Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

Reductive dehalogenation and dehalogenative sulfonation of phenols and heteroaromatics with sodium sulfite in an aqueous medium

Monika Tomanová, Lukáš Jedinák and Petr Cankař *

Department of Organic Chemistry, Palacký University, 17. Listopadu 1192/12, 77146, Olomouc, Czech Republic.

*Corresponding author email: petr.cankar@upol.cz

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1. General information

1.1 Chemicals

Starting materials and reagents were purchased from various commercial sources (VWR, Sigma-Aldrich, Fluorochem, Acros Organics) and used as received. Starting compounds **25** and **26** were prepared according literature procedures.[1,2] Concentrated hydrochloric acid was purchased from VWR (37%, AnalR NORMAPUR®). Ethyl acetate, $CHCl_3$ and hexane for a reaction workup and for a column chromatography were purchased from VWR (HiPerSolv CHROMANORM® for HPLC) and used as received. Deuterated solvents for NMR spectroscopy were purchased from VWR (> 99.8%, without TMS) and stored in a desiccator at ambient temperature. Dimethyl sulfone used as a standard for quantitative NMR was purchased from Sigma-Aldrich (TraceCERT®) and stored in a fridge. **Anhydrous sodium sulfite** was purchased from Lach-Ner (98.8%), stored at ambient temperature and used without further purification. Local tap water was purified by reverse osmosis and purged with a stream of nitrogen before use.

1.2 Reaction monitoring

The reactions were monitored with LC/MS (ACQUITY UPLC, Waters) consisting of auto-sampler, quaternary solvent manager system, PDA detector and quadrupole mass spectrometer. The separations were performed using C18 column (tempered to 30 °C) and a mobile phase consisted of: (A) 0.01 mol/L ammonium acetate in water and (B) acetonitrile. A linearly programmed gradient elution was used at a flow rate of 0.6 mL/min.

The quantitative ^{1}H NMR NMR was performed on JEOL 400 MHz spectrometer. A stock solution of the NMR standard (dimethyl sulfone) was added to a crude reaction mixture, which was then diluted with DMSO-d_6 and filtered to remove precipitated salts. An aliquot (0.6 mL) of a filtrate was then withdrawn for the NMR analysis.

1.3 Compound characterization

Compounds were characterized by their ^{1}H and ^{13}C NMR spectra, high resolution mass spectra (HRMS), and melting point.

NMR spectra were recorded at room temperature on JEOL 400 MHz spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) using $CDCl_3$, DMSO-d_6 or D_2O as a solvent. Chemical shifts (δ) for proton and carbon signals were referenced to the residual solvent peak and are reported in parts per million (ppm). Coupling constants (*J*) are reported in Hertz (Hz) and multiplicity reported according to the

following convention: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, brs = broad singlet.

HRMS analyses were performed on Thermo Exactive Plus high resolution mass spectrometer with electrospray ionization (ESI) and Orbitrap analyzer operating at positive or negative full scan mode in the range of 60-800 m/z.

1.4 Microwave reactor

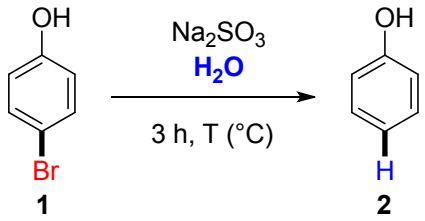
All reactions carried out under microwave irradiation were performed with the CEM Discover® SP microwave synthesizer, using the Dynamic mode in the following settings: maximum amount of microwave power (150 W), premixing time (1 minute), stirring speed (high), hold time (depending on the reaction), temperature control point (depending on the reaction), simultaneous cooling (PowerMax **ON**/~~OFF~~). In the Dynamic mode a specified amount of power (150 W) is applied in order to reach the reaction temperature (temperature control point); then the power is modulated automatically, based on the temperature sensor feedback data, to hold the set temperature for a specific reaction time (hold time). A simultaneous cooling of the reaction vessel provided by a compressed air (24 psi) was applied during entire experiment (PowerMax option “ON”).

All 0.5 mmol scale reactions were performed in a 10 mL borosilicate glass reaction vessel closed with a disposable silicon cap and equipped with Teflon coated egg-shaped magnetic stir bar. The temperature was monitored by an external infrared sensor.

The 5 mmol scale reaction was performed in an 80 mL borosilicate glass reaction vessel equipped with Teflon coated egg-shaped magnetic stir bar. The reaction vessel was equipped with a cover assembly allowing introduction of a fiber optic temperature sensor, used for monitoring a reaction temperature.

2. Dehalogenation of 4-bromophenol at various temperatures

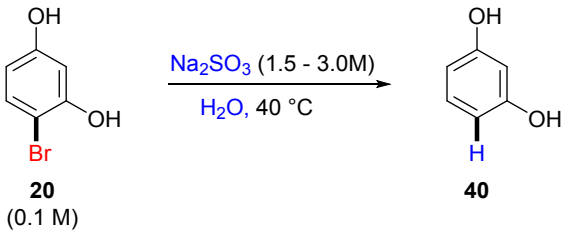
The mixture of substrate **1** (0.5 mmol), Na_2SO_3 (6.0 mmol) and water (2.5 mL) was stirred at given temperature for 3h. The reaction was performed either under microwave irradiation (150 W) or in a glass pressure tube inserted into preheated oil bath. Yield of **2** was detrmined by a quantitative HPLC. No significant difference between convective and microwave heating was observed at 100 °C.



1 **2**

Entry	Heating	T (°C)	**2** (%)
1	microwave	130	>98
2	microwave	120	76
3	microwave	110	33
4	microwave	100	14
5	convective	100	11

3. Kinetic study



A 10 mL Shlenk flask was charged with sodium sulfite (7.5 – 15.0 mmol, 15.0 – 30.0 equivalents, 1.5 – 3.0 M) and water (5 mL). The mixture was heated in oil bath to 40 °C (internal temperature) under nitrogen atmosphere. When the internal temperature reached 40 °C, 4-bromoresorcinol **20** (94 mg, 0.5 mmol) was added in a single portion to start the reaction, which was monitored by HPLC.

The reaction was carried out under pseudo first order conditions using at least 15 equivalents of sodium sulfite. The slope of a graph (-ln[SM] vs. time) corresponded to k´ (for the pseudo first order reaction). Rate constant k´ was determined at six different concentrations of sodium sulfite: 1.50, 2.00, 2.25, 2.50, 2.75 and 3.00 mol/L.

$[Na_2SO_3]$ (mol/L)	k´ (s^{-1})
1.50	5.81×10^{-4}
2.00	8.05×10^{-4}
2.25	10.05×10^{-4}
2.50	11.68×10^{-4}
2.75	12.75×10^{-4}
3.00	14.02×10^{-4}

The slope of a graph (k´ vs. $[Na_2SO_3]$) corresponded to k_1 (second order): $k_1 = 5.65 \times 10^{-4}$ $M^{-1}s^{-1}$).

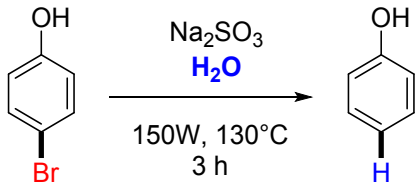
The reaction of 4-bromoresorcinol **20** (0.5 mmol) with sodium sulfite (15 equivalents) at 40 °C was repeated in D_2O (5 mL). The pseudo first order rate constant was determined: k´ = 1.14×10^{-4} s^{-1}, providing $k'_{H/D} = 5.81/1.14 = 5.09$.

4. General procedure

A 10 mL reaction vessel equipped with a magnetic stir bar was charged with aryl halide (0.5 mmol), anhydrous sodium sulfite (amount specified for every compound), and demineralized water (2.5 mL). Without microwave irradiation: the mixture was stirred at ambient temperature or in preheated oil bath in closed vessel for specified time. Under microwave irradiation: the vessel was sealed and premixed for one minute at high stirring speed in the CEM Discover SP microwave synthesizer. Then, the reaction mixture was irradiated at maximum power of 150 W with simultaneous cooling by a compressed air (24 psi). When the desired temperature was reached (ramping time ~ 1 min), the power was automatically adjusted in order to maintain the set reaction temperature for specified time. Finally, the vessel was cooled to approximately 40 °C by a compressed air (cooling time ~ 1 min). The workup procedure is described for individual compounds. Generally, hydrodehalogenated products were obtained after liquid-liquid extraction in a sufficient purity, no chromatographic purification was required. Sulfonated products were obtained after acidification with hydrochloric acid.

5. Procedures and analytical data for individual compounds

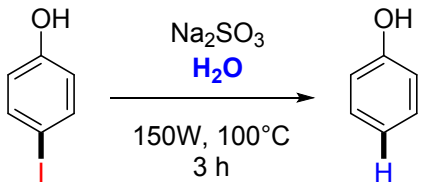
Phenol 2 (Table 2, entry 1)



Compound **2** was prepared according to the general procedure from 4-bromophenol **1** (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$ and evaporation under reduced pressure yielded compound **2** as a pale brown crystalline solid (42 mg, 88 %).

Melting point 38-39 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.32 (brs, 1 H), 7.15 (t, J = 7.8 Hz, 2 H), 6.82 – 6.65 (m, 4 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.3, 129.4, 118.8, 115.2 ppm; HRMS: m/z calculated for C_6H_6O $[M - H]^-$ 93.0335, found 93.0337.

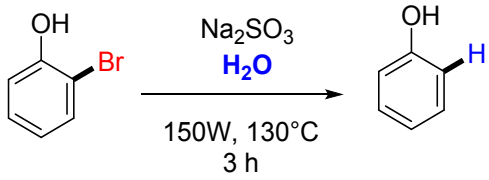
Phenol 2 (Table 2, entry 2)



Compound **2** was prepared according to the general procedure from 4-iodophenol **3** (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **2** as a pale brown crystalline solid (43 mg, 91 %).

Analytical data were in accordance with compound **2** obtained from 4-bromophenol **1**.

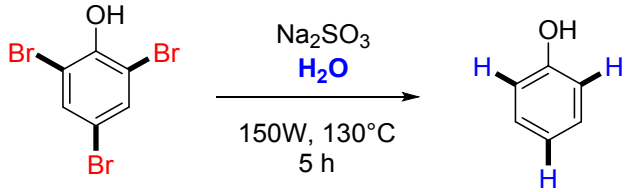
Phenol 2 (Table 2, entry 3)



Compound **2** was prepared according to the general procedure from 2-bromophenol **4** (87 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **2** as a pale brown crystalline solid (42 mg, 88 %).

Analytical data were in accordance with compound **2** obtained from 4-bromophenol **1**.

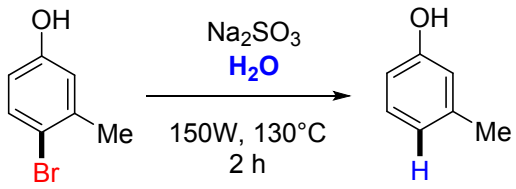
Phenol 2 (Table 2, entry 4)



Compound **2** was prepared according to the general procedure from 2,4,6-tribromophenol **5** (166 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 5 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **2** as a pale brown crystalline solid (37 mg, 78 %).

Analytical data were in accordance with the compound **2** obtained from 4-bromophenol **1**.

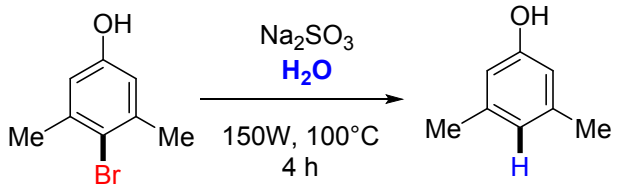
3-Methylphenol 27 (Table 2, entry 5)



Compound **27** was prepared according to the general procedure from 4-bromo-3-methylphenol **6** (94 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 2 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **27** as a pale yellow oil (43 mg, 80 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.13 (t, *J* = 7.7 Hz, 1 H), 6.76 (d, *J* = 7.4 Hz, 1 H), 6.68 – 6.63 (m, 2 H), 4.49 (brs, 1 H), 2.32 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 139.9, 129.5, 121.7, 116.1, 112.4, 21.4 ppm; HRMS: m/z calculated for C_7H_8O $[M - H]^-$ 107.0491, found 107.0494.

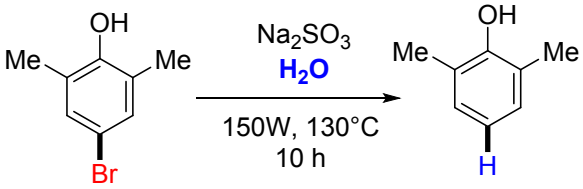
3,5-Dimethylphenol 28 (Table 2, entry 6)



Compound **28** was prepared according to the general procedure from 4-bromo-3,5-dimethylphenol **7** (101 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100°C for 4 hour. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **28** as a white crystalline solid (51 mg, 84 %).

Melting point 60-61 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (s, 1 H), 6.48 (s, 2 H), 5.00 (brs, 1 H), 2.27 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 139.9, 122.63, 113.13, 21.4 ppm; HRMS: m/z calculated for $C_8H_{10}O$ $[M - H]^-$ 121.0648, found 121.0643.

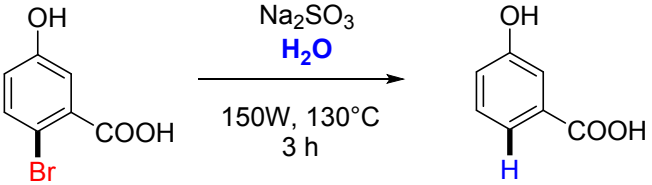
2,6-Dimethylphenol 29 (Table 2, entry 7)



Compound **29** was prepared according to the general procedure from 4-bromo-2,6-dimethylphenol **8** (101 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 10 hours. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **29** as a pale brown solid (53 mg, 87 %).

Melting point 40-42 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (d, *J* = 7.4 Hz, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 4.58 (s, 1H), 2.25 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.27, 128.72, 123.08, 120.33, 15.98 ppm; HRMS: m/z calculated for $C_8H_{10}O$ $[M - H]^-$ 121.0648, found 121.0641.

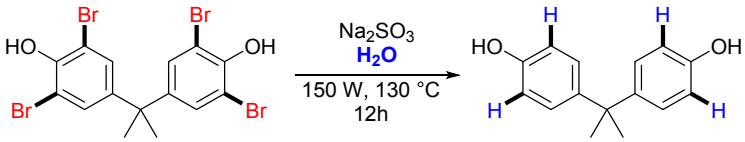
3-Hydroxybenzoic acid 31 (Table 2 , entry 9)



Compound **31** was prepared according to the general procedure from 2-bromo-3-hydroxybenzoic acid **10** (109 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 3 hours. Then, a clear colorless solution was acidified with concentrated hydrochloric acid to pH ≈ 1. The precipitate was collected via filtration and washed with water (1 mL), yielding 3-hydroxybenzoic acid **31** as a pale yellow crystalline solid (58 mg, 85%).

Melting point 199-200°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.38 – 7.32 (m, 2 H) 7.28 (t, *J* = 7.8 Hz, 1 H), 6.99 (ddd, *J* = 8.2, 2.6, 1.1 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 167.8, 157.9, 132.6, 130.1, 120.5, 120.4, 116.3 ppm; HRMS: m/z calculated for $C_7H_6O_3$ $[M - H]^-$ 137.0233, found 137.0233.

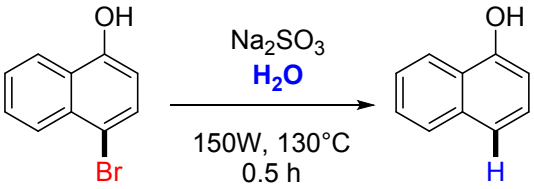
4,4'-(Propane-2,2-diyl)diphenol 32 (Table 2, entry 10)



Compound **32** was prepared according to the general procedure from Tetrabromobisphenol A **11** (272 mg, 0.5 mmol) and sodium sulfite (1.01 g, 8.0 mmol, 16.0 equivalents) in a two-fold amount of water (5 mL). The reaction mixture was irradiated with the microwave reactor at 130 °C for 12 hours. Extraction to EtOAc (3x5 mL), washing with 10% aqueous solution of Na_2CO_3, drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **32** as a white amorphous solid (91 mg, 80%).

Melting point 155-157 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.13 (s, 2 H), 6.99 – 6.95 (m, 4 H), 6.65 – 6.62 (m, 4 H), 1.52 (s, 6 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 154.9, 141.1, 127.3, 114.5, 40.9, 30.9 ppm; HRMS: m/z calculated for $C_{15}H_{16}O_2$ $[M – H]^-$ 227.1067, found 227.1065.

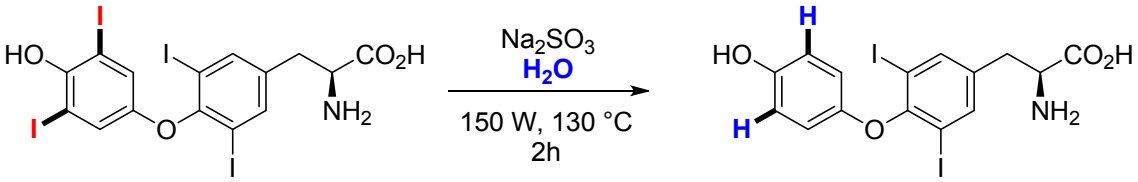
Naphtalen-1-ol 37 (Table 2, entry 15)



Compound **37** was prepared according to the general procedure from 4-bromonaphthalen-1-ol **16** (112 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 30 minutes. Extraction to EtOAc (2x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure provided a crude product. The purification by a column chromatography (silica gel, hexane - ethyl acetate 20:1) yielded compound **37** as a white crystalline solid (43 mg, 60%).

Melting point 92-93°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 – 8.16 (m, 1 H), 7.84 – 7.80 (m, 1 H), 7.53 – 7.47 (m, 2 H), 7.45 (d, *J* = 8.2 Hz, 1 H), 7.32 (dd, *J* = 8.2, 7.5 Hz, 1 H), 6.82 (d, *J* = 7.5, 1 H), 5.21 (brs, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.4, 134.9, 127.8, 126.58, 126.0, 125.4, 124.4, 121.6, 120.9, 108.8 ppm; HRMS: m/z calculated for $C_{10}H_8O$ $[M – H]^-$ 143.0491, found 143.0493.

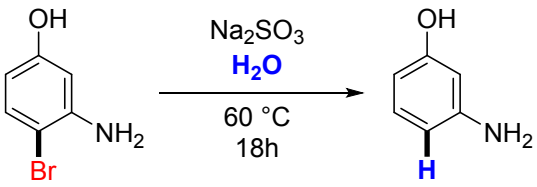
2-Amino-3-(4-(4-hydroxyphenoxy)-3,5-diiodophenyl)propanoic acid 38 (Table 2, entry 16)



Compound **38** was prepared according to the general procedure from L-thyroxine **17** (78 mg, 0.1 mmol) and sodium sulfite (126 mg, 10.0 mmol, 10.0 equivalents) in water (2 mL). The reaction mixture was irradiated with the microwave reactor at 130°C for 2 hours. Then, the white precipitate was collected and washed with water (3x 2 mL). After drying under high vacuum, compound **38** was obtained as a white solid (48 mg, 92%).

Melting point 248-250 °C; ^{1}H NMR (400 MHz, D_2O, NaOH): 7.60 (s, 2 H), 6.45 – 6.41 (m, 2 H), 6.38 – 6.34 (m, 2 H), 3.28 (dd, *J* = 7.5, 5.5 Hz, 1 H), 2.74 (dd, *J* = 13.6, 5.5 Hz, 1 H), 2.55 (dd, *J* = 13.6, 7.5 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, D_2O-H_2O 1:6, NaOH): δ = 181.6, 161.1, 152.5, 146.0, 140.9, 139.4, 118.8, 116.5, 91.0, 57.4, 39.4 ppm; HRMS: m/z calculated for $C_{15}H_{13}I_2NO_4$ $[M + H]^+$ 525.9007, found 525.9008.

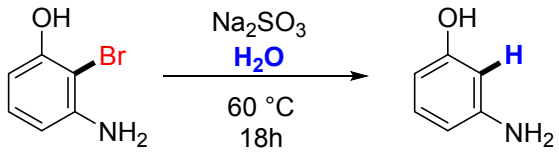
3-Aminophenol 39 (Table 2, entry 17)



Compound **39** was prepared according to the general procedure from 3-amino-4-bromophenol **18** (96 mg, 0.5 mmol) and sodium sulfite (630 mg, 5.0 mmol, 10.0 equivalents). The reaction mixture was heated on an oil bath at 60 °C for 18 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **39** as a white crystalline solid (52 mg, 96 %).

Melting point 118-120°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.80 (s, 1 H), 6.77 (t, *J* = 8.2 Hz, 1 H), 6.04 – 5.95 (m, 2 H), 5.95 – 5.84 (m, 1 H), 4.85 (s, 2 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.1, 149.9, 129.5, 105.4, 103.3, 101.0 ppm; HRMS: m/z calculated for C_6H_7NO $[M – H]^-$ 108.0444, found 108.0441.

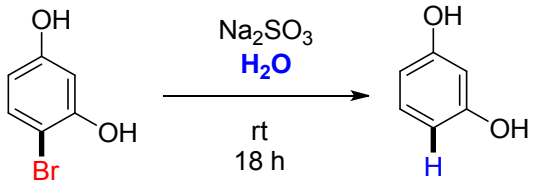
3-Aminophenol 39 (Table 2, entry 18)



Compound **39** was prepared according to the general procedure from 3-amino-2-bromophenol **19** (96 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was heated on an oil bath at 60 °C for 18 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **39** as a white crystalline solid (50 mg, 91 %).

Analytical data were in accordance with compound **39** obtained from 3-amino-4-bromophenol **18**.

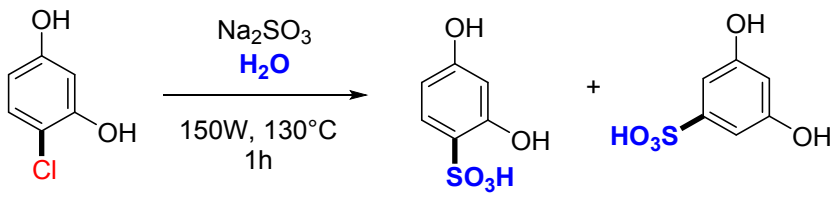
Resorcinol 40 (Table 2, entry 19)



Compound **40** was prepared according to the general procedure from 4-bromoresorcinol **20** (95 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was mixed for 18 hours at ambient temperature. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **40** as a pale brown crystalline solid (53 mg, 96%).

Melting point 101-103 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.14 (s, 2 H), 6.93 – 6.89 (m, 1 H), 6.21 – 6.17 (m, 3 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.0, 130.2, 106.7, 103.0 ppm; HRMS: m/z calculated for $C_6H_6O_2$ $[M - H]^-$ 109.0284, found 109.0282.

Mixture of sulfonic acids 41 and 42 (Table 2, entry 20)



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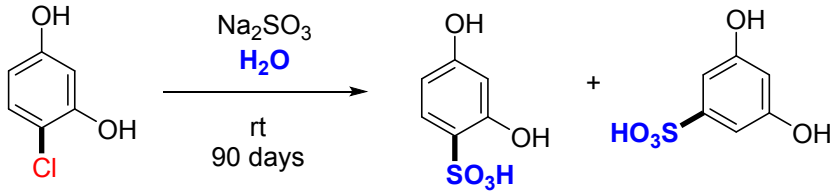
The mixture of sulfonic acids **41** and **42** was prepared according to the general procedure from 4-chlororesorcinol **21** (72 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 1 hour. Then, the solution was acidified with concentrated hydrochloric acid to pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds **41**/**42** (89:11) as a pale pink amorphous solid (76 mg, 73%).

The ratio of **41**/**42** was determined by ^{1}H NMR (the copy of the ^{1}H spectrum is provided in section 5).

Mixture of sulfonic acids 41 and 42 (Table 2, entry 21)

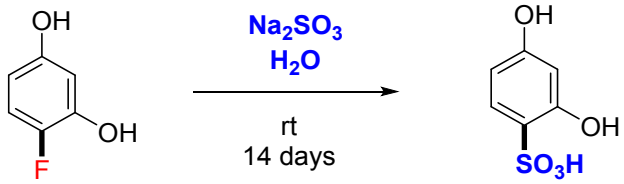


59 : 41

The mixture of sulfonic acids **41** and **42** was prepared according to the general procedure from 4-chlororesorcinol **21** (72 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was stirred at ambient temperature for 90 days. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds **41**/**42** (59:41) as a pale pink amorphous solid (85 mg, 82%).

The ratio of **41**/**42** was determined by ^{1}H NMR (the copy of the ^{1}H spectrum is provided in section 5).

2,4-Dihydroxybenzenesulfonic acid 41 (Table 2, entry 22)

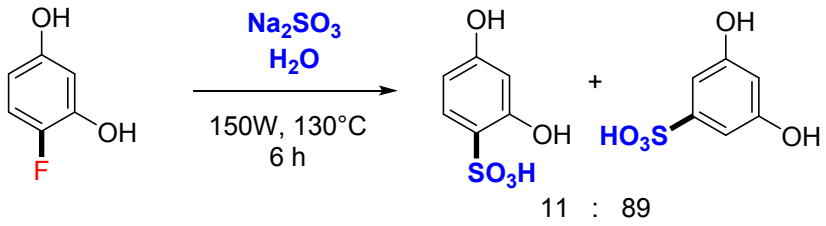


Compound **41** was prepared according to the general procedure from 4-fluoroesorcinol **22** (64 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was mixed at ambient temperature for 14 days. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by a filtration and washed with acetone (2 mL). The

filtrate was concentrated under reduced pressure to yield compound **41** as a white crystalline solid (86 mg, 83%).

Melting point 308-310°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.17 (d, *J* = 8.4 Hz, 1 H), 6.15 (dd, *J* = 8.4, 2.3 Hz, 1 H), 6.06 (d, *J* = 2.3 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 159.6, 154.7, 128.2, 122.4, 106.3, 102.2 ppm; HRMS: m/z calculated for $C_6H_6O_5S$ $[M - H]^-$ 188.9852, found 188.9855.

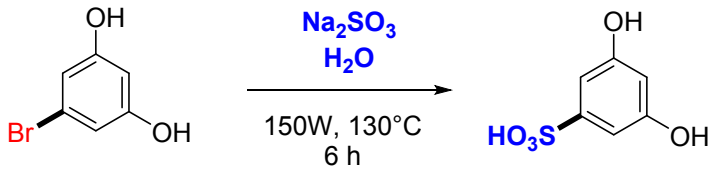
Mixture of sulfonic acids 41 and 42 (Table 2, entry 23)



The mixture of sulfonic acids **41** and **42** was prepared according to the general procedure from 4-fluoroesorcinol **22** (64 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 6 hours. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compounds **41**/**42** (11:89) as a pale yellow amorphous solid (95 mg, 91%).

The ratio of **41**/**42** was determined by ^{1}H NMR (the copy of the ^{1}H spectrum is provided in section 5).

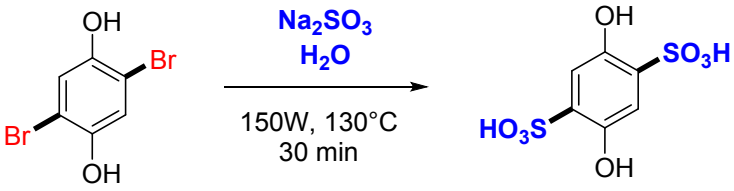
3,5-Dihydroxybenzenesulfonic acid 42 (Table 2, entry 24)



Compound **42** was prepared according to the general procedure from 5-bromoresorcinol **23** (64 mg, 0.5 mmol) and sodium sulfite (756 mg, 6.0 mmol, 12.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 6 hours. Then, the solution was acidified with concentrated hydrochloric acid pH ≈ 1 and freeze dried. The residue was treated with acetone (2 mL) at ambient temperature for 30 minutes. Precipitated solids were removed by filtration and washed with acetone (2 mL). The filtrate was concentrated under reduced pressure to yield compound **42** as a pale yellow crystalline solid (69 mg, 66%).

Melting point 286-288°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.26 (s, 2 H), 6.52 (d, *J* = 2.2 Hz, 2 H), 6.15 (t, *J* = 2.2 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.6, 149.6, 104.1, 102.7 ppm; HRMS: m/z calculated for $C_6H_6O_5S$ $[M-H]^-$ 188.9852, found 188.9854.

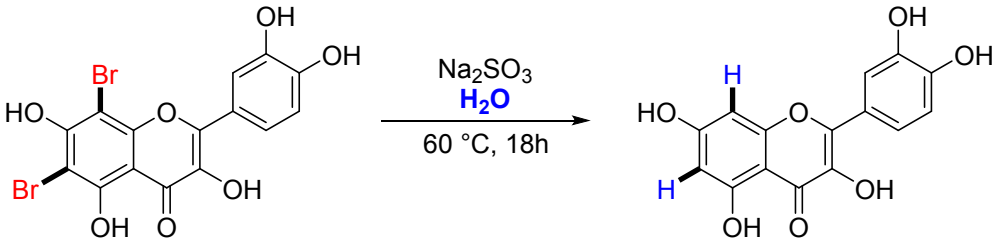
2,5-Dihydroxybenzene-1,4-disulfonic acid 43 (Table 2, entry 25)



Compound **43** was prepared according to the general procedure from 2,5-dibromobenzene-1,4-diol **24** (134 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130°C for 30 minutes. Then, the mixture was acidified with concentrated hydrochloric acid to pH ≈ 1 and stirred at room temperature overnight. The precipitate was filtered off and washed with water (1 mL) to yield compound **43** as a white crystalline solid (118 mg, 77%).

Melting point >360 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.77 (s, 2 H), 6.81 (s, 2 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 145.15, 132.88, 114.01 ppm; HRMS: m/z calculated for $C_6H_6O_8S_2$ [M – H]- 268.9431, found 268.9429.

Quercetin 44 (Table 2, entry 26)

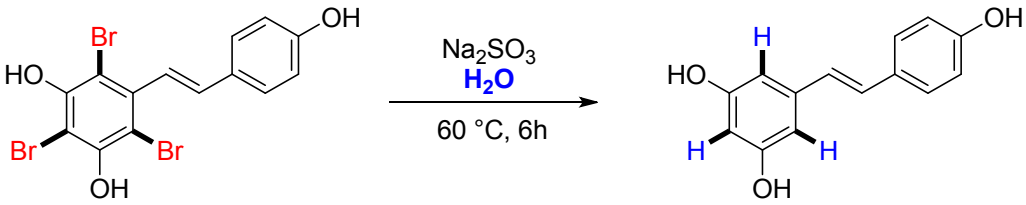


Compound **44** was prepared according to the general procedure from brominated Quercetin **25**[ref. 1] (114 mg, 0.25 mmol) and sodium sulfite (315 mg, 2.5 mmol, 10.0 equivalents) in water (5 mL). The reaction mixture was vigorously stirred on an oil bath at 60 °C for 18 hours. Then the mixture was cooled in ice water bath and acidified with concentrated hydrochloric acid to pH ≈ 1. The precipitated solid was collected by filtration, washed with water (2x2 mL), and dried under reduced pressure to yield Quercetin **44** as a yellow crystalline solid (66 mg, 87%).

Melting point 314-316 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.49 (s, 1 H), 10.77 (brs, 1 H), 9.51 (brs, 1 H), 9.36 (brs, 2 H), 7.68 (d, *J* = 2.3 Hz, 1 H), 7.54 (dd, *J* = 8.5, 2.3 Hz, 1 H), 6.88 (d, *J* = 8.5 Hz, 1

H), 6.40 (d, *J* = 2.0 Hz, 1 H), 6.18 (d, *J* = 2.0 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 175.9, 163.9, 160.7, 156.2, 147.7, 146.8, 145.1, 135.8, 122.0, 120.0, 115.6, 115.1, 103.0, 98.2, 93.4 ppm; HRMS: m/z calculated for $C_{15}H_{10}O_7$ $[M - H]^-$ 301.0354, found 301.0356.

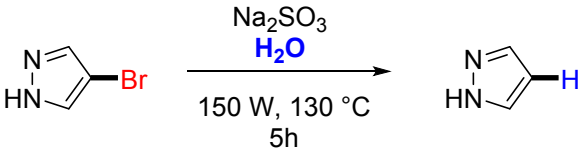
Resveratrol 45 (Table 2, entry 27)



Compound **45** was prepared according to the general procedure from brominated Resveratrol **26**[ref. 2] (116 mg, 0.25 mmol) and sodium sulfite (473 mg, 3.75 mmol, 15.0 equivalents) in water (5 mL). The reaction mixture was vigorously stirred on an oil bath at 60 °C for 6 hours. Then the mixture was cooled on an ice water bath and acidified with concentrated hydrochloric acid to pH ≈ 1. The precipitated solid was collected by filtration, washed with water (2x2 mL), and dried under reduced pressure to yield Resveratrol **45** as a white crystalline solid (51 mg, 90%).

Melting point 255-256 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.54 (s, 1 H), 9.19 (s, 1 H), 7.39 (d, *J* = 8.4 Hz, 2 H), 6.93 (d, *J* = 16.1 Hz, 1 H), 6.81 (d, *J* = 16.1 Hz, 1 H), 6.75 (d, *J* = 8.4 Hz, 2 H), 6.38 (d, *J* = 2.0 Hz, 2 H), 6.11 (t, *J* = 2.0 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 158.5, 157.2, 139.3, 128.1, 127.9, 125.7, 115.5, 104.3, 101.8 ppm; HRMS: m/z calculated for $C_{14}H_{12}O_3$ $[M - H]^-$ 227.0703, found 227.0706.

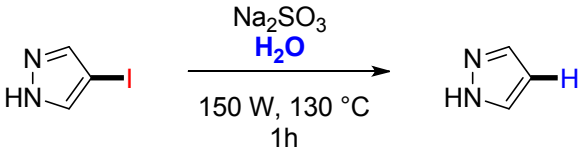
1*H*-Pyrazole 60 (Table 3, entry 1)



Compound **60** was prepared according to the general procedure from 4-bromo-1*H*-pyrazole **46** (73 mg, 0.5 mmol) and sodium sulfite (504 mg, 4.0 mmol, 8.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 5 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **60** as a white crystalline solid (31 mg, 91%).

Melting point 67-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.02 (s, 1 H), 7.64 (d, *J* = 2.1 Hz, 2 H), 6.36 (t, *J* = 2.1 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.7, 104.9 ppm; HRMS: m/z calculated for $C_3H_4N_2$ $[M + H]^+$ 69.0453, found 69.0452.

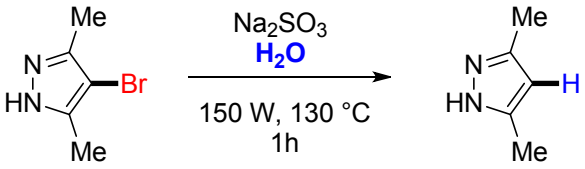
1*H*-Pyrazole 60 (Table 3, entry 2)



Compound **60** was prepared according to the general procedure from 4-iodo-1*H*-pyrazole **47** (97 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **60** as a white crystalline solid (32 mg, 94%).

Analytical data are in accordance with the compound **60** obtained from 4-bromo-1*H*-pyrazole **46**.

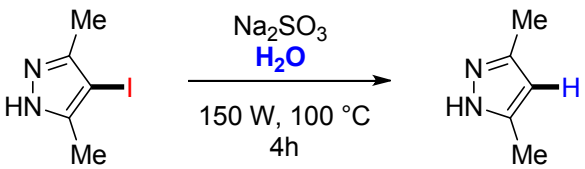
3,5-Dimethyl-1*H*-pyrazole 61 (Table 3, entry 3)



Compound **61** was prepared according to the general procedure from 4-bromo-3,5-Dimethyl-1*H*-pyrazole **48** (88 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **61** as a white crystalline solid (43 mg, 90%).

Melting point 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.20 (s, 1 H), 5.82 (s, 1 H), 2.28 (s, 6 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.3, 104.0, 12.2 ppm; HRMS: m/z calculated for $C_5H_8N_2$ $[M + H]^+$ 97.0760, found 97.0760.

3,5-Dimethyl-1*H*-pyrazole 61 (Table 3, entry 4)

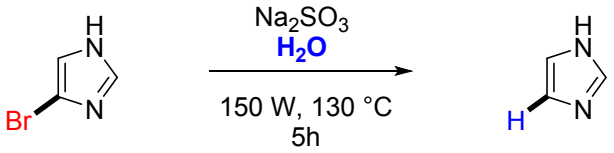


Compound **61** was prepared according to the general procedure from 4-iodo-3,5-dimethyl-1*H*-pyrazole **49** (111 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction

mixture was irradiated with the microwave reactor at 100 °C for 4 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **61** as a white crystalline solid (44 mg, 92%).

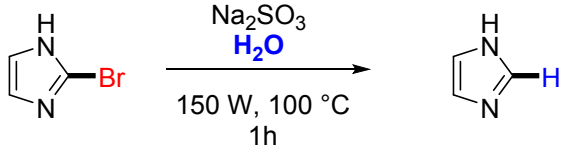
Analytical data are in accordance with compound **61** obtained from 4-bromo-3,5-dimethyl-1*H*-pyrazole **48.**

1*H*-Imidazole 63 (Table 3, entry 6)



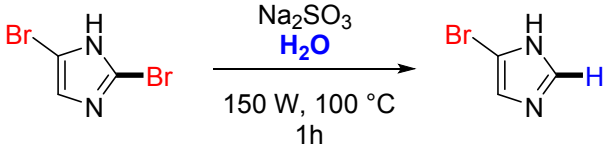
Compound **63** was prepared according to the general procedure from 4-bromo-1*H*-imidazole **51** (73 mg, 0.5 mmol) and sodium sulfite (504 mg, 4.0 mmol, 8.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 5 hours. The product was not extracted due to its high water solubility. The yield was determined by a quantitative ^{1}H NMR using dimethyl sulfone as an internal standard. Compound **63** was obtained in the 84% NMR yield together with the two minor impurities.

1*H*-Imidazole 63 (Table 3, entry 7)



Compound **63** was prepared according to the general procedure from 2-bromo-1*H*-imidazole **52** (73 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 1 hour. The product was not extracted due to its high water solubility. The yield was determined by a quantitative ^{1}H NMR using dimethyl sulfone as an internal standard. Compound **63** was obtained in the 97% NMR yield.

4-Bromo-1*H*-imidazole 51 (Table 3, entry 8)

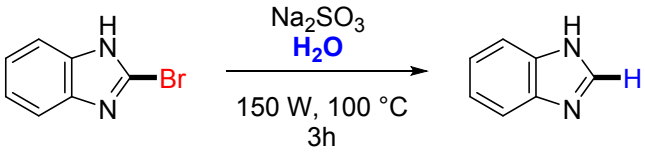


Compound **51** was prepared from 2,4-dibromo-1*H*-imidazole **53** (113 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave

reactor at 100 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **51** as a white amorphous solid (52 mg, 71%).

Melting point 130 – 132 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.42 (brs, 1 H), 7.63 (d, *J* = 1.2 Hz, 1 H), 7.25 (d, *J* = 1.2 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 135.9, 115.7, 113.5 ppm; HRMS: m/z calculated for $C_3H_3BrN_2$ $[M - H]^-$ 144.9396 and 146.9375, found 144.9392 and 146.9370.

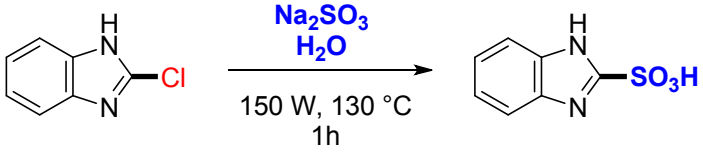
1*H*-Benzo[*d*]imidazole 64 (Table 3, entry 9)



Compound **64** was prepared according to the general procedure from 2-bromo-1*H*-benzo[*d*]imidazole **54** (99 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **64** as a white crystalline solid (54 mg, 92%).

Melting point 169-170 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.42 (s, 1 H), 8.20 (s, 1 H), 7.56 – 7.57 (m, 2 H), 7.20 – 7.16 (m, 2 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 142.0, 138.1, 121.7, 115.3 ppm; HRMS: m/z calculated for $C_7H_6N_2$ $[M - H]^-$ 117.0447, found 117.0445.

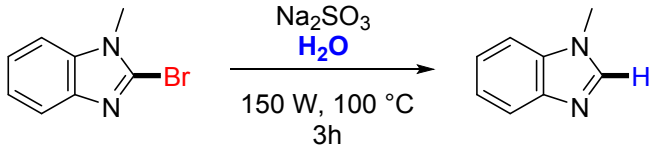
1*H*-Benzo[*d*]imidazole-2-sulfonic acid 65 (Table 3, entry 10)



Compound **65** was prepared according to the general procedure from 2-chloro-1*H*-benzo[*d*]imidazole **55** (76 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Then, the solution was acidified with concentrated hydrochloric acid to pH ≈ 1. The resulting white suspension was stirred at ambient temperature for 4h. After that, the white precipitate was collected by filtration, washed with water (1 mL), and dried under stream of nitrogen for 4h to yield compound **65** as a white crystalline solid (93 mg, 94%).

Melting point > 360 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.75 – 7.70 (m, 2 H), 7.60 – 7.56 (m, 2 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 152.8, 130.6, 126.6, 114.7 ppm; HRMS: m/z calculated for $C_7H_6N_2O_3S$ $[M - H]^-$ 197.0015, found 197.0012.

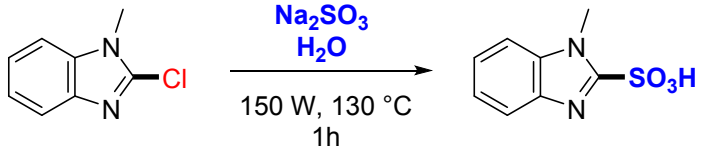
1-Methyl-1*H*-benzo[*d*]imidazole 66 (Table 3, entry 11)



Compound **66** was prepared according to the general procedure from 2-bromo-1-methyl-1*H*-benzo[*d*]imidazole **56** (105 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100 °C for 3 hours. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **64** as a colorless amorphous solid (45 mg, 68%).

Melting point 60-62 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (s, 1 H), 7.83 – 7.80 (m, 1 H), 7.43 – 7.39 (m, 1 H), 7.36 – 7.28 (m, 2 H), 3.86 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.7, 143.6, 134.6, 123.0, 122.2, 120.3, 109.4, 31.1 ppm; HMRS: m/z calculated for $C_8H_8N_2$ 133.0760, found 133.0761.

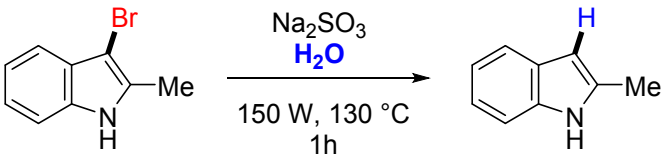
1-Methyl-1*H*-benzo[*d*]imidazole-2-sulfonic acid 67 (Table 3, entry 12)



Compound **67** was prepared according to the general procedure from 2-chloro-1-methyl-1*H*-benzo[*d*]imidazole **57** (83 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Then the mixture was diluted with 10% aqueous Na_2CO_3 (10 mL) and washed with EtOAc (3x5 mL). The aqueous layer was acidified with concentrated hydrochloric acid to pH ≈ 1. The precipitated solid was collected by filtration, washed with water (3x2 mL), and dried under stream of nitrogen to yield compound **67** as a white amorphous solid (65 mg, 61%).

Melting point 328 – 330 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.99 – 7.96 (m, 1 H), 7.75 – 7.72 (m, 1 H), 7.68 – 7.60 (m, 2 H), 4.18 (s, 3 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 151.6, 132.7, 129.0, 127.1, 126.7, 114.9, 113.6, 32.2 ppm; HRMS: m/z calculated for $C_8H_8N_2O_3S$ $[M - H]^-$ 213.0328, found 213.0329.

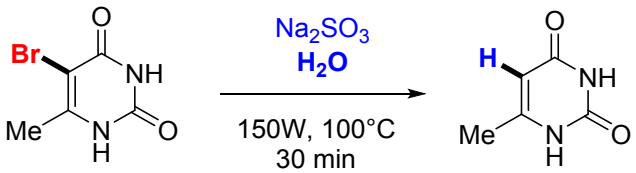
2-Methyl-1*H*-indole 68 (Table 3, entry 13)



Compound **68** was prepared according to the general procedure from 3-bromo-2-methyl-1*H*-indole **58** (104 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 130 °C for 1 hour. Extraction to EtOAc (3x5 mL), drying over anhydrous $MgSO_4$, and evaporation under reduced pressure yielded compound **68** as a colorless amorphous solid (60 mg, 92%).

Melting point 56-58 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 10.86 (s, 1 H), 7.37 (d, *J* = 7.7 Hz, 1 H), 7.25 (dd, *J* = 7.7, 1.1 Hz, 1 H), 6.96 (ddd, *J* = 7.7, 7.3, 1.1 Hz, 1 H), 6.90 (ddd, *J* = 7.7, 7.3, 1.1 Hz, 1 H), 6.10 – 6.08 (m, 1 H), 2.37 (d, *J* = 0.9 Hz, 3 H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ = 136.1, 135.5, 128.7, 119.9, 118.9, 118.6, 110.5, 99.0, 13.4 ppm; HRMS: m/z calculated for C_9H_9N $[M + H]^+$ 132.0808, found 132.0809.

6-Methylpyrimidine-2,4(1*H*,3*H*)-dione 69 (Table 3, entry 14)

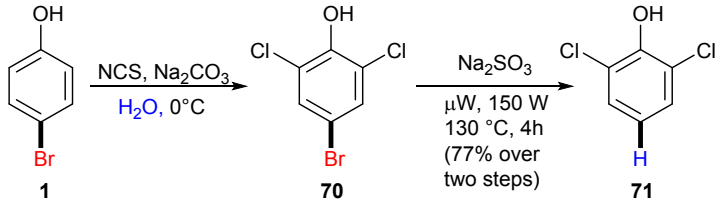


Compound **69** was prepared according to the general procedure from 5-bromo-6-methylpyrimidine-2,4(1*H*,3*H*)-dione **59** (102 mg, 0.5 mmol) and sodium sulfite (252 mg, 2.0 mmol, 4.0 equivalents). The reaction mixture was irradiated with the microwave reactor at 100°C for 30 minutes. After cooling on an ice bath, the white solid was collected by filtration and washed with water (1 mL) to yield compound **69** as a white crystalline solid (50 mg, 80%).

Melting point 272-274 °C (decomp.); ^{1}H NMR (400 MHz, DMSO-d_6) δ = 10.82 (s, 2 H), 5.31 (s, 1 H), 2.00 (s, 3 H) ppm; ^{13}C NMR (101 MHz, DMSO-d_6) δ = 164.11, 152.88, 151.57, 98.72, 18.22 ppm; HRMS: m/z calculated for $C_5H_6N_2O_2$ $[M – H]^-$ 125.0346, found 125.0343.

6. One-pot chlorination/debromination:

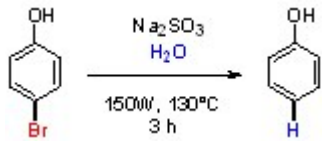
2,6-Dichlorophenol 71

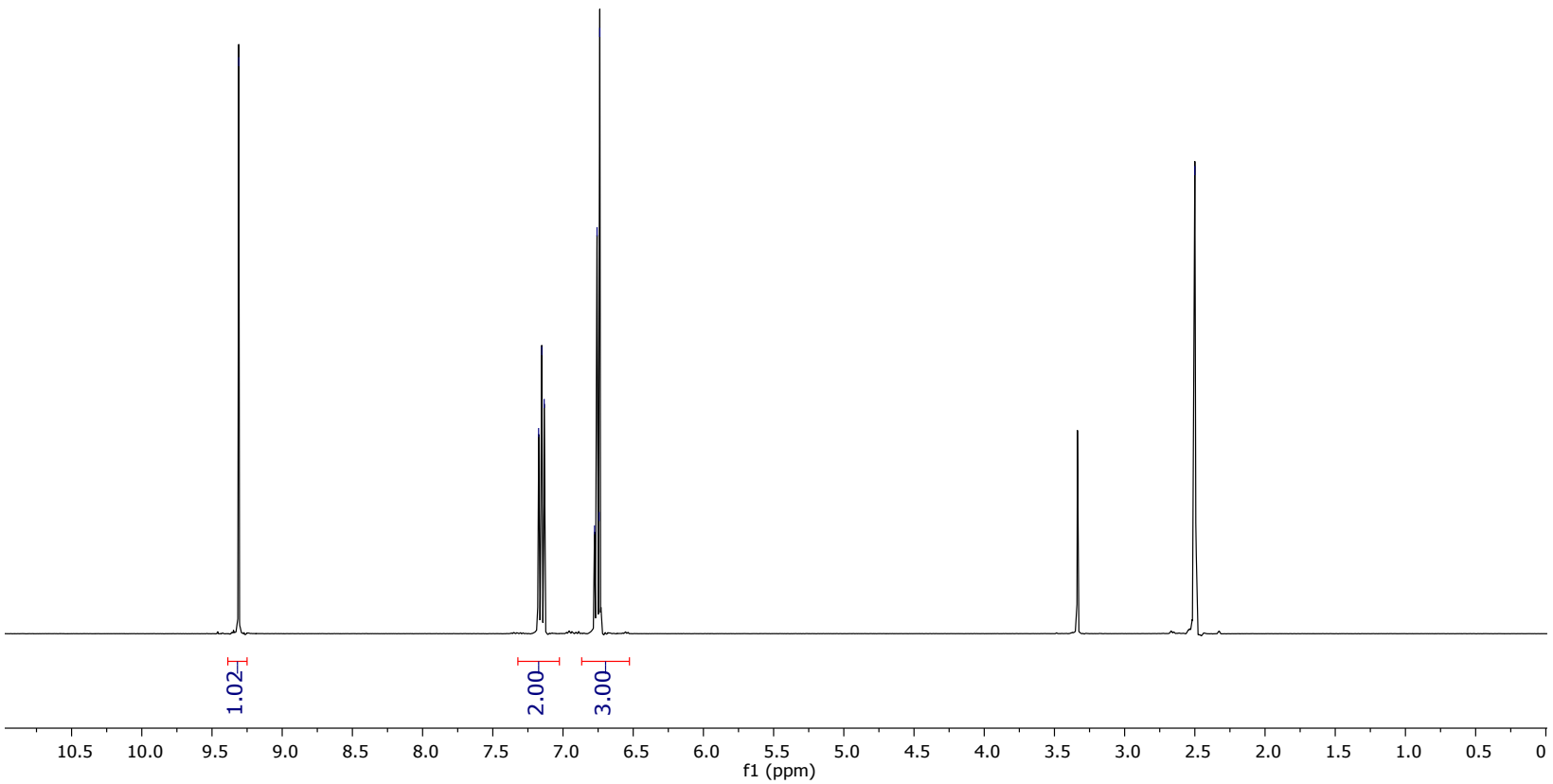


A 10 mL microwave reaction vessel equipped with a magnetic stir bar was charged with 4-bromophenol (87 mg, 0.5 mmol), sodium carbonate (106 mg, 1.0 mmol, 2.0 eq.), and water (2.5 mL). The mixture was vigorously stirred until both reagents dissolved, forming a pale red (or pink) solution. The reaction mixture was cooled to 0 °C using an ice-water bath and freshly crystalized *N*-chlorosuccinimide (168 mg, 1.25 mmol, 2.5 equiv.) was added in several portions. The reaction mixture was vigorously stirred at 0 °C for 90 minutes. After that time, anhydrous sodium sulfite (630 mg, 5.0 mmol, 10.0 equivalents) was added and the vessel was removed from the ice-water bath, flushed with argon, sealed with disposable silicon cap, and inserted into the CEM Discover SP microwave synthesizer. The content of the flask was premixed at high stirring speed for one minute, and then irradiated at the maximum power of 150 W with simultaneous cooling (compressed air, 24 psi). The power input was automatically adjusted in order to hold the reaction temperature at 130 °C for 4h. After that time, the HPLC showed complete consumption of intermediate 4-bromo-2,6-dichlorophenol **70**. Finally, the reaction mixture was extracted with EtOAC (3x5 mL), dried over anhydrous magnesium sulfate, and evaporated under reduced pressure to yield 2,6-dichlorophenol **71** as a colorless oil, which formed colorless needles upon standing (63 mg, 77% over two steps).

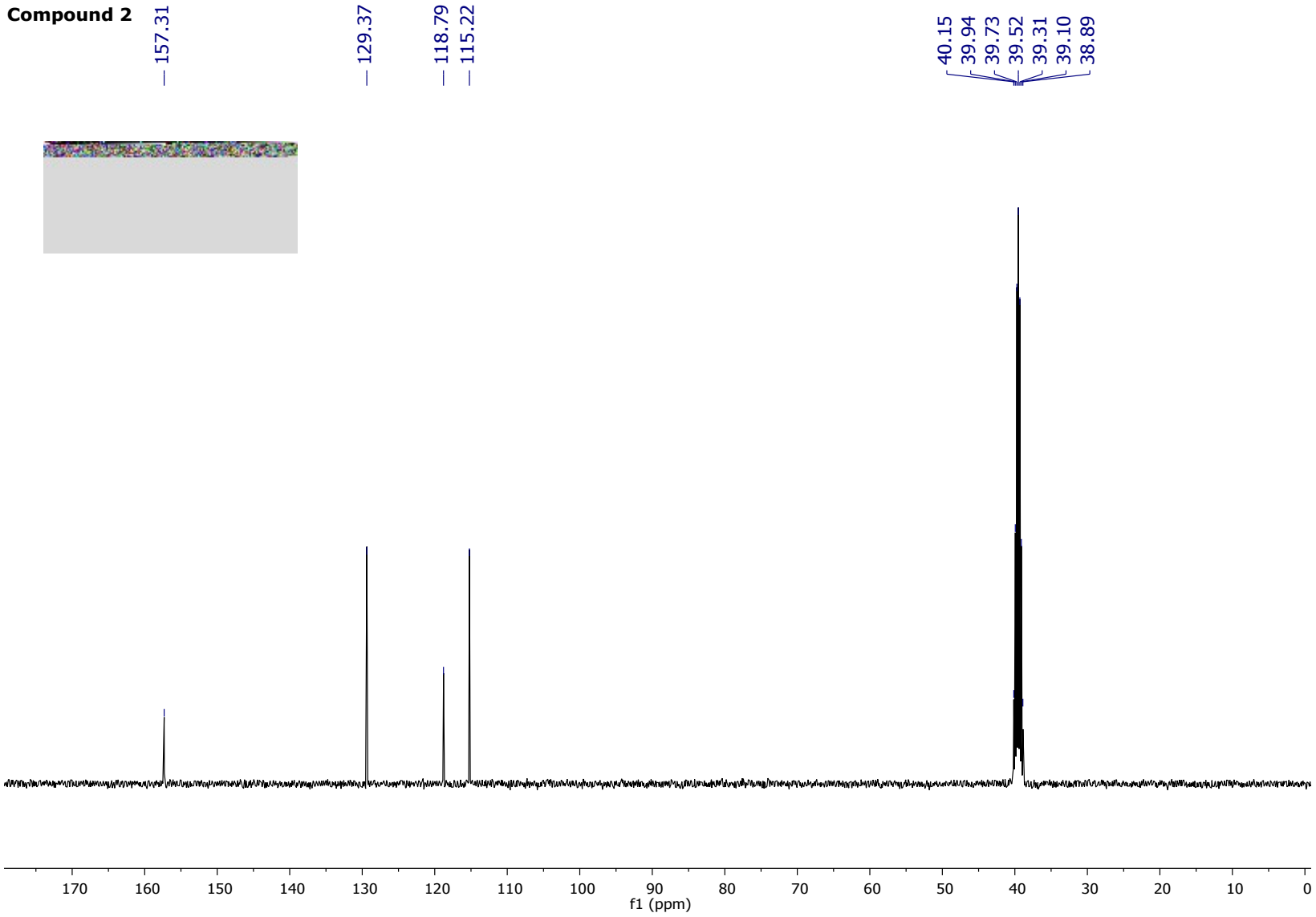
Melting point 63-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 8.2 Hz, 2 H), 6.82 (t, *J* = 8.2 Hz, 1 H), 5.85 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.0, 128.4, 121.3, 121.2 ppm; HRMS: m/z calculated for $C_6H_4Cl_2O$ $[M - H]^-$ 160.9555 and 162.9526, found 160.9555 and 162.9527.

Compound 2

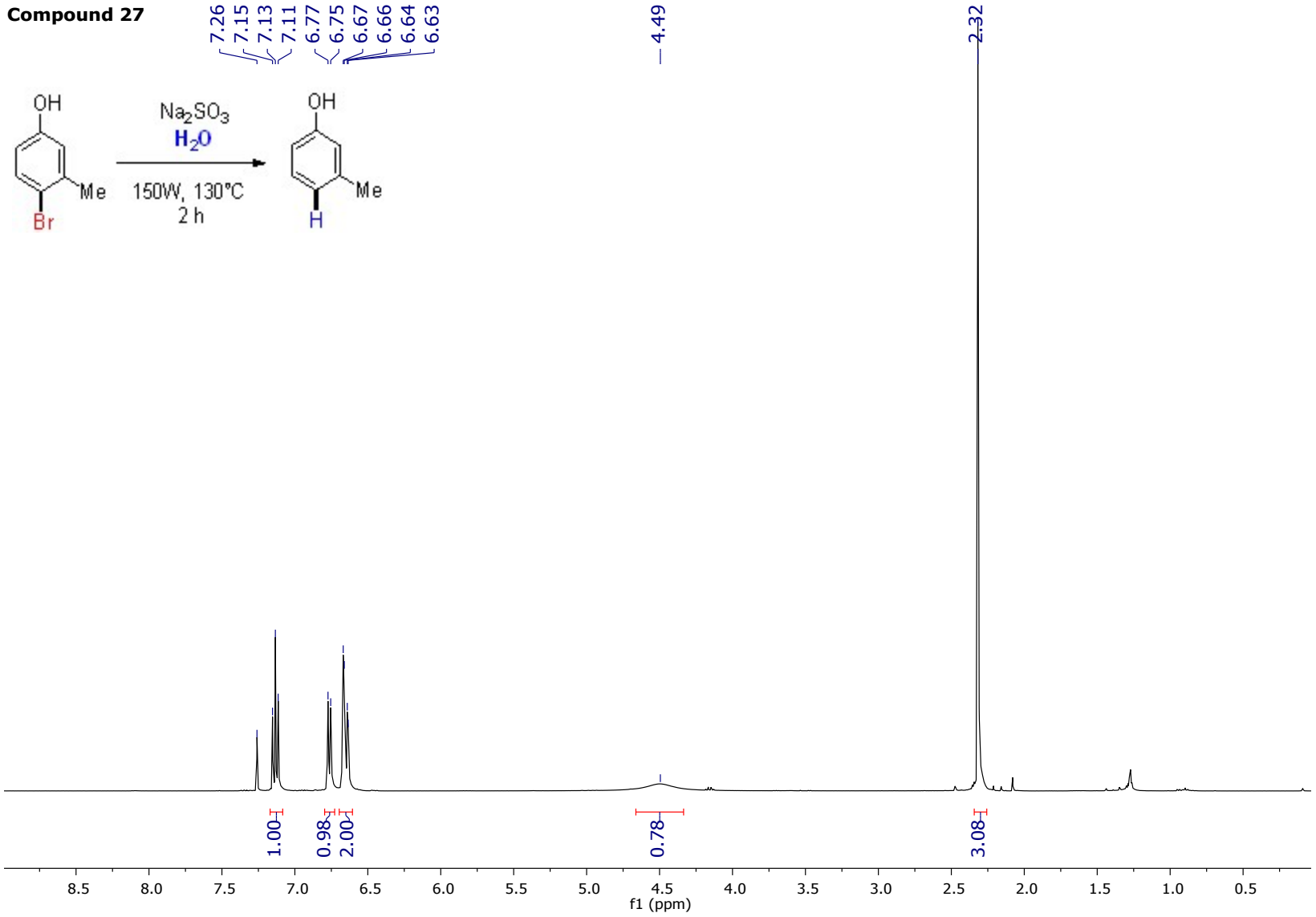

OH
Br
Na_2SO_3
H_2O
150W, 130°C
3 h
OH
H


9.31
7.17
7.15
7.13
6.78
6.76
6.74
6.74
2.50
1.02
2.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

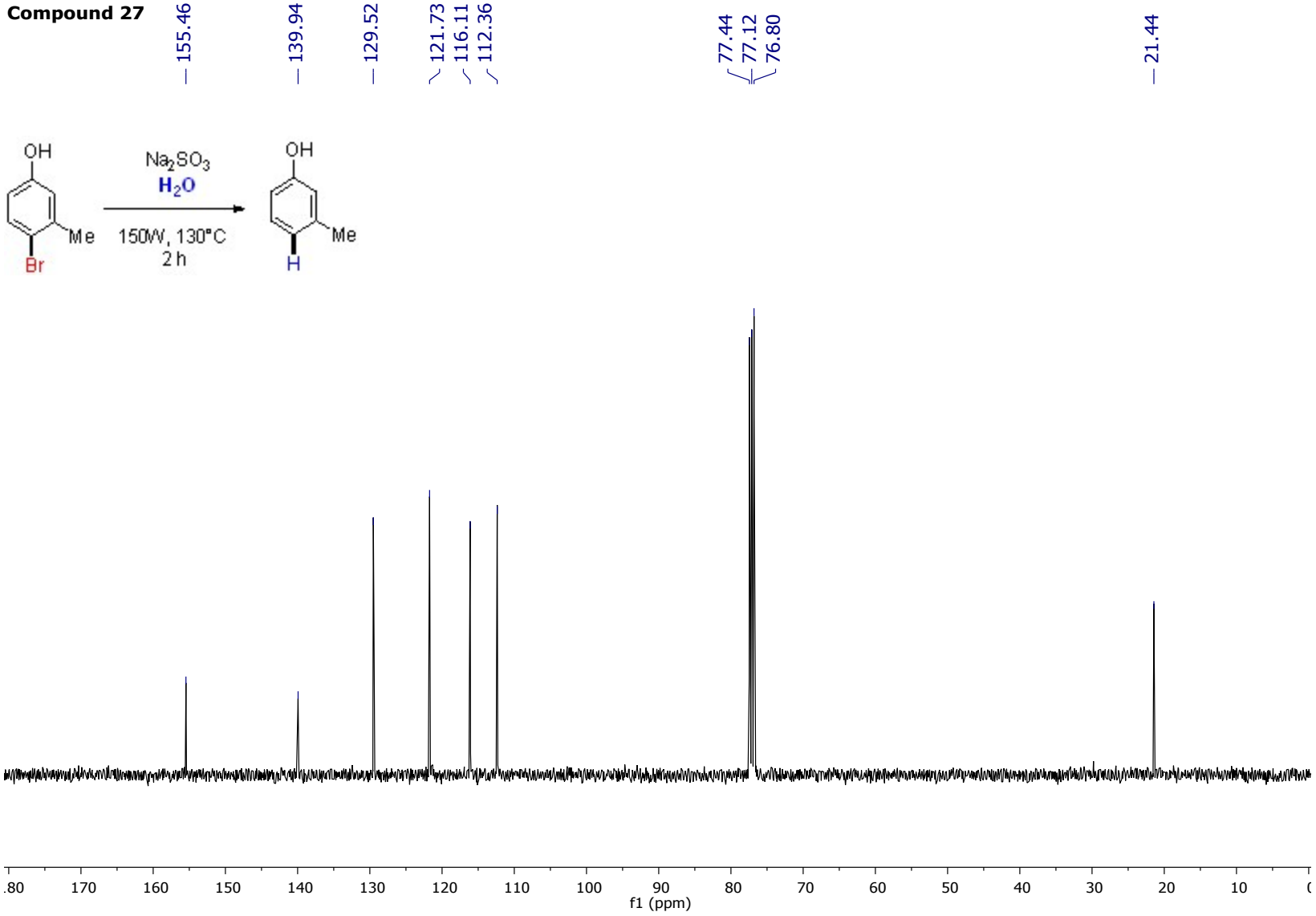
Compound 2


157.31
129.37
118.79
115.22
40.15
39.94
39.73
39.52
39.31
39.10
38.89
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

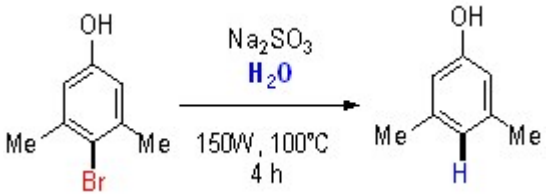
Compound 27


7.26
7.15
7.13
7.11
6.77
6.75
6.67
6.66
6.64
6.63
4.49
2.32
OH
Me
Br
Na_2SO_3
H_2O
150W, 130°C
2 h
OH
Me
H
1.00
0.98
2.00
0.78
3.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

Compound 27

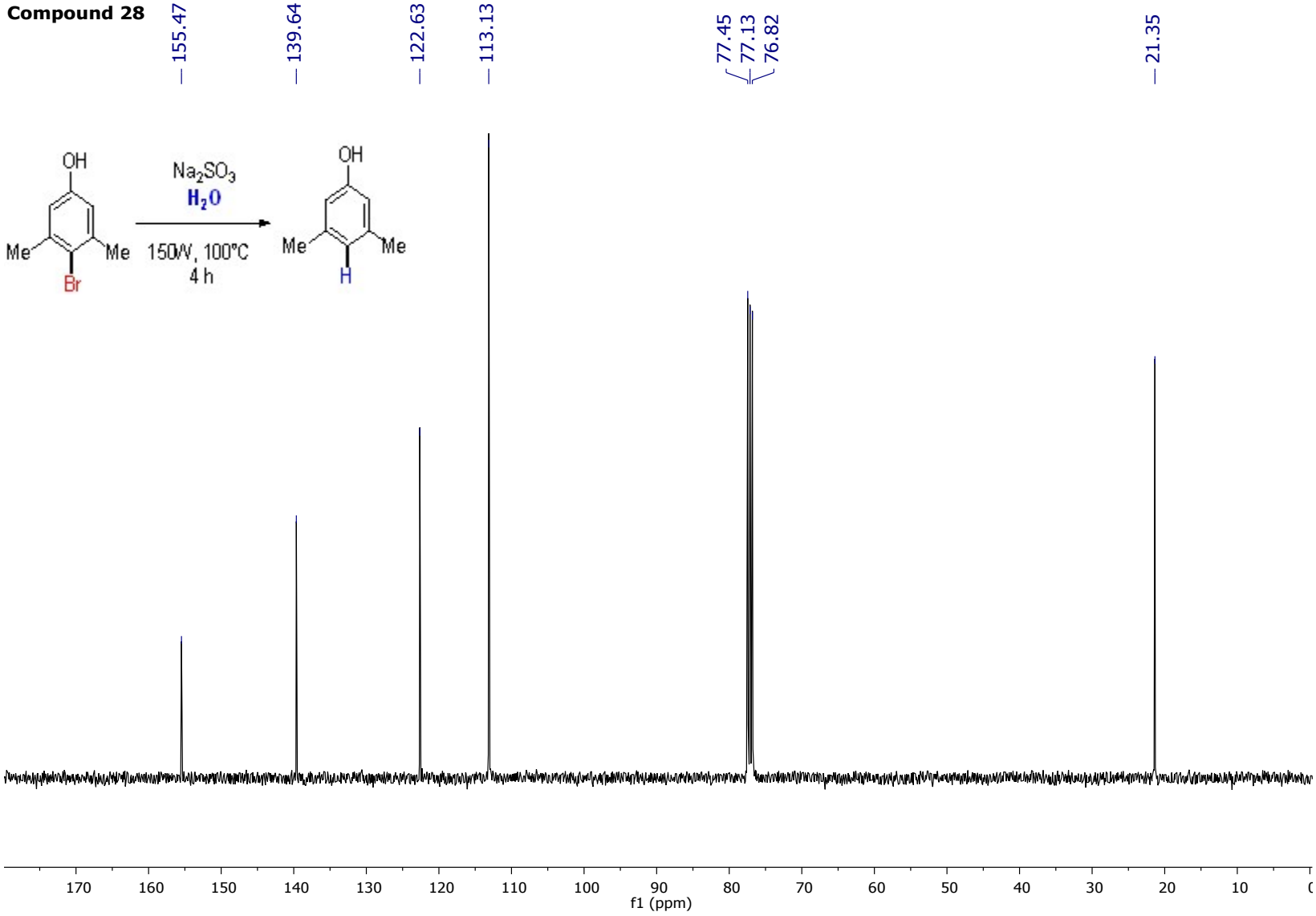

155.46
139.94
129.52
121.73
116.11
112.36
77.44
77.12
76.80
21.44
OH
Me
Br
Na_2SO_3
H_2O
150W, 130°C
2 h
OH
Me
H
f1 (ppm)

Compound 28

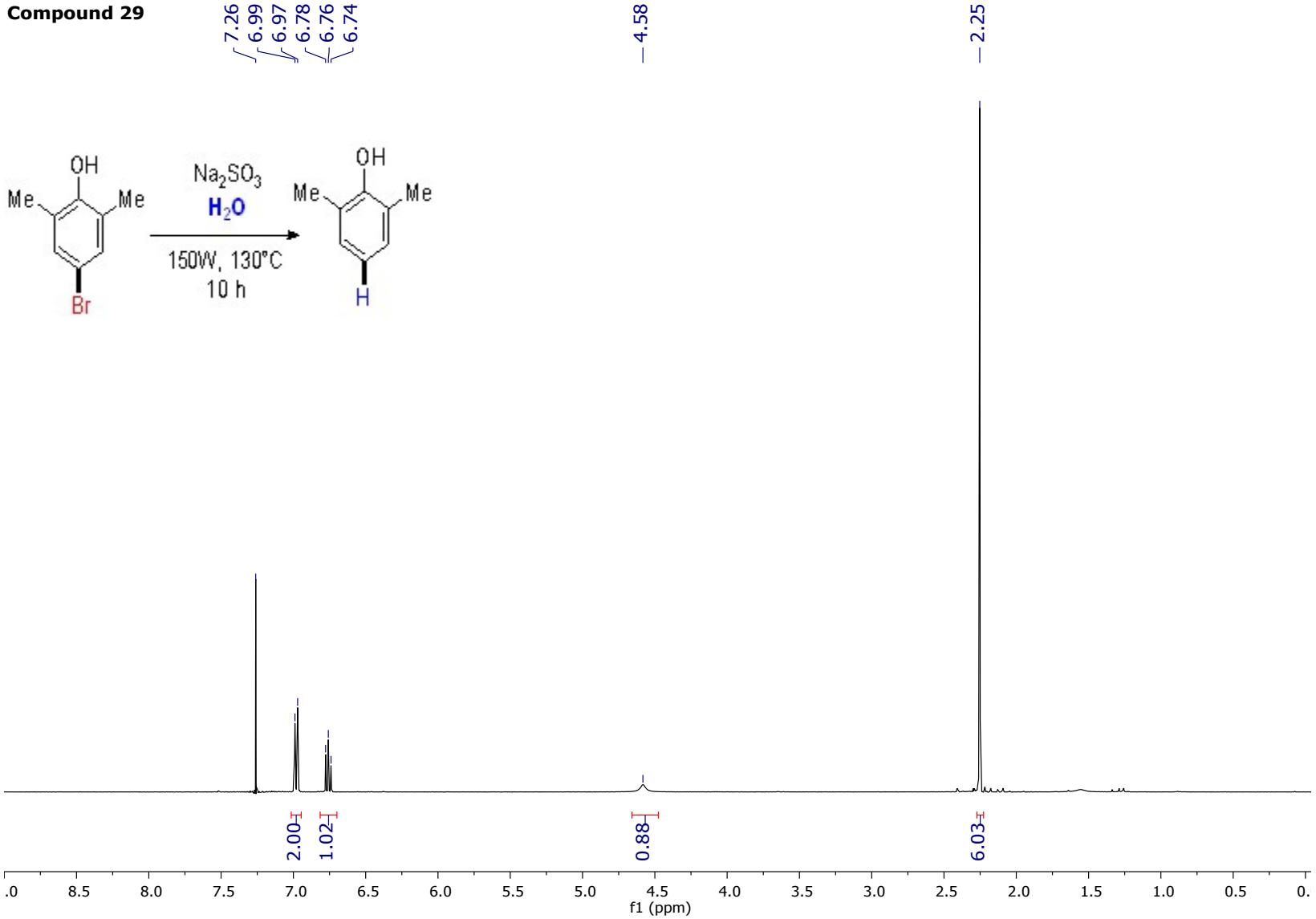

OH
Me
Me
Br
Na_2SO_3
H_2O
150W, 100°C
4 h
OH
Me
Me
H

7.26
6.59
6.48
5.00
2.27
1.00
2.00
0.97
6.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

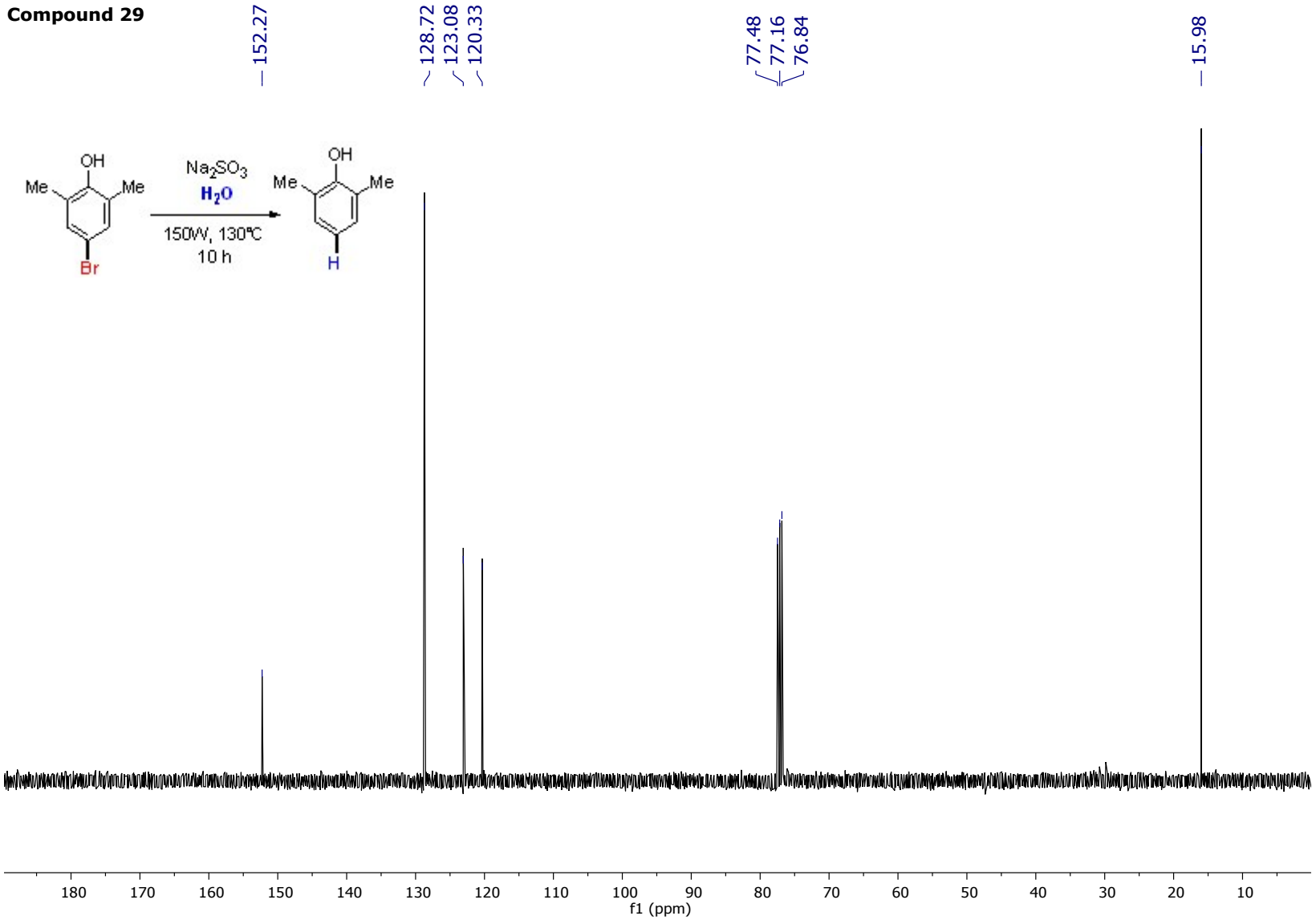
Compound 28


155.47
139.64
122.63
113.13
77.45
77.13
76.82
21.35
OH
Me
Me
Br
Na2SO3
H2O
150W, 100°C
4 h
OH
Me
Me
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

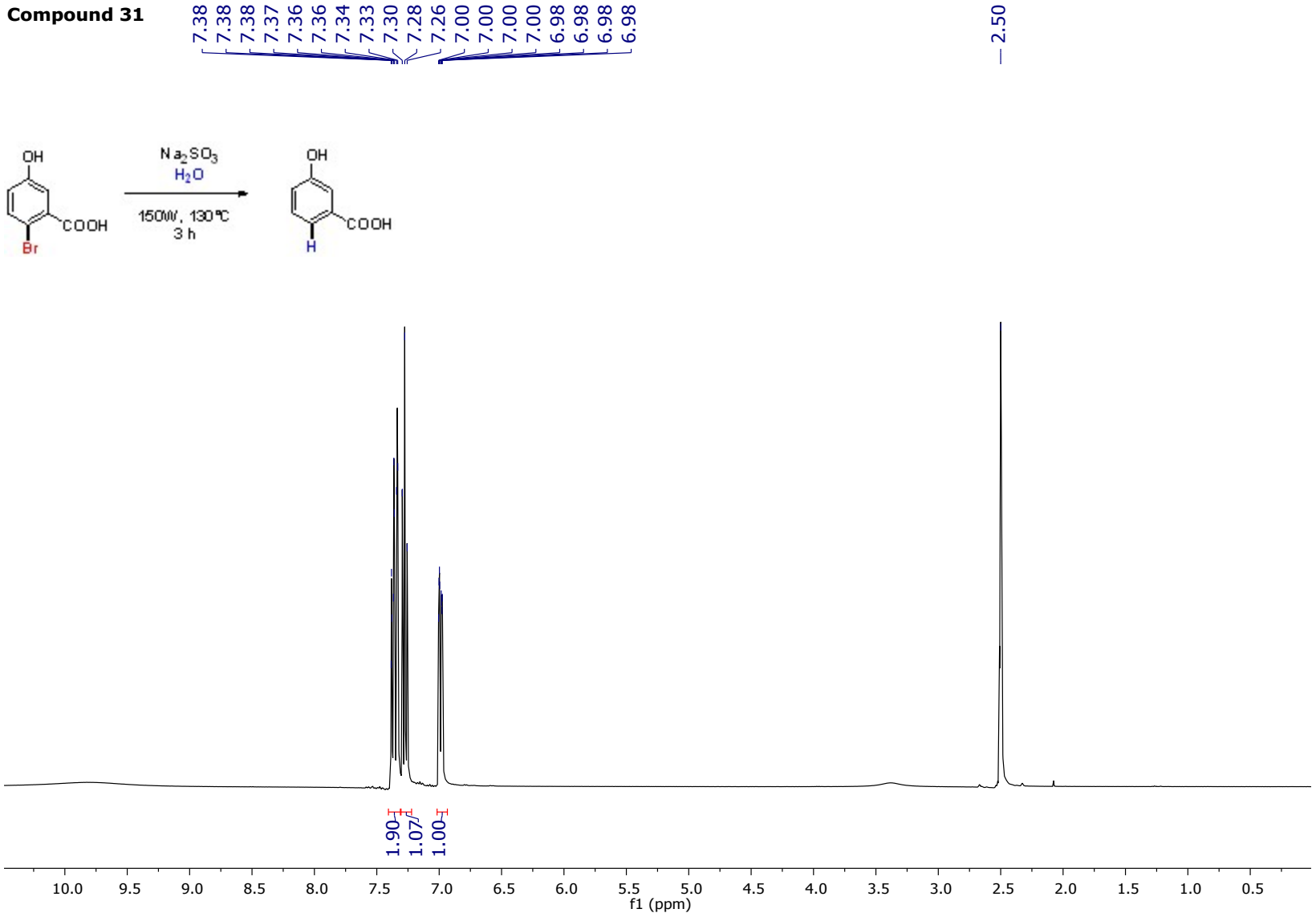
Compound 29

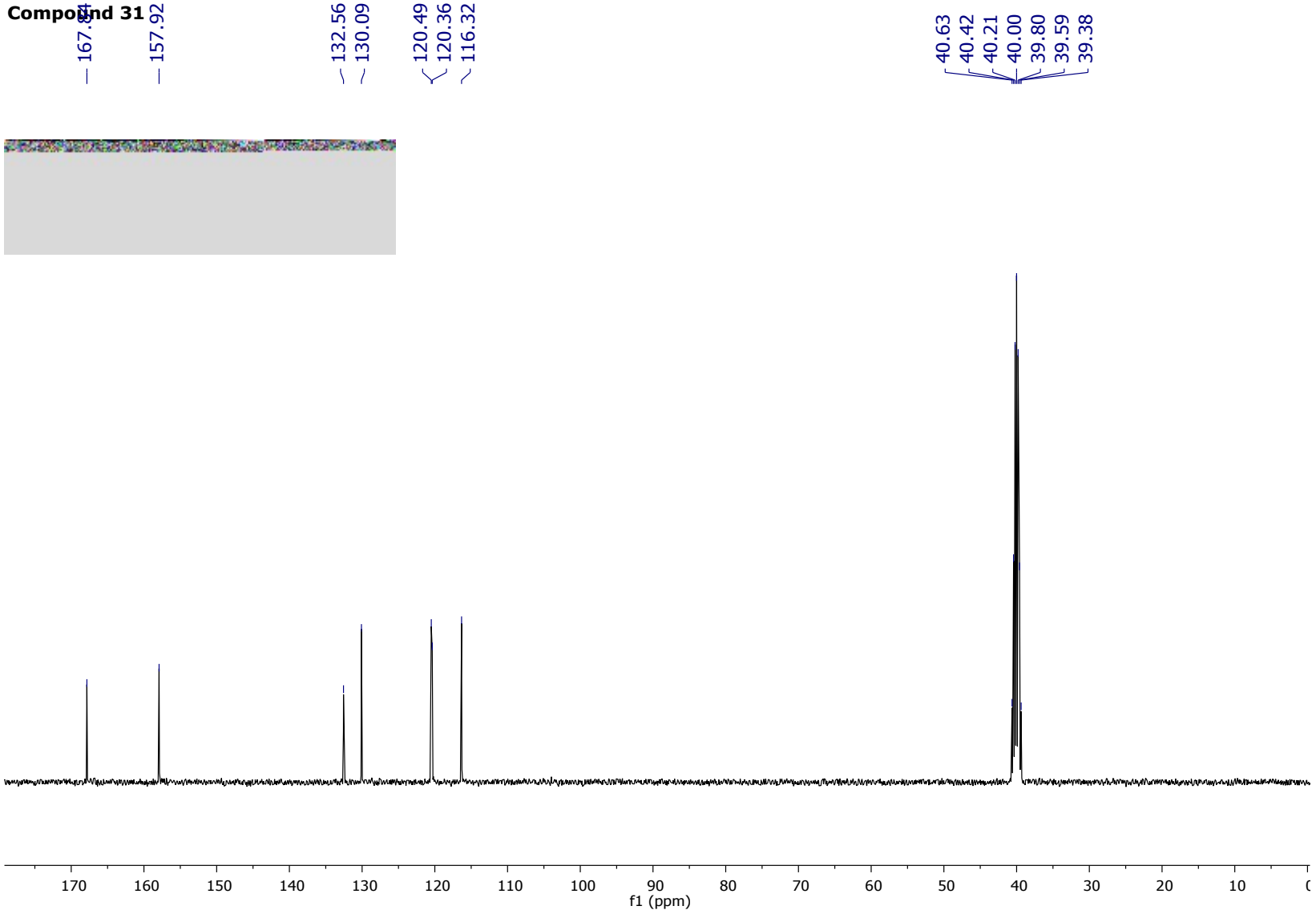

7.26
6.99
6.97
6.78
6.76
6.74
4.58
2.25
OH
Me
Me
Br
Na_2SO_3
H_2O
150W, 130°C
10 h
OH
Me
Me
H
2.00
1.02
0.88
6.03
f1 (ppm)

Compound 29

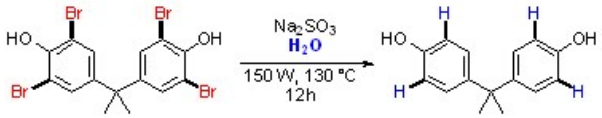

152.27
128.72
123.08
120.33
77.48
77.16
76.84
15.98
OH
Me
Me
Br
Na2SO3
H2O
150W, 130℃
10 h
OH
Me
Me
H
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Compound 31

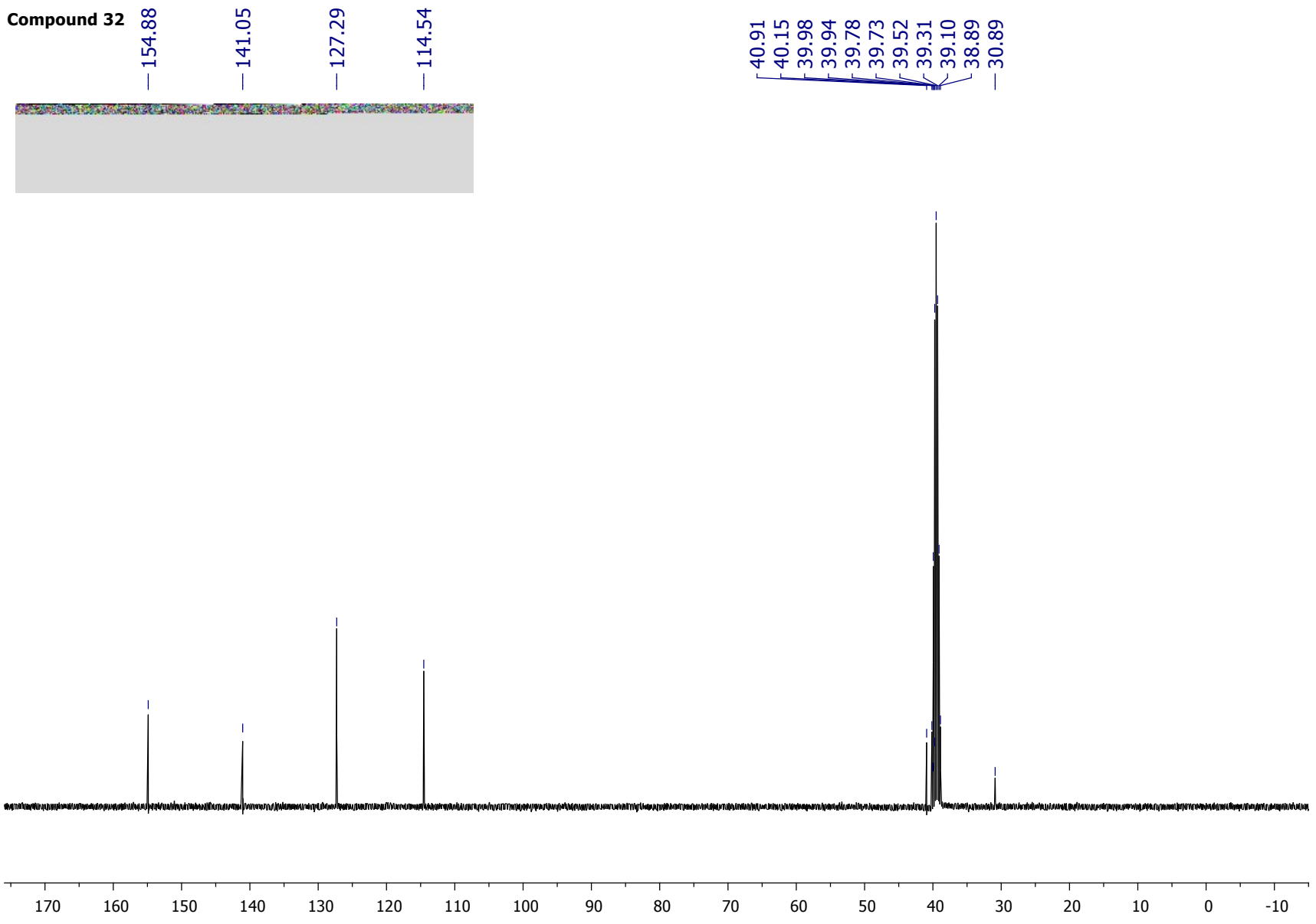

7.38
7.38
7.38
7.37
7.36
7.36
7.34
7.33
7.30
7.28
7.26
7.00
7.00
7.00
7.00
6.98
6.98
6.98
6.98
2.50
OH
COOH
Br
Na2SO3
H2O
150W, 130°C
3 h
OH
COOH
H
1.90
1.07
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


Compound 31
167.84
157.92
132.56
130.09
120.49
120.36
116.32
40.63
40.42
40.21
40.00
39.80
39.59
39.38
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

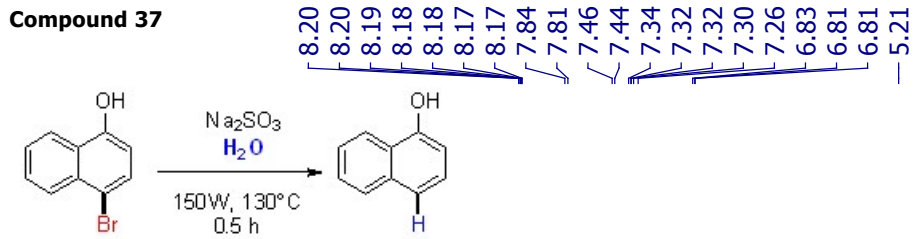
Compound 32

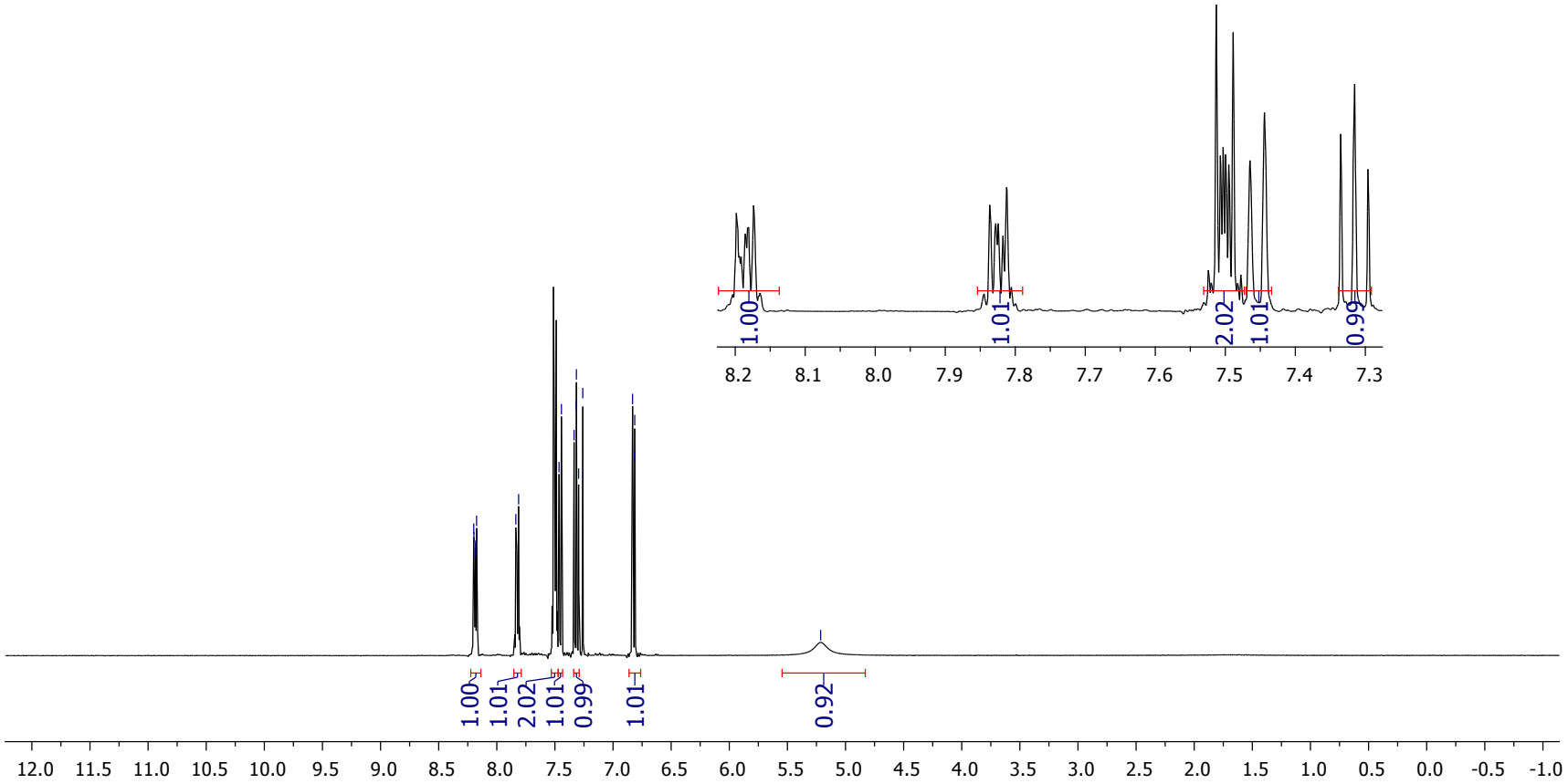

Br
Br
HO
OH
Br
Br
Na2SO3
H2O
150 W, 130 °C
12h
H
H
HO
OH
H
H

9.13
6.98
6.96
6.64
6.62
3.34
2.50
2.50
2.50
1.52
2.08
3.93
4.00
6.08
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4


Compound 32
154.88
141.05
127.29
114.54
40.91
40.15
39.98
39.94
39.78
39.73
39.52
39.31
39.10
38.89
30.89
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

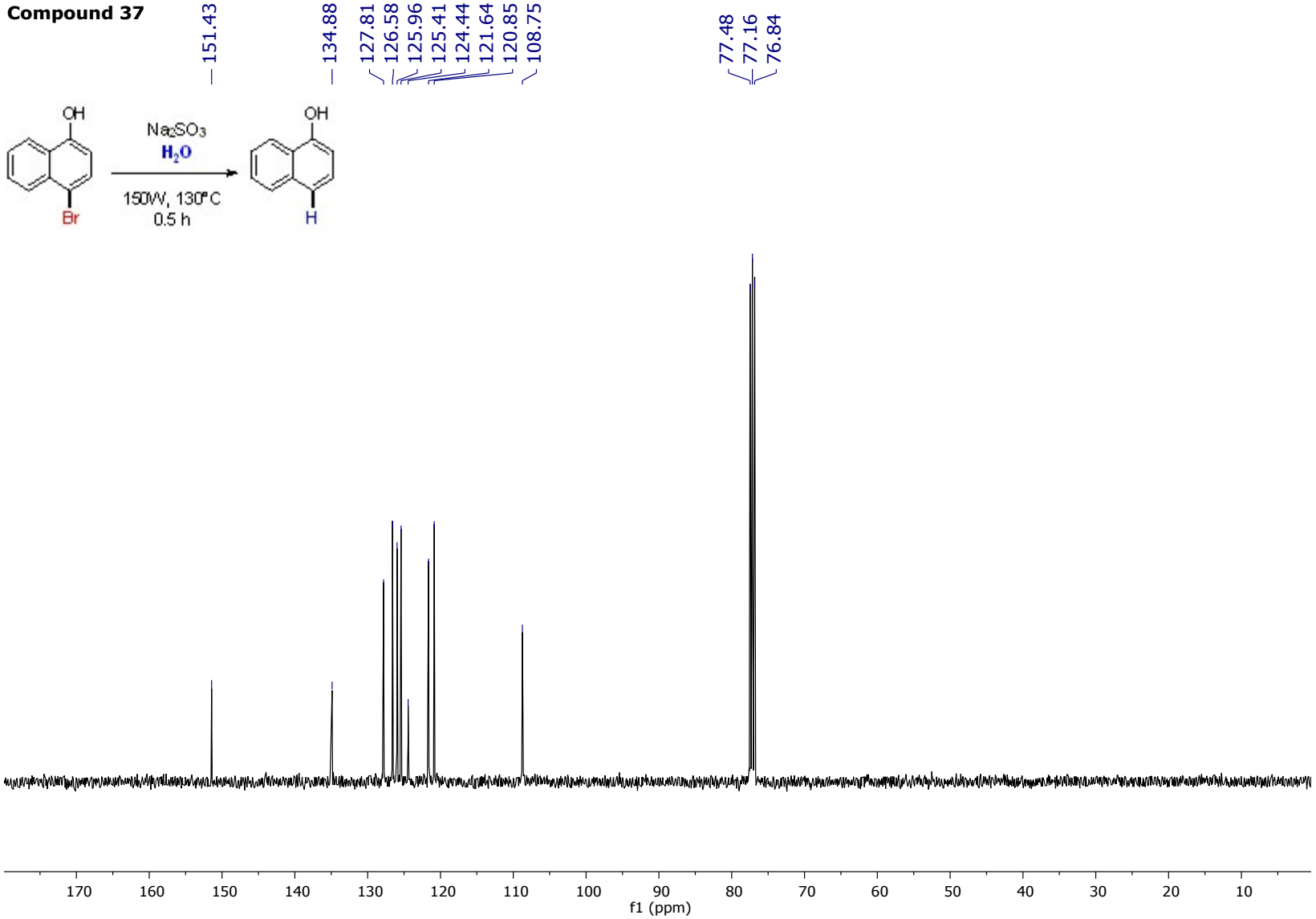
Compound 37


8.20
8.20
8.19
8.18
8.18
8.17
8.17
7.84
7.81
7.46
7.44
7.34
7.32
7.32
7.30
7.26
6.83
6.81
6.81
5.21
OH
Br
Na2SO3
H2O
150W, 130°C
0.5 h
OH
H

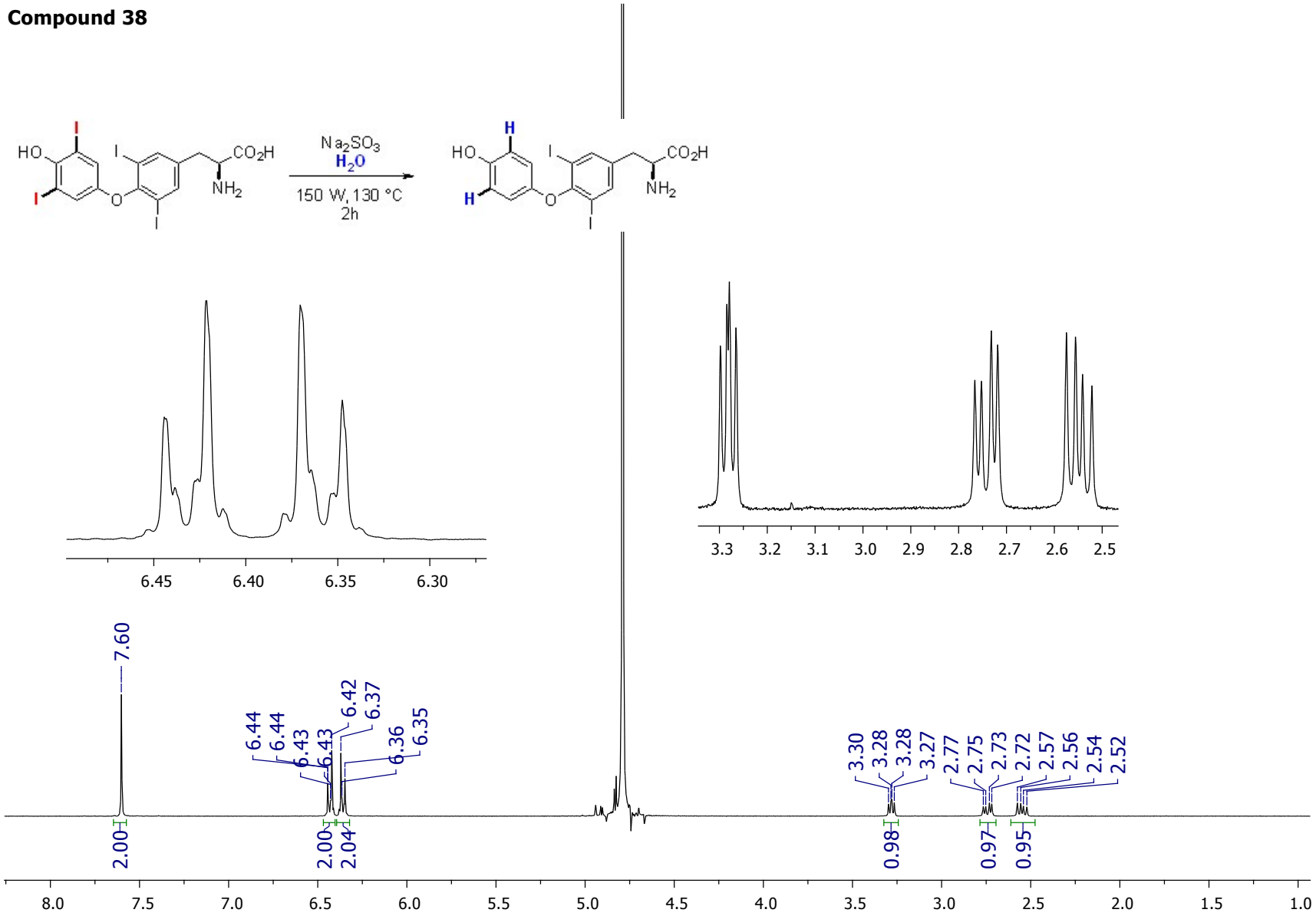

1.00
1.01
2.02
1.01
0.99
1.01
0.92
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0

1.00
1.01
2.02
1.01
0.99
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3

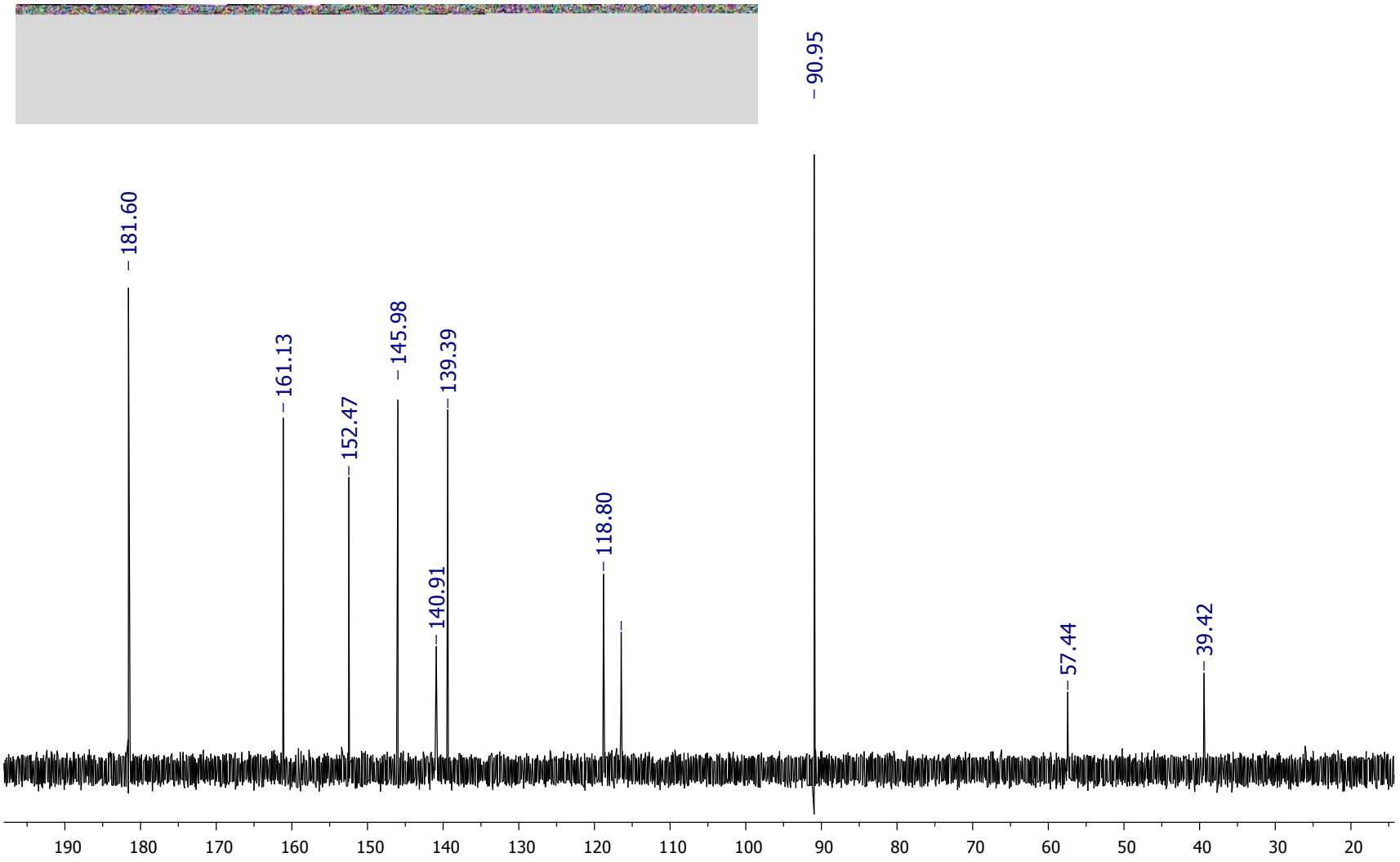
Compound 37


151.43
134.88
127.81
126.58
125.96
125.41
124.44
121.64
120.85
108.75
77.48
77.16
76.84
OH
Br
Na2SO3
H2O
150W, 130°C
0.5 h
OH
H
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

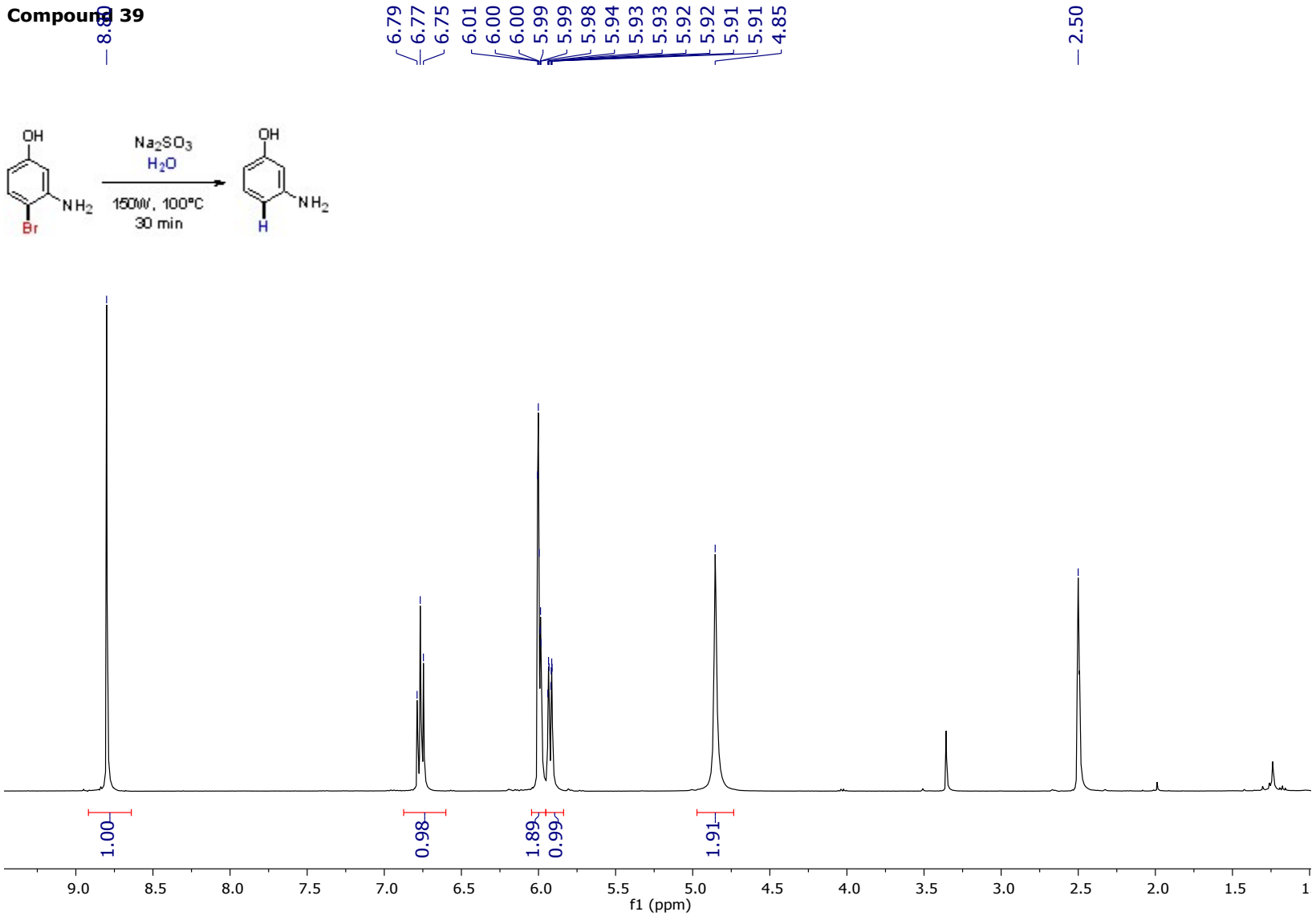
Compound 38


HO
I
I
O
I
CO2H
NH2
Na2SO3
H2O
150 W, 130 °C
2h
H
H
7.60
6.44
6.44
6.43
6.43
6.42
6.37
6.36
6.35
3.30
3.28
3.28
3.27
2.77
2.75
2.73
2.72
2.57
2.56
2.54
2.52
2.00
2.00
2.04
0.98
0.97
0.95

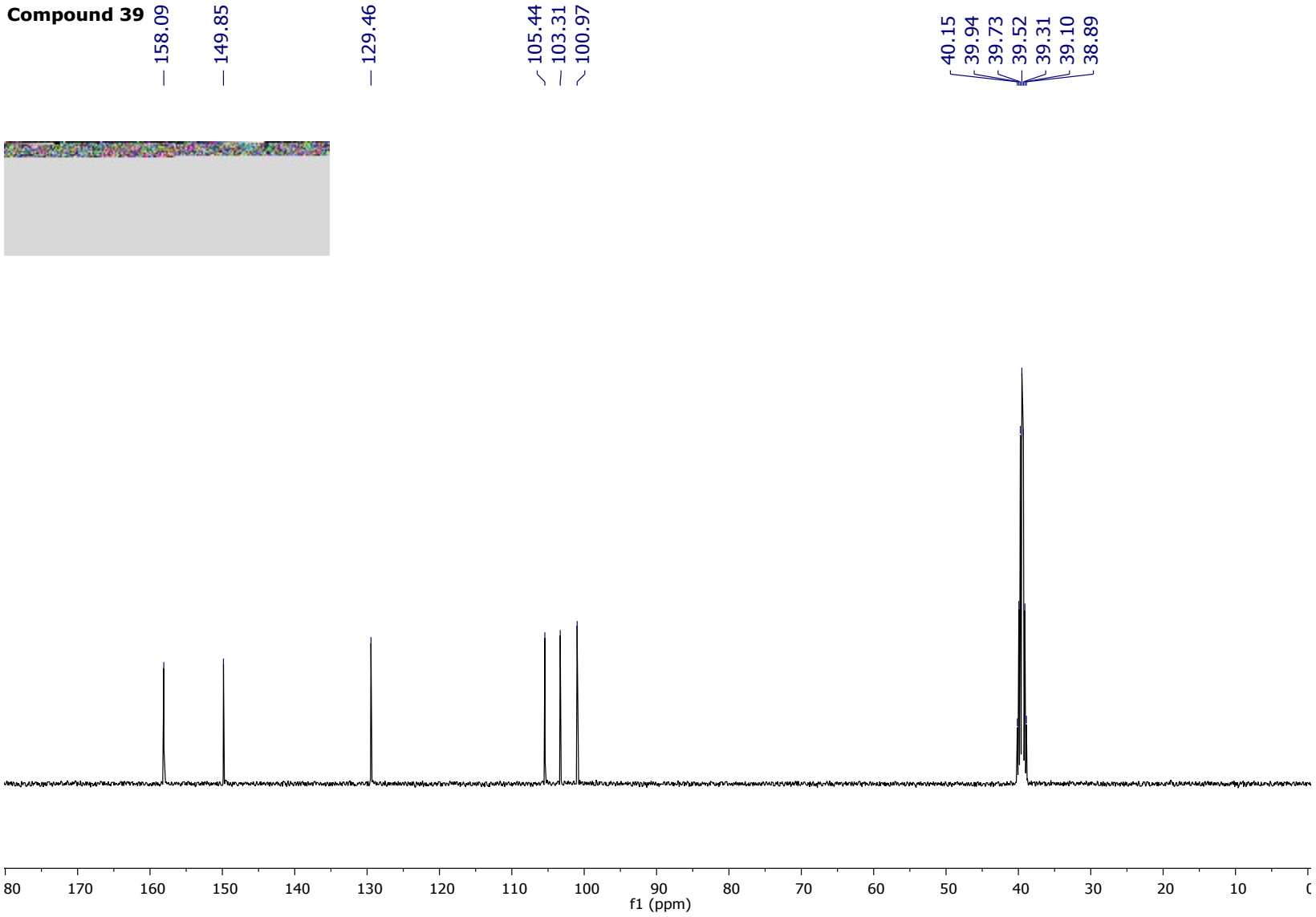
Compound 38


181.60
161.13
152.47
145.98
140.91
139.39
118.80
90.95
57.44
39.42
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

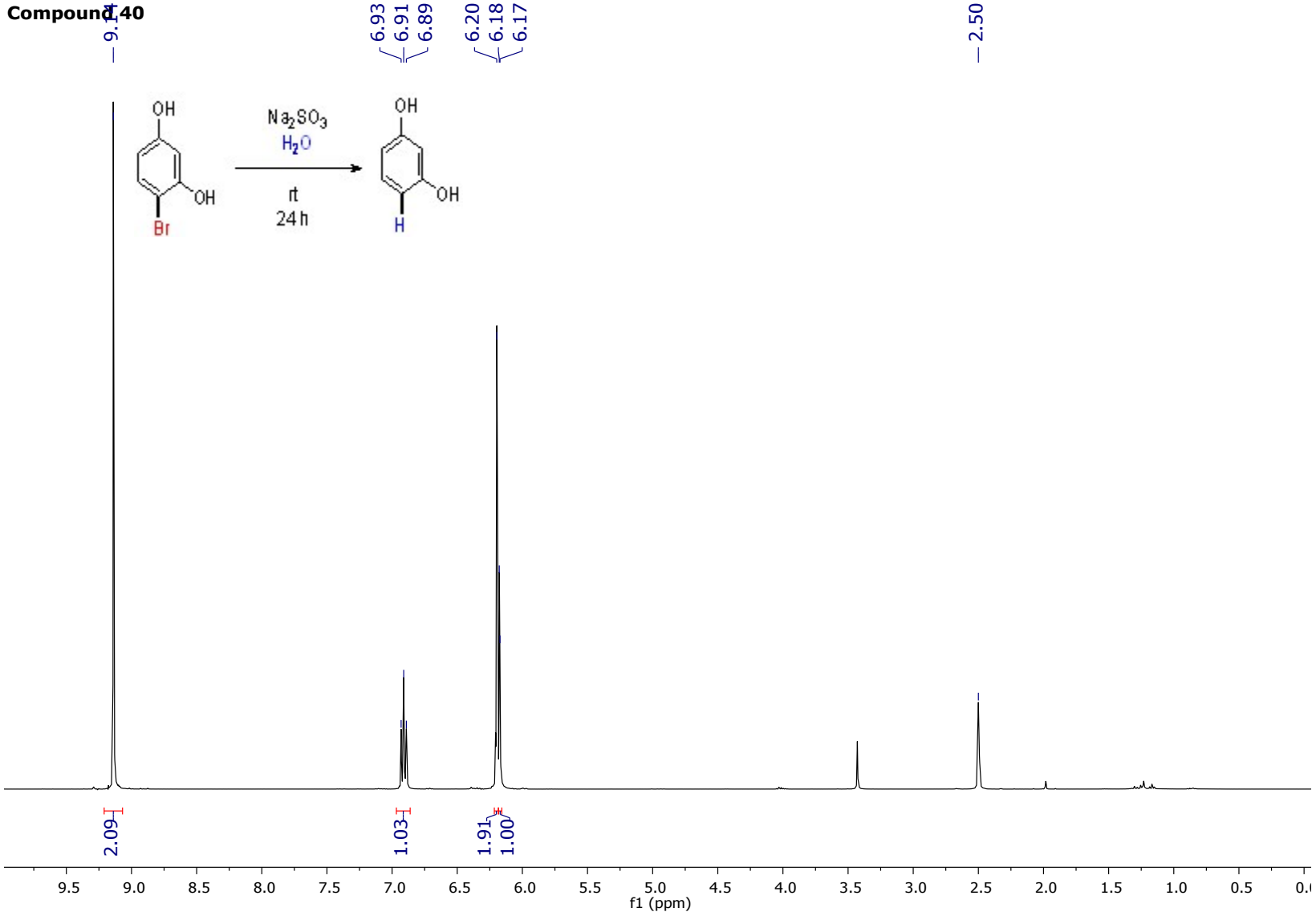
Compound 39


8.80
6.79
6.77
6.75
6.01
6.00
6.00
5.99
5.99
5.98
5.94
5.93
5.93
5.92
5.92
5.91
5.91
4.85
2.50
OH
NH2
Br
Na2SO3
H2O
150W, 100°C
30 min
OH
NH2
H
1.00
0.98
1.89
0.99
1.91
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1
f1 (ppm)

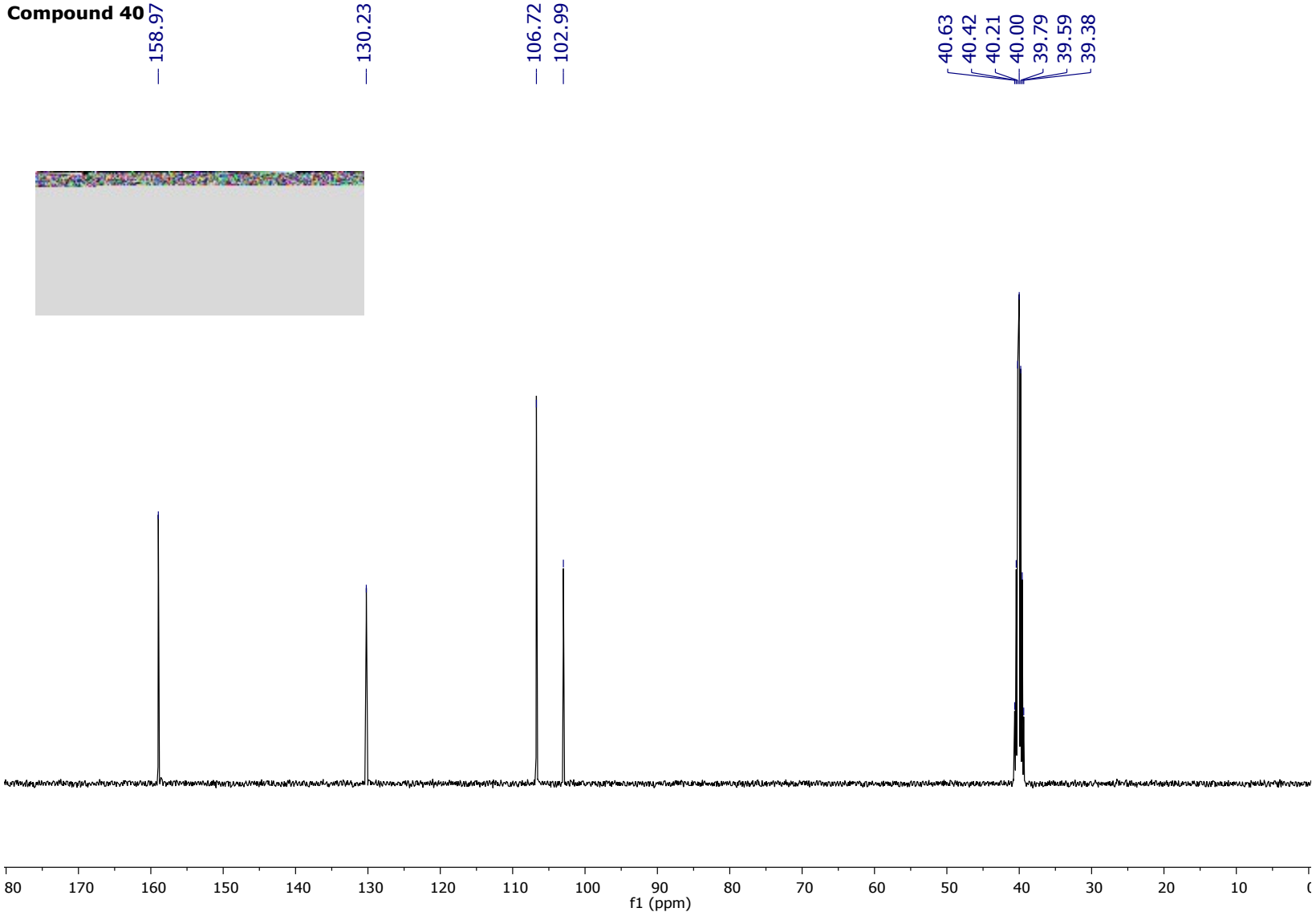
Compound 39


158.09
149.85
129.46
105.44
103.31
100.97
40.15
39.94
39.73
39.52
39.31
39.10
38.89
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

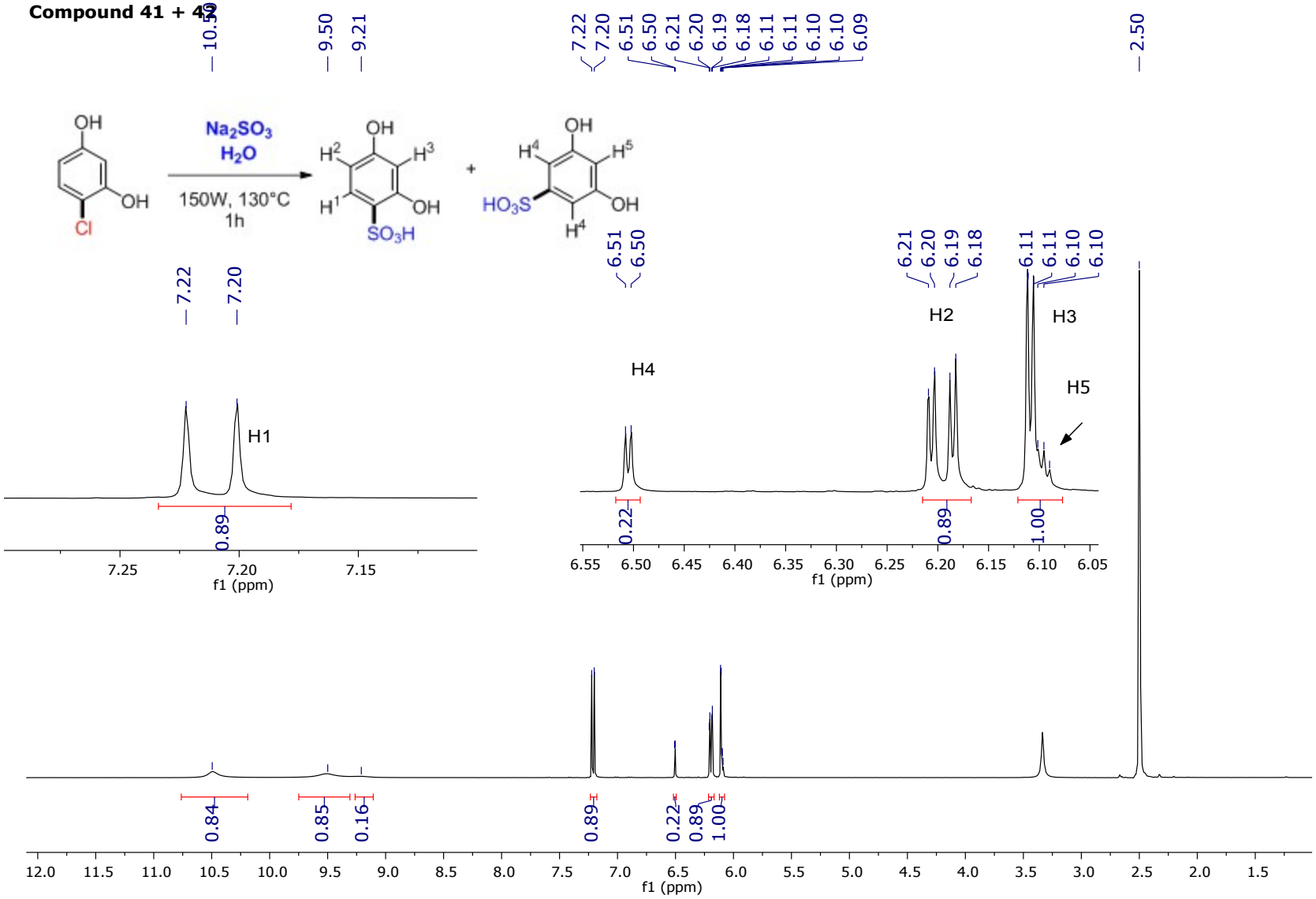
Compound 40


9.14
6.93
6.91
6.89
6.20
6.18
6.17
2.50
OH
OH
Br
Na2SO3
H2O
rt
24 h
OH
OH
H
2.09
1.03
1.91
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

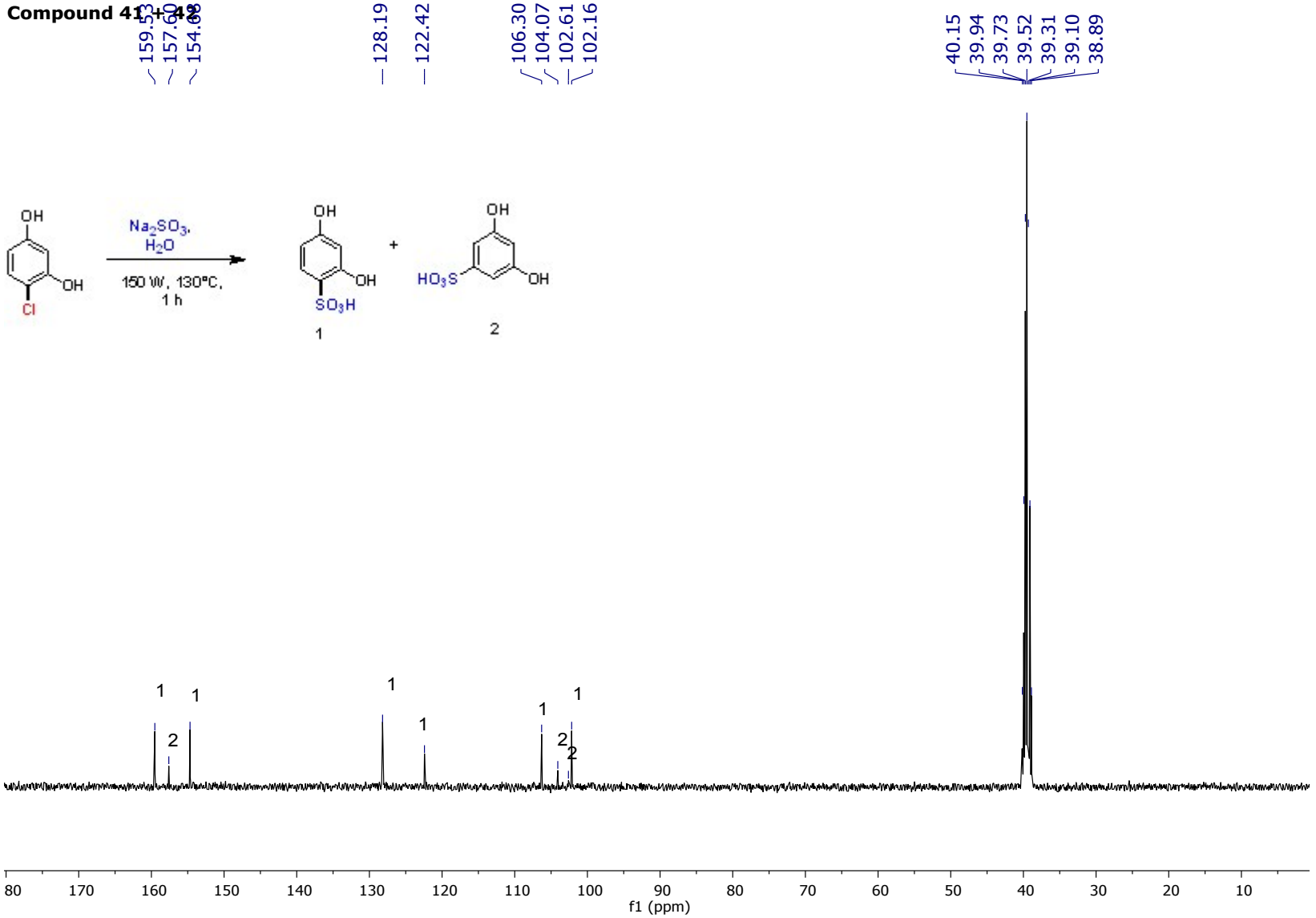
Compound 40


158.97
130.23
106.72
102.99
40.63
40.42
40.21
40.00
39.79
39.59
39.38
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

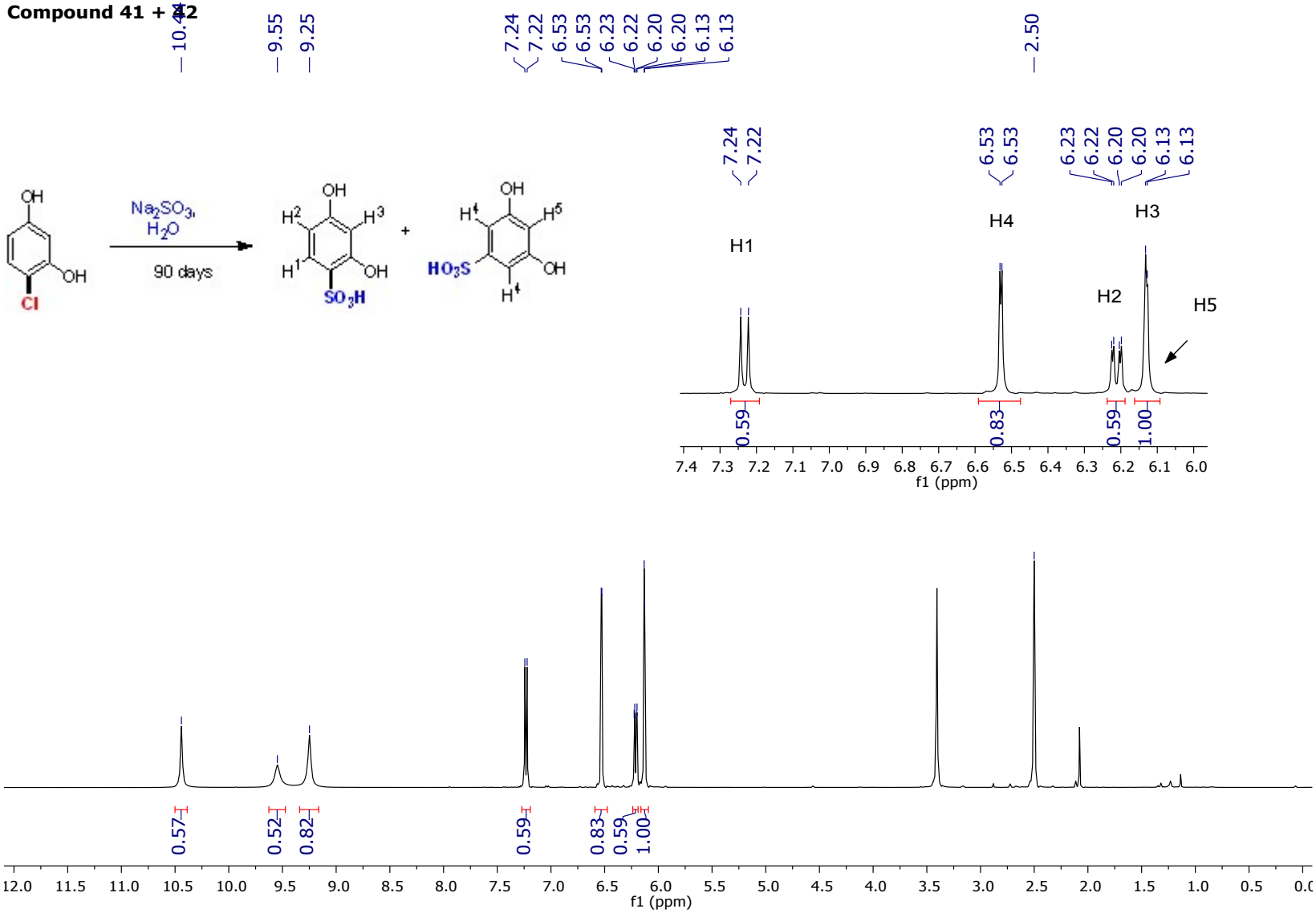
Compound 41 + 42



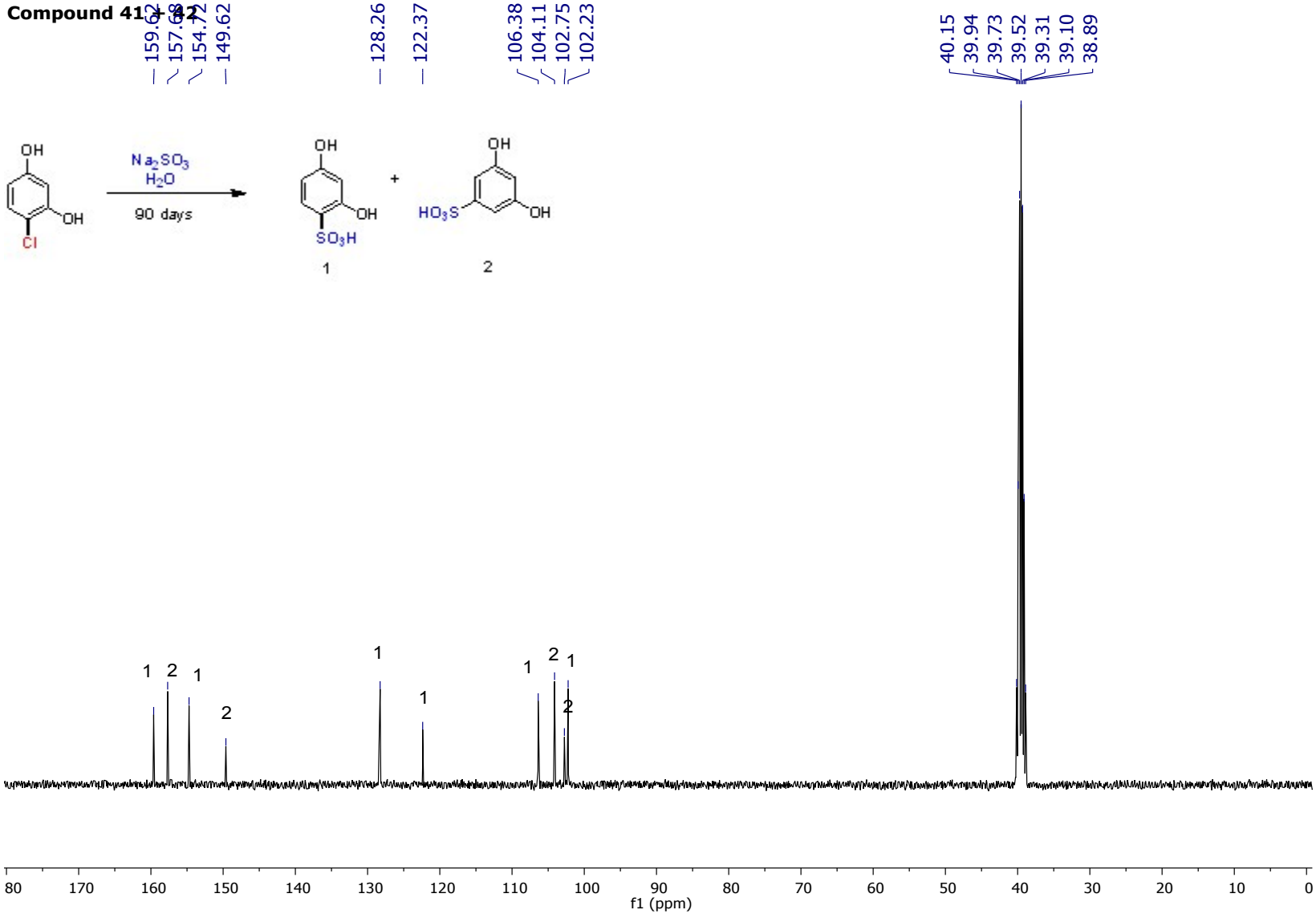
Compound 41 + 42



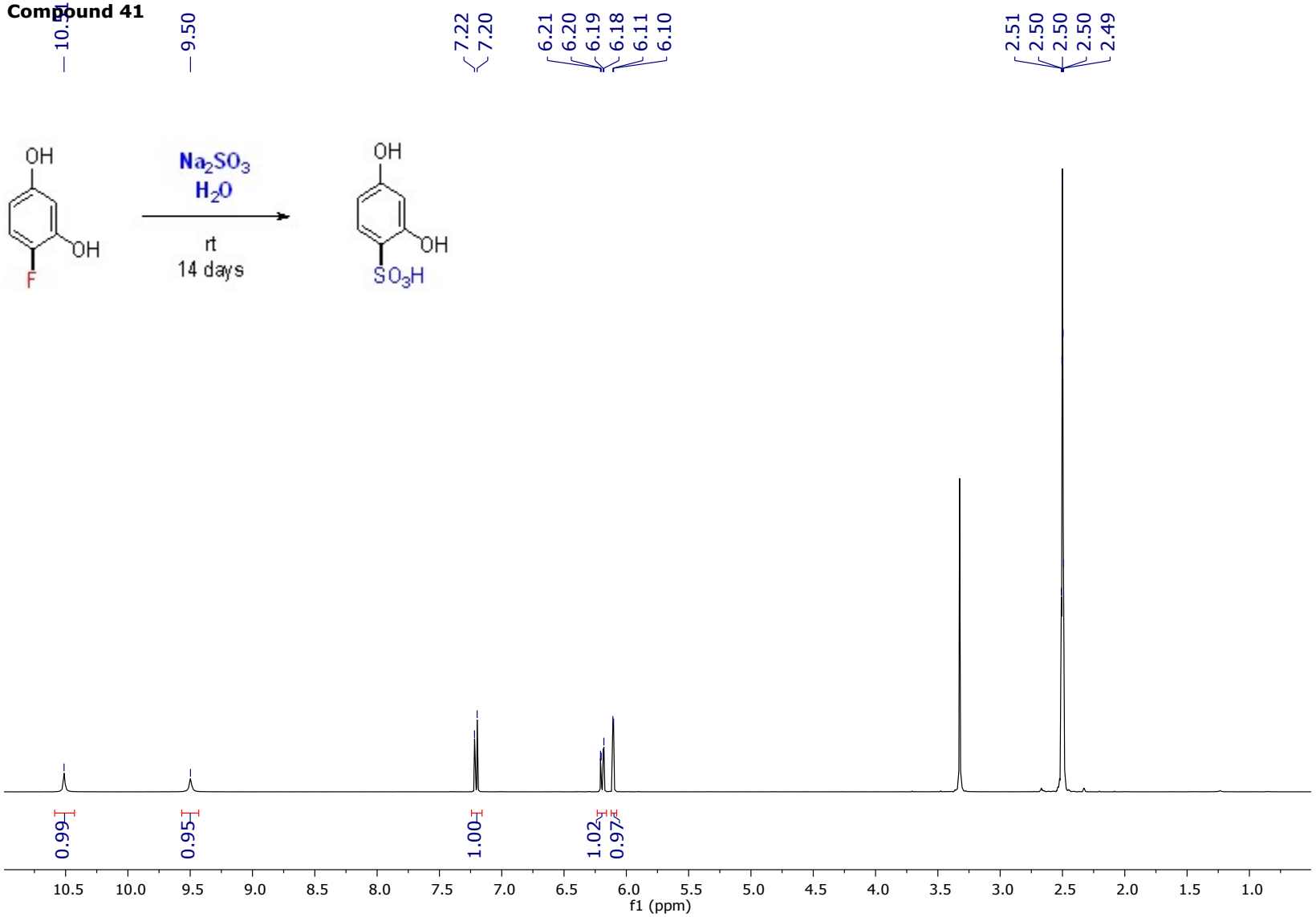
Compound 41 + 42



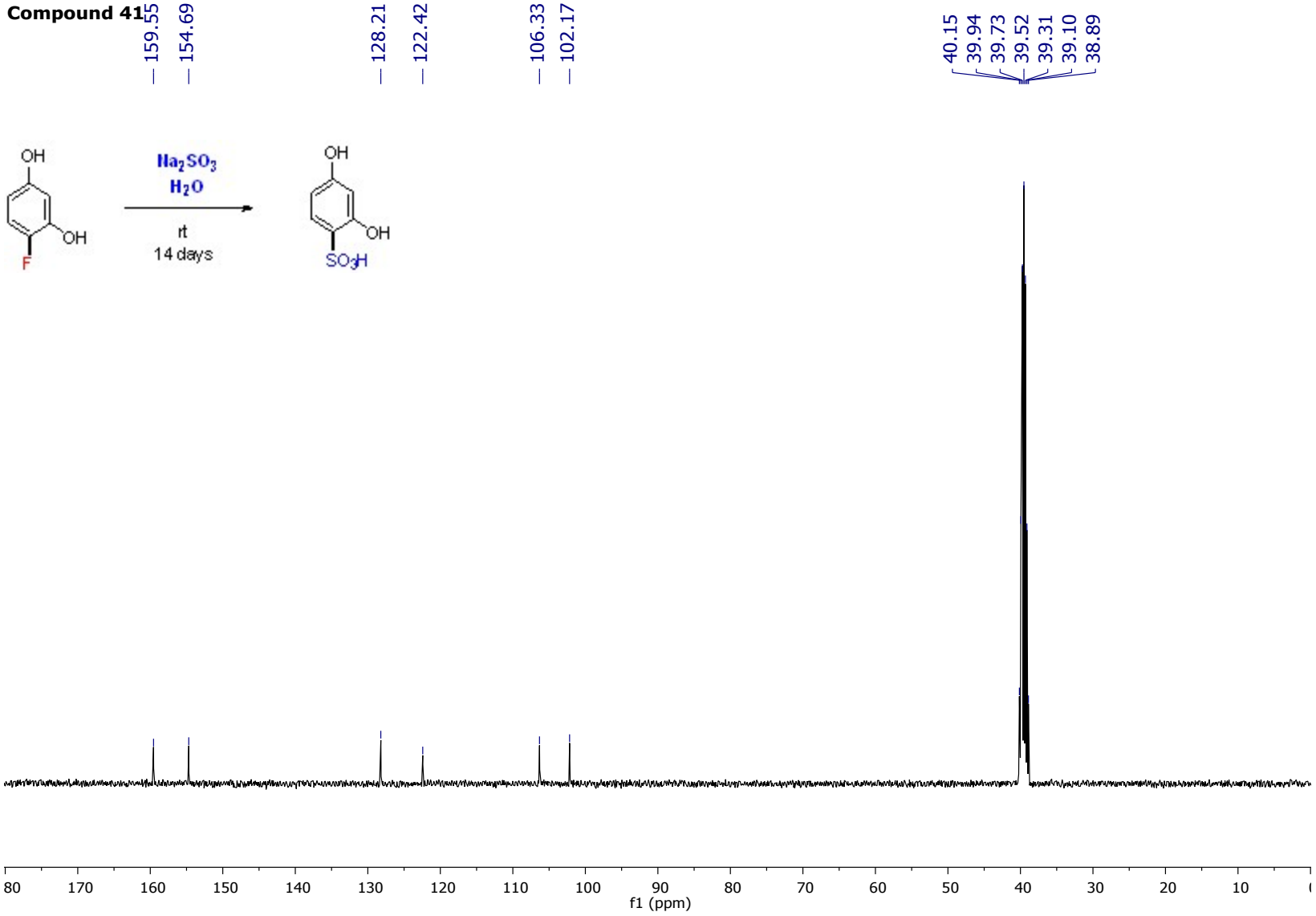
Compound 41 + 42



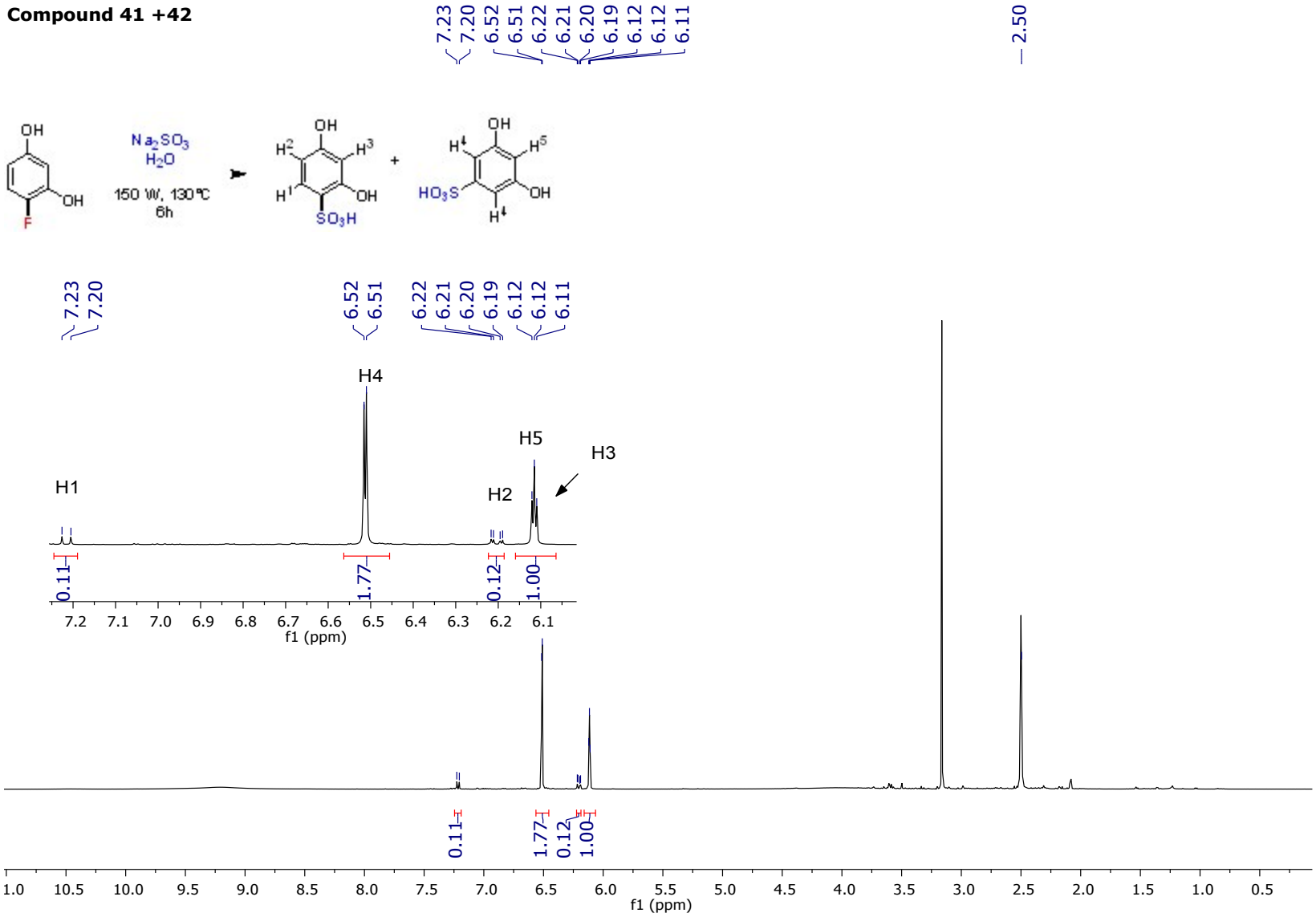
Compound 41


10.51
9.50
7.22
7.20
6.21
6.20
6.19
6.18
6.11
6.10
2.51
2.50
2.50
2.50
2.49
OH
OH
F
Na2SO3
H2O
rt
14 days
OH
OH
SO3H
0.99
0.95
1.00
1.02
0.97
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

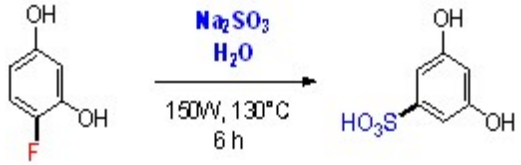
Compound 41


159.55
154.69
128.21
122.42
106.33
102.17
40.15
39.94
39.73
39.52
39.31
39.10
38.89
OH
OH
F
Na2SO3
H2O
rt
14 days
OH
OH
SO3H
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

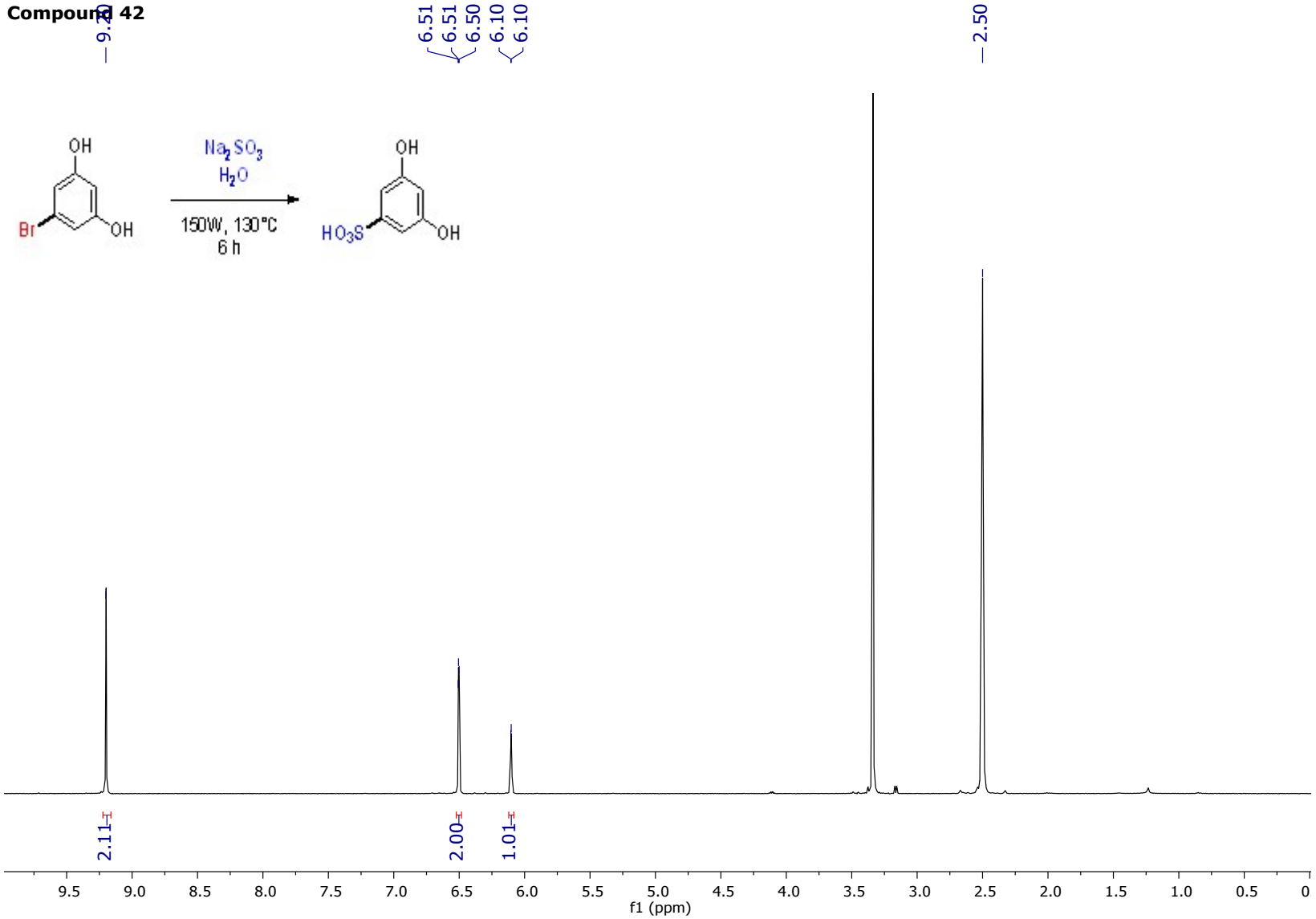
Compound 41 +42



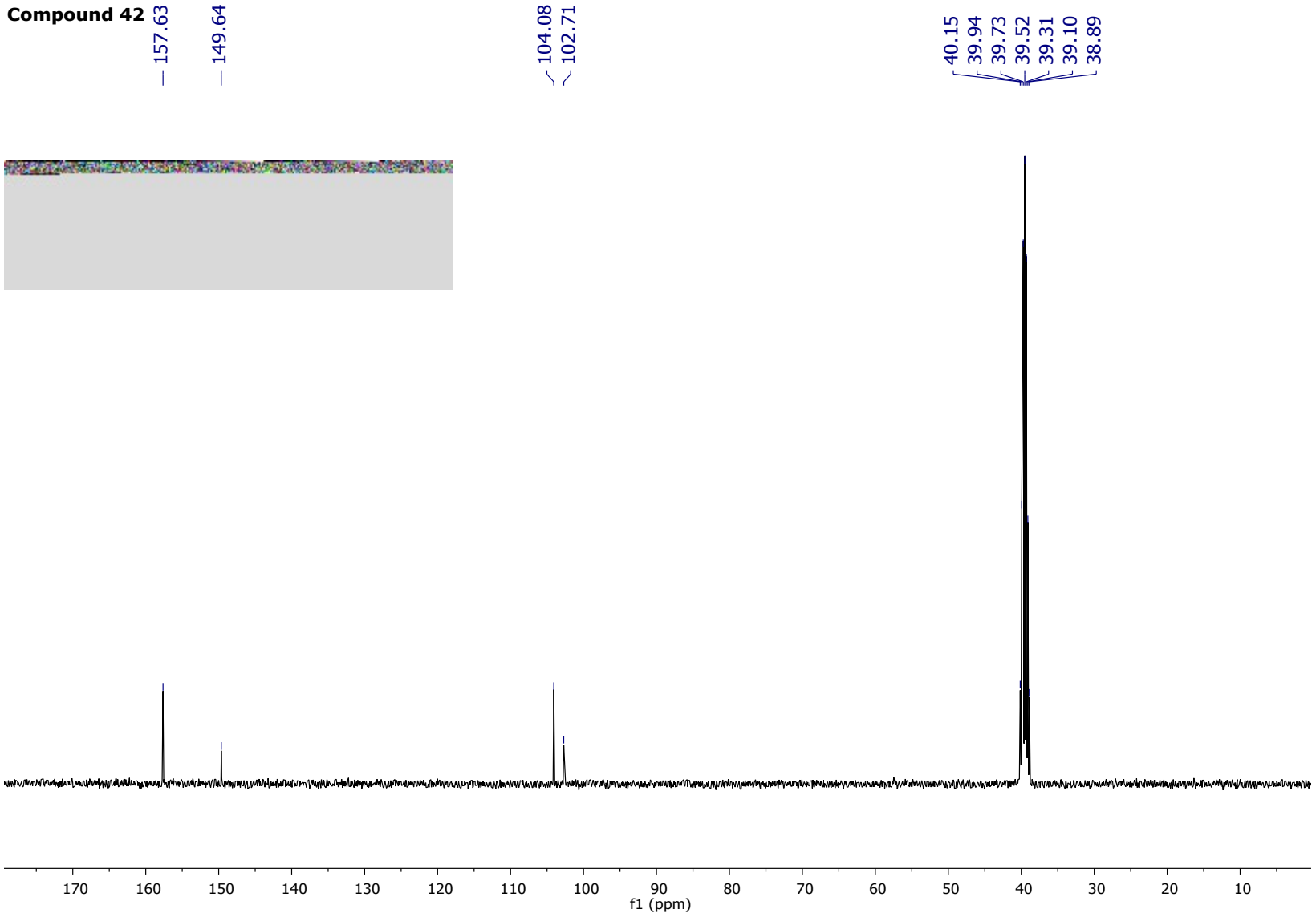
Compound 41 + 42



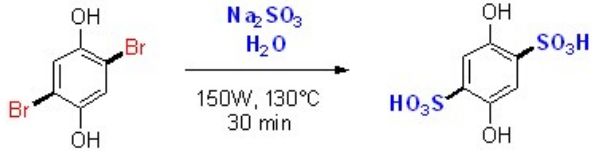
Compound 42

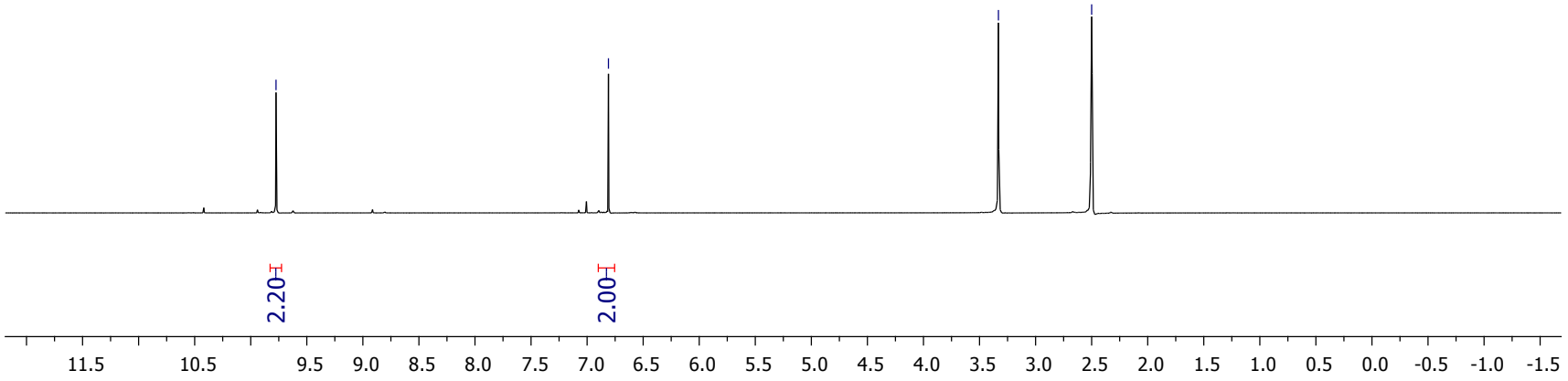

9.20
6.51
6.51
6.50
6.10
6.10
2.50
OH
Br
OH
Na2SO3
H2O
150W, 130°C
6 h
OH
HO3S
OH
2.11
2.00
1.01
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

Compound 42

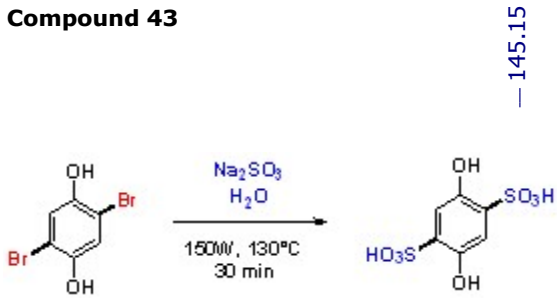

157.63
149.64
104.08
102.71
40.15
39.94
39.73
39.52
39.31
39.10
38.89
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Compound 43


OH
Br
Br
OH
Na_2SO_3
H_2O
150W, 130°C
30 min
OH
SO_3H
HO_3S
OH

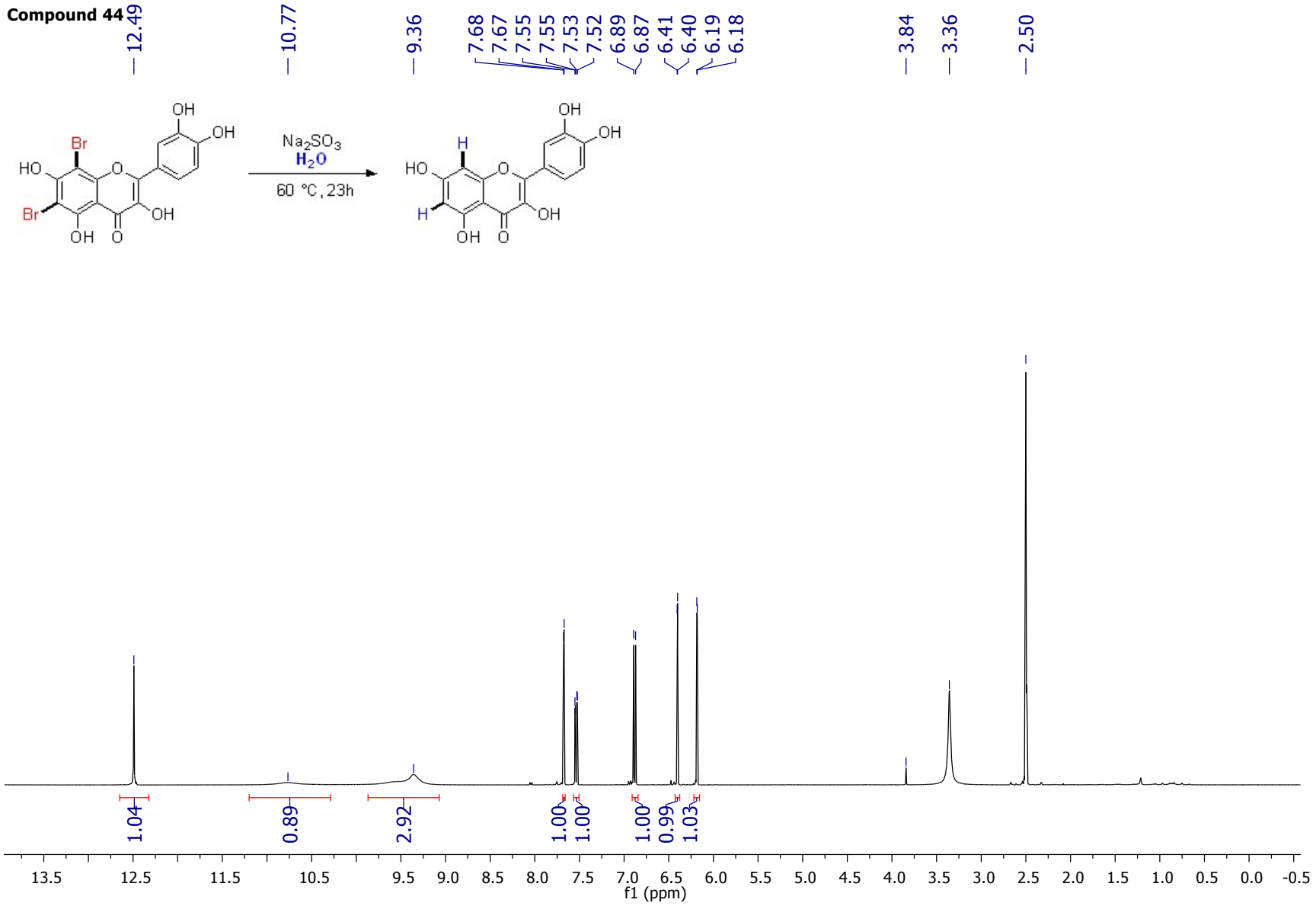

9.77
6.81
3.33
2.50
2.20
2.00
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5

Compound 43

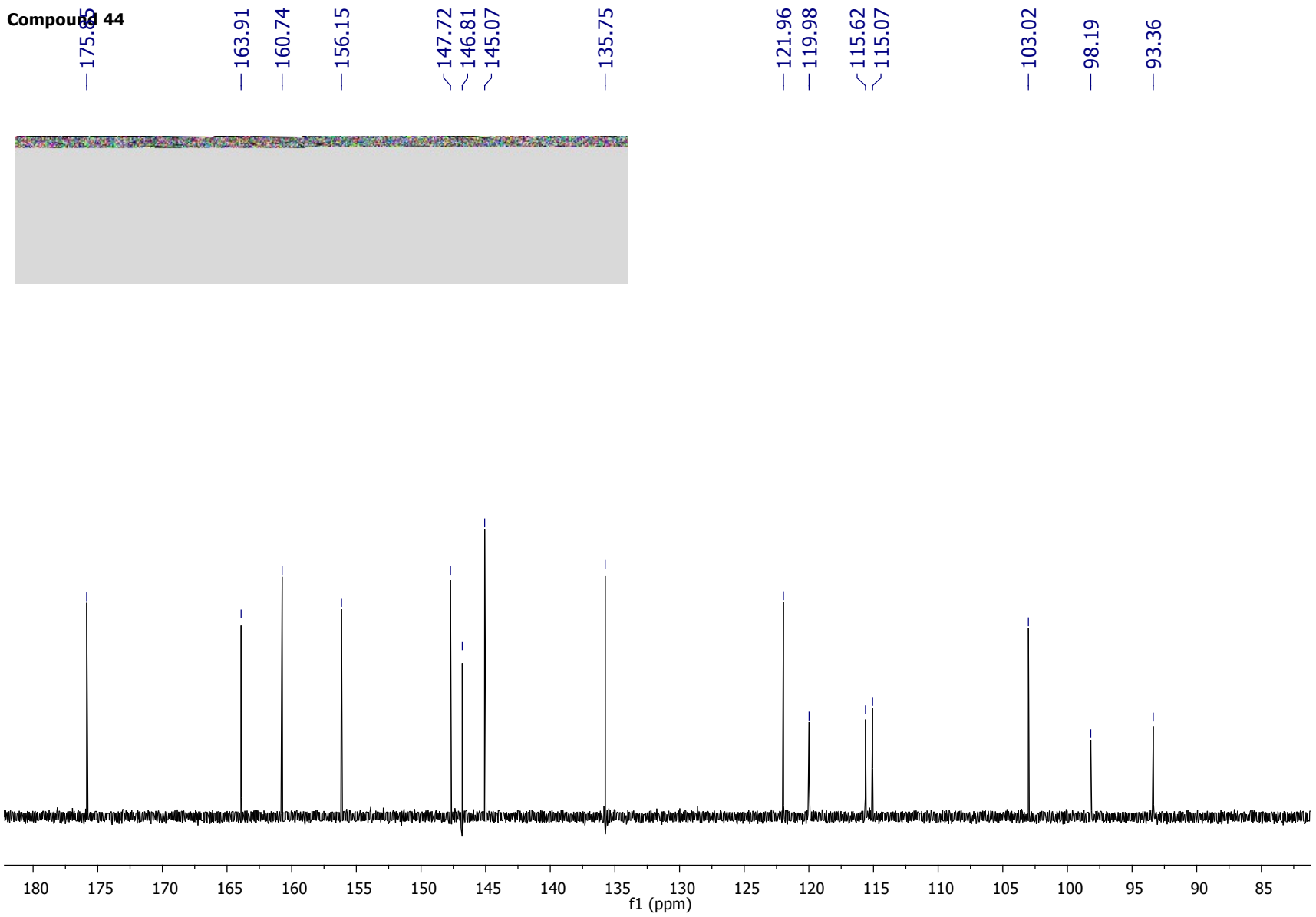

OH
Br
Br
OH
Na_2SO_3
H_2O
150W, 130°C
30 min
OH
SO_3H
HO_3S
OH

145.15
132.88
114.01
40.15
39.94
39.73
39.52
39.31
39.10
38.89
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

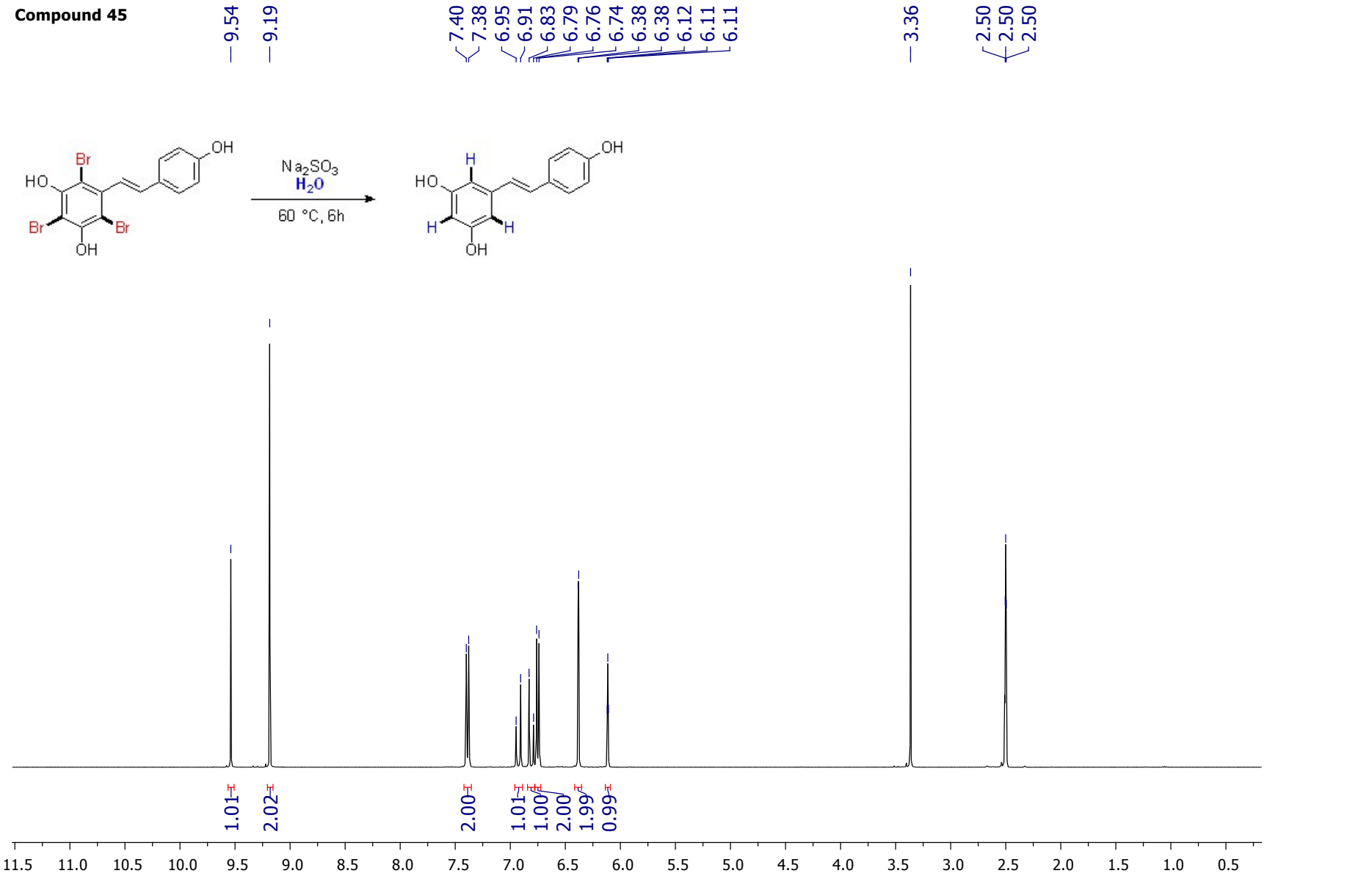
Compound 44


12.49
10.77
9.36
7.68
7.67
7.55
7.55
7.53
7.52
6.89
6.87
6.41
6.40
6.19
6.18
3.84
3.36
2.50
Br
HO
OH
OH
Br
OH
O
Na2SO3
H2O
60 °C, 23h
H
H
1.04
0.89
2.92
1.00
1.00
1.00
0.99
1.03
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

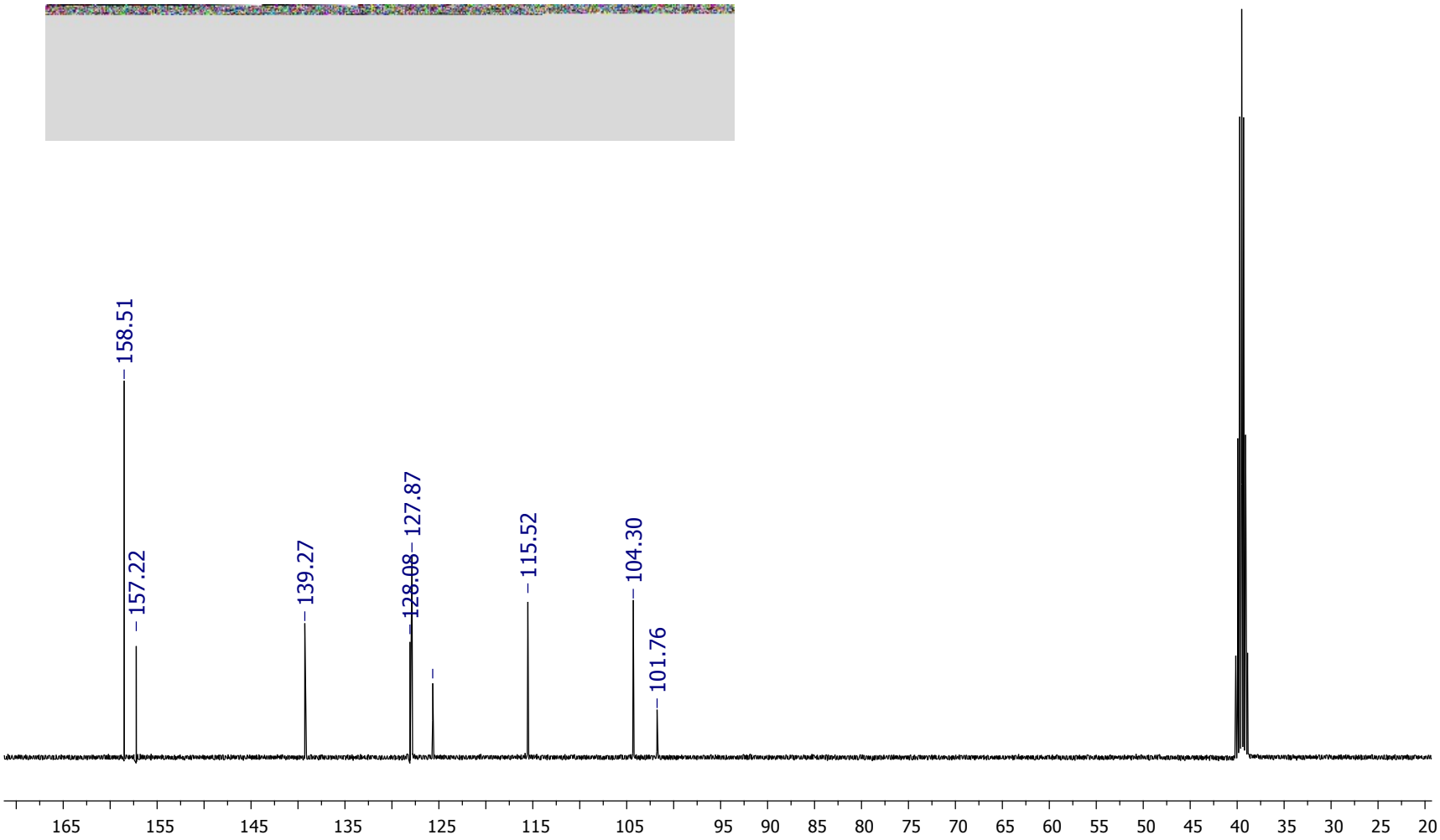
Compound 44


175.65
163.91
160.74
156.15
147.72
146.81
145.07
135.75
121.96
119.98
115.62
115.07
103.02
98.19
93.36
180
175
170
165
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
f1 (ppm)

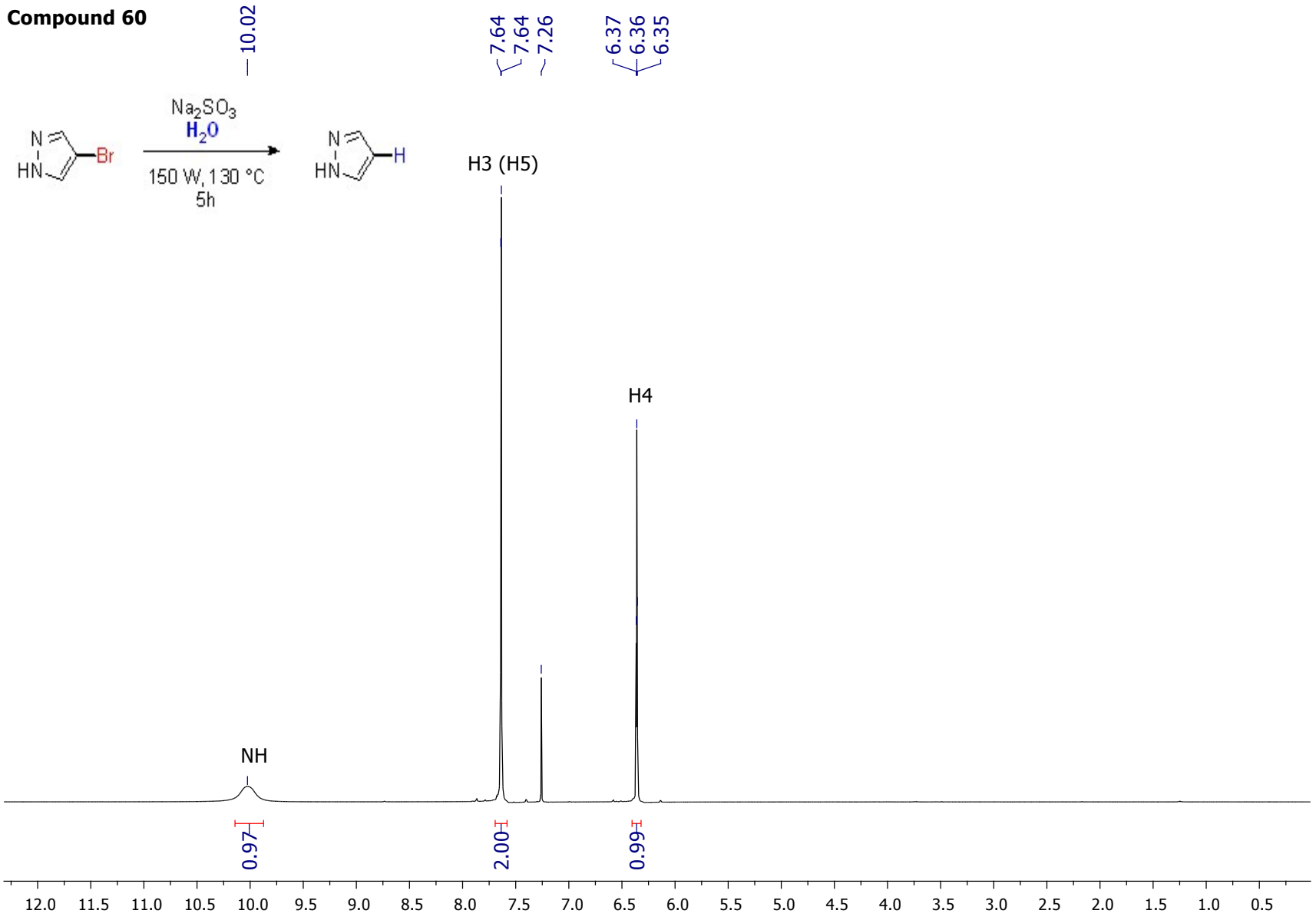
Compound 45


9.54
9.19
7.40
7.38
6.95
6.91
6.83
6.79
6.76
6.74
6.38
6.38
6.12
6.11
6.11
3.36
2.50
2.50
2.50
Br
HO
OH
Br
Br
OH
Na2SO3
H2O
60 °C, 6h
H
HO
OH
H
H
OH
1.01
2.02
2.00
1.01
1.00
2.00
1.99
0.99
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

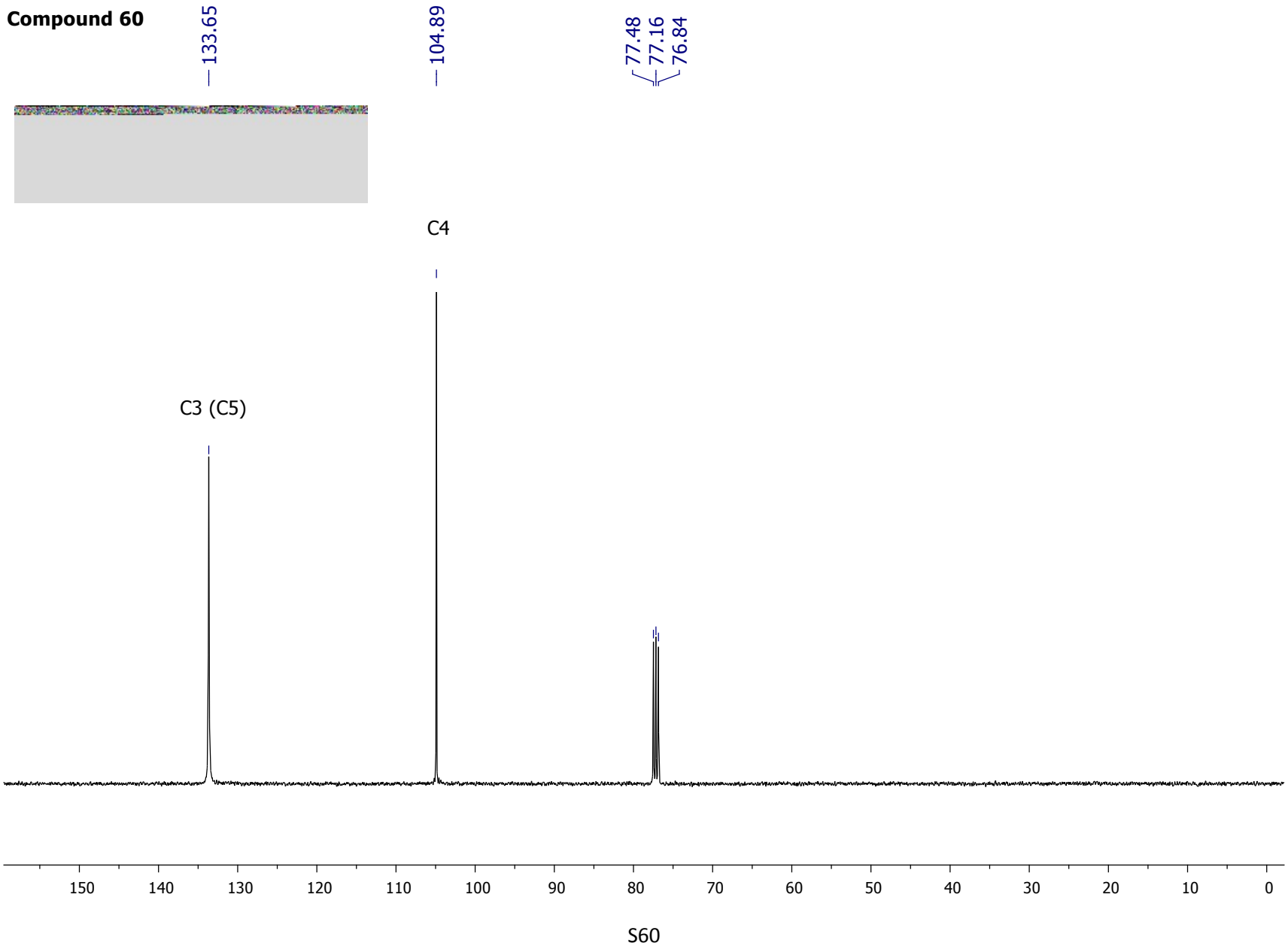
Compound 45


158.51
157.22
139.27
128.08
127.87
115.52
104.30
101.76
165
155
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20

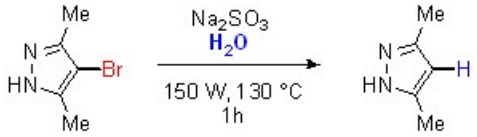
Compound 60


10.02
7.64
7.64
7.26
6.37
6.36
6.35
Na2SO3
H2O
150 W, 130 °C
5h
N
HN
Br
H
H3 (H5)
H4
NH
0.97
2.00
0.99
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

Compound 60

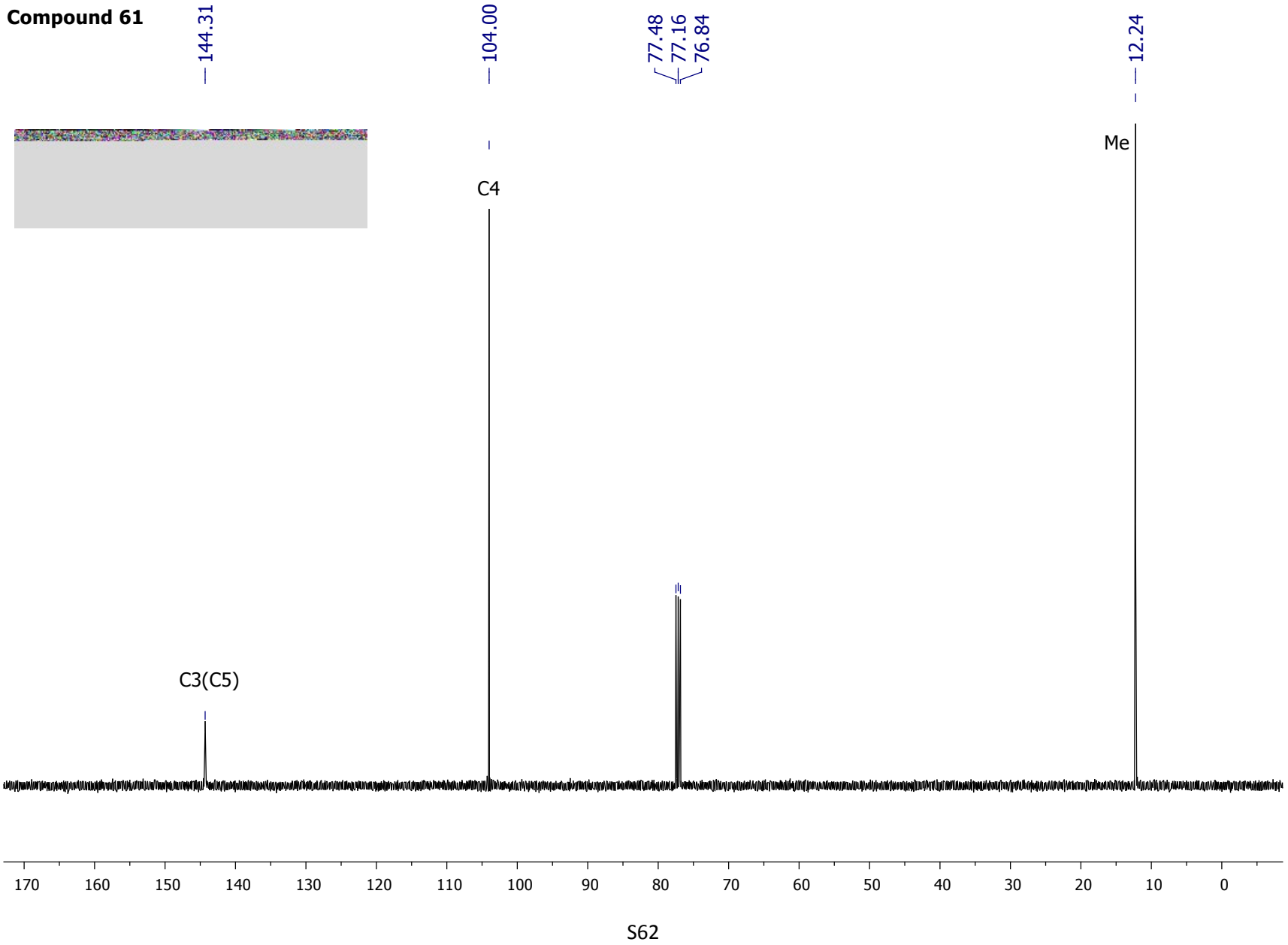

133.65
104.89
77.48
77.16
76.84
C4
C3 (C5)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

Compound 61

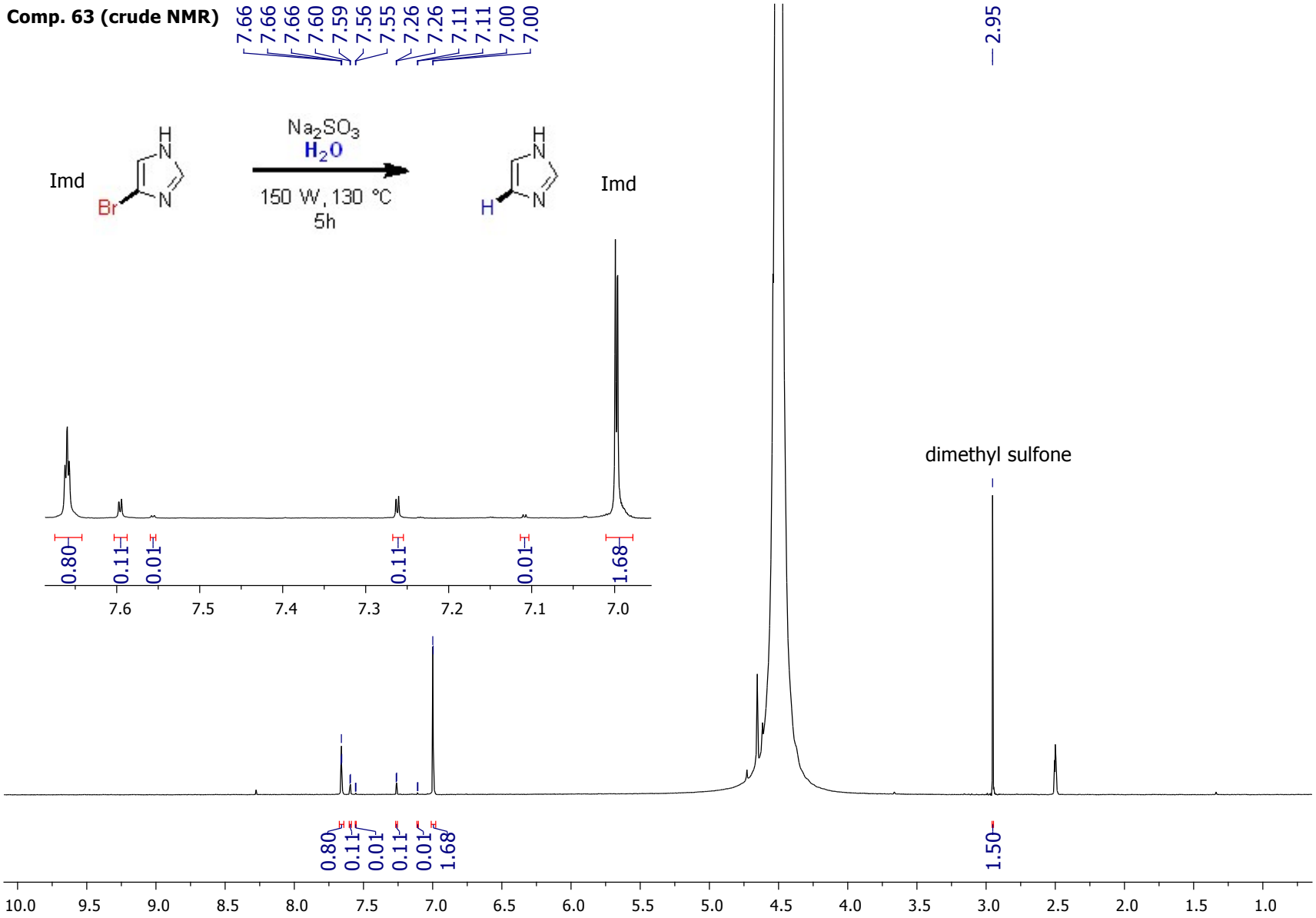

Me
N
HN
Br
Me
Na2SO3
H2O
150 W, 130 °C
1h
Me
N
HN
H
Me

11.20
7.26
5.82
2.28
Me
H4
NH
CHCl3
1.06
0.96
6.00
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

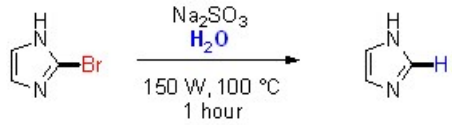
Compound 61


144.31
104.00
77.48
77.16
76.84
12.24
C4
Me
C3(C5)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

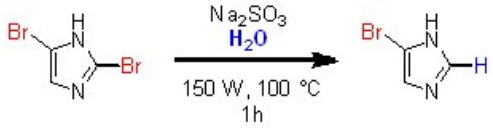
Comp. 63 (crude NMR)

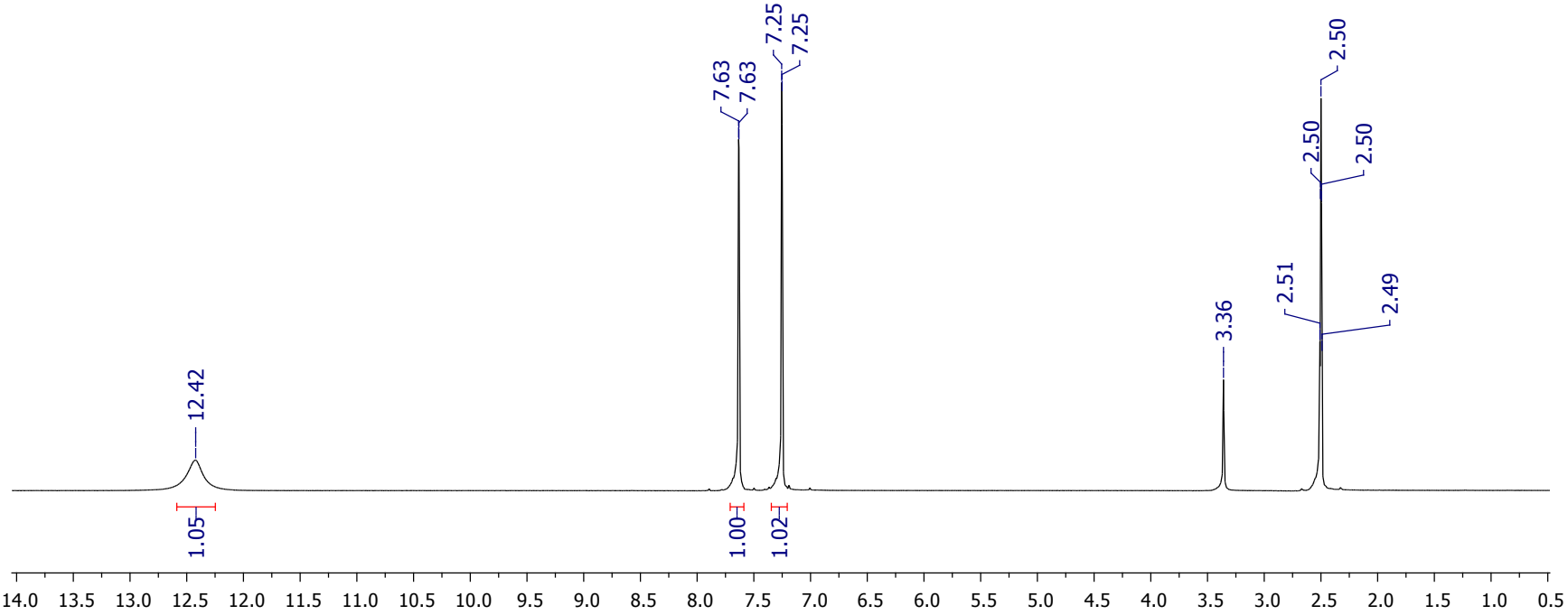


Comp. 63 (crude NMR)

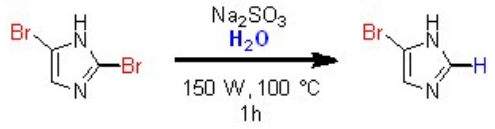


Compound 51


Br
H
N
Br
N
Na2SO3
H2O
150 W, 100 °C
1h
Br
H
N
H
N

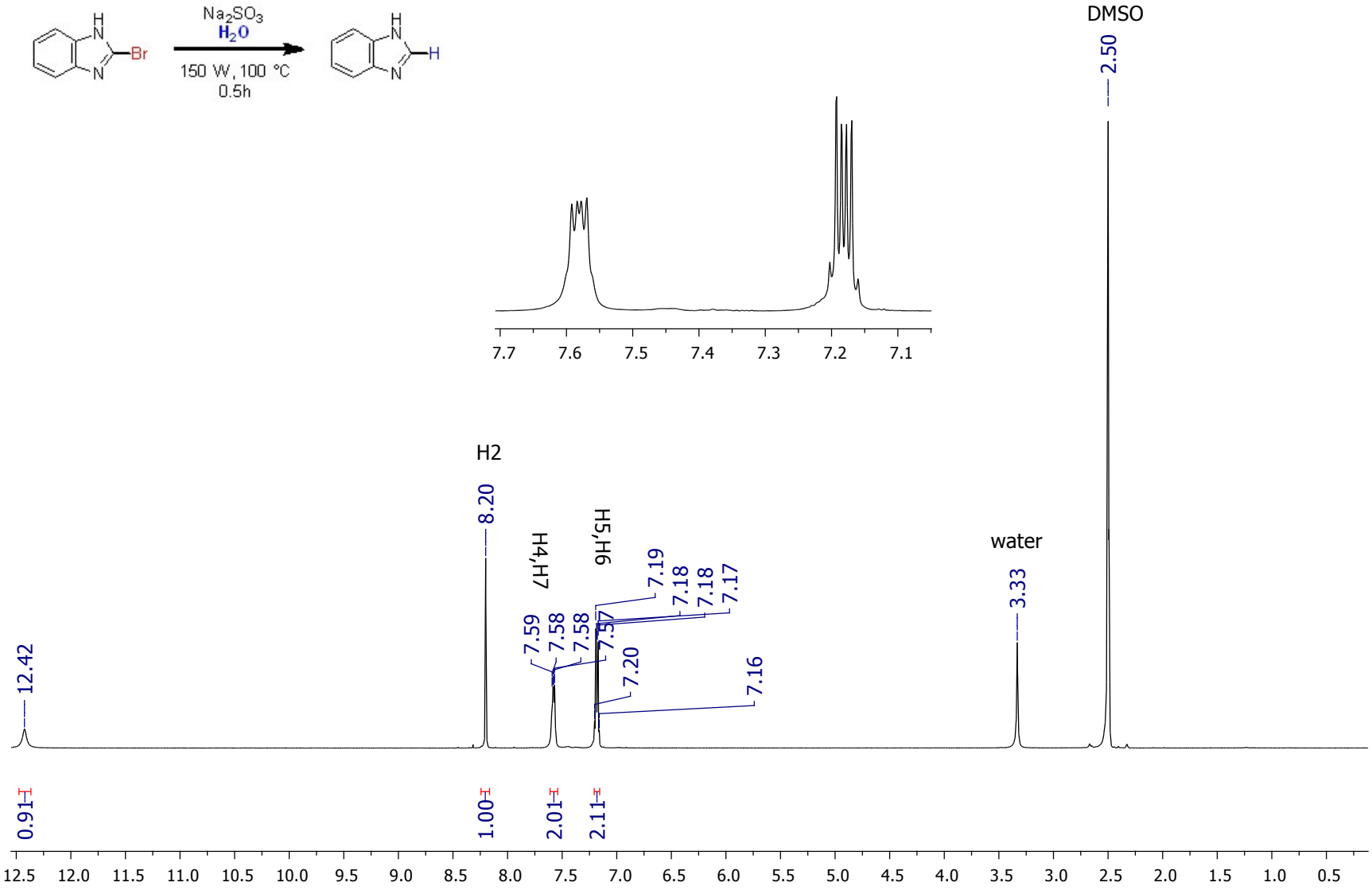

12.42
7.63
7.63
7.25
7.25
3.36
2.51
2.50
2.50
2.50
2.49
1.05
1.00
1.02
14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

Compound 51

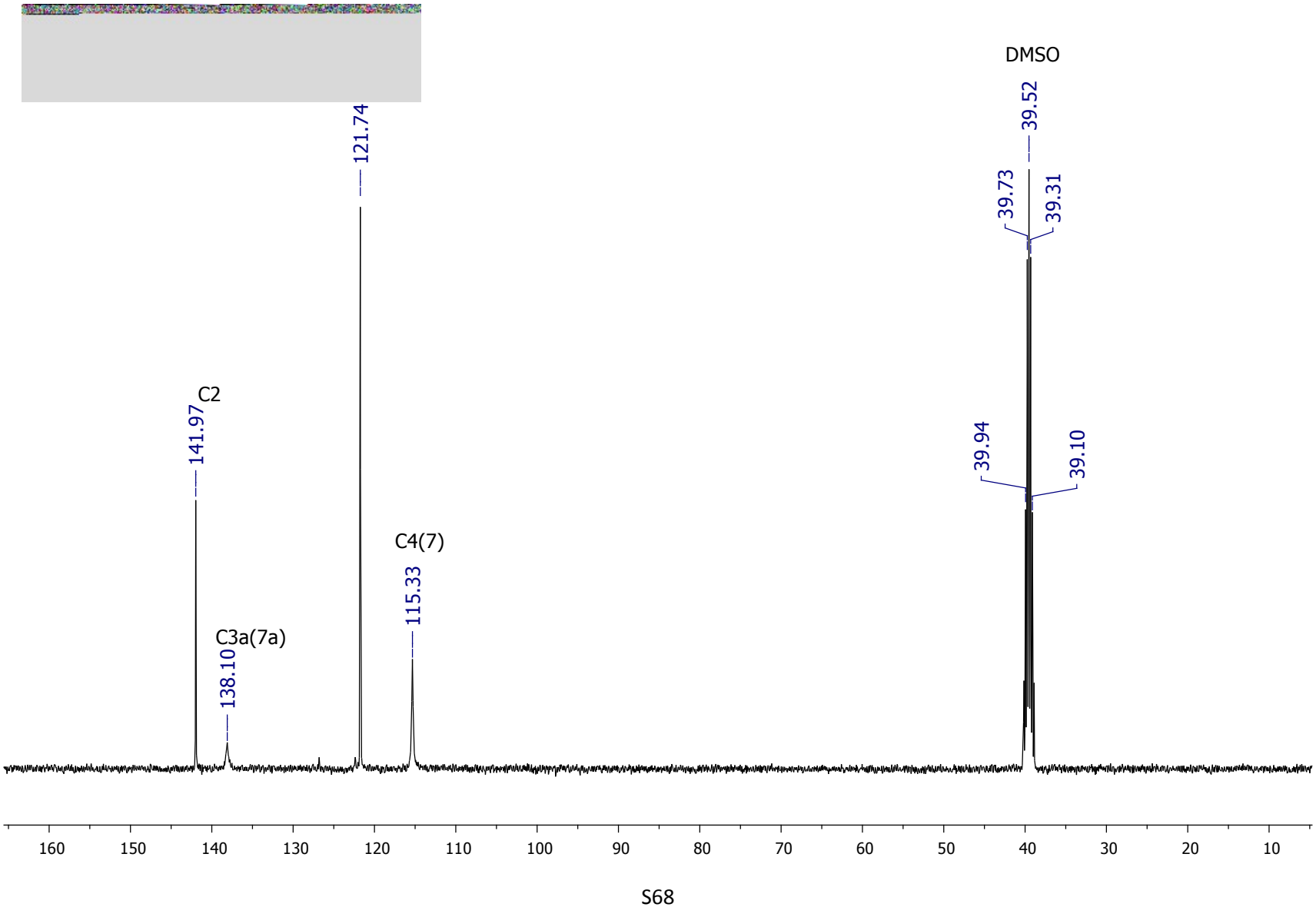

Br
H
N
Br
N
Na_2SO_3
H_2O
150 W, 100 °C
1h
Br
H
N
H
N

39.52
39.73
39.31
39.94
39.10
135.92
115.68
113.52
150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15

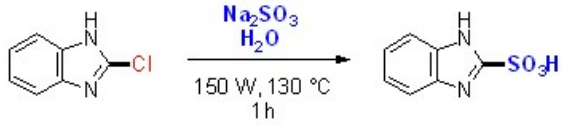
Compound 64

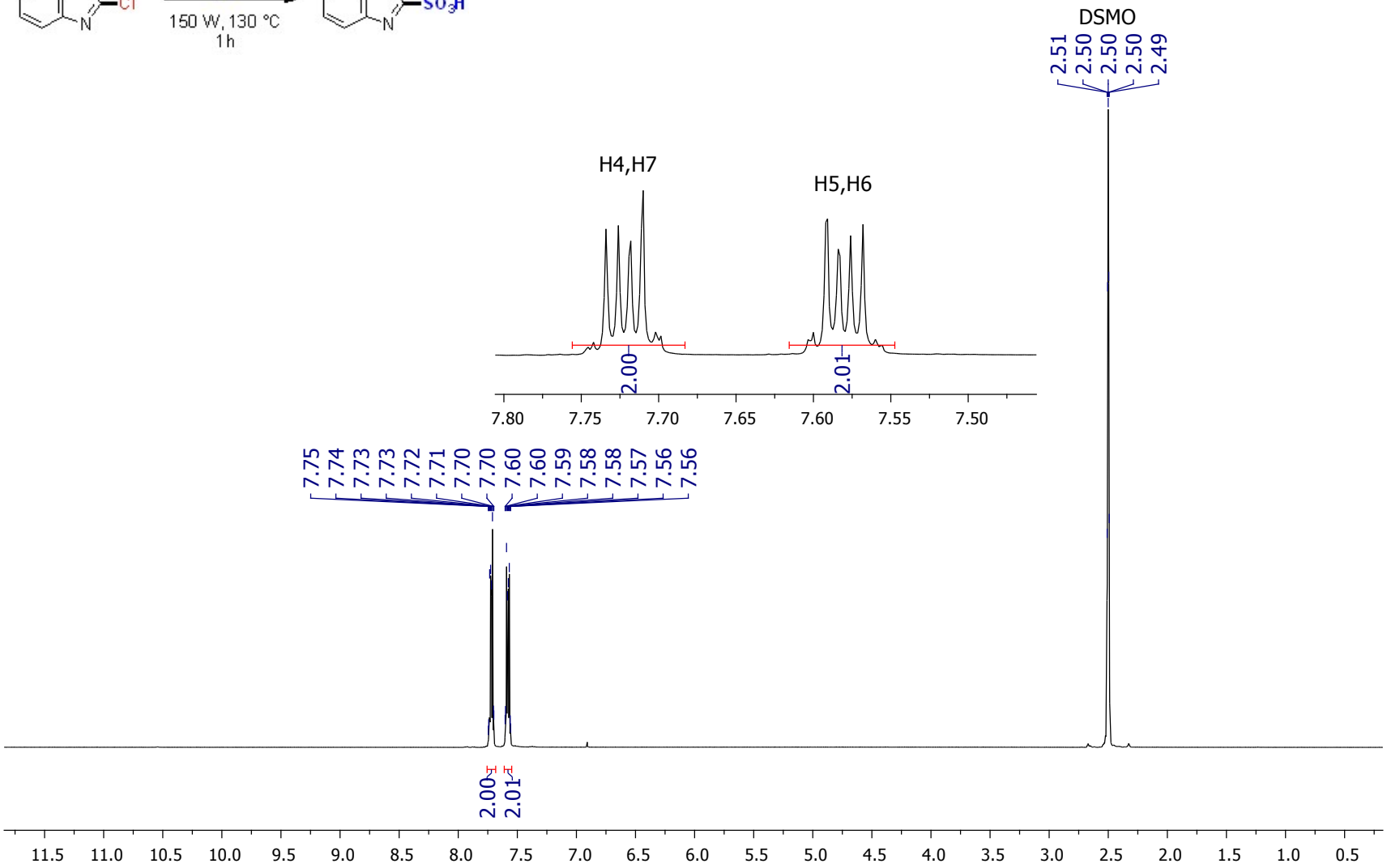

Na2SO3
H2O
150 W, 100 °C
0.5h
Br
H
DMSO
2.50
H2
8.20
H4,H7
H5,H6
7.19
7.18
7.18
7.17
7.59
7.58
7.58
7.57
7.20
7.16
water
3.33
12.42
0.91
1.00
2.01
2.11

Compound 64

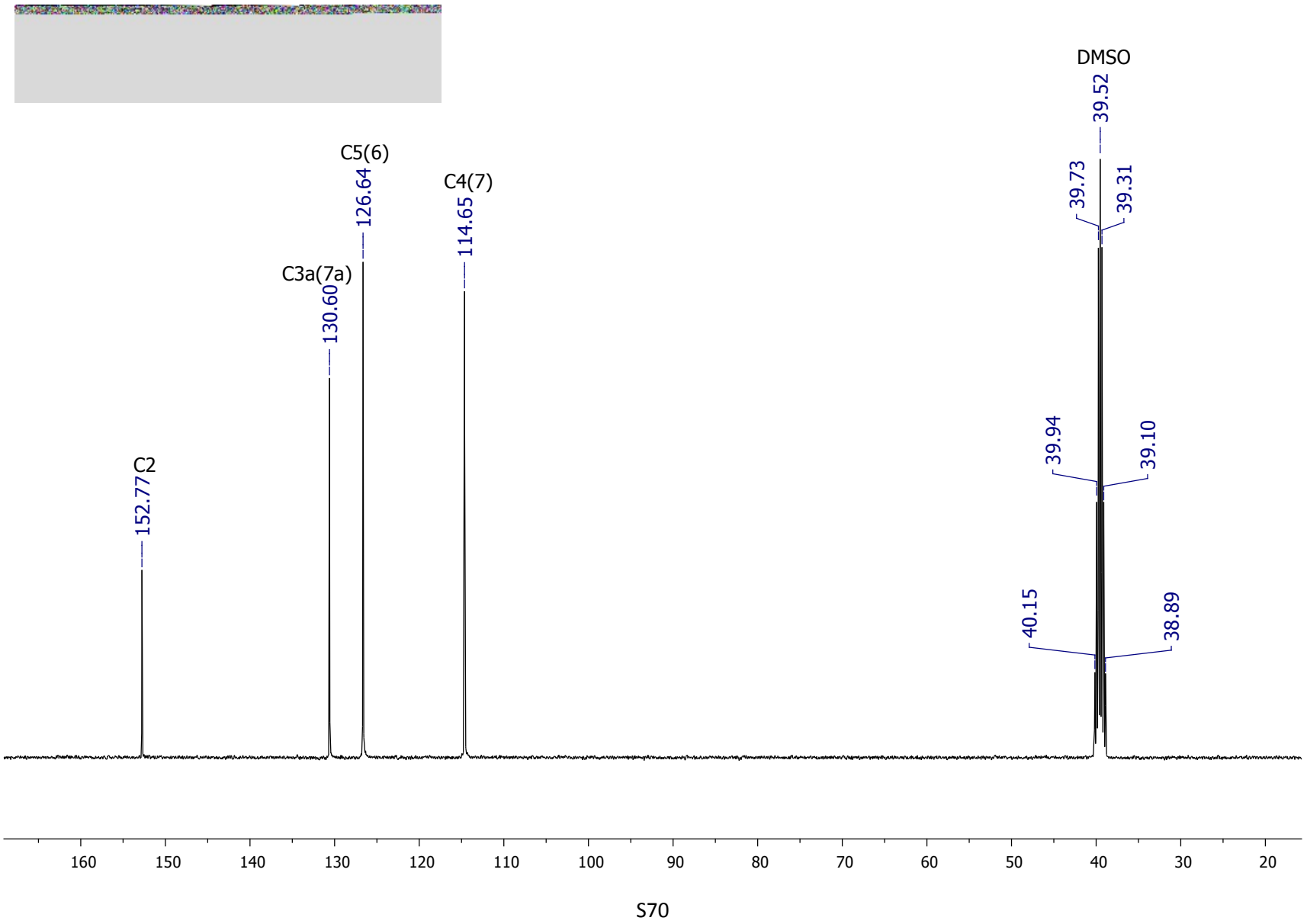

DMSO
39.52
39.73
39.31
39.94
39.10
121.74
C2
141.97
C4(7)
115.33
C3a(7a)
138.10
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

Compound 65

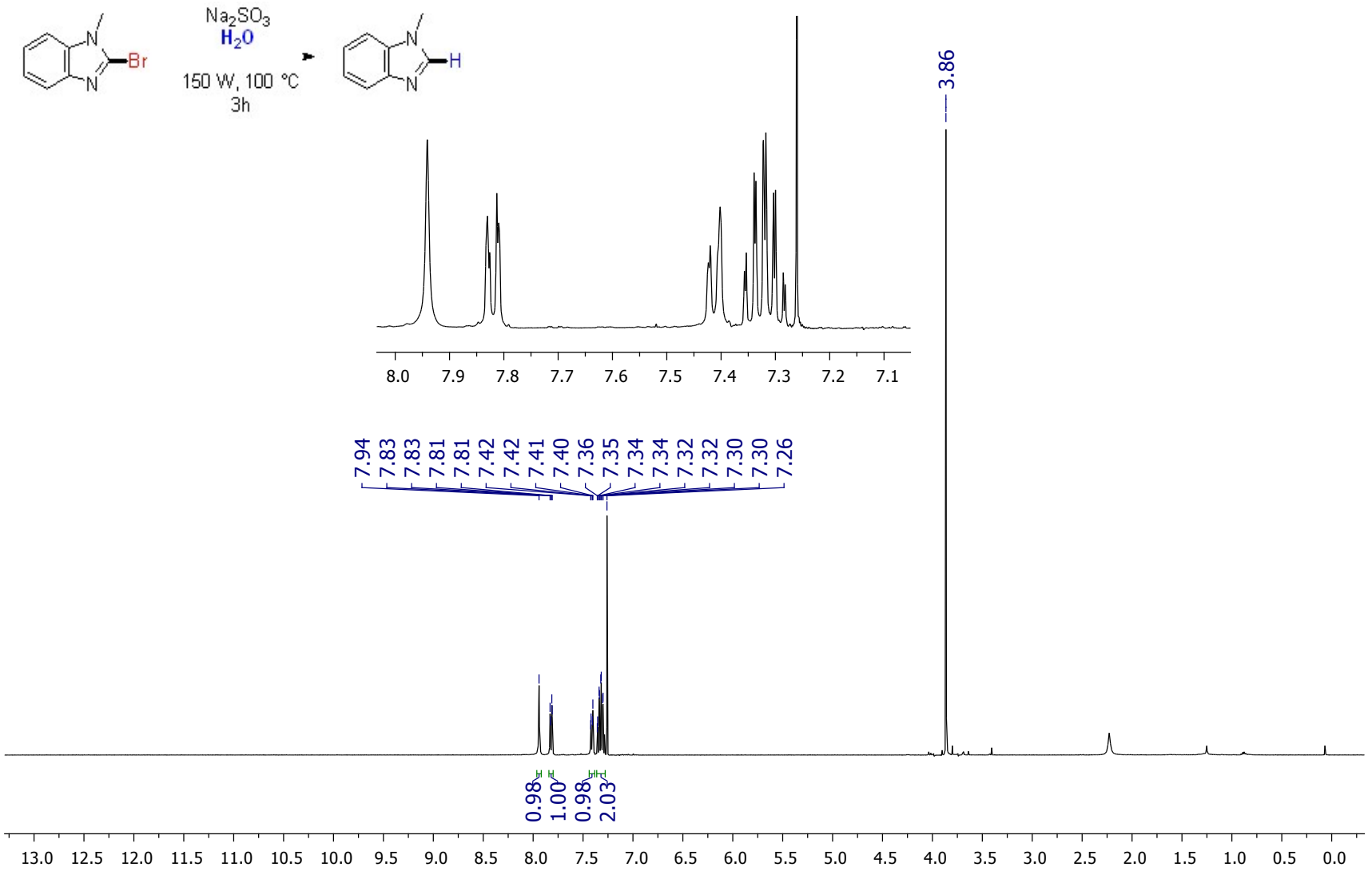

Na2SO3
H2O
150 W, 130 °C
1h
Cl
SO3H


DSMO
2.51
2.50
2.50
2.50
2.49
H4,H7
H5,H6
2.00
2.01
7.80
7.75
7.70
7.65
7.60
7.55
7.50
7.75
7.74
7.73
7.73
7.72
7.71
7.70
7.70
7.60
7.60
7.59
7.58
7.58
7.57
7.56
7.56
2.00
2.01
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

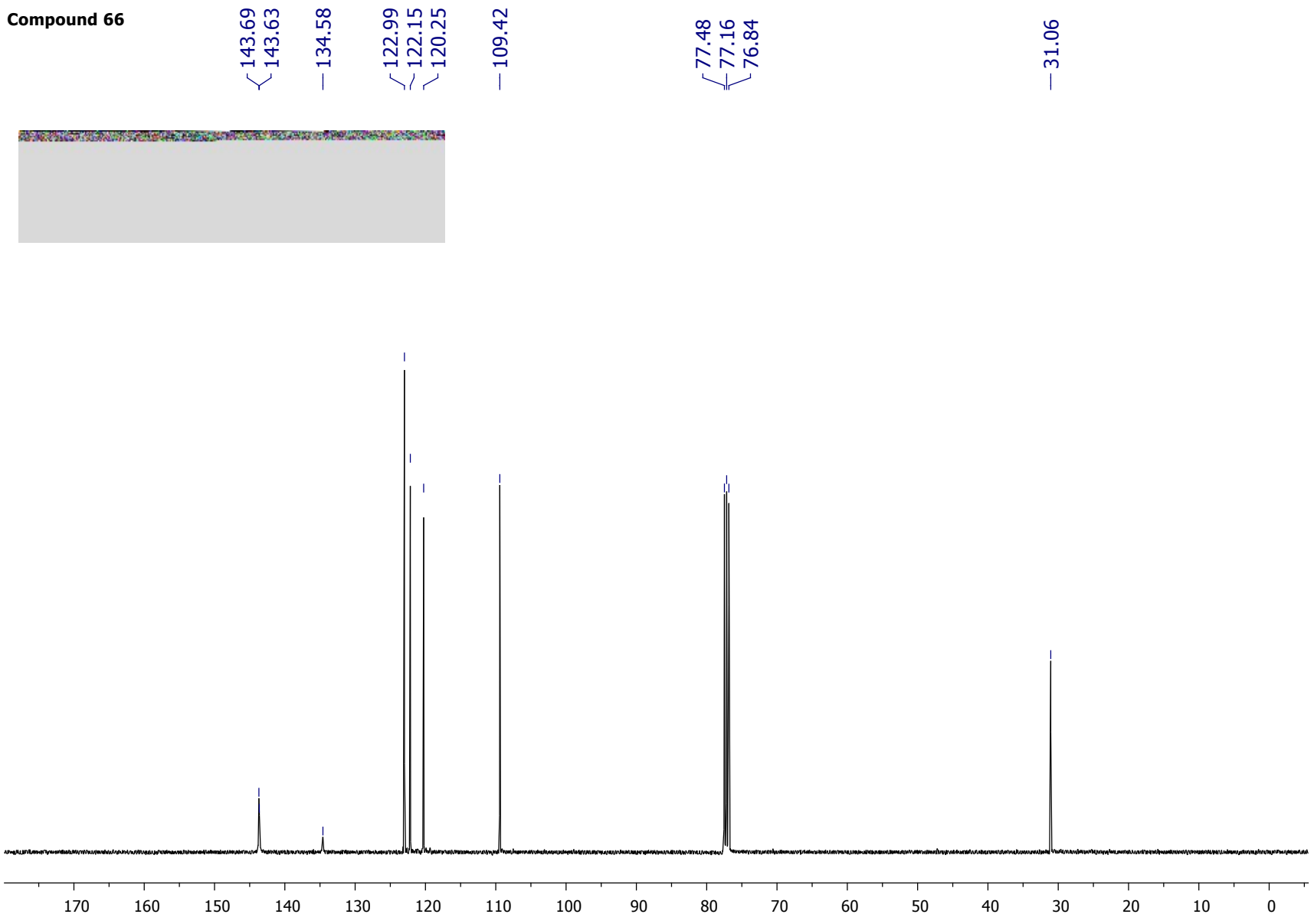
Compound 65


DMSO
39.52
39.73
39.31
C5(6)
126.64
C4(7)
114.65
C3a(7a)
130.60
C2
152.77
39.94
39.10
40.15
38.89
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

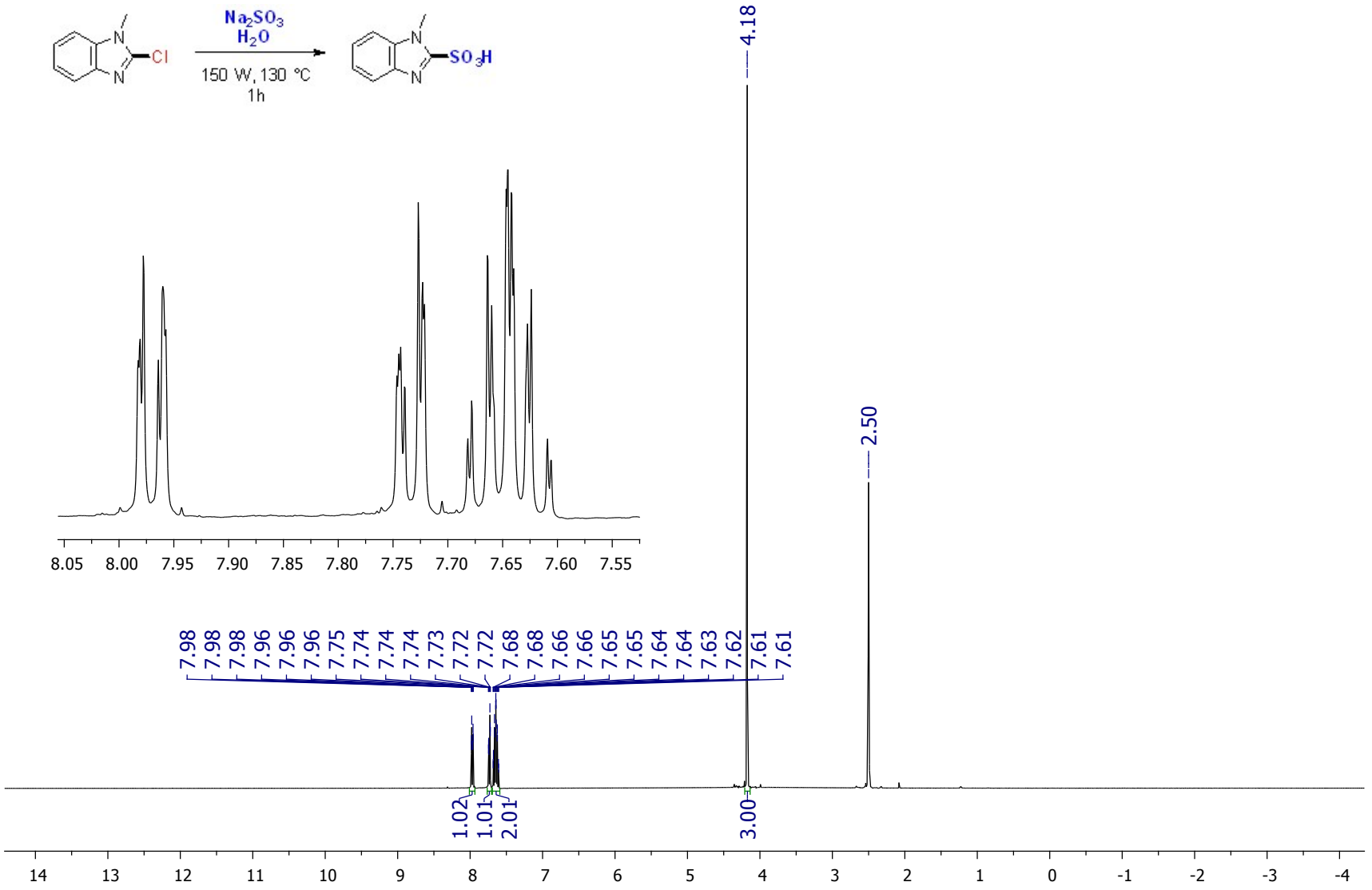
Compound 66


Na2SO3
H2O
150 W, 100 °C
3h
Br
H
3.86
7.94
7.83
7.83
7.81
7.81
7.42
7.42
7.41
7.40
7.36
7.35
7.34
7.34
7.32
7.32
7.30
7.30
7.26
0.98
1.00
0.98
2.03

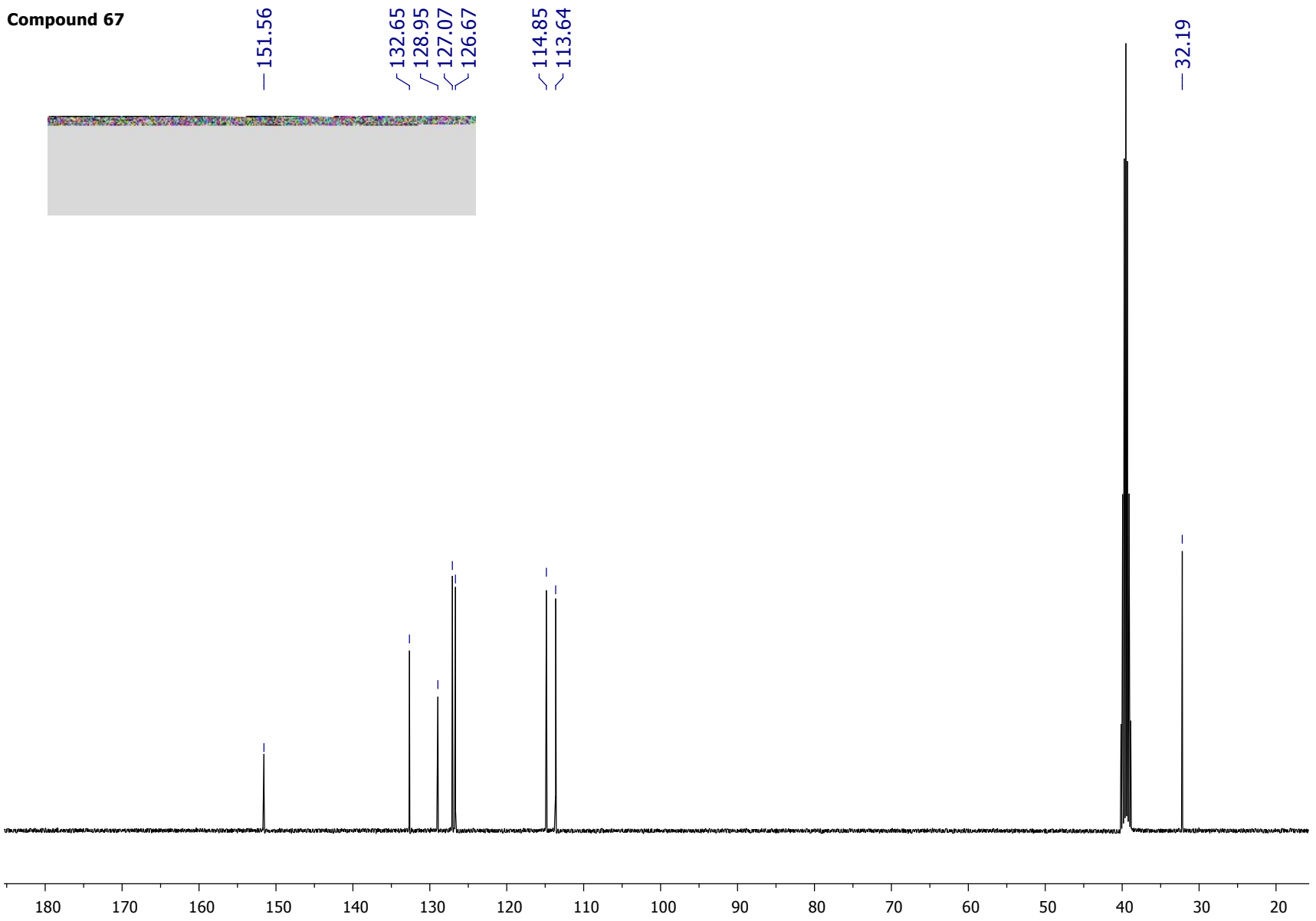
Compound 66


143.69
143.63
134.58
122.99
122.15
120.25
109.42
77.48
77.16
76.84
31.06
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

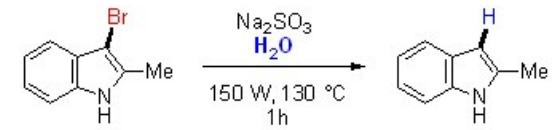
Compound 67


Na2SO3
H2O
150 W, 130 °C
1h
Cl
SO3H
4.18
2.50
7.98
7.98
7.98
7.96
7.96
7.96
7.75
7.74
7.74
7.74
7.73
7.72
7.72
7.68
7.68
7.66
7.66
7.65
7.65
7.64
7.64
7.63
7.62
7.61
7.61
1.02
1.01
2.01
3.00
8.05
8.00
7.95
7.90
7.85
7.80
7.75
7.70
7.65
7.60
7.55
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4

Compound 67

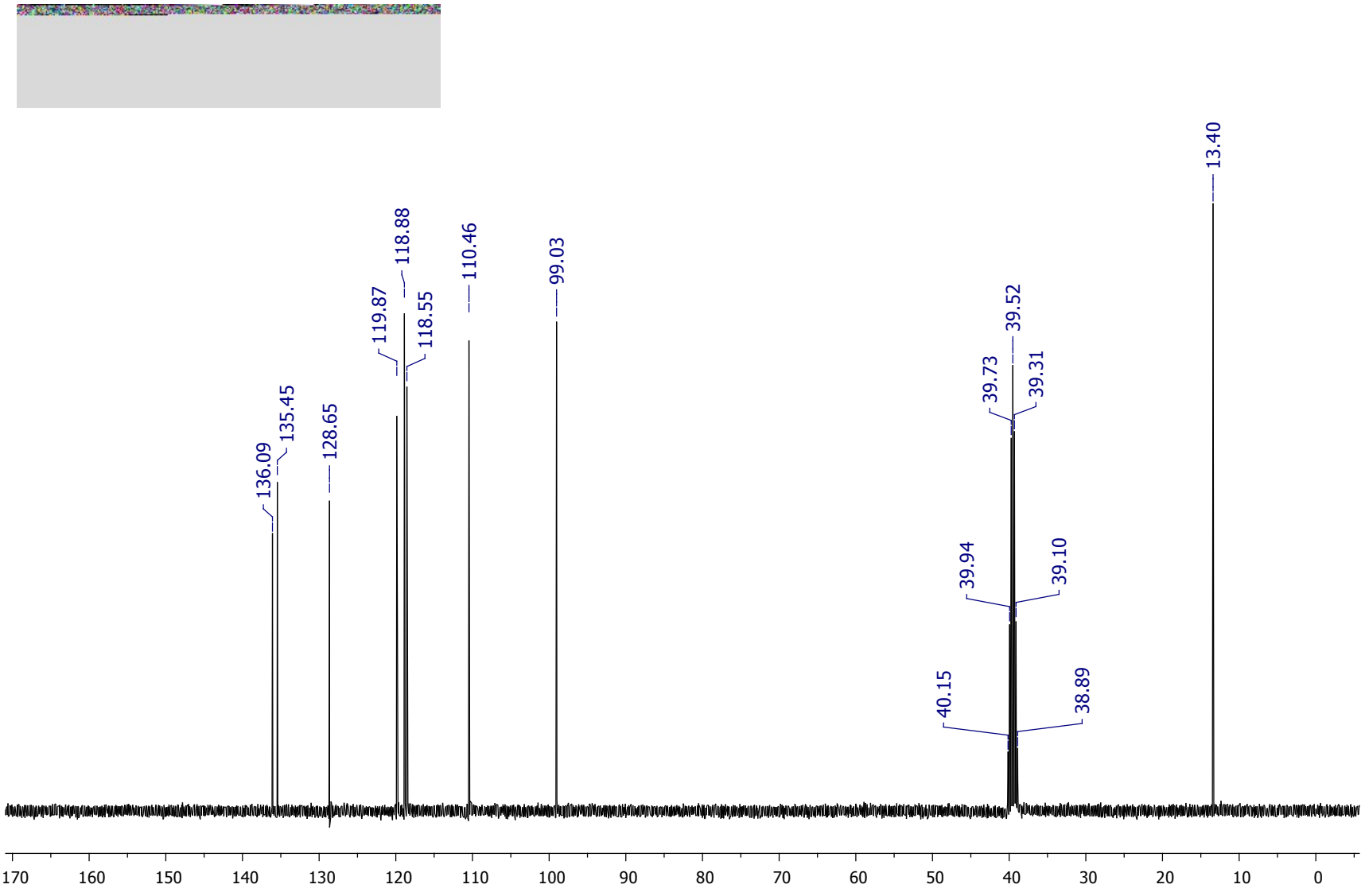

151.56
132.65
128.95
127.07
126.67
114.85
113.64
32.19
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

Compound 68

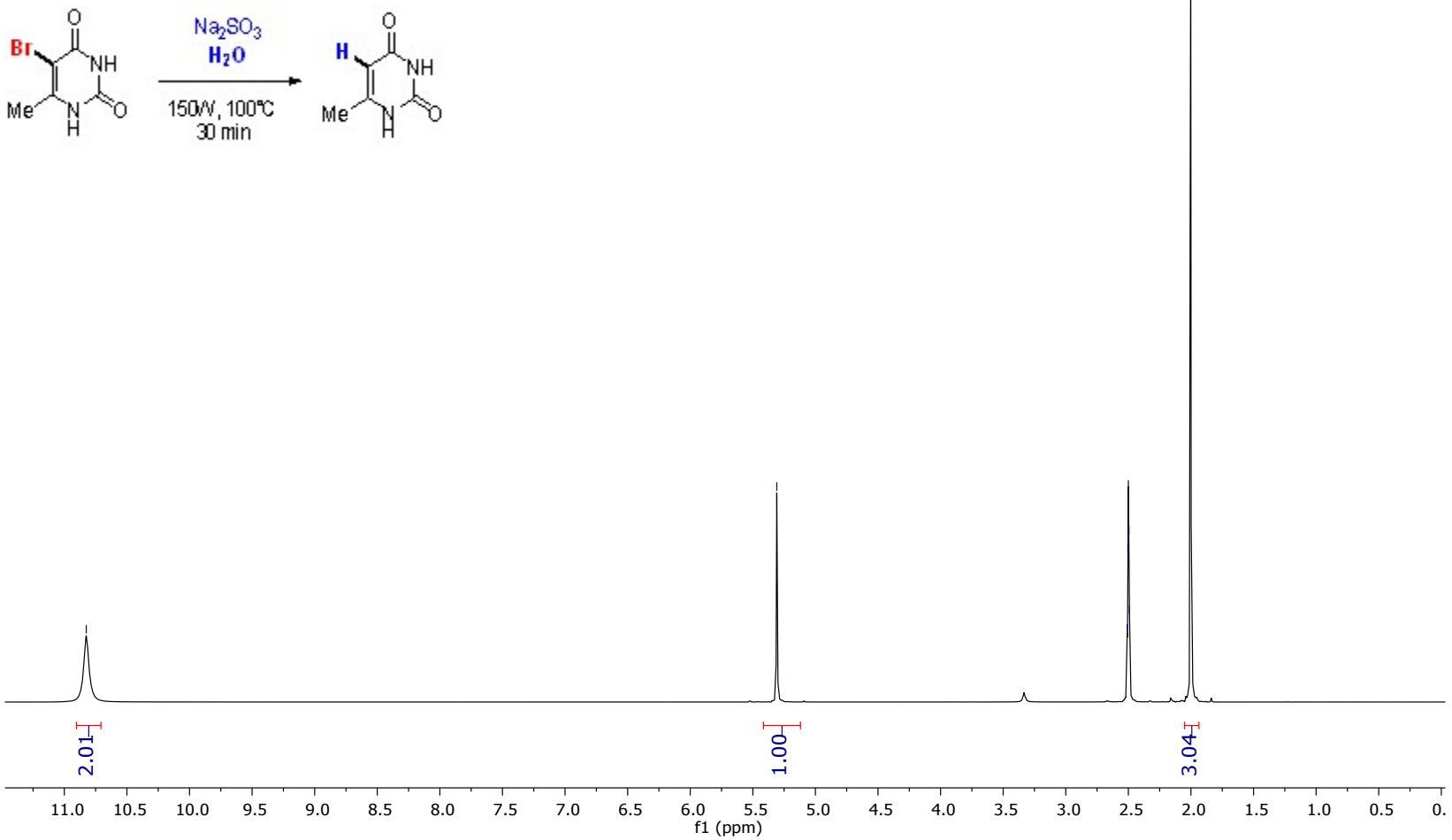

Br
Me
N
H
Na2SO3
H2O
150 W, 130 °C
1h
H
Me
N
H

2.51
2.50
2.50
2.49
2.49
2.37
2.37
7.38
7.36
7.26
7.25
7.24
7.23
6.98
6.98
6.97
6.96
6.95
6.94
6.92
6.92
6.90
6.90
6.90
6.88
6.88
6.10
6.09
6.09
6.09
6.09
3.34
10.86
0.99
1.00
1.01
1.01
1.05
0.98
3.03
7.5
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

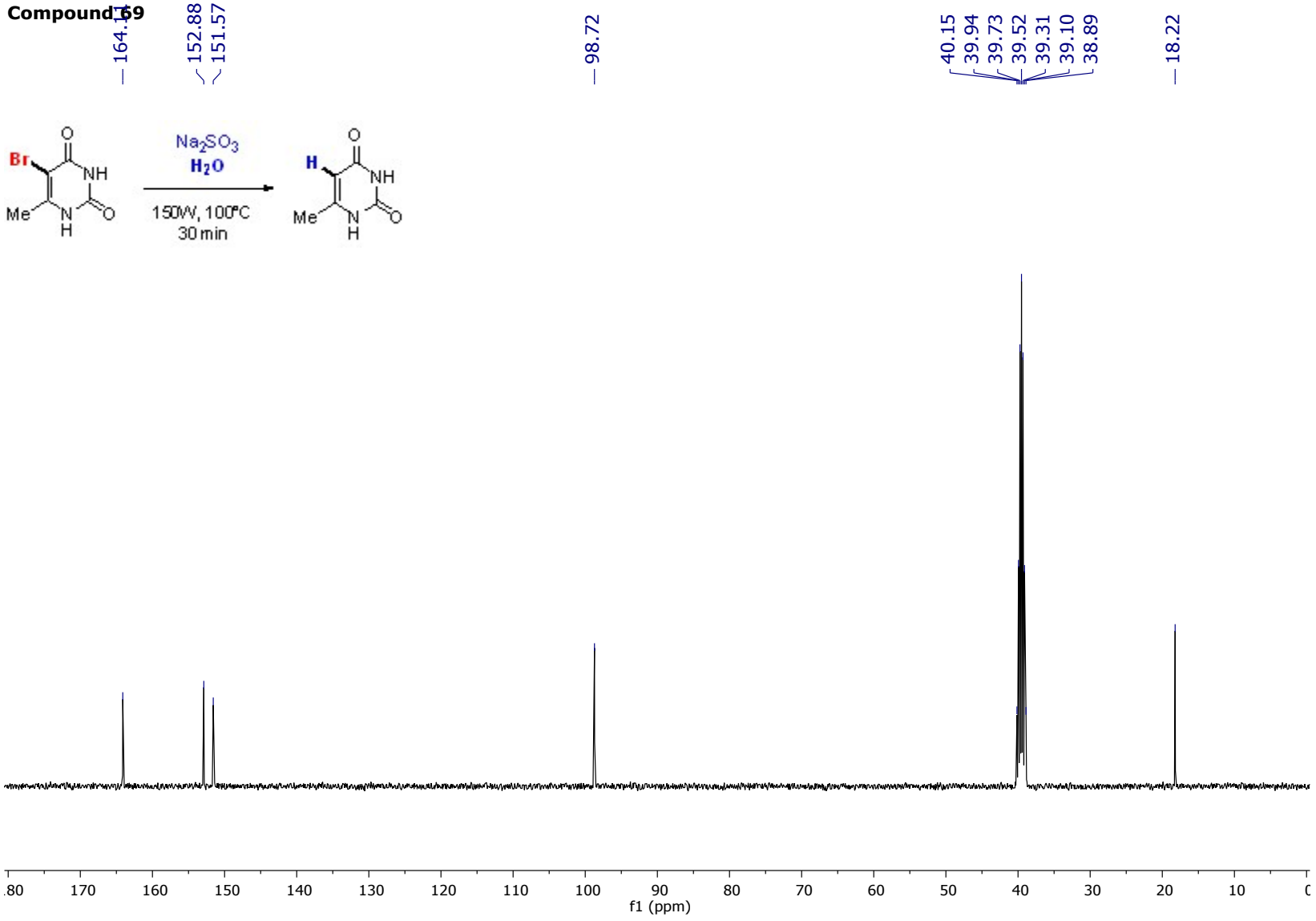
Compound 68


136.09
135.45
128.65
119.87
118.88
118.55
110.46
99.03
40.15
39.94
39.73
39.52
39.31
39.10
38.89
13.40
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

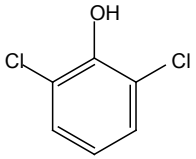
Compound 69


10.82
5.31
2.51
2.50
2.50
2.50
2.49
2.00
Br
O
NH
Me
N
H
O
Na_2SO_3
H_2O
150W, 100℃
30 min
H
O
NH
Me
N
H
O
2.01
1.00
3.04
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
f1 (ppm)

Compound 69

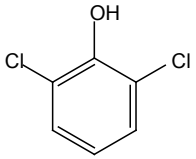

164.11
152.88
151.57
98.72
40.15
39.94
39.73
39.52
39.31
39.10
38.89
18.22
Br
NH
Me
N
H
O
Na_2SO_3
H_2O
150W, 100°C
30 min
H
f1 (ppm)

Compound 71


OH
Cl
Cl

7.27
7.26
7.25
6.84
6.82
6.80
5.85
2.43
1.00
0.04
2.43
1.00
1.08
0.05
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

Compound 71


OH
Cl
Cl

148.00
128.42
121.31
121.27
77.48
77.16
76.84
121.31
121.27
121.6
121.4
121.2
121.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

8. References

1. M. Peng, F. Liu, X. Feng, F. Yang and X. Yang, *Asian J. Chem.*, 2014, **26**, 4701.

2. X.-Z. Li, X. Wei, Ch.-J. Zhang, X.-L. Jin, J.-J. Tang, G.-J. Fan and B. Zhou, *Food Chem.*, 2012, **135**, 1239.