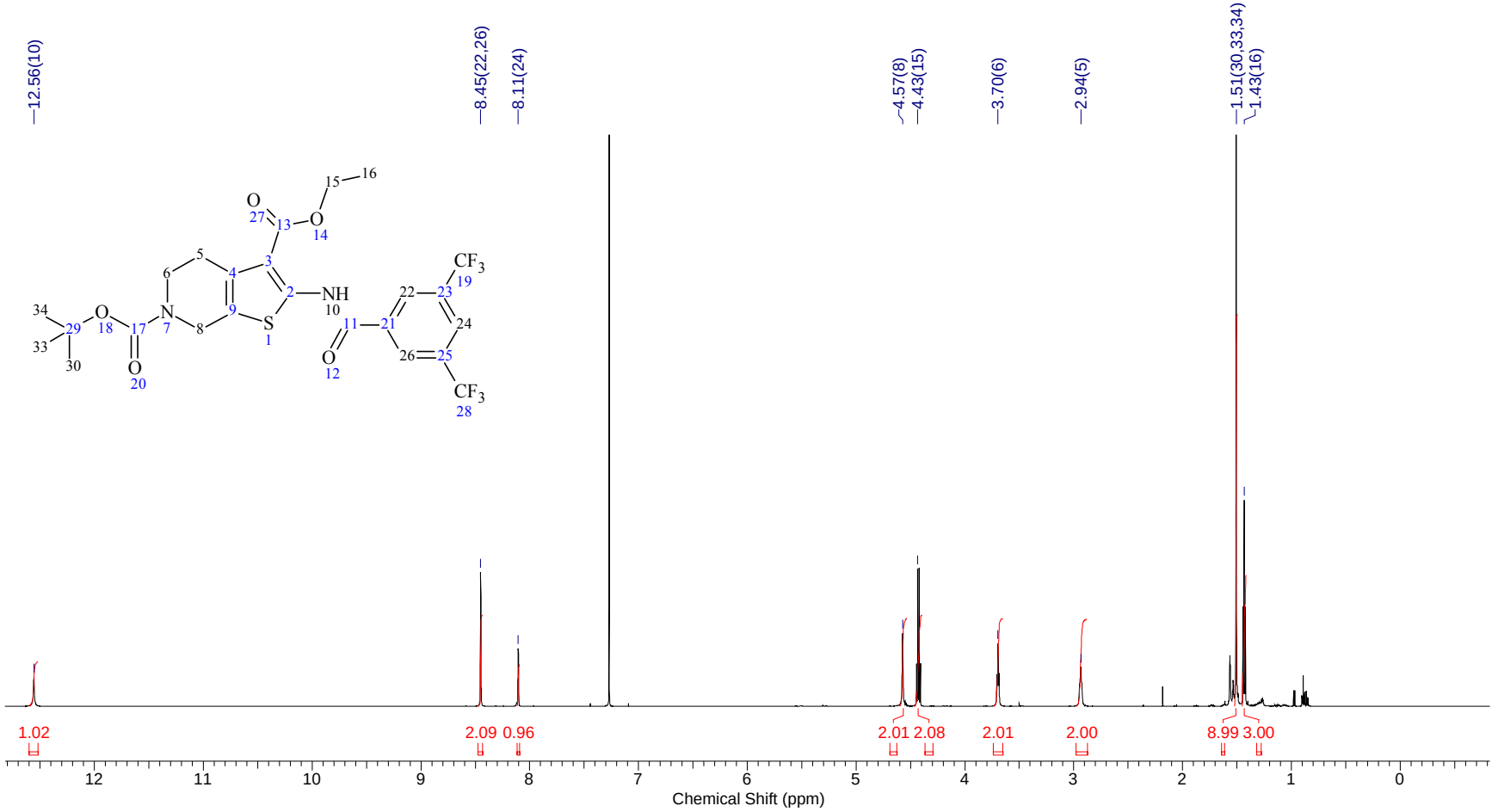
^{1}H-NMR of compound 6-(t*ert*-butyl) 3-ethyl 2-(perfluorobenzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(29**, $CDCl_3$**)**



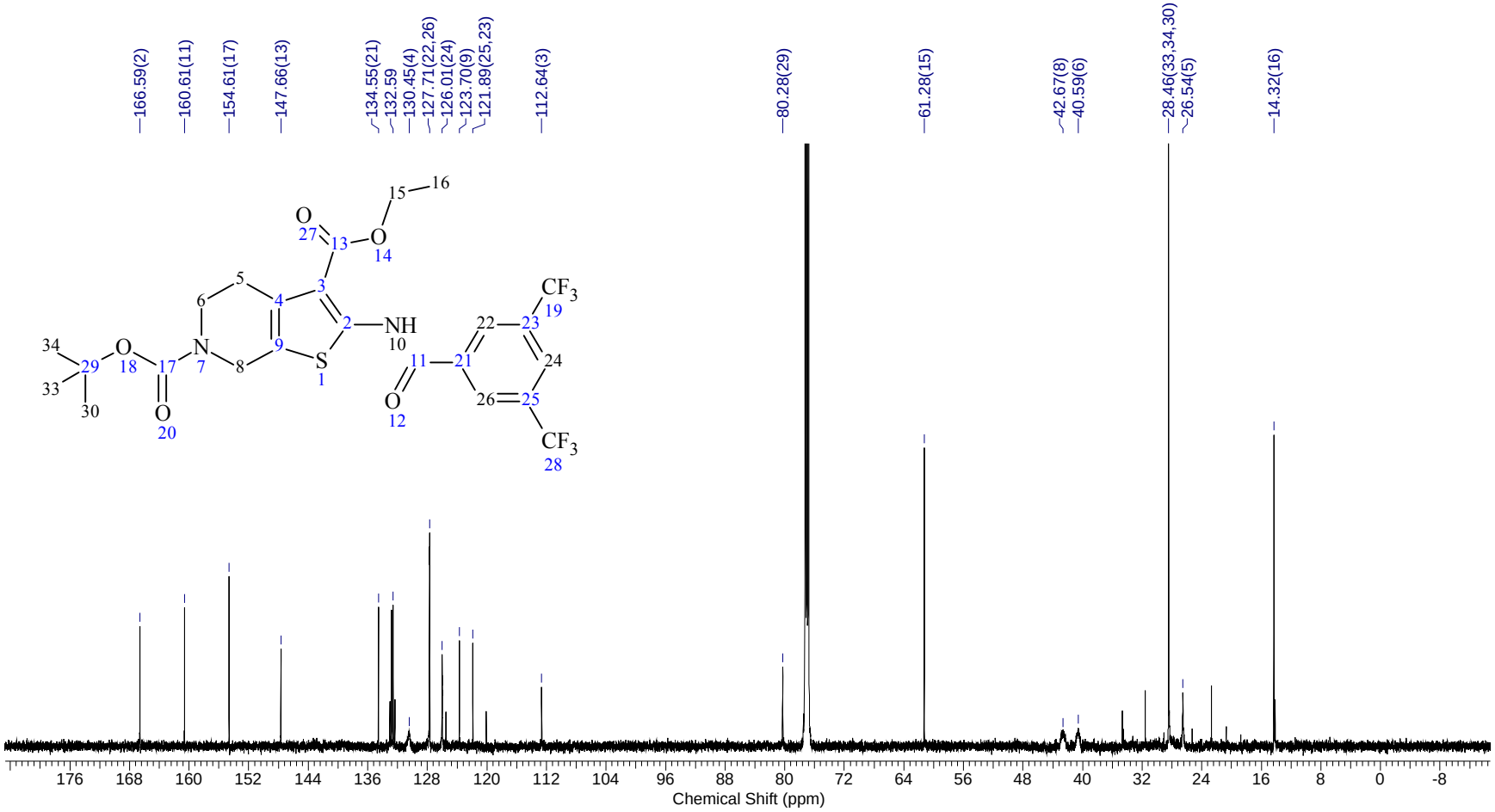
^{13}C-NMR of compound 6-(t*ert*-butyl) 3-ethyl 2-(perfluorobenzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(29**, $CDCl_3$**)**



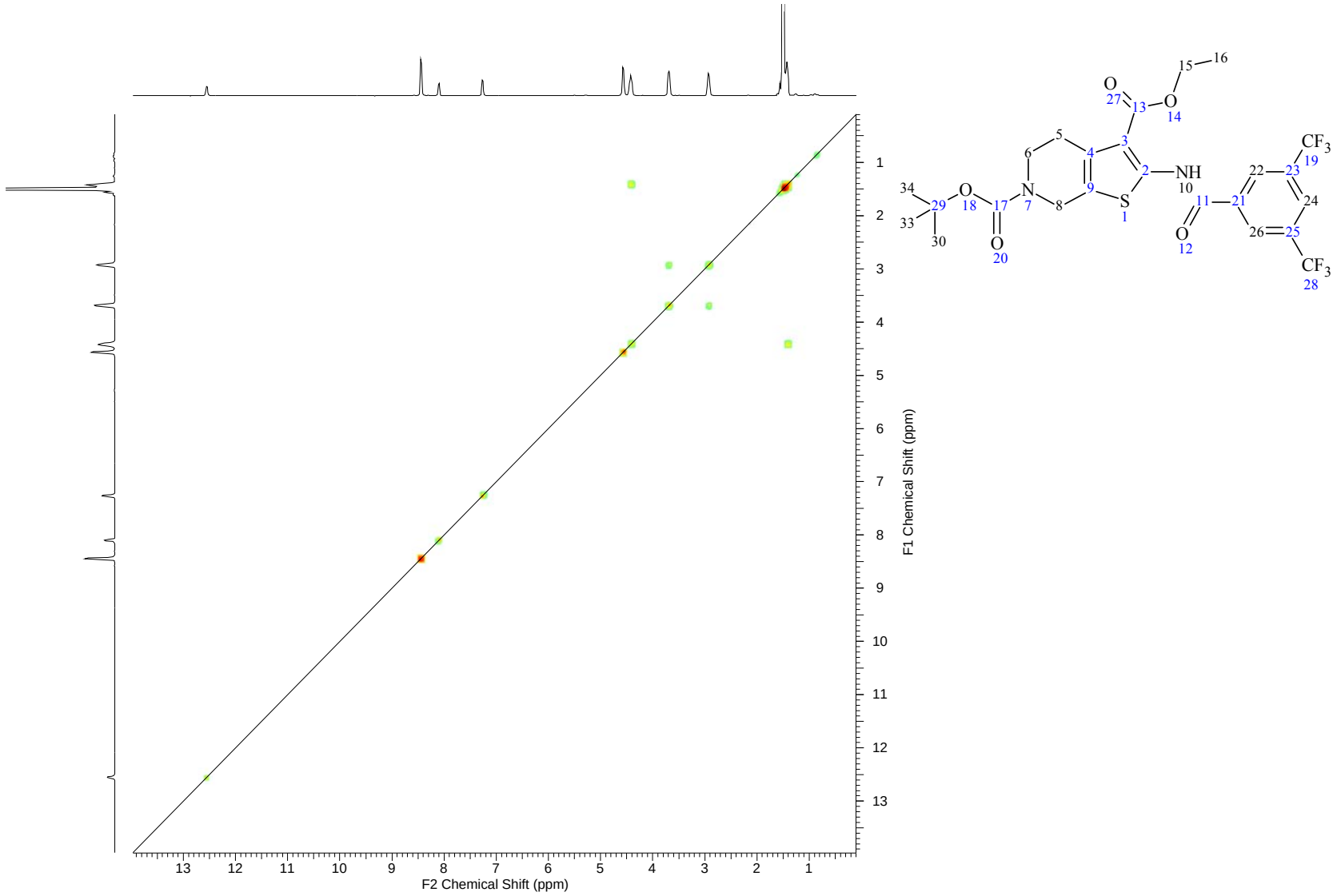
^{1}H-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30**, $CDCl_3$**)**



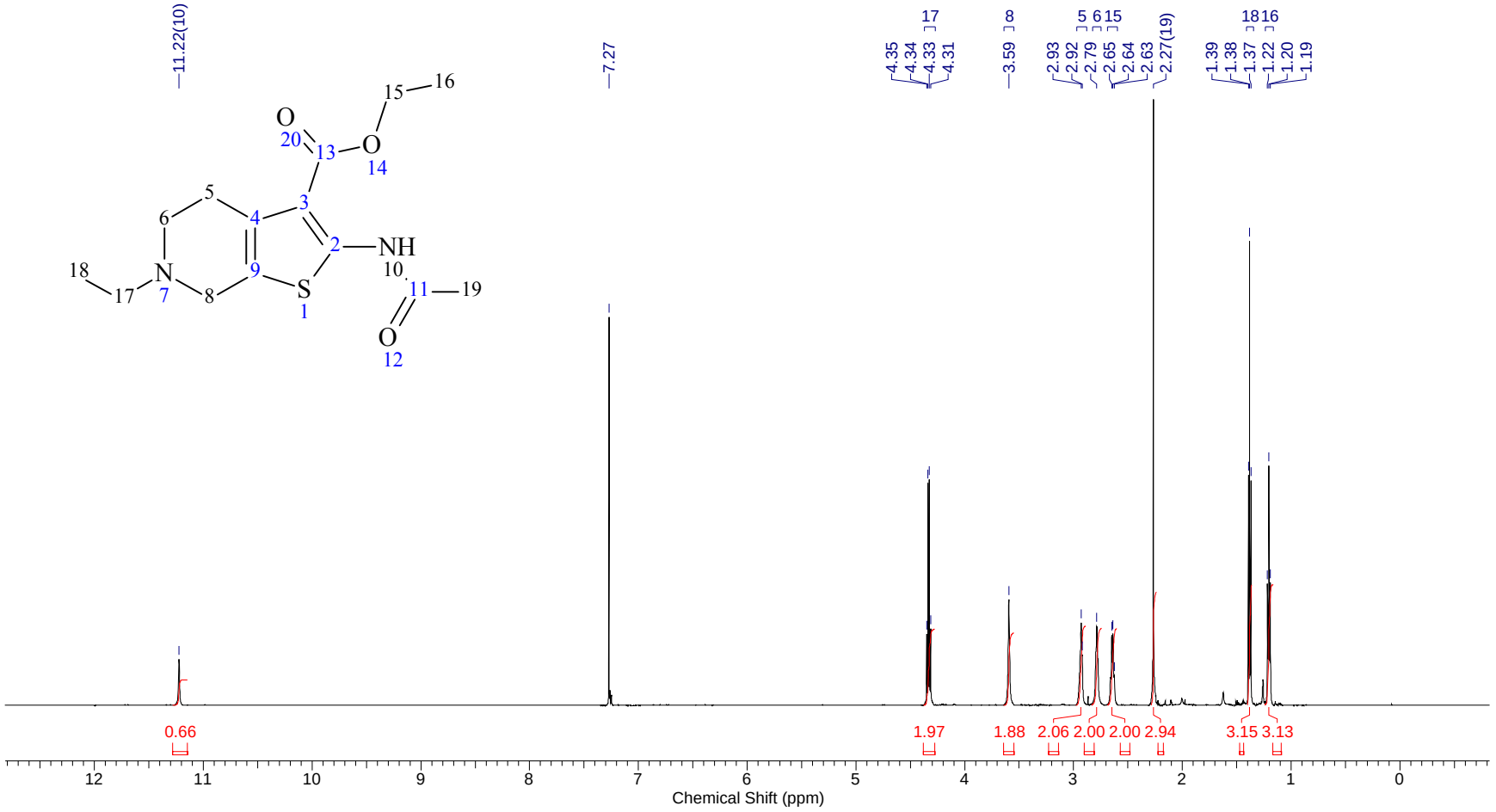
^{13}C-NMR of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30**, $CDCl_3$**)**



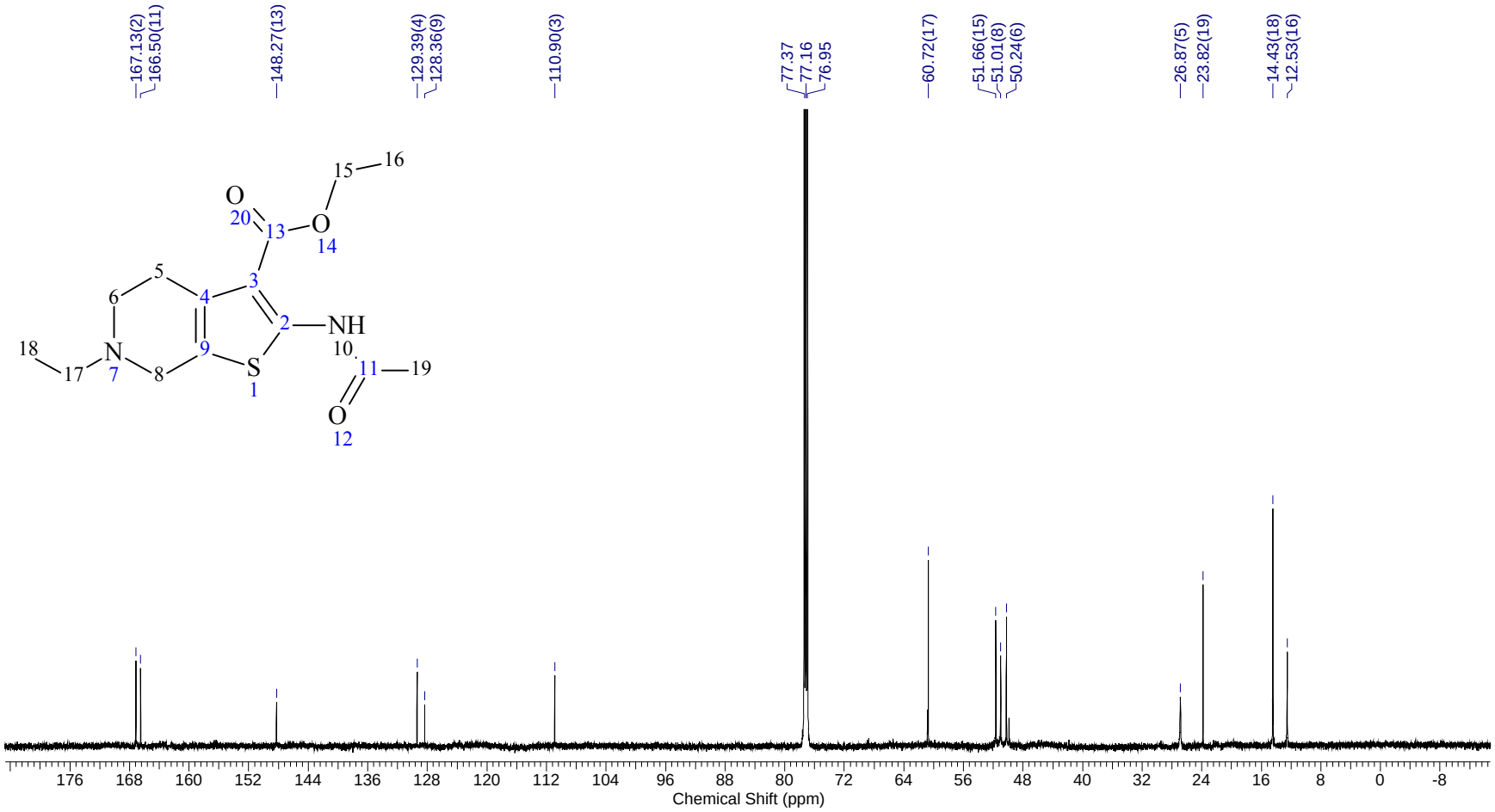
COSY of compound 6-(*tert*-butyl) 3-ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-4,7-dihydrothieno[2,3-*c*]pyridine-3,6(5*H*)-dicarboxylate **(30)**



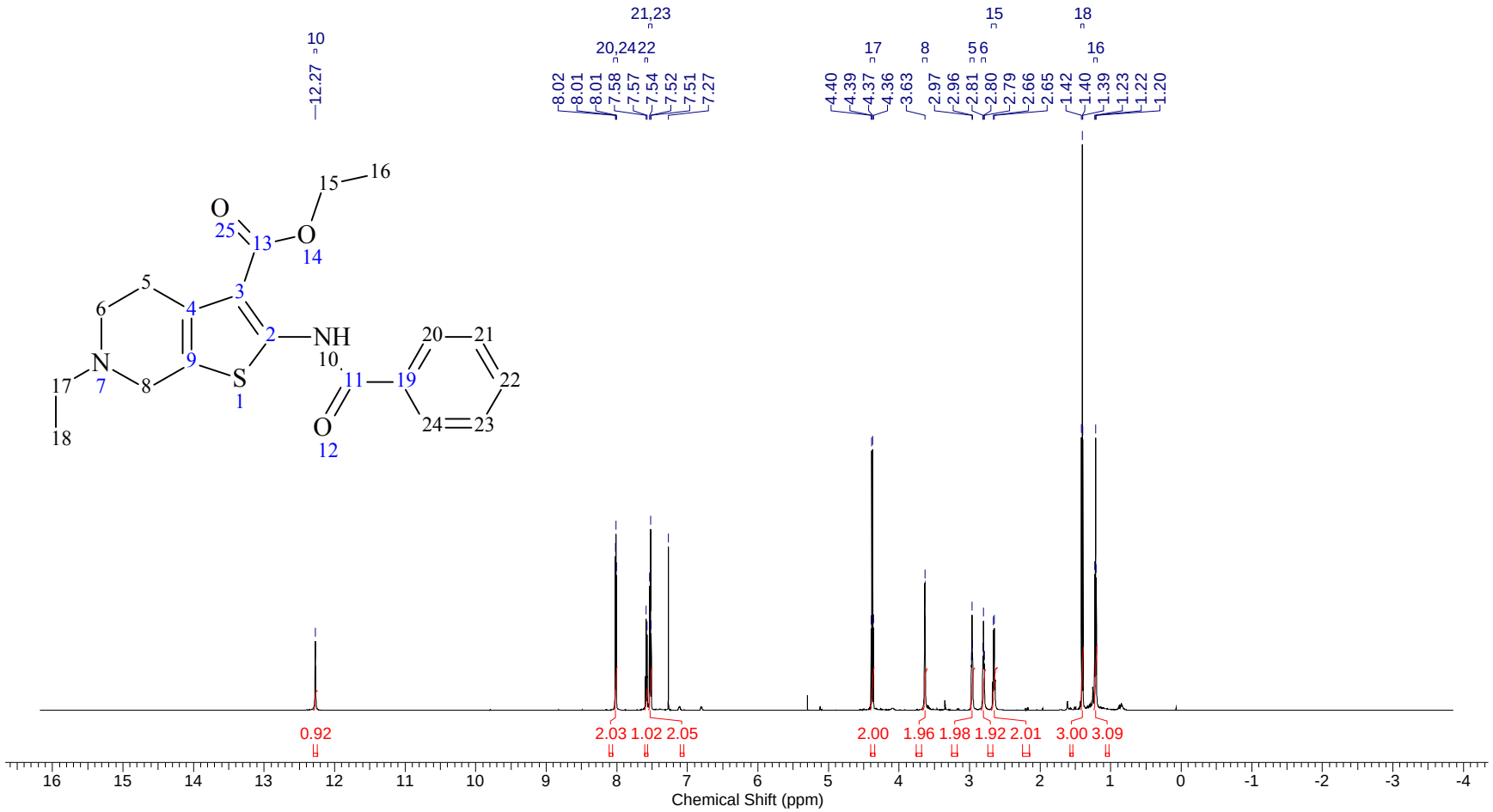
^{1}H-NMR of compound ethyl 2-acetamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(31,** $CDCl_3$**)**[6]



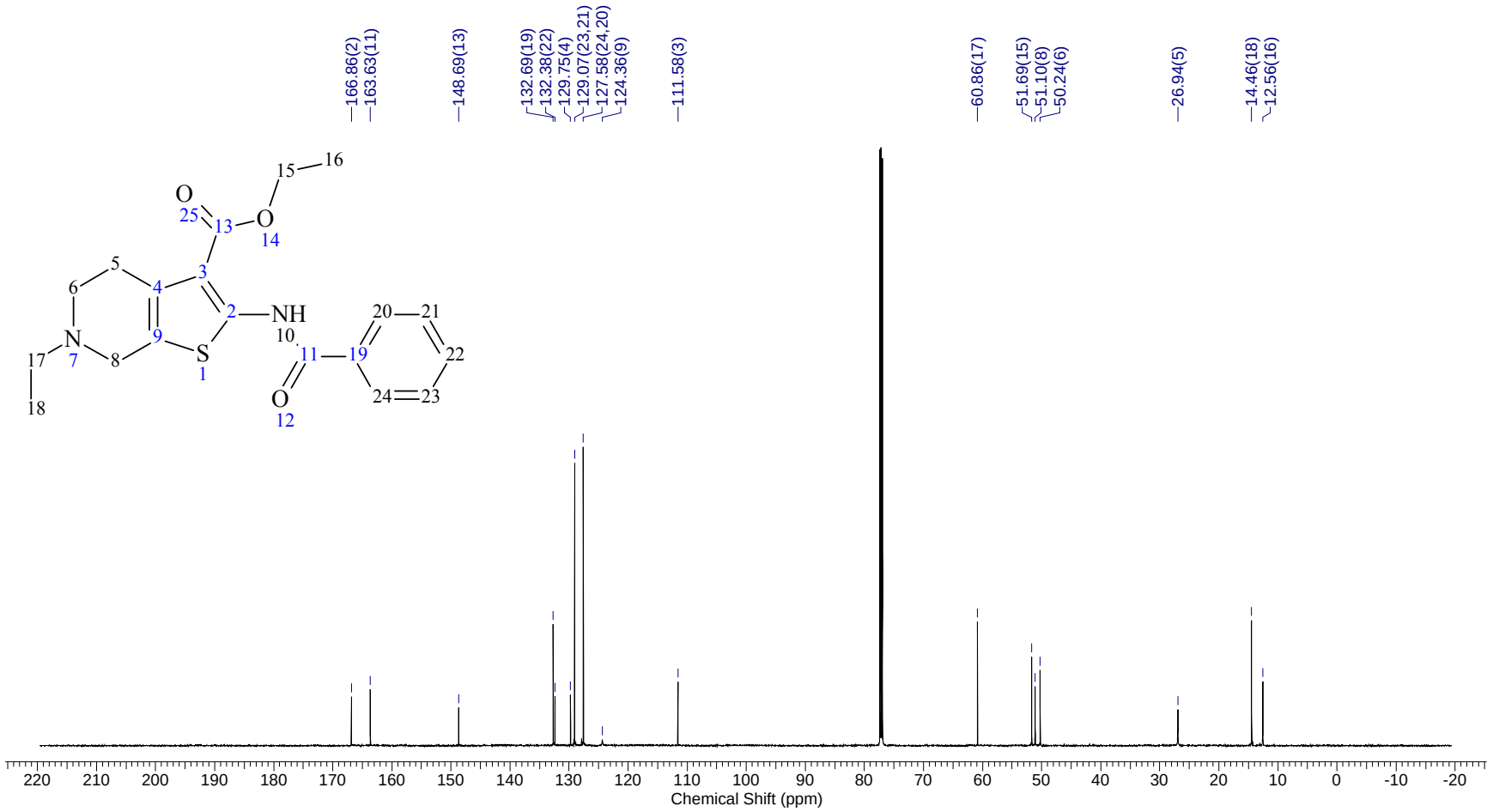
^{13}C-NMR of compound ethyl 2-acetamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(31**, $CDCl_3$**)**[6]



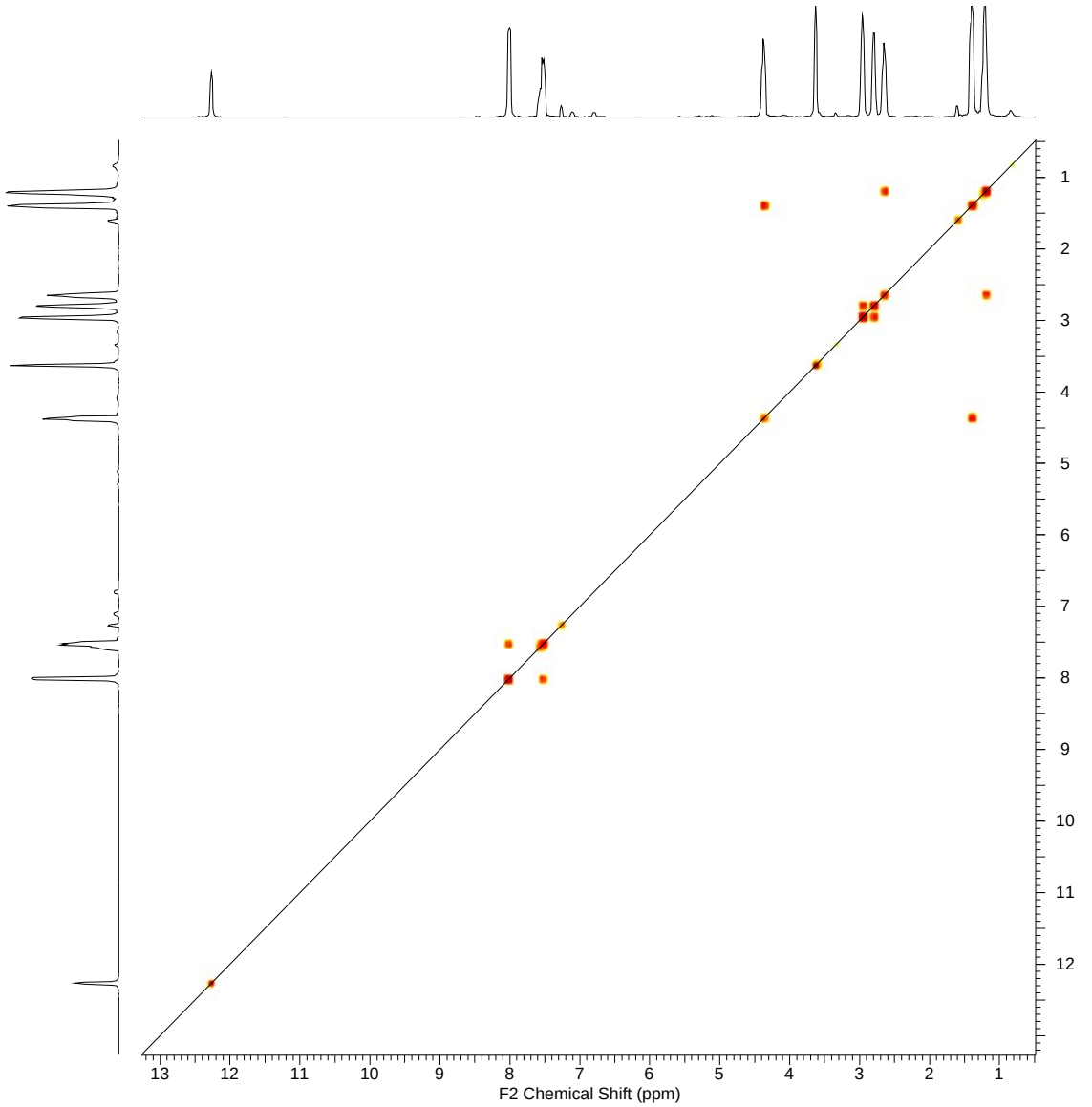
^{1}H-NMR of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32**, $CDCl_3$**)**

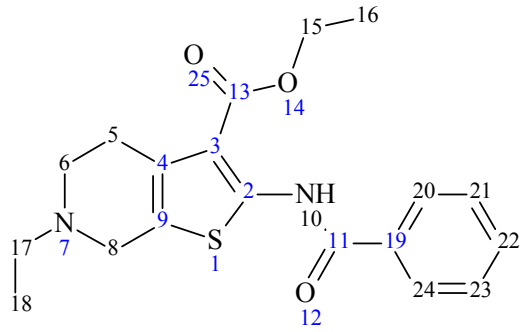


^{13}C-NMR of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32,** $CDCl_3$**)**

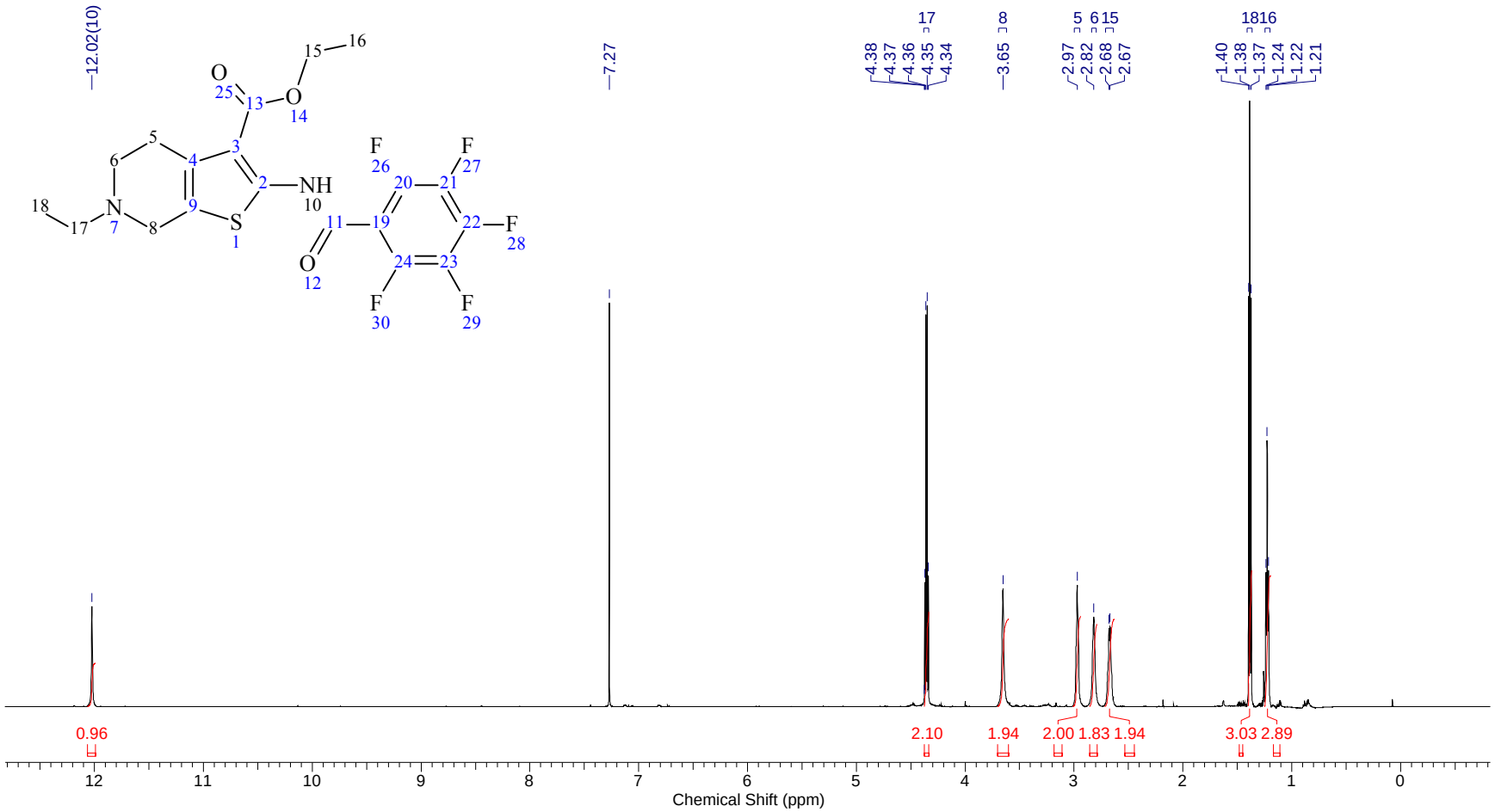


COSY of compound ethyl 2-benzamido-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(32**, $CDCl_3$**)**

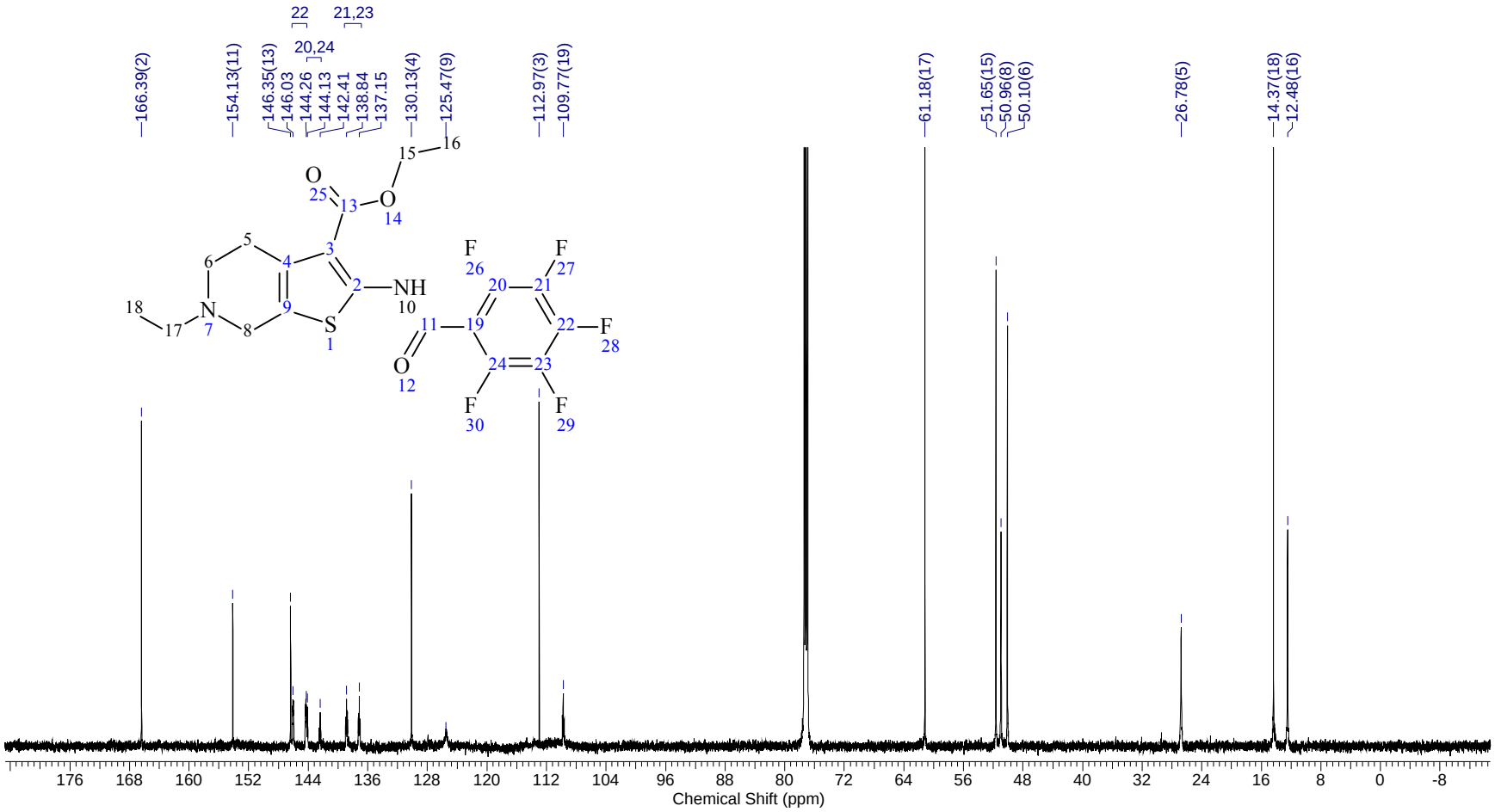




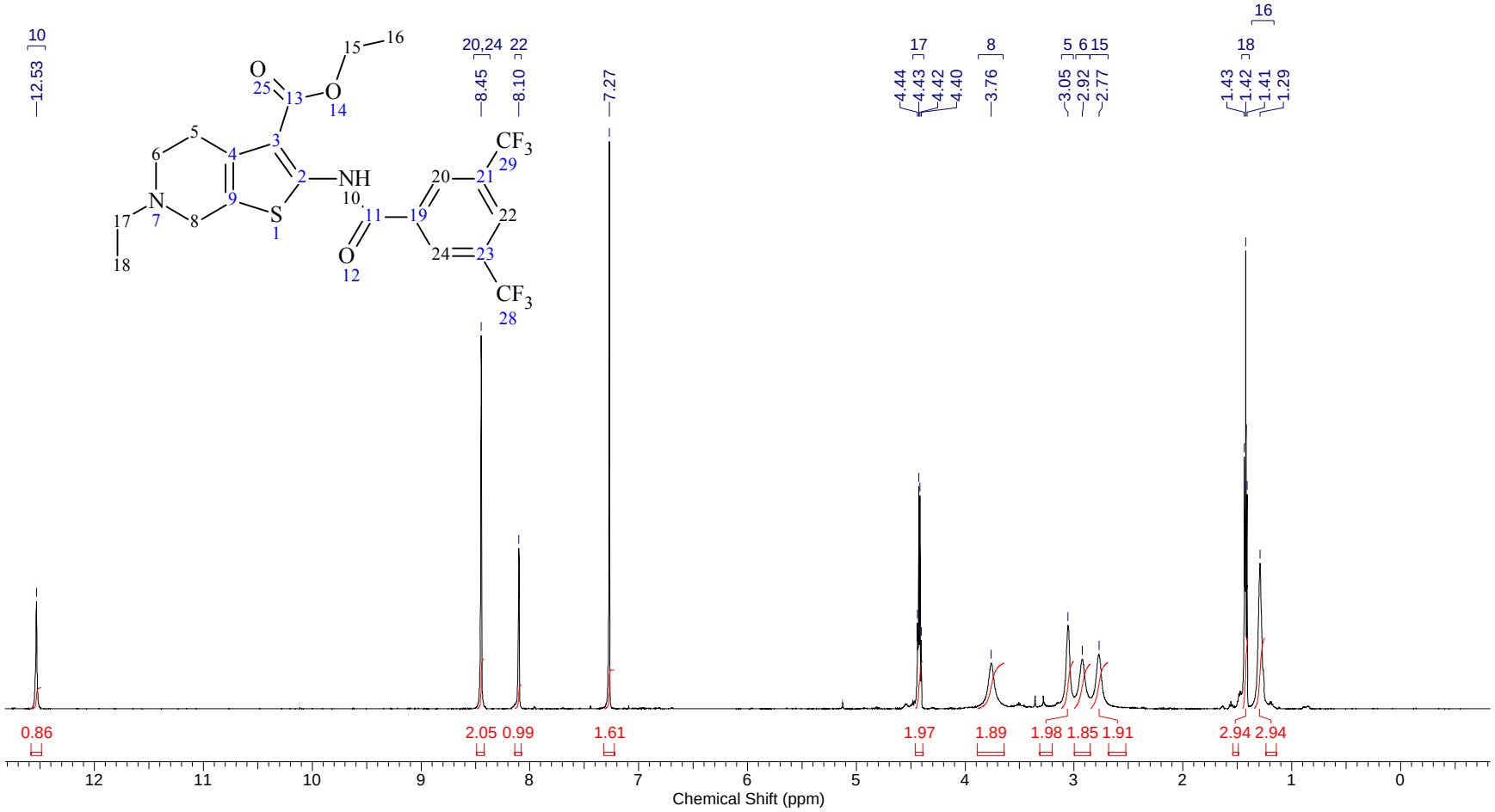
^{1}H-NMR of compound ethyl 6-ethyl-2-(perfluorobenzamido)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(33**, $CDCl_3$**)**



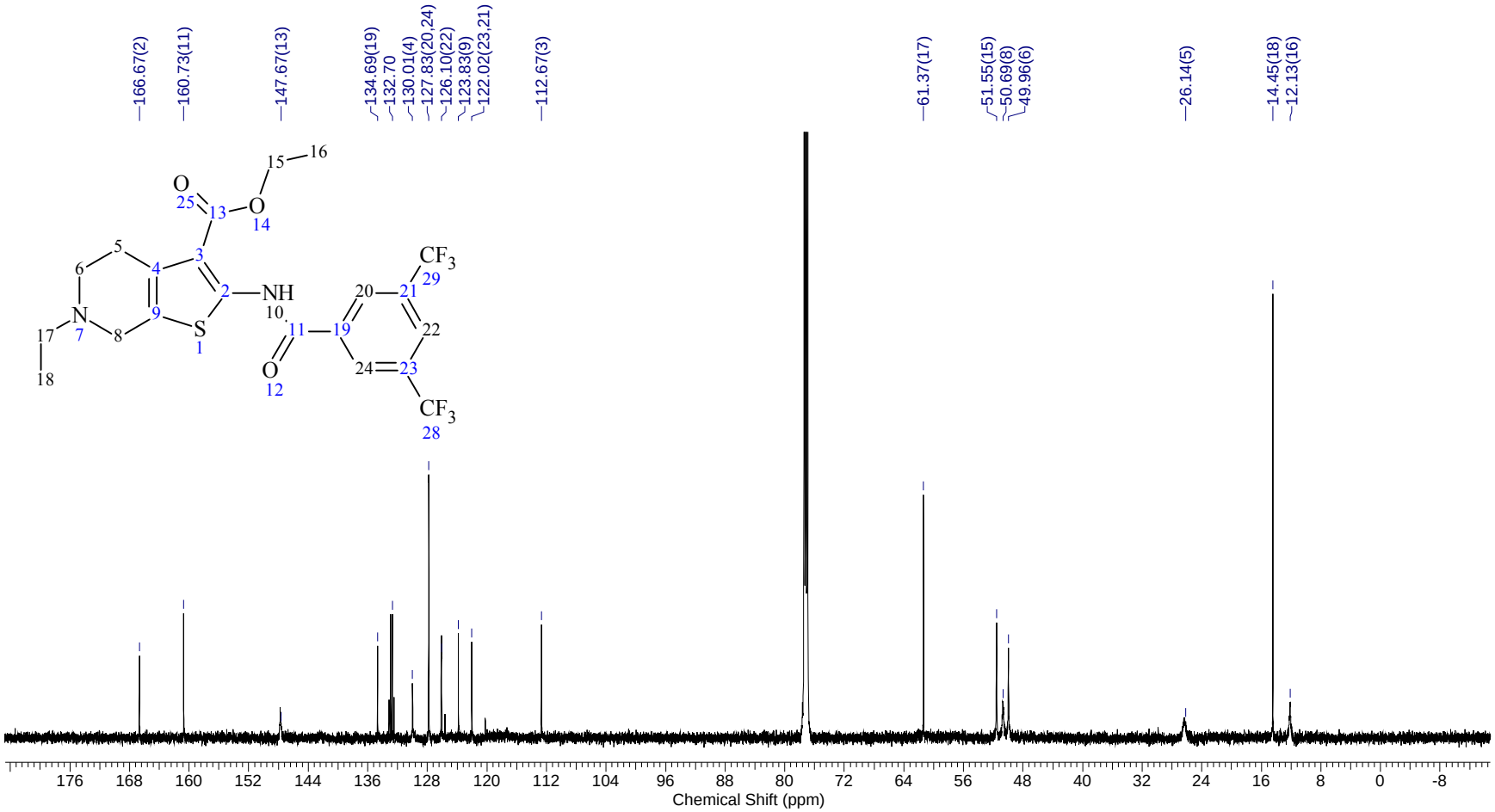
^{13}C-NMR of compound ethyl 6-ethyl-2-(perfluorobenzamido)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(33**, $CDCl_3$**)**



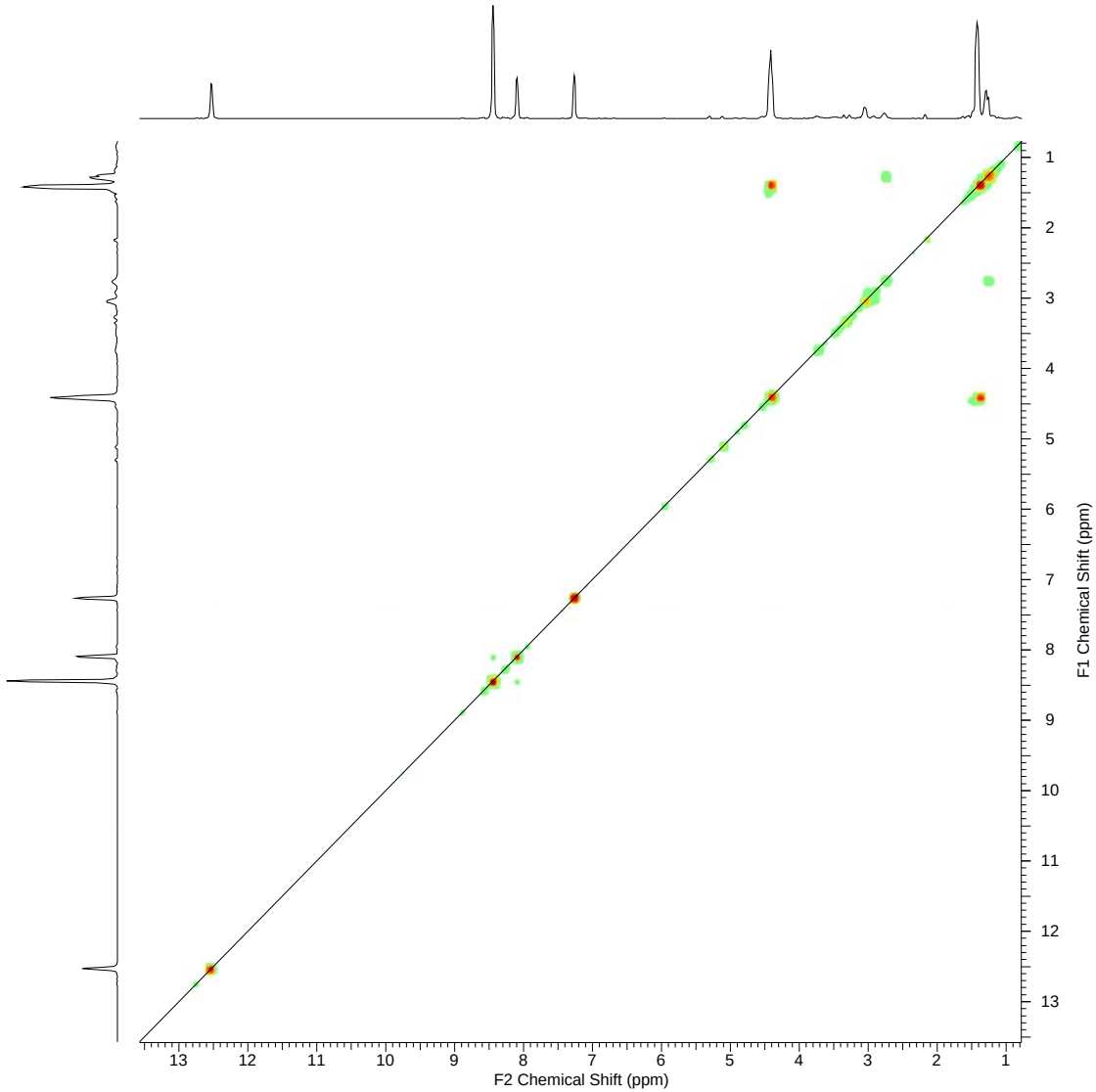
^{1}H-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34**, $CDCl_3$**)**

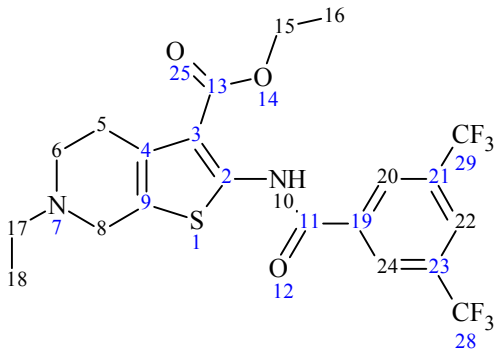


^{13}C-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34**, $CDCl_3$**)**

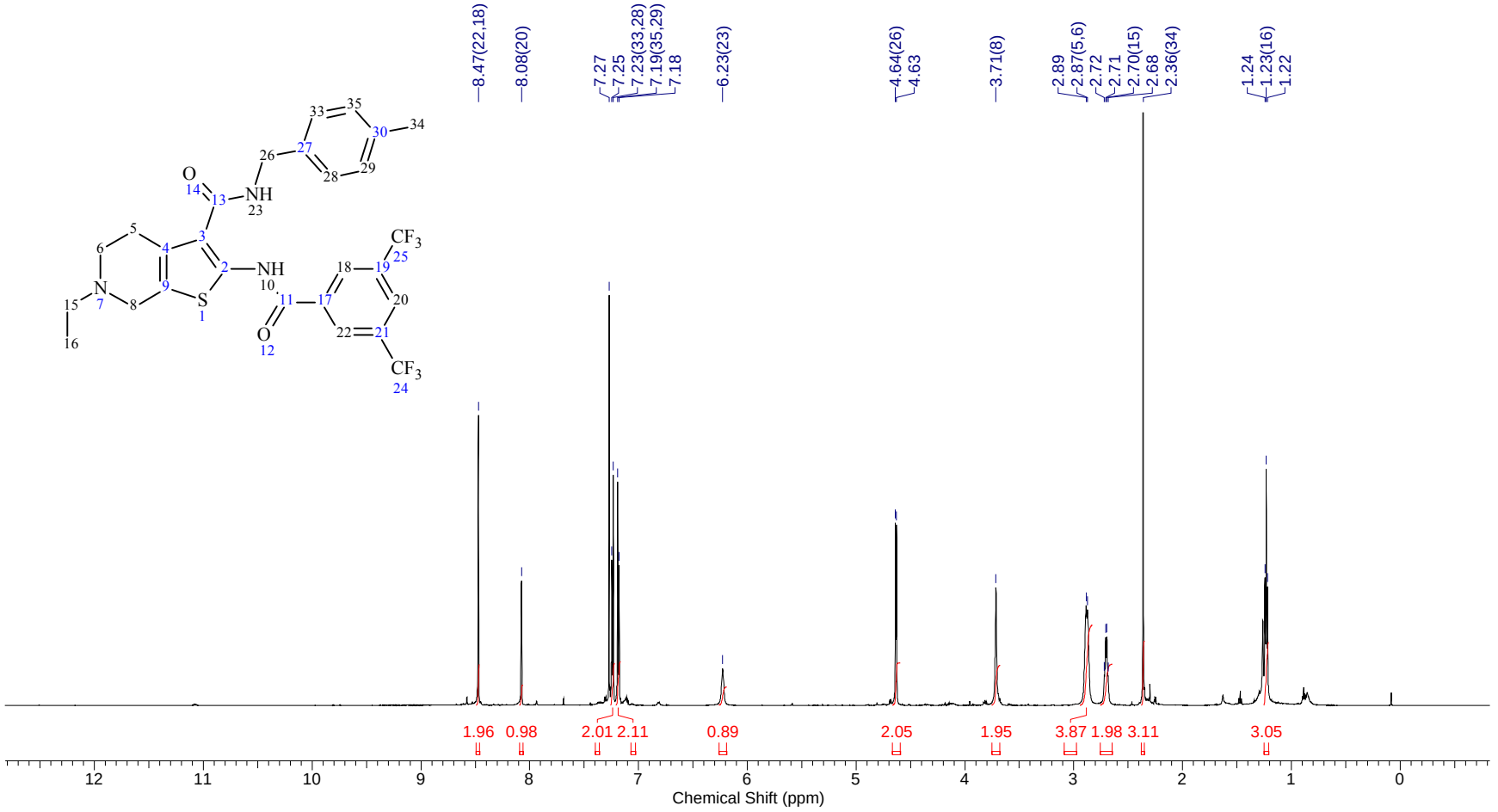


COSY of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylate **(34**, $CDCl_3$**)**

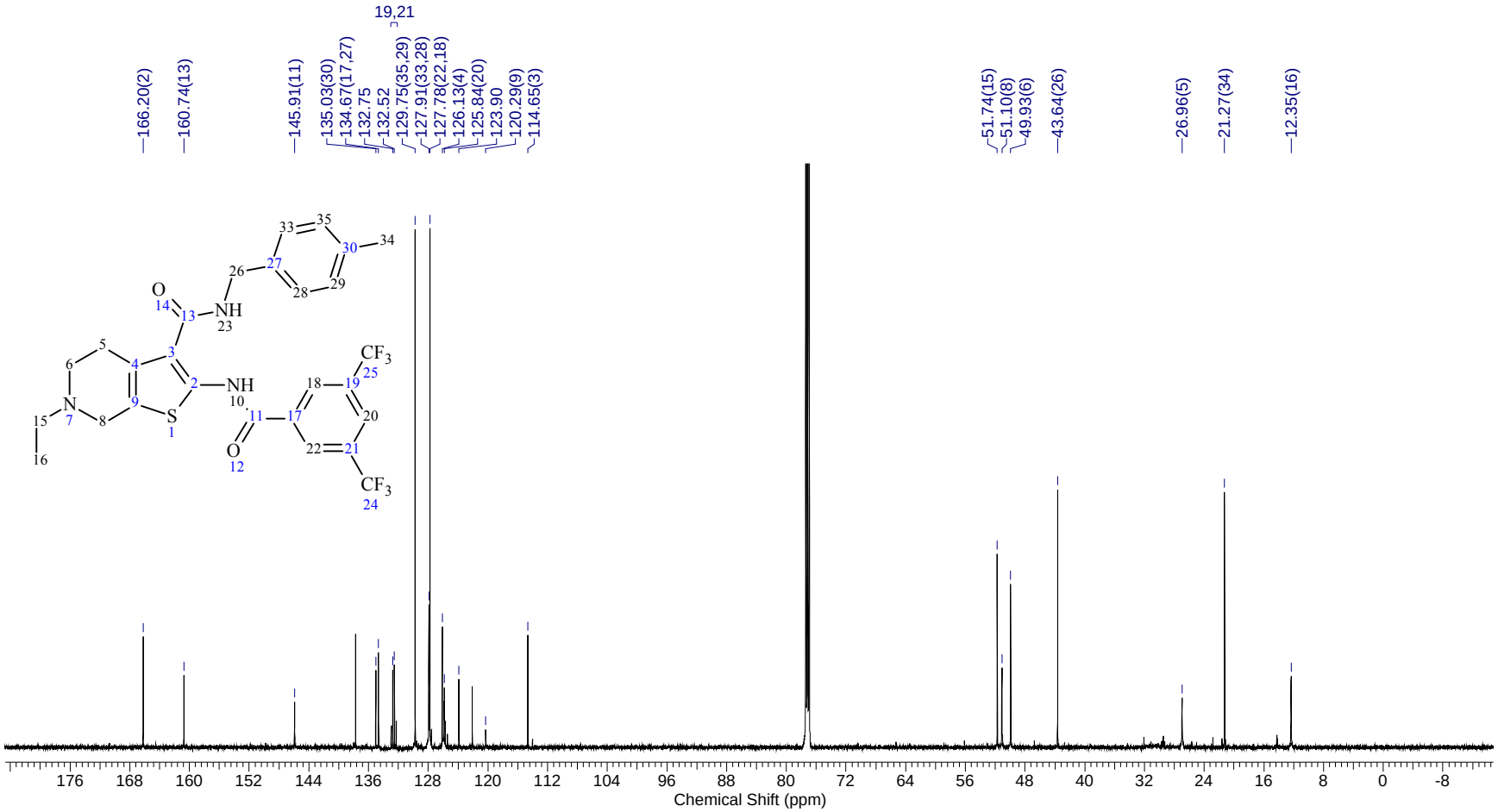




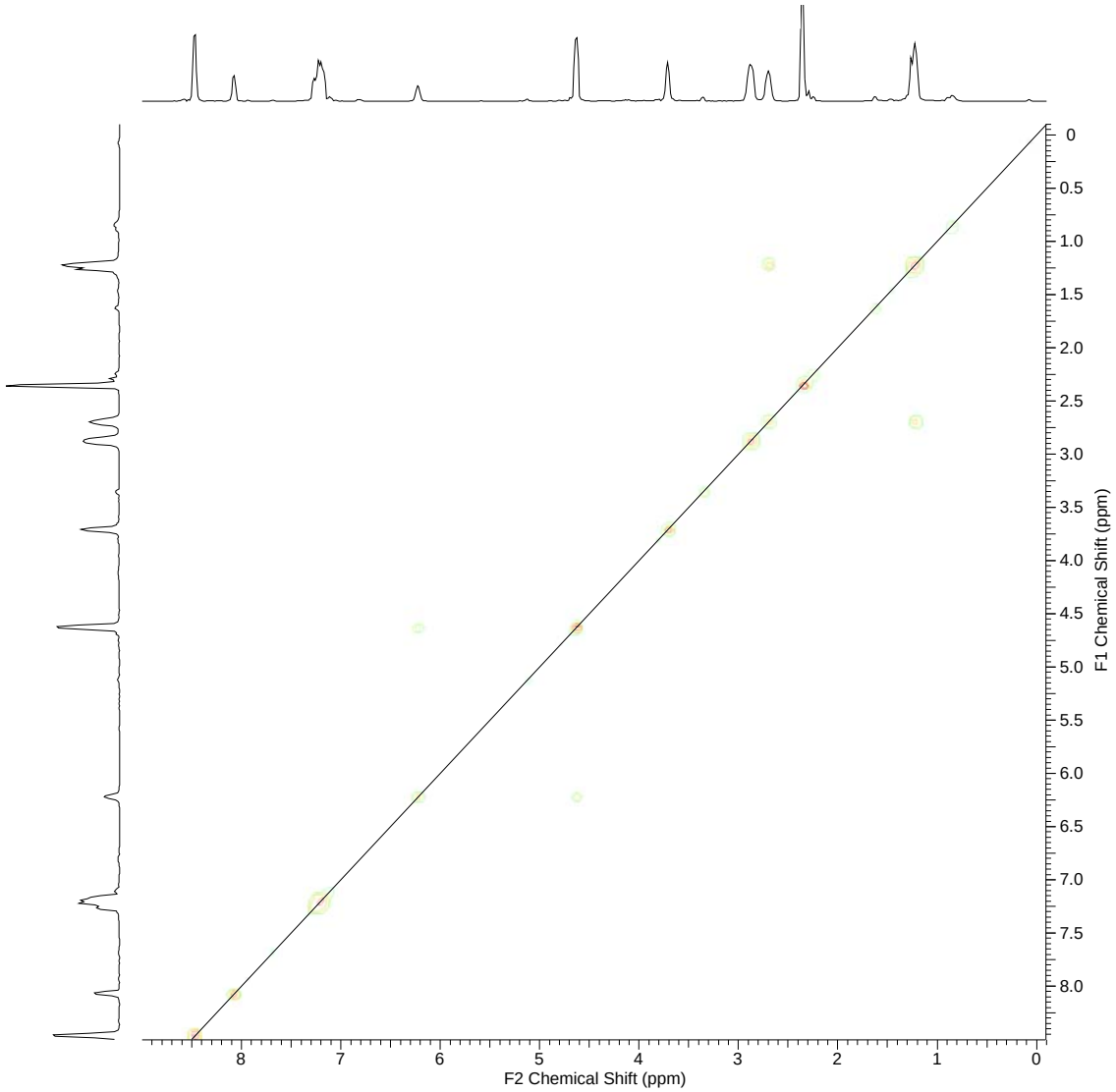
^{1}H-NMR of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35**, $CDCl_3$**)**

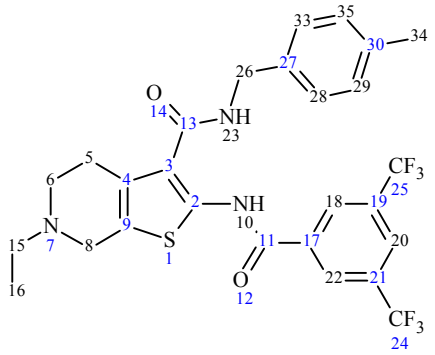


^{13}C-NMR of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35**, $CDCl_3$**)**

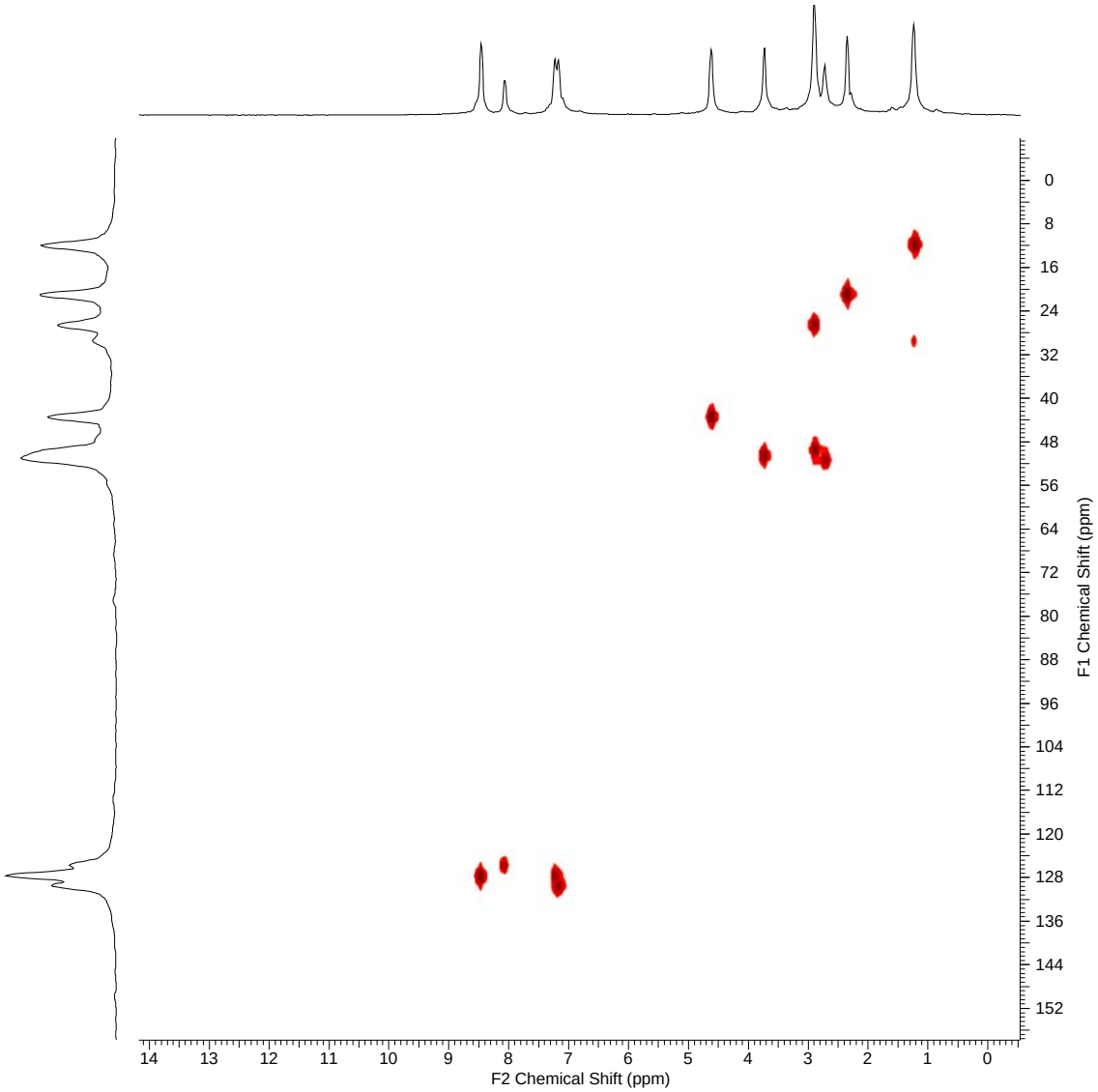


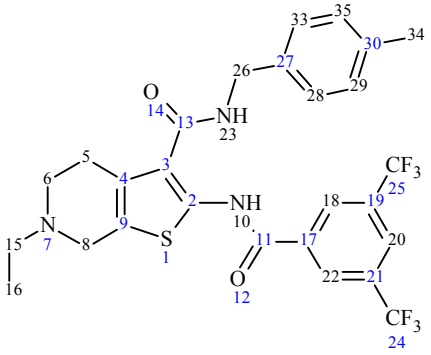
COSY of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35**, $CDCl_3$**)**



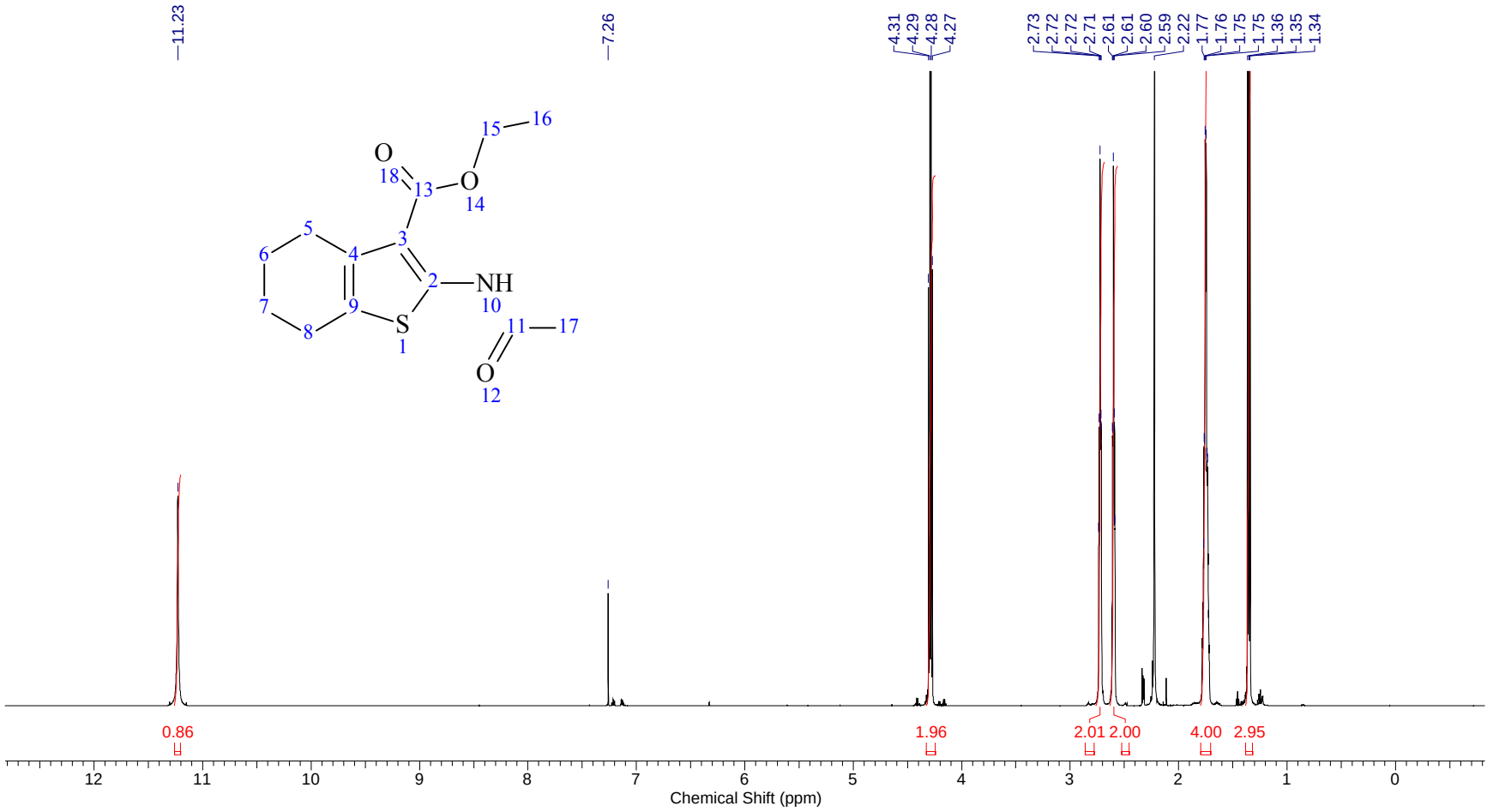


HMQC of compound 2-(3,5-Bis(trifluoromethyl)benzamido)-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide **(35**, $CDCl_3$**)**

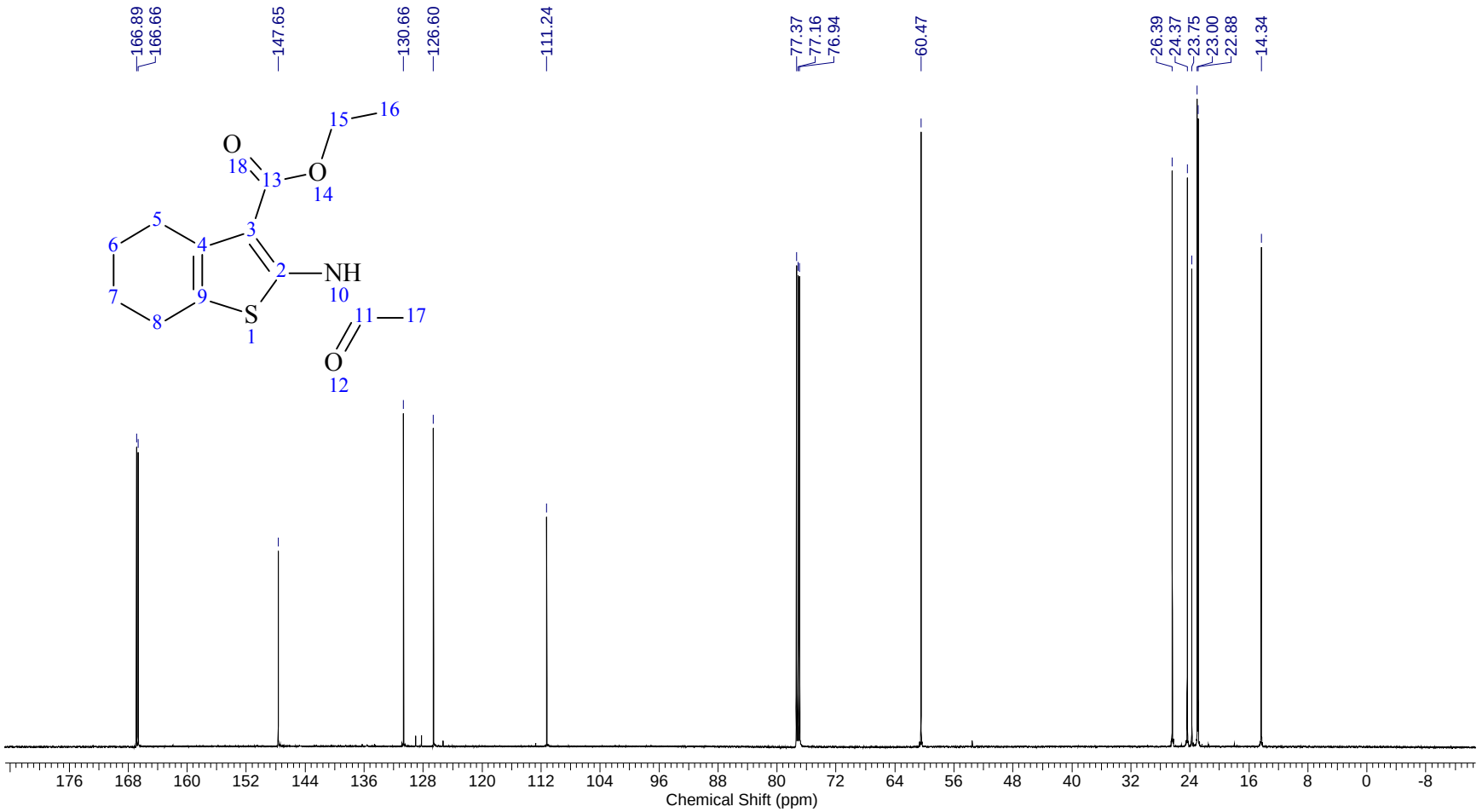




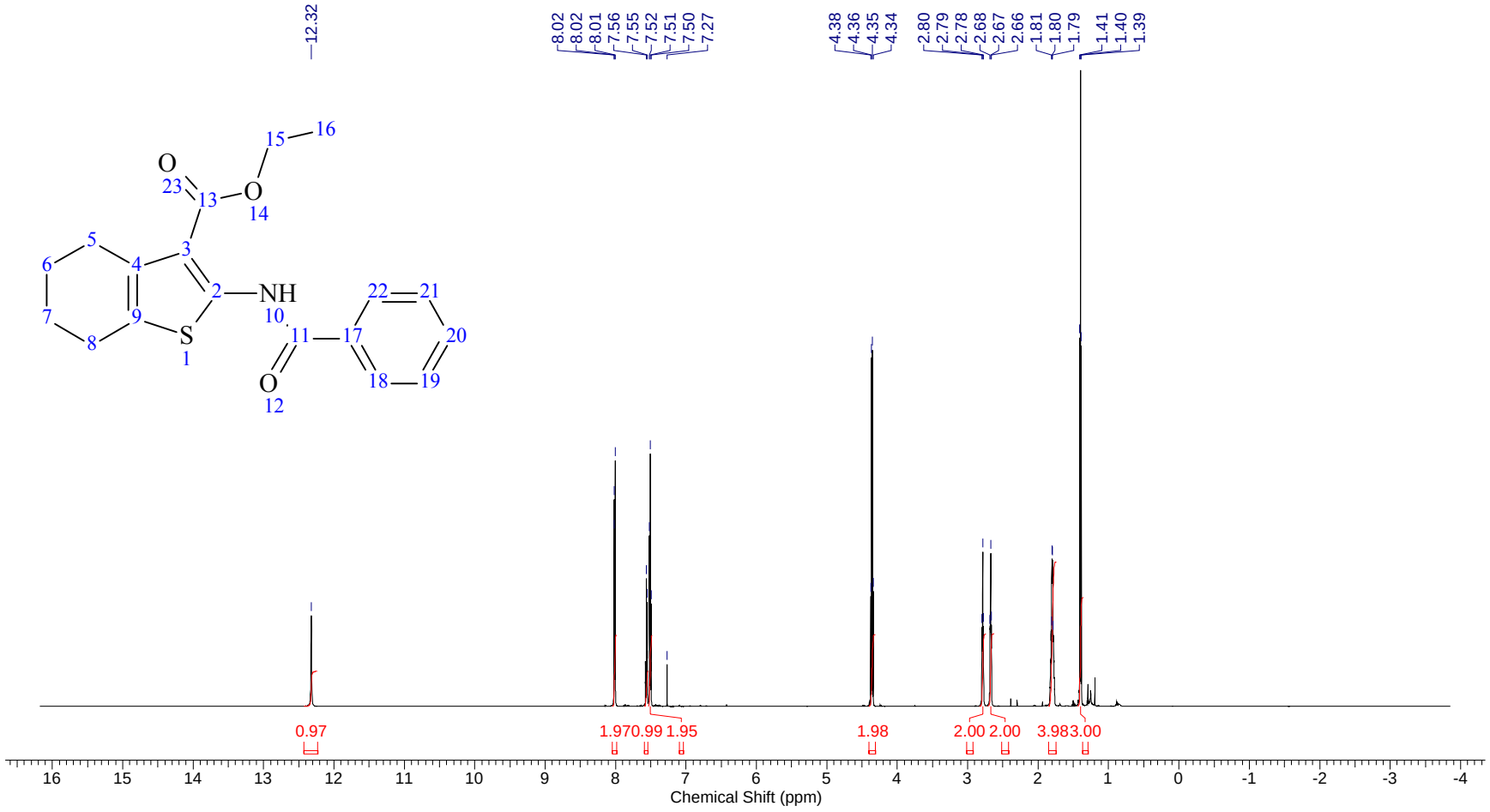
^{1}H-NMR of compound Ethyl 2-acetamido-4,5,6,7-tetrahydrobenzo[*b*] thiophene-3-carboxylate (**36**, $CDCl_3$)[7]



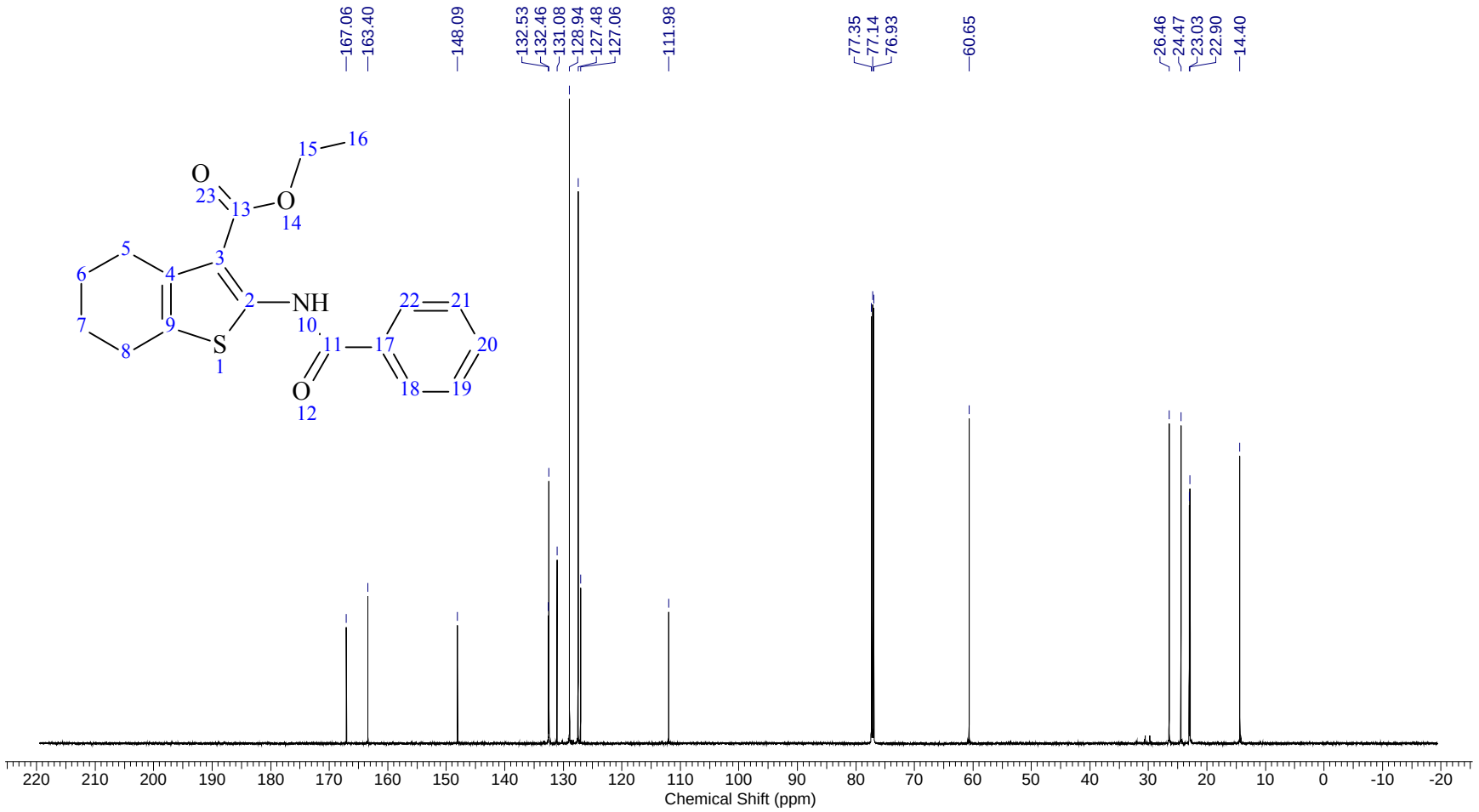
^{13}C-NMR of compound ethyl 2-acetamido-4,5,6,7-tetrahydrobenzo[*b*] thiophene-3-carboxylate (**36,** $CDCl_3$)[7]



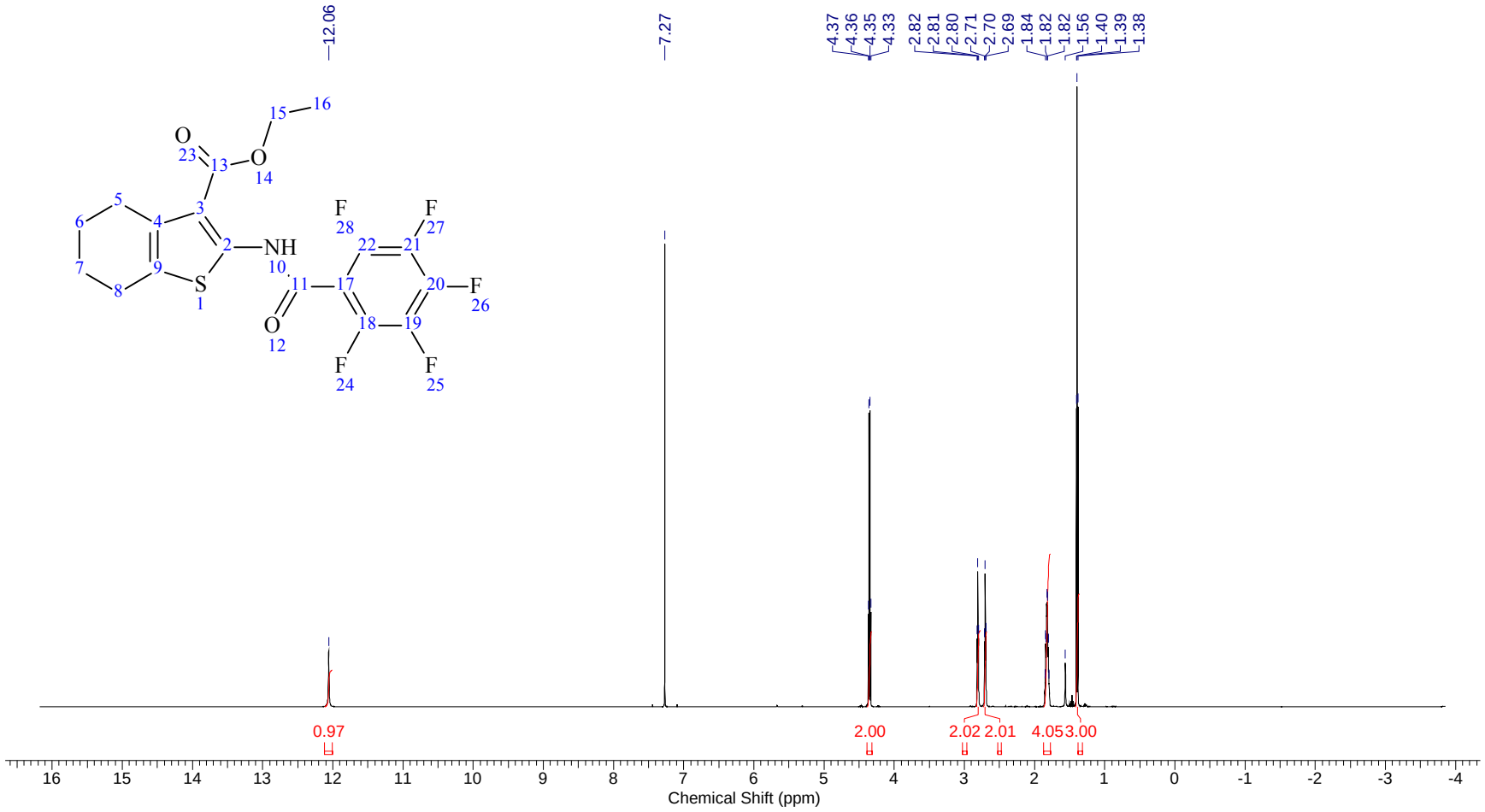
^{1}H-NMR of compound ethyl-2-benzamido-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**37,** $CDCl_3$)[8]



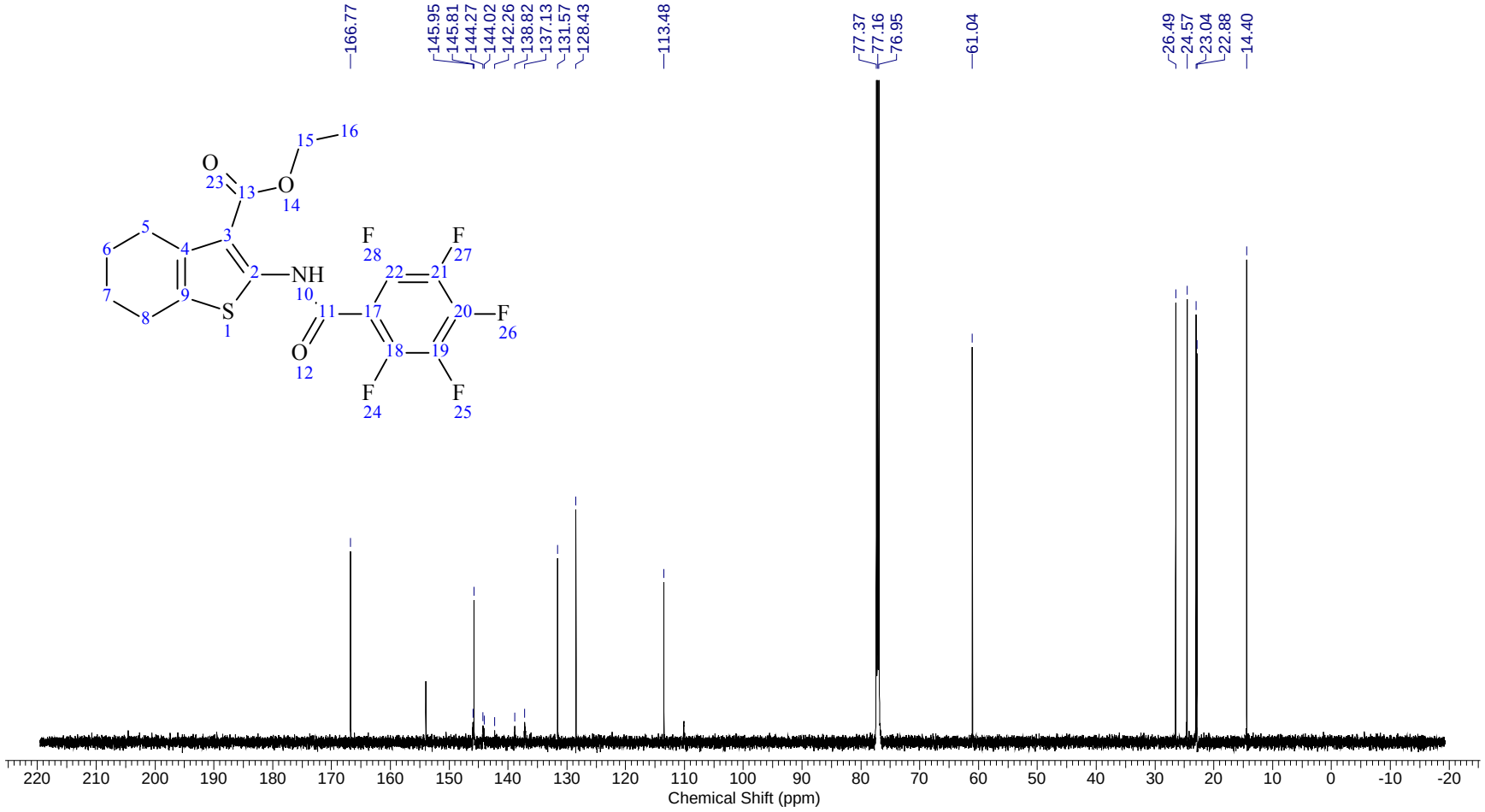
^{13}C-NMR of compound ethyl-2-benzamido-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**37**, $CDCl_3$)[8]



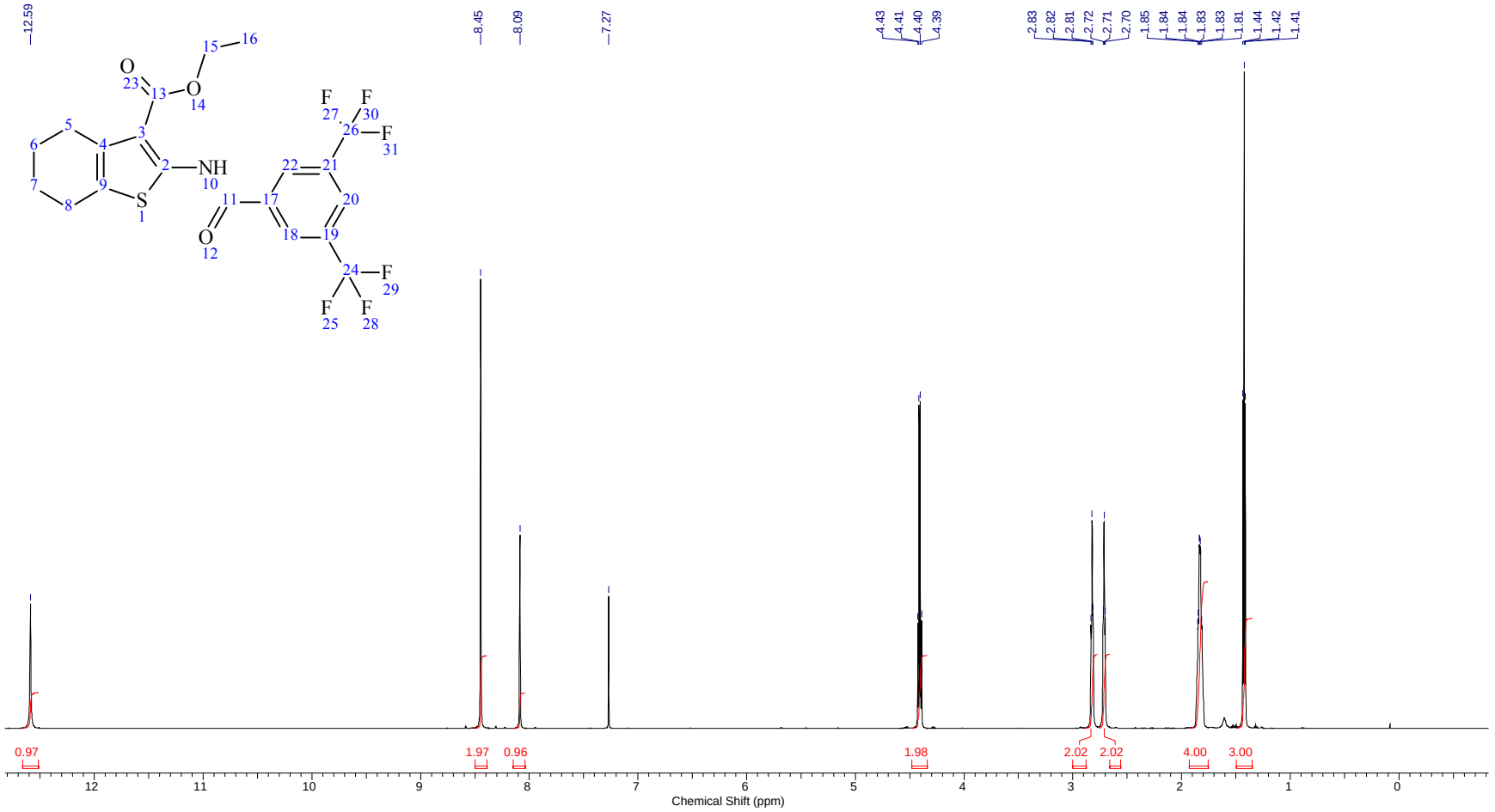
^{1}H-NMR of compound ethyl 2-(perfluorobenzamido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**38**, $CDCl_3$)



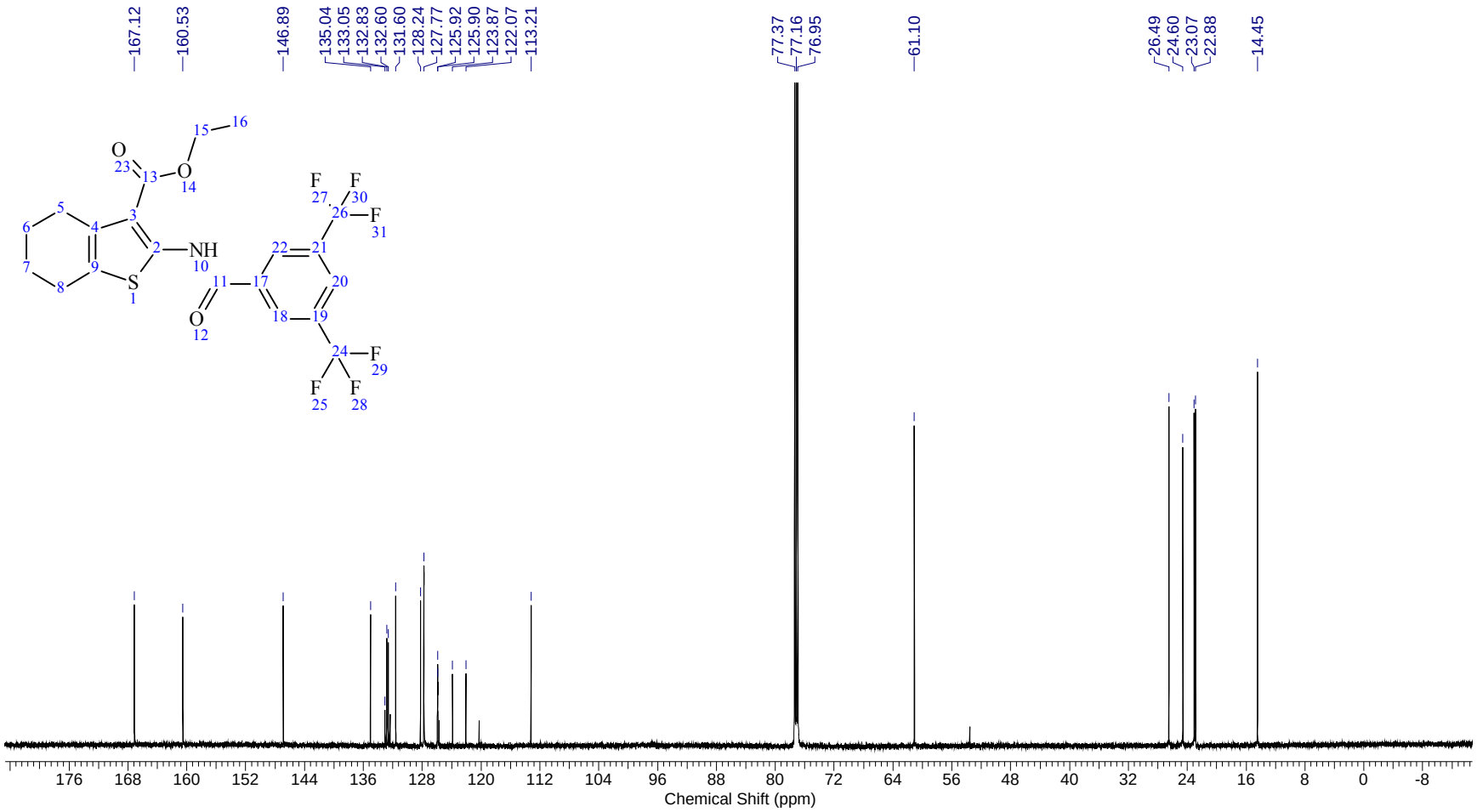
^{13}C-NMR of compound ethyl 2-(perfluorobenzamido)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**38**, $CDCl_3$)



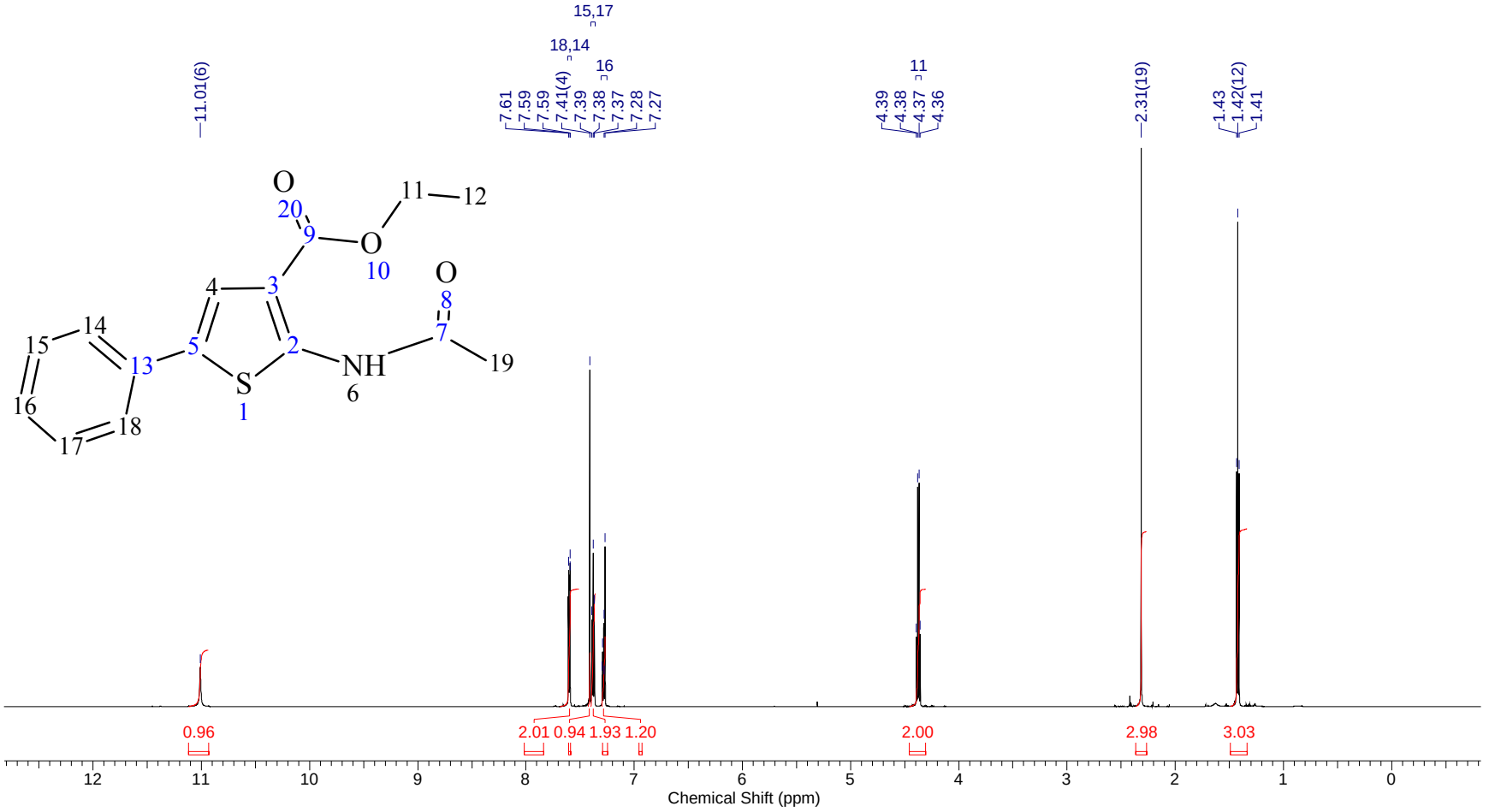
^{1}H-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzaimdo)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**39**, $CDCl_3$)



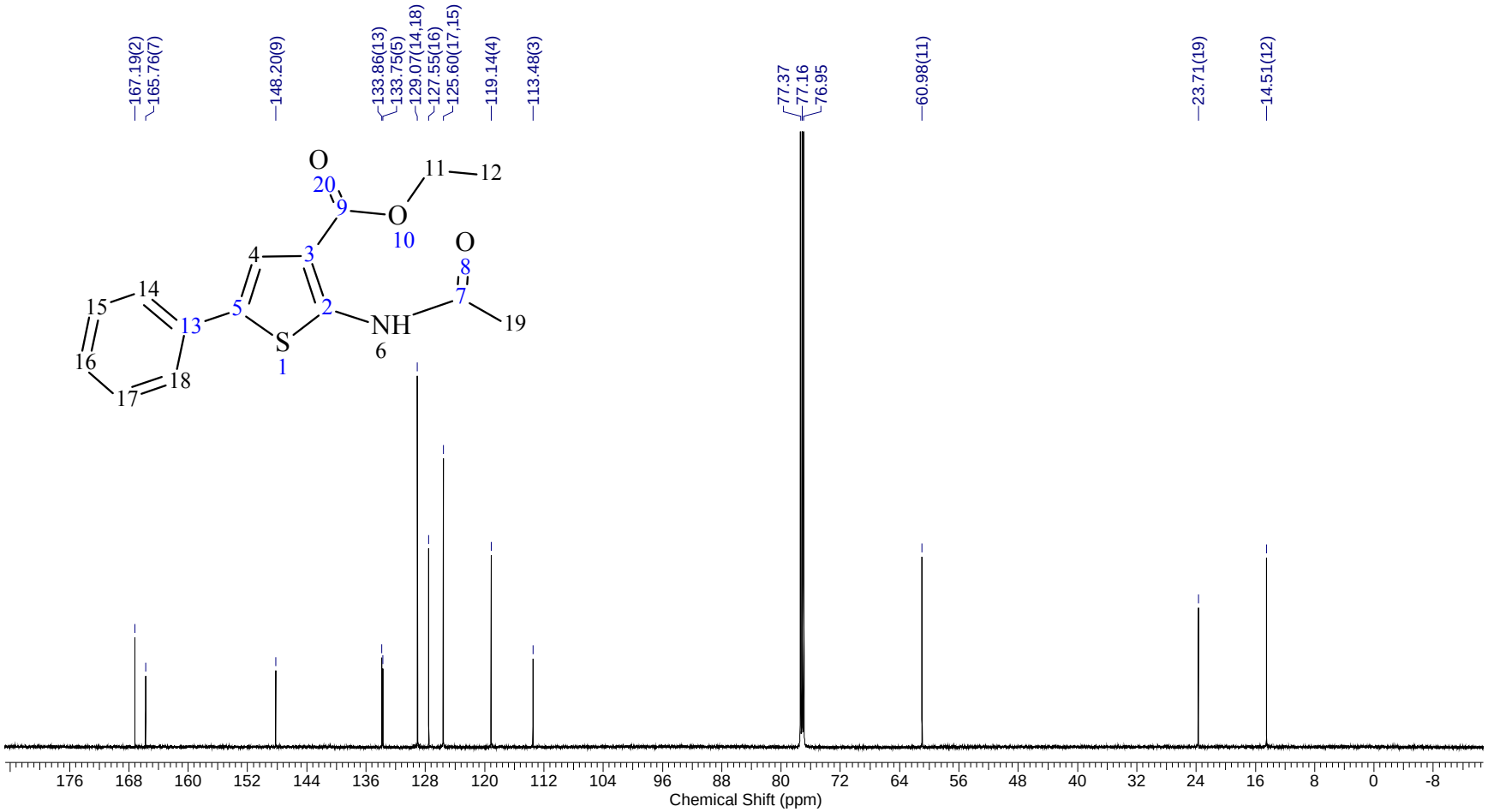
^{13}C-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzaimdo)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylate (**39**, $CDCl_3$)



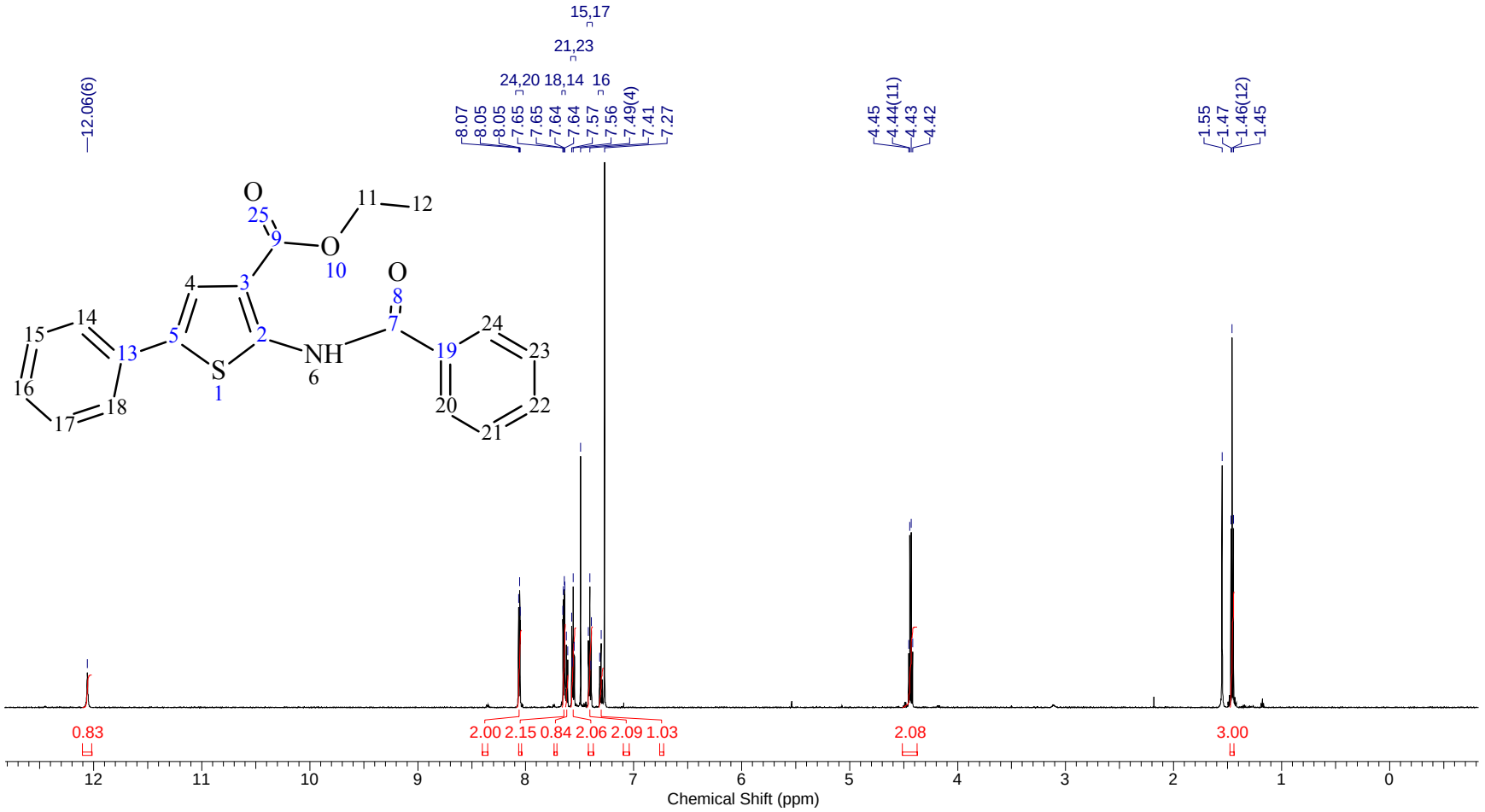
^{1}H-NMR of compound ethyl 2-acetamido-5-phenylthiophene-3-carboxylate (**54**, $CDCl_3$)[9]



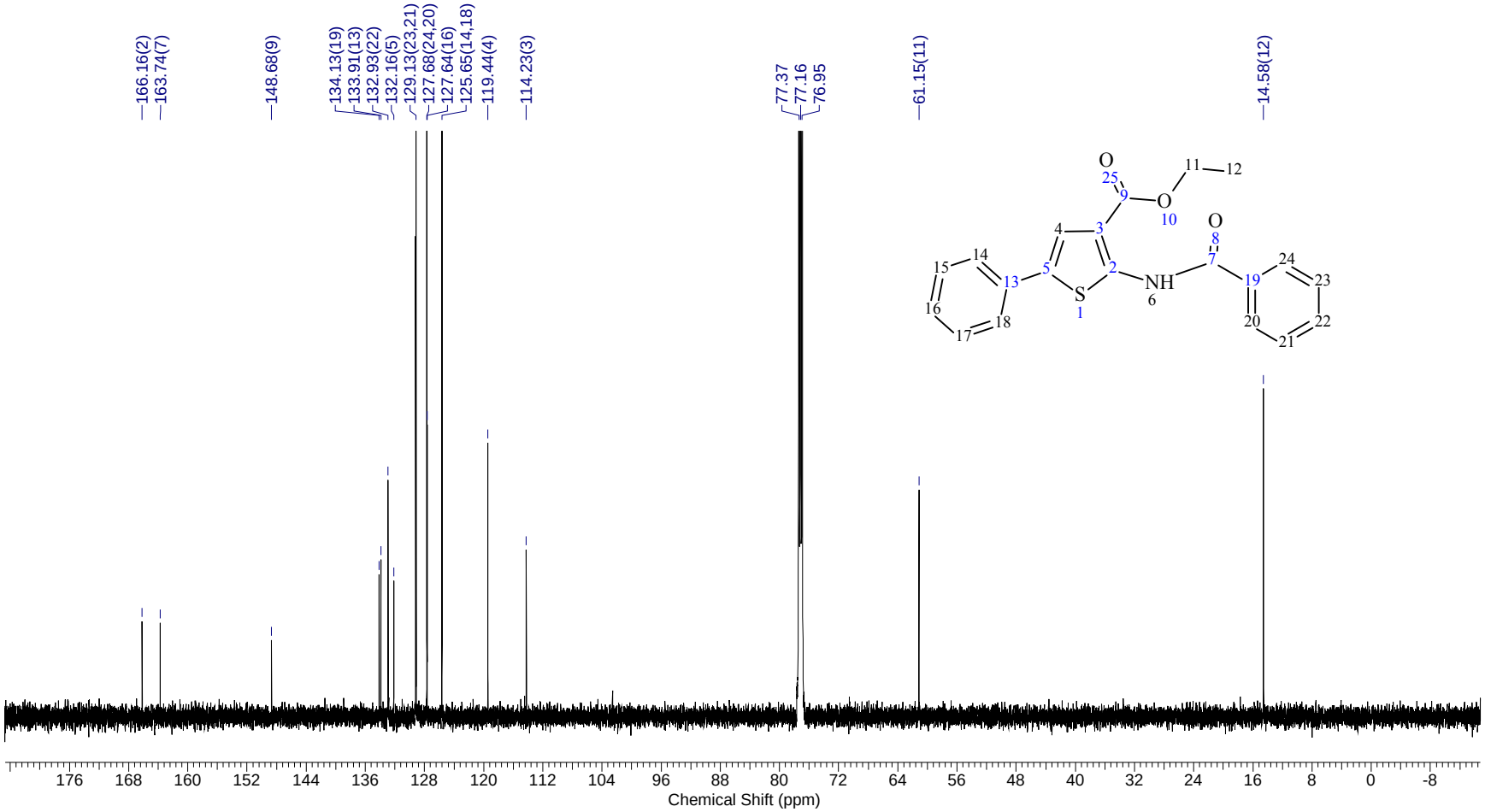
^{13}C-NMR of compound ethyl 2-acetamido-5-phenylthiophene-3-carboxylate (**54**, $CDCl_3$)[9]



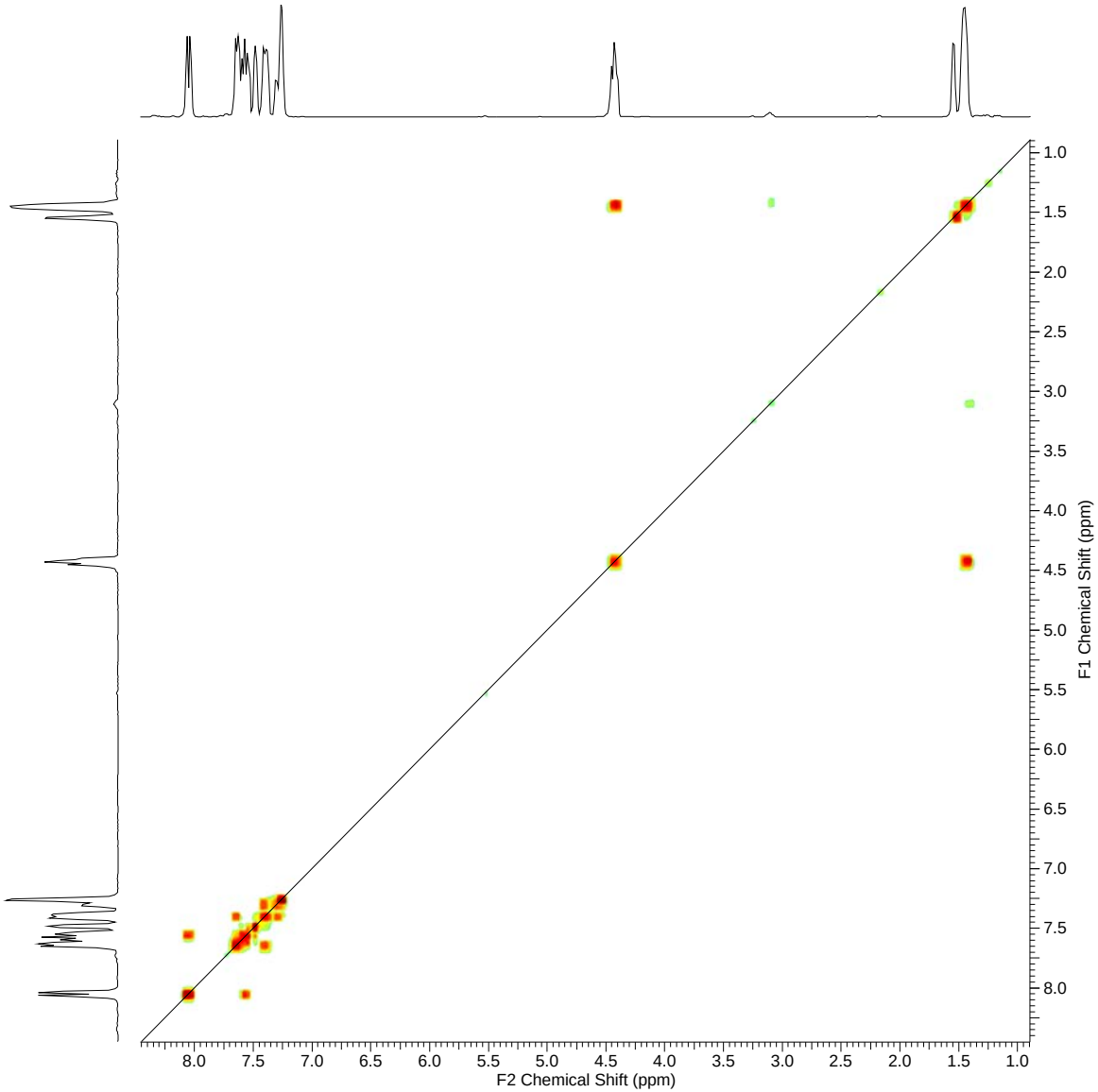
[1]H-NMR of compound ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (**55**, $CDCl_3$)[9]

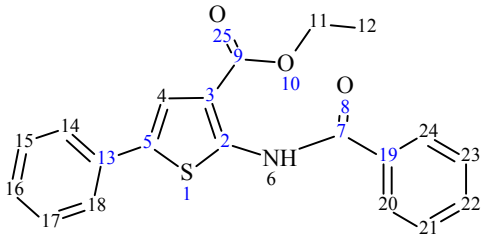


^{13}C-NMR of compound ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (**55**, $CDCl_3$)[9]

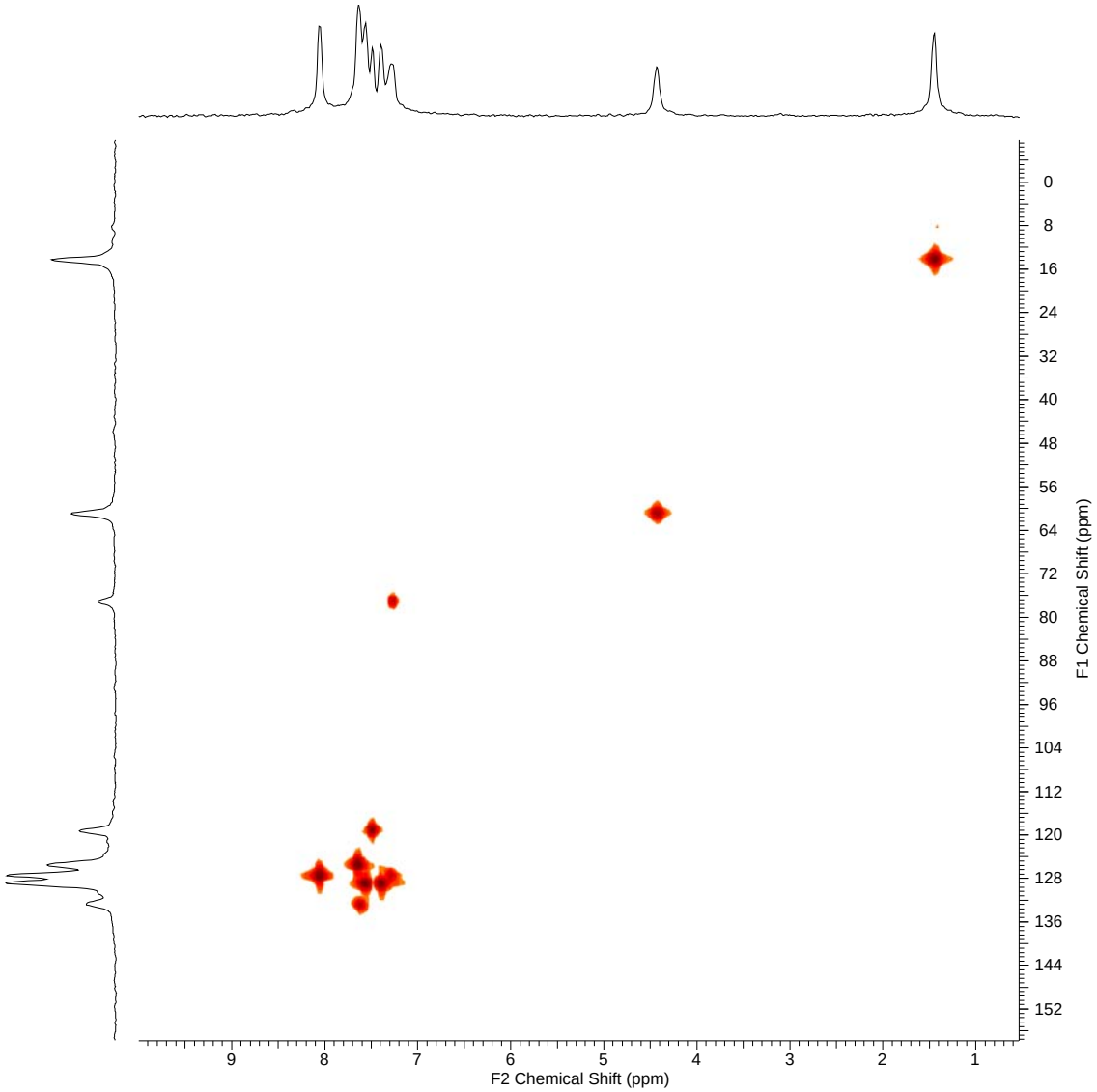


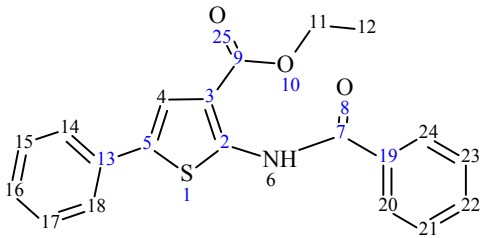
COSY of compound ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (**55**, $CDCl_3$)[9]



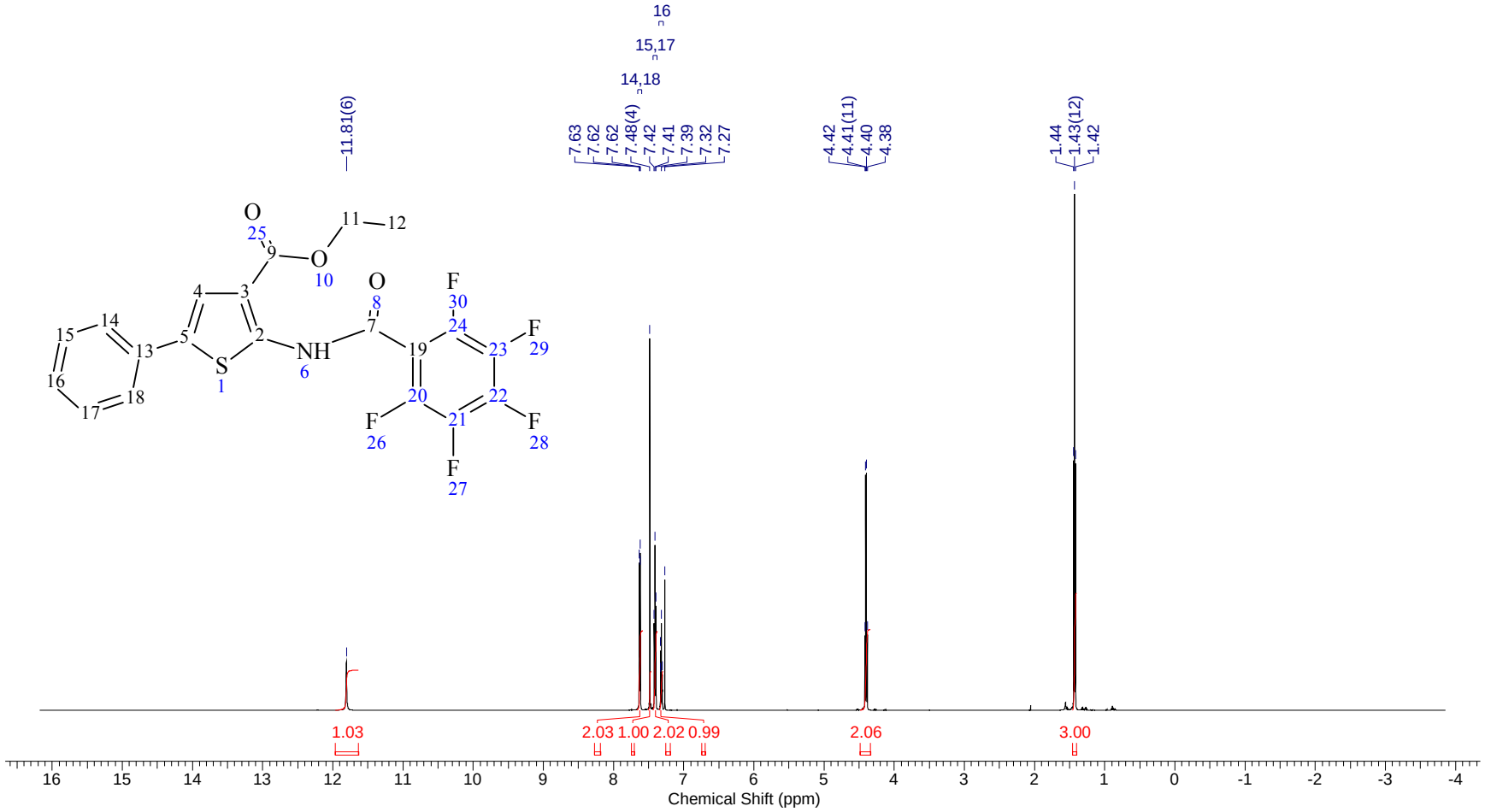


HMQC of compound ethyl 2-benzamido-5-phenylthiophene-3-carboxylate (**55,** $CDCl_3$)[9]

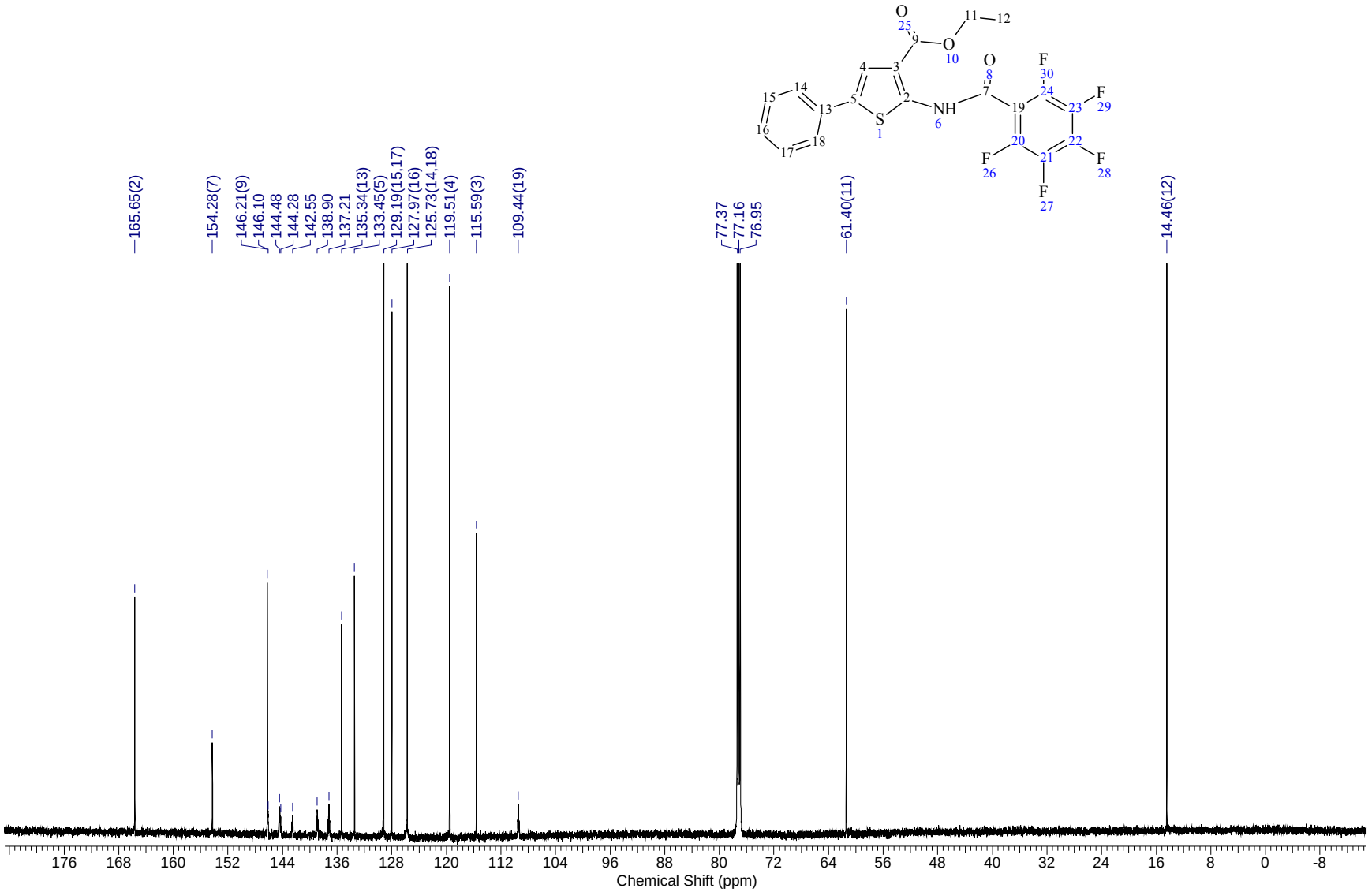




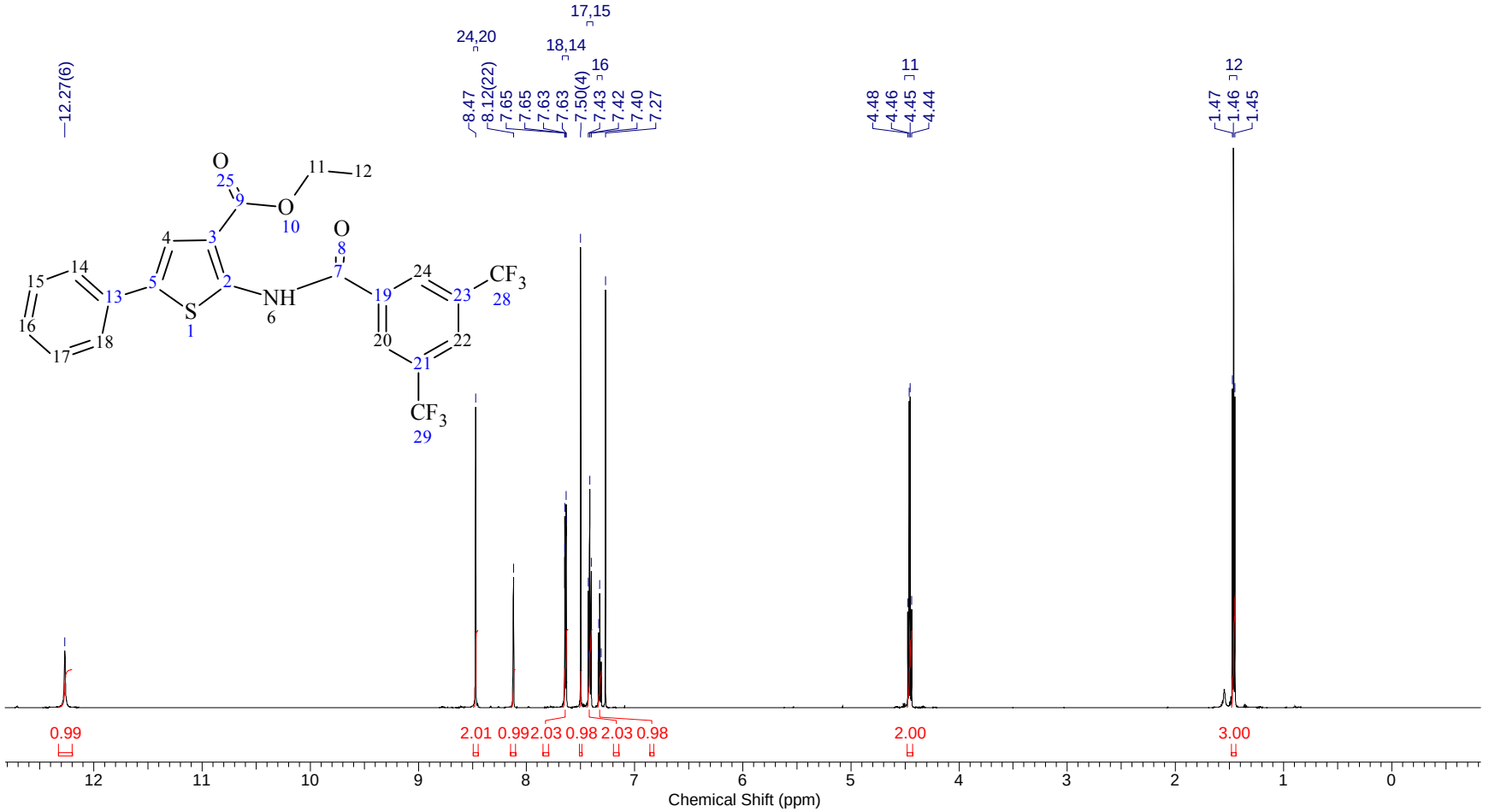
^{1}H-NMR of compound ethyl 2-(perfluorobenzamido)-5-phenylthiophene-3-carboxylate (**56**, $CDCl_3$)



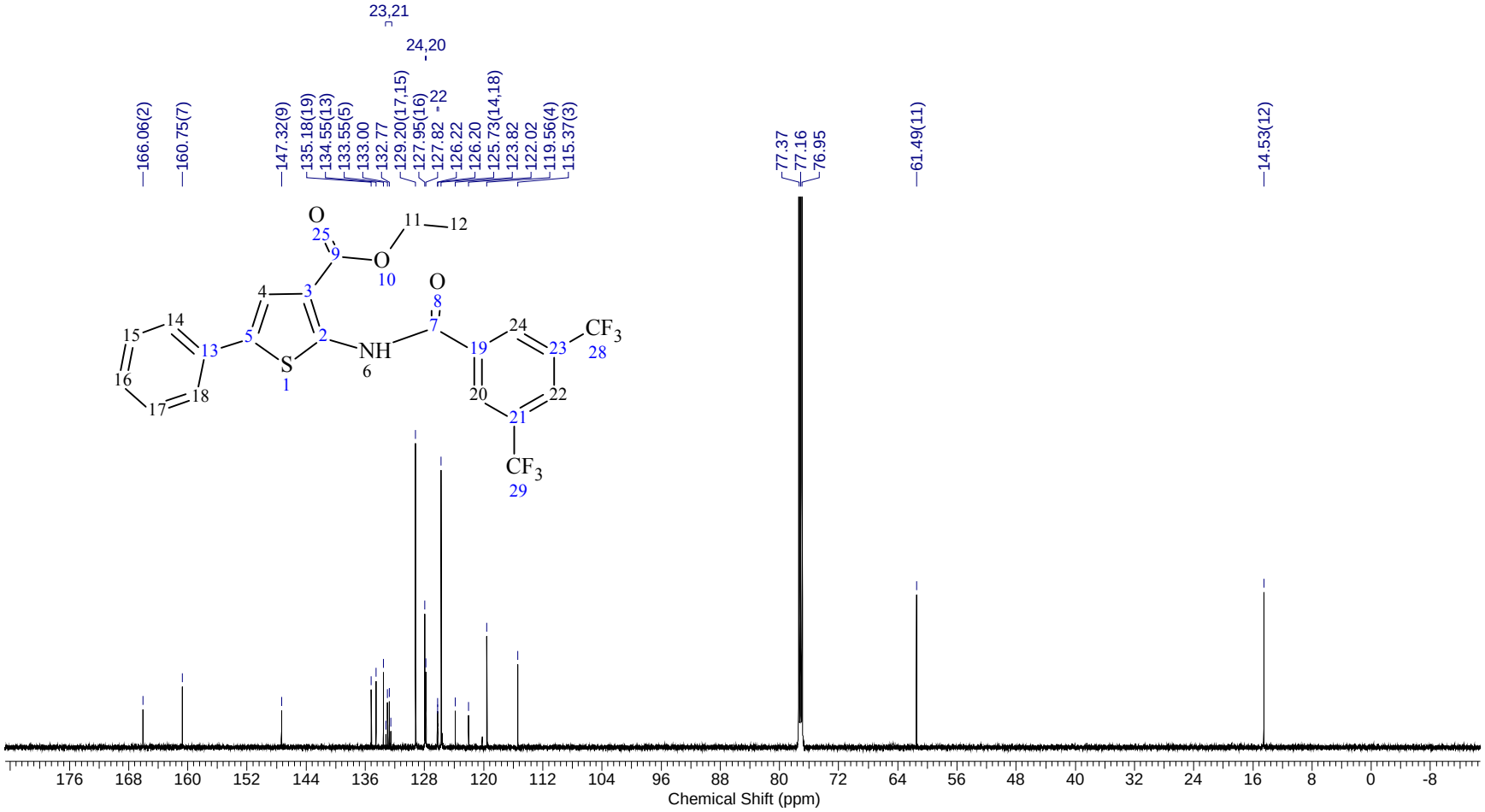
^{13}C-NMR of compound ethyl 2-(perfluorobenzamido)-5-phenylthiophene-3-carboxylate (**56**, $CDCl_3$)



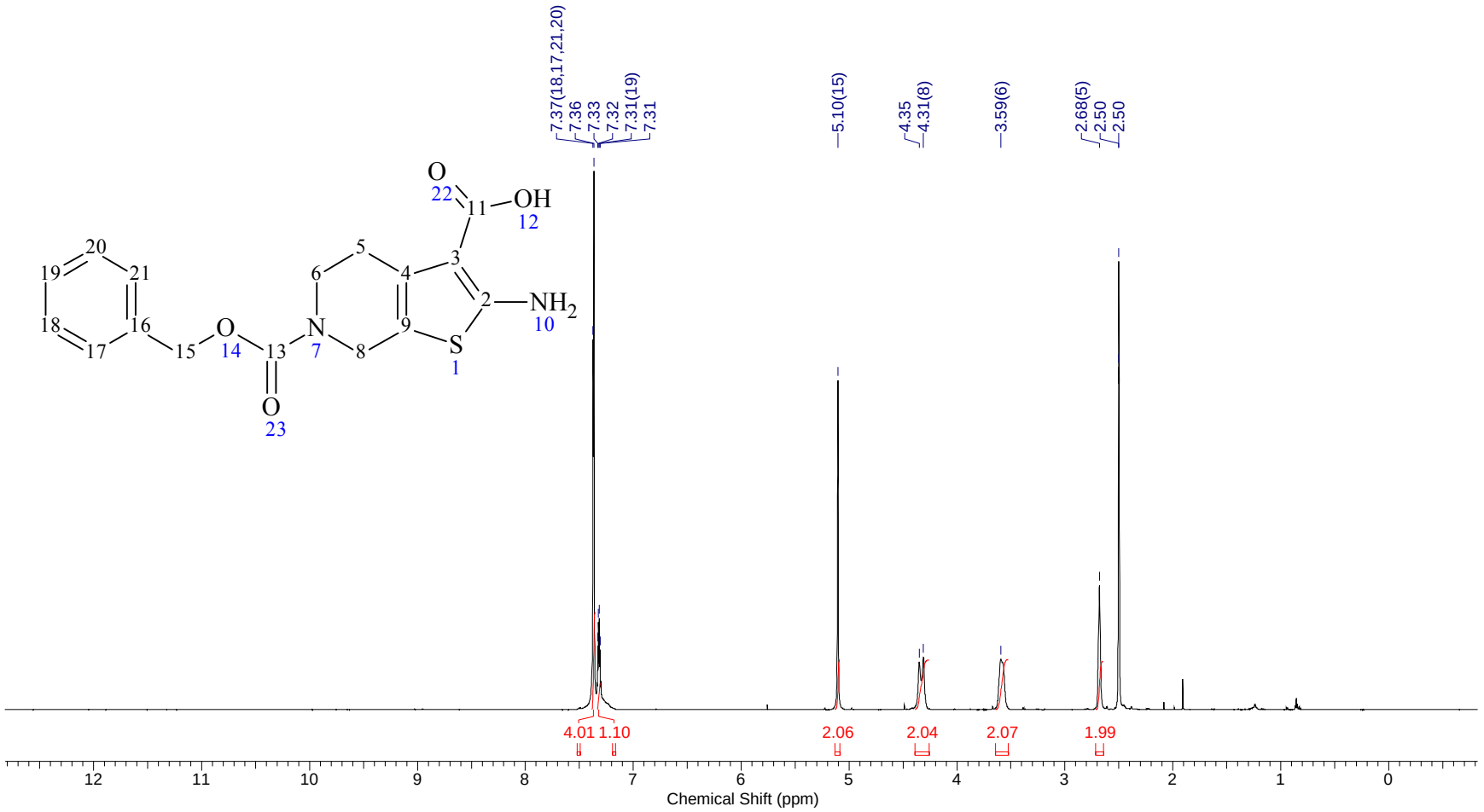
^{1}H-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-5-phenylthiophene-3-carboxylate (**57**, $CDCl_3$)



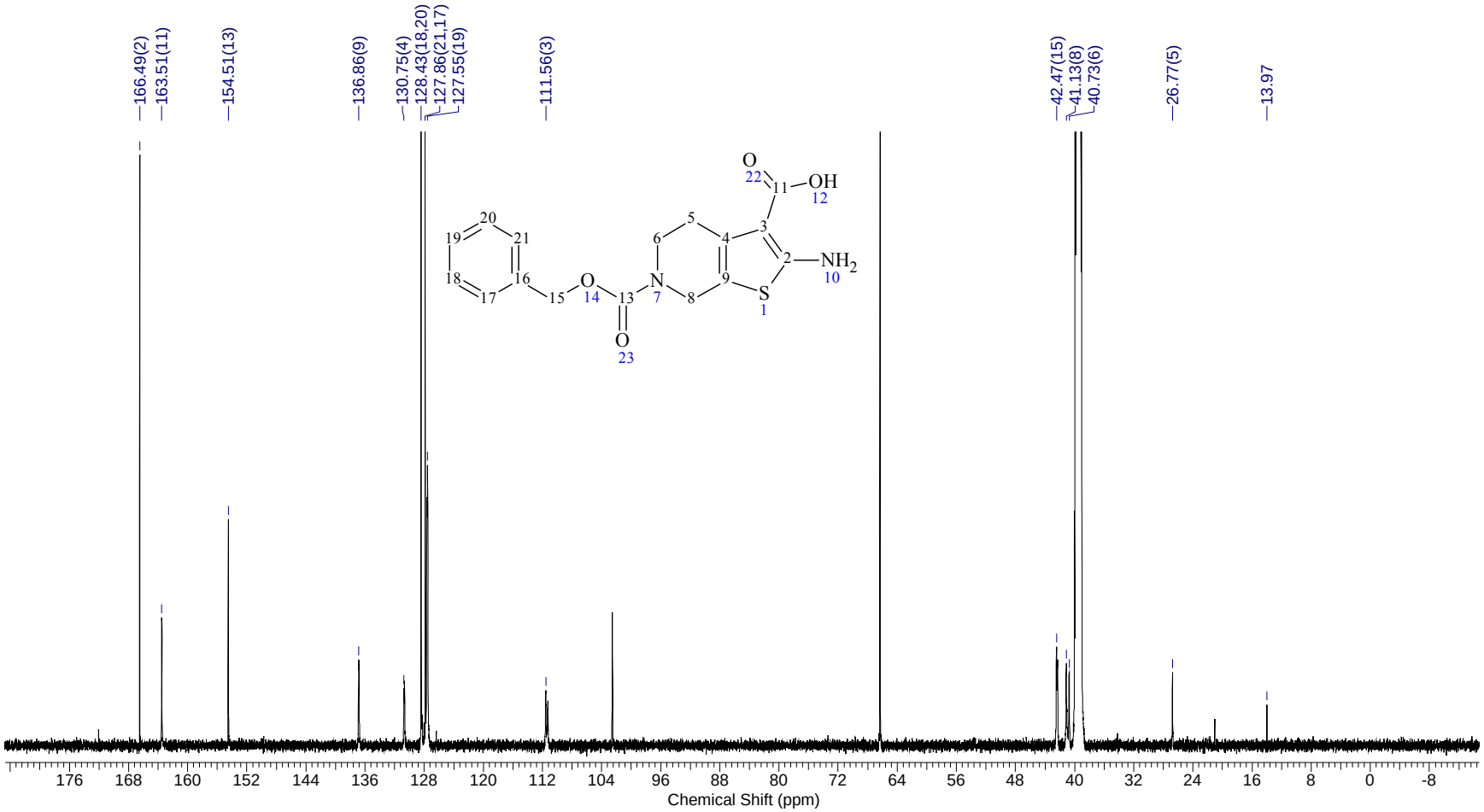
^{13}C-NMR of compound ethyl 2-(3,5-bis(trifluoromethyl)benzamido)-5-phenylthiophene-3-carboxylate (**57**, $CDCl_3$)



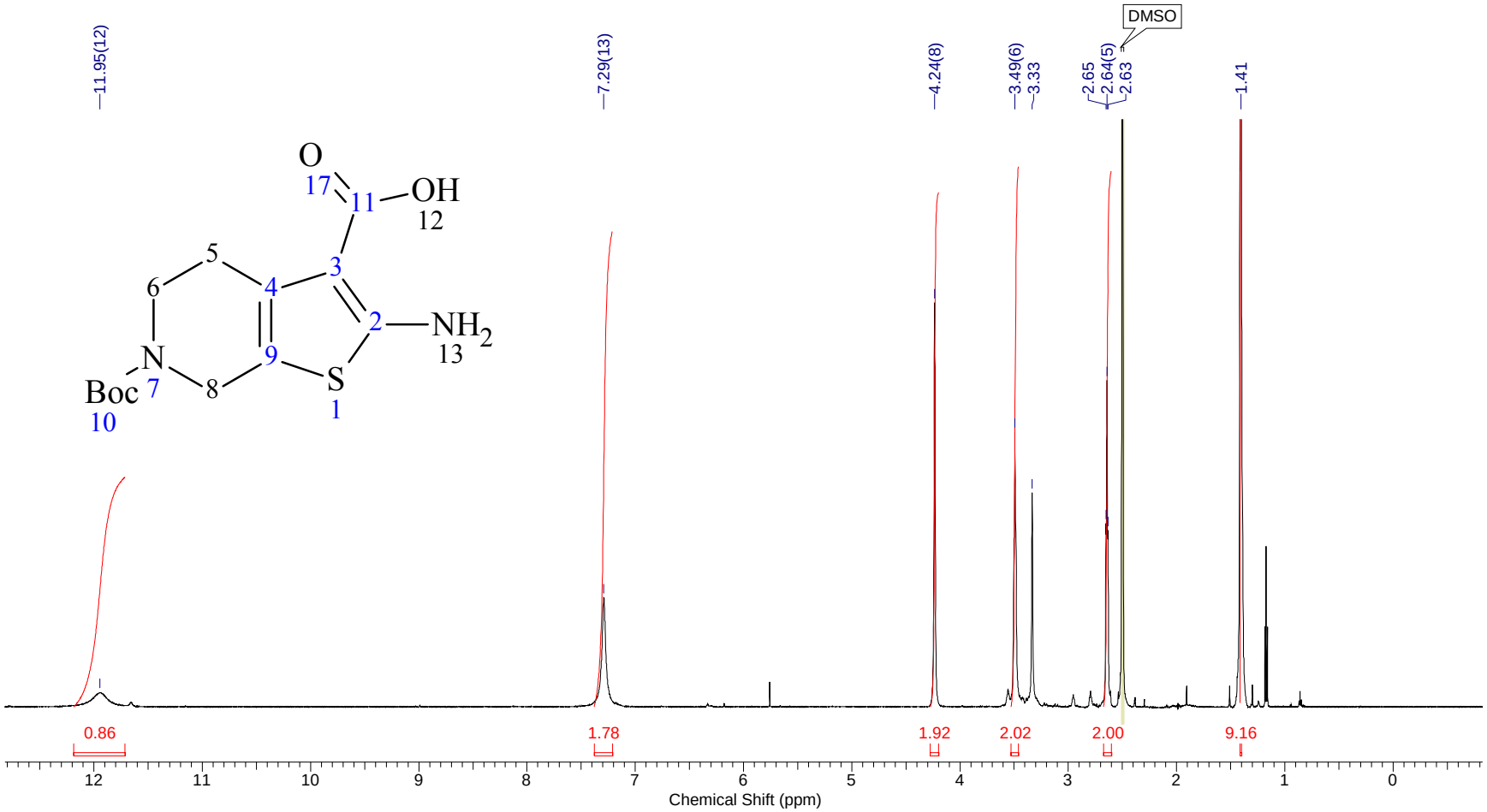
^{1}H-NMR of compound 2-Amino-6-((benzyloxy)carbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**40**, $(CD_3)_2SO$)



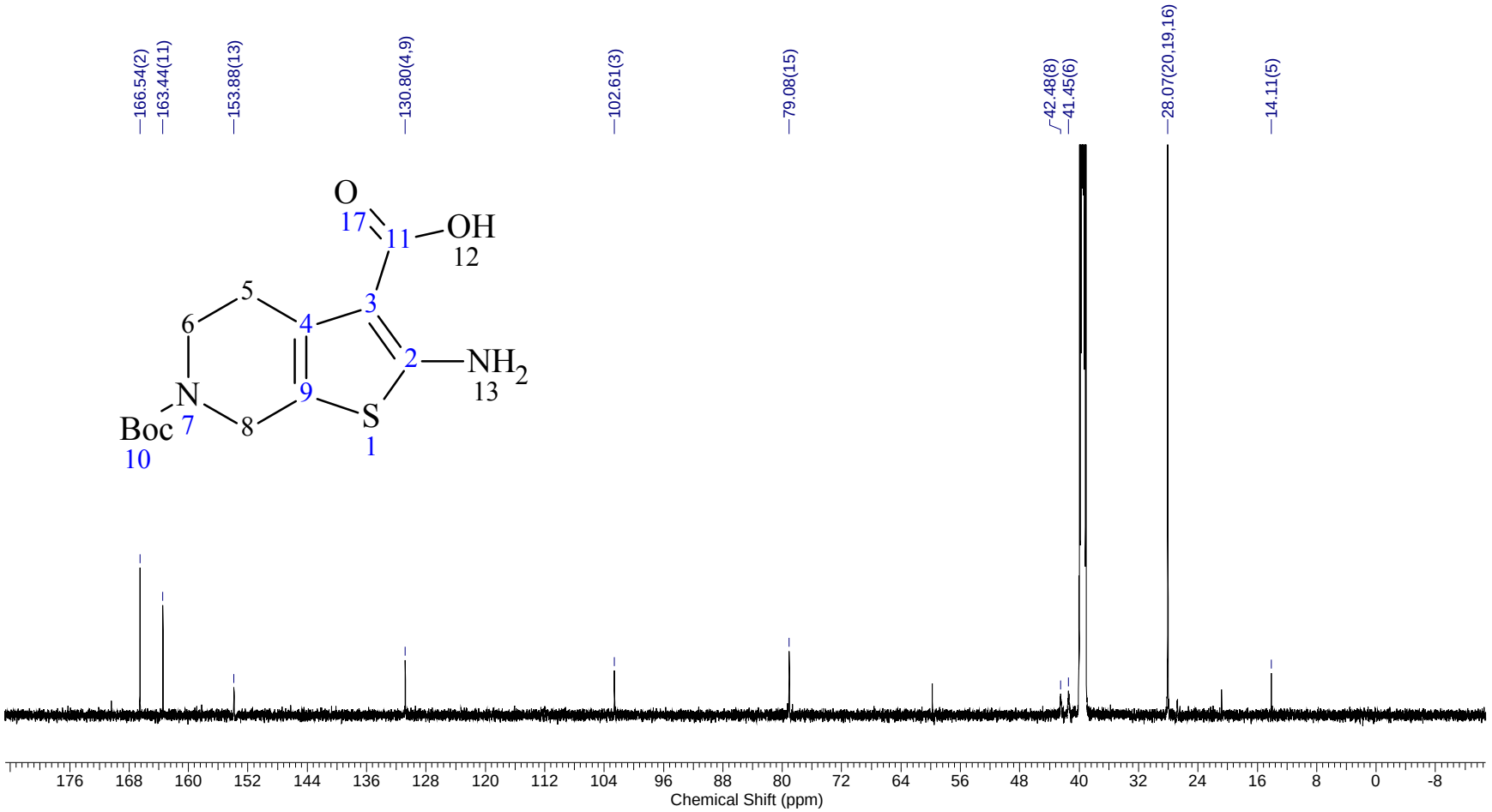
^{13}C-NMR of compound 2-Amino-6-((benzyloxy)carbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**40**, $(CD_3)_2SO$)



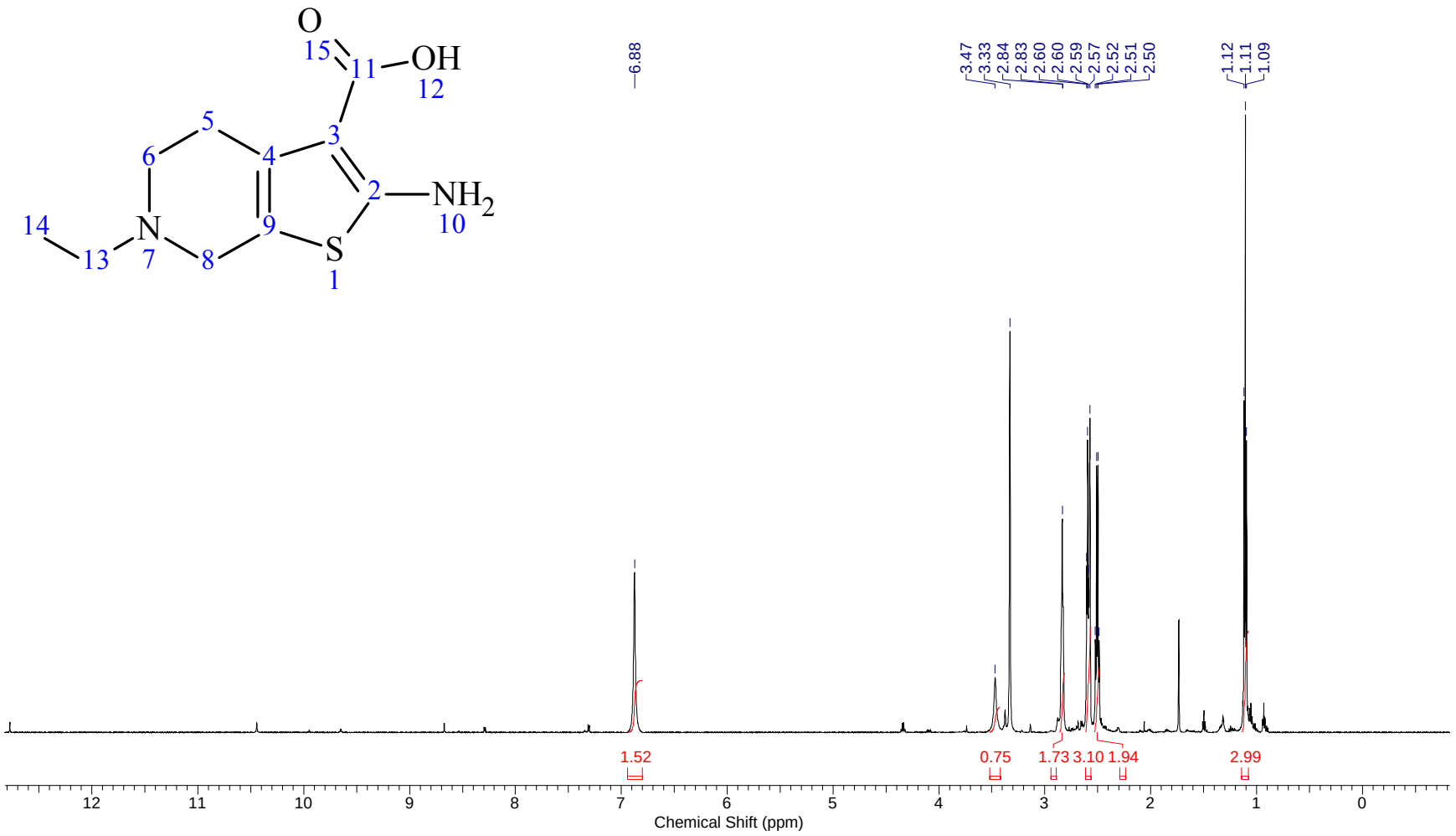
^{1}H-NMR of compound 2-Amino-6-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**41**, $(CD_3)_2SO$)[10]



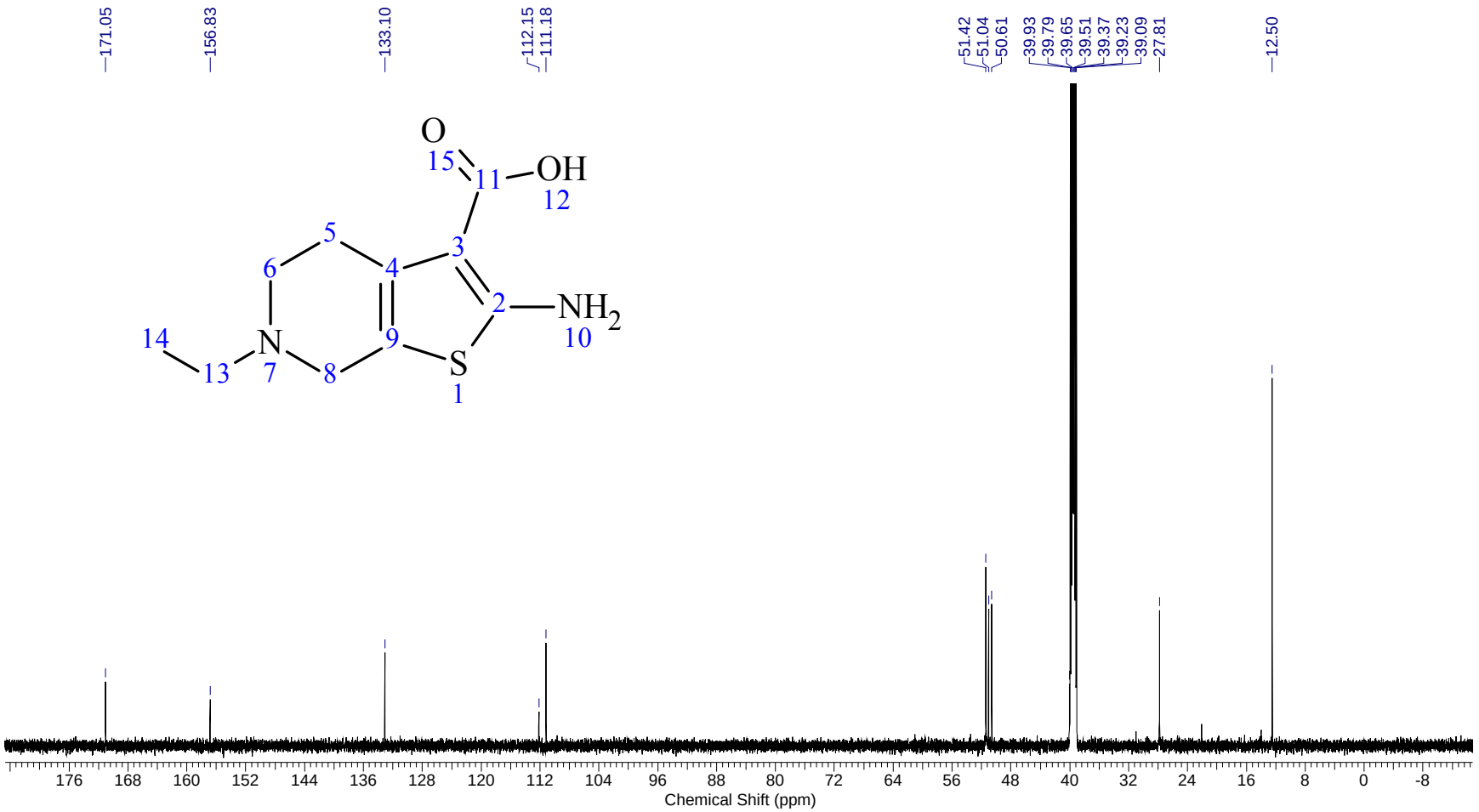
^{13}C-NMR of compound 2-amino-6-(*tert*-butoxycarbonyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**41**, $(CD_3)_2SO$)[10]



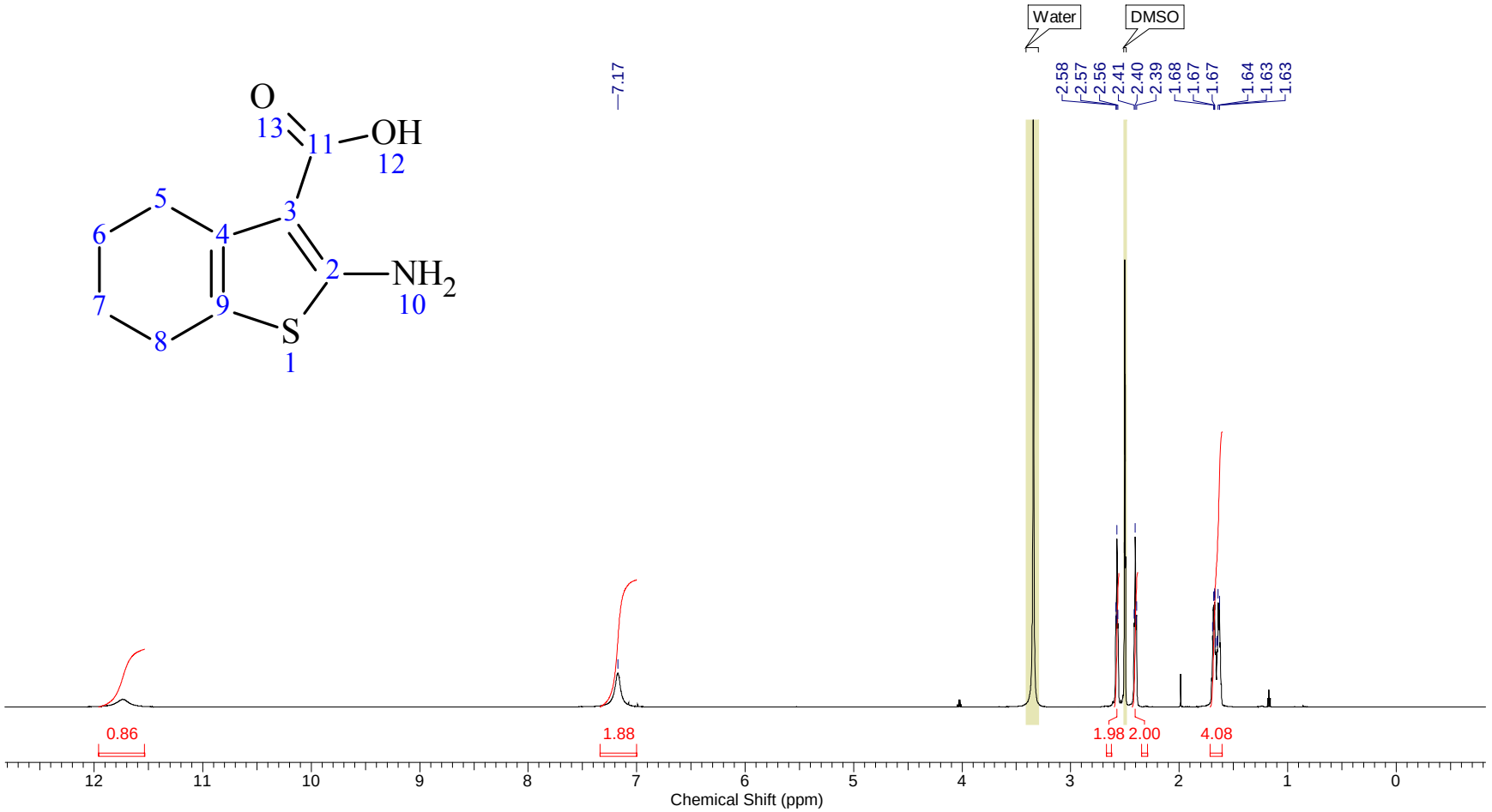
^{1}H-NMR of compound 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**42**, $(CD_3)_2SO$)



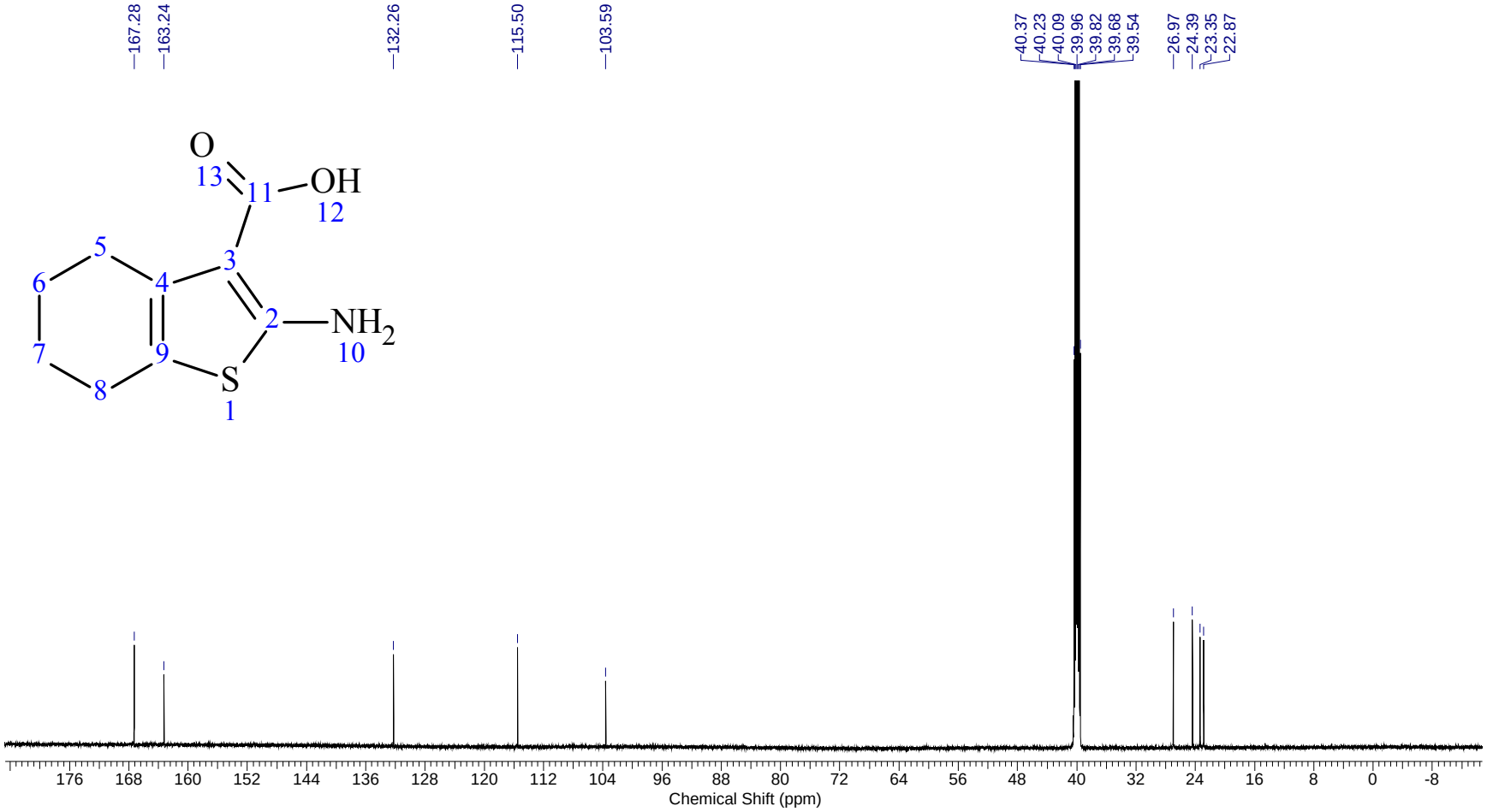
^{13}C-NMR of compound 2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxylic acid (**42**, $(CD_3)_2SO$)



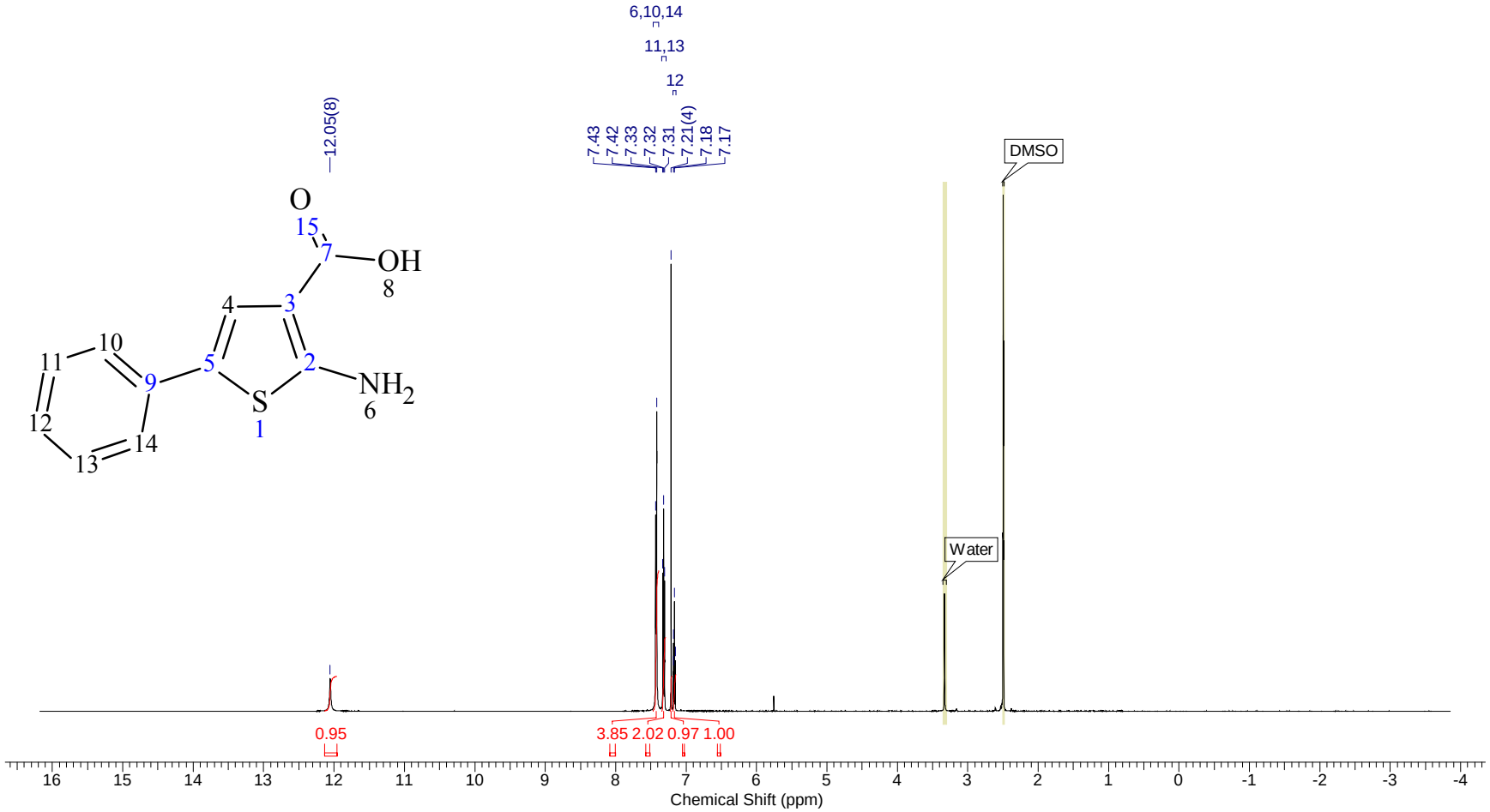
^{1}H-NMR of compound 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**43**, $(CD_3)_2SO$)[11]



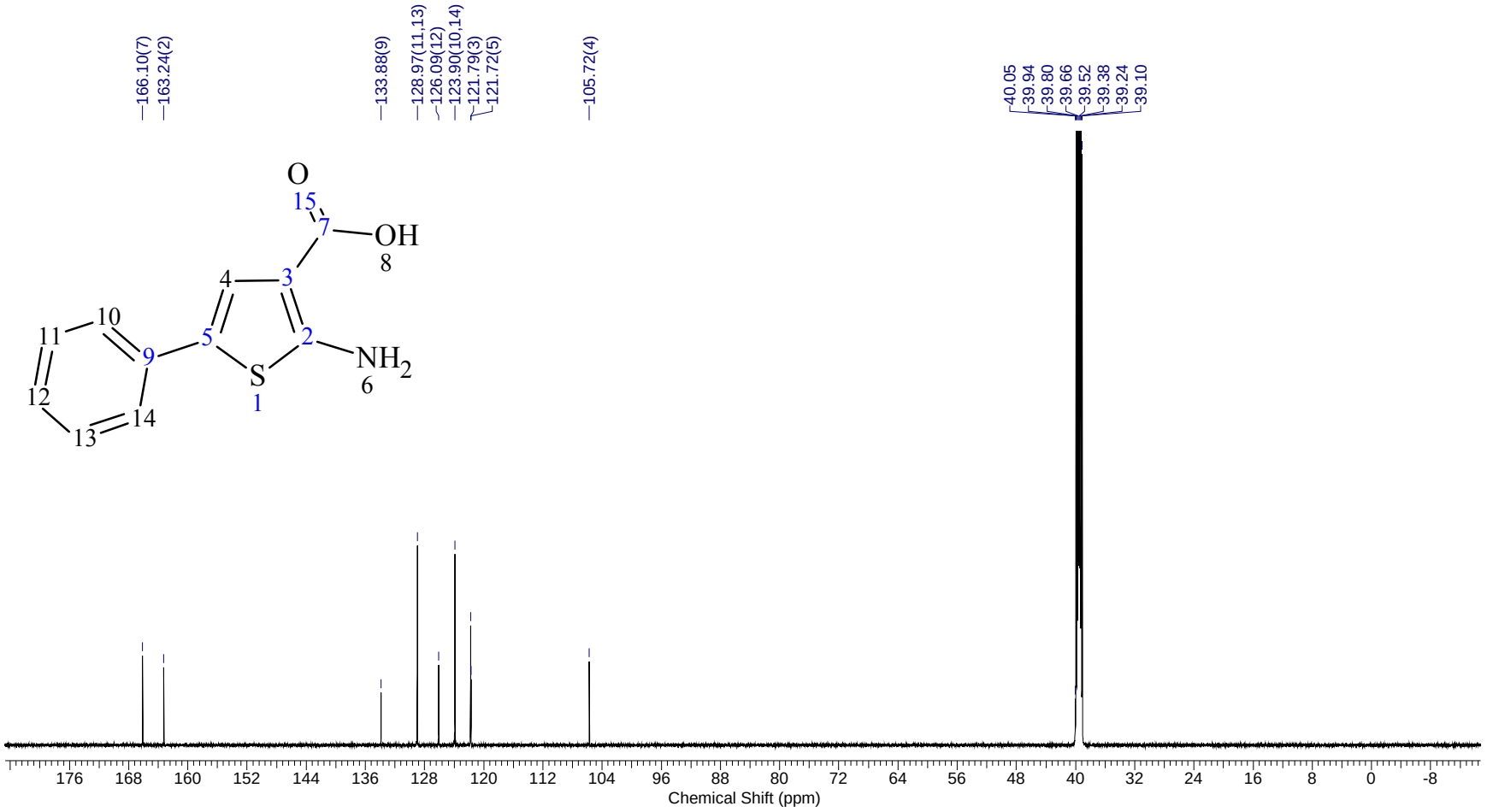
^{13}C-NMR of compound 2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxylic acid (**43**, $(CD_3)_2SO$)[11]



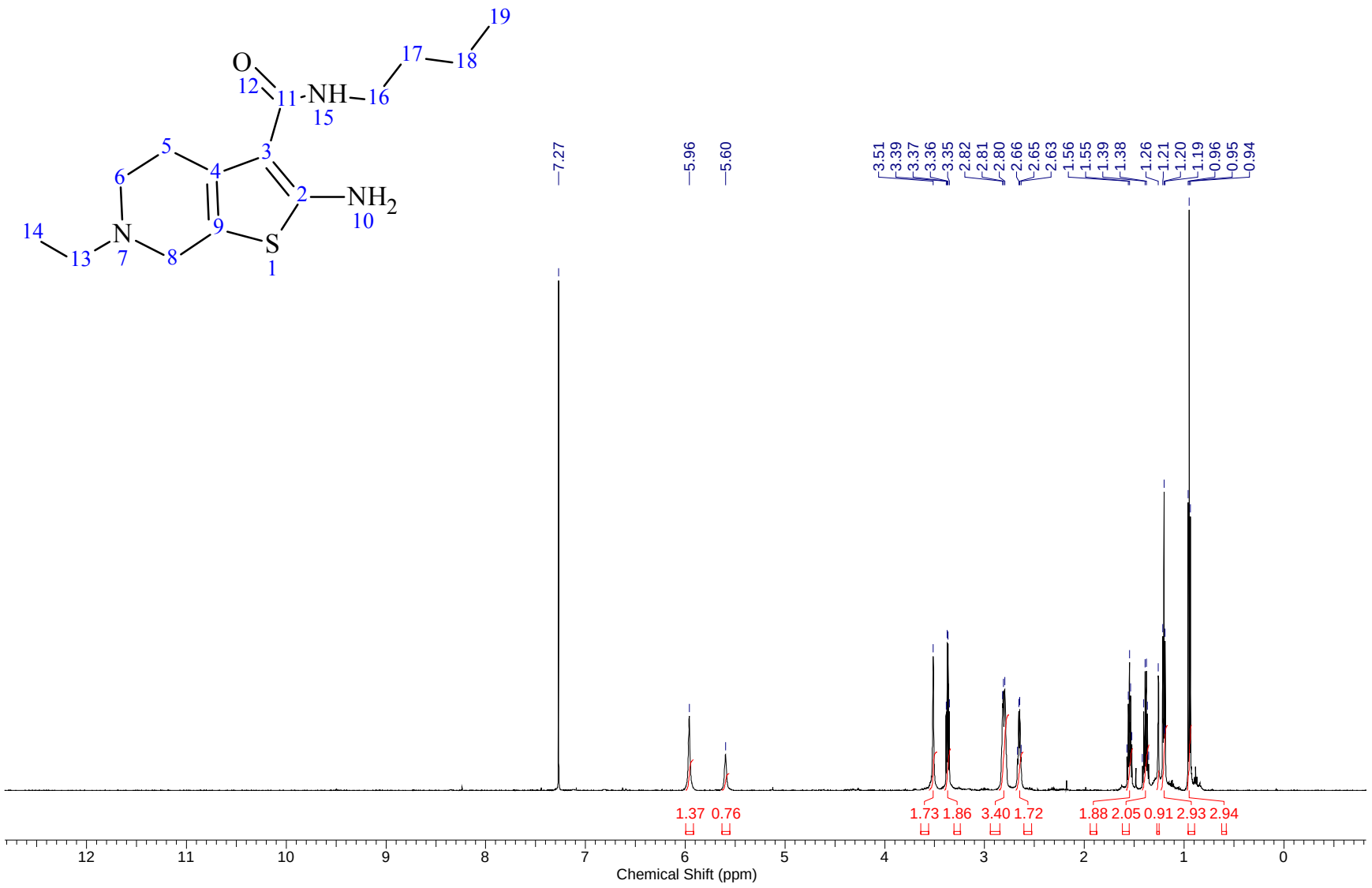
[1]H-NMR of compound 2-Amino-5-phenylthiophene-3-carboxylic acid (**58**, $(CD_3)_2SO$)[12]



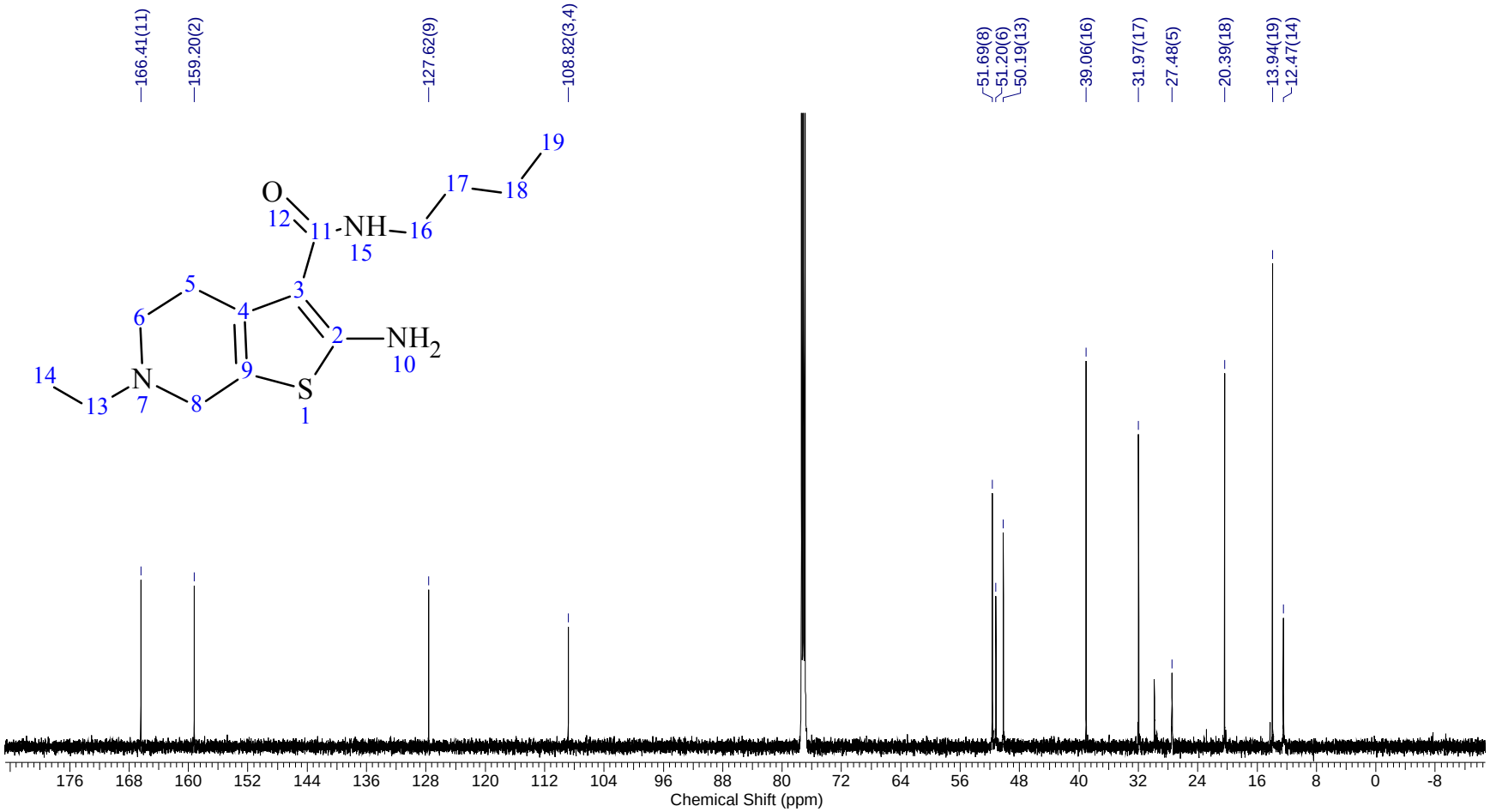
^{13}C-NMR of compound 2-Amino-5-phenylthiophene-3-carboxylic acid (**58**, $(CD_3)_2SO$)[12]



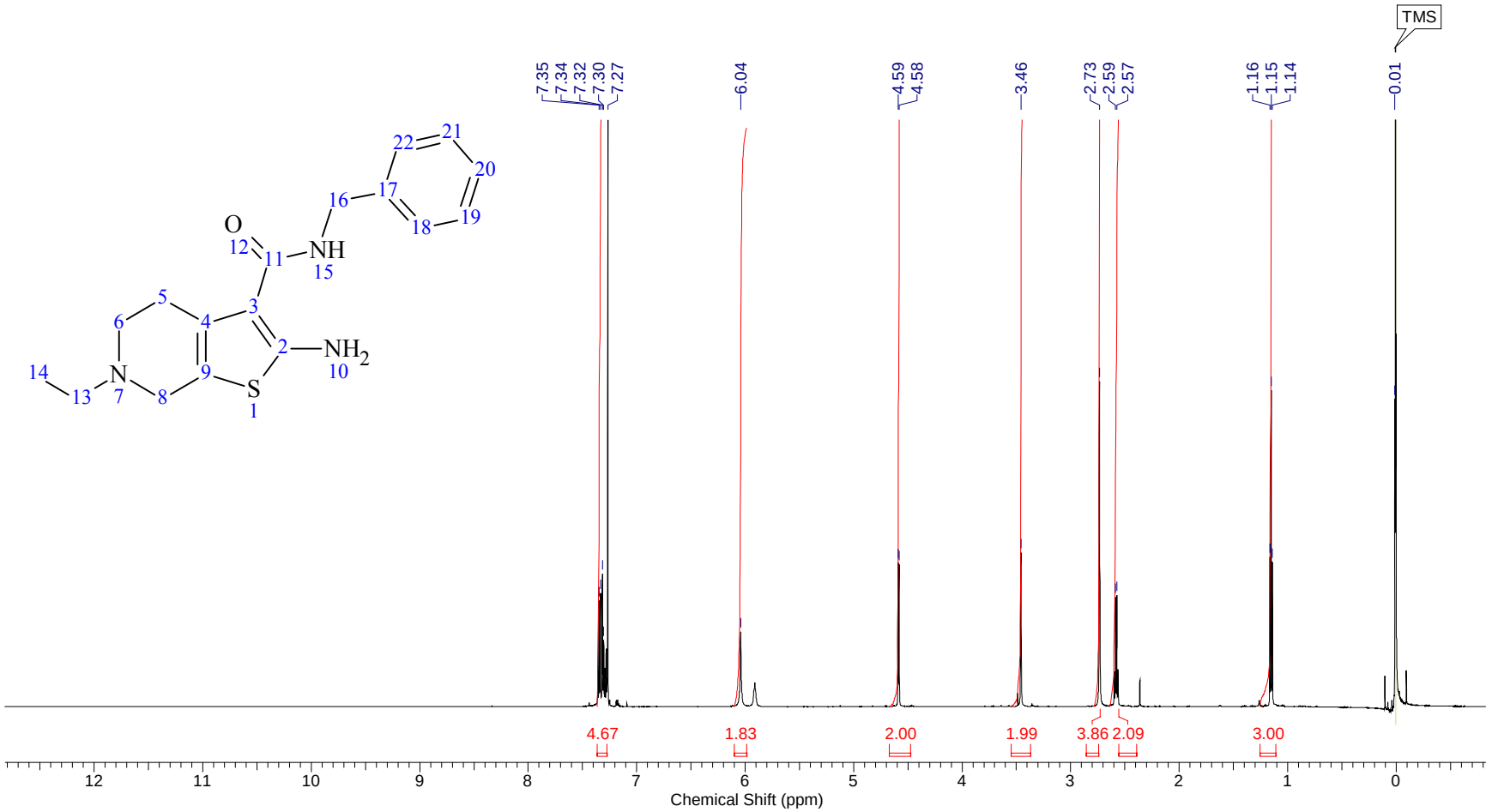
^{1}H-NMR of compound 2-amino-*N*-butyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**44**, $CDCl_3$)



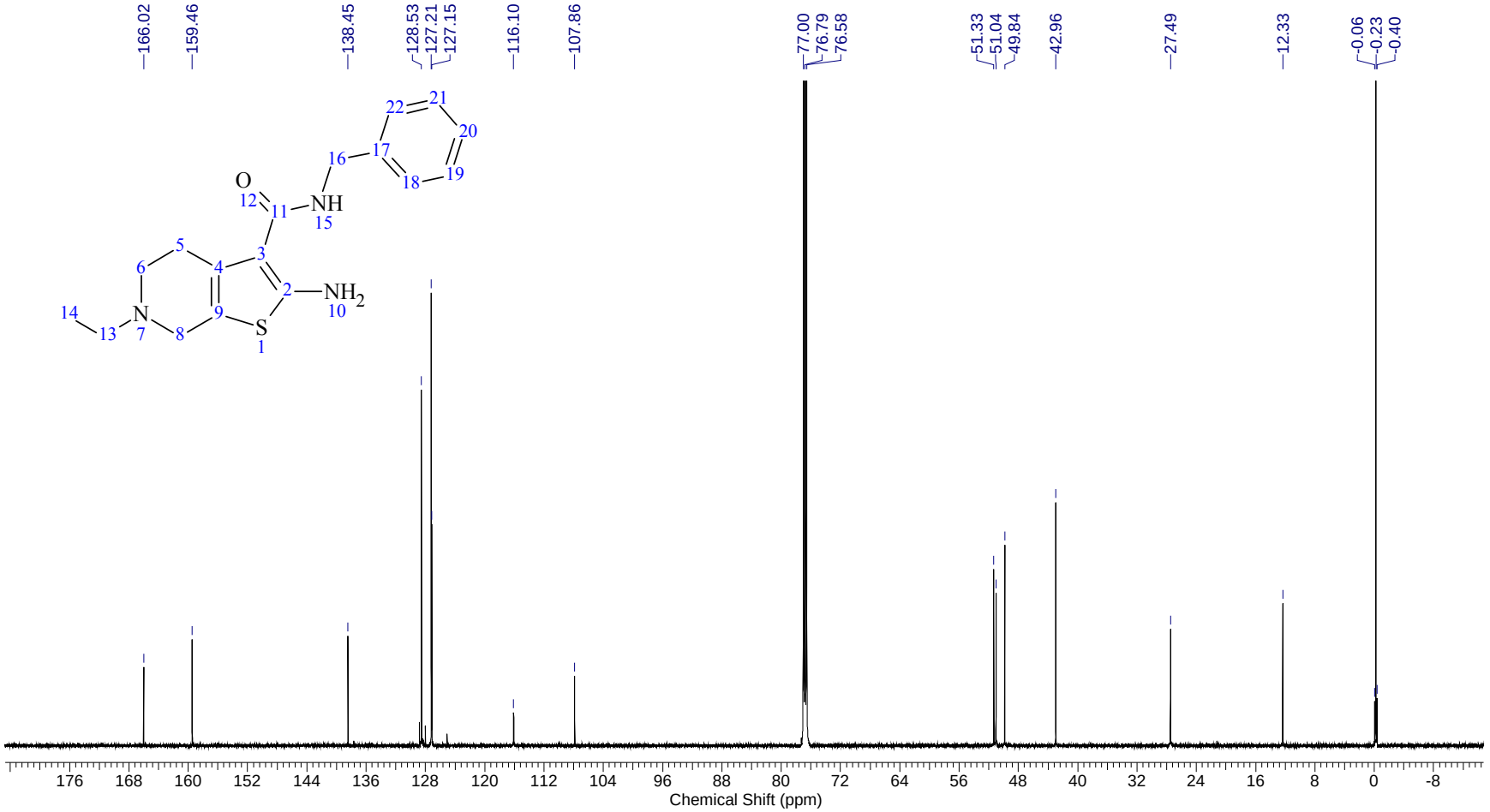
^{13}C-NMR of compound 2-amino-*N*-butyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**44**, $CDCl_3$)



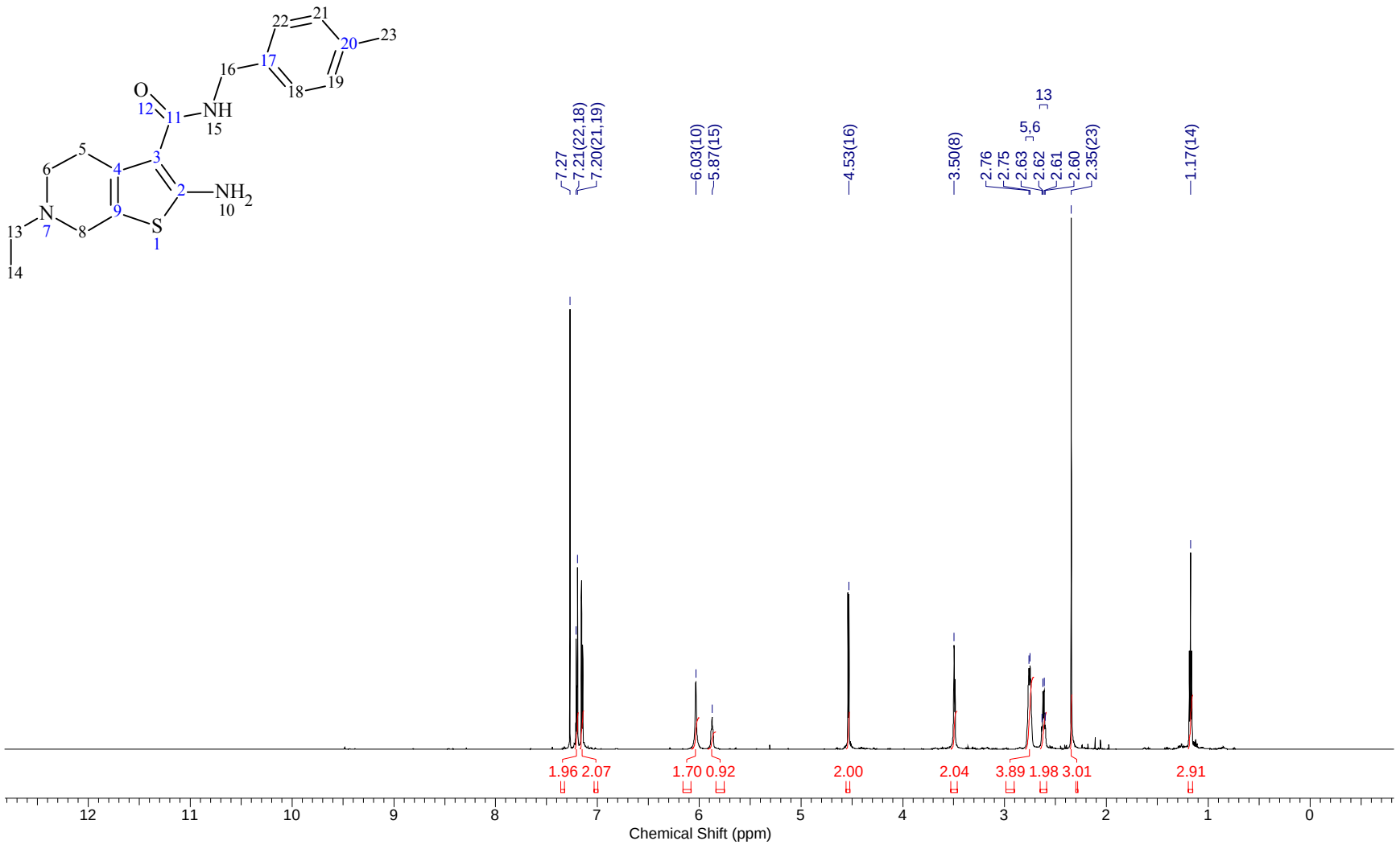
^{1}H-NMR of compound 2-amino-*N*-benzyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**45**, $CDCl_3$)



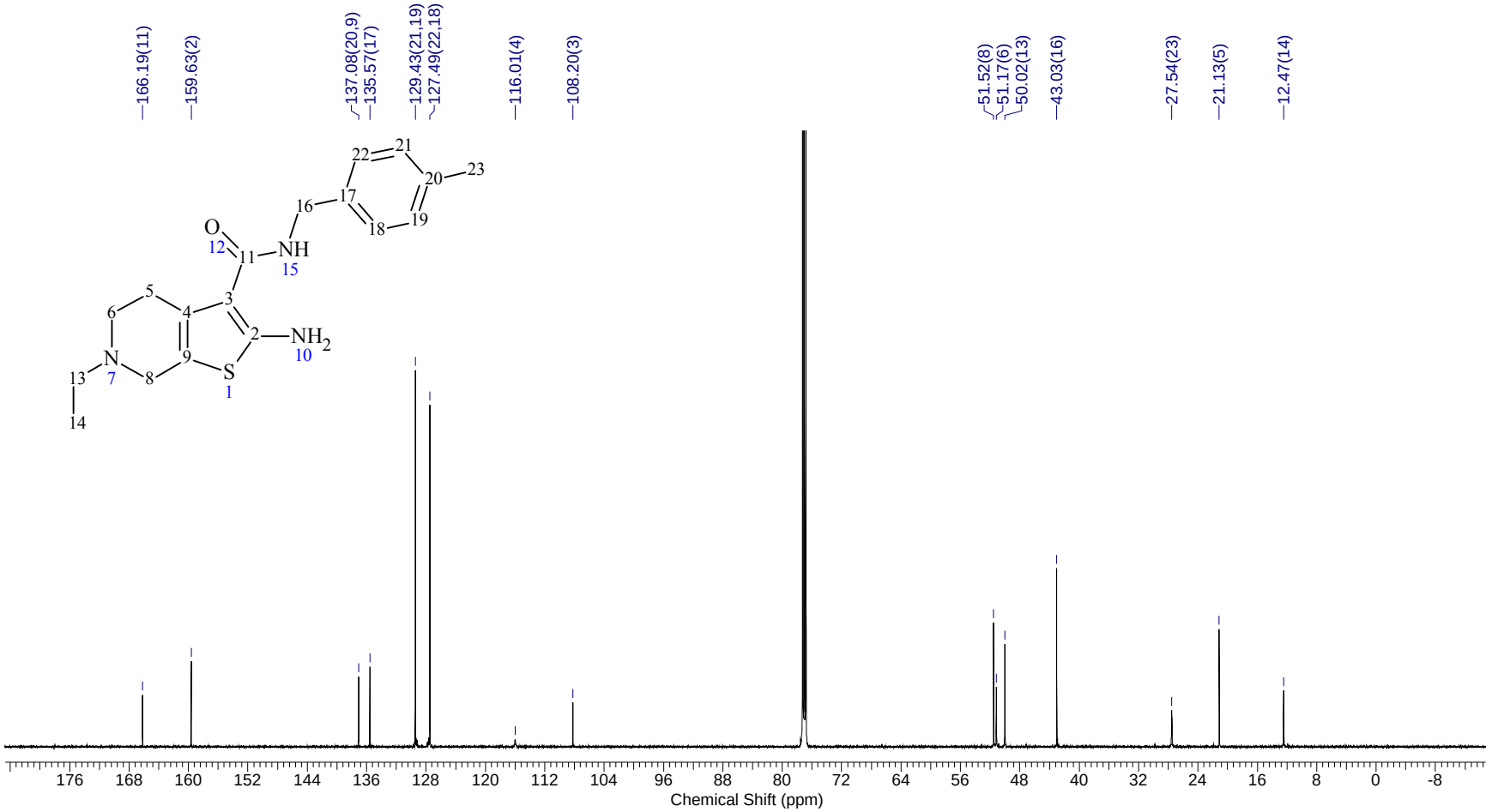
^{13}C-NMR of compound 2-amino-*N*-benzyl-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**45**, $CDCl_3$)



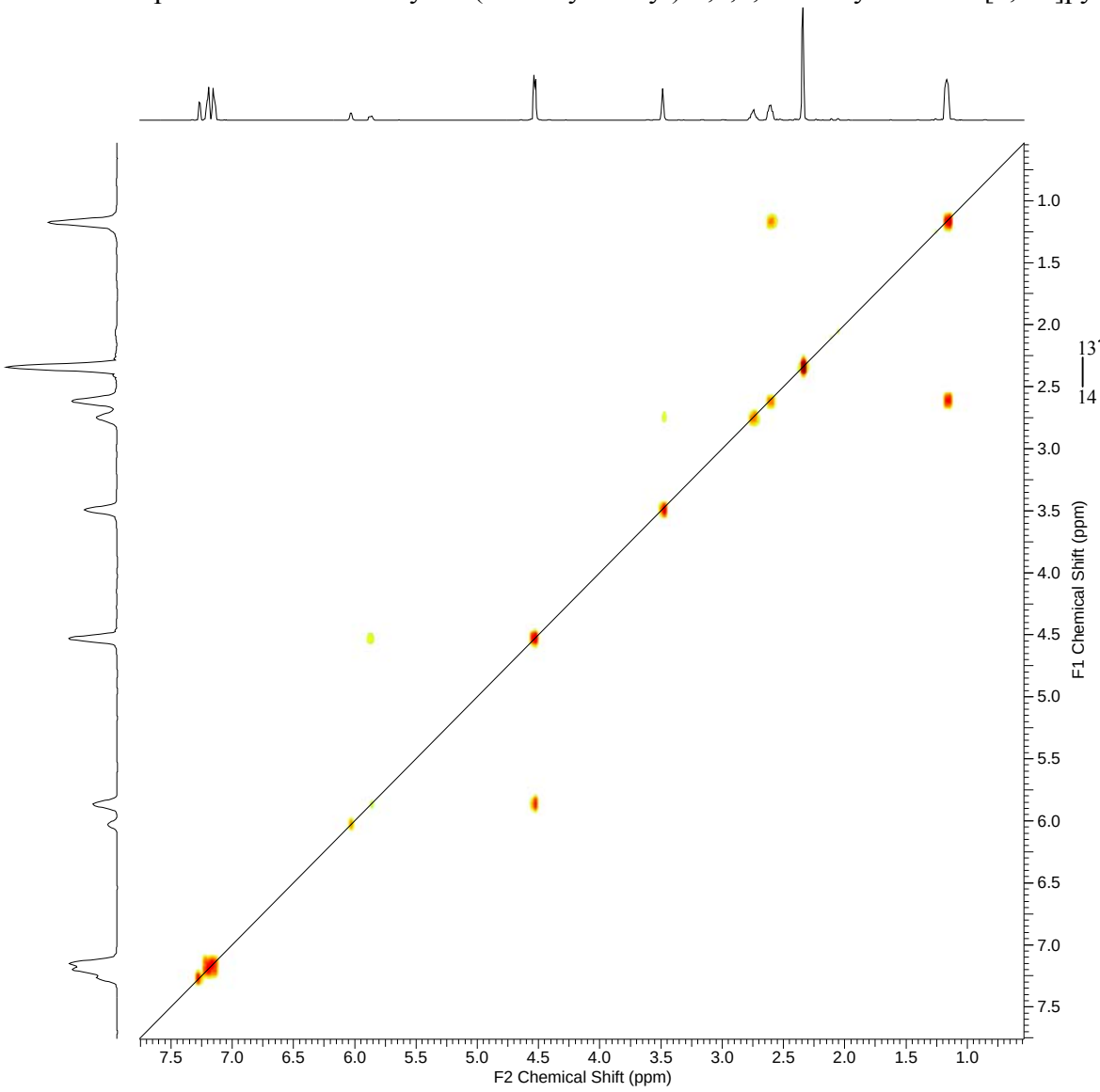
^{1}H-NMR of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46**, $CDCl_3$)

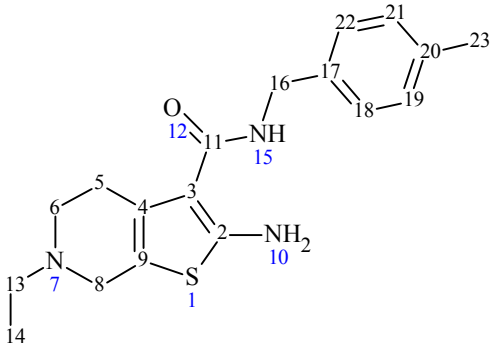


^{13}C-NMR of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46**, $CDCl_3$)

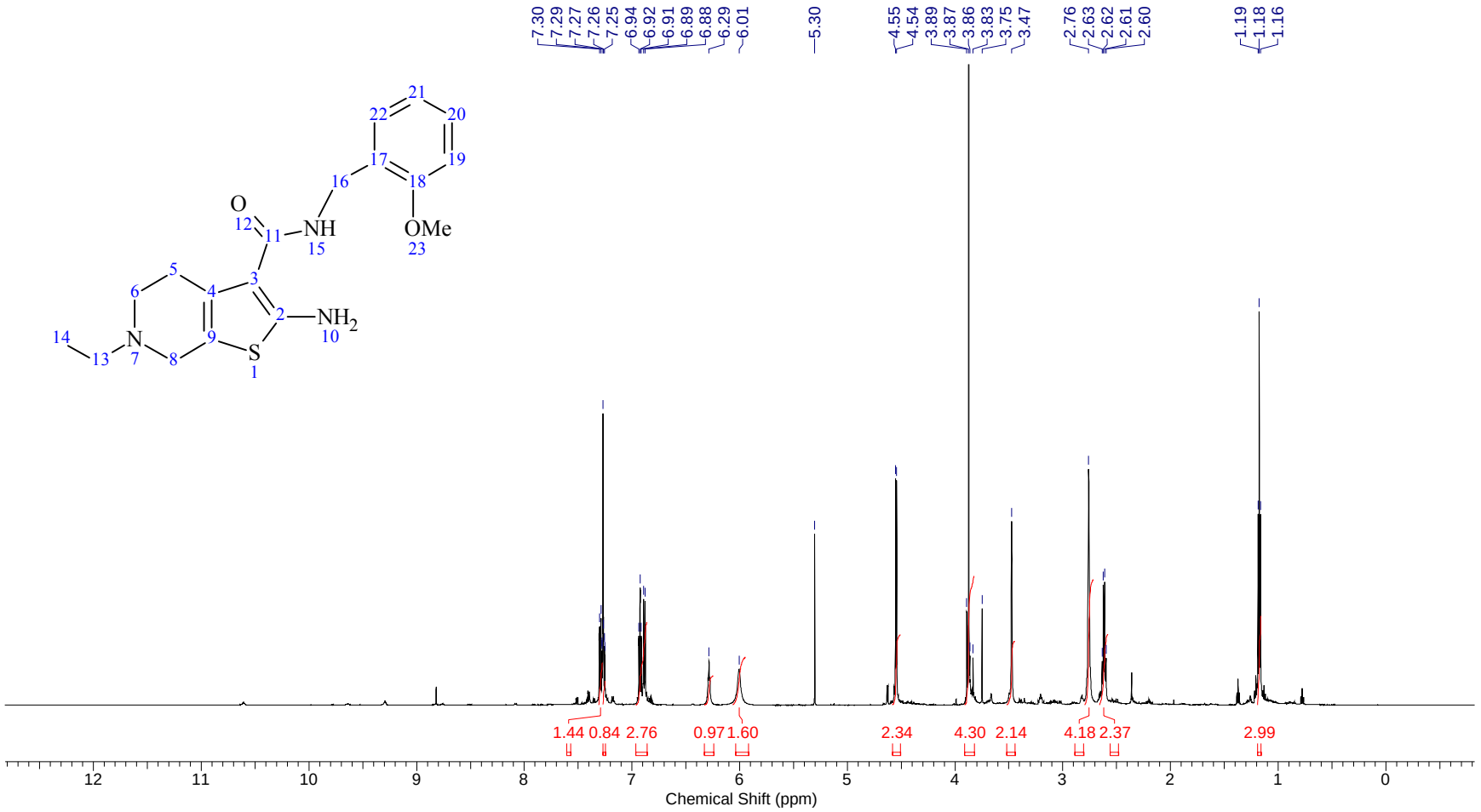


COSY of compound 2-amino-6-ethyl-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**46,** $CDCl_3$)

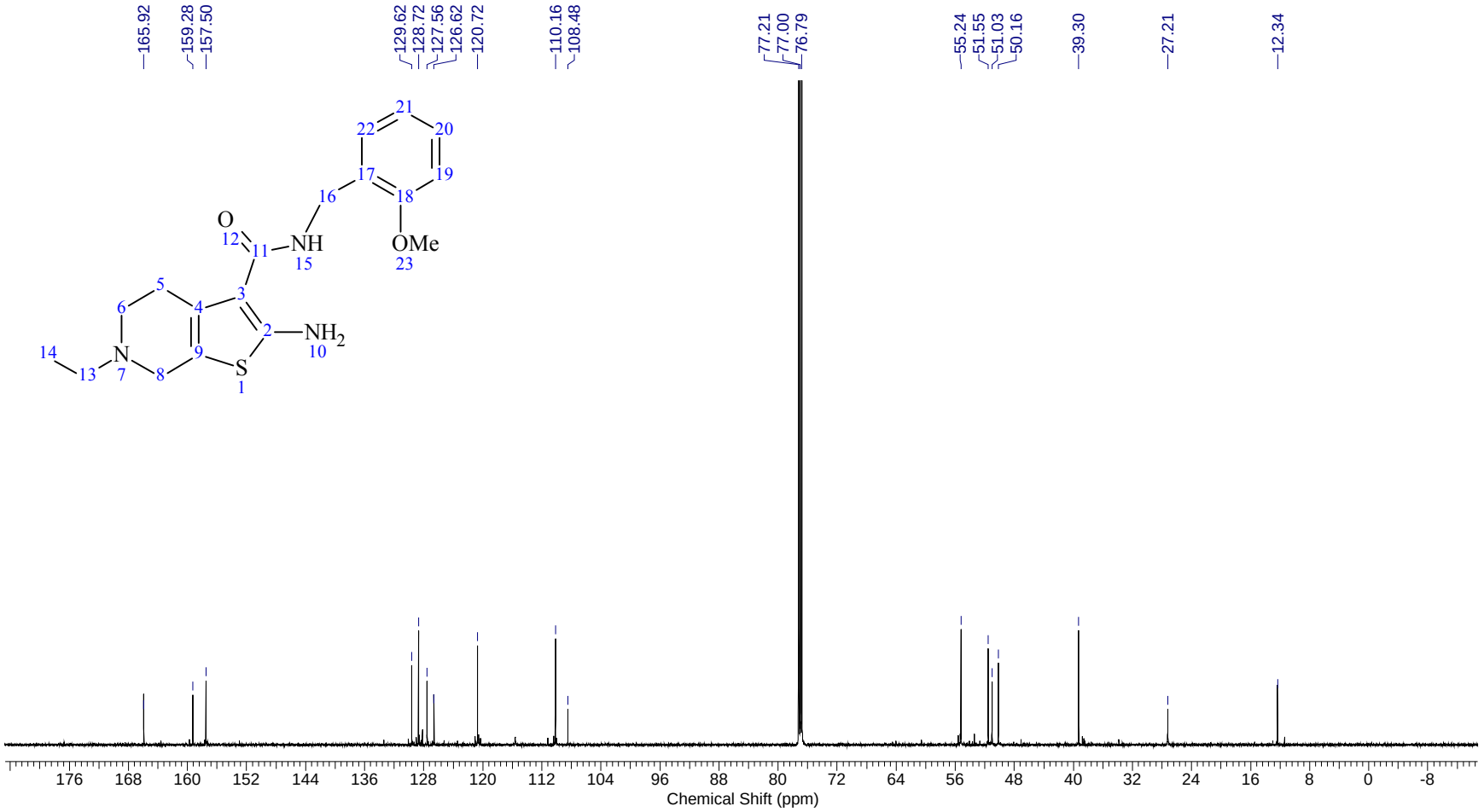




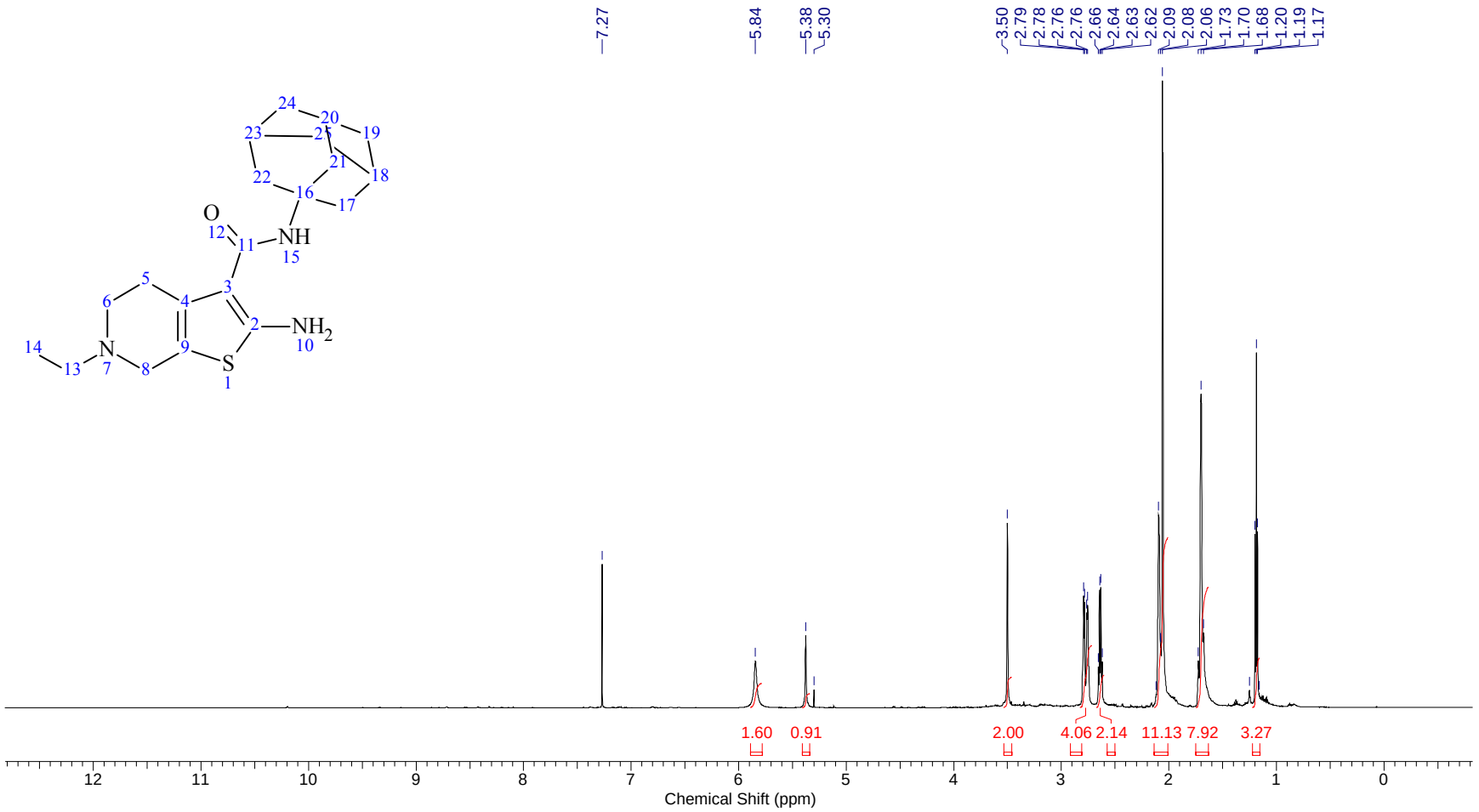
^{1}H-NMR of compound 2-amino-6-ethyl-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**47**, $CDCl_3$)



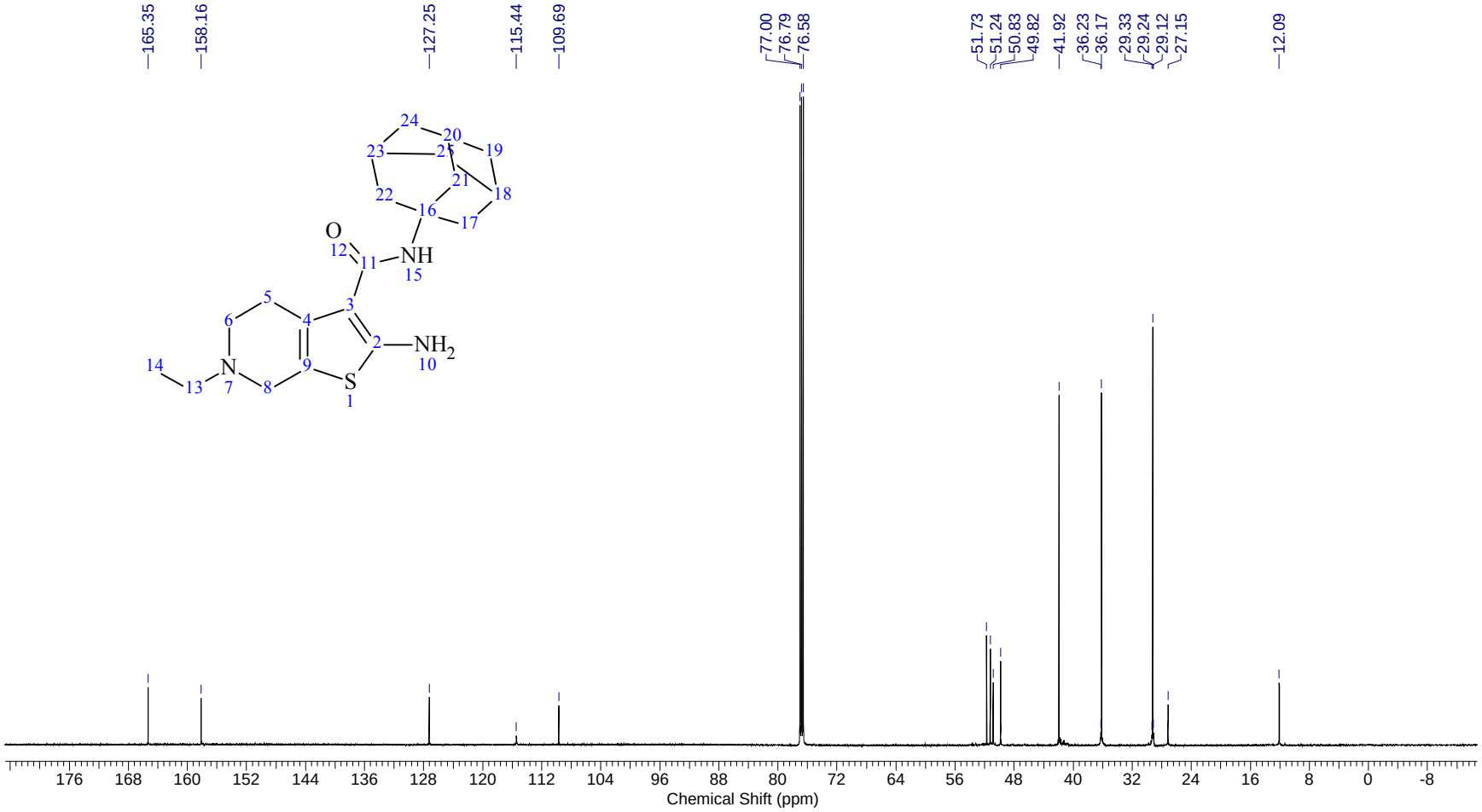
^{13}C-NMR of compound 2-amino-6-ethyl-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**47**, $CDCl_3$)



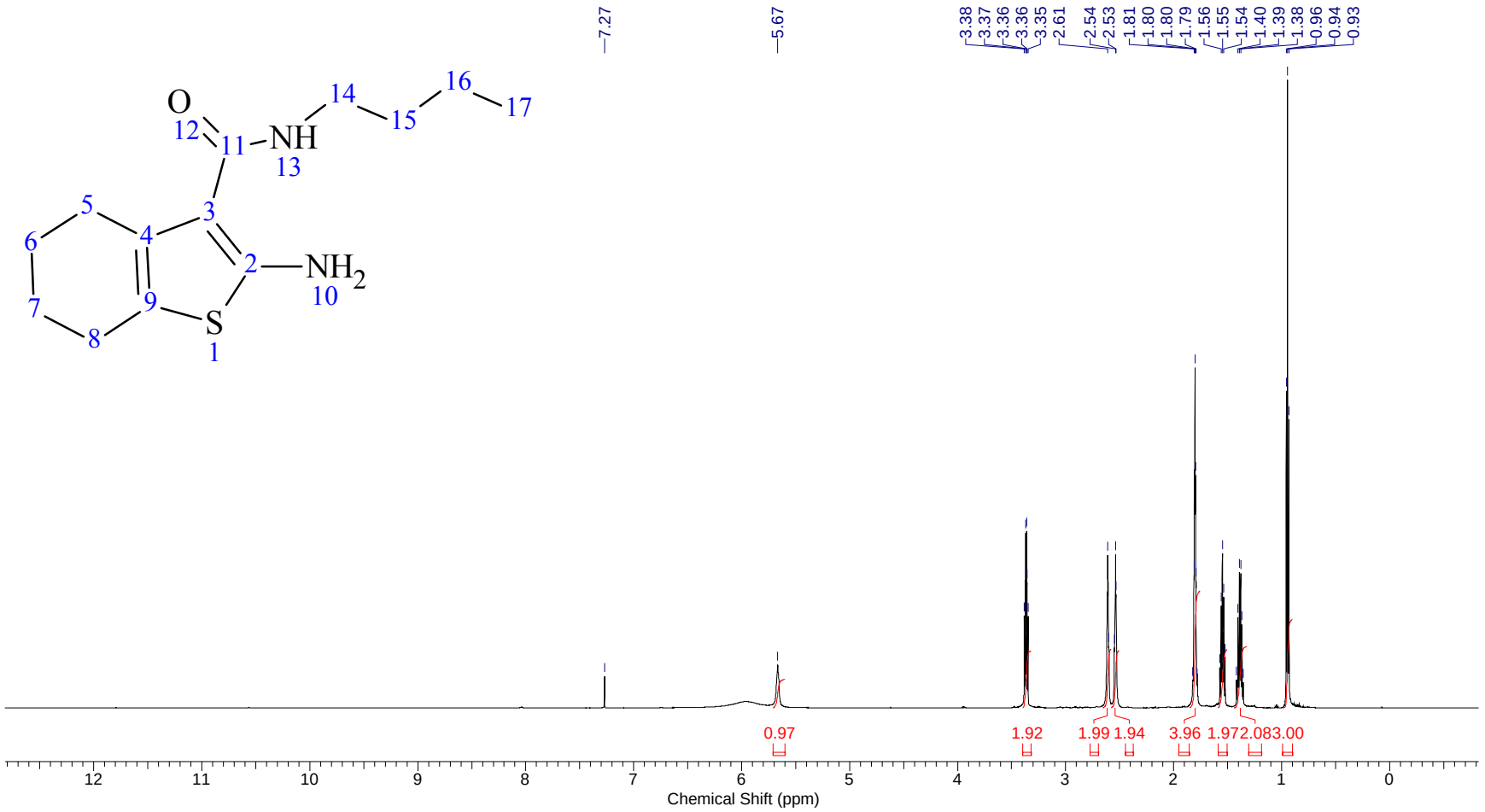
^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**48**, $CDCl_3$)



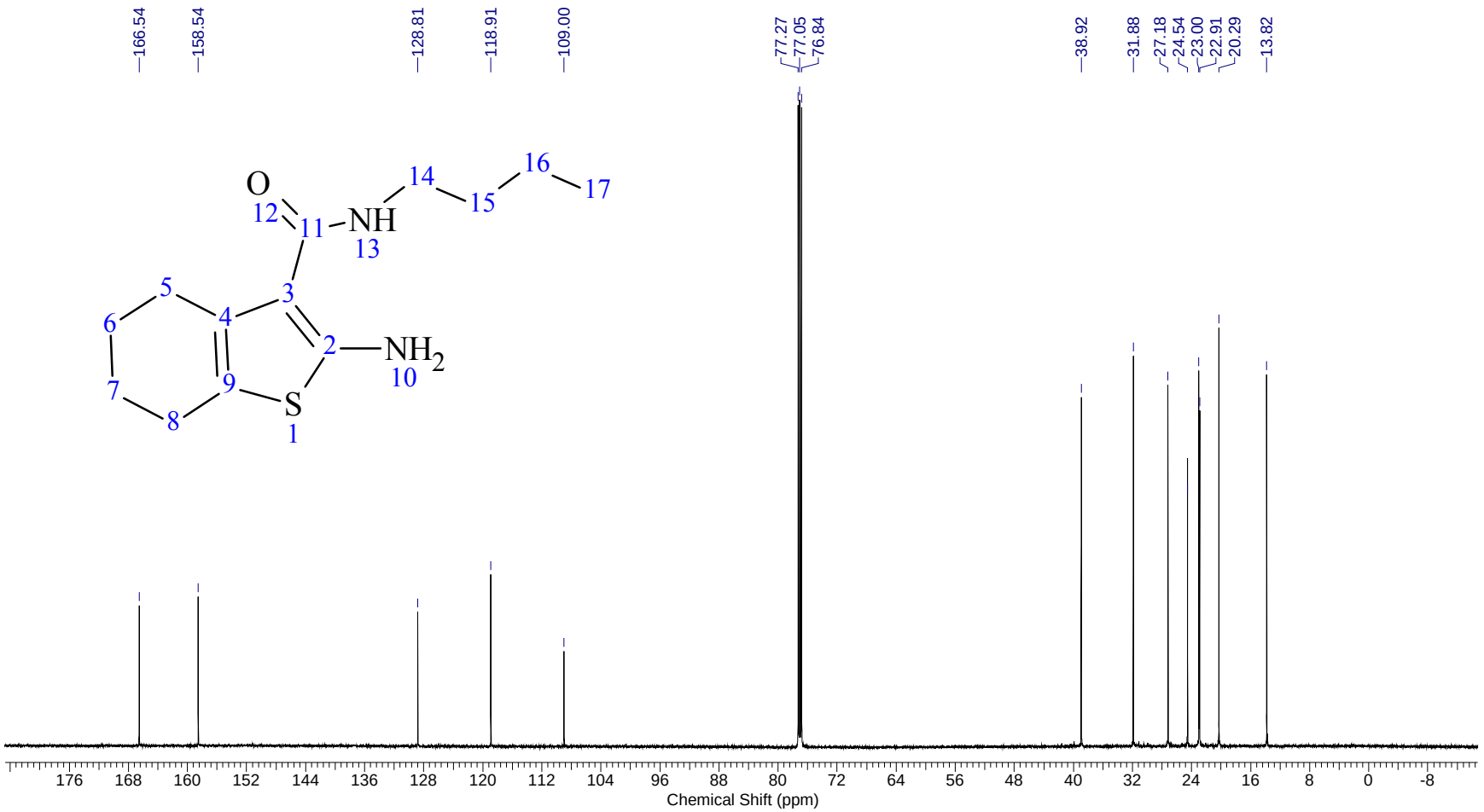
^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-6-ethyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-3-carboxamide (**48**, $CDCl_3$)



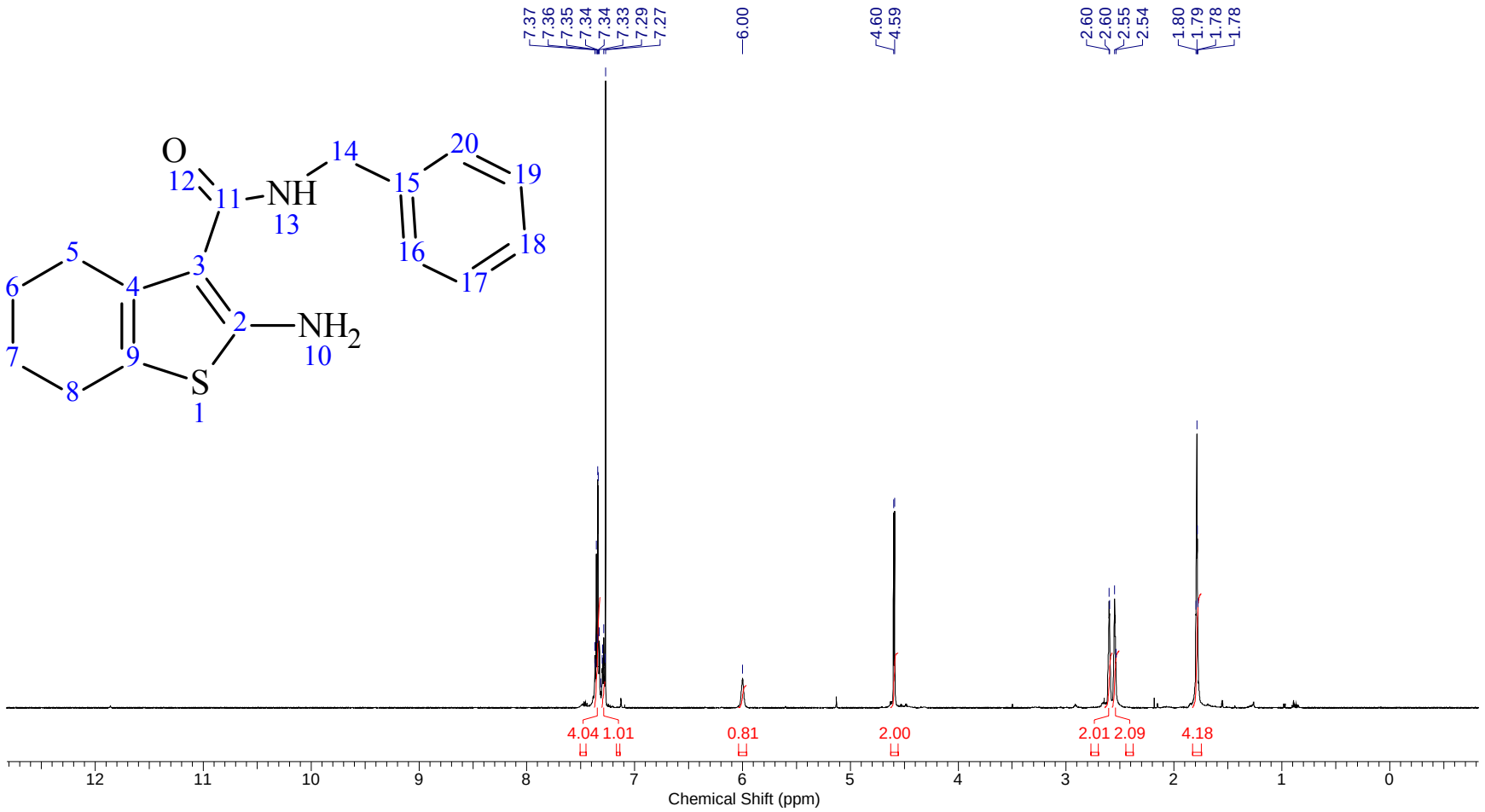
^{1}H-NMR of compound 2-amino-*N*-butyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**49,** $CDCl_3$)



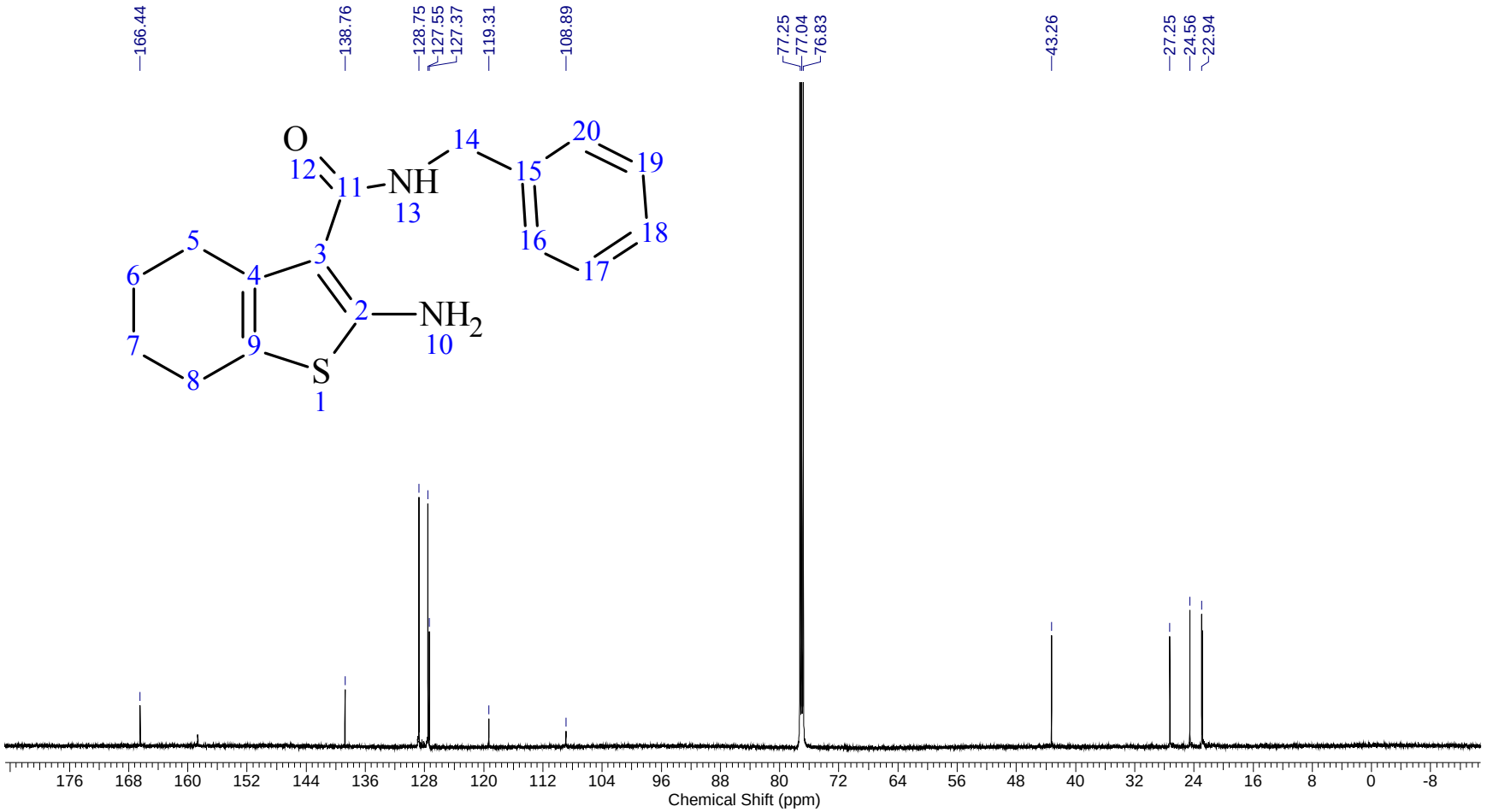
^{13}C-NMR of compound 2-amino-*N*-butyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**49,** $CDCl_3$)



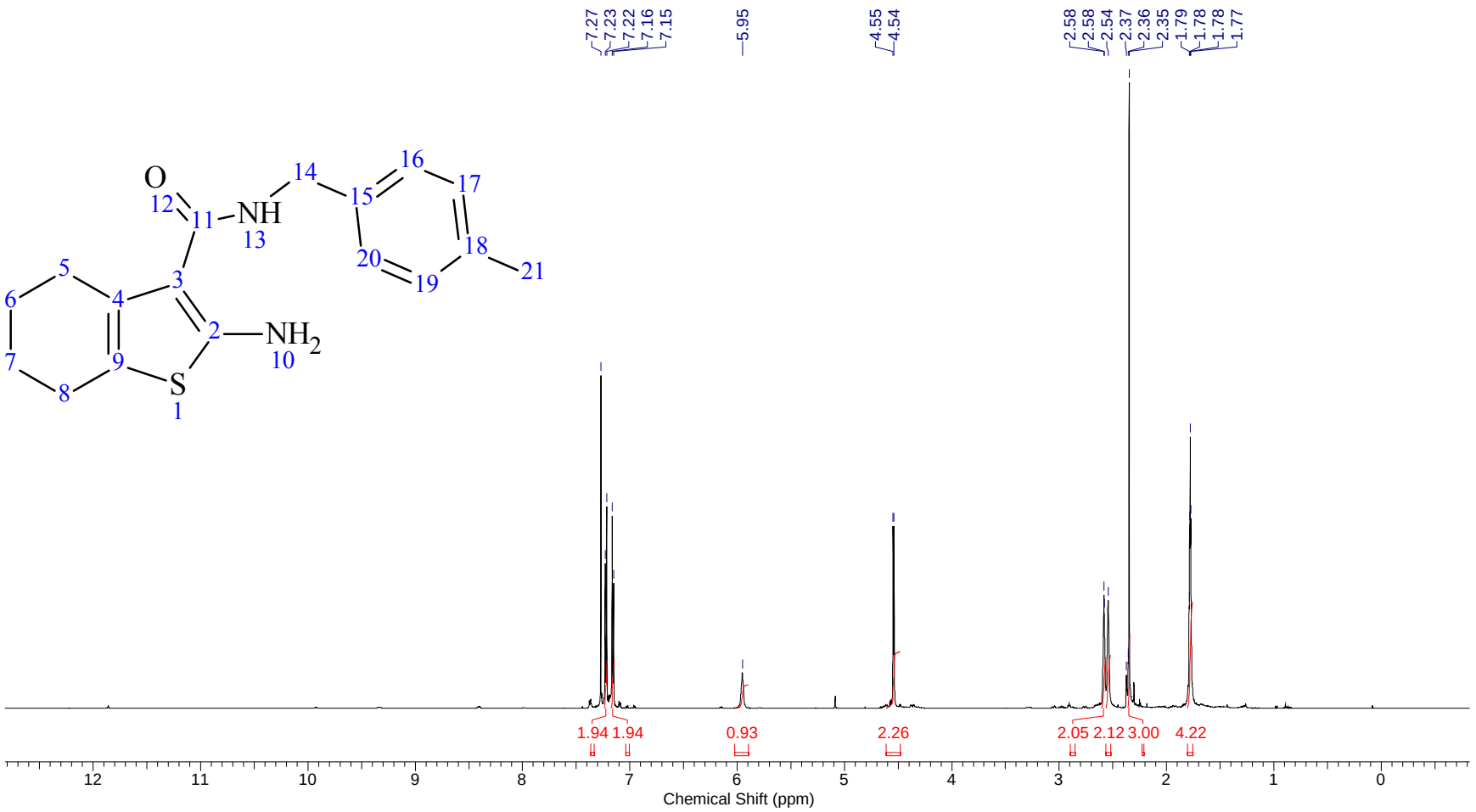
^{1}H-NMR of compound 2-amino-*N*-benzyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**50,** $CDCl_3$)[13]



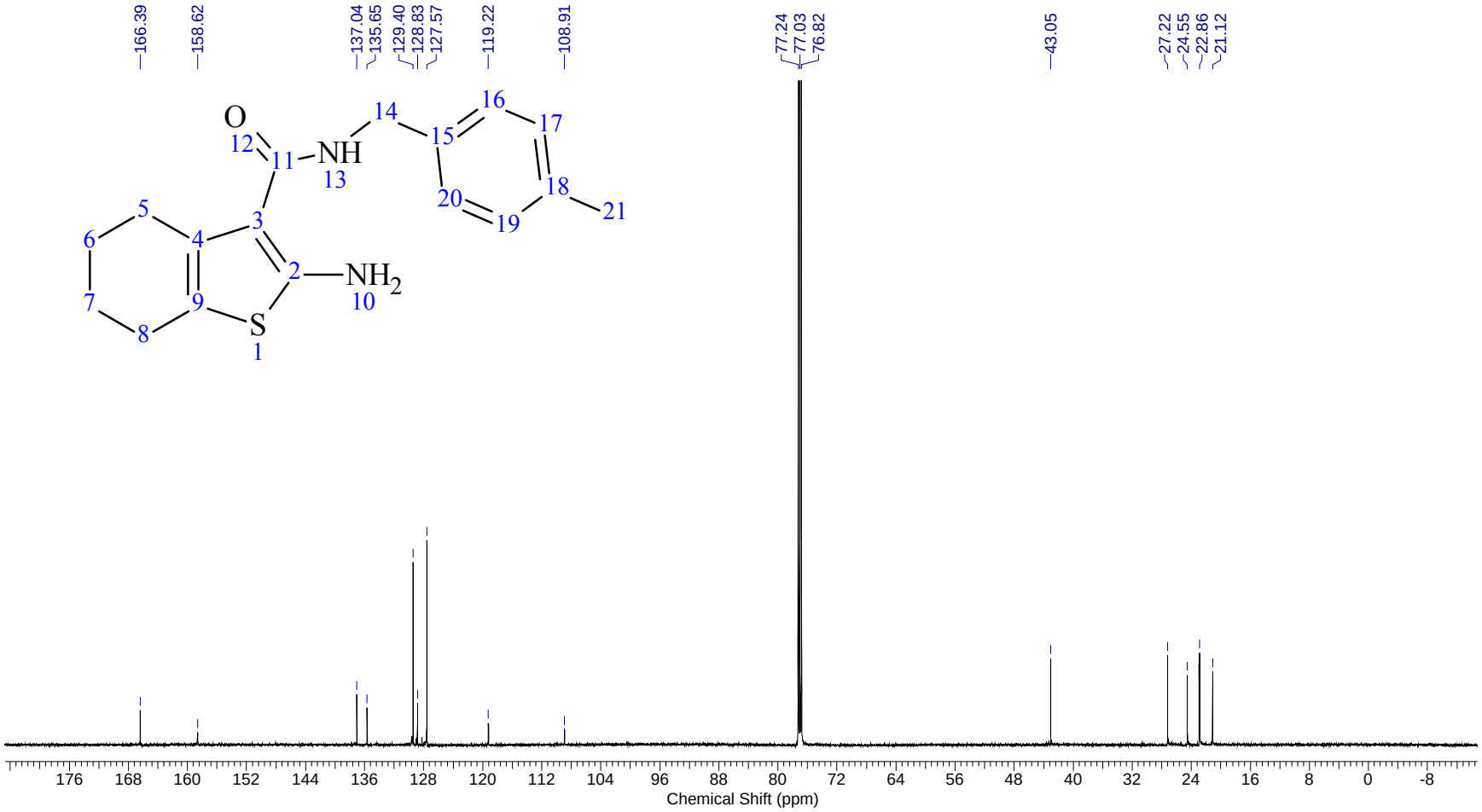
^{13}C-NMR of compound 2-amino-*N*-benzyl-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**50,** $CDCl_3$)[13]



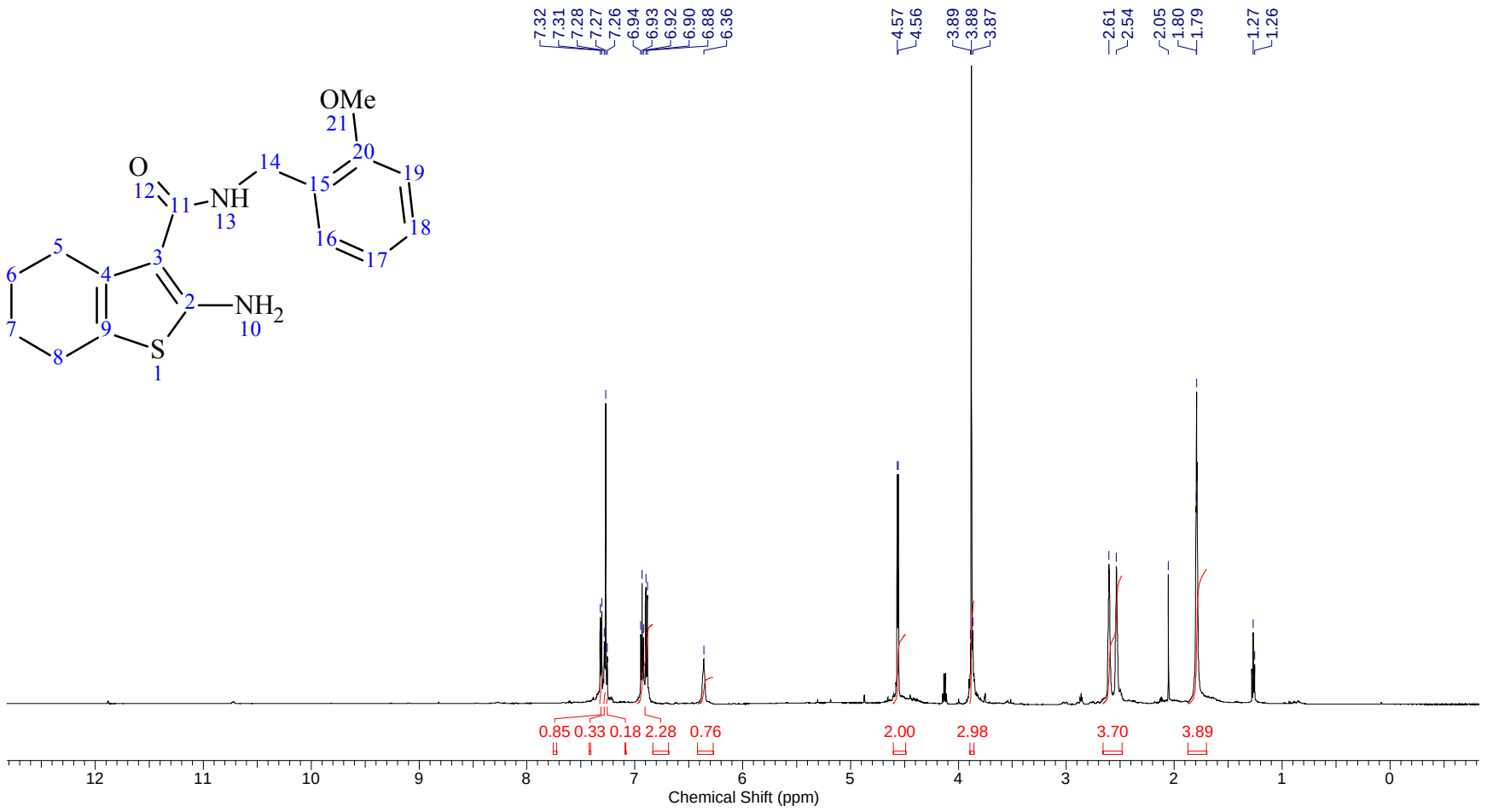
^{1}H-NMR of compound 2-amino-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**51**, $CDCl_3$)



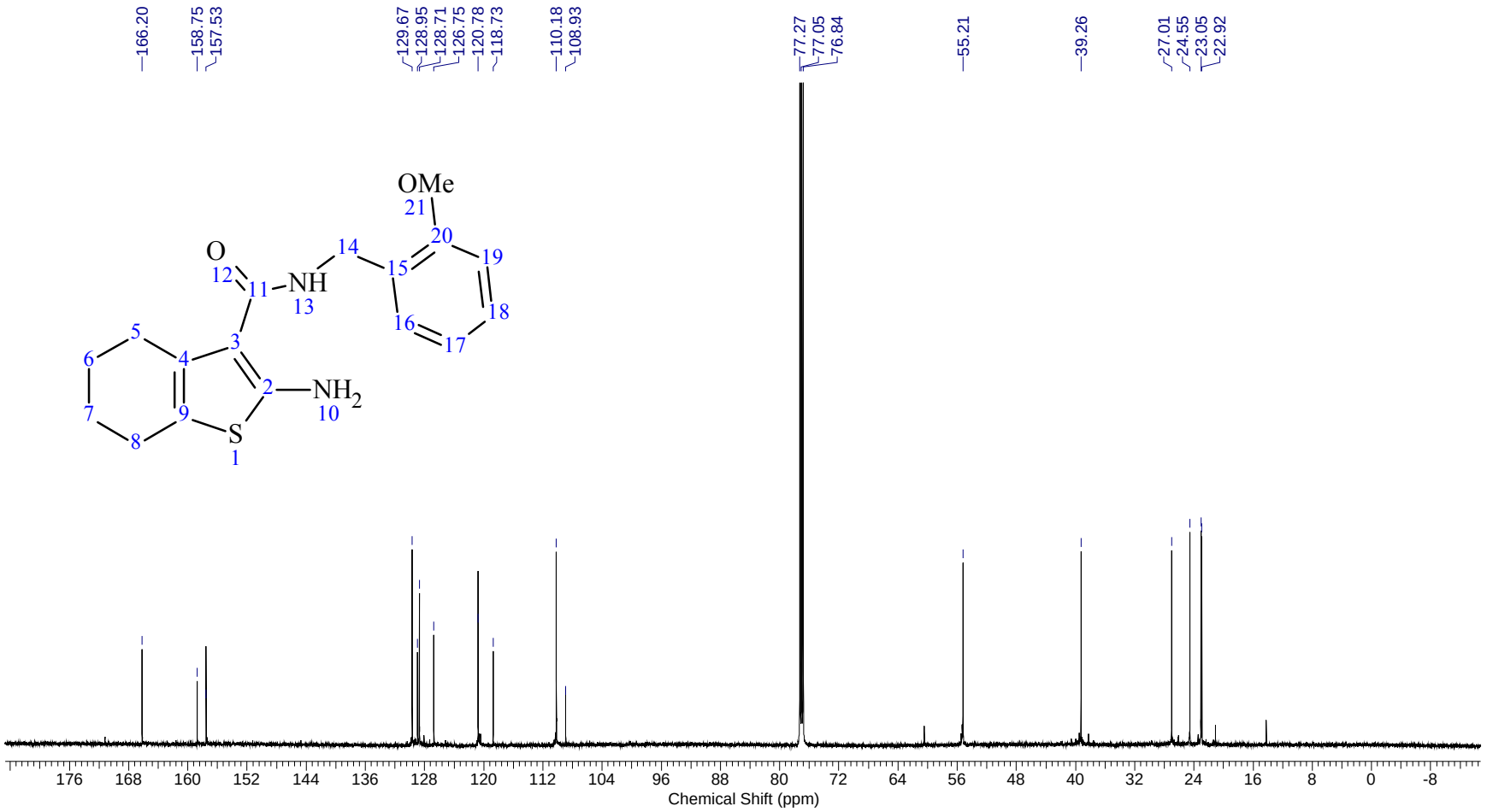
^{13}C-NMR of compound 2-amino-*N*-(4-methylbenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**51**, $CDCl_3$)



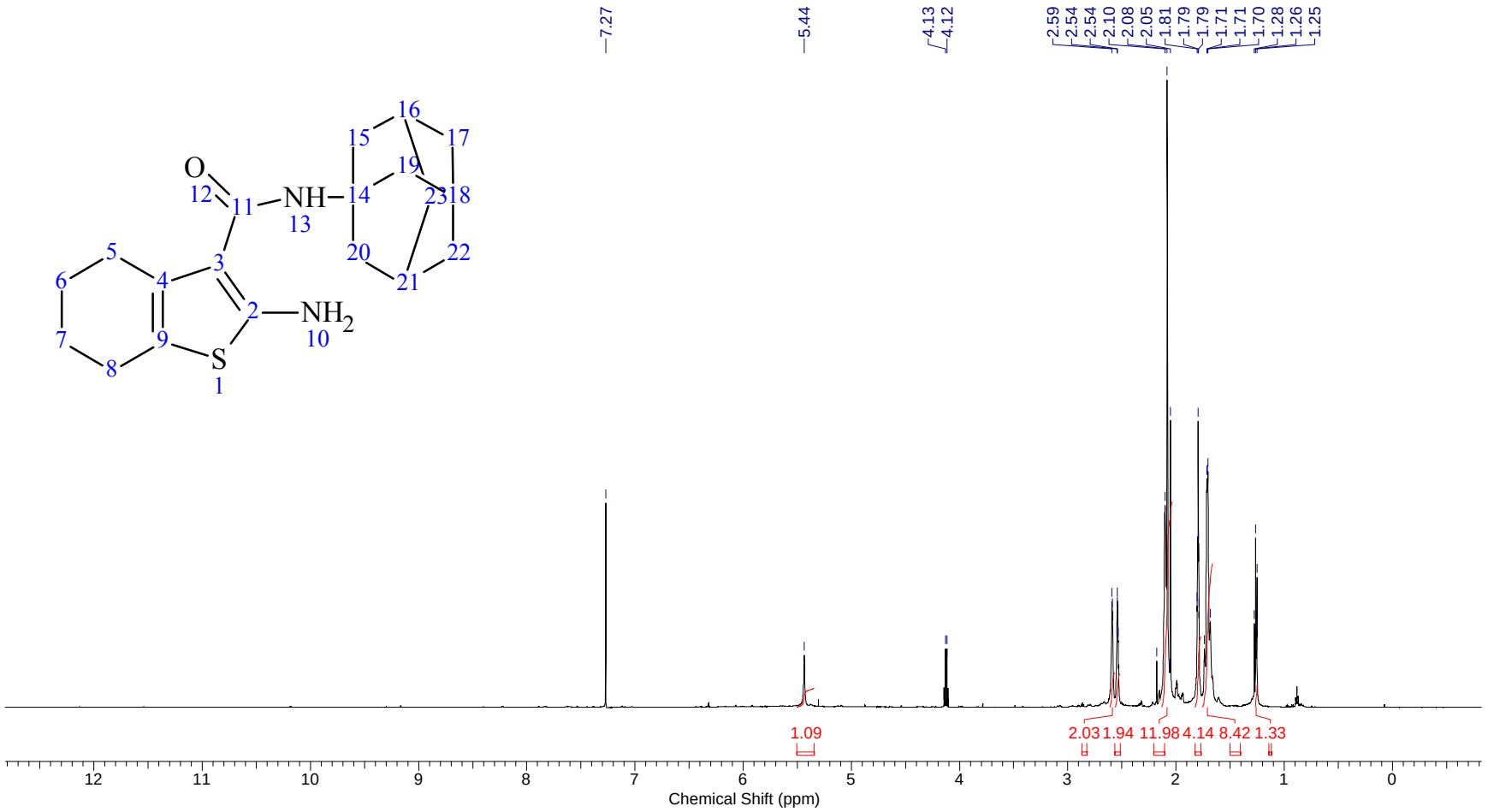
^{1}H-NMR of compound 2-amino-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**52**, $CDCl_3$)



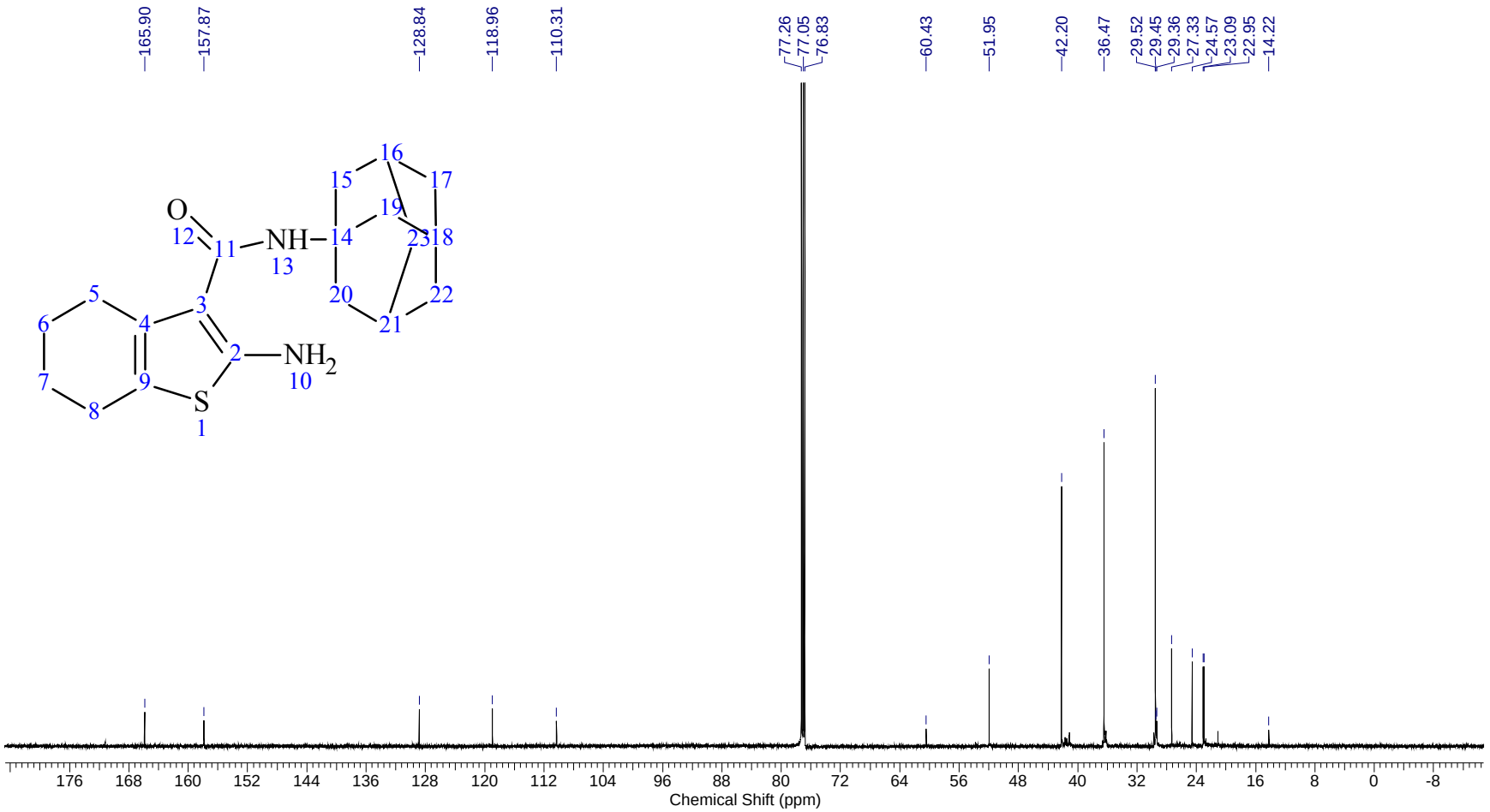
^{13}C-NMR of compound 2-amino-*N*-(2-methoxybenzyl)-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**52,** $CDCl_3$)



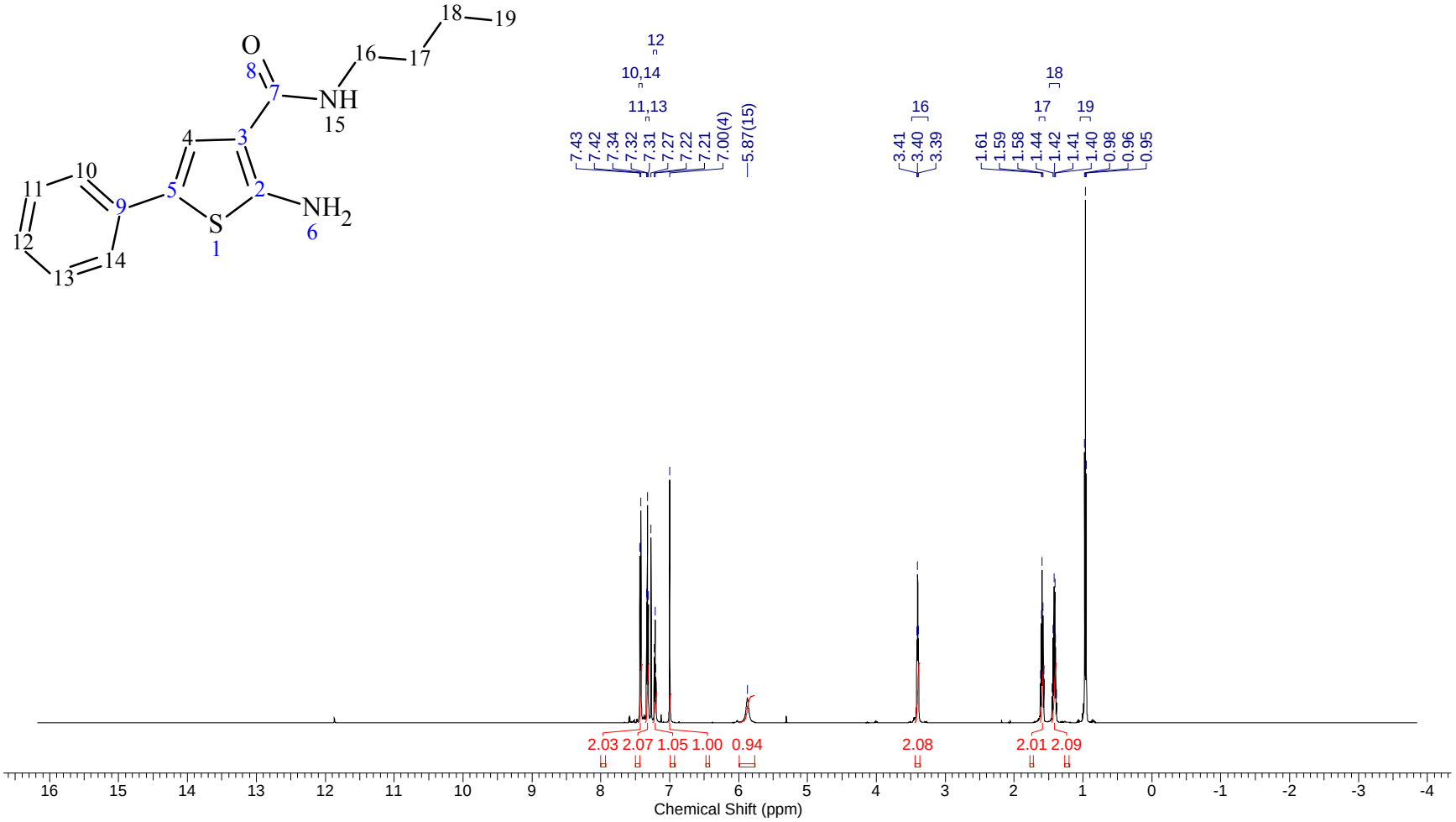
^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**53**, $CDCl_3$)



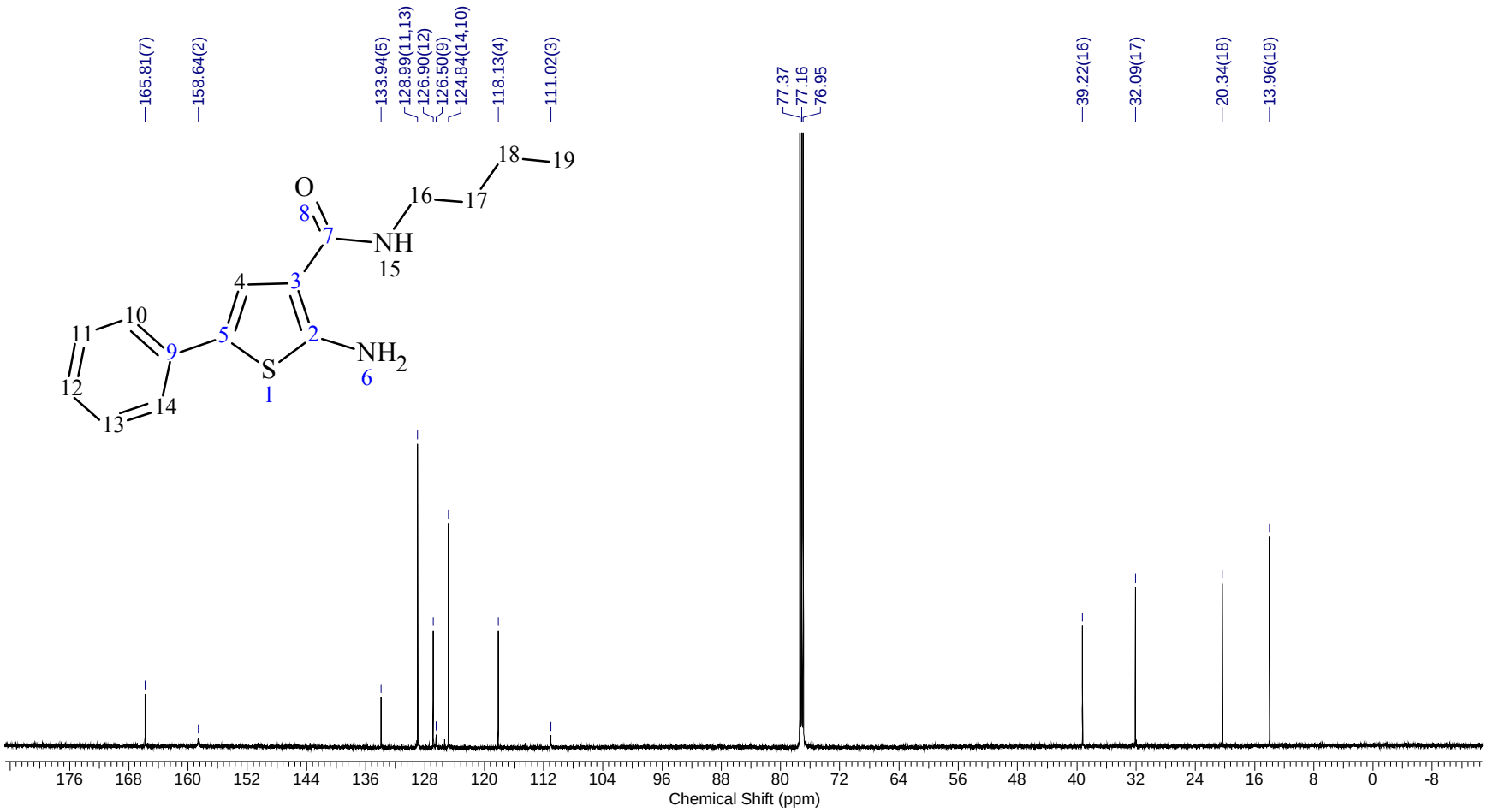
^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-4,5,6,7-tetrahydrobenzo[*b*]thiophene-3-carboxamide (**53**, $CDCl_3$)



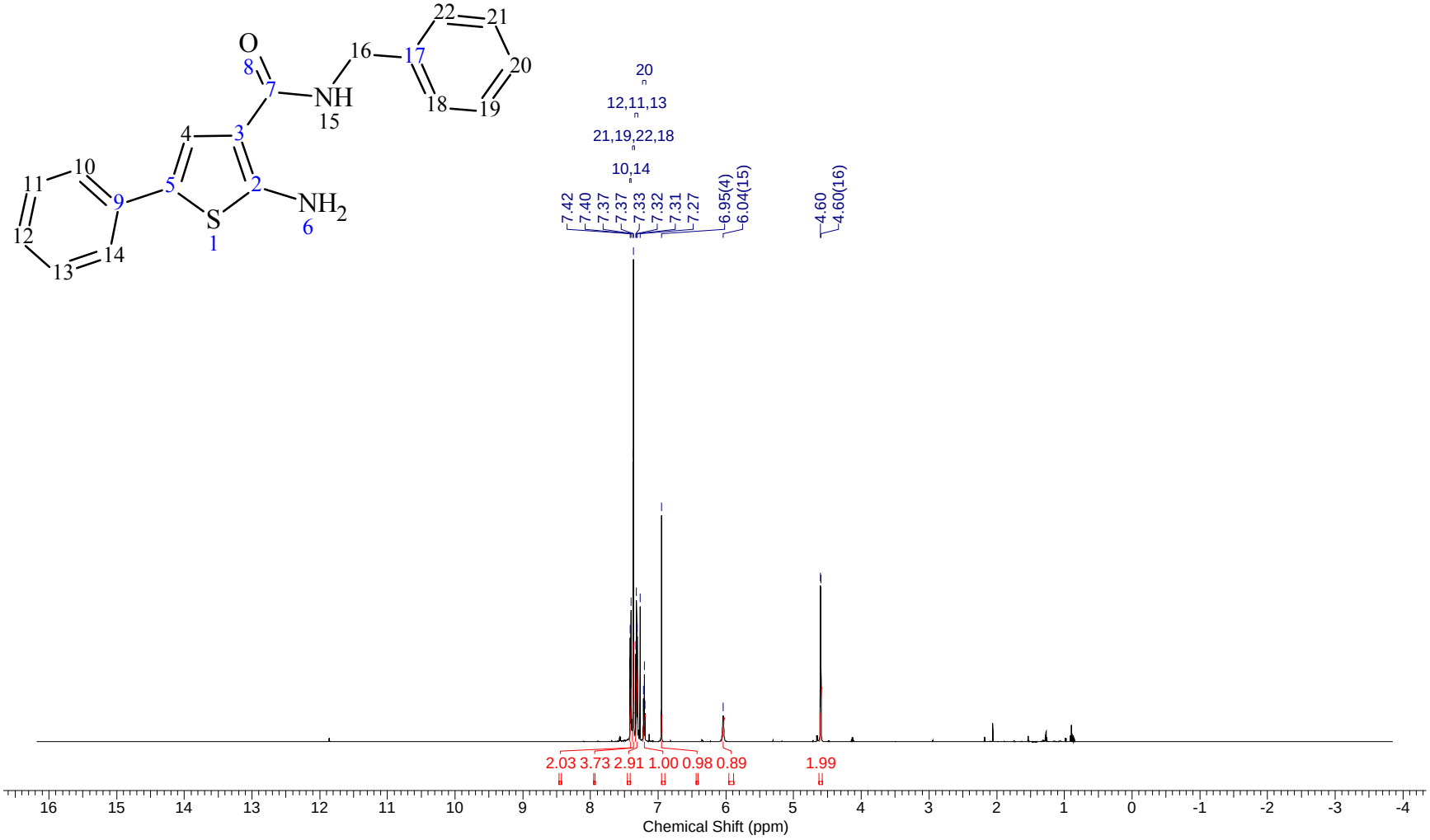
^{1}H-NMR of compound 2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (**59**, $CDCl_3$)[14]



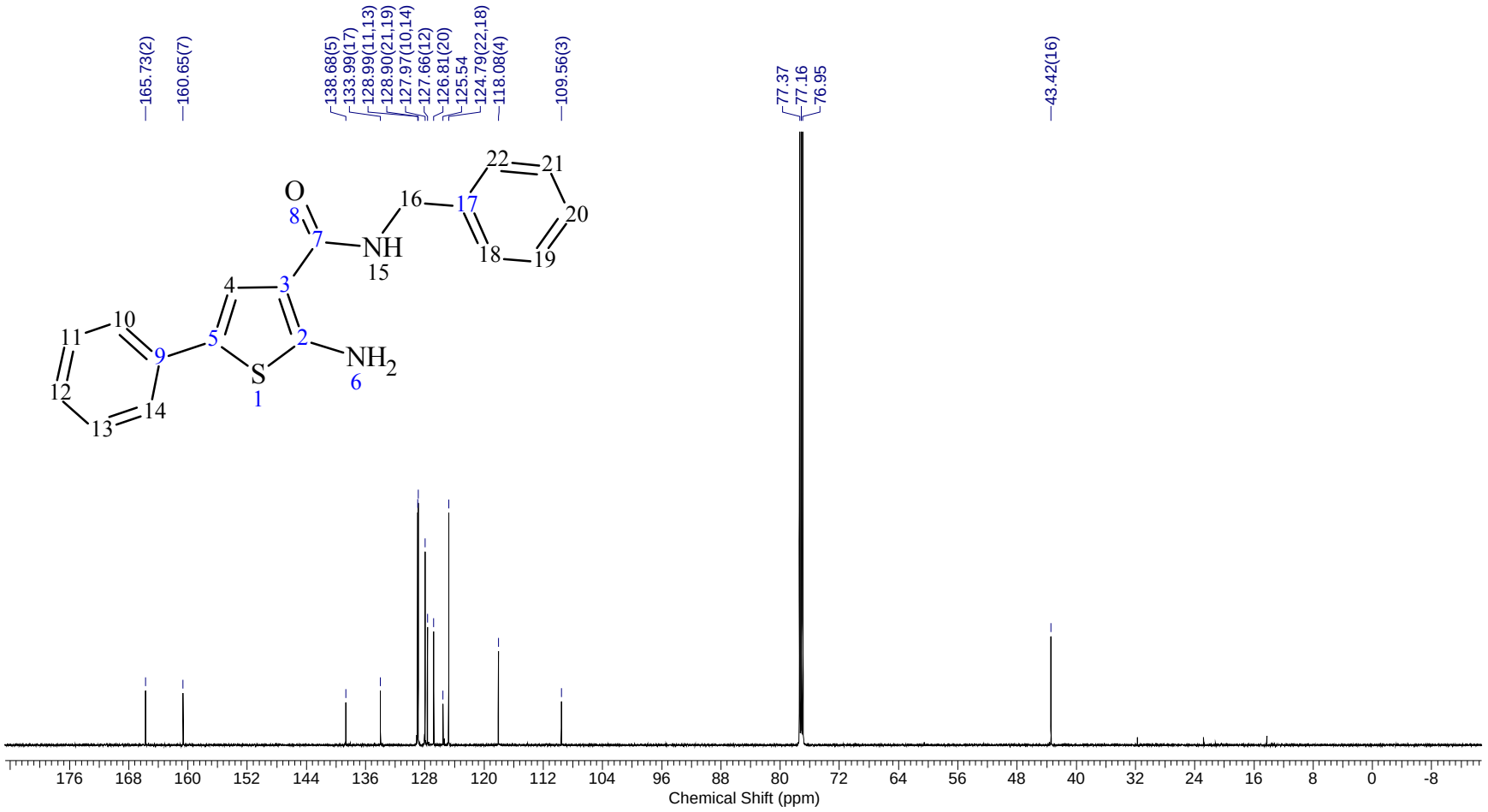
^{13}C-NMR of compound 2-Amino-*N*-butyl-5-phenylthiophene-3-carboxamide (**59**, $CDCl_3$)[14]



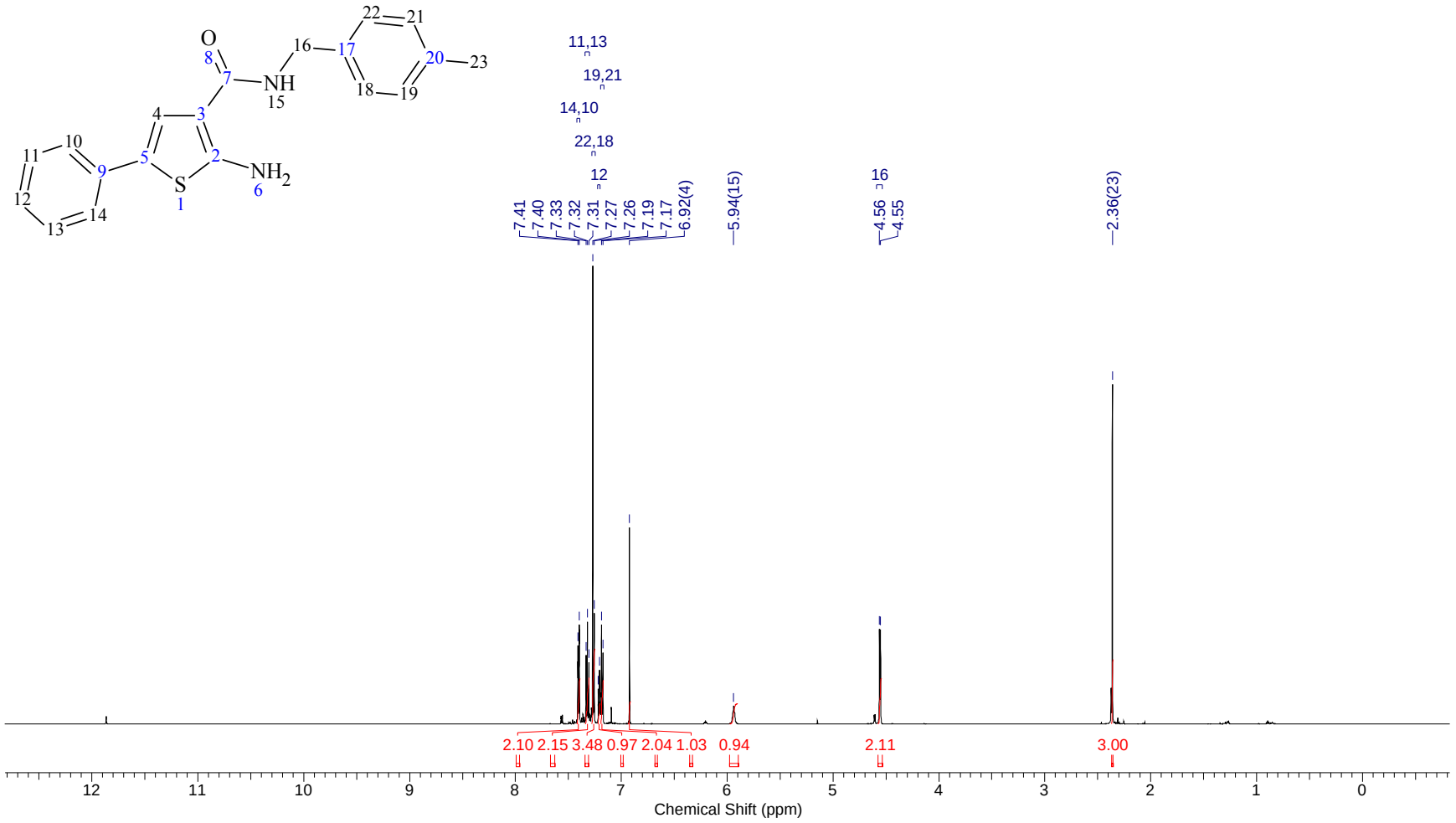
^{1}H-NMR of compound 2-amino-*N*-benzyl-5-phenylthiophene-3-carboxamide (**60,** $CDCl_3$)



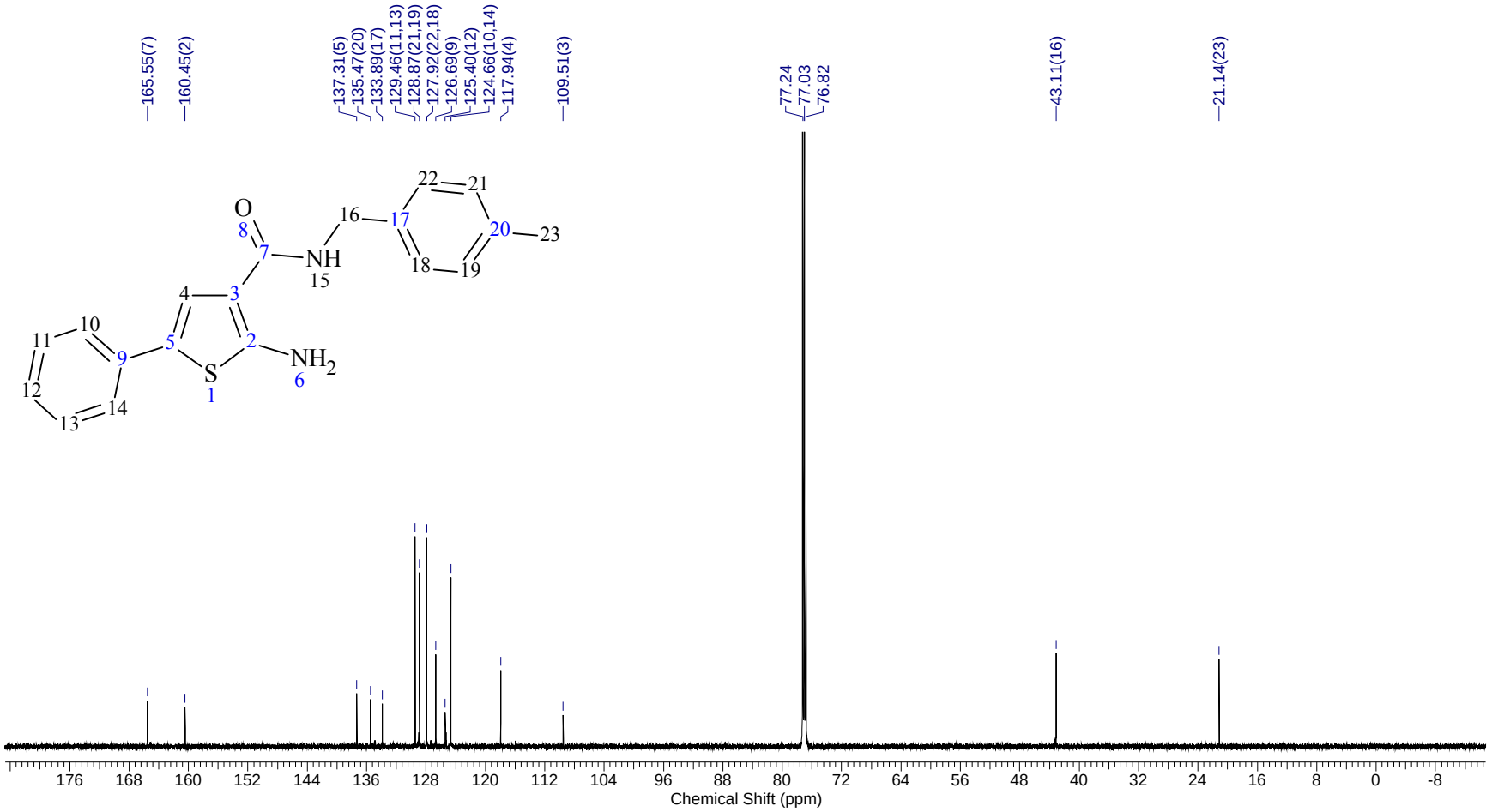
^{13}C-NMR of compound 2-amino-*N*-benzyl-5-phenylthiophene-3-carboxamide (**60**, $CDCl_3$)



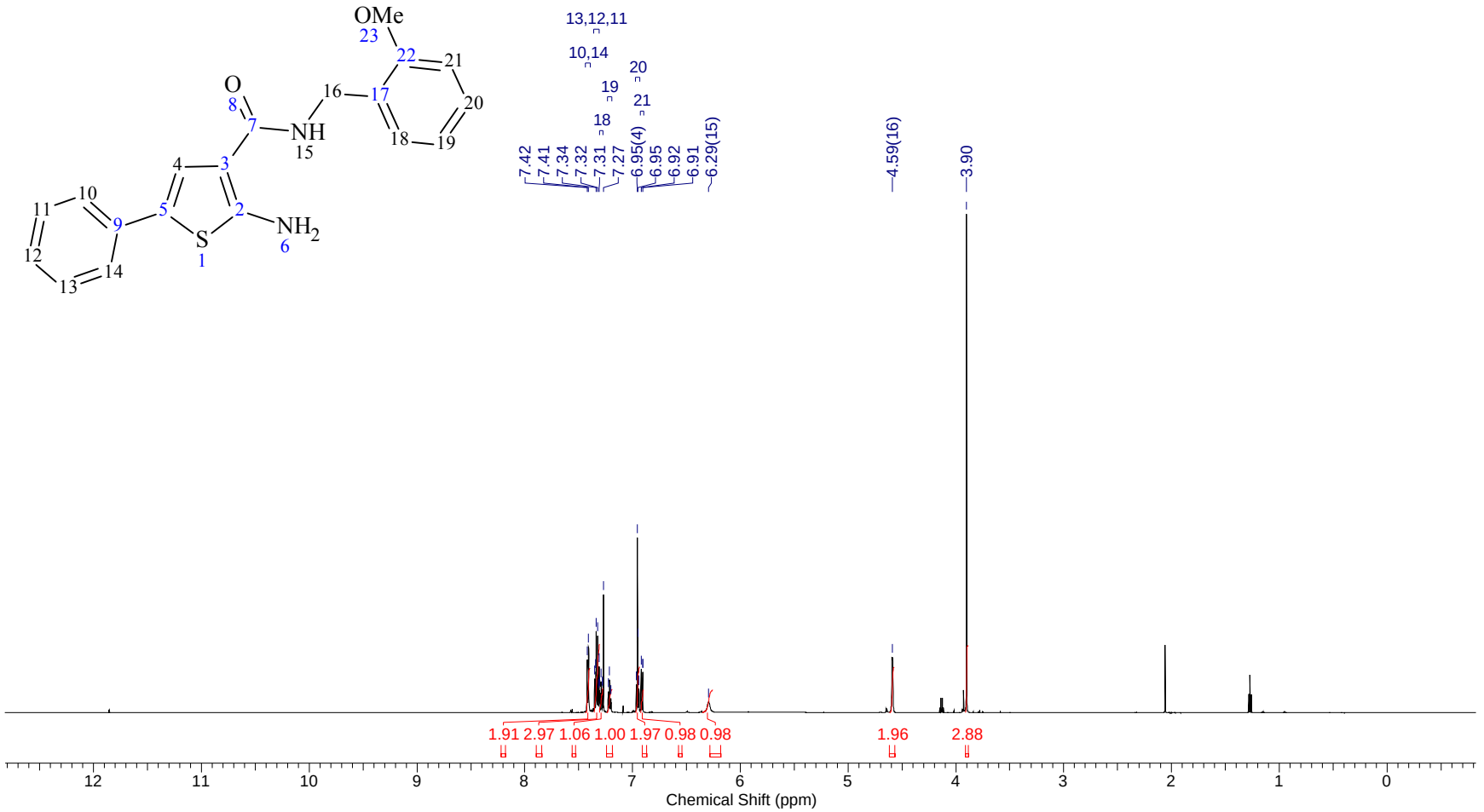
^{1}H-NMR of compound 2-amino-*N*-(4-methylbenzyl)-5-phenylthiophene-3-carboxamide (**61,** $CDCl_3$)



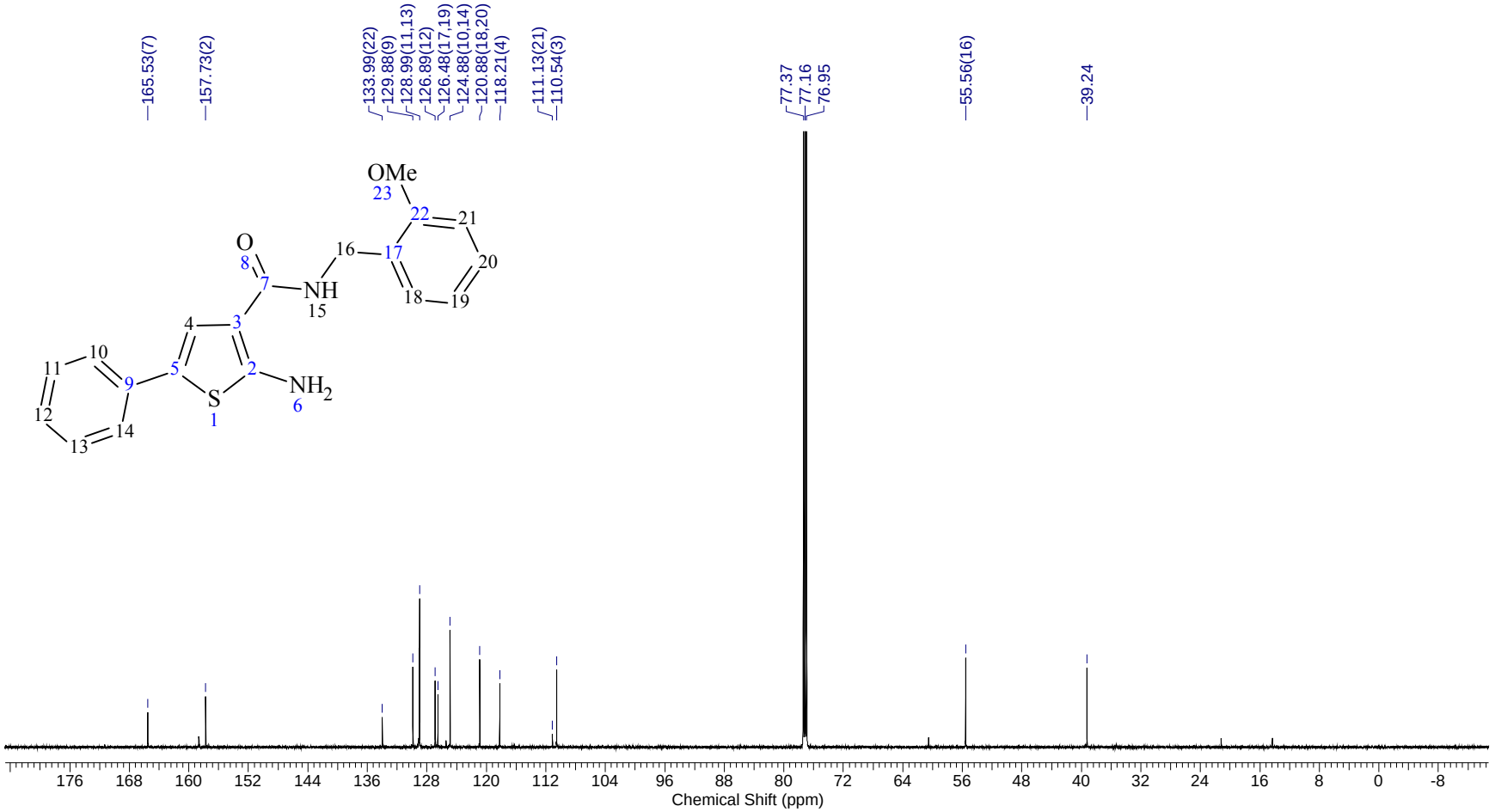
^{13}C-NMR of compound 2-amino-*N*-(4-methylbenzyl)-5-phenylthiophene-3-carboxamide (**61**, $CDCl_3$)



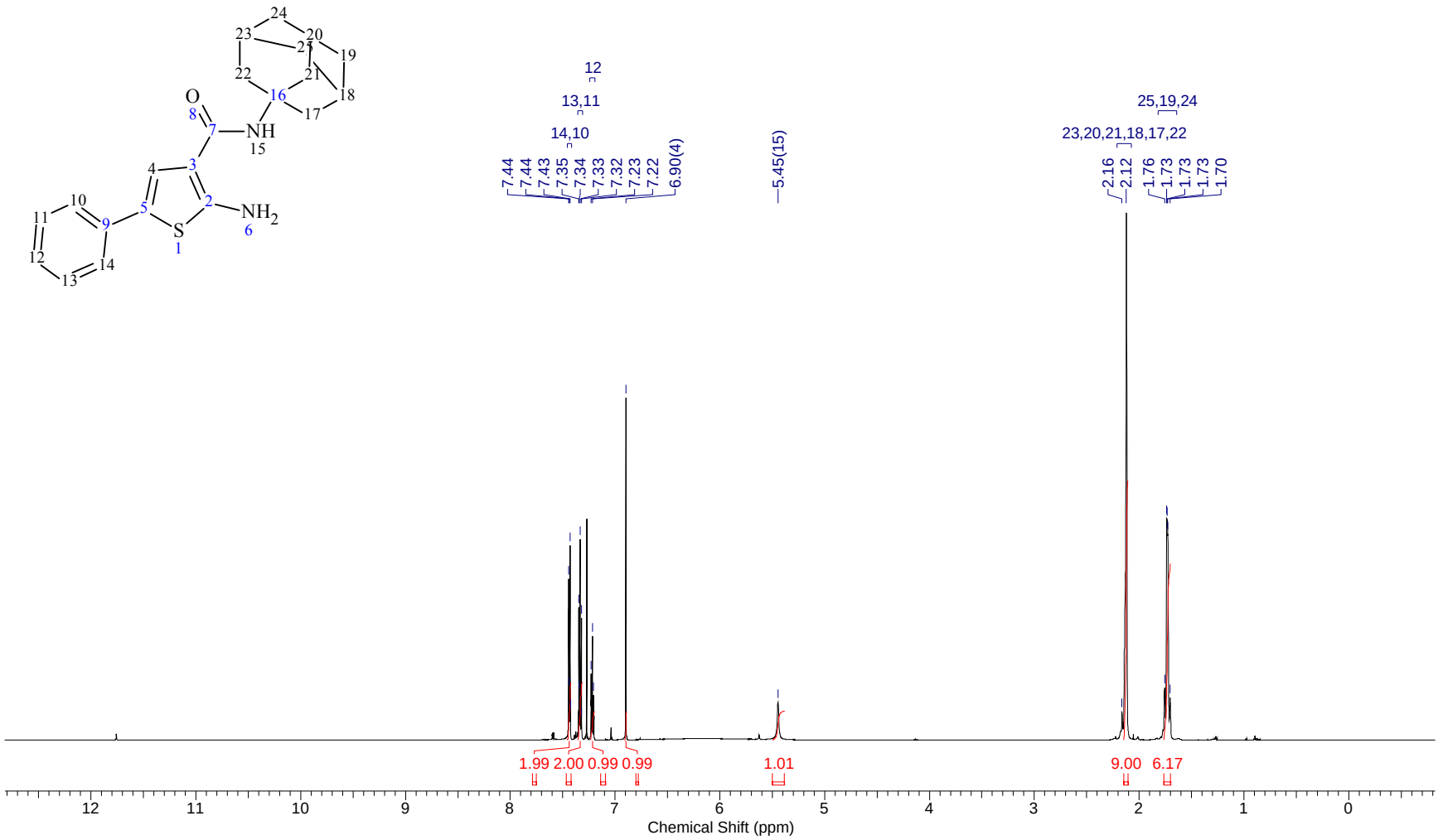
^{1}H-NMR of compound 2-Amino-*N*-(2-methoxybenzyl)-5-phenylthiophene-3-carboxamide (**62**, $CDCl_3$)



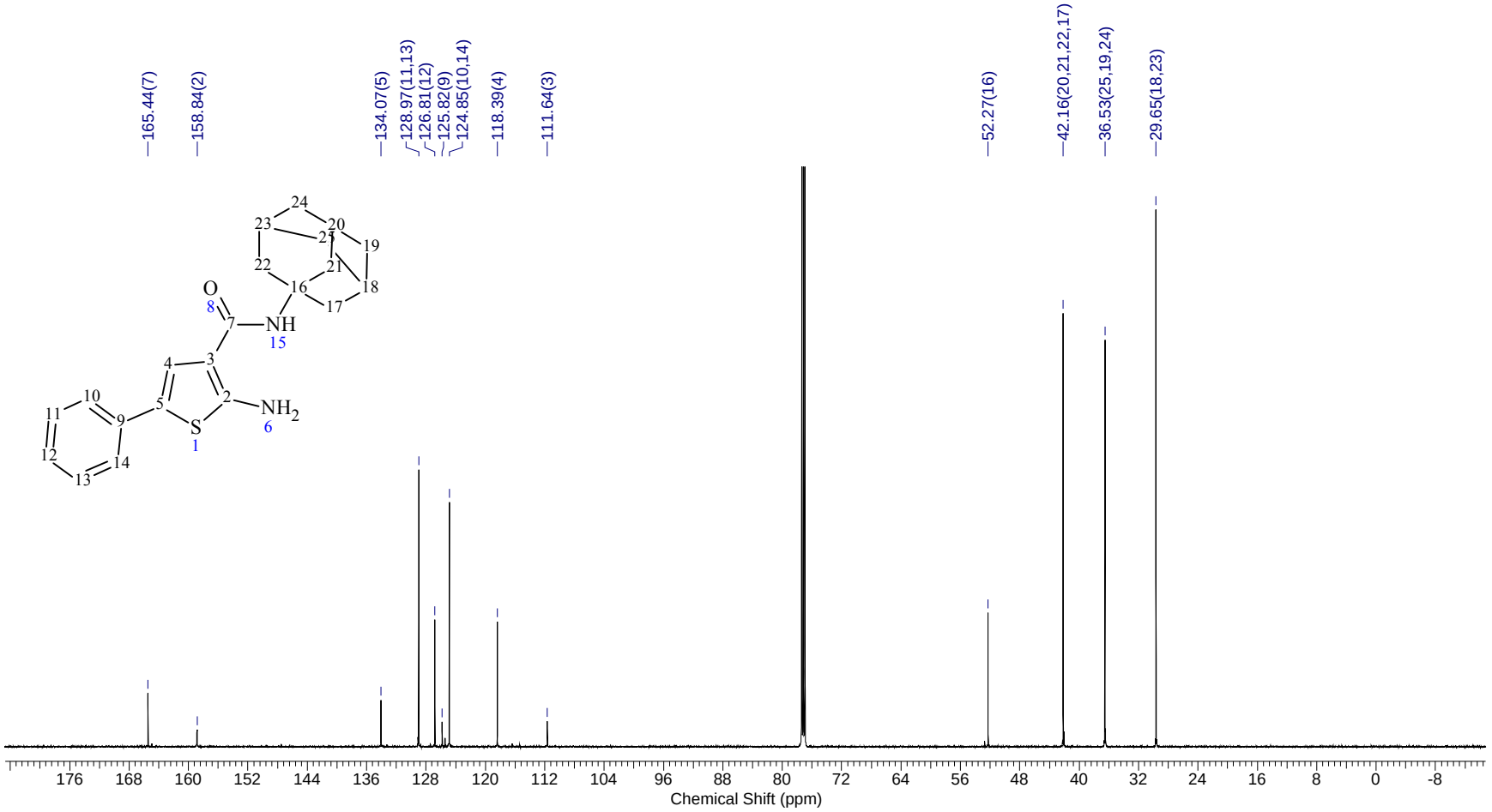
^{13}C-NMR of compound 2-Amino-*N*-(2-methoxybenzyl)-5-phenylthiophene-3-carboxamide (**62**, $CDCl_3$)



^{1}H-NMR of compound *N*-(adamantan-1-yl)-2-amino-5-phenylthiophene-3-carboxamide (**63**, $CDCl_3$)



^{13}C-NMR of compound *N*-(adamantan-1-yl)-2-amino-5-phenylthiophene-3-carboxamide (**63**, $CDCl_3$)



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