Electronic supplementary materials *Mendeleev Commun.*, 2022, **32**, 795–797

Novel recyclization of 3,4-dihydroisoquinolines as an efficient route to a new type of heteroarylated derivatives of β-arylethylamines

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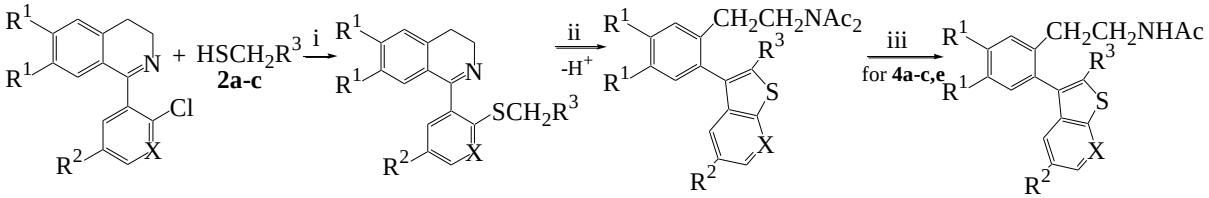
1. General Information

The solvents were purified according to standard procedures. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded in DMSO-d_6 at 30ºC on Bruker Avance 600 spectrometer. Chemical shifts of nuclei ^{1}H and ^{13}C were measured relatively the residual signals of DMSO-d_6 (δ =2.49 ppm for protons and 39.09 ppm for carbon). Coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined by using Fisher-Johns Melting Point Apparatus (Fisher Scientific) and are uncorrected. The reaction and purity of the obtained compounds (for base) were monitored by TLC (plates with Al_2O_3 III activity grade, eluent $CHCl_3$, development of TLC plates by exposition to iodine vapors in 'iodine chamber').

The experimental data for structure **5c** were obtained on an Agilent SuperNova diffractometer by using a microfocus X-ray source with copper anode and an Atlas S2 two-dimensional CCD detector. The reflections were collected, unit cell parameters determined and refined by using the specialized CrysAlisPro 1.171.38.41 software suite (Rigaku Oxford Diffraction, 2015).[S1] The structures were solved by using the ShelXT program (Sheldrick, 2015)[S2] and refined with the ShelXL program (Sheldrick, 2015).[S3] Molecular graphics and presentation of structures for publication were performed with the Olex^2 ver 1.5 software suite.[S4] CCDC 2161739 (crystal from MeCN) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

Quantum chemical calculations [B3LYP/6-311+G(d,p)] were performed using quantum chemical program package Gaussian 2016.[S5]

The general reactions scheme:



1a-c **3a-e** **4a-e** **5a-c, e**

Compounds **3c,e** and **4a,e** were used without isolation from the reaction solutions to carry out the next step in one-pot regime.

4b - 97%
4c - 69%
4d - 69%

5a - 76%
5b- 65%
5c - 54%
5e - 66%

1 R^1 = H, R^2= NO_2, X = CH (**a**); R^1 = OMe, R^2= NO_2, X = CH (**b**); R^1 = OMe, R^2 = H, X = N (**c**);

2 R^3 = benzimidazol-2-yl (**a**), COOEt (**b**), $CONH_2$ (**c**);

3 R^1 = H, R^2= NO_2, R^3 = benzimidazol-2-yl, X = CH (**a**); R^1 = OMe, R^2= NO_2, X = CH, R^3 = COOEt (**b**), benzimidazol-2-yl (**c**), $CONH_2$ (**d**); R^1 = OMe, R^2= H, R^3 = benzimidazol-2-yl, X = N (**e**);

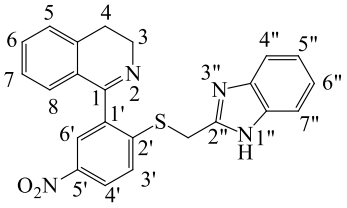
4 R^1 = H, R^2= NO_2, X = CH, R^3 = benzimidazol-2-yl (**a**); R^1 = OMe, R^2= NO_2, X = CH, R^3 = COOEt (**b**), benzimidazol-2-yl (**c**), CN (**d**); R^1 = OMe, R^2= H, X = N, R^3 = benzimidazol-2-yl (**e**);

5 R^1 = H, R^2= NO_2, X = CH, R^3 = benzimidazol-2-yl (**a**); R^1 = OMe, R^2= NO_2, X = CH, R^3 = COOEt (**b**), benzimidazol-2-yl (**c**); R^1 = OMe, R^2= H, X = N, R^3 = benzimidazol-2-yl (**e**)

2. Synthesis and characterization of compounds 3-5.

Starting compounds **1a**, **b**[S6] and **1c**[S7] were synthesized as described previously.

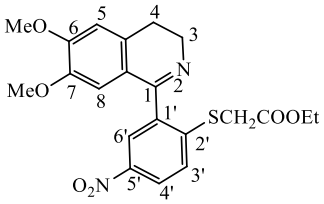
1-{2-[((1*H*-Benzo[*d*]imidazol-2-yl)methyl)thio]-5-nitrophenyl}-3,4-dihydroisoquinoline (**3a**).



To a solution of sodium metal (0.046 g 0.002 g-at) in EtOH (10 ml) under a nitrogen atmosphere 1*H*-benzo[*d*]imidazole-2-thiol **2a** (0.33 g, 0.002 mol) was added in portions at 25°C. The mixture was stirred for 5 min, and 1-(2-chloro-5-nitrophenyl)-3,4-dihydroisoquinoline **1a** (0.57 g, 0.002 mol) was added and then boiled at 2 h in a nitrogen atmosphere. Water (20 ml) and saturated NaCl solution (20 ml) were added, the precipitate was filtered off, wash with water (3×5 ml). Yield of dihydroisoquinoline **3a** was 0.51 g (61%). Colourless crystals with mp 225-228°C (EtOH). ^{1}H NMR (600 MHz), δ: 2.78-2.82 (m, 2H, H-3), 3.78-3.83 (m, 2H, H-4), 4.54 (s, 2H, SCH_2), 6.75 (d, *J* 8.2, 1H, H-3'), 7.07 (t, *J* 7.5, 1H, H-7), 7.12-7.15 (m, 2H, H-5", H-6"), 7.32 (d, *J* 7.5, 1H, H-5), 7.37-7.43 (m, 2H, H-4", H-7"), 7.54 (d, *J* 7.9, 1H, H-8), 8.01-8.06 (m, 2H, H-6, H-6'), 8.27 (dd, *J* 8.9, 2.6, 1H, H-4'), 12.40 (s, 1H, NH). ^{13}C NMR (150 MHz), δ: 25.00, 29.84, 47.12,

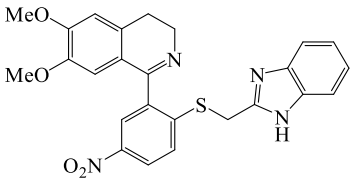
111.21, 118.57, 121.28, 122.25, 123.40, 123.59, 126.20, 126.91, 127.05, 127.15, 127.63, 127.65, 127.71, 131.24, 137.35, 138.09, 144.52, 145.72, 150.00, 163.90. Found (%): C 66.38; H 4.21; N 13.24; S 7.40. Calc. for $C_{23}H_{18}N_4O_2S$ (%): C 66.65; H 4.38; N 13.52; S 7.74.

Ethyl 2-((2-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)-4-nitrophenyl)thio)acetate (3b).



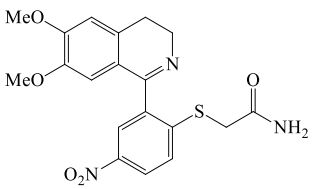
To a solution ethyl 2-mercaptoacetate (1.2 g, 0.01 mol) **2b** in DMF (15 ml) under a nitrogen atmosphere, NaH (0.29 g, 0.012 mol) was added in portions at 25°C. The mixture was stirred for 1 h, and 1-(2-chloro-5-nitrophenyl)-6,7-dimethoxy-3,4-dihydroisoquinoline **1b** (3.47 g, 0.01mol) was added, and this was stirred at 24 h in a nitrogen atmosphere at 25°C. Water (50 ml) was added, the precipitate was filtered off, wash with water (3×15 ml). Yield was 3.36 g (78%). Colourless crystals with mp 157-159°C (MeOH). ^{1}H NMR (600 MHz), δ: 1.00 (t, *J* 7.1, 3H, $CH_2\underline{Me}$), 2.65-2.86 (m, 4H, H-3, H-4), 3.17 (s, 1H, CH_2S), 3.58 (s, 3H, OMe), 3.77 (s, 3H, OMe), 3.90-4.09 (m, 2H, $\underline{CH_2}CH_3$), 5.67 (s, 1H, CH_2S), 6.74 (s, 1H, H-8), 6.77 (s, 1H, H-5), 7.25 (d, *J* 2.4, 1H, H-6'), 7.62 (d, *J* 8.6, 1H, H-3'), 8.09 (dd, *J* 8.6, 2.4, 1H, H-4'). ^{13}C NMR (150 MHz), δ: 13.65, 29.10, 38.19, 55.35, 55.67, 60.76, 66.00, 70.59, 110.81, 111.53, 118.62, 123.06, 124.07, 127.56, 129.65, 144.69, 147.02, 147.58, 147.74, 147.88, 167.37. Found (%): C 58.32; H 5.00; N 6.36; S 7.71. Calc. for $C_{21}H_{22}N_2O_6S$ (%): C 58.59; H 5.15; N 6.51; S 7.45.

1-{2-[((1*H*-Benzo[*d*]imidazol-2-yl)methyl)thio]-5-nitrophenyl}-6,7-dimethoxy-3,4-dihydroisoquinoline (**3c**).



Compound **3c** was obtained from dihydroisoquinoline **1b** analogously to compound **3a** and, after isolation from the reaction mixture, was introduced into further transformation without additional purification.

2-{[2-(6,7-Dimethoxy-3,4-dihydroisoquinolin-1-yl)-4-nitrophenyl]thio}acetamide (3d).



The compound was obtained analogously to the compound **3a** from 3,4-dihydroisoquinoline **1b** and 2-mercaptoacetamide. The isolated product was treated with boiling ethyl acetate, cooled and filtered off; yield: 0.52 g (65%). Colourless crystals with mp 201-203°C (EtOAc). ^{1}H NMR (600 MHz), δ: 2.73 (t, *J* 7.7, 2H, H-4), 3.30 (s, 2H, H-3), 3.53 (s, 3H, OMe), 3.72-3.86 (m, 7H, OMe, SCH_2, H_2O), 6.40 (s, 1H, H-5), 6.98 (s, 1H, H-8), 7.19 (s, 1H, NH_2), 7.57 (s, 1H, NH_2), 7.70 (d, *J* 8.9, 1H, H-3'), 7.98-8.05 (s, 1H, H-6'), 8.21-8.28 (m, 1H, H-4'). ^{13}C NMR (150 MHz), δ: 24.82, 35.54, 47.20, 55.68, 55.81, 110.64, 111.15, 120.31, 123.39, 123.46, 126.55, 131.26, 138.07, 144.26, 146.62, 147.16, 151.39, 163.53, 168.97. Found (%): C 58.59; H 4.49; N 10.28; S 8.23. Calc. for $C_{19}H_{19}N_3O_5S$ (%): C 56.85; H 4.77; N 10.47; S 7.99.

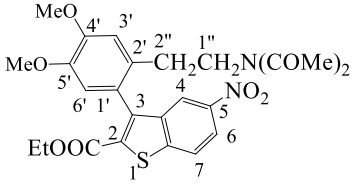
General procedure for the synthesis of compounds **4b-d**. A mixture of 3,4-dihydroisoquinoline derivative **3b-d** (0.002 mol) and Ac_2O was boiled, cooled, H_2O (15 ml) and conc. NH_4OH (to pH 8) were added, the precipitate **4b-d** was filtered off, washed with water (3×5 ml). Conditions for reaction are given in Table S1.

Table S1. Reaction conditions and yields of compound **4b-d**.

Substrate	Product	Ac_2O, ml	Reaction time, h	Yield, %
3b	**4b**	7	2	97
3c	**4c**	10	3	69 (crude)
3d	**4d**	6	8	69

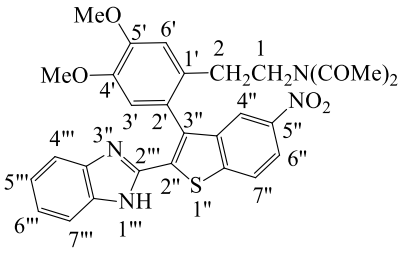
Compounds **4a,e** were obtained from **3a,e** in a similar way and, after isolation from the reaction mixture, were introduced into further recyclization without additional purification (see preparation procedures **5a** and **5e**)

Ethyl 3-{2-[2-(*N*-acetylacetamido)ethyl]-4,5-dimethoxyphenyl}-5-nitrobenzo[*b*]thiophene-2-carboxylate (4b).



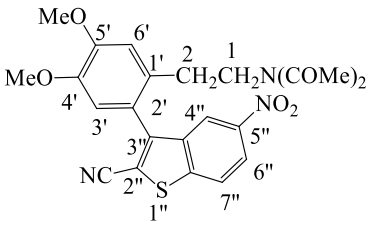
Yield was 1.00 g (97%). Colourless crystals with mp 178-180°C (EtOH). ^{1}H NMR (600 MHz), δ: 1.08 (t, *J* 7.2, 3H, CH_2Me), 1.96 (s, 6H, 2COMe), 2.30-2.41 (m, 1H, H-2"), 2.50-2.65 (m, 1H, H-2"), 3.37-3.50 (м, 1H, H-1"), 3.51-3.60 (м, 1H, H-1"), 3.69 (s, 3H, OMe), 3.87 (s, 3H, OMe), 4.12-4.20 (m, 2H, CH_2Me), 6.83 (s, 1H, H-3'), 7.04 (s, 1H, H-6'), 7.98 (d, *J* 2.1, 1H, H-4), 8.31-8.35 (m, 1H, H-7), 8.41 (d, *J* 8.9, 1H, H-6). HRMS (ESI): m/z $[M + Na]^+$ calc. for $C_{23}H_{19}N_3NaO_3S$: 440.1039; found: 440.1028.

***N*-{2-[2-(1*H*-Benz[*d*]imidazol-2-yl)-5-nitrobenzo[*b*]thiophen-3-yl]-4,5-dimethoxyphenethyl}-*N*-acetylacetamide (4c).**



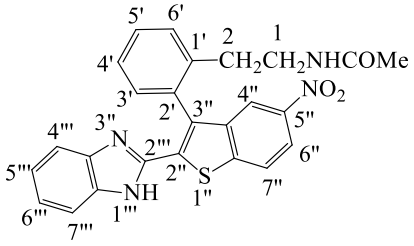
Yield was 0.77 g (69%, calculated relative to the amount of crude dihydroisoquinoline **3c** used in the reaction). Colorless crystals with mp 267-270°C (EtOH). ^{1}H NMR (600 MHz), δ: 1.89 (s, 6H, 2COMe), 2.39-2.43 (m, 1H, H-2), 2.50-2.54 (m, 1H, H-2), 3.40-3.49 (m, 2H, H-1), 3.73 (s, 3H, OMe), 3.91 (s, 3H, OMe), 7.01 (s, 1H, H-3'), 7.09 (s, 1H, H-6'), 7.17-7.21 (m, 2H, H-4''', 7'''), 7.48-7.52 (m, 1H, H-5'''), 7.63-7.67 (m, 1H, H-6'''), 7.94 (d, *J* 2.2, 1H, H-4''), 8.26 (dd, *J* 8.8, 2.2, 1H, H-6''), 8.37 (d, *J* 8.8, 1H, H-7''), 11.28 (s, 1H, NH). ^{13}C NMR (150 MHz), δ: 22.30, 25.49, 31.79, 45.24, 55.46, 55.72, 112.54, 113.93, 114.02, 118.38, 118.96, 119.79, 122.30, 123.20, 123.40, 123.95, 130.26, 133.76, 134.44, 135.10, 140.95, 142.86, 144.83, 144.96, 145.59, 148.07, 149.47, 172.37. Found (%): C 62.08; H 4.43; N 9.75; S 5.92. Calc. for $C_{29}H_{26}N_4O_6S$ (%): C 62.35; H 4.69; N 10.03; S 5.74.

***N*-Acetyl-*N*-[2-(2-cyano-5-nitrobenzo[*b*]thiophen-3-yl)-4,5-dimethoxyphenethyl]acetamide (4d).**



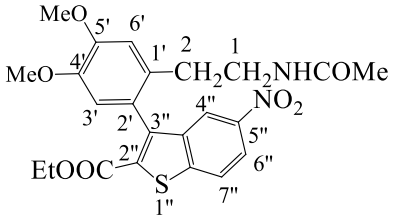
The starting compound was 2-{{2-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)-4-nitrophenyl}thio}acetamide **3d**. Yield was 0.65 g (69%). Colorless crystals with mp 188-190°C (EtOAc). ^{1}H NMR (600 MHz), δ: 1.99 (2s, 6H, 2COMe), 2.50-2.72 (m, 2H, H-2), 3.43-3.61 (m, 2H, H-1), 3.75 (s, 3H, OMe), 3.90 (s, 3H, OMe), 7.01 (s, 1H, H-3'), 7.14 (s, 1H, H-6'), 8.14 (d, *J* 2.2, 1H, H-4''), 8.35-8.46 (m, 1H, H-6''), 8.52 (d, *J* 9.0, 1H, H-7''). ^{13}C NMR (150 MHz), δ: 25.59, 25.68, 31.59, 45.63, 55.64, 55.85, 110.85, 113.57, 113.85, 119.75, 121.89, 121.92, 125.06, 130.24, 137.25, 145.72, 146.21, 147.70, 148.27, 149.99, 160.98, 172.41. HRMS (ESI): m/z $[M + Na]^+$ calc. for $C_{23}H_{21}N_3NaO_6S$: 490.1043; found: 490.1050.

***N*-{2-[2-(1*H*-Benz[*d*]imidazol-2-yl)-5-nitrobenzo[*b*]thiophen-3-yl]phenethyl}acetamide (5a).**



A mixture of dihydroisoquinoline **3a** (0.83 g, 0.002 mol) and Ac_2O was boiled for 8 h, cooled, H_2O (15 ml) and conc. NH_4OH (to pH 8) was added, the precipitate of **4a** was filtered off, washed with water (3×5 ml). Then it was dissolved in EtOH (5 ml) and treated with hydrazine hydrate (0.5 ml), and the mixture was stirred at 20-25°C for 24 h. Water (10 ml) was added, the precipitate **5a** was filtered off and washed with water (3×5 ml). Yield was 0.69 g (76%). Colorless crystals with mp 292-295°C (EtOH). ^{1}H NMR (600 MHz), δ: 1.57 (s, 3H, Me), 2.43-2.52 (m, 4H, H-1, HDO), 2.88-2.94 (m, 1H, H-1), 3.06-3.14 (м, 1H, H-2), 3.39-3.42 (м, 1H, H-2), 7.15-7.18 (м, 2H, H-5''', H-6'''), 7.24 (d, *J* 7.5, 1H, H-6'), 7.37-7.40 (m, 2H, H-4', H-5'), 7.45-7.53 (m, 2H, H-4''', H-6''), 7.58-7.67 (m, 1H, H-3'), 7.84 (d, *J* 2.3, 1H, H-4''), 7.91-7.99 (m, 1H, NHCO), 8.25 (dd, 1H, H-6''), 8.38 (d, *J* 8.8, 1H, H-7''), 11.74 (c, 1H, H-1'''). ^{13}C NMR (150 MHz), δ: 18.53, 22.34, 33.65, 112.43, 118.08, 119.89, 122.36, 123.44, 124.23, 127.49, 129.36, 130.74, 130.81, 131.6, 133.94, 134.81, 135.23, 138.93, 140.17, 142.97, 144.84, 144.87, 145.65, 169.48. HRMS (ESI): m/z $[M + H]^+$ calc. for $C_{25}H_{21}N_4O_3S$: 457.1329; found: 457.1322.

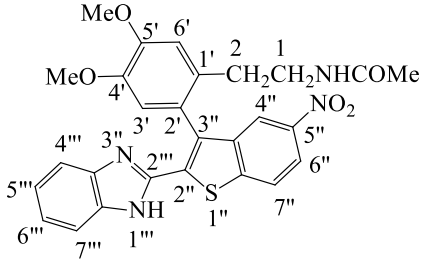
Ethyl 3-[2-(2-acetamidoethyl)-4,5-dimethoxyphenyl]-5-nitrobenzo[*b*]thiophene-2-carboxylate (5b).



A mixture of diacetyl derivative **4b** (1.03 g, 0.002 mol), EtOH (5 ml) and hydrazine hydrate (0.5 ml) was kept 24 h at 20-25°C, then H_2O (10 ml) was added The precipitate **5b** was filtered off and washed with water (3×5 ml). Yield was 0.61 g (65%). Colourless crystals with mp 83-85°C (cyclohexane). ^{1}H NMR (600 MHz), δ: 1.05 (t, *J* 7.1, 3H, $CH_2\underline{Me}$), 1.48 (s, 3H, COMe), 2.23-2.40 (m, 2H, H-2), 2.88-3.04 (m, 2H, H-1), 3.65 (s, 3H, OMe), 3.83 (s, 3H, OMe), 4.13 (q, *J* 7.1, 2H, $\underline{CH_2}Me$), 6.76 (s, 1H, H-6'), 6.99 (s, 1H, H-3'), 7.58 (t, 1H, *J* 5.6, NHCO), 8.02 (d, *J* 2.0, 1H, H-4''), 8.31 (dd, *J* 8.9, 2.3, 1H, H-6''), 8.38 (d, *J* 8.9, 1H, H-7''). ^{13}C NMR (150 MHz), δ: 13.69, 22.25, 32.48, 39.95, 55.54, 55.73, 61.39, 112.60, 113.27, 120.01, 121.19, 124.38, 124.68, 130.58, 132.62,

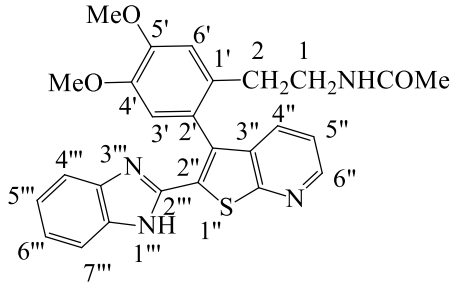
139.97, 142.80, 145.07, 145.71, 146.96, 148.95, 161.13, 168.63. Found (%): 58.40; H, 5.11; N, 5.62, S, 6.85. Calc. for $C_{23}H_{24}N_2O_7S$. (%): C, 58.46; H, 5.12; N, 5.93, S, 6.79.

_N_-{2-[2-(1_H_-Benz[_d_]imidazol-2-yl)-5-nitrobenzo[_b_]thiophen-3-yl]-4,5-dimethoxyphenethyl}acetamide (5c).



Acetamide **5c** was obtained analogously to compound **5b** from diacetyl derivative **4c**.Yield was 0.56 g (54%). Colorless crystals with mp 288-291°C (EtOH). ^{1}H NMR (600 MHz), δ: 1.57 (s, 3H, COMe), 2.35-2.47 (m, 2H, H-2), 2.93 (dt, *J* 13.1, 5.9, 1H,H-1), 3.07–3.13 (m, 1H, H-1), 3.64 (s, 3H, OMe), 3.91 (s, 3H, OMe), 6.87 (s, 1H, H-6'), 7.08 (s, 1H, H-3'), 7.18-7.24 (m, 2H, H-5''', H-6'''), 7.45-7.51 (m, 1H, H-4'''), 7.63-7.69 (m, 1H, H-7'''), 7.80 (t, *J* 6.0, 1H, NHCO), 7.94 (d, *J* 2.3, 1H, H-4''), 8.25 (dd, *J* 8.8, 2.3, 1H, H-6''), 8.37 (d, *J* 8.8, 1H, H-7''), 11.47 (s, 1H, H-1'''). ^{13}C NMR (150 MHz), δ: 22.30, 33.07, 39.58, 55.39, 55.65, 112.54, 113.84, 113.87, 118.28, 118.88, 119.78, 122.28, 122.89, 123.37, 124.02, 131.38, 133.93, 134.69, 135.22, 140.61, 142.81, 144.81, 145.02, 145.60, 147.87, 149.31, 169.23. HRMS (ESI): m/z $[M + H]^+$ calc. for $C_{27}H_{25}N_4O_5S$: 517.1540; found: 517.1531.

_N_-{2-[2-(1_H_-Benz[_d_]imidazol-2-yl)thieno[2,3-_b_]pyridin-3-yl]-4,5-dimethoxyphenethyl}acetamide (5e).



To a solution 1*H*-benz[*d*]imidazole-2-thiol (1.65 g, 0.01 mol) in DMF (10 ml) under a nitrogen atmosphere, NaH (0.29 g, 0.012 mol) was added in portions at 25°C. The mixture was stirred for 30 min, 1-(2-chloropyridin-3-yl)-6,7-dimethoxy-3,4-dihydroisoquinoline **1c** (3.03 g, 0.01 mol) was added, and the mixture was heated at 110-115°C for 3 h. Water (20 ml) was added, the precipitate **3e** was filtered off, washed with water (3×5 ml). After drying at 80°C compound **3e** (0.83 g, 0.002 mol) and Ac_2O (10 ml) were boiled for 6 h. After cooling, water (20 ml) and NH_4OH were added to pH 7.0-7.5, the diacetyl derivative **4e** was filtered off, washed with water (3×5 ml). Then the crude diacetyl derivative **4e** (1.03 g, 0.002 mol) was treated with EtOH (5 ml), hydrazine hydrate (0.5 ml) and kept at 20-25°C for 24 h. Water (10 ml) was added, the precipitate of **5e** was

filtered off, washed with water (3×5 ml). Yield was 0.62 g (66%). Colourless crystals with mp 278 - 280°C (EtOH). ^{1}H NMR (600 MHz), δ: 1.60 (s, 3H, COMe), 2.32-2.45 (m, 2H, H-2), 2.90-2.93 (м, 1H, H-1), 3.05-3.09 (м, 1H, H-1), 3.61 (s, 3H, OMe), 3.87 (s, 3H, OMe), 6.82 (s, 1H, H-6'), 7.03 (s, 1H, H-3'), 7.15-7.24 (m, 2H, H-5''', H-6'''), 7.41-7.65 (m, 4H, H-5'', H-4''', H-7''', NHCO), 7.87 (t, *J* 6.0, 1H, H-4''), 8.63 (d, *J* 4.5, 1H, H-6''), 11.42 (br. s, 1H, H-1'''). ^{13}C NMR (150 MHz), δ: 22.42, 33.16, 39.12, 55.43, 55.63, 113.81, 120.67, 123.40, 129.58, 129.71, 129.84,131.27, 131.30, 132.69, 134.13, 145.47, 147.79, 148.01, 149.12, 159.91, 169.31. Found (%): C 65.71; H 5.00; N 11.54; S 6.92. Calc. for $C_{26}H_{24}N_4O_3S$ (%): C 66.08; H 5.12; N 11.86; S 6.79.

3. Structure and X-ray data for compound 5c.

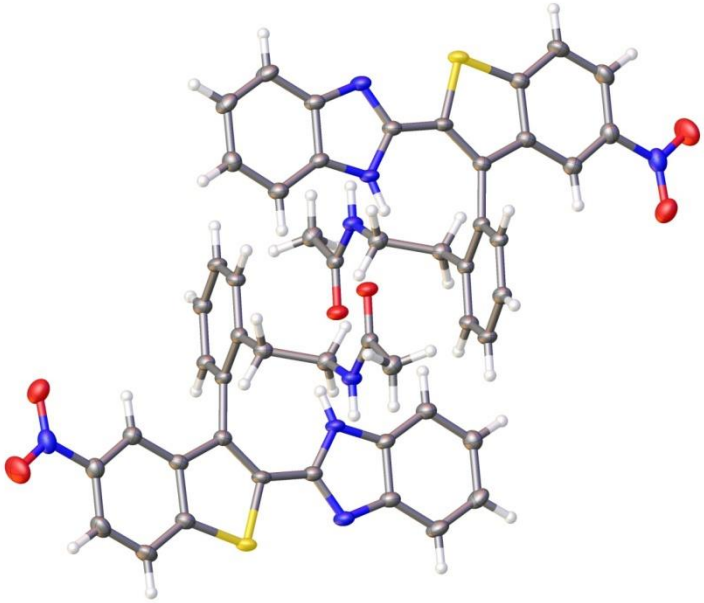


Figure S1 Structure for compound **5c**.

Table S2. Crystal data and structure refinement for compound **5c**.

CCDC Number	2161739
Empirical formula	$C_{25}H_{20}N_4O_3S$
Formula weight	456.51
Temperature/K	100.15
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.0803(2)
b/Å	15.0856(4)
c/Å	14.3380(4)
α/°	90
β/°	106.089(3)
γ/°	90
Volume/Å^3	2094.94(10)
Z	4
ρ_{calc}g/cm^3	1.447
μ/mm^{-1}	1.687
F(000)	952.0
Crystal size/mm^3	0.317 × 0.139 × 0.089
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.692 to 156.252
Index ranges	$-12 \leq h \leq 9$, $-18 \leq k \leq 18$, $-17 \leq l \leq 18$
Reflections collected	21849
Independent reflections	4365 [R_{int} = 0.0665, R_{sigma} = 0.0410]
Data/restraints/parameters	4365/0/307
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0508, wR_2 = 0.1485
Final R indexes [all data]	R_1 = 0.0592, wR_2 = 0.1549
Largest diff. peak/hole / e Å^{-3}	0.52/-0.42

Table S3 Bond Lengths for compound **5c.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	C11	1.730(2)	C7	C6	1.402(3)
S1	C8	1.7445(18)	C3	C4	1.382(3)
O1	C24	1.233(2)	C21	C20	1.400(3)
O2	N4	1.231(3)	C21	C22	1.505(3)
N1	C1	1.371(2)	C18	C19	1.386(3)
N1	C2	1.382(3)	C9	C10	1.444(3)
N2	C1	1.320(3)	C9	C8	1.371(3)
N2	C7	1.379(3)	C24	C25	1.512(3)
N3	C24	1.345(3)	C20	C19	1.388(3)
N3	C23	1.446(3)	C15	C10	1.401(3)
O3	N4	1.229(3)	C15	C14	1.383(3)
N4	C14	1.467(3)	C10	C11	1.410(3)

Table S3 Bond Lengths for compound **5c.**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C1	C8	1.452(3)	C6	C5	1.377(3)
C17	C16	1.397(3)	C12	C11	1.398(3)
C17	C18	1.391(3)	C12	C13	1.375(3)
C16	C21	1.405(3)	C14	C13	1.401(3)
C16	C9	1.494(2)	C4	C5	1.405(3)
C2	C7	1.404(3)	C22	C23	1.536(3)
C2	C3	1.391(3)			

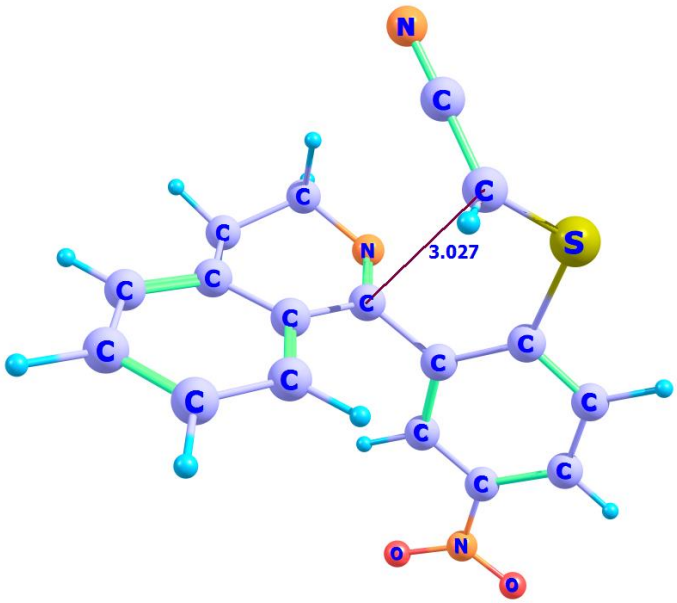
Table S4. Bond Angles for compound **5c**.

Atom	**Atom**	**Atom**	**Angle/°**	**Atom**	**Atom**	**Atom**	**Angle/°**
C11	S1	C8	91.44(10)	C8	C9	C10	111.33(17)
C1	N1	C2	106.75(16)	O1	C24	N3	122.78(19)
C1	N2	C7	105.32(16)	O1	C24	C25	122.15(19)
C24	N3	C23	121.90(16)	N3	C24	C25	115.07(17)
O2	N4	C14	118.81(19)	C19	C20	C21	121.13(18)
O3	N4	O2	122.9(2)	C14	C15	C10	117.64(19)
O3	N4	C14	118.3(2)	C15	C10	C9	128.32(18)
N1	C1	C8	126.55(18)	C15	C10	C11	118.95(19)
N2	C1	N1	112.65(18)	C11	C10	C9	112.72(18)
N2	C1	C8	120.76(17)	C5	C6	C7	117.67(18)
C18	C17	C16	120.70(18)	C13	C12	C11	118.32(18)
C17	C16	C21	119.88(17)	C15	C14	N4	118.79(19)
C17	C16	C9	119.19(17)	C15	C14	C13	123.4(2)
C21	C16	C9	120.90(18)	C13	C14	N4	117.82(19)
N1	C2	C7	105.27(17)	C3	C4	C5	121.7(2)
N1	C2	C3	132.22(17)	C21	C22	C23	109.95(17)
C3	C2	C7	122.50(19)	C10	C11	S1	111.22(15)
N2	C7	C2	109.99(18)	C12	C11	S1	126.45(16)
N2	C7	C6	130.01(18)	C12	C11	C10	122.3(2)
C6	C7	C2	119.99(19)	C6	C5	C4	121.6(2)
C4	C3	C2	116.55(18)	C18	C19	C20	120.15(17)
C16	C21	C22	121.21(17)	C1	C8	S1	114.62(14)
C20	C21	C16	118.52(19)	C9	C8	S1	113.24(15)
C20	C21	C22	120.12(18)	C9	C8	C1	132.13(18)
C19	C18	C17	119.60(19)	N3	C23	C22	112.58(17)
C10	C9	C16	122.89(17)	C12	C13	C14	119.31(19)
C8	C9	C16	125.71(18)				

4. Quantum chemical data.

Minimum energy structures of possible spirointermediates **A**, **B, C** and transiton state **TS** [R^1 = R^2 = H and R^3 = CN, X=CH); B3LYP/6-311+G(d,p)]

C-anion **A:**



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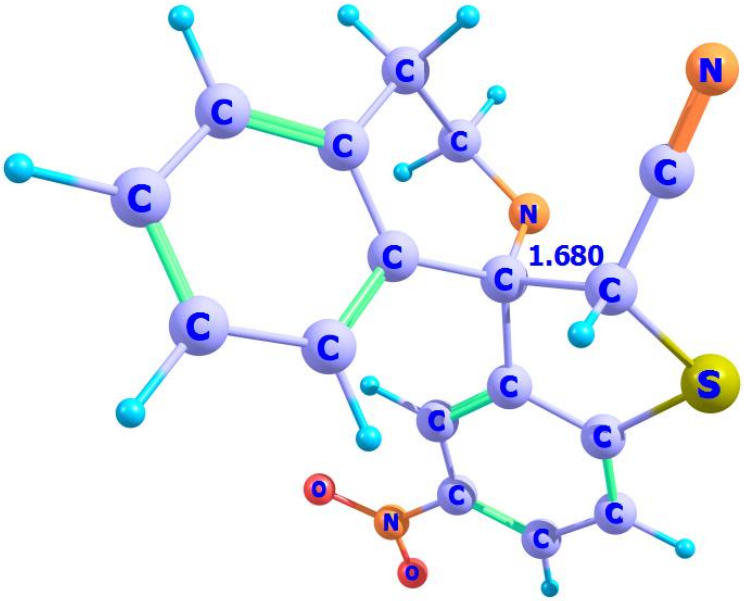
	35		
	symmetry c1		
C	3.164232000	-2.607976000	-0.348145000
C	2.415132000	-1.714635000	0.417552000
C	1.360218000	-1.004976000	-0.182928000
C	1.071676000	-1.215279000	-1.535985000
C	1.823883000	-2.108929000	-2.291681000
C	2.875844000	-2.806276000	-1.697105000
C	2.656671000	-1.496162000	1.890569000
C	2.277810000	-0.068385000	2.289502000
N	0.950148000	0.335707000	1.821454000
H	3.983359000	-3.149064000	0.116472000
H	0.259964000	-0.665382000	-1.996432000
H	1.594234000	-2.257829000	-3.341235000
H	3.470597000	-3.499721000	-2.282585000
H	2.043668000	-2.209358000	2.461175000
H	2.295657000	0.039399000	3.377584000
C	0.578724000	-0.061309000	0.665506000
C	-0.801227000	0.351904000	0.224202000
C	-1.806375000	-0.600105000	0.347466000
C	-1.136379000	1.665055000	-0.189241000
C	-3.142833000	-0.273055000	0.100431000
C	-2.498455000	1.970344000	-0.417787000
C	-3.496189000	1.031300000	-0.267398000
H	-1.568061000	-1.604711000	0.672101000
H	-2.752840000	2.975316000	-0.738825000
H	-4.535411000	1.274593000	-0.441312000
S	0.003201000	2.992894000	-0.542148000
C	1.527144000	2.294173000	-0.981737000
H	1.612287000	1.850578000	-1.964063000
N	-4.167319000	-1.280885000	0.243251000
O	-3.831253000	-2.428202000	0.562627000
O	-5.345879000	-0.954782000	0.042098000
H	3.701398000	-1.699734000	2.145628000
H	2.996063000	0.652177000	1.879772000
C	2.670599000	2.519798000	-0.232027000
N	3.648897000	2.690659000	0.392598000

Spiro-transition state TS for transformation **A** → **B**:



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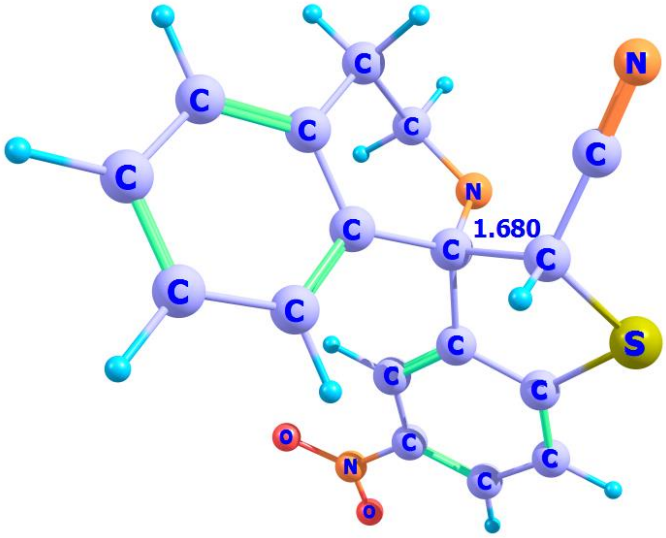
35

symmetry c1

C	3.164525000	-2.499469000	-0.123781000
C	2.508402000	-1.389960000	0.422418000
C	1.459529000	-0.790830000	-0.296086000
C	1.101246000	-1.322030000	-1.541729000
C	1.767090000	-2.419391000	-2.081719000
C	2.807373000	-3.012894000	-1.367148000
C	2.857790000	-0.844412000	1.782381000
C	1.575943000	-0.302111000	2.444159000
N	0.901561000	0.695701000	1.658842000
H	3.964785000	-2.965702000	0.444228000
H	0.282462000	-0.874458000	-2.095639000
H	1.470870000	-2.812270000	-3.049005000
H	3.329049000	-3.874331000	-1.771998000
H	3.330422000	-1.628802000	2.389022000
H	0.940378000	-1.185712000	2.686527000
C	0.761103000	0.446242000	0.295567000
C	-0.748830000	0.506304000	-0.014976000
C	-1.634749000	-0.536562000	0.222786000
C	-1.264312000	1.760510000	-0.376066000
C	-3.007016000	-0.316447000	0.090559000
C	-2.642232000	1.986579000	-0.475793000
C	-3.526148000	0.945827000	-0.241201000
H	-1.278067000	-1.513106000	0.521621000
H	-3.020414000	2.966783000	-0.745993000
H	-4.595460000	1.081903000	-0.313102000
S	-0.033320000	2.994066000	-0.670462000
C	1.306629000	1.731959000	-0.637199000
H	1.449946000	1.391916000	-1.664433000
N	-3.926514000	-1.420157000	0.313622000
O	-3.464423000	-2.544922000	0.525728000
O	-5.140743000	-1.183999000	0.286557000
H	3.574291000	-0.020134000	1.684976000
H	1.831448000	0.144847000	3.413358000
C	2.552620000	2.288061000	-0.160674000
N	3.576522000	2.699758000	0.181903000

spiro-N-anion **B:**



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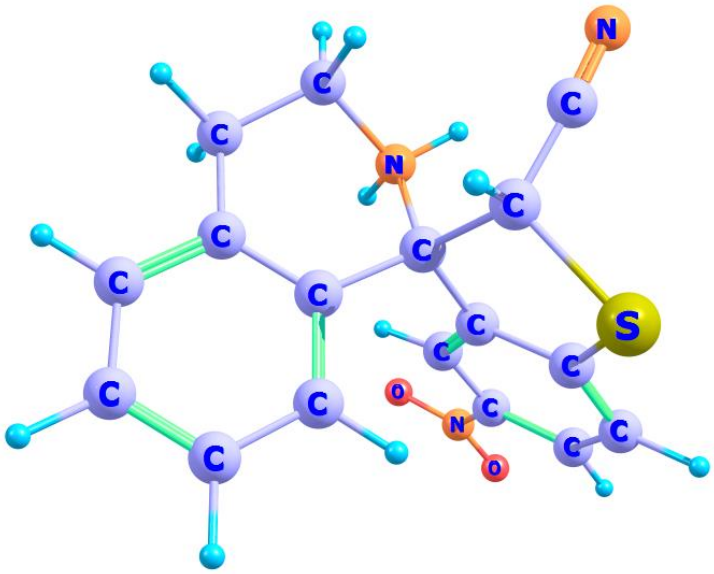
35

symmetry c1

C	2.647168200	3.065553751	0.595846288
C	2.184836549	1.993021317	-0.163167970
C	1.438927182	0.986242302	0.456074192
C	1.175240114	1.104558001	1.820972399
C	1.635618256	2.176449333	2.564184098
C	2.381539878	3.166497509	1.947465184
C	2.482144415	1.929048276	-1.644646553
C	2.314915886	0.496371657	-2.154899308
N	1.048645794	-0.050438810	-1.779166834
H	3.225528454	3.833395308	0.107644868
H	0.593242935	0.351066483	2.318056714
H	1.408652794	2.237727779	3.615372932
H	2.749239461	4.007012266	2.512342067
H	1.773927444	2.568027448	-2.169984798
H	2.389459530	0.497563650	-3.241750502
C	0.924823892	-0.208670299	-0.403842035
C	-0.541598875	-0.488453240	-0.072220575
C	-1.579129886	0.219326262	-0.653000661
C	-0.834698068	-1.501215727	0.820776575
C	-2.876741226	-0.079241684	-0.280643540
C	-2.143780448	-1.804648989	1.186114826
C	-3.176704293	-1.081788081	0.635137403
H	-1.350179824	0.963220248	-1.388016712
H	-2.349337150	-2.603046295	1.876244524
H	-4.197017047	-1.288912854	0.887264345
S	0.587804412	-2.361655273	1.419893608
C	1.680655558	-1.548466927	0.190851924
H	2.600118736	-1.283031147	0.692044076
N	-3.974689339	0.667216436	-0.869592998
O	-3.717937646	1.545500448	-1.636990955
O	-5.093716039	0.369520730	-0.552147314
H	3.480593703	2.328019993	-1.832265633
H	3.193647989	-0.080325712	-1.808050347
C	2.019432005	-2.511099142	-0.868782326
N	2.335661562	-3.309497189	-1.612997445

Cationic spiroform **C:**



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37

symmetry c1

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C	2.273016064	1.962805623	-0.178291630	C	-2.908378326	-0.115422472	-0.252478473
C	1.427059531	1.025959105	0.445295868	C	-2.157139670	-1.943370785	1.117520283
C	1.049269667	1.216986289	1.784740008	C	-3.201418112	-1.195752963	0.577870682
C	1.509754484	2.314530407	2.503313765	H	-1.456421025	1.130065181	-1.182563318
C	2.349269590	3.245187429	1.888020690	H	-2.369001786	-2.786466997	1.765784996
C	2.674922450	1.849057485	-1.635500424	H	-4.236346979	-1.436140905	0.789210646
C	2.515999922	0.439446516	-2.173381826	S	0.594102279	-2.392388493	1.468432741
N	1.147176904	-0.076176903	-1.776984639	C	1.688064521	-1.544703039	0.229848338
H	3.366286146	3.794553441	0.077317154	H	2.619226296	-1.271650704	0.730210050
H	0.386877195	0.507836554	2.268069354	N	-4.009892152	0.683538035	-0.823181198
H	1.207814431	2.445735908	3.536839993	O	-3.696318463	1.608804067	-1.571319650
H	2.710697739	4.106256111	2.440252215	O	-5.151919954	0.367289350	-0.513632265
H	2.083314284	2.545524478	-2.246417826	H	3.718795278	2.148943820	-1.768714861
H	2.572357387	0.387147772	-3.262484560	H	3.245103931	-0.257018253	-1.756948059
C	0.921521551	-0.232650938	-0.264742478	C	1.970083672	-2.457980126	-0.876625101
C	-0.560552172	-0.513292934	-0.045995317	N	2.151295174	-3.096660909	-1.831143338
C	-1.601810143	0.248837436	-0.564770874	H	0.978920933	-0.986661771	-2.226738244
				H	0.432937299	0.566218431	-2.135184089

5. References

S1 *CrysAlisPro Software System, version 1.171.38.41,* Rigaku Oxford Diffraction, Oxford, 2015.

S2 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.*, 2015, **A71**, 3.

S3 G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, 2015, **C71**, 3.

S4 O. V. Dolomanov, L. J. Bourhis,; R. J. Gildea, J. A. K. Howard and H. J. Puschmann, *Appl. Crystallogr.*, 2009, **42**, 339.

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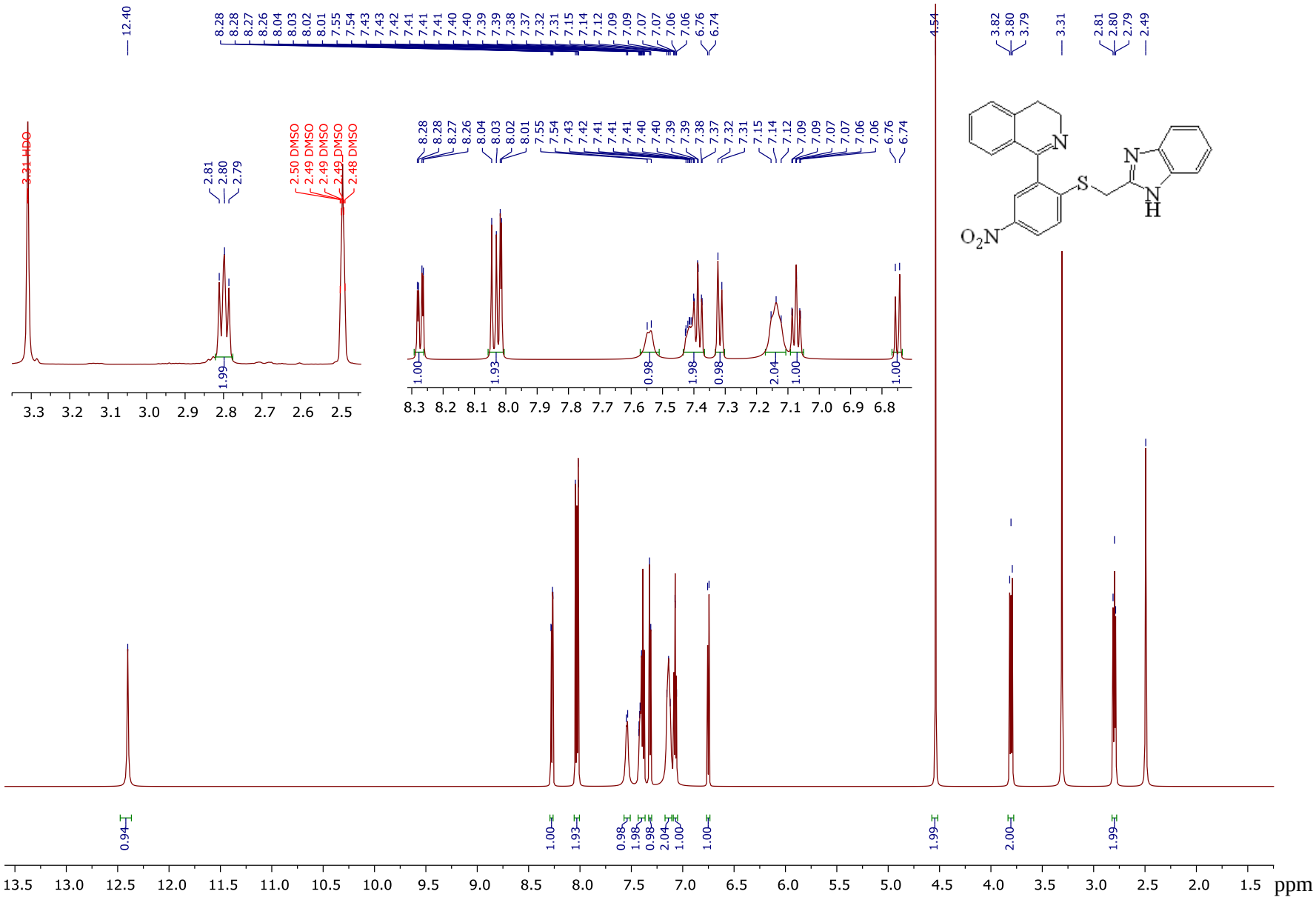
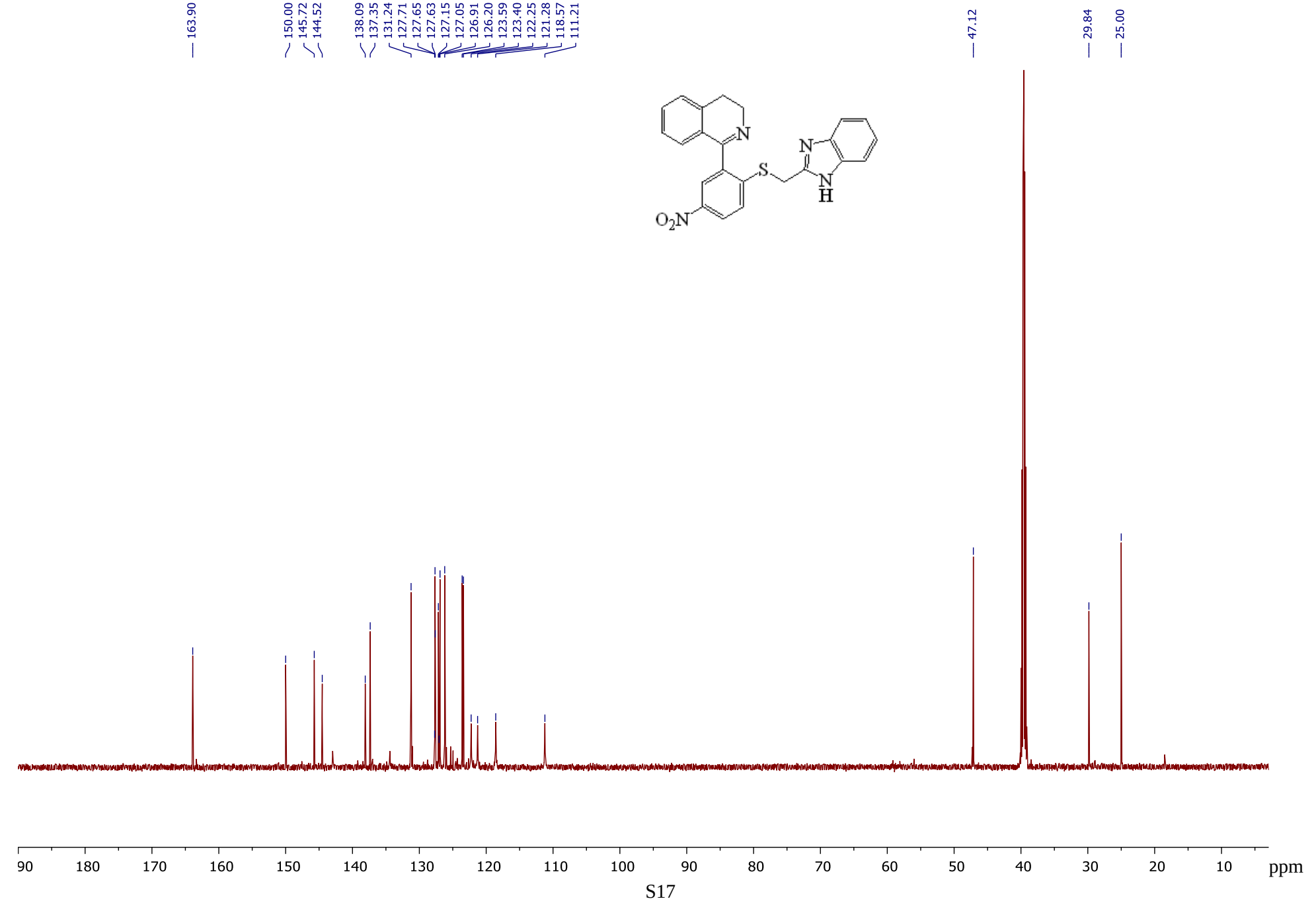
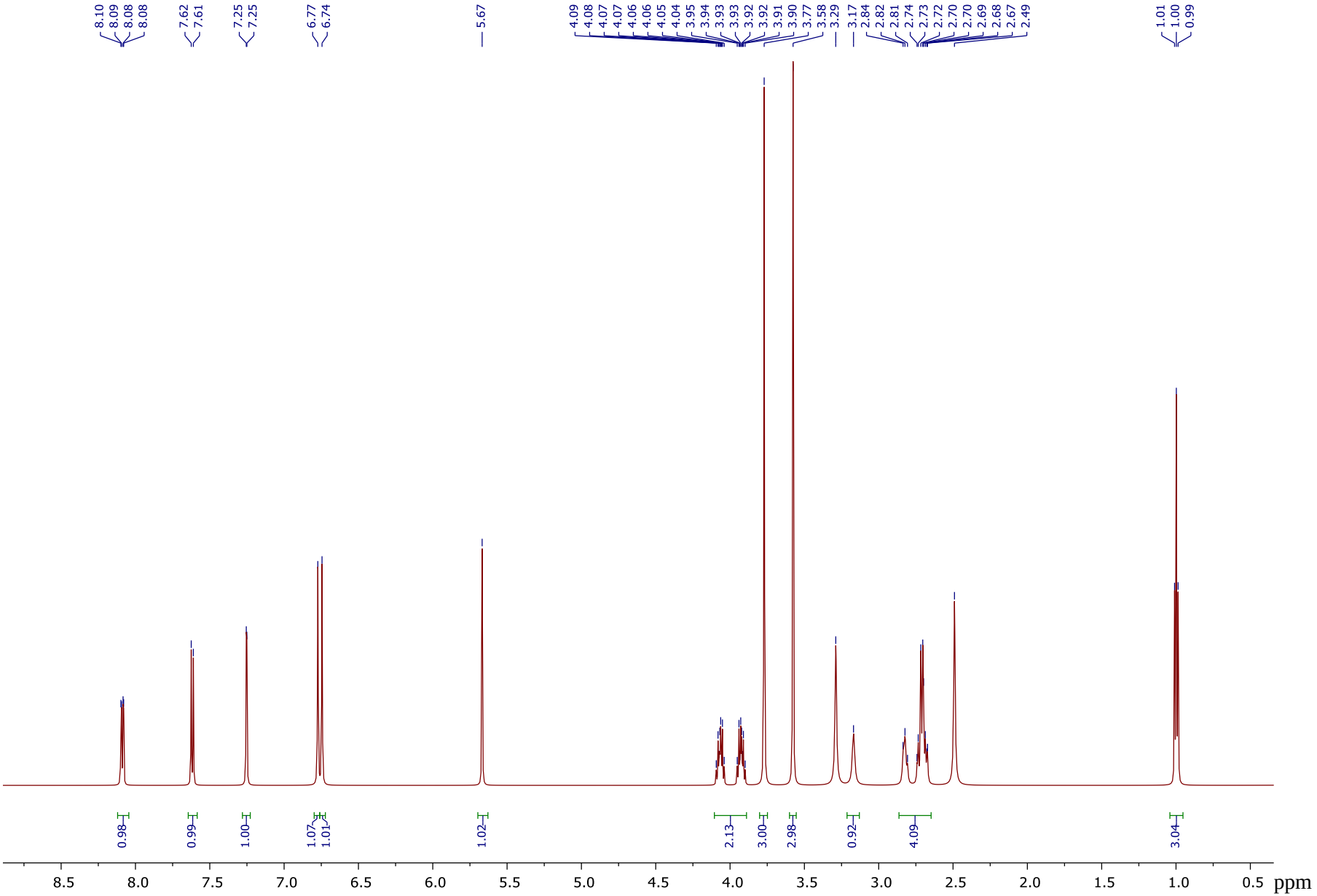
6. NMR Spectra of compounds 3-5.

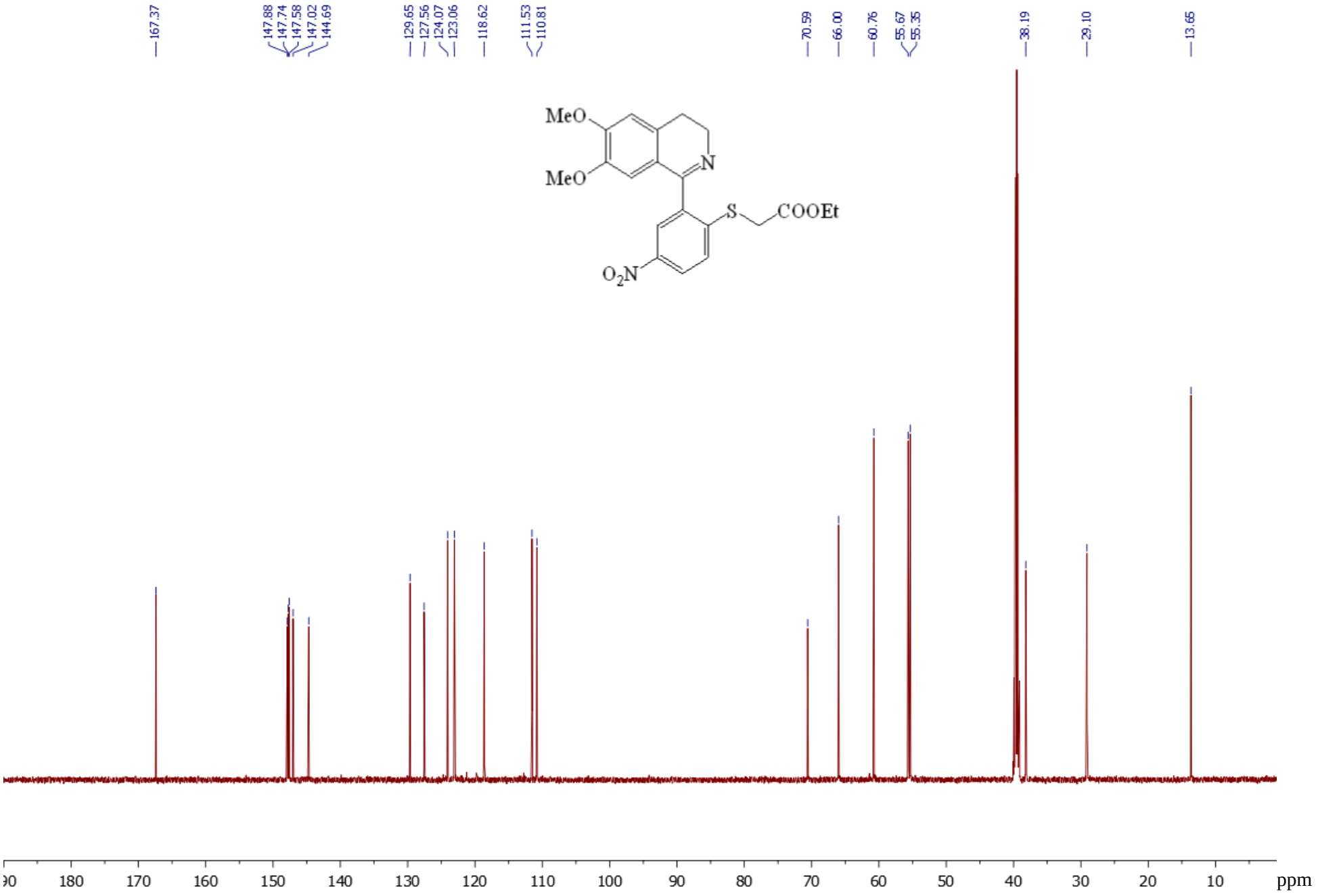
1-{2-[((1*H*-Benz[*d*]imidazol-2-yl)methyl)thio]-5-nitrophenyl}-3,4-dihydroisoquinoline (**3a**).



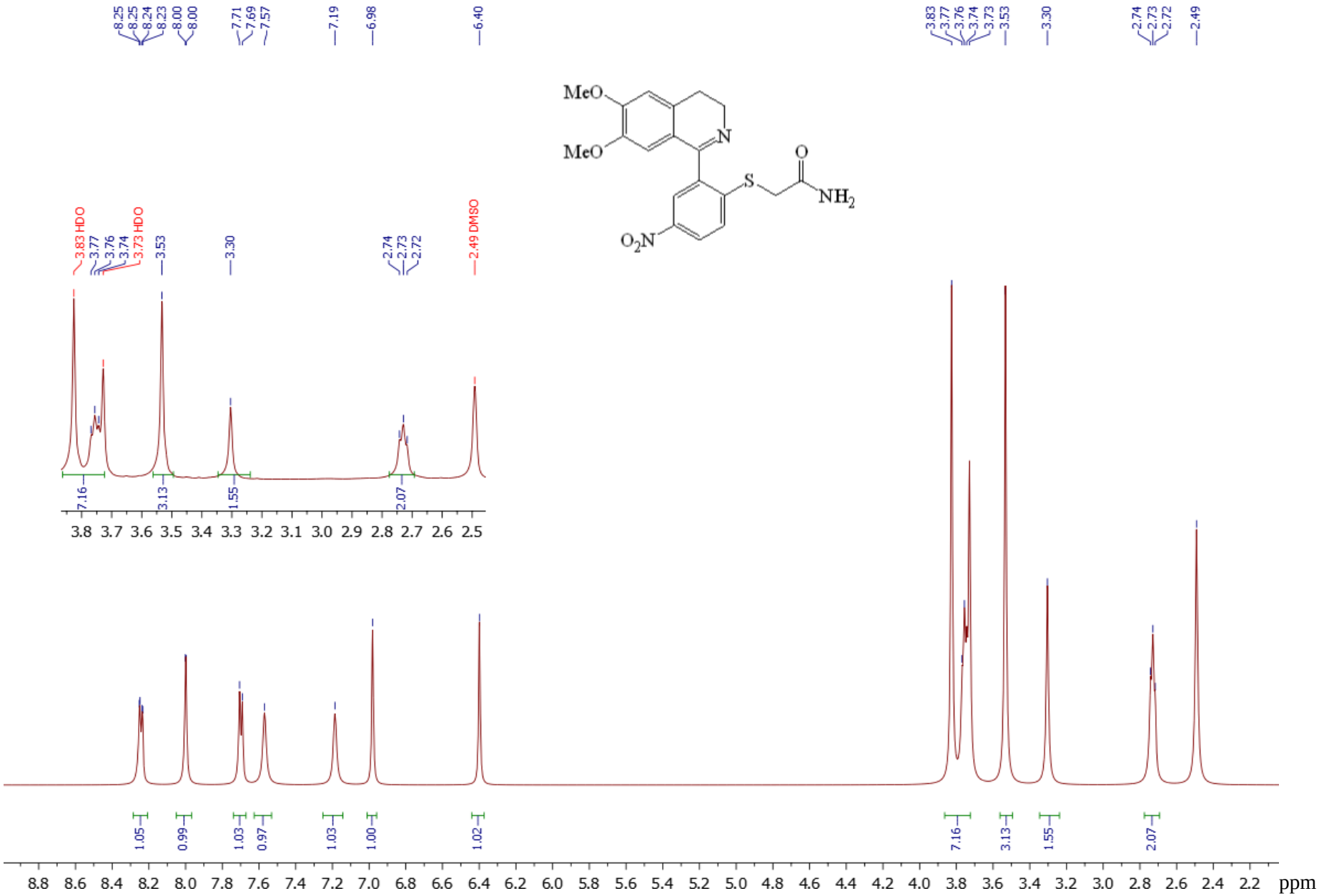

163.90
150.00
145.72
144.52
138.09
137.35
131.24
127.71
127.65
127.63
127.15
127.05
126.91
126.20
123.59
123.40
122.25
121.28
118.57
111.21
47.12
29.84
25.00
N
S
N
N
H
O2N
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

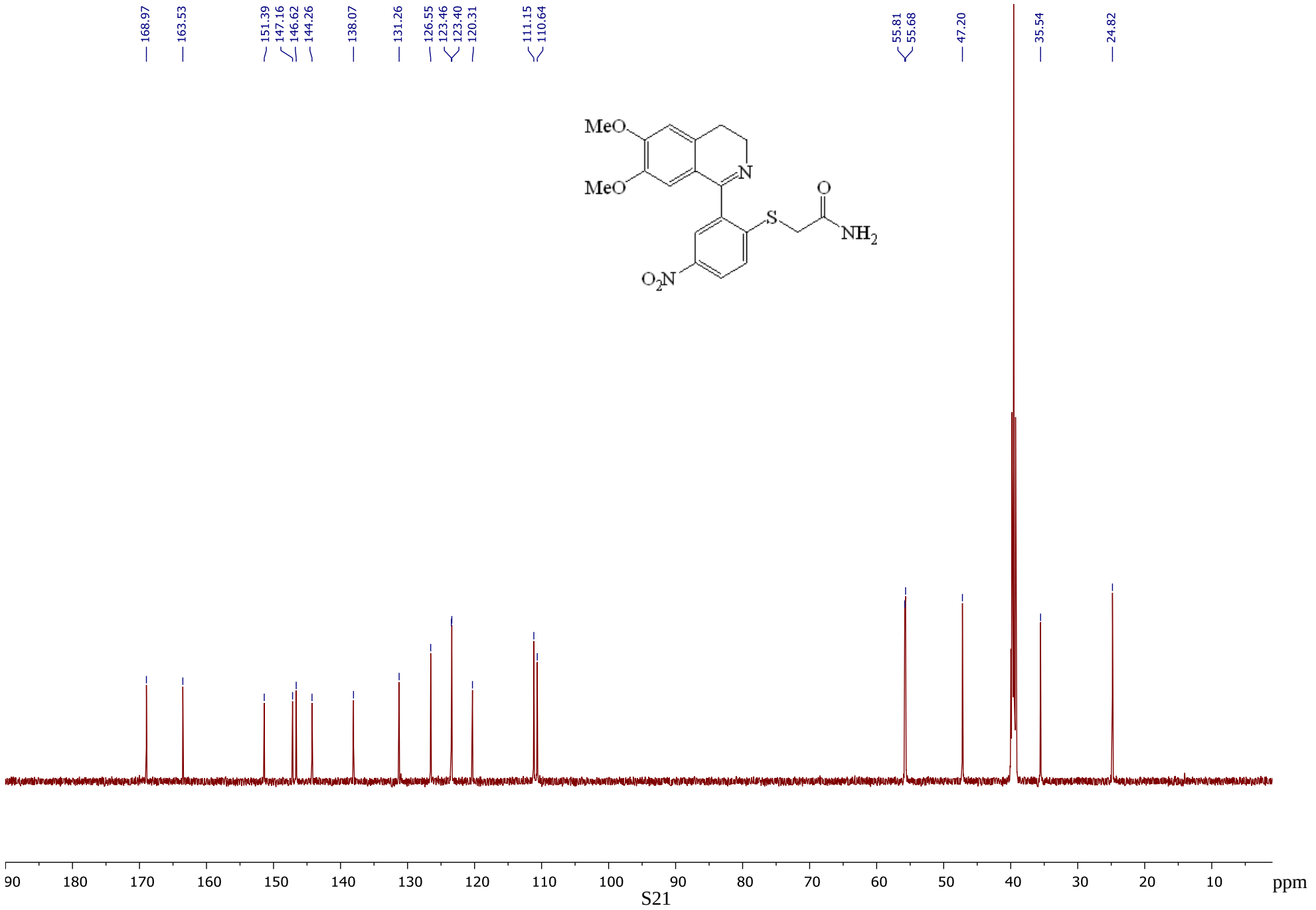
Ethyl 2-((2-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)-4-nitrophenyl)thio)acetate **(3b).**



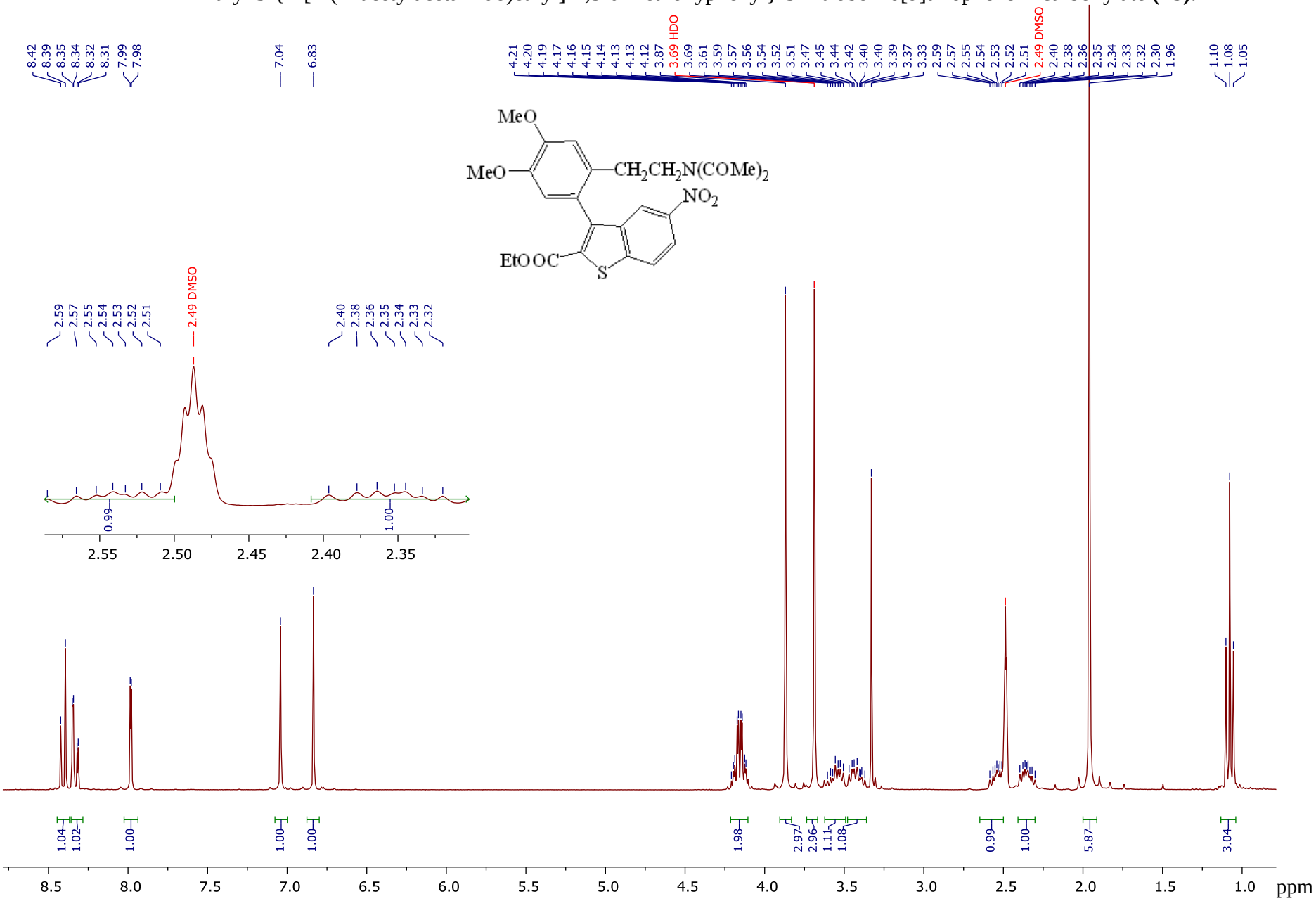

167.37
147.88
147.74
147.58
147.02
144.69
129.65
127.56
124.07
123.06
118.62
111.53
110.81
70.59
66.00
60.76
55.67
55.35
38.19
29.10
13.65
MeO
MeO
N
S
COOEt
O2N
ppm

2-{[2-(6,7-Dimethoxy-3,4-dihydroisoquinolin-1-yl)-4-nitrophenyl]thio}acetamide **(3d).**

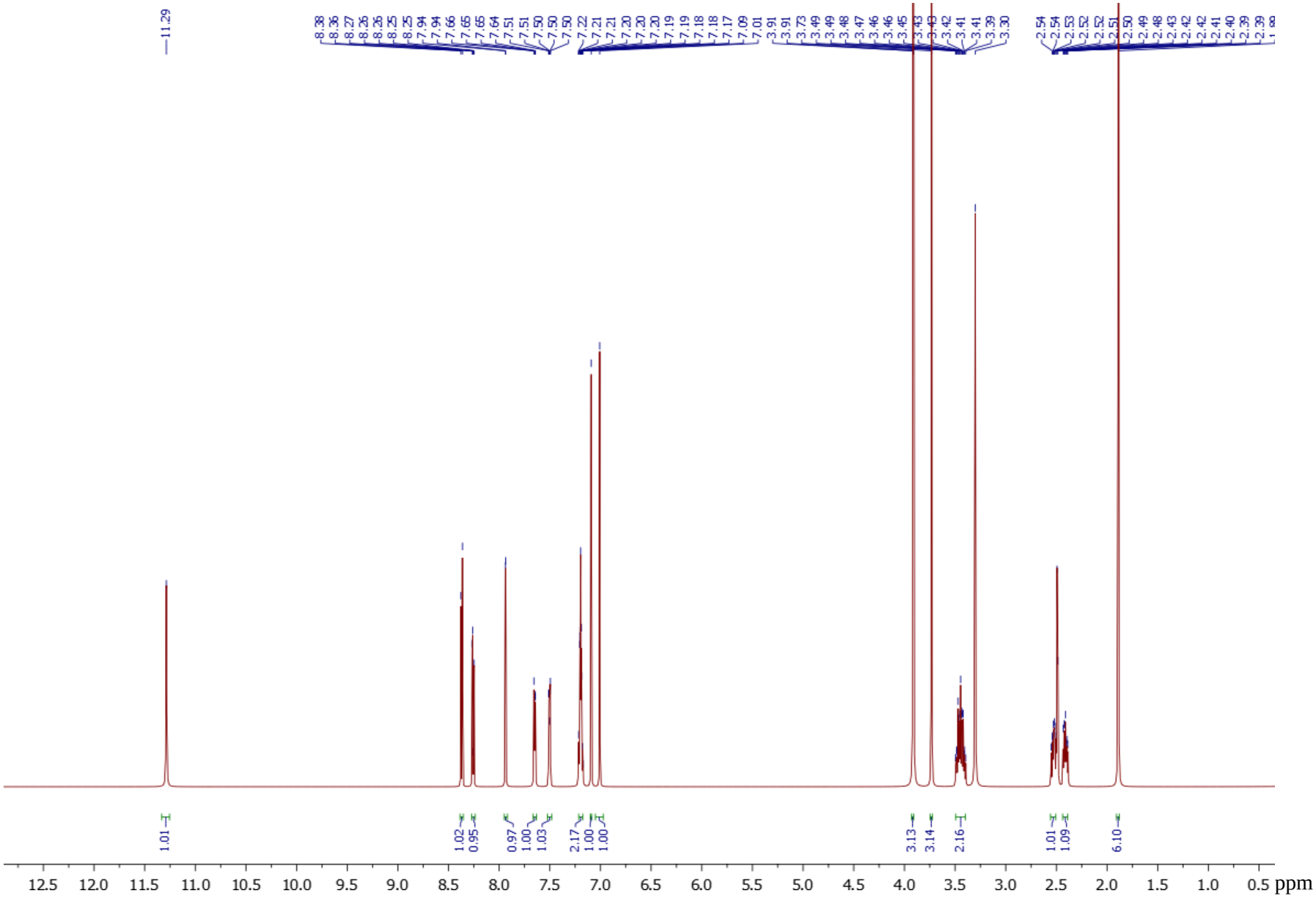


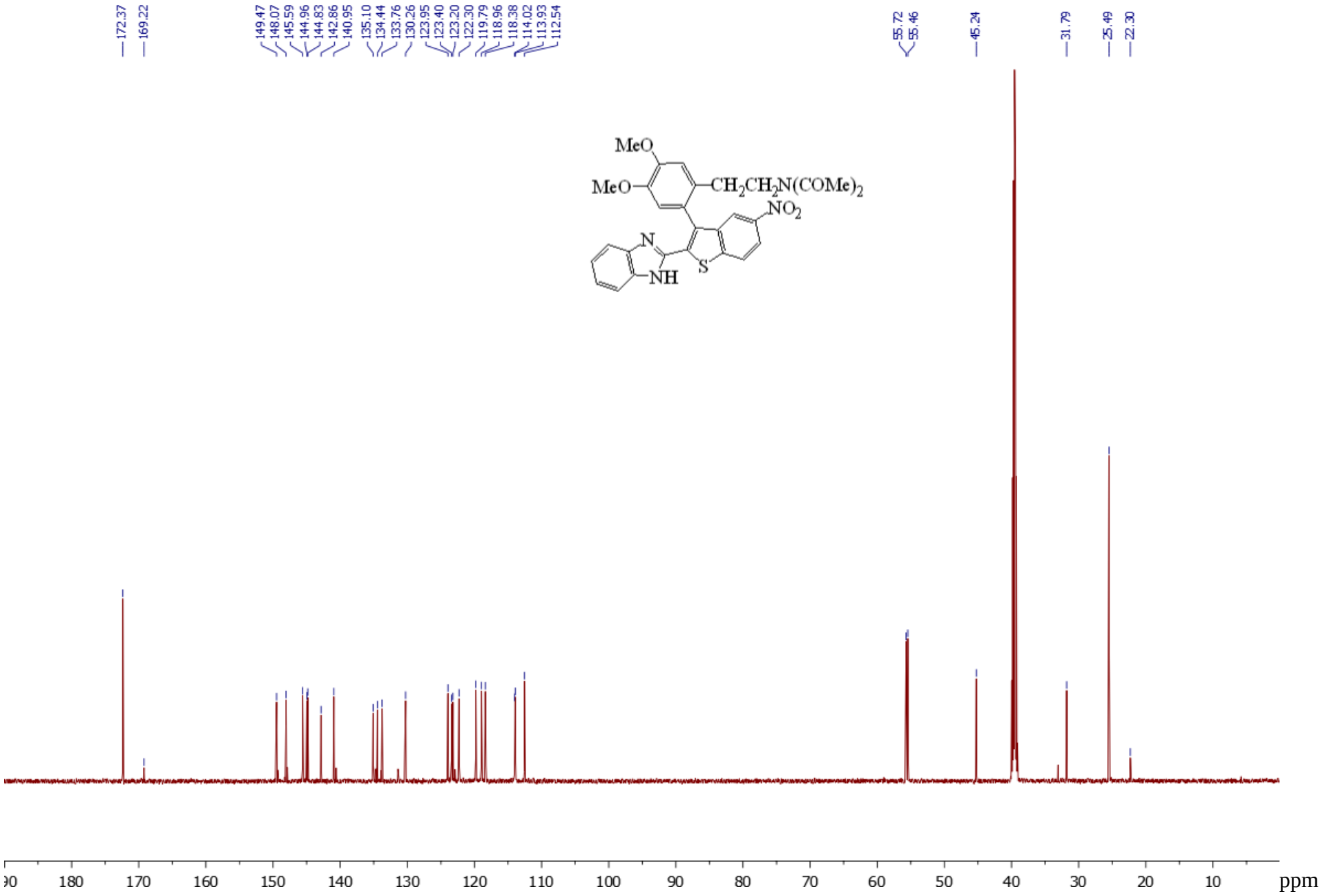

168.97
163.53
151.39
147.16
146.62
144.26
138.07
131.26
126.55
123.46
123.40
120.31
111.15
110.64
55.81
55.68
47.20
35.54
24.82
MeO
MeO
N
O
S
NH2
O2N
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

Ethyl 3-{2-[2-(*N*-acetylacetamido)ethyl]-4,5-dimethoxyphenyl}-5-nitrobenzo[*b*]thiophene-2-carboxylate **(4b).**

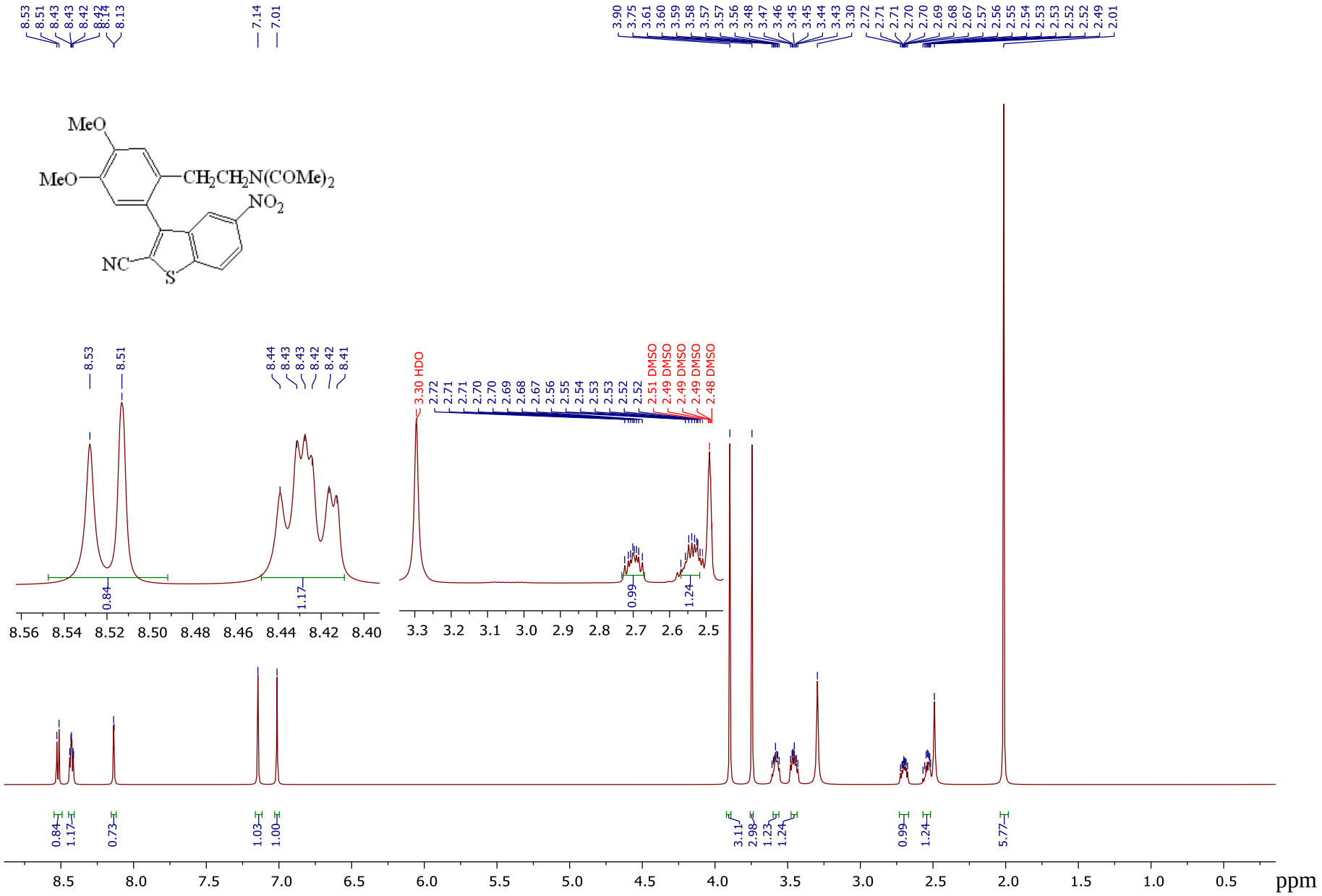


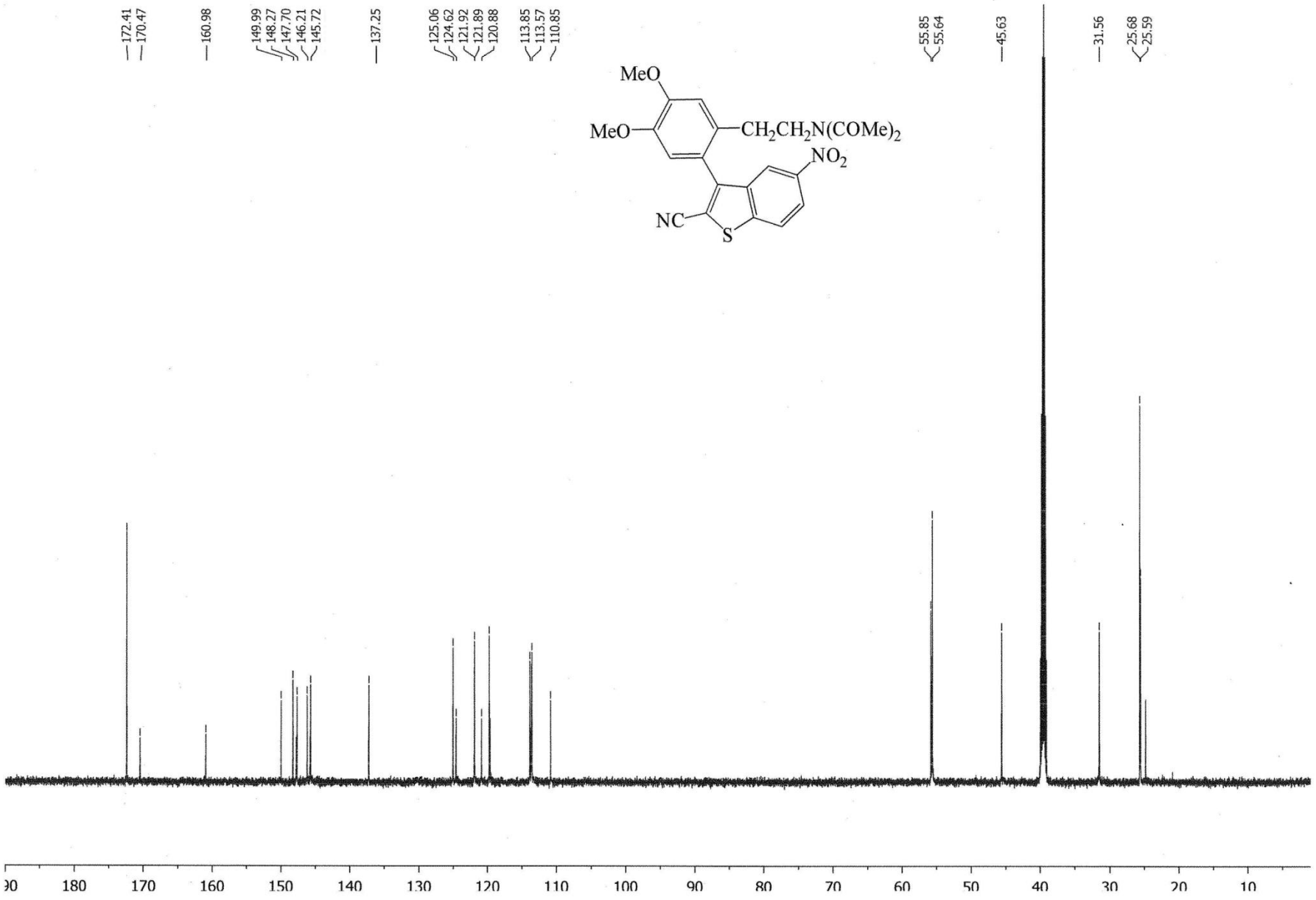
N-{2-[2-(1*H*-Benzo[*d*]imidazol-2-yl)-5-nitrobenzo[*b*]thiophen-3-yl]-4,5-dimethoxyphenethyl}-*N*-acetylacetamide **(4c).**



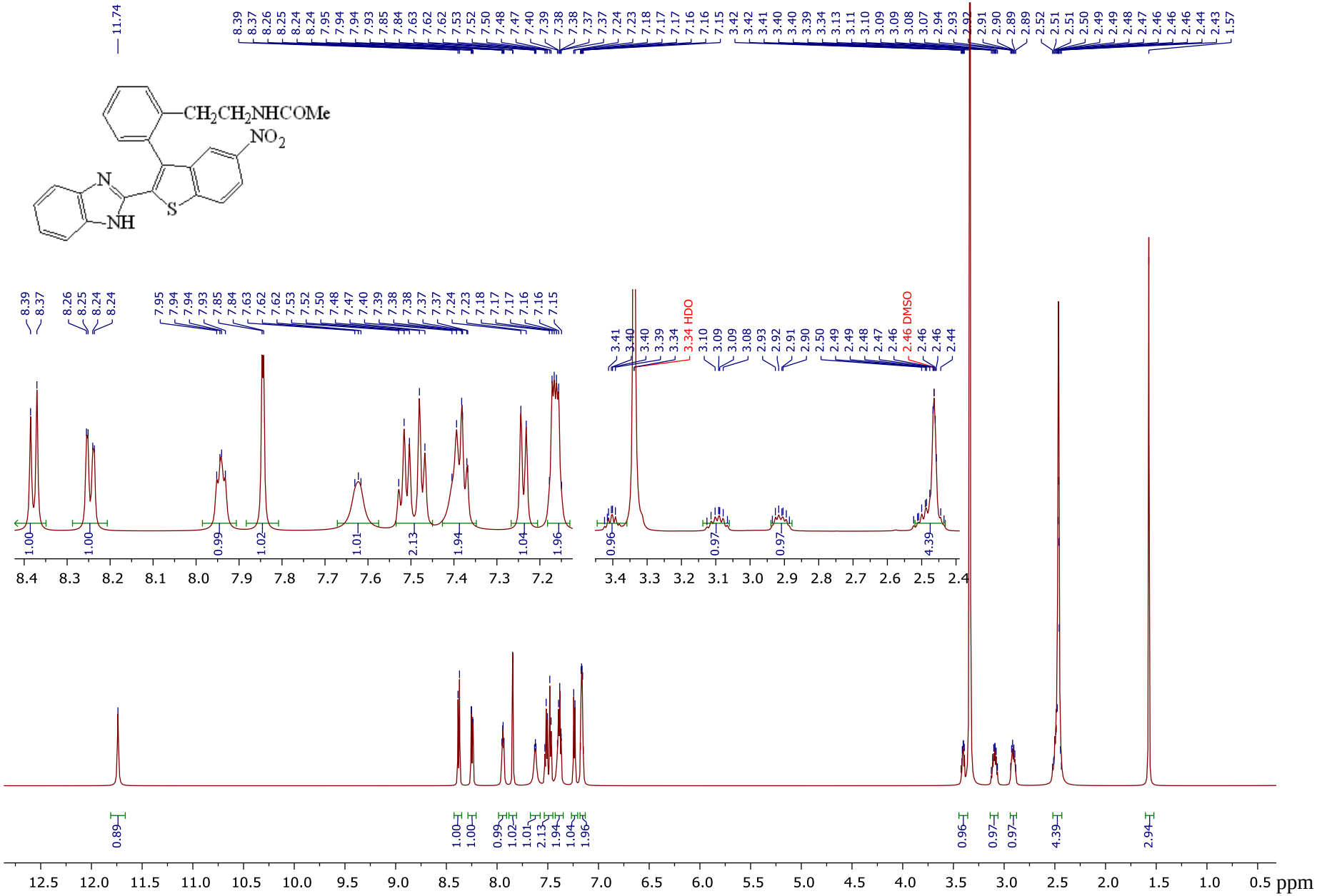

172.37
169.22
149.47
148.07
145.59
144.96
144.83
142.86
140.95
135.10
134.44
133.76
130.26
123.95
123.40
123.20
122.30
119.79
118.96
118.38
114.02
113.93
112.54
55.72
55.46
45.24
31.79
25.49
22.30
MeO
MeO
CH2CH2N(COMe)2
NO2
N
NH
S
ppm

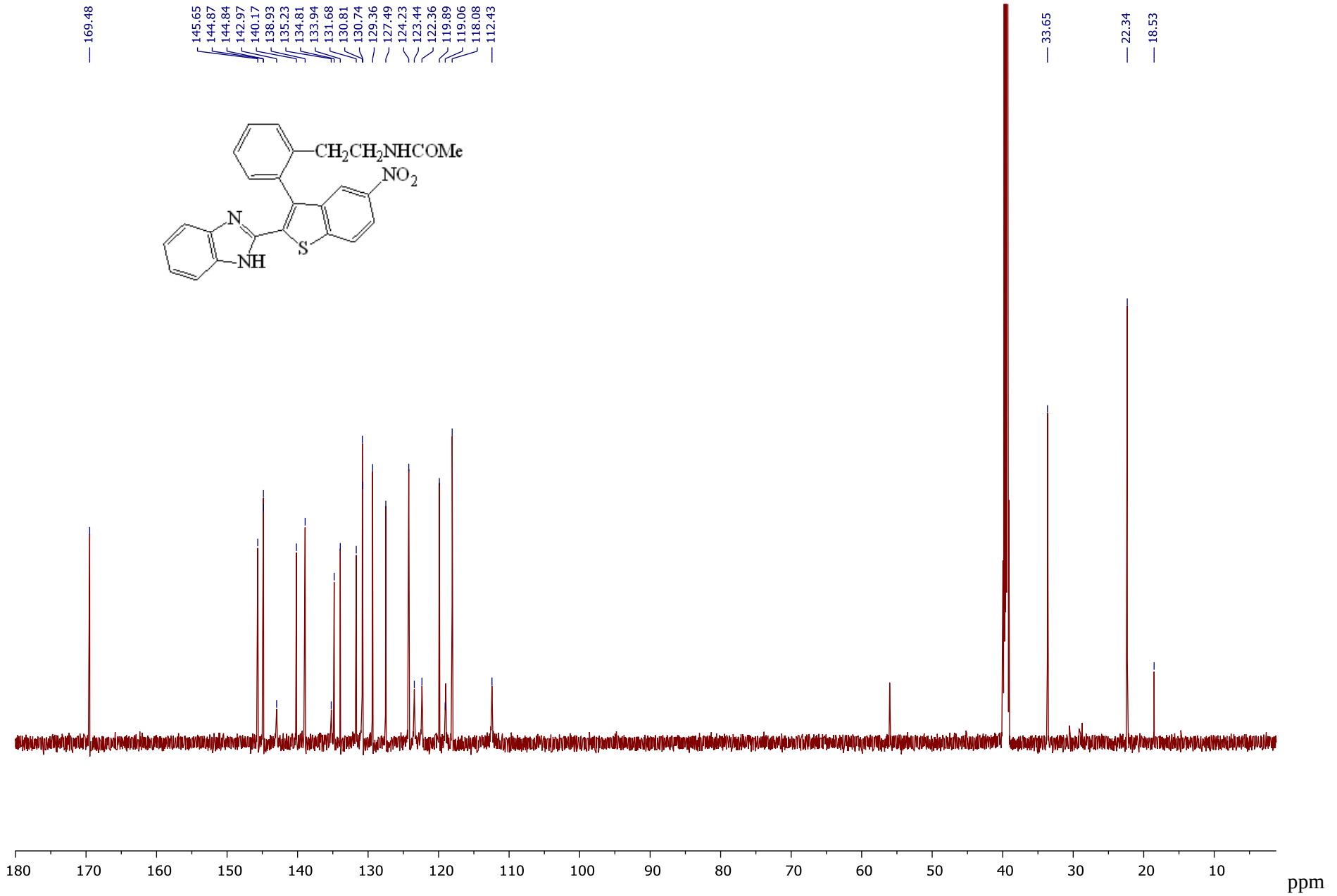
N-Acetyl-*N*-[2-(2-cyano-5-nitrobenzo[*b*]thiophen-3-yl)-4,5-dimethoxyphenethyl]acetamide **(4d).**



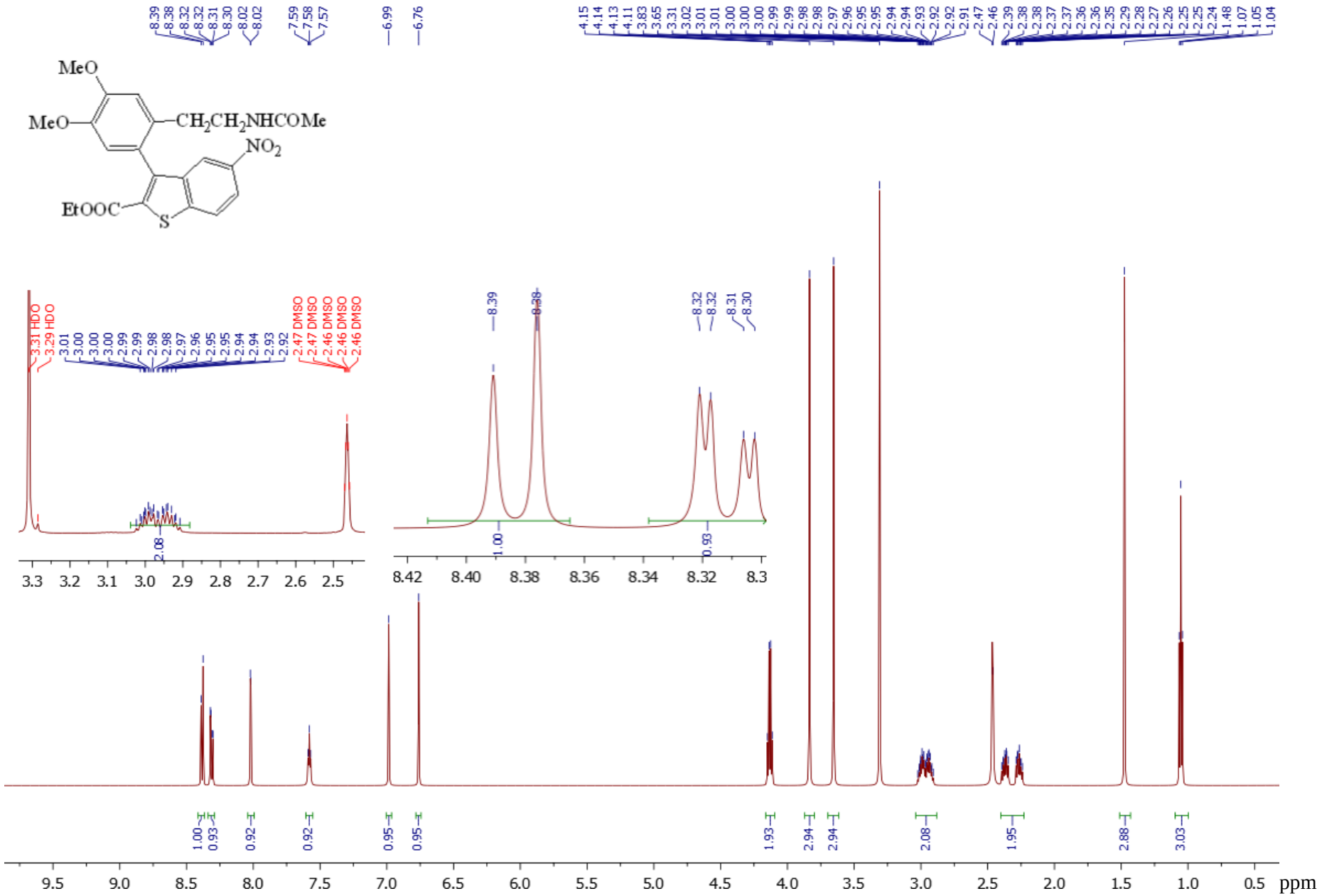

172.41
170.47
160.98
149.99
148.27
147.70
146.21
145.72
137.25
125.06
124.62
121.92
121.89
120.88
113.85
113.57
110.85
55.85
55.64
45.63
31.56
25.68
25.59
MeO
MeO
CH2CH2N(COMe)2
NO2
NC
S
ppm

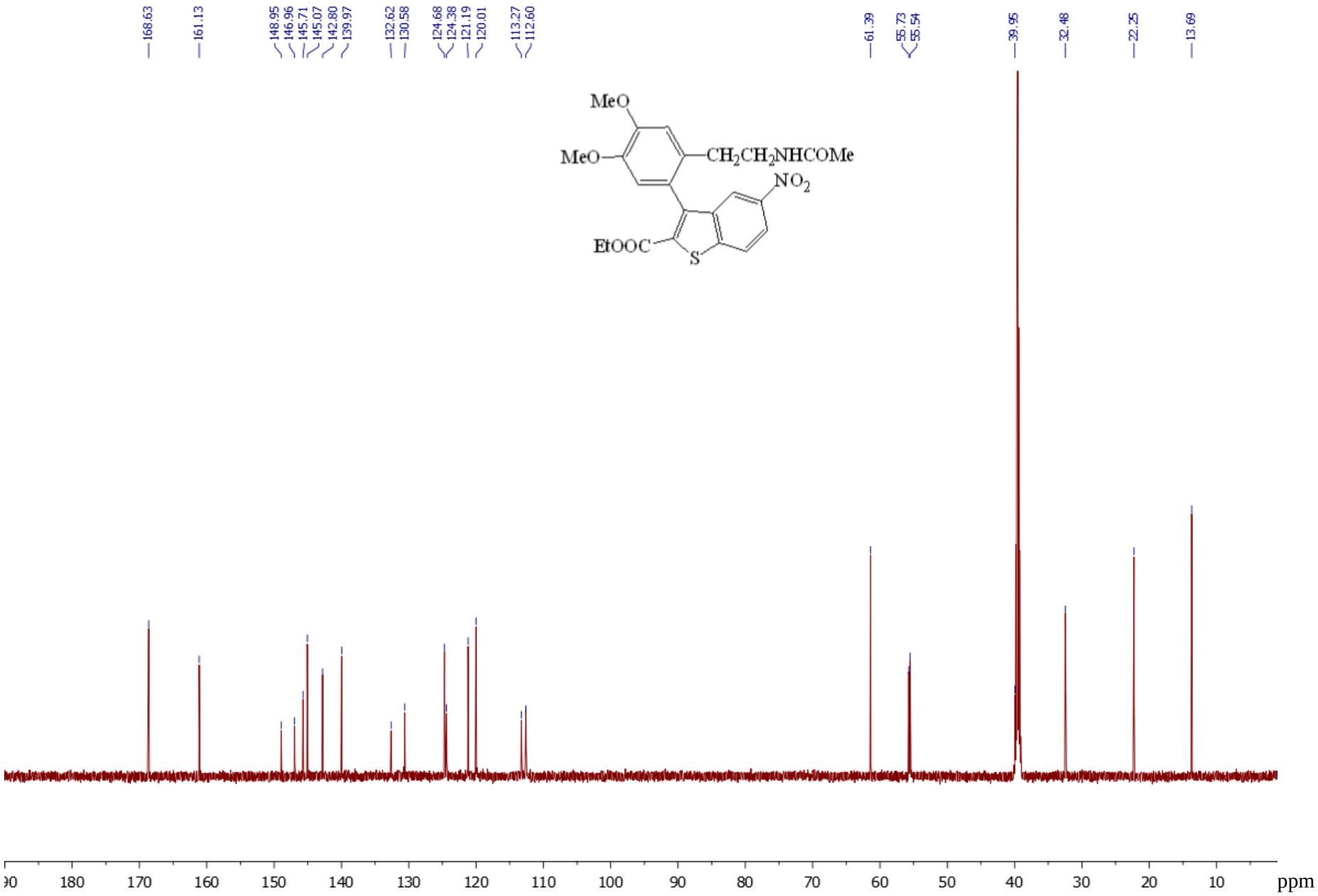
N-{2-[2-(1*H*-Benz[*d*]imidazol-2-yl)-5-nitrobenzo[*b*]thiophen-3-yl]phenethyl}acetamide (**5a**).



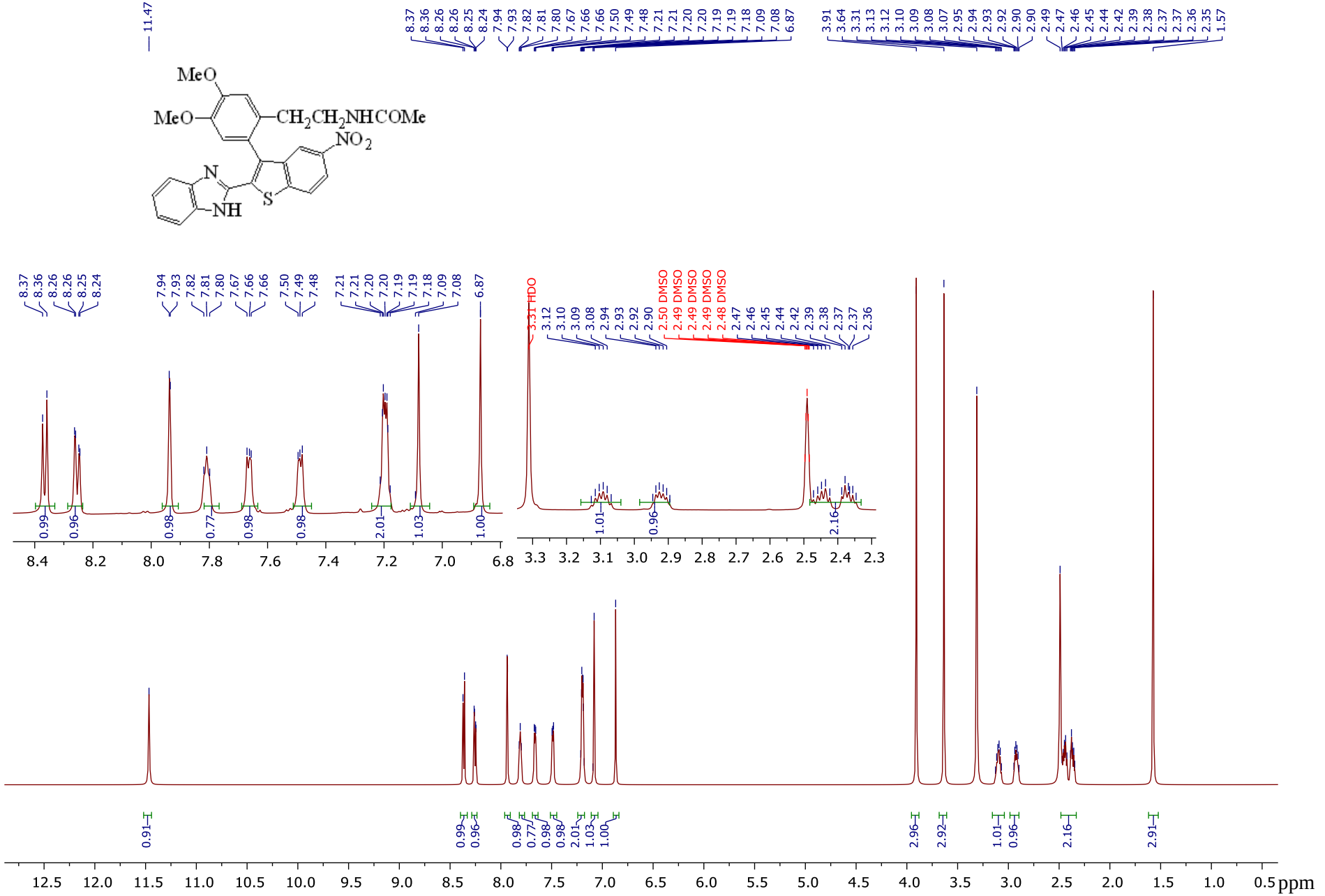

169.48
145.65
144.87
144.84
142.97
140.17
138.93
135.23
134.81
133.94
131.68
130.81
130.74
129.36
127.49
124.23
123.44
122.36
119.89
119.06
118.08
112.43
33.65
22.34
18.53
CH2CH2NHCOMe
NO2
N
NH
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

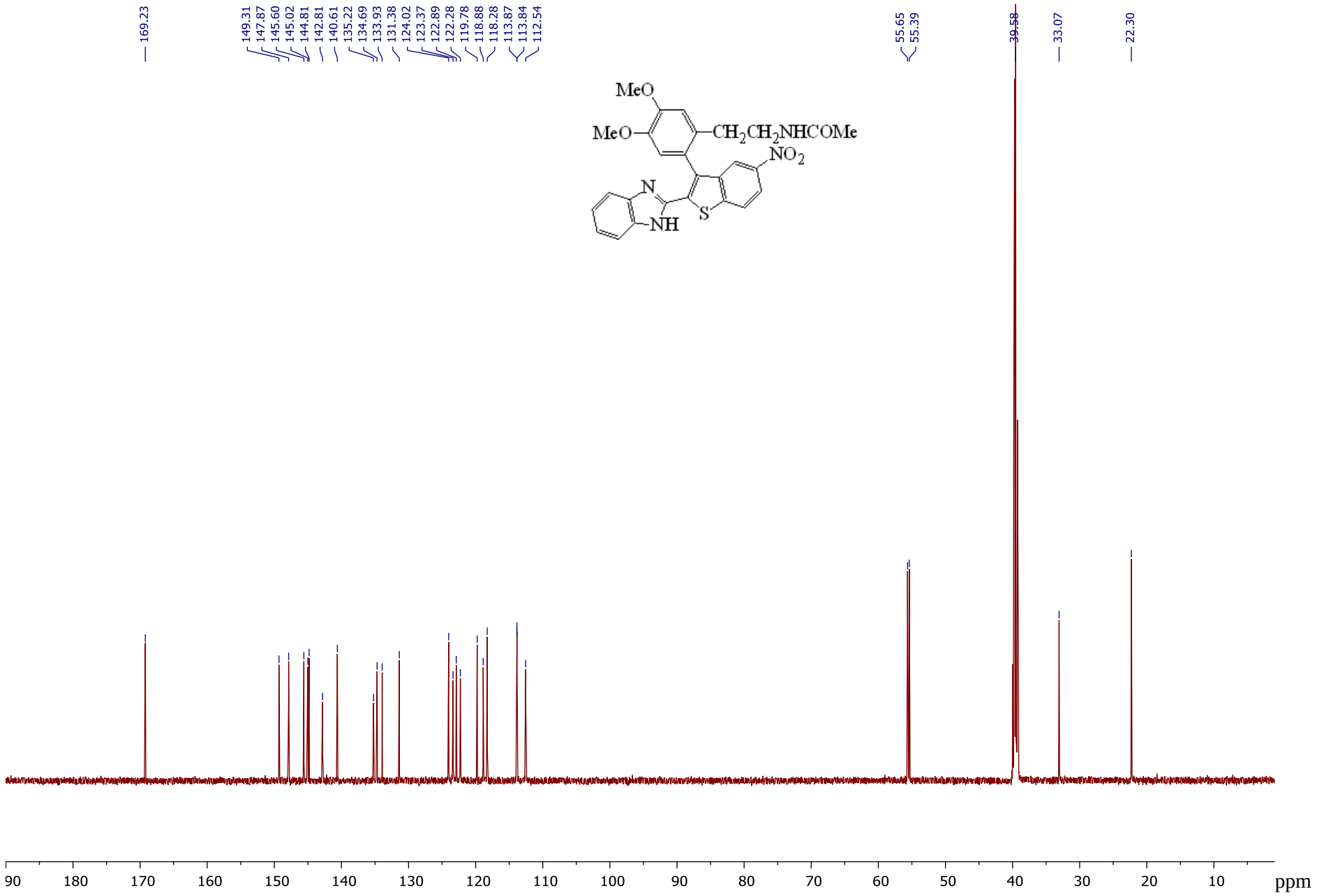
Ethyl 3-[2-(2-acetamidoethyl)-4,5-dimethoxyphenyl]-5-nitrobenzo[*b*]thiophene-2-carboxylate **(5b).**



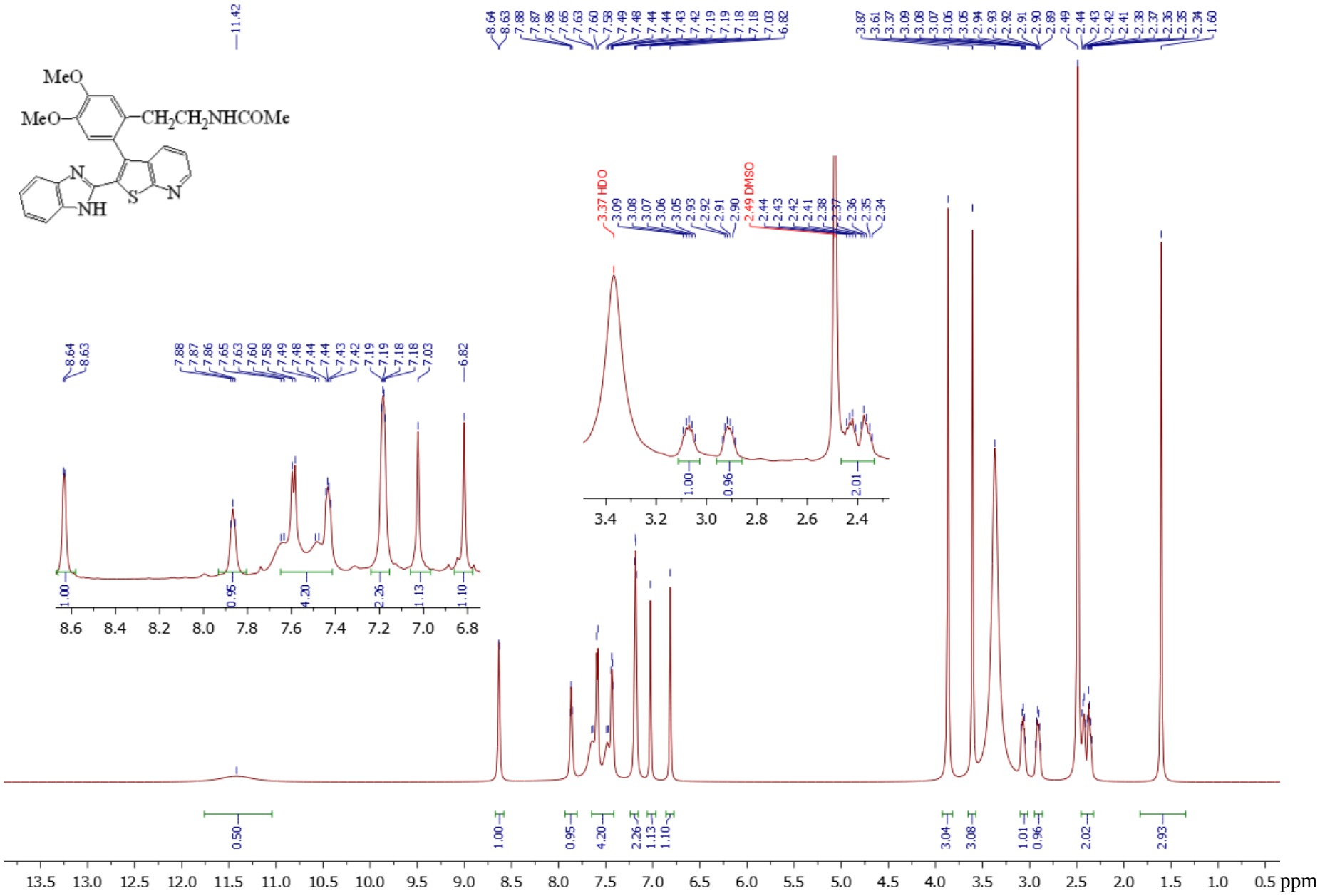

168.63
161.13
148.95
146.96
145.71
145.07
142.80
139.97
132.62
130.58
124.68
124.38
121.19
120.01
113.27
112.60
61.39
55.73
55.54
39.95
32.48
22.25
13.69
MeO
MeO
CH2CH2NHCOMe
NO2
EtOOC
S
ppm

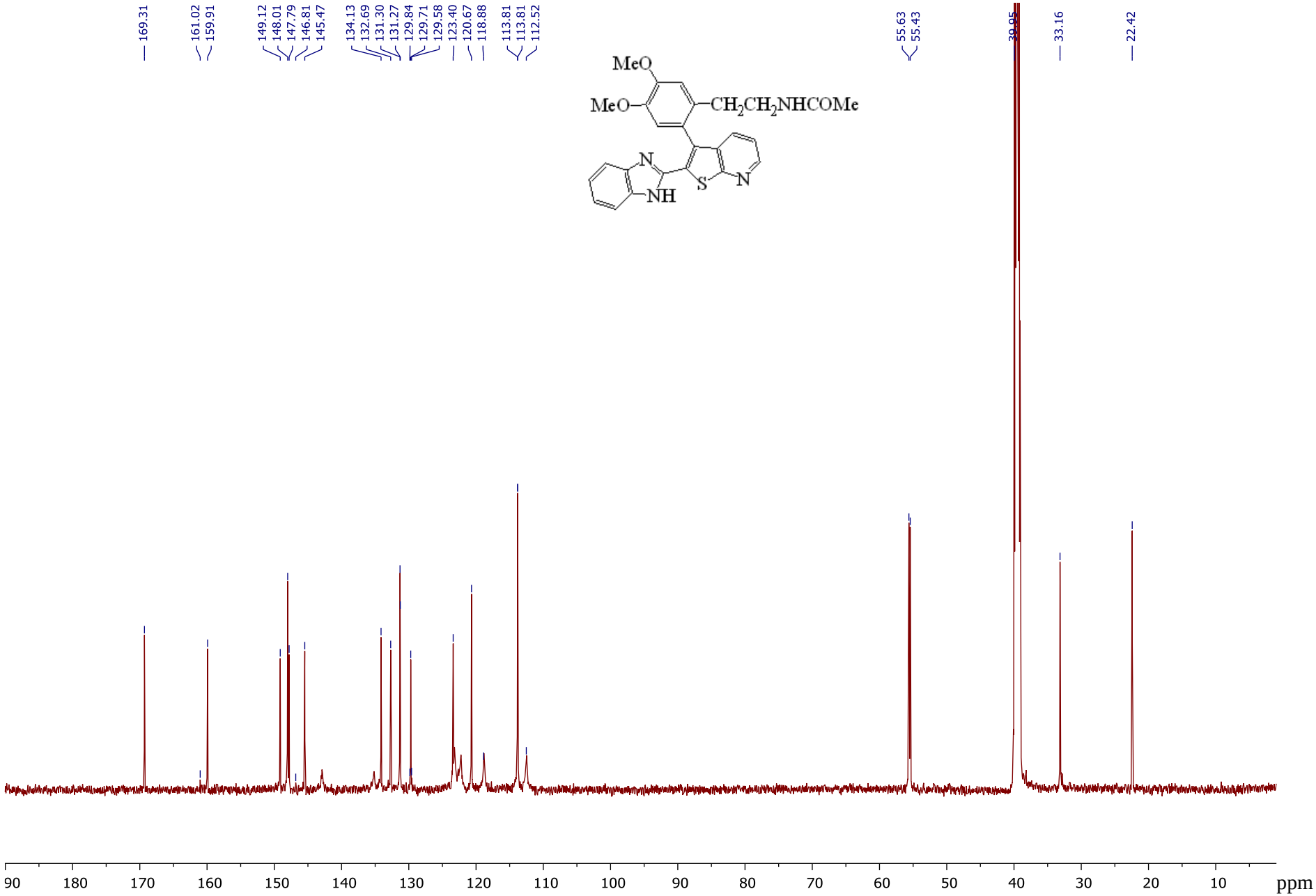
N-{2-[2-(1*H*-Benzo[*d*]imidazol-2-yl)-5-nitrobenzo[*b*]thiophen-3-yl]-4,5-dimethoxyphenethyl}acetamide **(5c).**




169.23
149.31
147.87
145.60
145.02
144.81
142.81
140.61
135.22
134.69
133.93
131.38
124.02
123.37
122.89
122.28
119.78
118.88
118.28
113.87
113.84
112.54
55.65
55.39
39.58
33.07
22.30
MeO
MeO
CH2CH2NHCOMe
NO2
N
NH
S
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

N-{2-[2-(1*H*-Benz[*d*]imidazol-2-yl)thieno[2,3-*b*]pyridin-3-yl]-4,5-dimethoxyphenethyl}acetamide **(5e).**




169.31
161.02
159.91
149.12
148.01
147.79
146.81
145.47
134.13
132.69
131.30
131.27
129.84
129.71
129.58
123.40
120.67
118.88
113.81
113.81
112.52
55.63
55.43
39.95
33.16
22.42
MeO
MeO
CH2CH2NHCOMe
N
NH
S
N
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm