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Amidino substituted 2-aminophenols: Biologically important building blocks for the amidino-functionalization of 2-substituted benzoxazoles

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ELECTRONIC SUPPLEMENTARY INFORMATION

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General information

Melting points were determined by means of Original Kofler Mikroheitztisch apparatus (Reichert, Wien). ^{1}H NMR and ^{13}C NMR spectra were recorded with the Bruker Avance DPX-300 or Bruker AV-600 using TMS as internal standard. Chemical shifts are reported in parts per million (ppm) relative to TMS. UPLC-MS spectra were recorded with Agilent 1290 Infiniti II/6120 Quadrupole LC/MS spectrometers using electrospray ionization (ESI). Elemental analyses for carbon, hydrogen and nitrogen were performed on Perkin-Elmer 2400 elemental analyser. Analyses are indicated as symbols of elements, and analytical results obtained are within 0.4 % of the theoretical value.

Synthesis of amidino substituted 2-aminophenols

4-Hydroxy-3-nitrobenzonitrile (2a)

A mixture of fuming nitric acid (7.0 ml, 170 mmol) and glacial acetic acid (12.5 ml) was added dropwise to the solution of 4-hydroxybenzonitrile **1a** (12.5 g, 105 mmol) in glacial acetic acid (50 ml) at 50 - 60 °C. Reaction mixture was stirred for 30 min at 50 °C then poured into ice – water mixture. The resulting precipitate was filtered, washed with cold water and dried at room temperature giving 16.4 g (95 %) of pure compound **2a** as pale yellow solid; mp = 140 – 144 °C (mp = 142 – 145 °C).[S1] UPLC (230 nm): 99.7 area %; MS (ESI) *m/z*: 163.2 (M-H$^+$) ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 12.32 (bs, 1H, –O*H*), 8.43 (d, 1H, *J* = 2.1 Hz, Ar–*H*), 7.95 (dd, 1H, *J* = 8.7 Hz, *J* = 2.1 Hz, Ar–*H*), 7.26 (d, 1H, *J* = 8.7 Hz, Ar–*H*).

3-Hydroxy-4-nitrobenzonitrile (2b), 3-hydroxy-2-nitrobenzonitrile (2c) and 5-hydroxy-2-nitrobenzonitrile (2d)

A mixture of fuming nitric acid (2.6 ml, 62.3 mmol) and glacial acetic acid (4.8 ml) was added dropwise to the solution of 3-hydroxybenzonitrile (5.0 g, 42.0 mmol) in glacial acetic acid (20 ml) at 30 – 35 °C. The reaction mixture was stirred for 2 h at 35 °C and then poured into ice – water mixture. The resulting precipitate was filtered, washed with cold water and dried at room temperature overnight giving the mixture of isomers **2b**, **2c** and **2d.** Crystallization from toluene gave 1.6 g (23 %) of pure isomer **2d** as pale yellow solid; mp = 195 – 202 °C (mp = 201 °C).[S2] UPLC (230 nm): 98.2 area %; MS (ESI) *m/z*: 163.2 (M-H$^+$) ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.73 (bs, 1H, –O*H*), 8.39 (d, 1H, *J* = 9.1 Hz, Ar–*H*), 7.23 (d, 1H, *J* = 2.7 Hz, Ar–*H*), 7.43 (dd, 1H, *J* = 9.1 Hz, *J* = 2.7 Hz, Ar–*H*). Evaporation of toluene filtrate under reduced pressure and chromatography on silica gel using toluene/EtOAc (97:3) gave pure isomers **2b** and **2c**. Yield of pure isomer **2b** was 1.6 g (23 %) as pale yellow solid; mp = 114 – 119 °C (mp = 121 °C).[S3] UPLC (230 nm): 97.0 area %; MS (ESI) *m/z*: 163.2 (M-H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.80 (bs, 1H, –O*H*), 8.01 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 7.51 (d, 1H, *J* = 1.6 Hz, Ar–*H*), 7.43 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar–*H*). Yield of pure isomer **2c** was 1.4 g (21 %) as pale yellow solid; mp = 135 – 138 °C. UPLC (230 nm): 98.1 area %; MS (ESI) *m/z*: 163.2 (M-H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.91 (bs, 1H, –O*H*), 7.65 (dd, 1H, *J* = 8.5 Hz, *J* = 7.8 Hz, Ar–*H*), 7.53 (dd, 1H, *J* = 7.8 Hz, *J* = 1.2 Hz, Ar–*H*), 7.47 (dd, 1H, *J* = 8.5 Hz, *J* = 1.2 Hz, Ar–*H*). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 151.1, 138.9, 133.7, 124.5, 124.1, 114.5, 106.2. Analysis calcd for $C_7H_4N_2O_3$ (164.12): C, 51.23; H, 2.46; N, 17.07. Found: C, 51.41; H, 2.40; *N, 16.98.*

General procedure for the preparation of 2-aminophenols (3a-3c)

A mixture of 2-nitrophenoles (**2a-2c**) and a solution of tin(II) chloride dihydrate (4 equiv.) dissolved in water : concd HCl 1:1 mixture was heated under reflux for 20 minutes and then poured into ice. The reaction mixture was neutralized with sodium hydroxide solution, extracted with diethyl ether and dried over $MgSO_4$. Evaporation of solvent gave pure amines.

3-Amino-4-hydroxybenzonitrile (3a) Using 4-hydroxy-3-nitrobenzonitrile **2a** (9.8 g, 60 mmol) and 140 ml of solution of tin(II) chloride dihydrate (54.2 g, 240 mmol) gave 7.2 g (90 %) of pure compound **3a** as white solid; mp = 145 – 148 °C (mp = 153 – 156 °C).[1] UPLC (230 nm): 98.3 %; MS (ESI) *m/z*: 135.2 (M+H$^+$). ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 9.75 (bs, 1H, –O*H*), 6.99 (dd, 1H, *J* = 8.1 Hz, *J* = 1.8 Hz, Ar–*H*), 6.87 (d, 1H, *J* = 1.8 Hz, Ar–*H*), 6.63 (d, 1H, *J* = 8.1 Hz, Ar–*H*), 5.54 (s, 2H, –NH_2).

4-Amino-3-hydroxybenzonitrile (3b) Using 3-hydroxy-4-nitrobenzonitrile **2b** (6.0 g, 36 mmol) and 120 ml of solution of tin(II) chloride dihydrate (32.8 g, 146 mmol) gave 4.54 g (94 %) of pure compound **3b** as bright yellow solid; mp = 141 – 145 °C (mp = 149 – 150 °C).[3] UPLC (230 nm): 98.0 area %; MS (ESI) *m/z*: 135.2 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 10.17 (bs, 1H, –O*H*), 6.87 – 6.82 (m, 2H, Ar–*H*), 6.74 (d, 1H, *J* = 8.0 Hz, Ar–*H*), 4.97 (bs, 2H, –NH_2).

2-Amino-3-hydroxybenzonitrile (3c) Using 3-hydroxy-2-nitrobenzonitrile **2c** (2.50 g, 15 mmol) and 50 ml of solution of tin(II) chloride dihydrate (13.8 g, 61 mmol) gave 2.0 g (97 %) of pure compound **3c** as bright yellow solid; mp = 149 – 150 °C. UPLC (230 nm): 99.7 area %; MS (ESI) *m/z*: 135.2 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 9.90 (bs, 1H, –O*H*), 6.86 (d, 2H, *J* = 7.8 Hz, Ar–*H*), 6.48 (dd, 1H, *J* = 7.8 Hz, Ar–*H*), 5.36 (s, 2H, –NH_2). ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 144.4, 141.1, 122.2, 118.2, 117.5, 116.6, 93.8. Analysis calcd for $C_7H_6N_2O$ (134.14): C, 62.68; H, 4.51; N, 20.88. Found: C, 62.64; H, 4.59; N, 20.91. The crystals suitable for X-ray analysis were obtained by slow evaporation from ethyl-acetate.

General procedure for carboximidates (5a-6c)

A solution of the corresponding nitrile **3a** or **3b** in dry alcohol was saturated with dry gaseous HCl at 10 – 15 °C. The flask was stoppered and obtained suspension stirred at room temperature for 5 days (TLC-control). From the reaction mixture the excess of HCl was removed with a stream of N_2 and poured into dry diethyl-ether (500 ml). Resulting precipitate was filtered, washed with dry diethyl-ether and dried under reduced pressure over KOH.

Methyl-(3-amino-4-hydroxyphenyl) carboximidate dihydrochloride (5a). Using general procedure nitrile **3a** (3.97 g, 29.6 mmol) and dry methanol (50 ml) gave 6.35 g (89%) of crude imidate salt **5a**, as very hygroscopic white solid salt which was immediately used in II step of Pinner reaction without purification and characterisation for the preparations of amidines **8c'** and **8d'**.

2-Methoxyethyl-(3-amino-4-hydroxyphenyl) carboximidate dihydrochloride (5b). Using general procedure nitrile **3a** (5.14 g 38.3 mmol) and dry 2-metoxyethanol (70 ml) gave 11.06 g (100%) of crude imidate salt **5b** as hygroscopic white solid. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.81 (bs, 2H, $-C=NH_2^+$), 7.88 (dd, 1H, J = 8.7 Hz, J = 1.8 Hz, Ar–H), 7.80 (d, 1H, J = 1.8 Hz, Ar–H), 7.19 (d, 1H, J = 8.7 Hz, Ar–H), 4.69 (t, 2H, J = 4.1 Hz, $CH_3OCH_2CH_2O-$), 3.78 (t, 2H, J = 4.1 Hz, $CH_3OCH_2CH_2O-$), 3.36 (s, 3H, CH_3O-). The crude imidate salt was used in II step of Pinner reaction without purification within 2 days for the preparations of amidines **8b** and **8d**.

2-(2-Ethoxyethoxy)ethyl-(3-amino-4-hydroxyphenyl) carboximidate dihydrochloride (5c). Using general procedure nitrile **3a** (5.00 g, 37.3 mmol) and dry 2-(2-ethoxyethoxy)ethanol (60 ml) gave 11.87 g (93%) of crude imidate salt **5c**, as hygroscopic white solid. ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 11.81 (bs, 2H, $-C=NH_2^+$), 7.91 (d, 1H, J = 8.7 Hz, Ar–H), 7.85 (s, 1H, Ar–H), 7.22 (d, 1H, J = 8.7 Hz, Ar–H), 4.70 (t, 2H, J = 4.1 Hz, $-OCH_2CH_2O-$), 3.87 (t, 2H, J = 4.1 Hz, $-OCH_2CH_2O-$), 3.64 (t, 2H, J = 4.7 Hz, $-OCH_2CH_2O-$), 3.51 (t, 2H, J = 4.7 Hz, $-OCH_2CH_2O-$), 3.42 (q, 2H, J = 6.9 Hz, CH_3CH_2O-), 1.07 (s, 3H, CH_3CH_2O-). The crude imidate salt was used in II step of Pinner reaction without purification within 3 days for the preparations of amidines **8a**, **8a'** and **8b'**

Methyl-(4-amino-3-hydroxyphenyl) carboximidate dihydrochloride (6a). Using general procedure nitrile **3b** (2.00 g, 14.9 mmol) and dry methanol (20 ml) gave crude imidate salt **4ba** as orange viscous liquid which was immediately used in II step of Pinner reaction without purification and characterisation for the preparations of amidine **8i'**.

2-Methoxyethyl-(4-amino-3-hydroxyphenyl) carboximidate dihydrochloride (6b). Using general procedure nitrile **3b** (5.00 g, 37.3 mmol) and dry 2-metoxyethanol (80 ml) gave 10.30 g (98%) of crude imidate salt **6b** as hygroscopic white solid. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.38 (bs, 1H, $-C=NH_2^+$), 10.73 (bs, 1H, $-C=NH_2^+$), 8.08-7.07 (bs, 4H, $-OH + -NH_3^+$), 7.62 (dd, 1H, J = 8.5 Hz, J =

2.1 Hz, Ar–*H*), 7.41 (d, 1H, *J* = 2.1 Hz, Ar–*H*), 6.85 (d, 1H, *J* = 8.5 Hz, Ar–*H*), 4.66 (t, 2H, *J* = 4.1 Hz, $CH_3OCH_2CH_2O$–), 3.76 (t, 2H, *J* = 4.1 Hz, $CH_3OCH_2CH_2O$–), 3.35 (s, 3H, CH_3O–). The crude imidate salt was used in II step of Pinner reaction without purification within 2 days for the preparations of amidines **8g**, **8g'**, and **8j**.

2-(2-Ethoxyethoxy)ethyl-(4-amino-3-hydroxyphenyl) carboximidate dihydrochloride (6c). Using general procedure nitrile **3b** (3.47 g, 25.8 mmol) and dry 2-(2-ethoxyethoxy)ethanol (50 ml) gave crude imidate salt **6c** as pale red viscous liquid which was immediately used in II step of Pinner reaction without purification and characterisation for the preparations of amidine **8h**

2-Amino-4-amidiniumphenolate hemihydrochloride hydrate (8a). A suspension of imidate salt **5c** (4.44 g, 13.0 mmol) in absolute ethanol (50 ml) was cooled to 10 °C and saturated with ammonia. The flask was stoppered and the reaction mixture was stirred at room temperature for 2 days. From the reaction mixture the excess of NH_3 was removed with a stream of N_2 and cooled overnight in refrigerator. The resulting precipitate was filtered and crystallized from water (charcoal) giving 1.08 g (44%) of beige solid; mp = 148-152 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 152.1 ($M+H^+$). ^1H NMR (600 MHz, DMSO-d_6) (δ ppm): 7.23 (bs, 4H, $-C(NH_2)_2^+$), 6.99 (dd, 1H, *J* = 8.3 Hz, *J* = 2.5 Hz, Ar–*H*), 6.96 (d, 1H, *J* = 2.5 Hz, Ar–*H*), 6.55 (d, 1H, *J* = 8.3 Hz, Ar–*H*), 4.68 (bs, 2H, $-NH_2$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.2, 157.6, 138.2, 119.1, 113.9, 112.2, 110.9. Analysis calcd for $C_7H_9N_3O$ x 0.5 HCl x H_2O (187.41): C, 44.86; H, 6.81; N, 22.42. Found: C, 44.91; H, 6.73; N, 22.41. The crystals suitable for X-ray analysis were obtained by slow evaporation from methanol.

2-Amino-4-amidiniumphenolate dihydrate (8a'). A suspension of imidate salt **5c** (3.14 g, 9.2 mmol) in absolute ethanol (40 ml) was cooled to 10 °C and saturated with ammonia. The flask was stoppered and the reaction mixture was stirred at room temperature for 2 days. From the reaction mixture the excess of NH_3 was removed with a stream of N_2 at room temperature, resulting in a precipitation of ammonium chloride which was separated by filtration. The ethanol filtrate was concentred, and the residue suspended in water (10 ml), and basified to pH 10-11 with a 2.5 M NaOH. The resulting crude product was filtered and crystallized from water giving 0.86 g (64%) of beige crystals suitable for X-ray analysis; mp = 155-158 °C. UPLC (230 nm): 100 area %; MS (ESI) m/z: 152.1 ($M+H^+$). ^1H NMR (300 MHz, DMSO-d_6) (δ ppm): 7.01 (dd, 1H, *J* = 8.5 Hz, *J* = 2.6 Hz, Ar–*H*), 6.83 (d, 1H, *J* = 2.6 Hz, Ar–*H*), 6.11 (d, 1H, *J* = 8.5 Hz, Ar–*H*), 4.27 (s, 2H, $-NH_2$). ^{13}C NMR (75 MHz, D_2O) (δ ppm): 165.3, 163.6, 137.4, 122.3, 117.2, 113.9, 110.5. Analysis calcd for $C_7H_9N_3O$ x 2 H_2O (187.20): C, 44.91; H, 7.00; N, 22.45. Found: C, 45.06; H, 6.96; N, 22.66.

2-Amino-4-(4,5-dihydro-1H-imidazol-3-ium-2-yl)phenolate hemihydrochloride dihydrate (8b). A suspension of imidate salt **5b** (4.25 g, 15.0 mmol) in absolute ethanol (50 ml) under nitrogen, ethylene-diamine (5.0 ml, 75 mmol) was added and reaction mixture was heated under reflux for 4h. After cooling overnight, the resulting precipitate was filtered and crystallized from ethanol giving 1.41 g (41%) of beige crystals suitable for X-ray analysis; mp = 150 – 153 °C. UPLC (230 nm): 99.8 area %; MS (ESI) *m/z*: 178.1 (M+H$^+$) calculated for free base 177.09. ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 7.06 (s, 1H, Ar–*H*), 6.93 (d, 1H, *J* = 7.4 Hz, Ar–*H*), 6.62 (d, 1H, *J* = 7.4 Hz, Ar–*H*), 4.65 (s, 2H, –NH_2), 3.63 (s, 4H, –CH_2CH_2–). ^{13}C NMR (150 MHz, D_2O) (δ ppm): 165.9, 161.6, 137.8, 123.2, 117.5, 115.0, 108.1, 44.6. Analysis calcd for $C_9H_{11}N_3O$ x 0.5 HCl x 2 H_2O (231.46): C, 46.70; H, 6.75; N, 18.15. Found: C, 46.63; H, 6.81; N, 18.22.

2-Amino-4-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate hydrate (8b'). A suspension of imidate salt **5c** (5.66 g, 16.6 mmol) in absolute ethanol (60 ml) under nitrogen, ethylene-diamine (5.6 ml, 84 mmol) was added and reaction mixture was heated under reflux for 4h. After cooling overnight, the resulting precipitate was filtered, and air dried. The crude product was suspended in water (20 ml), and basified to pH 10-11 with a 2.5 M NaOH. The resulting solid was filtered and washed with cold ethanol giving 2.54 g (78%) of beige solid; mp = 153-158 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 178.1 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 7.07 (d, 1H, *J* = 2.1 Hz, Ar–*H*), 6.87 (dd, 1H, *J* = 8.1 Hz, *J* = 2.1 Hz, Ar–*H*), 6.56 (d, 1H, *J* = 8.1 Hz, Ar–*H*), 4.55 (s, 2H, –NH_2), 3.54 (s, 4H, –CH_2CH_2–). ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 164.6, 151.4, 137.0, 117.7, 116.5, 113.7, 112.3, 47.9. Analysis calcd for $C_9H_{11}N_3O$ x H_2O (195.10): C, 55.37; H, 6.71; N, 21.52. Found: C, 55.28; H, 6.76; N, 21.61. The crystals suitable for X-ray analysis were obtained by slow evaporation from water.

2-Amino-4-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate hydrate (8c'). A suspension of imidate salt **5a** (1.90 g, 14.5 mmol) in absolute ethanol (35 ml) under nitrogen, 1,3-propanediamine (5.0 ml, 60 mmol) was added and reaction mixture was heated under reflux for 4 h. The reaction mixture was cooled, resulting in a precipitation of 1,3-propanediamine dihydrochloride which was separated by filtration. The ethanol filtrate was concentred and the residue dissolved in water. The solution was basified to pH 10-11 with a 2.5 M NaOH and the resulting solid, filtered and washed with cold ethanol giving 2.28 g (75%) of beige solid; mp = 218 – 223 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 192.2 (M+H$^+$). ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 6.84 – 6.79 (m, 2H, Ar–*H*), 6.24 (d, 1H, *J* = 8.0 Hz, Ar–*H*), 4,33 (bs, 2H, –NH_2), 3.32 (t, 4H, *J* = 5.5 Hz, –CH_2CH$_2$CH_2–), 1.79 (m, 2H, –CH$_2$CH_2CH$_2$–). ^{13}C NMR (75 MHz, D_2O) (δ ppm): 162.8, 160.1, 138.1, 121.2, 117.8, 113.6, 113.0, 39.3, 18.8. Analysis calcd for $C_{10}H_{13}N_3O$ x H_2O (209.24): C, 57.40; H, 7.23; N, 20.08. Found: C, 57.37; H, 7.31; N, 20.10. The crystals suitable for X-ray analysis were obtained by slow evaporation from water.

2-Amino-4-(*N*-isopropylamidino)phenol hydrochloride ethanol solvate (8d). A suspension of imidate salt **5b** (5.5 g, 19.4 mmol) in absolute ethanol (30 mL) under nitrogen, *i*-propylamine (4.1 ml, 47.7 mmol) was added and reaction mixture was heated under reflux for 2 h. After cooling overnight, the resulting precipitate was filtered, and crystallized from ethanol giving 2.45 g (46%) of pale yellow crystals suitable for X-ray analysis; mp = 247 – 250 °C . UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 194.2 (M+H$^+$) calcd for free base 193.12. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 10.25 (bs, 1H, –O*H*), 9.16 – 8.76 (m, 3H, –C(N*H*$_2$)$^+$N*H*–), 6.89 (d, 1H, *J* = 2.0 Hz, Ar–*H*), 6.86 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 6.81 (dd, 1H, *J* = 8.2 Hz, *J* = 2.0 Hz, Ar–*H*), 4.98 (bs, 2H, –N*H*$_2$), 4.02 (m, 1H, *J* = 6.4 Hz, –C*H*(CH$_3$)$_2$), 1.23 (d, 6H, *J* = 6.4 Hz, –CH(C*H*$_3$)$_2$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 162.2, 148.7, 137.1, 119.9, 116.9, 113.8, 112.8, 44.6, 21.3. Analysis calcd for $C_{10}H_{15}N_3O$ x HCl x C_2H_5OH (275.77): C, 55.27; H, 7.58; N, 16.63. Found: C, 55.44; H, 7.49; N, 16.57.

2-Amino-4-(*N*-isopropylamidinium)phenolate (8d'). A suspension of imidate salt **5a** (6.0 g, 25.1 mmol) in absolute ethanol (30 mL) under nitrogen, *i*-propylamine (5.0 ml, 61.1 mmol) was added and reaction mixture was heated under reflux for 2 h. After cooling overnight, the resulting precipitate was filtered, and washed with cold ethanol. The crude product was suspended in cold water (3 ml) and basified to pH 10-11 with a 2.5 M NaOH. After cooling overnight, the resulting precipitate was filtered giving 2.48 g (51%) of pale yellow solid; mp = 232 – 234 °C. UPLC (230 nm): 98.7 area %; MS (ESI) *m/z*: 194.2 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 6.82-6.78 (m, 2H, Ar–*H*), 6.38 (d, 1H, *J* = 8.8 Hz, Ar–*H*), 4.50 (bs, 2H, –N*H*$_2$), 3.91 (m, 1H, *J* = 6.4 Hz, –C*H*(CH$_3$)$_2$), 1.18 (d, 6H, *J* = 6.4 Hz, –CH(C*H*$_3$)$_2$). ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 162.2, 148.7, 137.1, 119.9, 116.9, 113.8, 112.8, 44.6, 21.3. Analysis calcd for $C_{10}H_{15}N_3O$ (193.25): C, 62.15; H, 7.82; N, 21.74. Found: C, 62.20; H, 7.77; N, 21.74.

2-Amino-4-(4,5,6,7-tetrahydro-1*H*-1,3-diazepinium-2-yl)phenolate (8e'). A suspension of imidate salt **5b** (2.6 g, 9.2 mmol) in absolute ethanol (60 mL) under nitrogen, 1,4-butanediamine (4.8 ml, 47.8 mmol) was added and reaction mixture was heated under reflux for 4 h. After cooling overnight, the resulting precipitate was filtered and washed with cold ethanol. The crude product obtained was suspended in cold water (10 ml) and basified to pH 10-11 with a 2.5 M NaOH. After cooling overnight, the resulting precipitate was filtered giving 1.19 g (61%) of beige solid; mp > 300 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 206.2 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 8.25 (bs, 2H, –C(N*H*–)$_2$$^+$), 6.85 (dd, 1H, *J* = 8.5 Hz, *J* = 2.4 Hz, Ar–*H*), 6.68 (d, 1H, *J* = 2.4 Hz, Ar–*H*), 6.13 (d, 1H, *J* = 8.5 Hz, Ar–*H*), 4.33 (bs, 2H, –N*H*$_2$), 3.35 (bs, 4H, –C*H*$_2$CH$_2$CH$_2$C*H*$_2$–), 1.68 (bs, 4H, –CH$_2$C*H*$_2$C*H*$_2$CH$_2$–). Analysis calcd for $C_{11}H_{15}N_3O$ (205.26): C, 64.37; H, 7.37; N, 20.47. Found: C, 64.33; H, 7.46; N, 20.40

2-Aminium-4-(4,5,6,7-tetrahydro-1*H*-1,3-diazepinium-2-yl)phenol dimethanesulphonate hydrate (8e). A solution of phenolate **8e'** (0.43 g, 2.1 mmol) in ethanol (5 ml) methanesulfonic acid (0.300 ml, 4.7 mmol) was added. After cooling overnight, the resulting precipitate was filtered giving 0.48 g (55%) of yellow crystals suitable for X-ray analysis; mp = 176 – 181 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 206.4 (M+H$^+$) calcd for free base 205.12. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 11.56 (bs, 1H, –O*H*), 9.47 (s, 2H, –C(N*H*–)$_2$$^+$), 7.53 (s, 1H, Ar–*H*), 7.46 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 7.10 (d, 1H, *J* = 8.4

Hz, Ar–*H*), 5.53 (bs, 3H, $–NH_3^+$), 3.63 (s, 4H, $–CH_2CH_2CH_2CH_2–$), 2.38 (s, 6H, $CH_3SO_3^-$), 1.93 (s, 4H, $–CH_2CH_2CH_2CH_2–$). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) (δ ppm): 164.1, 154.3, 128.1, 122.9, 120.5, 115.7, 43.7, 39.7, 25.5. Analysis calcd for $C_{11}H_{15}N_3O$ x 2 CH_3SO_3H x H_2O (415.48): C, 37.58; H, 6.06; N, 10.11. Found: C, 37.77; H, 5.98; N, 10.03.

2,2'-Bis(3-amino-4-phenolate)butane-1,4-diimidamide (8f'). A suspension of imidate salt **5b** (3.1 g, 10.8 mmol) in absolute ethanol (100 ml) under nitrogen, 1,4-butanediamine (2.7 mL, 26.9 mmol) was added and reaction mixture was heated under reflux for 4 h. After cooling overnight, the resulting precipitate was filtered and washed with cold ethanol. The crude product was suspended in cold water (5 ml) and basified to pH 10-11 with a 2.5 M NaOH. After cooling overnight, the resulting precipitate was filtered giving 0.85 g (22%) of yellow solid; mp = 173 – 178 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 357.2 ($M+H^+$). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) (δ ppm): 6.88 (d, 2H, *J* = 2.3 Hz, Ar–*H*), 6.83 (dd, 2H, *J* = 8.2 Hz, *J* = 2.3 Hz, Ar–*H*), 6.58 (d, 2H, *J* = 8.2 Hz, Ar–*H*), 4.70 (bs, 6H, –N*H*–, $–NH_2$), 3.35 (m, 4H, $–CH_2CH_2CH_2CH_2–$), 1.66 (m, 4H, $–CH_2CH_2CH_2CH_2–$). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) (δ ppm): 162.7, 153.3, 137.7, 117.7, 116.9, 113.7, 111.6, 42.0, 25.2. Analysis calcd for $C_{18}H_{24}N_6O_2$ (356.42): C, 60.66; H, 6.79; N, 23.58. Found: C, 60.70; H, 6.70; N, 23.64.

2-Amino-5-amidinophenol dihydrochloride (8g). A suspension of imidate salt **6b** (2.30 g, 8.1 mmol) in absolute ethanol (35 ml) was cooled to 10 °C and saturated with ammonia. The flask was stoppered and the reaction mixture was stirred at room temperature for 2 days. From the reaction mixture the excess of NH_3 was removed with a stream of N_2 at room temperature, resulting in a precipitation of ammonium chloride which was separated by filtration. The ethanol filtrate was saturated with dry gaseous HCl and resulting precipitate filtered and crystallized from ethanol giving 1.30 g (72%) of colourless crystals suitable for X-ray analysis; mp = 191 – 194 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 152.1 ($M+H^+$) calculated for free base 151.07. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) (δ ppm): 10.39 (bs, 1H, –O*H*), 9.04 (s, 2H, $–C(NH_2)_2^+$), 8.87 (s, 2H, $–C(NH_2)_2^+$), 7.26 – 7.18 (m, 2H, Ar–*H*), 7.02 (d, 1H, *J* = 8.0 Hz, Ar–*H*), 6.19 (bs, 3H, $–NH_3^+$). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) (δ ppm): 165.4, 147.5, 133.3, 121.6, 120.1, 119.1, 114.7. Analysis calcd for $C_7H_9N_3O$ x 2 HCl (224.09): C, 37.52; H, 4.95; N, 18.75. Found: C, 37.41; H, 5.08; N, 18.72.

2-Amino-5-(4,5-dihydro-1*H*-imidazol-2-yl)phenol hydrochloride dihydrate (8h). A solution of imidate salt **6c** prepared from nitrile **3b** (3.47 g, 25.8 mmol) in absolute ethanol (50 ml) under nitrogen, ethylene-diamine (4.3 ml, 65 mmol) was added and reaction mixture was heated under reflux for 4 h. After cooling overnight, the resulting precipitate was filtered, and crystallized from water giving 3.88 g (60%) of pale yellow solid; mp = 198 – 202 °C. UPLC (230 nm): 99.4 area %; MS (ESI) *m/z*: 178.1 ($M+H^+$) calculated for free base 177.09. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) (δ ppm): 9.87 (bs, 3H, –O*H* + $–C(NH–)_2^+$), 7.33 (dd, 1H, *J* = 8.3 Hz, *J* = 2.0 Hz, Ar–*H*), 7.21 (d, 1H, *J* = 2.0 Hz, Ar–*H*), 6.68 (d, 1H, *J*

= 8.3 Hz, Ar–*H*), 5.90 (s, 2H, –N*H*$_2$), 3.86 (s, 4H, –C*H*$_2$C*H*$_2$–). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) (δ ppm): 164.7, 144.5, 143.0, 122.6, 113.9, 112.6, 107.5, 43.8. Analysis calcd for $C_9H_{11}N_3O$ x HCl x 2 H_2O (249.69): C, 43.29; H, 6.46; N, 16.83. Found: C, 43.31; H, 6.28; N, 16.78. The crystals suitable for X-ray analysis were obtained by slow evaporation from water.

2-Amino-5-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate hydrate (8h'). A suspension of imidate salt **6b** (3.4 g, 12.0 mmol) in absolute ethanol (30 mL) under nitrogen, ethylene-diamine (2.0 ml, 30 mmol) was added and reaction mixture was heated under reflux for 4 h. After cooling overnight, the resulting precipitate was filtered, suspended in water (15 ml) and basified to pH 10-11 with a 2.5 M NaOH and cooled overnight. The resulting precipitate was filtered giving 1.73 g (81%) of beige solid; mp = 191 – 194 °C. UPLC (230 nm): 100 area %; MS (ESI) *m/z*: 178.1 (M+H$^+$). ^{1}H NMR (300 MHz, DMSO-*d*$_6$) (δ ppm): 7.72 (bs, 2H, –C(N*H*–)$_2$$^+$), 7.18 (d, 1H, *J* = 1.6 Hz, Ar–*H*), 7.00 (dd, 1H, *J* = 8.0 Hz, *J* = 1.6 Hz, Ar–*H*), 6.53 (d, 1H, *J* = 8.0 Hz, Ar–*H*), 4.89 (s, 2H, –N*H*$_2$), 3.50 (s, 4H, –C*H*$_2$C*H*$_2$–).^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 164.2, 143.3, 139.3, 119.1, 118.5, 113.3, 112.7, 49.4. Analysis calcd for $C_9H_{11}N_3O$ (177.20): C, 55.37; H, 6.71; N, 21.52. Found: C, 55.54; H, 6.58; N, 21.48.

2-Amino-5-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate (8i'). A solution of imidate salt **6a** prepared from nitrile **3b** (2.00 g, 14.9 mmol) in absolute ethanol (50 ml) under nitrogen, 1,3-propanediamine (5.0 mL, 60 mmol) was added and reaction mixture was heated under reflux for 4 h. The reaction mixture was cooled, resulting in a precipitation of 1,3-propanediamine dihydrochloride which was separated by filtration. The ethanol filtrate was concentred, the residue dissolved in water and basified to pH 10-11 with a 2.5 M NaOH. The resulting precipitate filtered and washed with cold ethanol giving 2.13 g (75%) of beige solid; mp = 218 – 223 °C. UPLC (254 nm): 100 area %; MS (ESI) *m/z*: 192.1 (M+H$^+$). ^{1}H NMR (600 MHz, DMSO-*d*$_6$) (δ ppm): 9.49 (bs, 2H, –C(N*H*–)$_2$$^+$), 6.82 – 6.76 (m, 2H, Ar–*H*), 6.23 (d, 1H, *J* = 7.8 Hz, Ar–*H*), 4.31 (bs, 2H, –N*H*$_2$), 3.31 (t, 4H, *J* = 5.7 Hz, –C*H*$_2$–), 1.91 (m, 2H, –C*H*$_2$–). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 158.8, 143.3, 142.7, 120.1, 114.3, 112.8, 112.7, 38.6, 18.3. Analysis calcd for $C_{10}H_{13}N_3O$ (191.23): C, 62.81; H, 6.85; N, 21.97. Found: C, 62.92; H, 6.80; N, 21.91.

2-Amino-5-(*N*-isopropylamidino)phenol hydrochloride (8j). A suspension of imidate salt **6b** (2.5 g, 8.9 mmol) in absolute ethanol (25 ml) under nitrogen, *i*-propylamine (2.0 ml, 23.3 mmol) was added and reaction mixture was heated under reflux for 2 h. After cooling overnight, the resulting precipitate was filtered, washed with cold ethanol giving 1.2 g (59%) of pale yellow solid; mp = 145 – 148 °C. UPLC (230 nm): 99.5 area %; MS (ESI) *m/z*: 194.2 (M+H$^+$) calcd for free base 193.12. ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ/ppm: 10.95 (bs, 1H, –O*H*), 9.43 – 9.05 (m, 3H, –C(N*H*$_2$)$^+$N*H*–), 7.29 – 7.27 (m, 2H, Ar–*H*), 7.13 (dd, 1H, *J* = 8.1 Hz, *J* = 1.9 Hz, Ar–*H*) 5.69 (bs, 2H, –N*H*$_2$), 4.09 (m, 1H, *J* = 6.5 Hz, –C*H*(CH$_3$)$_2$), 1.25 (d, 6H, *J* = 6.5 Hz, –CH(C*H*$_3$)$_2$). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 161.4, 148.1, 130.8, 124.3, 120.1, 119.8, 115.0, 44.9, 21.3. Analysis calcd for $C_{10}H_{15}N_3O$ x HCl (229.71): C, 52.29; H, 7.02; N, 18.29. Found: C, 52.38; H, 6.98; N, 18.14.

General procedure for the preparation of amidino-substituted 2-arylbenzoxazoles (10a-10l)

A mixture of amidino-substituted 2-aminophenol **8a’-8c’**, **8g** and **8h’** (0.5 mmol) and benzoic acid (**7a**), 1-naphthoic acid (**7b**) or 2-naphthoic acid (**7c**) (0.5 mmol) in polyphosphoric acid (10-12 g) was gradually heated to 160 °C until the mixture became homogenous and then at 180 °C for 2 h. The reaction mixture was poured in water (150 mL), cooled and made alkaline with 20 % NaOH. The obtained free base was filtered, washed with water and dried under vacuum over KOH. To a mixture of crude base in ethanol (5 ml) methanesulfonic acid (35 µL, 0.55 mmol) was added and stirred at room temperature for 1-2 h, diethyl ether (10 ml) was added, and then cooled overnight. The resulting precipitate was filtered and purified by crystallization.

5-Amidinium-2-phenylbenzoxazole methansulfonate (10a) Using zwitterion **8a’** (94 mg), acid **9a** (61 mg) and crystallization from ethanol/diethyl ether gave 93 mg (56 %) of white solid; mp = 268 – 271 °C. UPLC (254 nm): 100 area %; MS (ESI) *m/z*: 238.2 ($M+H^+$) calcd for free base 237.09. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 9.41 (s, 2H, $–C(NH_2)_2^+$), 9.13 (s, 2H, $–C(NH_2)_2^+$), 8.32 (s, 1H, Ar–*H*), 8.26 (d, 2H, *J* = 6.5 Hz, Ar–*H*), 8.08 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 7.89 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 7.71 – 7.67 (m, 3H, Ar–*H*), 2.33 (s, 3H, $CH_3SO_3^-$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.3, 164.2, 153.2, 141.6, 132.7, 129.5, 127.6, 125.8, 125.7, 125.0, 120.3, 111.7, 39.8. Analysis calcd for $C_{15}H_{15}N_3O_4S$ (333.36): C, 54.04; H, 4.54; N, 12.60. Found: C, 54.12; H, 4.52; N, 12.57.

6-Amidinium-2-phenylbenzoxazole methansulfonate dihydrate (10b) Using hydrochloride **8g** (112 mg), acid **9a** (61 mg) and crystallization from ethanol gave 102 mg (55 %) of beige solid; mp = 276 – 280 °C. UPLC (254 nm): 98.1 area %; MS (ESI) *m/z*: 238.2 ($M+H^+$) calcd for free base 237.09. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 9.38 (bs, 4H, $–C(NH_2)_2^+$), 8.34 – 8.12 (m, 3H, Ar–*H*), 8.00 (bs, 1H, Ar–*H*), 7.86 (bs, 1H, Ar–*H*), 7.66 (bs, 3H, Ar–*H*), 2.33 (s, 3H, $CH_3SO_3^-$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.1, 164.8, 149.7, 145.5, 132.8, 129.5, 127.7, 125.6, 125.1, 125.1, 120.1, 111.3, 39.8. Analysis calcd for $C_{15}H_{15}N_3O_4S$ x 2 H_2O (369.39): C, 48.77; H, 5.18; N, 11.38. Found: C, 48.65; H, 5.22; N, 11.41.

5-(4,5-Dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (10c) Using zwitterion **8b'** (98 mg), acid **9a** (61 mg) and crystallization from ethanol gave 100 mg (56 %) of white solid; mp = 167 – 170 °C. UPLC (254 nm): 99.7 area %; MS (ESI) *m/z*: 264.2 ($M+H^+$) calcd for free base 263.11. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 10.56 (bs, 2H, $–C(NH–)_2^+$), 8.43 (d, 1H, *J* = 1.4 Hz, Ar–*H*), 8.28 (dd, 2H, *J* = 7.2 Hz, *J* = 1.4 Hz, Ar–*H*), 8.11 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 7.99 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6

Hz, Ar–*H*), 7.73 (t, 1H, *J* = 7.2 Hz, Ar–*H*), 7.68 (t, 2H, *J* = 1.4 Hz, Ar–*H*), 7.75 – 7.63 (m, 3H, Ar–*H*), 4.07 (s, 4H, –C*H*$_2$C*H*$_2$–), 2.32 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 165.6, 164.6, 149.9, 146.3, 133.0, 129.5, 127.9, 125.5, 125.4, 120.6, 118.7, 111.5, 44.5, 39.7. Analysis calcd for $C_{17}H_{17}N_3O_4S$ (359.40): C, 56.81; H, 4.77; N, 11.69. Found: C, 56.88; H, 4.61; N, 11.77.

6-(4,5-Dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (10d) Using zwitterion **8h'** (89 mg), acid **9a** (61 mg) and crystallization from ethanol gave 83 mg (46 %) of beige solid; mp = 223 – 225 °C. UPLC (254 nm): 98.1 area %; MS (ESI) *m/z*: 264.2 (M+H$^+$) calcd for free base 263.11. ^{1}H NMR (600 MHz, DMSO-*d*$_6$) (δ ppm): 10.58 (bs, 2H, –C(N*H*–)$_2^+$), 8.42 (d, 1H, *J* = 1.6 Hz, Ar–*H*), 8.28 (dd, 2H, *J* = 7.2 Hz, *J* = 1.4 Hz, Ar–*H*), 8.11 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 7.99 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar–*H*), 7.75 – 7.65 (m, 3H, Ar–*H*), 4.07 (s, 4H, –C*H*$_2$C*H*$_2$–), 2.32 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 165.6, 164.6, 149.9, 146.3, 133.0, 129.5, 127.9, 125.5, 125.4, 120.6, 118.7, 111.5, 44.5, 39.7. Analysis calcd for $C_{17}H_{17}N_3O_4S$ (359.40): C, 56.81; H, 4.77; N, 11.69. Found: C, 56.91; H, 4.75; N, 11.64.

5-Amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (10e) Using zwitterion **8a’** (94 mg), acid **9b** (86 mg) and crystallization from ethanol gave 65 mg (34 %) of orange solid; mp = 273 – 277 °C. UPLC (254 nm): 98.5 area %; MS (ESI) *m/z*: 288.2 (M+H$^+$) calcd for free base 287.11. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) (δ ppm): 9.44 (s, 2H, –C(N*H*$_2$)$_2^+$), 9.41 (s, 1H, Ar–*H*), 9.14 (s, 2H, –C(N*H*$_2$)$_2^+$), 8.52 (dd, 1H, *J* = 7.4 Hz, *J* = 1.0 Hz, Ar–*H*), 8.45 (d, 1H, *J* = 1.6 Hz, Ar–*H*), 8.30 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 8.14 (d, 2H, *J* =8.7 Hz, Ar–*H*), 7.94 (dd, 1H, *J* = 8.7 Hz, *J* = 1.6 Hz, Ar–*H*), 7.85 – 7.67 (m, 3H, Ar–*H*), 2.38 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (150 MHz, DMSO-*d*$_6$) (δ ppm): 165.3, 163.8, 152.6, 141.7, 133.6, 133.4, 130.0, 129.8, 129.0, 128.3, 126.8, 126.0, 125.4, 125.4, 124.9, 121.7, 120.5, 111.6, 39.8. Analysis calcd for $C_{19}H_{17}N_3O_4S$ (383.42): C, 59.52; H, 4.47; N, 10.96. Found: C, 59.50; H, 4.58; N, 10.90.

6-Amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (10f) Using hydrochloride **8g** (112 mg), acid **9b** (86 mg) and crystallization from ethanol gave 73 mg (38 %) of white solid; mp = 265 – 268 °C. UPLC (254 nm): 99.3 area %; MS (ESI) *m/z*: 288.2 (M+H$^+$) calcd for free base 287.11. ^{1}H NMR (300 MHz, DMSO-*d*$_6$) (δ ppm): 9.45 (bs, 2H, –C(N*H*$_2$)$^+$), 9.42 (s, 1H, Ar–*H*), 9.17 (bs, 2H, –C(N*H*$_2$)$^+$), 8.53 (d, 1H, *J* = 7.1 Hz, Ar–*H*), 8.38 (s, 1H, Ar–*H*), 8.31 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 8.20 – 8.11 (m, 2H, Ar–*H*), 7.91 (dd, 1H, *J* = 8.4 Hz, *J* = 1.4 Hz, Ar–*H*), 7.86 – 7.67 (m, 3H, Ar–*H*), 2.35 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (75 MHz, DMSO-*d*$_6$) (δ ppm): 165.1, 164.9, 149.0, 145.8, 133.6, 130.2, 129.8, 129.1, 128.4, 126.9, 125.5, 125.4, 125.2, 125.1, 121.7, 120.3, 111.4, 39.8. Analysis calcd for $C_{19}H_{17}N_3O_4S$ (383.42): C, 59.52; H, 4.47; N, 10.96. Found: C, 59.43; H, 4.55; N, 10.99.

6-(4,5-Dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (10g) Using zwitterion **8h'** (89 mg), acid **9b** (86 mg) and crystallization from ethanol gave 84 mg (41 %) of white solid; mp = 248 – 252 °C. UPLC (254 nm): 100 area %; MS (ESI) *m/z*: 314.2 (M+H$^+$) calcd for free base 313.12. ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 10.62 (s, 2H, –C(N*H*–)$_2^+$), 9.43 (d, 1H, *J* = 8.6 Hz, Ar–*H*), 8.55 (dd, 1H, *J* = 7.3 Hz, *J* = 0.9 Hz, Ar–*H*), 8.47 (d, 1H, *J* = 1.7 Hz, Ar–*H*), 8.31 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 8.22 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 8.14 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 8.03 (dd, 1H, *J* = 8.4 Hz, *J* = 1.7 Hz, Ar–*H*), 7.73 – 7.70 (m, 3H, Ar–*H*), 4.09 (s, 4H, –C*H*$_2$C*H*$_2$–), 2.33 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.2, 164.6, 149.1, 146.3, 133.7, 133.6, 130.3, 129.8, 129.1, 128.4, 126.8, 125.4, 121.5, 120.7, 118.9, 111.4, 44.5, 39.8. Analysis calcd for $C_{21}H_{19}N_3O_4S$ (409.46): C, 61.60; H, 4.68; N, 10.26. Found: C, 61.66; H, 4.61; N, 10.24.

6-(3,4,5,6-Tetrahydropyrimidinium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (10h) Using zwitterion **8c'** (105 mg), acid **9b** (86 mg) and crystallization from ethanol gave 74 mg (35 %) of beige solid; mp = 277 – 282 °C. UPLC (254 nm): 99.9 area %; MS (ESI) *m/z*: 328.1 (M+H$^+$) calcd for free base 327.14. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 10.05 (bs, 2H, –C(N*H*–)$_2^+$), 9.44 (d, 1H, *J* = 8.7 Hz, Ar–*H*), 8.53 (dd, 1H, *J* = 7.4 Hz, *J* = 1.0 Hz, Ar–*H*), 8.31 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 8.27 (d, 1H, *J* = 1.3 Hz, Ar–*H*), 8.19 (d, 1H, *J* = 8.3 Hz, Ar–*H*), 8.15 (d, 1H, *J* = 8.2 Hz, Ar–*H*), 7.85 – 7.68 (m, 3H, Ar–*H*), 3.56 (m, 4H, –C*H*$_2$CH$_2$C*H*$_2$–), 2.30 (s, 3H, C*H*$_3$SO$_3^-$), 2.04 (m, 2H, –CH$_2$C*H*$_2$CH$_2$–). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 164.6, 159.0, 149.0, 145.2, 133.6, 133.5, 130.1, 129.8, 129.0, 128.4, 126.8, 125.7, 125.4, 124.6, 121.7, 120.5, 110.9, 39.7, 38.9, 17.7. Analysis calcd for $C_{22}H_{21}N_3O_4S$ (423.48): C, 62.40; H, 5.00; N, 9.92. Found: C, 62.45; H, 4.92; N, 9.98.

5-Amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (10i) Using zwitterion **8a’** (94 mg), acid **9c** (86 mg) and crystallization from water/acetone gave 86 mg (41 %) of beige solid; mp = 250 – 254 °C. UPLC (254 nm): 96.5 area %; MS (ESI) *m/z*: 288.2 (M+H$^+$) calcd for free base 287.11. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 9.42 – 9.20 (m, 4H, –C(N*H*$_2$)$_2^+$), 8.88 (s, 1H, Ar–*H*), 8.33 – 8.05 (m, 6H, Ar–*H*), 7.91 (bs, 1H, Ar–*H*), 7.68 (bs, 2H, Ar–*H*), 2.36 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 165.3, 164.4, 153.3, 141.8, 134.6, 132.5, 129.2, 129.1, 128.6, 128.5, 127.9, 127.4, 125.8, 125.1, 123.6, 123.0, 120.3, 111.6. Analysis calcd for $C_{19}H_{17}N_3O_4S$ x $2H_2O$ (419.45): C, 54.41; H, 5.05; N, 10.02. Found: C, 54.36; H, 5.12; N, 10.01.

6-Amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (10j) Using hydrochloride **8g** (112 mg), acid **9c** (86 mg) and crystallization from water/acetone gave 96 mg (46 %) of pale yellow solid; mp = 276 – 281 °C. UPLC (254 nm): 96.5 area %; MS (ESI) *m/z*: 288.2 (M+H$^+$) calcd for free base 287.11. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 9.43 – 9.22 (m, 4H, –C(N*H*$_2$)$_2^+$), 8.91 (s, 1H, Ar–*H*), 8.33 – 8.16 (m, 4H, Ar–*H*), 8.07 (bs, 2H, Ar–*H*), 7.89 (d, 1H, *J* = 7.1 Hz, Ar–*H*), 7.69 (bs, 2H, Ar–*H*), 2.37 (s, 3H, C*H*$_3$SO$_3^-$). ^{13}C NMR (75 MHz, DMSO-d_6) (δ ppm): 165.4, 165.1, 149.8, 145.8, 134.7, 132.5, 129.3, 129.2, 128.7, 127.9, 127.4, 125.2, 125.0, 123.6, 122.9, 120.1, 111.4. Analysis calcd for $C_{19}H_{17}N_3O_4S$ x $2H_2O$ (419.45): C, 54.41; H, 5.05; N, 10.02. Found: C, 54.32; H, 5.18; N, 9.97.

6-(4,5-Dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (10k) Using zwitterion **8h'** (89 mg), acid **9c** (86 mg) and crystallization from water/acetone gave 104 mg (51 %) of pale yellow solid; mp = 272 – 276 °C. UPLC (254 nm): 97.3 area %; MS (ESI) *m/z*: 314.2 ($M+H^+$) calcd for free base 313.12. ^{1}H NMR (600 MHz, DMSO-d_6) (δ ppm): 10.62 (s, 2H, $-C(NH-)_2^+$), 8.92 (s, 1H, Ar–*H*), 8.41 (d, 1H, *J* = 1.3 Hz, Ar–*H*), 8.29 (dd, 1H, *J* = 8.6 Hz, *J* = 1.6 Hz, Ar–*H*), 8.23 (d, 1 H, *J* = 8.0 Hz, Ar–*H*), 8.18 (d, 1H, *J* = 8.6 Hz, Ar–*H*), 8.12 (d, 1H, *J* = 8.4 Hz, Ar–*H*), 8.07 (d, 1H, *J* = 8.0 Hz, Ar–*H*), 8.00 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar–*H*), 7.73 – 7.67 (m, 2H, Ar–*H*), 4.08 (s, 4H, $-CH_2CH_2-$), 2.36 (s, 3H, $CH_3SO_3^-$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.7, 164.5, 149.9, 146.4, 134.7, 132.4, 129.2, 128.8, 128.7, 127.9, 127.4, 125.5, 123.6, 122.7, 120.5, 118.7, 111.4, 44.5, 39.7. Analysis calcd for $C_{21}H_{19}N_3O_4S$ (409.46): C, 61.60; H, 4.68; N, 10.26. Found: C, 61.56; H, 4.76; N, 10.28.

6-(3,4,5,6-Tetrahydropyrimidinium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (10l) Using zwitterion **8c'** (105 mg), acid **9c** (86 mg) and crystallization from water/acetone gave 123 mg (58 %) of pale yellow solid; mp = 246 - 251 °C. UPLC (254 nm): 100 area %; MS (ESI) *m/z*: 328.1 ($M+H^+$) calcd for free base 327.14. ^{1}H NMR (300 MHz, DMSO-d_6) (δ ppm): 10.04 (bs, 2H, $-C(NH-)_2^+$), 8.92 (s, 1H, Ar–*H*), 8.31 (dd, 1H, *J* = 8.6 Hz, *J* = 1.6 Hz, Ar–*H*), 8.24 (d, 1H, *J* = 8.6 Hz, Ar–*H*), 8.19 (d, 1H, *J* = 8.8 Hz, Ar–*H*), 8.11 – 8.06 (m, 2H, Ar–*H*), 7.79 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz, Ar–*H*), 7.75 – 7.65 (m, 2H, Ar–*H*), 3.56 (bs, 4H, $-CH_2CH_2CH_2-$), 2.30 (s, 3H, $CH_3SO_3^-$), 2.07 – 2.00 (m, 2H, $-CH_2CH_2CH_2-$). ^{13}C NMR (150 MHz, DMSO-d_6) (δ ppm): 165.2, 158.9, 149.8, 145.3, 134.6, 132.5, 129.2, 129.1, 128.6, 127.9, 127.4, 125.5, 124.7, 123.6, 123.0, 120.2, 110.9, 39.7, 38.9, 17.7. Analysis calcd for $C_{22}H_{21}N_3O_4S$ (423.48): C, 62.40; H, 5.00; N, 9.92. Found: C, 62.48; H, 5.01; N, 9.89.

II. Single crystal X-ray diffraction

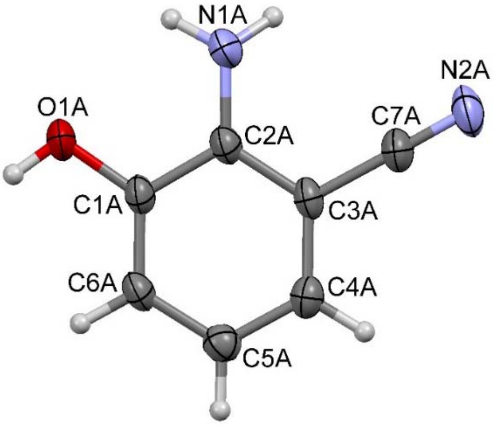


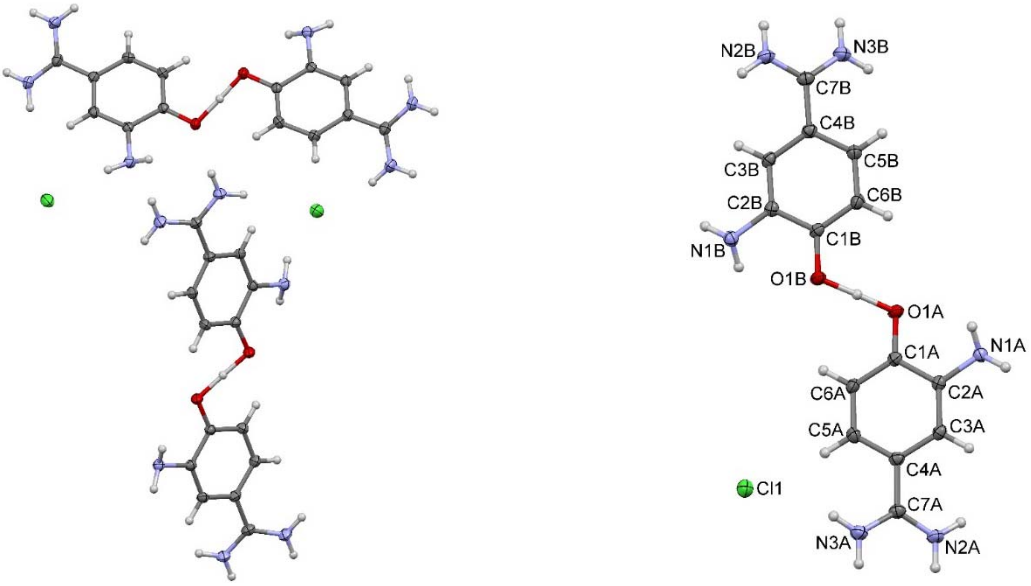
Figure S1. Molecular structure of **3c**, with atom numbering scheme. Displacement ellipsoids for non-hydrogen atoms are drawn at the 40 % probability level.

Table S1 Selected bond lengths for 4- and 5-amidino-substituted aminophenols

Compound	**C7–N2**	**C7–N3**	**C1–O1** (4-Am)[a]/ **C2–O1** (5-Am)[b]	**C2–N1** (4-Am)[a]/ **C1–N1** (5-Am)[b]
8a I [a]	1.314(3)	1.309(2)	1.335(2)	1.407(2)
8a II [a]	1.317(3)	1.320(3)	1.328(2)	1.407(2)
	1.323(3)	1.312(3)	1.338(2)	1.409(2)
	1.323(3)	1.318(3)	1.339(2)	1.411(2)
8a’ [a]	1.325(6)	1.315(5)	1.325(4)	1.417(5)
8b [a]	1.322(3)	1.318(3)	1.339(2)	1.409(2)
	[illegible]	[illegible]	[illegible]	[illegible]
8b’ [a,c]	1.319(4)	1.325(4)	1.323(4)	1.407(4)
	1.323(5)	1.324(5)	1.319(5)	1.401(5)
8c’ [a]	1.322(3)	1.321(3)	1.305(3)	1.407(3)
8d [a]	1.3160(18)	1.3211(18)	1.3551(17)	1.4107(18)
8e [a]	1.313(3)	1.316(3)	1.347(2)	1.461(3)
8g [b]	1.314(3)	1.304(3)	1.361(3)	1.459(3)
8h [b,c]	1.319(2)	1.327(2)	1.371(2)	1.364(2)

[a] 4-amidino-substituted 2-aminophenols; [b] 5-amidino-substituted 2-aminophenols; [c] bond lengths are given only for major disorder components

Data for compound **8a** were collected at 295 K and due to disorder present in structure, new data collection was done at 223 K. Two data collections revealed two temperature-dependent polymorphic forms of this compound, monoclinic designated as **8a I** (295 K) and triclinic designated as **8a II** (223 K). In **8a I** (Figure 1a), the negatively charged oxygen atom O1 and a symmetry related atom of a neighbouring molecule share the same proton located on the inversion centre, thus forming a cationic dimer. However, in the structure **8a II** the bridging proton is located on a general position, with the cationic dimers comprising two symmetry independent halves (Figure S2). Furthermore, the asymmetric unit of the salt solvate form **I** contains one cationic dimer, one chloride anion and two water molecules, while the asymmetric unit of form **II** contains twice the number of respective species. Accordingly, while the form **8a I** was refined in a monoclinic space group $P2_1/c$, the structure **8a II** was refined in triclinic space group $P\overline{1}$, with a unit cell doubled along the *a* axis relative to that of **8a I**.



(a) (b)

Figure S2. Molecular structure of **8a II**, showing (a) two cationic dimers and two chlorides in the asymmetric unit, and (b) atom numbering scheme of one cationic dimer. Displacement ellipsoids for non-hydrogen atoms are drawn at the 40 % probability level. Water molecules are omitted for clarity.

In **8b**, again, the dimeric cations are formed by two zwitterionic molecules bridged by a proton, with **8b** crystallizing as a hemihydrochloride monohydrate (Figure S3). However, the proton in the cationic dimer of **8b** lies on a crystallographic two-fold axis.

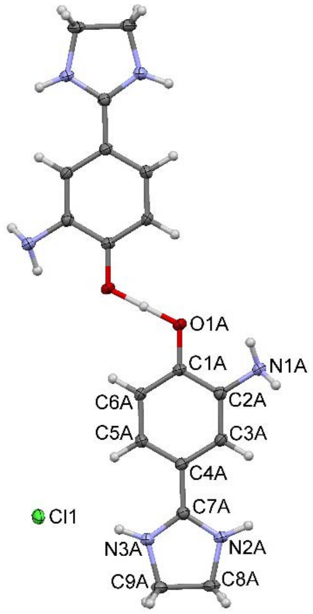


Figure S3. Molecular structure of **8b**, with atom numbering scheme. Displacement ellipsoids for non-hydrogen atoms are drawn at the 50 % probability level. Only one cationic dimer and chloride anion are shown. Water molecules are omitted for clarity.

Structures **8d** and **8h** contain one ethanol molecule or two water molecules, respectively, in the asymmetric unit. The C1–N1 bond in the structure of 5-amidino-substituted derivative **8h** (Figure S4) is significantly shorter (*ca*. 0.05 Å) than the C–NH_2 bond in the previously described 4-amidino-substituted structures.

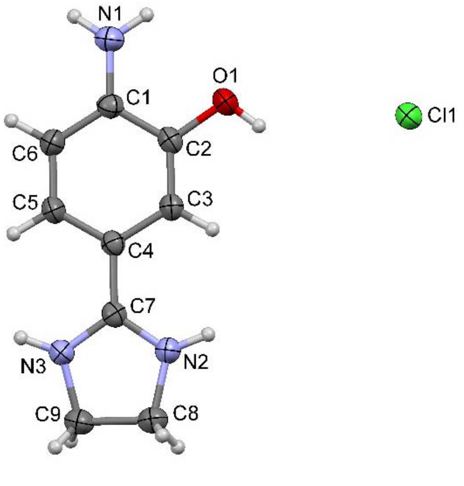
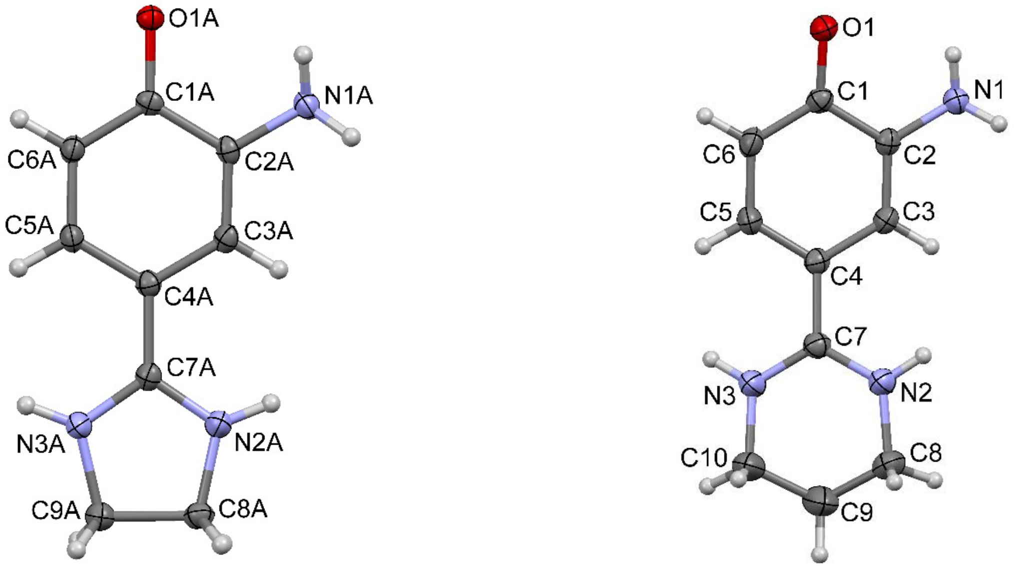


Figure S4. Molecular structure of **8h**, with atom numbering scheme. Displacement ellipsoids for non-hydrogen atoms are drawn at the 40 % probability level. Only major components of disordered atoms are presented. Solvent molecules are omitted for clarity.

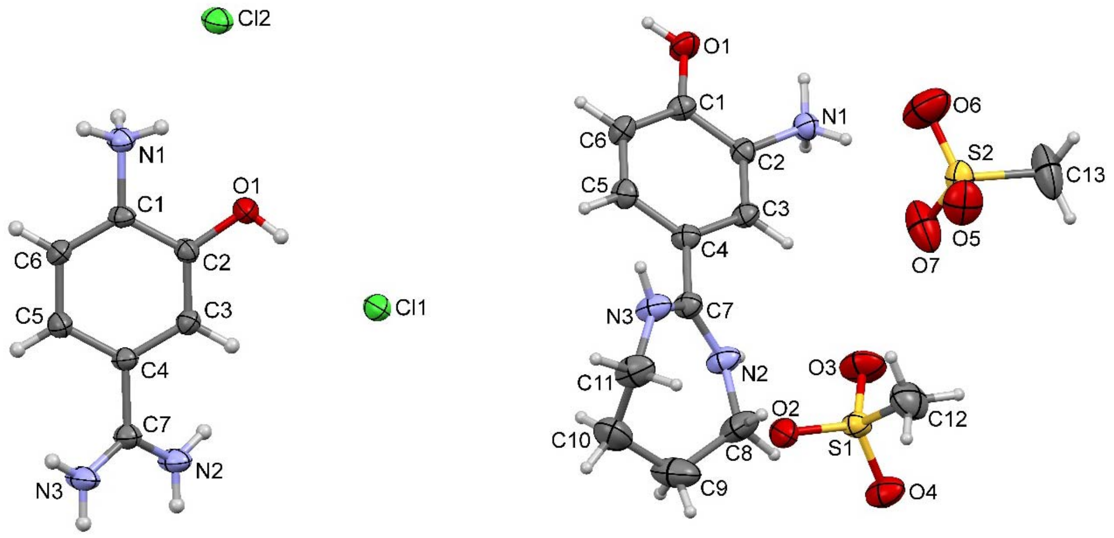
Compound **8c’** crystallized as monohydrate, **8a’** as dihydrate, while compound **8b’** crystallized with three independent molecules and *ca*. 14.2 water molecules in the asymmetric unit (Figure S5).



(a) (b)

Figure S5. Molecular structures of (a) **8b’** and (b) **8c’**, with atom numbering schemes. Displacement ellipsoids for non-hydrogen atoms are drawn at the 40 % probability level. Only the major disorder component of one of the symmetry-independent molecules in **8b’** is presented. Water molecules are omitted for clarity.

Isolation of 5-amidino-substituted derivative **8g** from ethanol solution with an excess of hydrogen chloride yielded a dihydrochloride. X-ray crystallographic study confirmed that this structure consists of one dication and two chlorides (Figure S6a). Besides the amidinium moiety, the amine N1 atom is also protonated, while the charge is balanced by two chloride anions. The C2–O1 bond distance in this salt structure is typical for a phenol C–O bond and corresponds to that observed in **8d**. On the other hand, the C1–N1 bond is 0.1 Å longer than the equivalent one in the 5-substituted amidino derivative **8h**, as expected for a $C–NH_3^+$ bond. Finally, another example of a dication with two anions is the structure of 4-amidino-substituted derivative **8e** in which amidinium moiety is a part of an 1,3-diazepinium ring (Figure S6b). Its asymmetric unit contains one dication, two methanesulfonate anions and one water molecule. The C2–N1 and phenol C–O bond lengths agree with the corresponding ones in **8g**. The two C–N bonds of the amidinium moieties are of equal length in both the **8e** and the **8g**, as observed in all other structures.



(a) **8g** (b) **8e**

Figure S6. Molecular structures of (a) **8g** and (b) **8e** with atom numbering schemes. Displacement ellipsoids for non-hydrogen atoms are drawn at the 40 and 30 % probability level for **8g** and **8e**, respectively. Water molecule in **8e** is omitted for clarity.

Experimental X-Ray details

Suitable single crystals for X-ray analysis were obtained by slow evaporation from water (**8a'**, **8b'** and **8h**), methanol (**8a I**, **8a II** and **8c'**), ethanol (**8d**, **8g** and **8e**) and ethyl acetate (**3c**) solutions, and from ethanol/water mixture (**8b**). Data for **3c**, **8a'**, **8d** and **8h** were collected at 170 K on a Bruker-Nonius Kappa Apex II diffractometer using graphite- monochromatized MoK$_\alpha$ radiation (λ = 0.71073 Å). COLLECT[S4] software was used for the data collection and DENZO-SMN[S5] for the data processing. The intensities were corrected for absorption using the multi-scan absorption correction method.[S6] Data for **8a I**, **8c'**, **8g** and **8e** were collected at 295 K on Oxford Diffraction Xcalibur2 diffractometer with a Sapphire 3 CCD detector using graphite-monochromatized MoK$_\alpha$ radiation (λ = 0.71073 Å). The *CrysAlisPro*[S7] program was used for the data collection and processing. The intensities were corrected for absorption using the multi-scan absorption correction method.[S7] Data for all other structures were collected on an Agilent SuperNova Dual diffractometer with Atlas detector (at 223 K for **8a II**, and at 123 K for **8b** and **8b'**) using mirror-monochromatized CuK$_\alpha$ radiation (λ = 1.54184 Å). The intensities were corrected for absorption using the multi-scan absorption correction method for **8b'**, while analytical absorption correction method was applied for **8a II** and **8b**.[S7] The structures were solved using direct methods with *SIR–97*,[S8] *SIR–2004*,[S9] *SIR–2014*[S10] and *SHELXS–97*,[S11] or by dual-space algorithm using *SHELXT*,[S12] and refined by full-matrix least-squares calculations based on F^2 using *SHELXL*[S13] program integrated in the *Olex*2[S14] or *WinGX*[S15] program package.

Hydrogen atoms attached to the nitrogen atoms N1-N3 and water oxygen atoms in **8a I** and **8c'** were found in the difference Fourier map, and subsequently refined using riding or rigid model, or a rotating group. The exception is hydrogen H1 atom in **8a I** (attached to O1 atom), which is fixed by crystallographic symmetry to lie on a special position. Hydrogen atoms attached to the nitrogen atoms N1-N3 and oxygen atom O1 in **8e** and **8g**, as well as to water oxygen atoms in **8e** were also found in the difference Fourier map, and subsequently refined using riding or rigid model, or a rotating group.

In **3c**, **8a II**, **8a'**, **8b**, **8b'** and **8d** hydrogen atoms bound to oxygen or nitrogen atoms were found in the difference Fourier map and subsequently refined using riding or rigid model, or a rotating group. In zwitterionic structures **8a II** and **8b**, hydrogen atoms half-way between the pairs of phenoxide oxygen atoms were found in the difference Fourier map. In **8b**, both $O^{-}\cdots H^{+}\cdots O^{-}$ hydrogen atoms were located on the special positions, an inversion centre and a two-fold axis, respectively, and could therefore be refined freely. On the other hand, the $O^{-}\cdots H^{+}\cdots O^{-}$ hydrogen atoms in **8a II** were restrained to lie half-way between the phenoxide oxygen atoms. In **8b'**, hydrogen atoms belonging to the minor disorder components of the water molecules could not be located and were omitted. All other hydrogen atoms were included in calculated positions, with *SHELXL*[S13] defaults.

Chloride ion in **8a I**, was disordered over two sites and have been refined with fixed occupancy ratio of 0.42 and 0.16 for Cl1 and Cl2, respectively (Cl2 atom lies on special, while Cl1 on general position), while water oxygen atom has been refined with fixed occupancy ratio of 55/45 %.

The structure of **8a II** was found to be twinned by pseudomerohedry, with a two-fold rotation around the reciprocal cell axis *c** as the twin operator. This was accounted for in the refinement, with the twin operator defined as [−1 0 0 0 −1 0 −1 0 1] and the batch scale factor refining to 0.2186(11). Extensive disorder was encountered in the structure of **8b'**, with all three molecules of **8b'** and 6 out of 14 water molecules in the asymmetric unit fully disordered, resulting in a non-stoichiometric hydrate. Disorder of the molecules **8b'** was modelled with all three symmetrically independent molecules split over two components each, with occupancies refining to 0.902(5)/0.098(5) for the molecule **8b'-A**, and 0.825(5)/0.175(5) for molecules **8b'-B** and **8b'-C**, whose disorders are correlated. Similarly, 5 out of 14 water molecules were modelled as split over two components each, while one was modelled as split over three components - one major and a hydrogen-bonded dimer of water molecules as a minor component, with the relative occupancies freely refined in all cases. Geometries of the molecules **8b'-A/B/C**, namely the 1,2 and 1,3 interatomic distances, were restrained to be the same. Amidino and aminophenol rings were restrained to be flat, respectively. Rigid bond and proximity restraints were applied to the anisotropic displacement parameters (ADPs) in **8b'-A/B/C**. Similarly, proximity restraints were applied to the ADPs of all the water molecules, while in two cases, the major and minor components of the disordered water molecules were constrained to have identical ADPs. The orientations of some hydrogen bond donor moieties and water molecules were adjusted using soft restraints to ensure a chemically plausible hydrogen bond network.

Disorder of the aminophenol ring was observed in the structure of **8h**, with the phenolic hydroxy group scrambled over the positions 1 and 3, i.e., over the two positions *ortho* to the amino and *meta* to the amidino group. A minor component of the hydroxy group was introduced at position 3, and the geometries (i.e. 1,2 and 1,3 distances) of the two possible orientations of the aminophenol ring restrained to be the same. Rigid bond restraints were applied to the aminophenol ring and both disorder components, and the ADPs of the oxygen atoms belonging to the two disorder components were constrained to be the same. The occupancies of the two disorder components refined to 0.948(3)/0.052(3). Soft restraints were used to adjust the orientations of the hydrogen bond donor moieties, to ensure a chemically plausible hydrogen bond network.

In the structure of **8d**, an ethanol solvate, the ethanol molecule was found to be disordered over two positions. Geometries, i.e. 1,2 and 1,3 distances of the two components were restrained to be the same, rigid bond and proximity restraints were applied to their ADPs, and their relative occupancies refined to 0.744(5)/0.256(5).

PLATON[S16] and Mercury[S17] programs were used for structure analysis and drawing preparation. Details of crystal data, data collection, and refinement parameters are given in Table S2. CCDC 2060884-2060894 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/structures.

Table S2 X-ray crystallographic data for structures described in this paper.

	3c	**8a I**	**8a II**	**8b**	**8h**	**8d**
CCDC Number	2060884	2060885	2060886	2060888	2060894	2060891
Formula	$C_7H_6N_2O$	$C_{14}H_{23}ClN_6O_4$	$C_{14}H_{23}ClN_6O_4$	$C_{18}H_{31}ClN_6O_6$	$C_9H_{16}ClN_3O_3$	$C_{12}H_{22}ClN_3O_2$
Formula weight	134.14	374.83	374.83	462.94	249.70	275.77
T / K	170	295	223	123	170	170
Crystal system	monoclinic	monoclinic	triclinic	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$	$P\bar{1}$	$I2/a$	$P\bar{1}$	$P2_1/n$
Unit cell dimensions						
a / Å	3.79610(10)	4.3443(4)	8.5903(2)	20.1831(3)	6.7656(2)	8.96920(10)
b / Å	7.4931(3)	14.5191(9)	14.7776(4)	7.18245(12)	9.4132(2)	18.2082(2)
c / Å	22.9246(9)	15.9472(15)	15.1797(4)	30.4640(5)	10.2539(2)	9.20580(10)
α / °	90	90	87.837(2)	90	108.3092(11)	90
β / °	99.5201(13)	113.446(11)	73.679(2)	102.6637(17)	96.7180(11)	106.4436(7)
γ / °	90	90	82.100(2)	90	102.1891(10)	90
V / Å^3	643.10(4)	922.83(15)	1831.77(8)	4308.76(12)	594.05(2)	1441.93(3)
Z	4	2	4	8	2	4
$D_{calc.}$ / g cm^{-3}	1.385	1.349	1.359	1.427	1.396	1.270
Absorption coef. μ / mm^{-1}	0.097	0.239	2.133	1.994	0.319	0.265
θ range for data collection/ °	2.864 - 27.333	4.409 - 25.239	3.019 - 76.510	4.813 - 74.334	2.572 - 27.377	2.564 - 28.037
Collected reflections No.	1431	3508	14914	7054	11385	27245
Independent refl. No. / $R_{Int.}$	1431 / 0.0	1661 / 0.0259	7457 / 0.0252	4185 / 0.0170	2641 / 0.0414	3461 / 0.0579
Reflections No. $I \geq 2\sigma(I)$	1196	1235	7125	3694	2227	2973
Data[a]/Restraints/Parameters	1431 / 0 / 96	1661 / 0 / 149	7457 / 6 / 484	4185 / 0 / 301	2641 / 73 / 160	3461 / 69 / 191
Goodness-of-fit on F^2, S	1.121	1.028	1.042	1.050	1.043	1.025
R [$I \geq 2\sigma(I)$] / R [all data]	0.0574 / 0.0688	0.0440 / 0.0635	0.0445 / 0.0460	0.0620 / 0.0664	0.0404 / 0.0497	0.0400 / 0.0485
wR [$I \geq 2\sigma(I)$] / wR [all data]	0.1432 / 0.1530	0.0975 / 0.1095	0.1209 / 0.1231	0.1830 / 0.1899	0.0979 / 0.1038	0.0936 / 0.0977
Max./min. el. density / e Å^{-3}	0.220 / -0.203	0.172 / -0.177	0.683 / -0.488	1.240 / -0.681	0.243 / -0.229	0.260 / -0.191

[a] Equal to independent reflections.

Table S2 Continued

	8a'	**8b'**	**8c'**	**8g**	**8e**
CCDC Number	2060887	2060889	2060890	2060893	2060892
Formula	$C_7H_{13}N_3O_3$	$C_9H_{19.669}N_3O_{5.73}$	$C_{10}H_{15}N_3O_2$	$C_7H_{11}Cl_2N_3O$	$C_{13}H_{25}N_3O_8S_2$
Formula weight	187.20	261.70	209.25	224.09	415.48
T / K	170	123	295	295	295
Crystal system	monoclinic	monoclinic	orthorhombic	monoclinic	triclinic
Space group	$P2_1$	$P2_1/c$	$P2_12_12_1$	$P2_1/c$	$P\overline{1}$
Unit cell dimensions					
a / Å	10.1400(8)	14.7267(7)	6.5770(2)	4.4199(3)	9.3183(7)
b / Å	4.0229(4)	36.3350(18)	10.7154(3)	11.7058(6)	9.8382(7)
c / Å	10.8744(12)	7.3619(4)	15.0191(4)	20.2357(15)	11.2711(8)
α / °	90	90	90	90	78.160(6)
β / °	98.890(7)	90.269(4)	90	93.014(6)	78.258(6)
γ / °	90	90	90	90	73.277(6)
V / Å^3	438.26(7)	3939.3(3)	1058.47(5)	1045.52(12)	956.96(13)
Z	2	12	4	4	2
$D_{calc.}$ / g cm^{-3}	1.419	1.324	1.313	1.424	1.442
Absorption coef. μ / mm^{-1}	0.112	0.940	0.094	0.587	0.324
θ range for data collection / °	1.895 - 28.025	3.864 - 74.349	4.494 - 25.224	4.394 - 25.250	4.397 - 25.249
Collected reflections No.	2959	23933	9382	1892	6996
Independent refl. No. / $R_{Int.}$	1918 / 0.0551	7808 / 0.0495	1899 / 0.0248	1892 / 0.0	3446 / 0.0191
Reflections No. $I \geq 2\sigma(I)$	1340	5659	1812	1596	2964
Data[a]/Restraints/Parameters	1918 / 1 / 127	7808 / 2744 /	1899 / 0 / 146	1892 / 0 / 129	3446 / 0 / 250
Goodness-of-fit on F^2, S	1.058	0.956	1.052	1.066	1.040
R [$I \geq 2\sigma(I)$] / R [all data]	0.0630 / 0.0998	0.0889 / 0.1146	0.0417 / 0.0435	0.0376 / 0.0472	0.0425 / 0.0505
wR [$I \geq 2\sigma(I)$] / wR [all data]	0.1466 / 0.1688	0.2339 / 0.2503	0.1072 / 0.1090	0.0908 / 0.0967	0.1101 / 0.1160
Max./min. el. density / e Å^{-3}	0.305 / -0.287	0.545 / -0.302	0.415 / -0.219	0.281 / -0.193	0.354 / -0.320

[a] Equal to independent reflections.

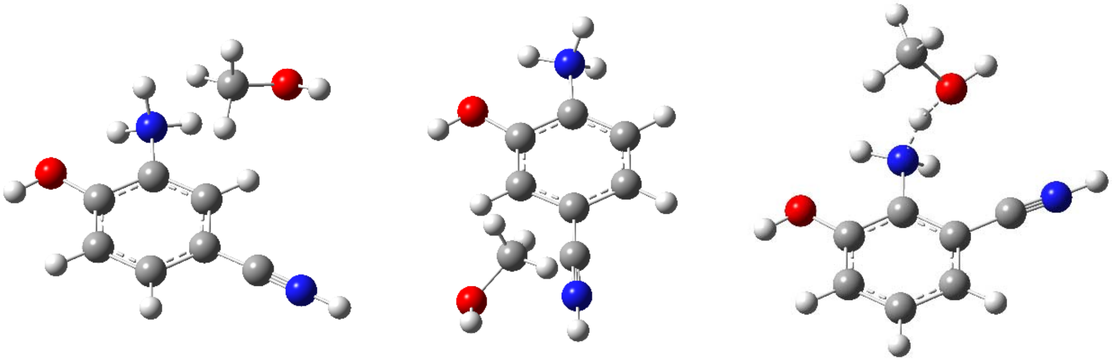
III. Computational Analysis

Computational Details

All molecular geometries were optimized using a very efficient M06–2X/6–31+G(d) model, which was designed to provide highly accurate thermodynamic and kinetic parameters for various organic systems. To account for the solvent effects, during geometry optimization, we included the implicit SMD solvation model corresponding to pure solvents. Thermal corrections were extracted from the corresponding frequency calculations, so that all of the presented results correspond to differences in the Gibbs free energies at room temperature and normal pressure. The choice of such computational setup was prompted by its success in reproducing various features of different organic,[S18,S19] organometallic[S20,S21] and enzymatic systems,[S22,S23] being particularly accurate for relative trends among similar reactants, which is the focus here. All transition state structures were located using the scan procedure, employing both 1D and 2D scans, the latter specifically utilized to exclude the possibility for concerted mechanisms. Apart from the visualization of the obtained negative frequencies, the validity of all transition state structures was validated by performing IRC calculations in both directions and identifying the matching reactant and product structures connected by the inspected transition state. All of the calculations were performed using the Gaussian 16 software.[S24]

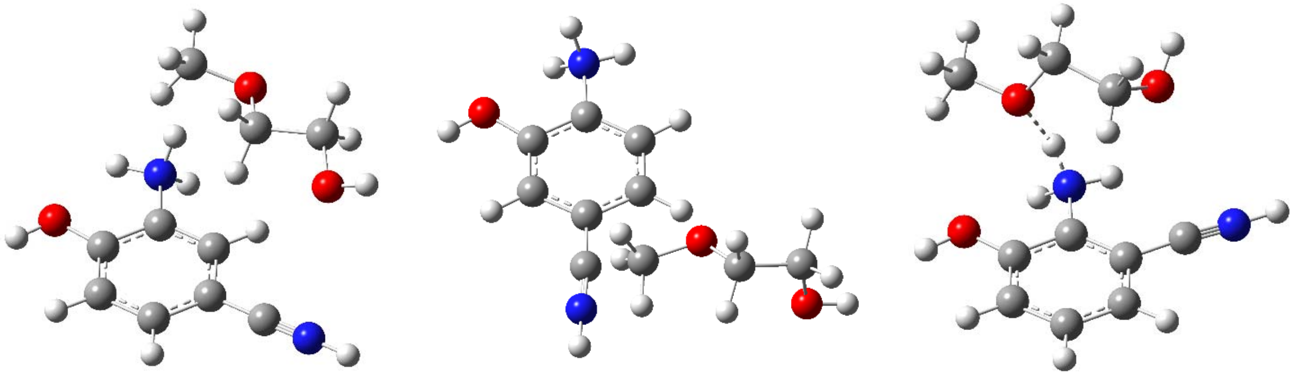
For the molecular dynamics simulations, investigated dications were parameterized through RESP charges at the HF/6–31G(d) level to be consistent with the employed GAFF force field. These were solvated in a 40 Å rectangular box, which allowed for 950 molecules of MeOH and 490 molecules of 2-methoxymethanol, calculated to match experimental solvent densities. All systems were neutralized by two Cl^- anions, whose position was maintained fixed at the opposite edges of the simulation boxes. These were submitted to geometry optimization in the AMBER 16 program[S25] by employing periodic boundary conditions in all directions. Optimized systems were gradually heated from 0 to 300 K and equilibrated during 30 ps using NVT conditions, followed by productive and unconstrained MD simulations of 300 ns by employing a time step of 2 fs at a constant pressure (1 atm) and temperature (300 K), the latter held constant using a Langevin thermostat with a collision frequency of 1 ps^{-1}. The nonbonded interactions were truncated at 11.0 Å, all in line with our earlier reports on similar systems.[S26]

In methanol



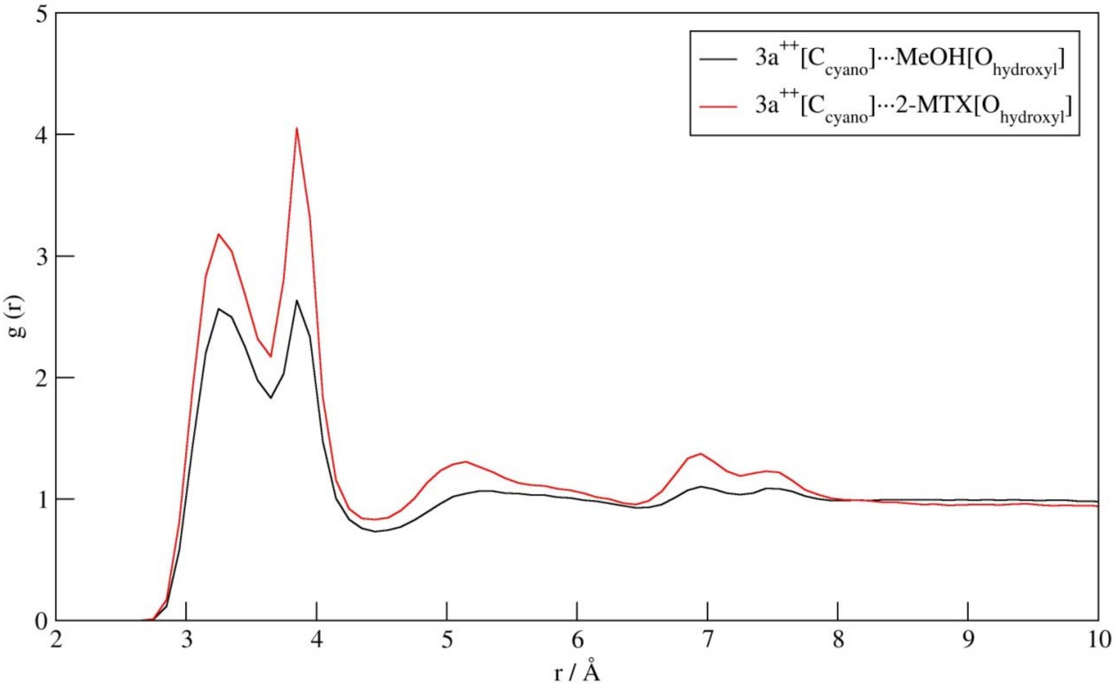
3a^{++} **3b**$^{++}$ **3c**$^{++}$

In 2-methoxyethanol



3a^{++} **3b**$^{++}$ **3c**$^{++}$

Figure S7. Geometries of reactive complexes for dications **3a**$^{++}$–**3c**$^{++}$ in methanol (top) and 2-methoxyethanol (bottom) preceding the nucleophilic attack of the solvent –OH group onto the C-atom of the substrate cyano moiety.



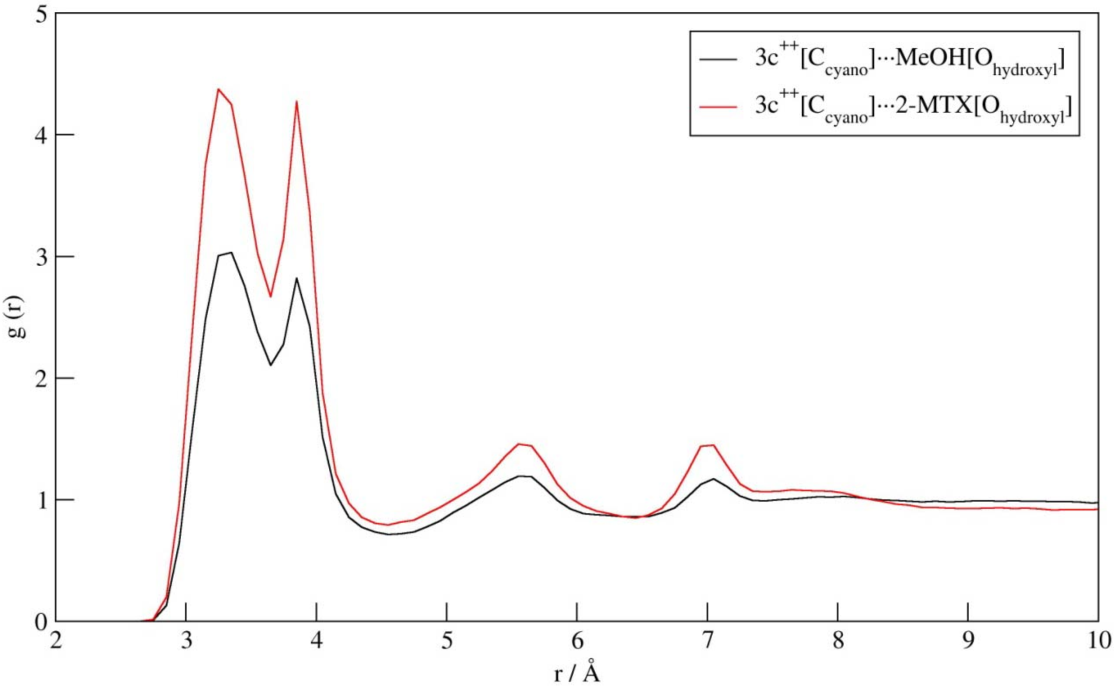
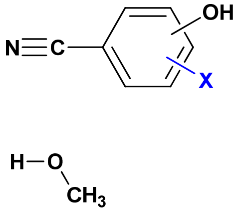
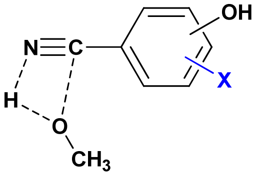


Figure S8. Radial distribution function (RDF) of distances between the hydroxyl O-atom in methanol (in black) and 2-methoxyethanol (in red) solutions, and the reactive cyano C-atom in dicationic **3a**$^{++}$ (top) and **3c**$^{++}$ (bottom), as obtained from the MD simulations in explicit solvents.

System:	
Name of the output file:	**01.log**
Description:	**SP1** in Figure 5 (X = NH_2) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,46660
Number of imaginary frequencies:	0

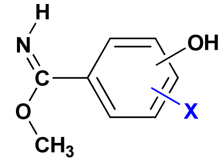
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center    Atomic     Atomic            Coordinates (Angstroms)
 Number    Number      Type          X          Y          Z
---------------------------------------------------------------------
    1        6          0       -0.194693  -1.380656  -1.009028
    2        1          0       -0.784244  -1.955853  -1.715450
    3        6          0        1.121564  -1.032869  -1.300601
    4        6          0        1.865549  -0.284783  -0.395158
    5        6          0        1.318546   0.131934   0.838199
    6        6          0        0.002638  -0.218017   1.126012
    7        6          0       -0.745440  -0.967603   0.206236
    8        1          0        1.579792  -1.337429  -2.238300
    9        8          0        3.153266   0.094258  -0.621314
   10        7          0        2.079879   0.935819   1.681421
   11        1          0       -0.445552   0.102379   2.062778
   12        6          0       -2.113514  -1.280753   0.505041
   13        7          0       -3.220770  -1.532873   0.739700
   14        1          0        1.773001   0.925673   2.649320
   15        1          0        3.081442   0.782356   1.610016
   16        1          0        3.468191  -0.249437  -1.475105
   17        8          0       -2.196881   1.988062  -0.027063
   18        1          0       -3.121230   2.210560  -0.218413
   19        6          0       -1.483229   1.922057  -1.257949
   20        1          0       -0.444656   1.682278  -1.015974
   21        1          0       -1.887606   1.140920  -1.912341
   22        1          0       -1.512503   2.883509  -1.783877
---------------------------------------------------------------------
```

System:	
Name of the output file:	**02.log**
Description:	**TS1** in Figure 5 (X = NH_2) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,37903
Number of imaginary frequencies:	1 (1871*i* cm^{-1})

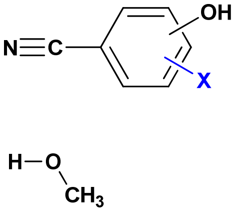
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0       -0.183164   -1.676000    0.170606
      2          1           0        0.324341   -2.624560    0.316877
      3          6           0       -1.564764   -1.584835    0.319194
      4          6           0       -2.209155   -0.366792    0.135757
      5          6           0       -1.488298    0.792210   -0.213869
      6          6           0       -0.105546    0.691800   -0.356769
      7          6           0        0.546377   -0.532763   -0.165714
      8          1           0       -2.152461   -2.460313    0.584639
      9          8           0       -3.557148   -0.206737    0.275203
     10          7           0       -2.163312    2.006447   -0.333459
     11          1           0        0.460266    1.578095   -0.632506
     12          6           0        1.991377   -0.669297   -0.349893
     13          7           0        2.872980   -1.492764   -0.567516
     14          1           0       -1.673636    2.692724   -0.899682
     15          1           0       -3.131129    1.914967   -0.628085
     16          1           0       -3.977005   -1.053472    0.504611
     17          8           0        2.789151    0.718669   -0.266318
     18          1           0        3.515721   -0.215842   -0.449807
     19          6           0        2.868658    1.341579    1.029767
     20          1           0        1.929979    1.860521    1.232288
     21          1           0        3.057315    0.582486    1.796286
     22          1           0        3.689990    2.058751    0.996647
---------------------------------------------------------------------
```

System:	
Name of the output file:	**03.log**
Description:	**SP2** in Figure 5 (X = NH_2) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,46647
Number of imaginary frequencies:	0

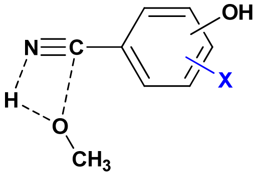
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
---------------------------------------------------------------------
      1          6           0        0.011015   -1.570379    0.284773
      2          1           0        0.591784   -2.460894    0.504638
      3          6           0       -1.374275   -1.575481    0.447295
      4          6           0       -2.113641   -0.433740    0.165427
      5          6           0       -1.488135    0.742276   -0.292895
      6          6           0       -0.102117    0.737600   -0.438433
      7          6           0        0.648661   -0.410005   -0.153812
      8          1           0       -1.890459   -2.466587    0.796885
      9          8           0       -3.472095   -0.369075    0.301500
     10          7           0       -2.259214    1.883165   -0.517910
     11          1           0        0.388358    1.637159   -0.804530
     12          6           0        2.117216   -0.410994   -0.372239
     13          7           0        2.705970   -1.389127   -0.933670
     14          1           0       -1.822600    2.553640   -1.143364
     15          1           0       -3.213888    1.687250   -0.804767
     16          1           0       -3.822721   -1.226426    0.597284
     17          8           0        2.819304    0.701291   -0.009209
     18          1           0        3.714603   -1.210836   -0.964542
     19          6           0        2.461320    1.374434    1.208977
     20          1           0        1.648325    2.084976    1.046980
     21          1           0        2.182502    0.652131    1.980923
     22          1           0        3.358868    1.911328    1.518661
---------------------------------------------------------------------
```

System:	
Name of the output file:	**04.log**
Description:	**SP1** in Figure 5 (X = NH_3^+) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,89081
Number of imaginary frequencies:	0

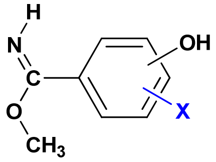
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.159675   -1.649370   -0.592625
      2          1           0       -0.739366   -2.426039   -1.081866
      3          6           0        1.152716   -1.416535   -0.979191
      4          6           0        1.890128   -0.413930   -0.347606
      5          6           0        1.287269    0.345457    0.660976
      6          6           0       -0.014383    0.128692    1.060419
      7          6           0       -0.742513   -0.883646    0.425079
      8          1           0        1.616398   -2.004682   -1.765805
      9          8           0        3.170027   -0.111558   -0.635071
     10          7           0        2.097684    1.389354    1.283127
     11          1           0       -0.460775    0.734376    1.844028
     12          6           0       -2.113859   -1.099096    0.788845
     13          7           0       -3.223606   -1.273213    1.071890
     14          1           0        1.578553    1.871744    2.029183
     15          1           0        2.957105    1.004622    1.703434
     16          1           0        3.530192   -0.709206   -1.314823
     17          8           0       -2.164874    1.933242   -0.404190
     18          1           0       -3.120134    2.101007   -0.420314
     19          6           0       -1.784698    1.367906   -1.654637
     20          1           0       -0.703262    1.208652   -1.623148
     21          1           0       -2.282037    0.405784   -1.827286
     22          1           0       -2.018614    2.047066   -2.482501
     23          1           0        2.392262    2.103350    0.600509
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**05.log**
Description:	**TS1** in Figure 5 (X = NH_3^+) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,80566
Number of imaginary frequencies:	1 (1843*i* cm^{-1})

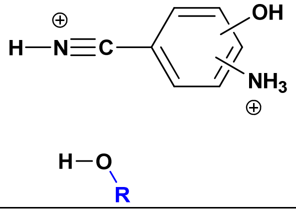
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.133136   -1.686965    0.173815
      2          1           0        0.396046   -2.624896    0.314715
      3          6           0       -1.512025   -1.645007    0.325082
      4          6           0       -2.189527   -0.438797    0.142244
      5          6           0       -1.459032    0.702878   -0.190677
      6          6           0       -0.085188    0.676738   -0.340278
      7          6           0        0.588798   -0.533107   -0.156489
      8          1           0       -2.073942   -2.537619    0.585052
      9          8           0       -3.524918   -0.285520    0.264742
     10          7           0       -2.210442    1.942219   -0.382559
     11          1           0        0.448932    1.583501   -0.612027
     12          6           0        2.037292   -0.646612   -0.344987
     13          7           0        2.911020   -1.476354   -0.574693
     14          1           0       -1.584870    2.732773   -0.589681
     15          1           0       -2.879276    1.864952   -1.162955
     16          1           0       -3.951718   -1.126418    0.508262
     17          8           0        2.806124    0.729824   -0.275410
     18          1           0        3.554060   -0.178410   -0.474447
     19          6           0        2.903127    1.358472    1.020887
     20          1           0        1.956991    1.854311    1.244535
     21          1           0        3.131068    0.604213    1.780493
     22          1           0        3.704948    2.094831    0.960311
     23          1           0       -2.757793    2.191675    0.454269
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**06.log**
Description:	**SP2** in Figure 5 (X = NH_3^+) in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-570,89454
Number of imaginary frequencies:	0

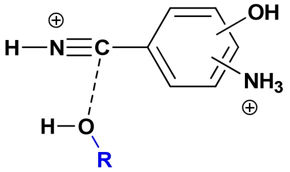
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0        0.013691   -1.604338    0.239257
      2          1           0        0.599548   -2.500406    0.420380
      3          6           0       -1.366444   -1.644068    0.395719
      4          6           0       -2.117856   -0.492656    0.161002
      5          6           0       -1.458887    0.676490   -0.222171
      6          6           0       -0.086267    0.730179   -0.370267
      7          6           0        0.664822   -0.426116   -0.141342
      8          1           0       -1.871521   -2.557261    0.697905
      9          8           0       -3.462193   -0.413386    0.275103
     10          7           0       -2.288084    1.854228   -0.470493
     11          1           0        0.389673    1.658309   -0.679460
     12          6           0        2.134222   -0.418459   -0.356902
     13          7           0        2.749398   -1.451731   -0.761892
     14          1           0       -1.717106    2.663641   -0.747272
     15          1           0       -2.972036    1.688210   -1.223614
     16          1           0       -3.843636   -1.268319    0.543077
     17          8           0        2.777230    0.775926   -0.179631
     18          1           0        3.751344   -1.250277   -0.833163
     19          6           0        2.673883    1.368719    1.125341
     20          1           0        1.642840    1.639828    1.366893
     21          1           0        3.064471    0.676628    1.877762
     22          1           0        3.291086    2.266468    1.092197
     23          1           0       -2.827138    2.126869    0.364395
---------------------------------------------------------------------
```

System:	
Name of the output file:	**07.log**
Description:	**SP1** in Figure 6 for **3a** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,27450
Number of imaginary frequencies:	0

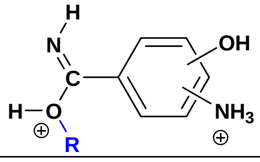
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.148313   -1.618455    0.488642
      2          1           0        0.764937   -2.402907    0.915461
      3          6           0       -1.168033   -1.468363    0.884662
      4          6           0       -1.945835   -0.449181    0.324796
      5          6           0       -1.381481    0.412392   -0.630943
      6          6           0       -0.075119    0.292255   -1.036091
      7          6           0        0.685950   -0.742187   -0.468859
      8          1           0       -1.608472   -2.131232    1.622961
      9          8           0       -3.224823   -0.219764    0.629874
     10          7           0       -2.245635    1.448972   -1.183218
     11          1           0        0.352445    0.974444   -1.765564
     12          6           0        2.044717   -0.868399   -0.831725
     13          7           0        3.146062   -1.000569   -1.119793
     14          1           0       -1.759308    1.990360   -1.911937
     15          1           0       -3.094439    1.046324   -1.609734
     16          1           0       -3.567380   -0.865193    1.275867
     17          1           0       -2.559237    2.112818   -0.458845
     18          1           0        4.124804   -1.103458   -1.375401
     19          8           0        2.293015    1.623452    0.529659
     20          1           0        3.250969    1.746235    0.621419
     21          6           0        1.762503    1.245331    1.796795
     22          1           0        0.675800    1.190266    1.689614
     23          1           0        2.141112    0.265297    2.112580
     24          1           0        2.004151    1.988370    2.564730
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**08.log**
Description:	**TS1** in Figure 6 for **3a** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,26182
Number of imaginary frequencies:	1 (331*i* cm^{-1})

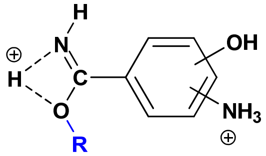
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.352033   -1.719749    0.138260
      2          1           0       -0.134363   -2.684498    0.244401
      3          6           0        1.726325   -1.617842    0.264105
      4          6           0        2.342201   -0.371517    0.123116
      5          6           0        1.555310    0.755925   -0.149155
      6          6           0        0.186460    0.680650   -0.270574
      7          6           0       -0.417761   -0.573326   -0.121683
      8          1           0        2.333271   -2.493862    0.472210
      9          8           0        3.660464   -0.161797    0.226486
     10          7           0        2.249645    2.030430   -0.305776
     11          1           0       -0.399727    1.568121   -0.485138
     12          6           0       -1.831327   -0.772723   -0.274902
     13          7           0       -2.717171   -1.477168   -0.582733
     14          1           0        1.587168    2.798599   -0.481581
     15          1           0        2.794346    2.275413    0.534889
     16          1           0        4.140610   -0.988924    0.415958
     17          1           0        2.913160    2.006978   -1.094873
     18          1           0       -3.717078   -1.658665   -0.591314
     19          8           0       -2.519410    0.995961    0.382401
     20          1           0       -2.235797    1.096640    1.310191
     21          6           0       -3.950900    1.022353    0.316952
     22          1           0       -4.222171    0.943166   -0.736666
     23          1           0       -4.381887    0.193984    0.887153
     24          1           0       -4.307317    1.974278    0.716526
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**09.log**
Description:	**SP2** in Figure 6 for **3a** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,27424
Number of imaginary frequencies:	0

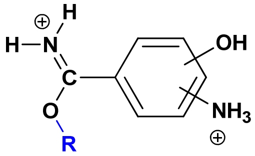
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.074146   -1.642362    0.204983
      2          1           0        0.481829   -2.558171    0.384456
      3          6           0       -1.450722   -1.646137    0.365501
      4          6           0       -2.171409   -0.468648    0.154709
      5          6           0       -1.484166    0.691431   -0.215282
      6          6           0       -0.115051    0.712019   -0.378406
      7          6           0        0.601766   -0.472321   -0.166885
      8          1           0       -1.977523   -2.548975    0.659887
      9          8           0       -3.503940   -0.353102    0.283800
     10          7           0       -2.284667    1.894414   -0.424476
     11          1           0        0.380598    1.633790   -0.673916
     12          6           0        2.055115   -0.516074   -0.356011
     13          7           0        2.885266   -1.409966   -0.614746
     14          1           0       -1.697648    2.699836   -0.679543
     15          1           0       -2.976791    1.765983   -1.177933
     16          1           0       -3.911061   -1.195955    0.554287
     17          1           0       -2.813336    2.152630    0.422264
     18          1           0        2.447673   -2.322201   -0.767458
     19          8           0        2.646241    0.810412   -0.231722
     20          1           0        3.521612    0.810432   -0.690837
     21          6           0        2.773536    1.355835    1.149782
     22          1           0        1.761685    1.444789    1.536102
     23          1           0        3.385039    0.659528    1.721605
     24          1           0        3.245785    2.326238    1.018667
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**10.log**
Description:	**TS2** in Figure 6 for **3a** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,24529
Number of imaginary frequencies:	1 (1869i cm^{-1})

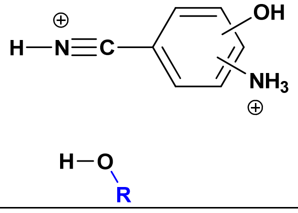
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.094656   -1.633967    0.206443
      2          1           0        0.472619   -2.545877    0.370535
      3          6           0       -1.470569   -1.649465    0.355676
      4          6           0       -2.197017   -0.472254    0.152309
      5          6           0       -1.518201    0.701529   -0.199074
      6          6           0       -0.149056    0.738749   -0.339529
      7          6           0        0.570917   -0.446224   -0.134619
      8          1           0       -1.995582   -2.559221    0.630943
      9          8           0       -3.528211   -0.369630    0.267560
     10          7           0       -2.331492    1.893507   -0.415642
     11          1           0        0.346490    1.664130   -0.624880
     12          6           0        2.005713   -0.468379   -0.312048
     13          7           0        2.884288   -1.343322   -0.579354
     14          1           0       -1.754914    2.699094   -0.693534
     15          1           0       -3.032572    1.746127   -1.157648
     16          1           0       -3.934922   -1.219656    0.516976
     17          1           0       -2.850885    2.162048    0.433783
     18          1           0        2.656449   -2.310409   -0.814990
     19          8           0        2.788931    0.701633   -0.235506
     20          1           0        3.630845   -0.167137   -0.475391
     21          6           0        2.840035    1.432572    1.037321
     22          1           0        1.887106    1.940517    1.175161
     23          1           0        3.046372    0.721434    1.838142
     24          1           0        3.650663    2.146267    0.910552
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**11.log**
Description:	**SP3** in Figure 6 for **3a** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,32931
Number of imaginary frequencies:	0

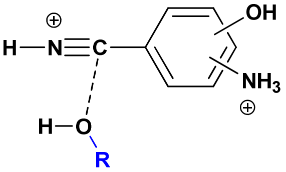
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.036277   -1.566904    0.348813
      2          1           0        0.635368   -2.437796    0.599643
      3          6           0       -1.341360   -1.625156    0.495046
      4          6           0       -2.115385   -0.506199    0.184444
      5          6           0       -1.481568    0.659140   -0.263167
      6          6           0       -0.112806    0.739264   -0.398118
      7          6           0        0.655970   -0.389035   -0.088942
      8          1           0       -1.828767   -2.529062    0.848186
      9          8           0       -3.453840   -0.456965    0.278388
     10          7           0       -2.334758    1.797278   -0.591292
     11          1           0        0.340789    1.653333   -0.771622
     12          6           0        2.113982   -0.358297   -0.269165
     13          7           0        2.728824   -1.359580   -0.833180
     14          1           0       -1.780703    2.602995   -0.912175
     15          1           0       -3.006993    1.566801   -1.338919
     16          1           0       -3.820951   -1.304241    0.590926
     17          1           0       -2.888401    2.106666    0.221631
     18          1           0        2.210261   -2.127252   -1.251768
     19          8           0        2.872044    0.633325    0.091115
     20          1           0        3.745289   -1.362810   -0.905759
     21          6           0        2.442354    1.656533    1.024287
     22          1           0        2.071000    2.512226    0.461211
     23          1           0        1.688475    1.262672    1.705915
     24          1           0        3.345753    1.925629    1.568821
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**12.log**
Description:	**SP1** in Figure 6 for **3b** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,27032
Number of imaginary frequencies:	0

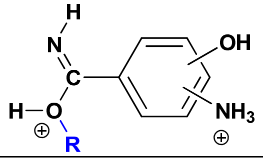
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
Center     Atomic      Atomic              Coordinates (Angstroms)
Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
    1          6           0       -0.020227   -0.241698   -1.042455
    2          1           0        0.472410   -0.862933   -1.783844
    3          6           0       -1.352814   -0.452211   -0.714102
    4          6           0       -1.945268    0.361337    0.259170
    5          6           0       -1.261122    1.370109    0.913917
    6          6           0        0.074356    1.595739    0.598144
    7          6           0        0.662154    0.782614   -0.376186
    8          8           0       -2.137327   -1.399082   -1.262225
    9          7           0       -3.346220    0.092590    0.564761
   10          1           0       -1.761949    1.973246    1.665419
   11          1           0        0.644074    2.374624    1.092374
   12          6           0        2.038299    0.987234   -0.683241
   13          7           0        3.135926    1.197877   -0.926083
   14          1           0        4.118332    1.358745   -1.138888
   15          8           0        2.390063   -1.587256    0.341760
   16          1           0        3.354554   -1.666798    0.408815
   17          6           0        1.855269   -1.440118    1.654292
   18          1           0        0.766901   -1.406713    1.556745
   19          1           0        2.126705   -2.289676    2.290459
   20          1           0        2.201591   -0.511622    2.124612
   21          1           0       -1.645526   -1.947262   -1.900342
   22          1           0       -3.698236    0.711073    1.308157
   23          1           0       -3.946980    0.228187   -0.263443
   24          1           0       -3.485582   -0.881472    0.875674
---------------------------------------------------------------------
```

System:	
Name of the output file:	**13.log**
Description:	**TS1** in Figure 6 for **3b** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,25835
Number of imaginary frequencies:	1 (324*i* cm^{-1})

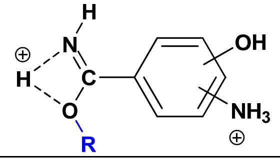
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
Center     Atomic      Atomic              Coordinates (Angstroms)
Number     Number      Type              X           Y           Z
---------------------------------------------------------------------
    1          6           0       -0.149624   -0.704798   -0.307479
    2          1           0        0.459752   -1.571486   -0.538023
    3          6           0       -1.528623   -0.834142   -0.189545
    4          6           0       -2.291842    0.298408    0.106387
    5          6           0       -1.728066    1.550964    0.275074
    6          6           0       -0.350721    1.695574    0.151976
    7          6           0        0.416445    0.559307   -0.131860
    8          8           0       -2.200801   -1.993851   -0.335377
    9          7           0       -3.732382    0.105495    0.236011
   10          1           0       -2.357380    2.406938    0.500759
   11          1           0        0.120021    2.664476    0.277372
   12          6           0        1.838120    0.781266   -0.280418
   13          7           0        2.717949    1.489808   -0.577300
   14          1           0        3.706682    1.718403   -0.634201
   15          8           0        2.544997   -0.992165    0.386225
   16          1           0        2.245739   -1.110558    1.306871
   17          6           0        3.976865   -0.985530    0.346336
   18          1           0        4.264834   -0.909215   -0.703117
   19          1           0        4.379208   -0.141827    0.915291
   20          1           0        4.349618   -1.924836    0.760770
   21          1           0       -1.596970   -2.731813   -0.536708
   22          1           0       -4.215409    0.993909    0.426747
   23          1           0       -4.142964   -0.295910   -0.621407
   24          1           0       -3.960994   -0.543365    1.005055
---------------------------------------------------------------------
```

System:	
Name of the output file:	**14.log**
Description:	**SP2** in Figure 6 for **3b** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,27219
Number of imaginary frequencies:	0

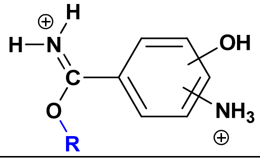
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.077090    0.746054   -0.413416
      2          1           0       -0.446380    1.642872   -0.734899
      3          6           0        1.460050    0.779965   -0.264871
      4          6           0        2.124426   -0.378939    0.142082
      5          6           0        1.452984   -1.561793    0.397411
      6          6           0        0.071710   -1.602480    0.244026
      7          6           0       -0.603621   -0.448858   -0.162365
      8          8           0        2.228206    1.867218   -0.489639
      9          7           0        3.575488   -0.295974    0.285704
     10          1           0        2.005315   -2.440766    0.717689
     11          1           0       -0.471657   -2.518285    0.452292
     12          6           0       -2.062412   -0.525198   -0.363641
     13          7           0       -2.848923   -1.438324   -0.677702
     14          1           0       -2.369919   -2.324079   -0.861338
     15          8           0       -2.699158    0.768216   -0.193387
     16          1           0       -3.591037    0.742883   -0.619733
     17          6           0       -2.785496    1.303197    1.195384
     18          1           0       -3.320485    2.243764    1.092029
     19          1           0       -3.323693    0.571792    1.796295
     20          1           0       -1.761752    1.453359    1.527596
     21          1           0        1.692308    2.628099   -0.776417
     22          1           0        3.968365   -1.167300    0.668243
     23          1           0        4.038590   -0.117908   -0.618158
     24          1           0        3.853619    0.470495    0.916934
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**15.log**
Description:	**TS2** in Figure 6 for **3b** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,24179
Number of imaginary frequencies:	1 (1857*i* cm^{-1})

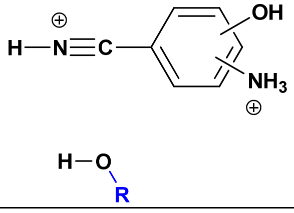
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.387091    1.114101    0.104317
      2          1           0       -0.092025    2.140376    0.306159
      3          6           0       -1.727893    0.756564    0.171158
      4          6           0       -2.083334   -0.571586   -0.082229
      5          6           0       -1.150742   -1.544232   -0.395663
      6          6           0        0.194566   -1.194823   -0.459277
      7          6           0        0.558804    0.131323   -0.207680
      8          8           0       -2.737309    1.599702    0.470253
      9          7           0       -3.503973   -0.895731    0.000191
     10          1           0       -1.471103   -2.563955   -0.588725
     11          1           0        0.938493   -1.939390   -0.722275
     12          6           0        1.954210    0.537070   -0.306923
     13          7           0        2.570856    1.622174   -0.519746
     14          1           0        2.100201    2.499909   -0.746444
     15          8           0        3.015470   -0.381493   -0.216875
     16          1           0        3.603075    0.693297   -0.400981
     17          6           0        3.215358   -1.122103    1.036027
     18          1           0        2.436753   -1.878898    1.110910
     19          1           0        4.196805   -1.577790    0.928712
     20          1           0        3.184837   -0.414673    1.865864
     21          1           0       -3.676896   -1.890230   -0.200323
     22          1           0       -3.886899   -0.696567    0.936983
     23          1           0       -4.059156   -0.343359   -0.671496
     24          1           0       -2.410814    2.502626    0.633080
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**16.log**
Description:	**SP3** in Figure 6 for **3b** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,32709
Number of imaginary frequencies:	0

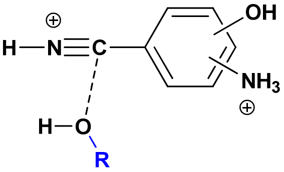
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.076896    0.756745   -0.500034
      2          1           0       -0.402901    1.633730   -0.926675
      3          6           0        1.460136    0.727022   -0.360485
      4          6           0        2.057927   -0.414451    0.181285
      5          6           0        1.325557   -1.524457    0.559659
      6          6           0       -0.057859   -1.511750    0.397899
      7          6           0       -0.661755   -0.366433   -0.122011
      8          8           0        2.288709    1.731650   -0.713651
      9          7           0        3.511031   -0.393671    0.321720
     10          1           0        1.830638   -2.391616    0.975729
     11          1           0       -0.652297   -2.370137    0.693796
     12          6           0       -2.131472   -0.345381   -0.296534
     13          7           0       -2.721057   -1.282538   -0.977025
     14          1           0       -2.179826   -2.001195   -1.452032
     15          8           0       -2.893173    0.581200    0.193720
     16          1           0       -3.736540   -1.293264   -1.070761
     17          6           0       -2.410576    1.525040    1.186464
     18          1           0       -3.308593    1.844937    1.711079
     19          1           0       -1.720896    1.030856    1.870866
     20          1           0       -1.943109    2.368602    0.680027
     21          1           0        1.797247    2.488100   -1.082126
     22          1           0        3.861814   -1.255299    0.762594
     23          1           0        3.979624   -0.301881   -0.592386
     24          1           0        3.827599    0.399825    0.899015
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**17.log**
Description:	**SP1** in Figure 6 for **3c** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,26682
Number of imaginary frequencies:	0

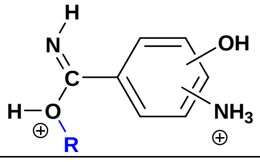
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0        0.690473    1.926194    0.536778
      2          1           0        0.262527    2.883513    0.812844
      3          6           0        1.984009    1.568534    0.909058
      4          6           0        2.515373    0.340466    0.540926
      5          6           0        1.760816   -0.569147   -0.212039
      6          6           0        0.467315   -0.232330   -0.586870
      7          6           0       -0.060125    1.012464   -0.210700
      8          1           0        2.583716    2.259357    1.491894
      9          1           0        3.525642    0.064793    0.831257
     10          8           0        2.206321   -1.778191   -0.605860
     11          7           0       -0.326444   -1.203181   -1.316932
     12          6           0       -1.375360    1.395080   -0.590943
     13          7           0       -2.412132    1.761891   -0.904748
     14          1           0       -3.352552    2.065852   -1.152558
     15          8           0       -2.333532   -1.005339    0.475575
     16          1           0       -3.223623   -1.334343    0.267221
     17          6           0       -1.929779   -1.507357    1.755800
     18          1           0       -0.935213   -1.100207    1.953902
     19          1           0       -2.620606   -1.167510    2.532307
     20          1           0       -1.883556   -2.600350    1.748662
     21          1           0       -0.550678   -0.892169   -2.274598
     22          1           0        0.184158   -2.094894   -1.399517
     23          1           0       -1.226041   -1.378815   -0.790176
     24          1           0        3.107604   -1.951379   -0.279262
---------------------------------------------------------------------
```

System:	
Name of the output file:	**18.log**
Description:	**TS1** in Figure 6 for **3c** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,25277
Number of imaginary frequencies:	1 (364*i* cm^{-1})

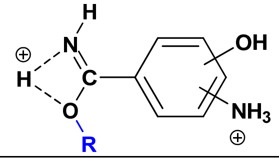
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.287570    1.883859    0.106446
      2          1           0       -0.364629    2.749558    0.148532
      3          6           0        1.632156    1.968362    0.466944
      4          6           0        2.454278    0.852905    0.409394
      5          6           0        1.943328   -0.379231   -0.015981
      6          6           0        0.602543   -0.477921   -0.367826
      7          6           0       -0.220830    0.652704   -0.311539
      8          1           0        2.038954    2.918458    0.796891
      9          1           0        3.502681    0.918189    0.687488
     10          8           0        2.674638   -1.508112   -0.114270
     11          7           0        0.113100   -1.775300   -0.814404
     12          6           0       -1.614209    0.629441   -0.688657
     13          7           0       -2.486046    1.133335   -1.296442
     14          1           0       -3.497344    1.097682   -1.419535
     15          8           0       -2.213562   -0.905004    0.386319
     16          1           0       -3.122759   -1.113190    0.095741
     17          6           0       -2.196538   -0.668620    1.812017
     18          1           0       -1.150153   -0.571203    2.103840
     19          1           0       -2.749053    0.244123    2.046423
     20          1           0       -2.641701   -1.530428    2.311733
     21          1           0       -0.082550   -1.787004   -1.827737
     22          1           0        0.819074   -2.505150   -0.632946
     23          1           0       -0.760674   -2.033498   -0.322739
     24          1           0        3.600371   -1.357846    0.147048
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**19.log**
Description:	**SP2** in Figure 6 for **3c** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,26328
Number of imaginary frequencies:	0

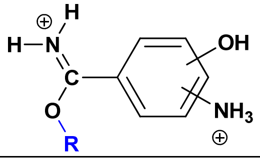
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.240075    1.830618    0.131960
      2          1           0        0.444622    2.670882    0.190492
      3          6           0       -1.597305    1.995142    0.406150
      4          6           0       -2.469314    0.917054    0.349853
      5          6           0       -1.987398   -0.350157    0.011452
      6          6           0       -0.632653   -0.516996   -0.264040
      7          6           0        0.248996    0.567974   -0.203216
      8          1           0       -1.976411    2.976266    0.673168
      9          1           0       -3.527592    1.038171    0.564111
     10          8           0       -2.758087   -1.456853   -0.076959
     11          7           0       -0.198614   -1.865322   -0.630922
     12          6           0        1.689435    0.445637   -0.502152
     13          7           0        2.487516    1.133844   -1.162152
     14          1           0        2.022275    1.917746   -1.630280
     15          8           0        2.272390   -0.734899    0.113537
     16          1           0        3.144233   -0.930147   -0.311799
     17          6           0        2.402339   -0.713380    1.602845
     18          1           0        1.385851   -0.701100    1.989053
     19          1           0        2.920223   -1.638262    1.843612
     20          1           0        2.970888    0.176845    1.867681
     21          1           0        0.249451   -2.359702    0.156804
     22          1           0       -1.014758   -2.430402   -0.912477
     23          1           0        0.460555   -1.872510   -1.422271
     24          1           0       -3.700227   -1.248776    0.053699
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**20.log**
Description:	**TS2** in Figure 6 for **3c** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,23201
Number of imaginary frequencies:	1 (1866*i* cm^{-1})

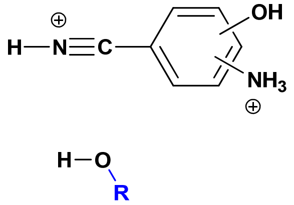
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0       -0.293827    1.834100    0.155685
      2          1           0        0.385240    2.678054    0.221510
      3          6           0       -1.656450    1.989312    0.406193
      4          6           0       -2.517563    0.903811    0.338458
      5          6           0       -2.023163   -0.363562    0.013056
      6          6           0       -0.663321   -0.525476   -0.233070
      7          6           0        0.206297    0.569632   -0.159160
      8          1           0       -2.048355    2.969043    0.658833
      9          1           0       -3.580904    1.019169    0.529954
     10          8           0       -2.787882   -1.471339   -0.091379
     11          7           0       -0.216438   -1.866857   -0.605604
     12          6           0        1.638101    0.452544   -0.418649
     13          7           0        2.498885    1.147969   -1.027319
     14          1           0        2.260614    1.977040   -1.575994
     15          8           0        2.402012   -0.643177    0.022842
     16          1           0        3.242552    0.056250   -0.565336
     17          6           0        2.522693   -0.866258    1.473756
     18          1           0        1.542655   -1.168214    1.844077
     19          1           0        3.248250   -1.670446    1.567077
     20          1           0        2.870284    0.057920    1.936733
     21          1           0        0.238832   -2.361380    0.178413
     22          1           0       -1.029221   -2.439326   -0.883332
     23          1           0        0.437530   -1.868536   -1.401398
     24          1           0       -3.734255   -1.265848    0.010614
---------------------------------------------------------------------
```

System:	
Name of the output file:	**21.log**
Description:	**SP3** in Figure 6 for **3c** in methanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-571,31600
Number of imaginary frequencies:	0

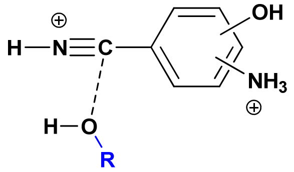
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
---------------------------------------------------------------------
      1          6           0        0.145472    1.806582    0.281098
      2          1           0       -0.565272    2.614957    0.419425
      3          6           0        1.507107    2.002995    0.512339
      4          6           0        2.412874    0.964349    0.351636
      5          6           0        1.961111   -0.296143   -0.047938
      6          6           0        0.602621   -0.497207   -0.279708
      7          6           0       -0.309198    0.546663   -0.107446
      8          1           0        1.862224    2.980226    0.822927
      9          1           0        3.474880    1.111825    0.527836
     10          8           0        2.758332   -1.367932   -0.241043
     11          7           0        0.219947   -1.839437   -0.717783
     12          6           0       -1.765185    0.371834   -0.322203
     13          7           0       -2.379936    1.117818   -1.188670
     14          1           0       -1.863036    1.763832   -1.781990
     15          8           0       -2.483217   -0.501540    0.309624
     16          1           0       -3.391739    1.048895   -1.302866
     17          6           0       -2.031055   -1.186533    1.508279
     18          1           0       -1.092199   -0.768473    1.871283
     19          1           0       -2.822339   -1.037414    2.241216
     20          1           0       -1.939893   -2.244105    1.259962
     21          1           0       -0.686814   -1.882092   -1.205250
     22          1           0        0.922971   -2.212979   -1.375103
     23          1           0        0.179560   -2.504118    0.072309
     24          1           0        3.698179   -1.138682   -0.129577
---------------------------------------------------------------------
```

System:	
Name of the output file:	**22.log**
Description:	**SP1** in Figure 6 for **3a** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,97943
Number of imaginary frequencies:	0

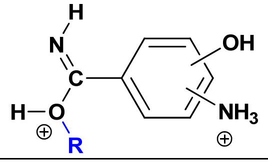
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.725846   -1.833537   -1.082691
      2          1           0       -1.448982   -2.189019   -1.809498
      3          6           0        0.627950   -1.902880   -1.349590
      4          6           0        1.546337   -1.423356   -0.407035
      5          6           0        1.081095   -0.877429    0.799972
      6          6           0       -0.258205   -0.811999    1.099220
      7          6           0       -1.162696   -1.294497    0.140451
      8          1           0        0.991235   -2.317794   -2.284746
      9          8           0        2.871316   -1.441501   -0.566416
     10          7           0        2.078533   -0.355433    1.725964
     11          1           0       -0.600411   -0.392612    2.041563
     12          6           0       -2.547725   -1.194473    0.398837
     13          7           0       -3.671310   -1.130506    0.614554
     14          1           0        1.637414    0.102686    2.535551
     15          1           0        2.693966   -1.100167    2.087627
     16          1           0        3.127164   -1.829807   -1.424477
     17          1           0        2.689162    0.343272    1.275963
     18          1           0       -4.668857   -1.062337    0.799573
     19          8           0       -2.441886    1.527612   -0.733291
     20          1           0       -3.315905    1.830528   -0.442267
     21          6           0       -1.450775    2.132794    0.088132
     22          6           0       -0.130408    2.016855   -0.649594
     23          1           0       -1.688243    3.186140    0.276443
     24          1           0       -1.384684    1.621405    1.058549
     25          8           0        0.919381    2.248170    0.270532
     26          1           0       -0.031709    1.014543   -1.095989
     27          1           0       -0.086674    2.751779   -1.466495
     28          6           0        2.173927    2.314953   -0.381854
     29          1           0        2.932335    2.512267    0.380296
     30          1           0        2.399995    1.369145   -0.898737
     31          1           0        2.191232    3.128701   -1.118671
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**23.log**
Description:	**TS1** in Figure 6 for **3a** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,96746
Number of imaginary frequencies:	1 (296*i* cm^{-1})

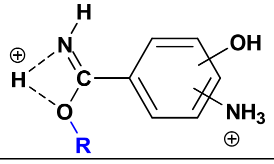
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
Center     Atomic      Atomic              Coordinates (Angstroms)
Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
    1          6           0        1.948328   -1.742817   -0.315873
    2          1           0        1.760139   -2.802018   -0.462008
    3          6           0        3.239520   -1.251791   -0.396431
    4          6           0        3.470879    0.114148   -0.215285
    5          6           0        2.388482    0.963146    0.051868
    6          6           0        1.096891    0.496583    0.146122
    7          6           0        0.879050   -0.873989   -0.039469
    8          1           0        4.075879   -1.913383   -0.601456
    9          8           0        4.675293    0.694839   -0.277706
   10          7           0        2.686168    2.381420    0.227924
   11          1           0        0.275785    1.176423    0.346572
   12          6           0       -0.436449   -1.456317   -0.024361
   13          7           0       -1.131165   -2.313132   -0.442025
   14          1           0        1.830035    2.926884    0.399730
   15          1           0        3.318661    2.544203    1.026135
   16          1           0        5.372928    0.046972   -0.488797
   17          1           0        3.145853    2.782785   -0.603757
   18          1           0       -2.038831   -2.759240   -0.336938
   19          8           0       -1.330452   -0.285725    1.255514
   20          1           0       -1.039672   -0.593532    2.135756
   21          6           0       -2.764237   -0.327320    1.170789
   22          6           0       -3.169127    0.575647    0.023119
   23          1           0       -3.102939   -1.356612    1.003403
   24          1           0       -3.174500    0.025801    2.119772
   25          8           0       -4.560246    0.431261   -0.140711
   26          1           0       -2.910064    1.619616    0.253878
   27          1           0       -2.640376    0.285570   -0.899378
   28          6           0       -5.059089    1.245641   -1.187163
   29          1           0       -6.135006    1.071823   -1.247299
   30          1           0       -4.872327    2.307487   -0.978601
   31          1           0       -4.592817    0.978623   -2.144970
---------------------------------------------------------------------
```

System:	
Name of the output file:	**24.log**
Description:	**SP2** in Figure 6 for **3a** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,98242
Number of imaginary frequencies:	0

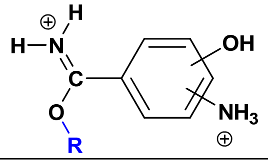
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.757468   -1.686655    0.033729
      2          1           0        0.209796   -2.621477   -0.041879
      3          6           0        2.061087   -1.627709   -0.439730
      4          6           0        2.774806   -0.433209   -0.345775
      5          6           0        2.161654    0.682115    0.236826
      6          6           0        0.871539    0.637318    0.719786
      7          6           0        0.161477   -0.563298    0.616927
      8          1           0        2.533030   -2.499113   -0.884006
      9          8           0        4.033721   -0.253907   -0.782157
     10          7           0        2.946782    1.912532    0.292908
     11          1           0        0.413248    1.524816    1.151432
     12          6           0       -1.202219   -0.611230    1.153491
     13          7           0       -1.779292   -0.084633    2.125275
     14          1           0        3.250217    2.212640   -0.645856
     15          1           0        2.408269    2.686757    0.704935
     16          1           0        4.388096   -1.064460   -1.190817
     17          1           0        3.800858    1.795150    0.858710
     18          1           0       -1.140294    0.480081    2.691036
     19          8           0       -2.048592   -1.530786    0.403377
     20          1           0       -2.862132   -1.707948    0.938173
     21          6           0       -2.415552   -1.206735   -1.022874
     22          6           0       -3.007968    0.170147   -1.093449
     23          1           0       -1.484576   -1.310968   -1.579046
     24          1           0       -3.119373   -1.996108   -1.281796
     25          8           0       -1.970007    1.100188   -0.879837
     26          1           0       -3.460653    0.297212   -2.087318
     27          1           0       -3.799411    0.281313   -0.337017
     28          6           0       -2.451828    2.381167   -0.510520
     29          1           0       -1.583615    3.035949   -0.413886
     30          1           0       -3.123840    2.783573   -1.279331
     31          1           0       -2.985801    2.331860    0.447861
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**25.log**
Description:	**TS2** in Figure 6 for **3a** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,95472
Number of imaginary frequencies:	1 (1815*i* cm^{-1})

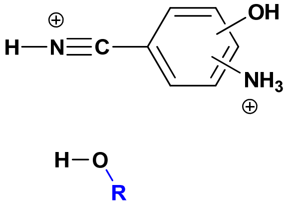
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0        0.650275   -1.608781   -0.028318
      2          1           0        0.019931   -2.487908   -0.126610
      3          6           0        1.948796   -1.647510   -0.510940
      4          6           0        2.769351   -0.527034   -0.376199
      5          6           0        2.268378    0.617569    0.259854
      6          6           0        0.982882    0.671294    0.750607
      7          6           0        0.164494   -0.455450    0.600169
      8          1           0        2.338112   -2.537882   -0.995288
      9          8           0        4.033854   -0.457086   -0.817624
     10          7           0        3.172236    1.758907    0.381449
     11          1           0        0.612337    1.574060    1.231441
     12          6           0       -1.183592   -0.407921    1.124861
     13          7           0       -1.795497    0.240831    2.028334
     14          1           0        3.516278    2.075381   -0.538015
     15          1           0        2.709072    2.562203    0.828483
     16          1           0        4.299416   -1.285189   -1.259003
     17          1           0        4.003152    1.528338    0.946683
     18          1           0       -1.330398    0.902918    2.650113
     19          8           0       -2.180372   -1.321278    0.712683
     20          1           0       -2.758812   -0.677678    1.587713
     21          6           0       -2.698307   -1.287944   -0.675256
     22          6           0       -3.124773    0.111420   -1.025420
     23          1           0       -1.896424   -1.657097   -1.316652
     24          1           0       -3.529167   -1.991974   -0.654939
     25          8           0       -1.954933    0.899974   -1.089496
     26          1           0       -3.649195    0.094487   -1.990458
     27          1           0       -3.815928    0.500110   -0.261839
     28          6           0       -2.205661    2.283785   -0.917679
     29          1           0       -1.249197    2.799243   -1.025378
     30          1           0       -2.903938    2.653250   -1.679364
     31          1           0       -2.621848    2.480117    0.080055
---------------------------------------------------------------------
```

System:	
Name of the output file:	**26.log**
Description:	**SP3** in Figure 6 for **3a** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-725,04235
Number of imaginary frequencies:	0

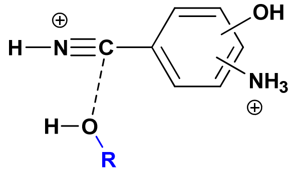
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -1.204265   -1.403340    0.209888
      2          1           0       -0.547320   -2.259271    0.318205
      3          6           0       -2.566212   -1.570010    0.399835
      4          6           0       -3.424037   -0.478807    0.257447
      5          6           0       -2.879508    0.769885   -0.065029
      6          6           0       -1.526415    0.951685   -0.251460
      7          6           0       -0.669325   -0.147264   -0.110717
      8          1           0       -2.977780   -2.542639    0.652450
      9          8           0       -4.756617   -0.530962    0.401501
     10          7           0       -3.810220    1.887301   -0.210749
     11          1           0       -1.175957    1.943217   -0.524669
     12          6           0        0.782457   -0.021386   -0.305764
     13          7           0        1.396893    1.122432   -0.397502
     14          1           0       -3.318527    2.756820   -0.458807
     15          1           0       -4.511349    1.708451   -0.945884
     16          1           0       -5.055162   -1.433923    0.617126
     17          1           0       -4.331620    2.066679    0.660522
     18          1           0        0.890969    1.998476   -0.308007
     19          8           0        1.421264   -1.154870   -0.377477
     20          1           0        2.429487    1.178862   -0.418636
     21          6           0        2.804905   -1.267635   -0.821161
     22          6           0        3.830648   -0.772831    0.174015
     23          1           0        2.915929   -2.340549   -0.970185
     24          1           0        2.896650   -0.753557   -1.783981
     25          8           0        4.058108    0.612386   -0.033184
     26          1           0        3.494681   -0.962139    1.203121
     27          1           0        4.764201   -1.324515    0.003194
     28          6           0        4.900205    1.184006    0.958518
     29          1           0        5.029579    2.236285    0.701156
     30          1           0        4.440735    1.097436    1.950705
     31          1           0        5.876020    0.683986    0.961296
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**27.log**
Description:	**SP1** in Figure 6 for **3b** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,97758
Number of imaginary frequencies:	0

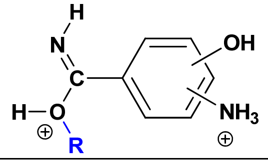
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
---------------------------------------------------------------------
      1          6           0       -1.212361    0.997295    0.740274
      2          1           0       -1.000398    2.021099    1.033790
      3          6           0       -2.423113    0.669770    0.141979
      4          6           0       -2.658329   -0.661255   -0.215759
      5          6           0       -1.732961   -1.668443   -0.005271
      6          6           0       -0.511433   -1.357801    0.580788
      7          6           0       -0.280074   -0.027619    0.940659
      8          8           0       -3.408835    1.545776   -0.127011
      9          7           0       -3.943864   -0.951124   -0.843157
     10          1           0       -1.961915   -2.687950   -0.301997
     11          1           0        0.244211   -2.115297    0.745603
     12          6           0        0.964522    0.338515    1.537262
     13          7           0        1.907052    0.691616    2.080915
     14          1           0        2.773982    0.966993    2.534967
     15          8           0        2.644648   -1.615173    0.399358
     16          1           0        2.678393   -2.580501    0.493371
     17          6           0        3.064788   -1.279995   -0.921429
     18          6           0        3.103415    0.220687   -1.051755
     19          1           0        4.068832   -1.676086   -1.116496
     20          1           0        2.371019   -1.698876   -1.662755
     21          8           0        1.782218    0.729339   -1.008416
     22          1           0        3.699541    0.655935   -0.233058
     23          1           0        3.578213    0.493491   -2.005542
     24          6           0        1.757295    2.141835   -1.086543
     25          1           0        0.710497    2.454435   -1.064569
     26          1           0        2.293139    2.592283   -0.238052
     27          1           0        2.217582    2.490086   -2.021051
     28          1           0       -4.051368   -1.956942   -1.034742
     29          1           0       -4.734383   -0.661242   -0.247048
     30          1           0       -4.049249   -0.451548   -1.739744
     31          1           0       -3.155152    2.453205    0.120336
---------------------------------------------------------------------
```

System:	
Name of the output file:	**28.log**
Description:	**TS1** in Figure 6 for **3b** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,96632
Number of imaginary frequencies:	1 (334*i* cm^{-1})

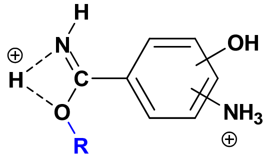
CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.925953    0.821616    0.732127
      2          1           0       -0.524177    1.763315    1.095204
      3          6           0       -2.209904    0.770044    0.203791
      4          6           0       -2.699418   -0.456079   -0.253936
      5          6           0       -1.949598   -1.617765   -0.205990
      6          6           0       -0.659603   -1.575580    0.314417
      7          6           0       -0.169120   -0.354723    0.777044
      8          8           0       -3.034921    1.830177    0.095334
      9          7           0       -4.053105   -0.461316   -0.801677
     10          1           0       -2.368365   -2.551884   -0.568892
     11          1           0       -0.066919   -2.480551    0.361355
     12          6           0        1.139981   -0.209121    1.380807
     13          7           0        1.795896    0.338937    2.188599
     14          1           0        2.758694    0.423587    2.506081
     15          8           0        2.303051   -1.496235    0.412137
     16          1           0        2.123164   -2.427468    0.639550
     17          6           0        2.472016   -1.351268   -1.013524
     18          6           0        2.939136    0.057712   -1.263858
     19          1           0        3.226455   -2.070838   -1.342685
     20          1           0        1.522442   -1.551008   -1.522535
     21          8           0        1.879947    0.931218   -0.918329
     22          1           0        3.823539    0.270282   -0.645216
     23          1           0        3.212059    0.178891   -2.321025
     24          6           0        2.313290    2.263053   -0.716223
     25          1           0        1.428446    2.864473   -0.496180
     26          1           0        3.014805    2.320045    0.127747
     27          1           0        2.802860    2.657802   -1.616351
     28          1           0       -4.375381   -1.418894   -0.998378
     29          1           0       -4.729745   -0.034665   -0.151147
     30          1           0       -4.110105    0.071647   -1.683421
     31          1           0       -2.626894    2.633315    0.466378
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**29.log**
Description:	**SP2** in Figure 6 for **3b** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,97997
Number of imaginary frequencies:	0

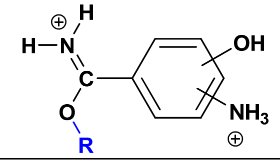
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0       -0.825500    0.704394    0.683285
      2          1           0       -0.327686    1.588268    1.075726
      3          6           0       -2.139970    0.791250    0.239424
      4          6           0       -2.752271   -0.352767   -0.279639
      5          6           0       -2.094774   -1.565760   -0.368313
      6          6           0       -0.775725   -1.655850    0.068687
      7          6           0       -0.158992   -0.519628    0.596061
      8          8           0       -2.887951    1.914440    0.261632
      9          7           0       -4.136184   -0.216807   -0.727413
     10          1           0       -2.607112   -2.433937   -0.772905
     11          1           0       -0.250883   -2.603613    0.012908
     12          6           0        1.213262   -0.590694    1.130014
     13          7           0        1.789905   -0.073361    2.105318
     14          1           0        1.161614    0.519583    2.654665
     15          8           0        2.036944   -1.538522    0.395979
     16          1           0        2.847704   -1.723911    0.932611
     17          6           0        2.409342   -1.245391   -1.036484
     18          6           0        3.031137    0.117594   -1.120295
     19          1           0        3.092802   -2.055507   -1.285448
     20          1           0        1.473657   -1.333360   -1.587399
     21          8           0        2.010241    1.065773   -0.900962
     22          1           0        3.830413    0.215113   -0.370573
     23          1           0        3.477368    0.232599   -2.118156
     24          6           0        2.505453    2.320147   -0.463078
     25          1           0        1.650029    2.993887   -0.385346
     26          1           0        2.990048    2.222730    0.517762
     27          1           0        3.224045    2.730730   -1.183617
     28          1           0       -4.766685    0.026916    0.051348
     29          1           0       -4.239228    0.526423   -1.434437
     30          1           0       -4.484732   -1.089845   -1.146700
     31          1           0       -2.393035    2.661812    0.643063
---------------------------------------------------------------------
```

System:	
Name of the output file:	**30.log**
Description:	**TS2** in Figure 6 for **3b** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,95165
Number of imaginary frequencies:	1 (1823*i* cm^{-1})

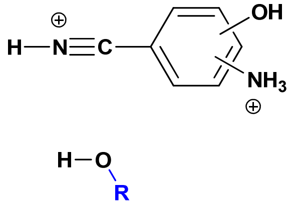
CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
---------------------------------------------------------------------
      1          6           0       -0.919044    0.718402    0.728163
      2          1           0       -0.491792    1.611275    1.178826
      3          6           0       -2.233927    0.730923    0.280861
      4          6           0       -2.756599   -0.427189   -0.302616
      5          6           0       -2.008714   -1.578792   -0.461904
      6          6           0       -0.686660   -1.594602   -0.026554
      7          6           0       -0.162143   -0.445991    0.568798
      8          8           0       -3.064447    1.789739    0.363029
      9          7           0       -4.148629   -0.376058   -0.741021
     10          1           0       -2.454952   -2.457051   -0.919465
     11          1           0       -0.090144   -2.494909   -0.130965
     12          6           0        1.201437   -0.454236    1.086631
     13          7           0        1.820095    0.129962    2.025403
     14          1           0        1.366496    0.774352    2.674527
     15          8           0        2.170932   -1.370967    0.632409
     16          1           0        2.767934   -0.781642    1.539220
     17          6           0        2.670294   -1.303807   -0.760306
     18          6           0        3.125762    0.097729   -1.061409
     19          1           0        3.481981   -2.029827   -0.778945
     20          1           0        1.846989   -1.627406   -1.399306
     21          8           0        1.974429    0.916546   -1.052625
     22          1           0        3.847996    0.433757   -0.302379
     23          1           0        3.619705    0.112958   -2.042170
     24          6           0        2.260595    2.279291   -0.787217
     25          1           0        1.317588    2.825200   -0.855623
     26          1           0        2.683996    2.395864    0.220011
     27          1           0        2.966175    2.681732   -1.524846
     28          1           0       -4.788585   -0.178823    0.043610
     29          1           0       -4.303218    0.363338   -1.443500
     30          1           0       -4.440686   -1.268635   -1.162728
     31          1           0       -2.623061    2.549569    0.783864
---------------------------------------------------------------------
```

System:	
Name of the output file:	**31.log**
Description:	**SP3** in Figure 6 for **3b** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-725,04054
Number of imaginary frequencies:	0

CARTESIAN COORDINATES

```
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        1.510298   -0.981594    0.361604
      2          1           0        1.149236   -1.939326    0.726725
      3          6           0        2.875228   -0.825697    0.142756
      4          6           0        3.352613    0.413037   -0.290068
      5          6           0        2.515670    1.493716   -0.499798
      6          6           0        1.151036    1.344997   -0.274956
      7          6           0        0.659009    0.106119    0.144269
      8          8           0        3.800039   -1.791116    0.323862
      9          7           0        4.792223    0.526760   -0.509182
     10          1           0        2.925567    2.442150   -0.834575
     11          1           0        0.480123    2.180132   -0.438717
     12          6           0       -0.799708   -0.032910    0.355140
     13          7           0       -1.408658   -1.178234    0.284904
     14          1           0       -0.891868   -2.020541    0.044613
     15          8           0       -1.419044    1.081554    0.602410
     16          1           0       -2.439562   -1.247530    0.316125
     17          6           0       -2.817227    1.140005    1.014390
     18          6           0       -3.805432    0.804783   -0.080323
     19          1           0       -2.939716    0.486770    1.884765
     20          1           0       -2.928025    2.179336    1.318674
     21          8           0       -4.060264   -0.590641   -0.074186
     22          1           0       -4.738088    1.346697    0.123367
     23          1           0       -3.421256    1.126288   -1.058612
     24          6           0       -4.842958   -1.006845   -1.184842
     25          1           0       -5.012550   -2.078875   -1.074221
     26          1           0       -5.805526   -0.481626   -1.189317
     27          1           0       -4.313359   -0.809233   -2.125063
     28          1           0        5.052019    1.483041   -0.788030
     29          1           0        5.328044    0.295364    0.340850
     30          1           0        5.119153   -0.112017   -1.249743
     31          1           0        3.393848   -2.622368    0.627387
 ---------------------------------------------------------------------
```

System:	
Name of the output file:	**32.log**
Description:	**SP1** in Figure 6 for **3c** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,97925
Number of imaginary frequencies:	0

CARTESIAN COORDINATES

```
---------------------------------------------------------------------
 Center     Atomic      Atomic              Coordinates (Angstroms)
 Number     Number       Type              X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -2.645002   -0.222961   -0.795694
      2          1           0       -3.443384    0.396385   -1.189242
      3          6           0       -2.466801   -1.537667   -1.217090
      4          6           0       -1.441543   -2.316188   -0.697195
      5          6           0       -0.563181   -1.789561    0.257801
      6          6           0       -0.723031   -0.477798    0.689706
      7          6           0       -1.762838    0.297675    0.158449
      8          1           0       -3.138326   -1.958303   -1.957864
      9          1           0       -1.303329   -3.343441   -1.024083
     10          8           0        0.456724   -2.471647    0.813022
     11          7           0        0.262066    0.015141    1.633812
     12          6           0       -1.971527    1.643199    0.563401
     13          7           0       -2.213534    2.713149    0.887517
     14          1           0       -2.398599    3.679567    1.149790
     15          8           0        0.550731    2.065440   -0.288080
     16          1           0        1.007037    2.896152   -0.073579
     17          6           0        1.182851    1.471692   -1.420993
     18          6           0        2.538815    0.906823   -1.068326
     19          1           0        0.517061    0.667617   -1.754536
     20          1           0        1.285737    2.198092   -2.234775
     21          8           0        2.353108   -0.098063   -0.079414
     22          1           0        3.007639    0.465620   -1.958236
     23          1           0        3.198491    1.693581   -0.673860
     24          6           0        3.570769   -0.682035    0.363121
     25          1           0        3.318595   -1.414070    1.133042
     26          1           0        4.073888   -1.185081   -0.470636
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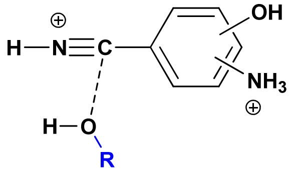
System:	
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Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,96576
Number of imaginary frequencies:	1 (310*i* cm^{-1})

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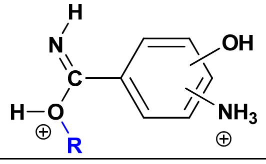
System:	
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Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,97553
Number of imaginary frequencies:	0

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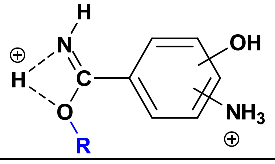
System:	
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Description:	**TS2** in Figure 6 for **3c** in 2-methoxyethanol
Total Gibbs Free Energy, M06–2X/6–31+G(d) (in a.u.):	-724,94651
Number of imaginary frequencies:	1 (1848*i* cm^{-1})

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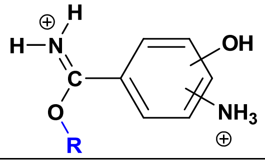
System:	
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Number of imaginary frequencies:	0

CARTESIAN COORDINATES

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---------------------------------------------------------------------
```

IV. Cell culturing and MTT proliferation assay

The cell lines HeLa (cervical carcinoma), SW620 (colorectal carcinoma), HepG2 (hepatocellular carcinoma) and CFPAC-1 (pancreatic adenocarcinoma, metastatic) were obtained from ATCC (American Type Culture Collection) and cultured as monolayers in Dulbecco's modified Eagle medium (DMEM) supplemented with 10 % foetal bovine serum (FBS), 2 mM L-glutamine, 100 U/ml penicillin and 100 μg/ml streptomycin in a humidified atmosphere with 5 % CO_2 at 37 °C. The panel cell lines were inoculated onto a series of standard 96-well microtiter plates on day 0, at 3000 cells per well. Test compounds were then added in five 10-fold dilutions (0.01 to 100 μM) followed by a 72-hour incubation. Working dilutions were freshly prepared on the day of testing in the growth medium. The solvent (DMSO) was also tested for eventual inhibitory activity by adjusting its concentration to be the same as in the working concentrations (DMSO concentration never exceeded 0.1 %). After 72 hours of incubation, the cell growth rate was evaluated by performing the MTT assay according to the manufacturer’s instructions. The absorbance was measured at 570 nm (TECAN SUNRISE Microtiter plate reader, Männedorf, Switzerland), and transformed into a cell percentage growth (PG) using the formulas proposed by National Institutes of Health (NIH) and described previously.[S27] The IC_{50} values for each compound were calculated from dose-response curves using linear regression analysis by fitting the mean test concentrations that give PG values above and below the reference value. Each test point was performed in quadruplicate in three individual experiments.

V. ^{1}H and ^{13}C NMR spectra

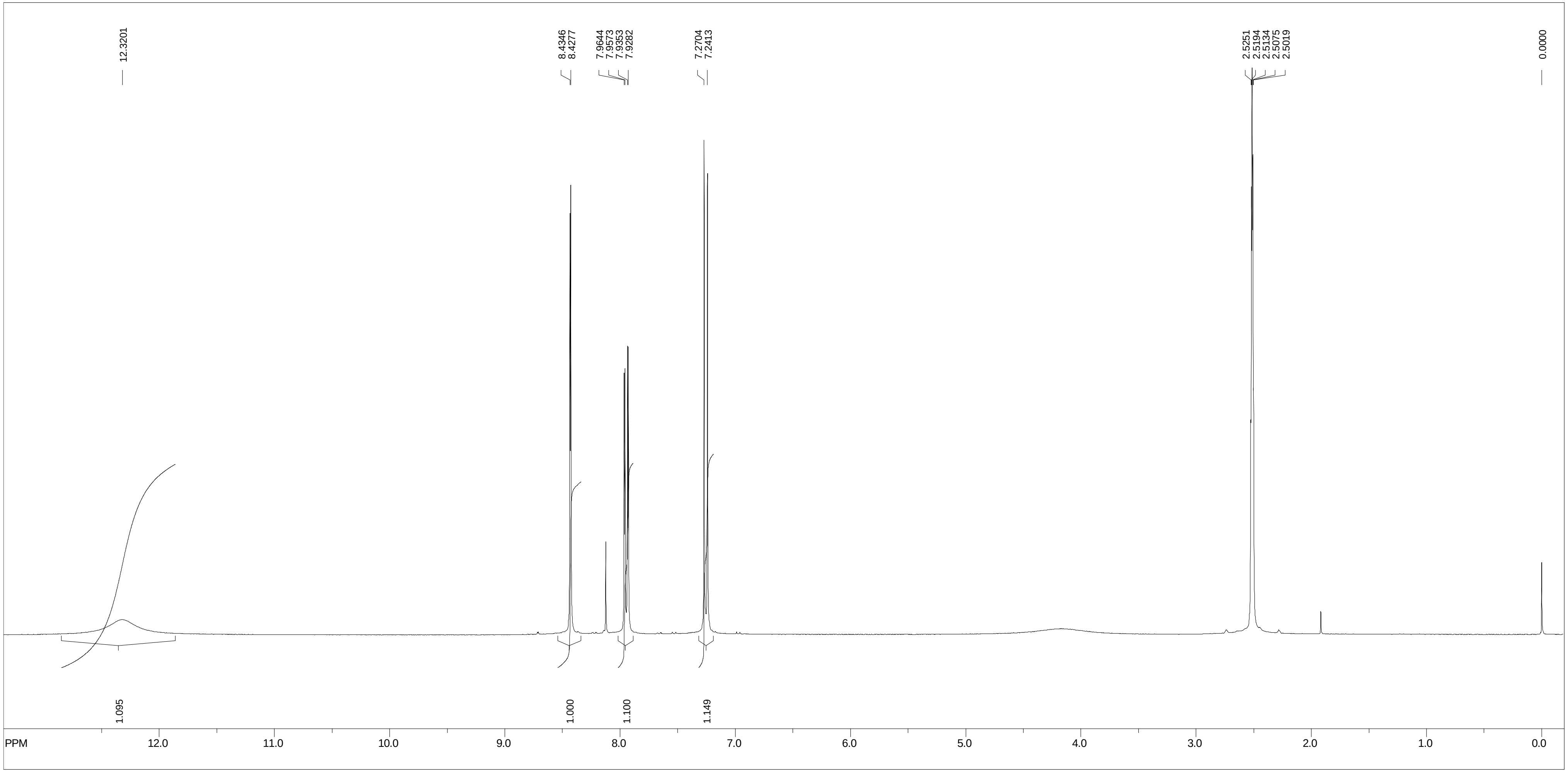

Figure S9. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 4-hydroxy-3-nitrobenzonitrile (**2a**)

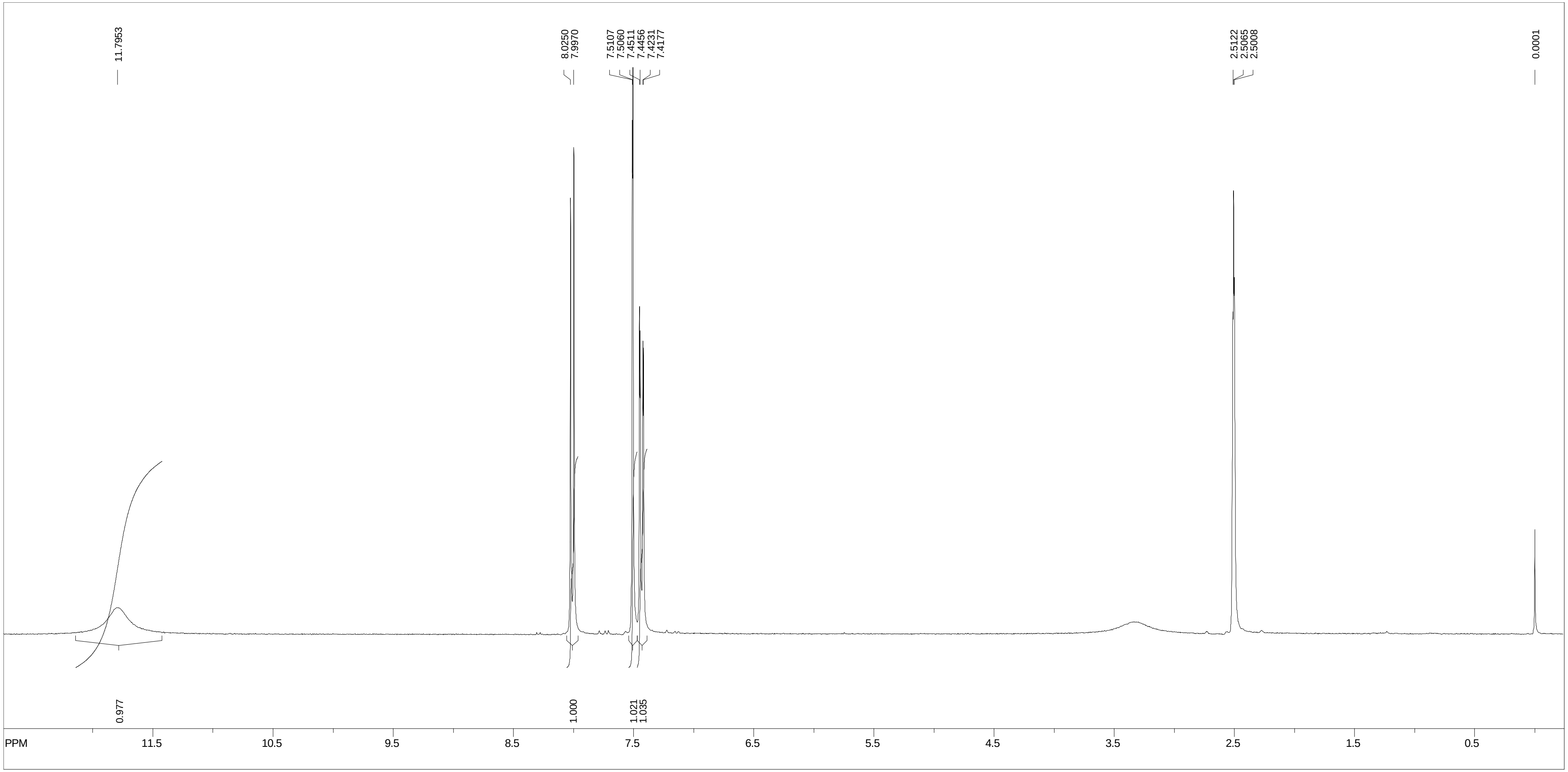

Figure S10. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 3-hydroxy-4-nitrobenzonitrile (**2b**)

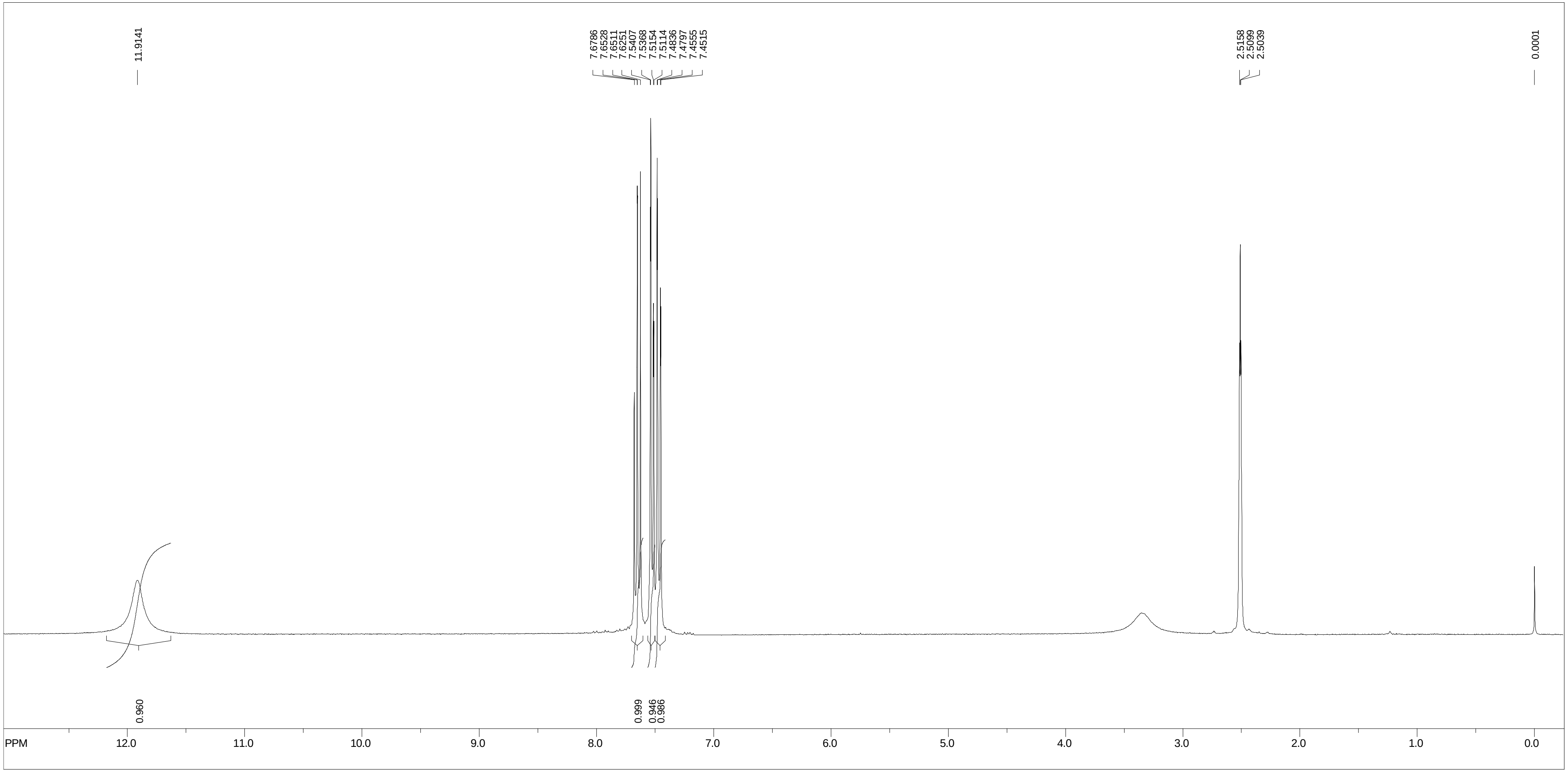

Figure S11. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 3-hydroxy-2-nitrobenzonitrile (**2c**)

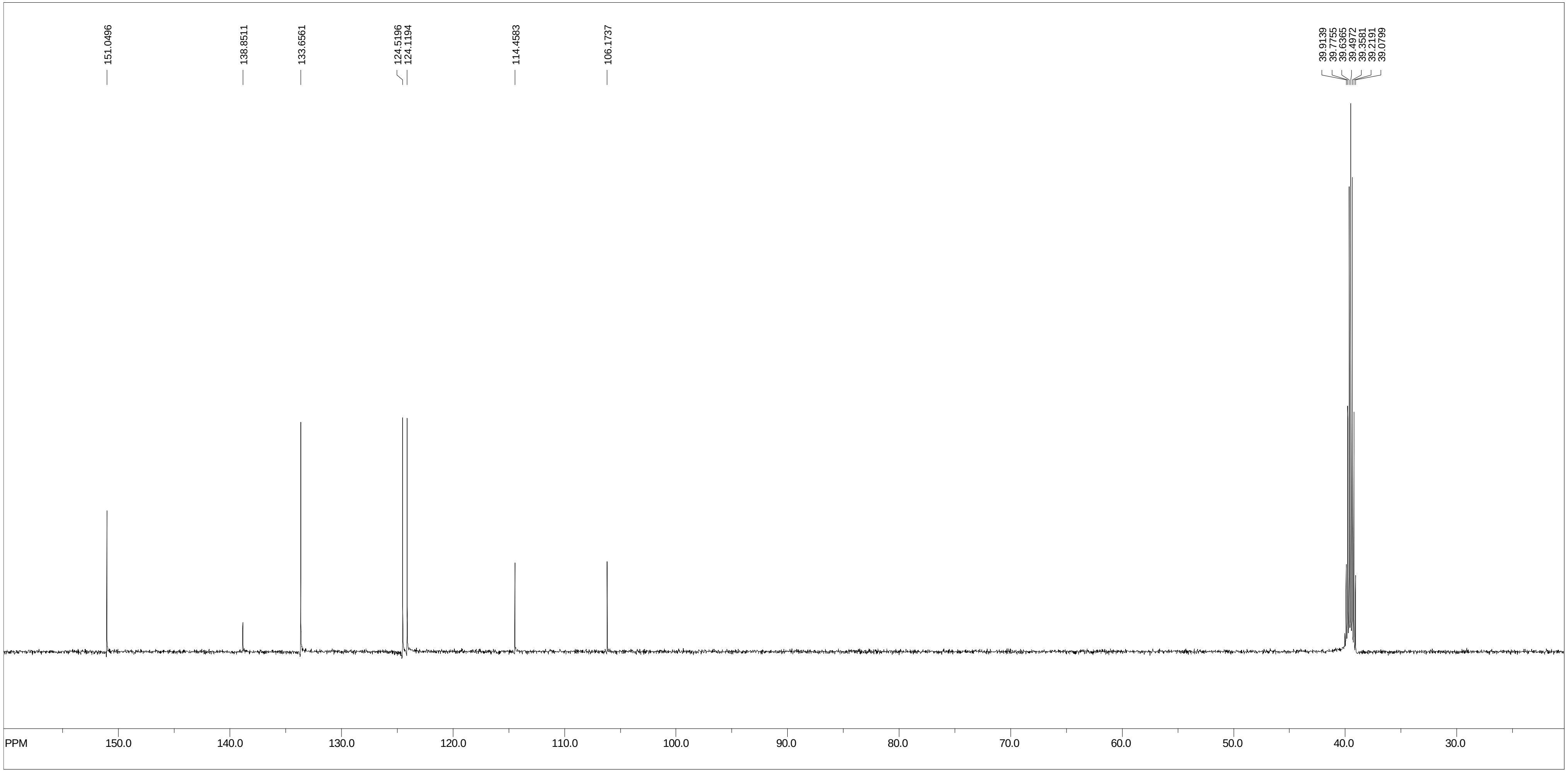

Figure S12. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 3-hydroxy-2-nitrobenzonitrile (**2c**)

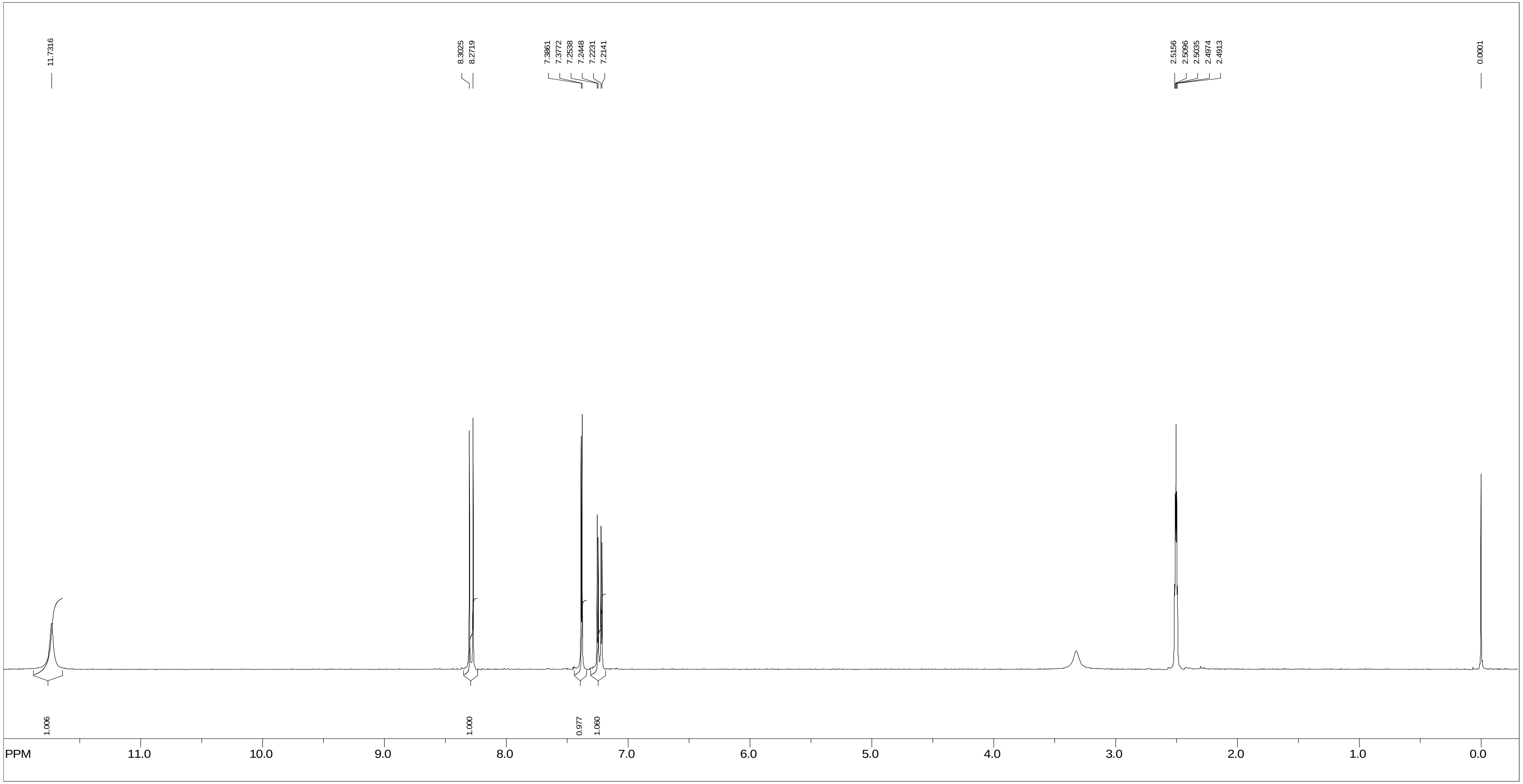

Figure S13. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 5-hydroxy-2-nitrobenzonitrile (**2d**)

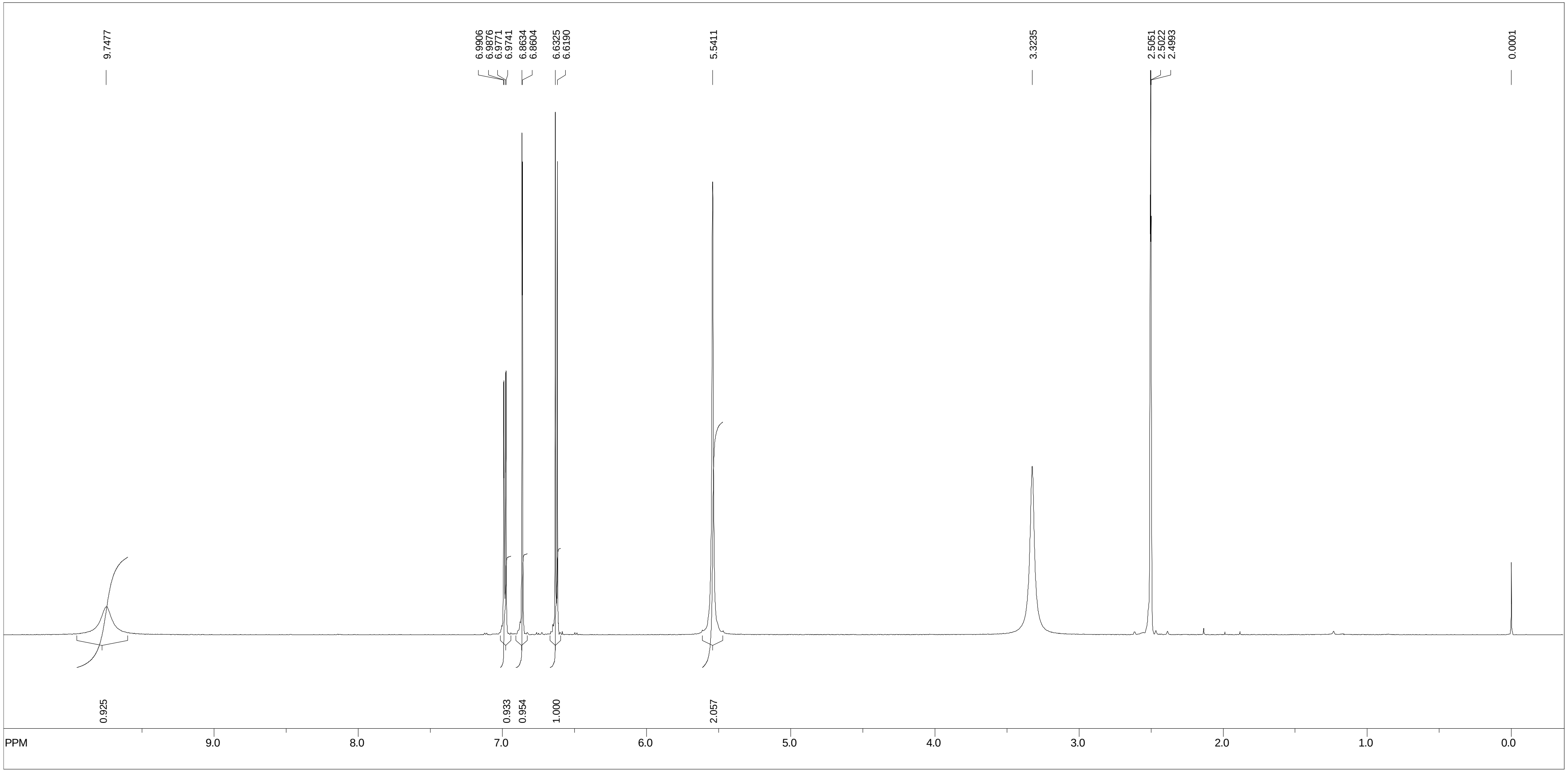

Figure S14. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 4-amino-3-hydroxybenzonitrile (**3a**)

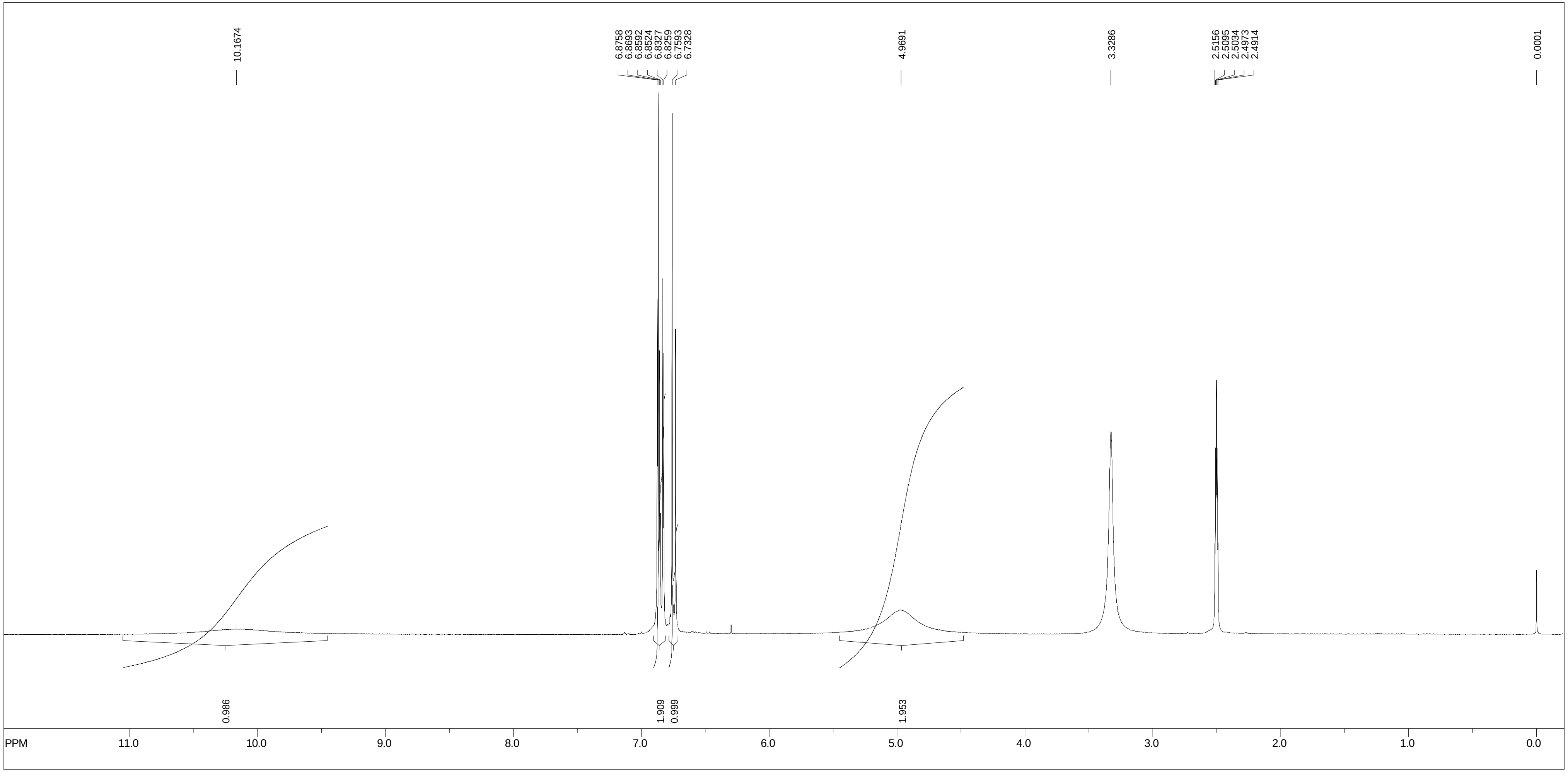

Figure S15. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 3-amino-4-hydroxybenzonitrile (**3b**)

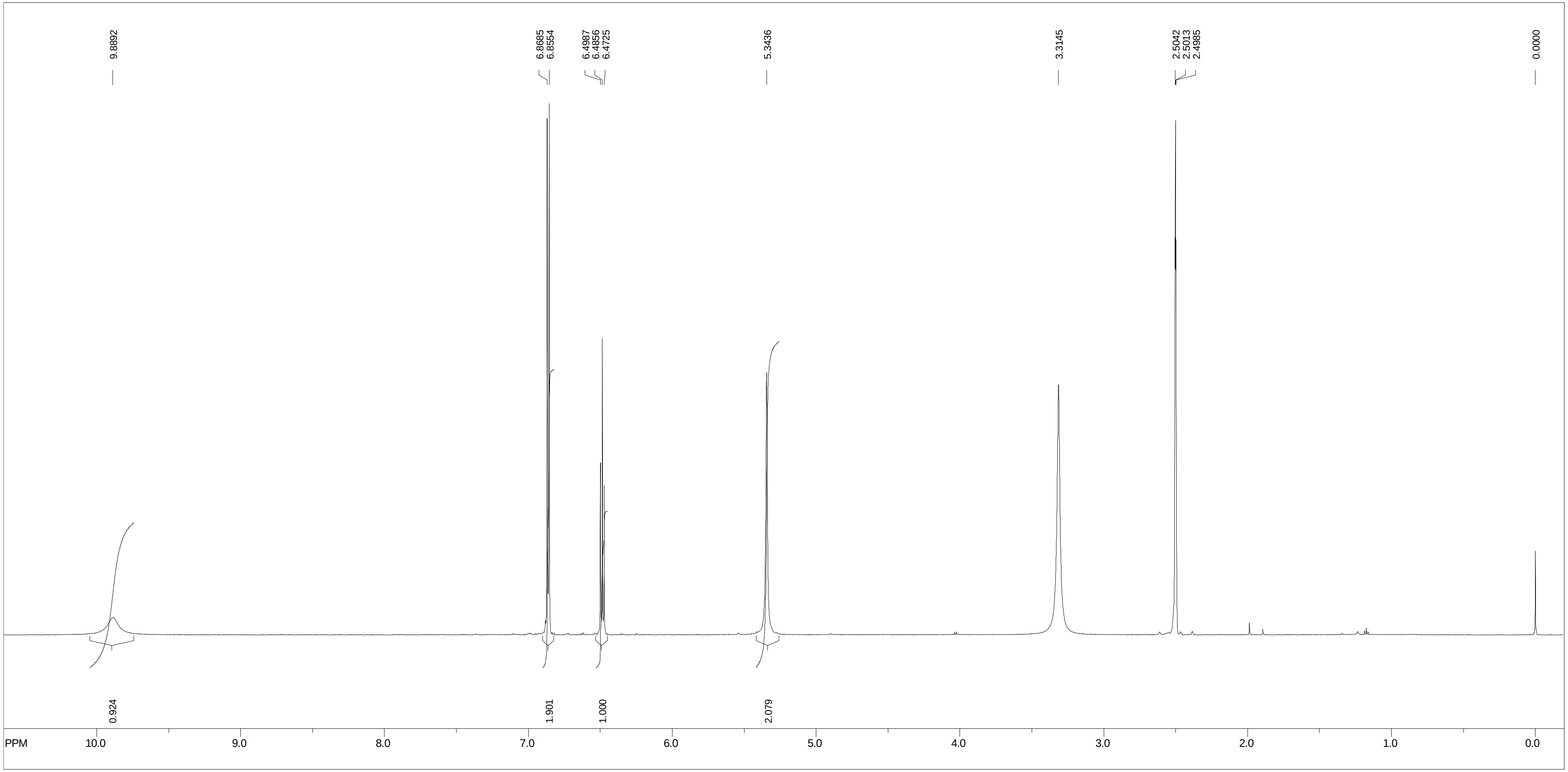

Figure S16. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-3-hydroxybenzonitrile (**3c**)

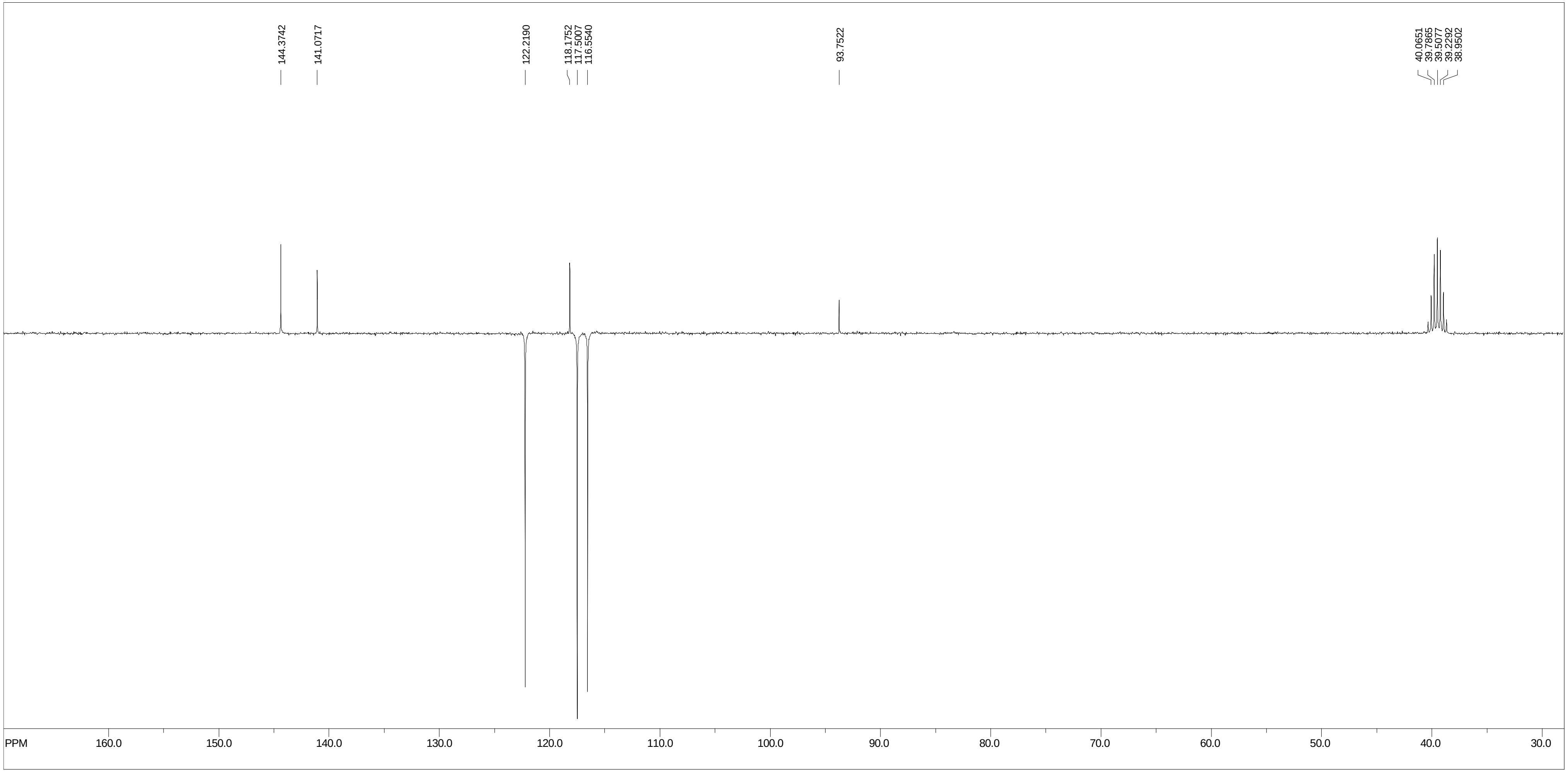

Figure S17. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-3-hydroxybenzonitrile (**3c**)

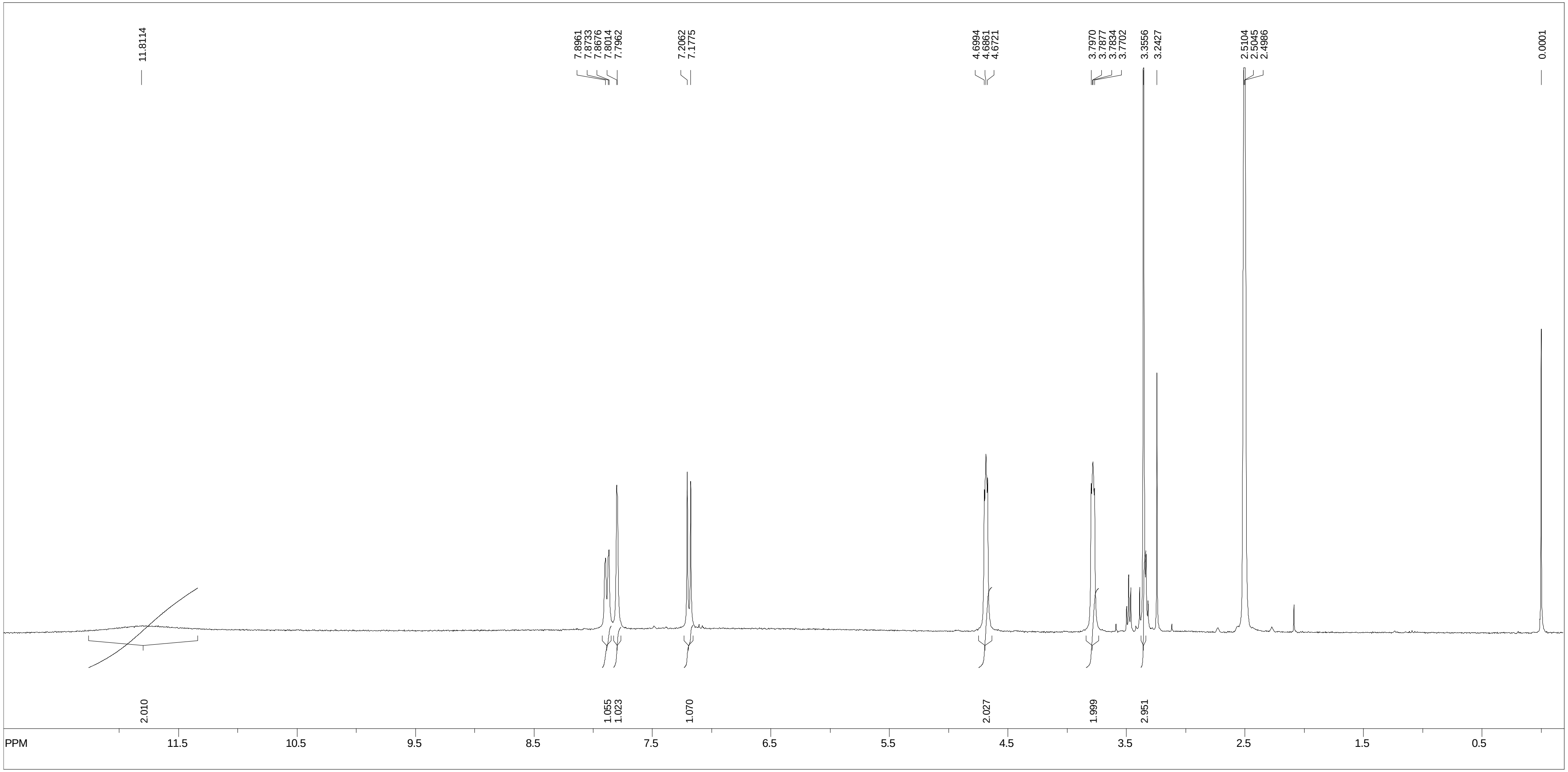

Figure S18. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-methoxyethyl-(3-amino-4-hydroxyphenyl) carboximidate dihydrochloride (**5b**)

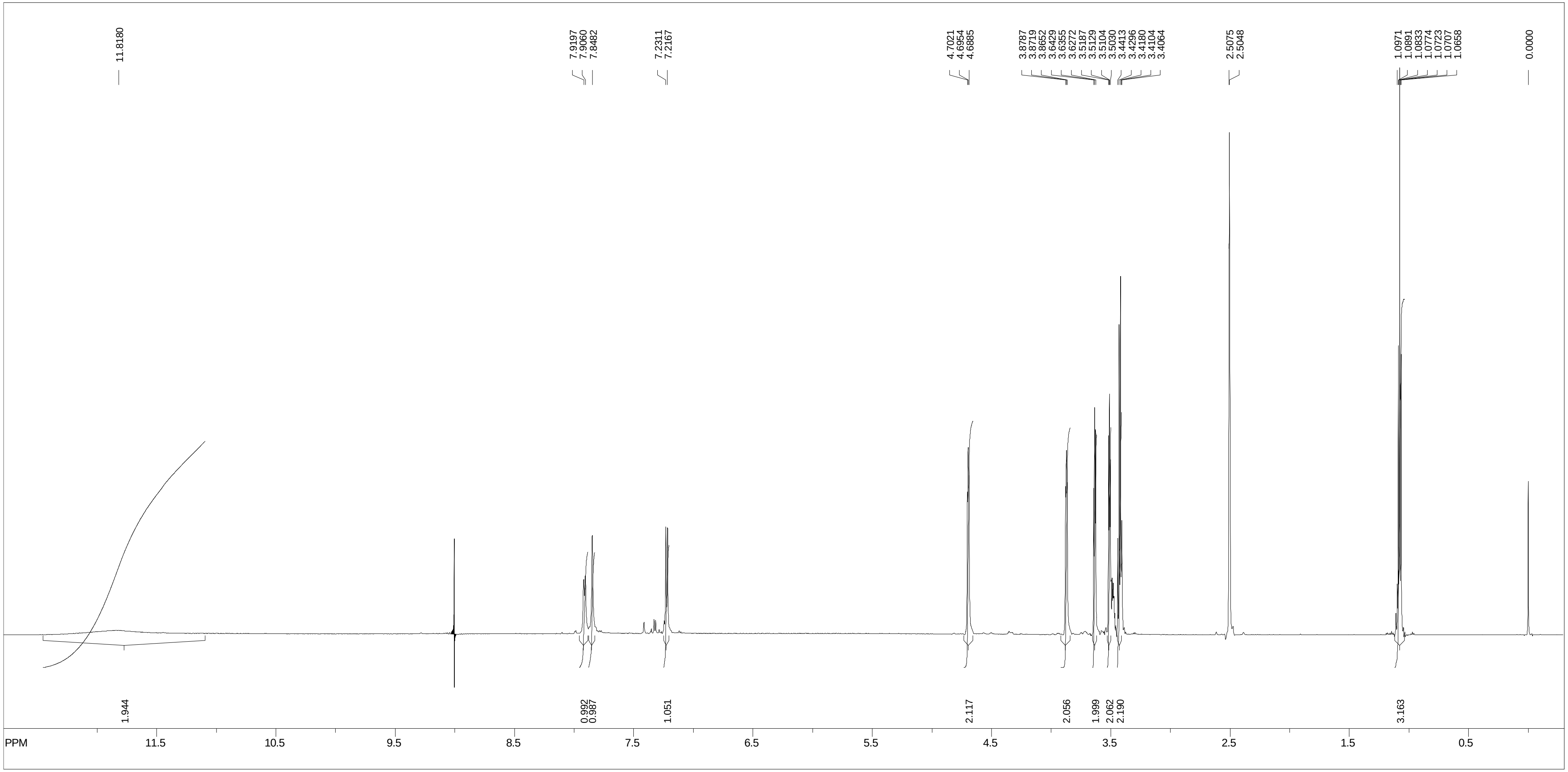

Figure S19. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-(2-ethoxyethoxy)ethyl-(3-amino-4-hydroxyphenyl) carboximidate dihydrochloride (**5c**)

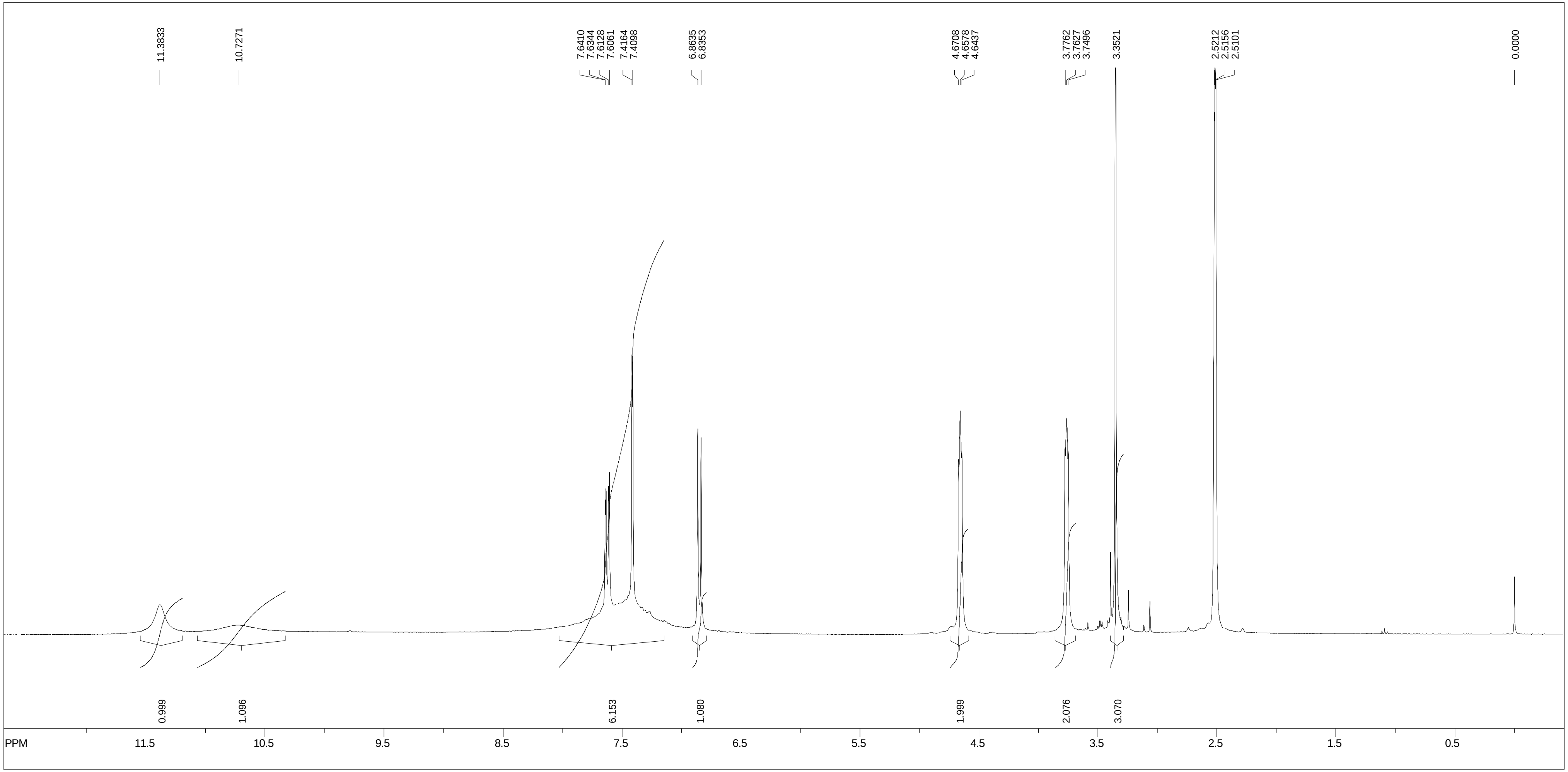

Figure S20. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-methoxyethyl-(4-amino-3-hydroxyphenyl) carboximidate dihydrochloride (**6b**)

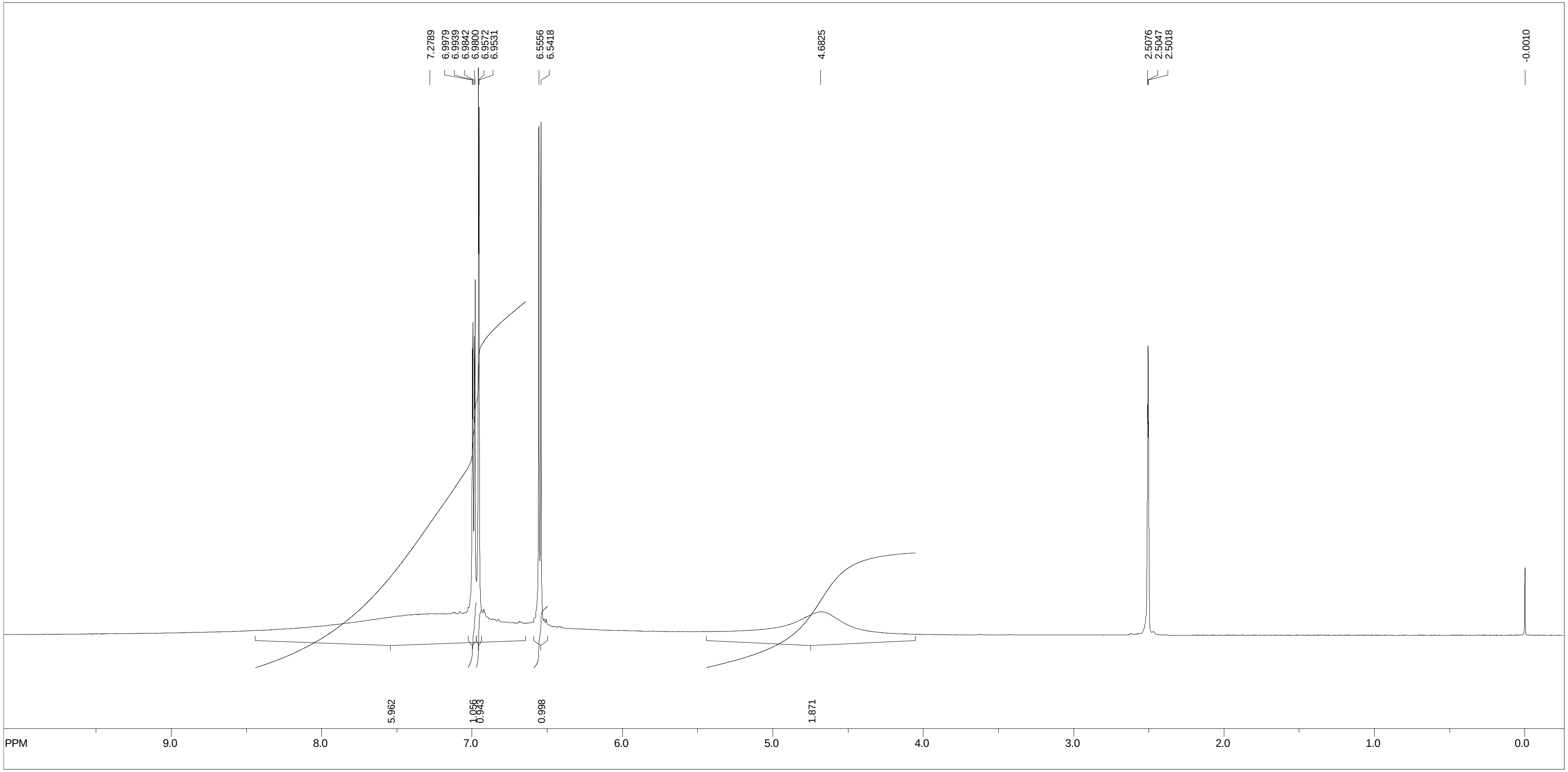

Figure S21. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-amino-4-amidiniumphenolate hemihydrochloride **8a**

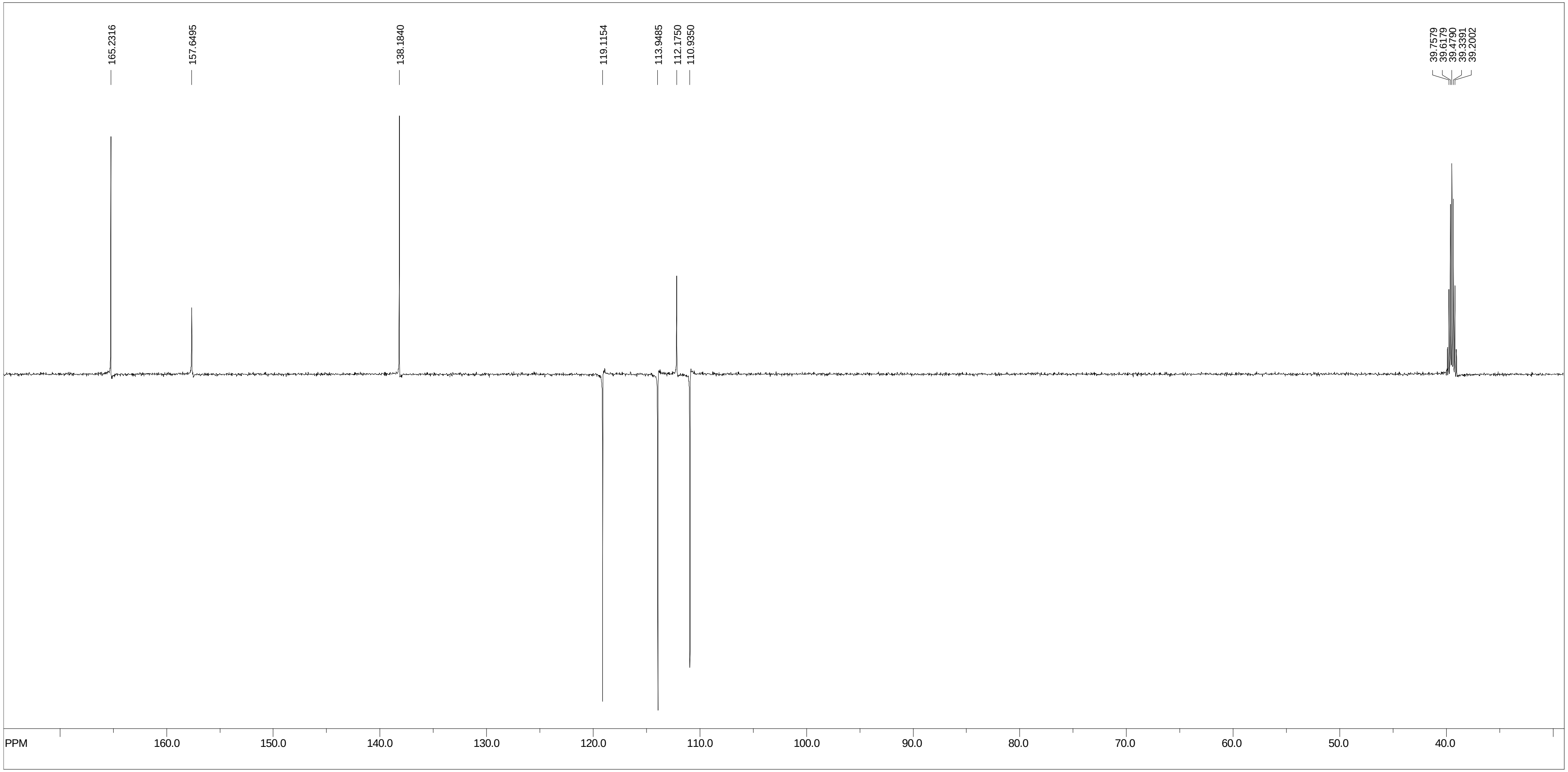

Figure S22. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2-amino-4-amidiniumphenolate hemihydrochloride **8a**

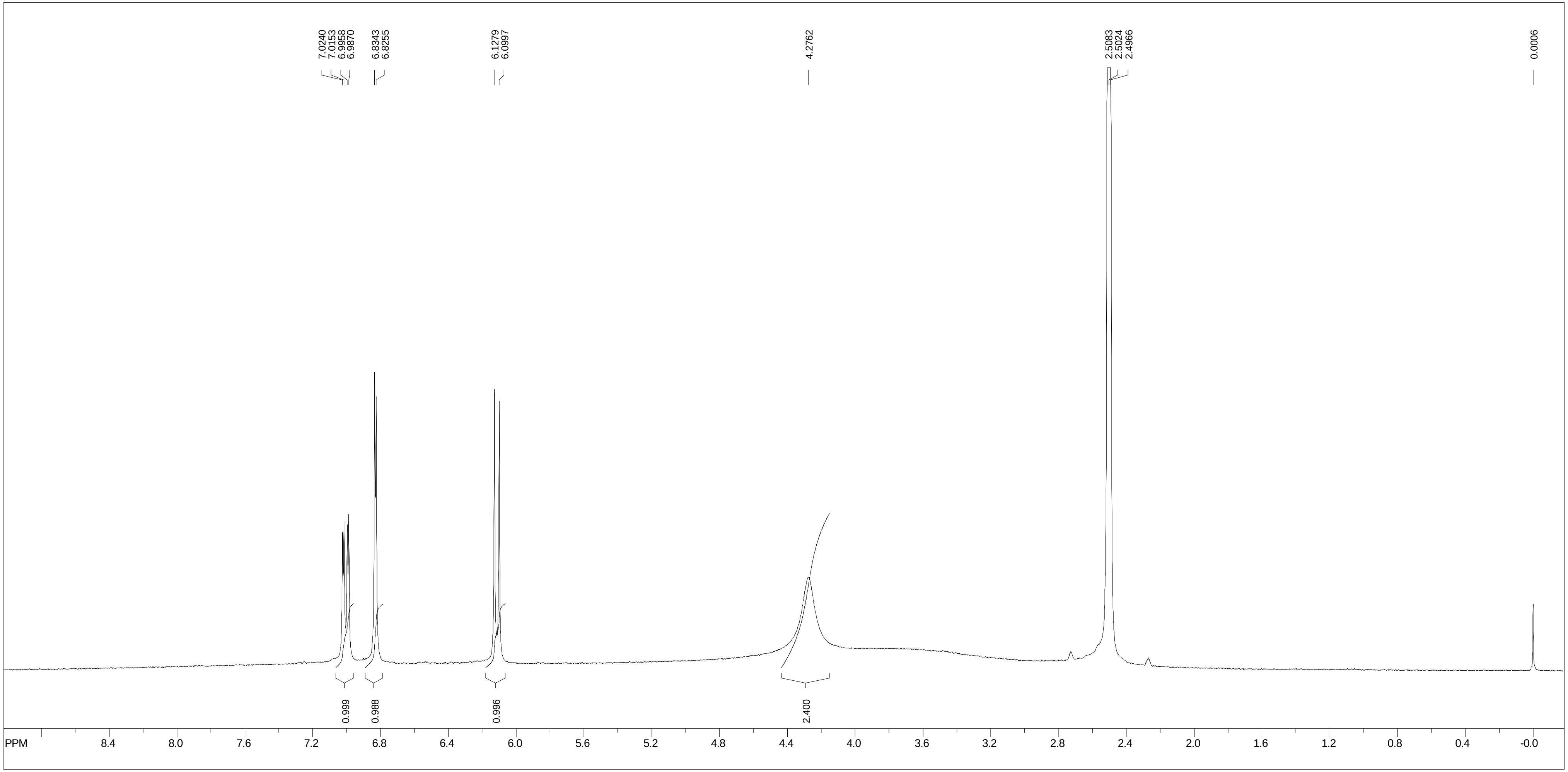

Figure S23. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-amidiniumphenolate **8a'**

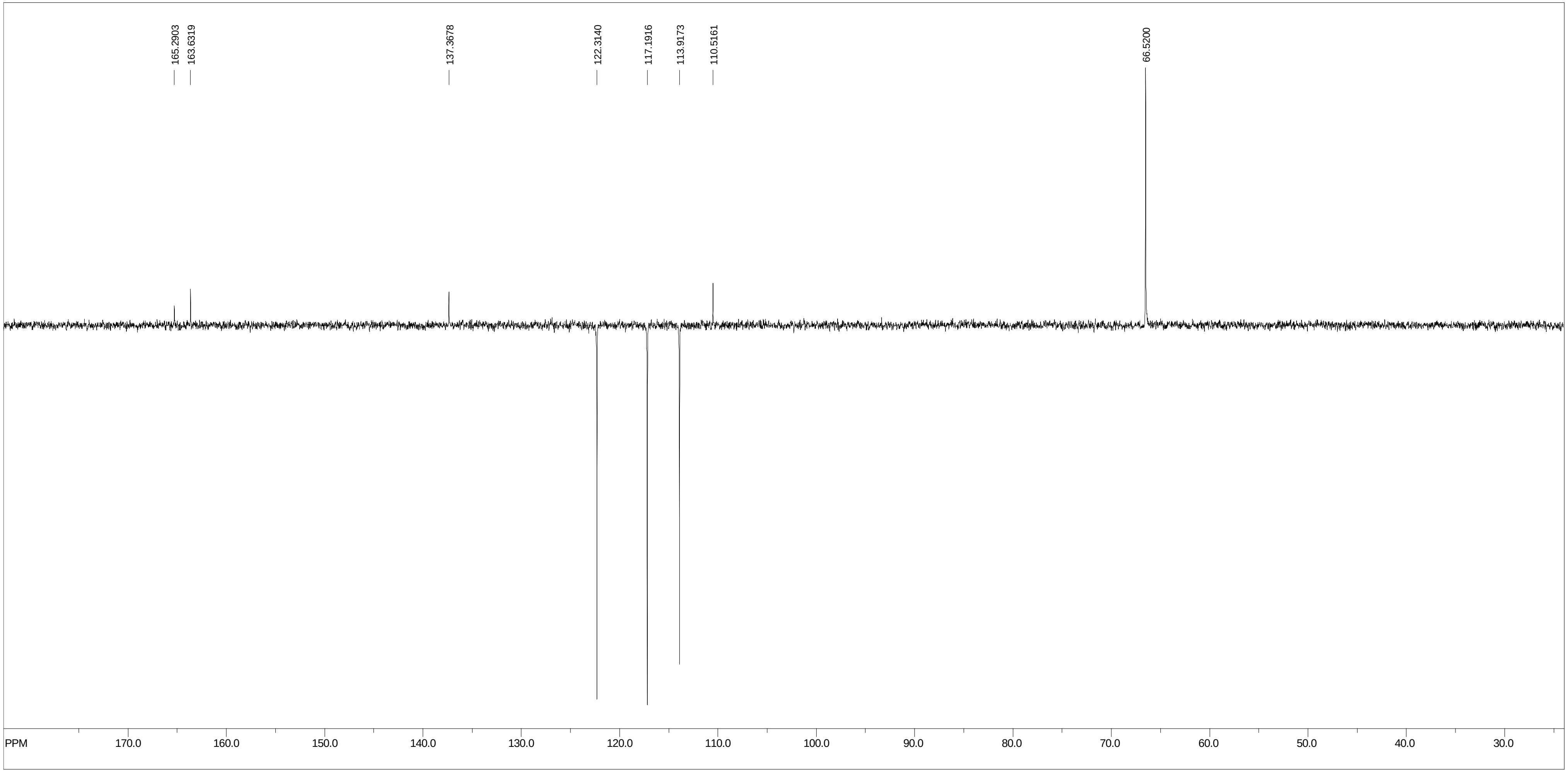

Figure S24. ^{13}C NMR spectrum (75 MHz, D_2O) of 2-amino-4-amidiniumphenolate **8a'**

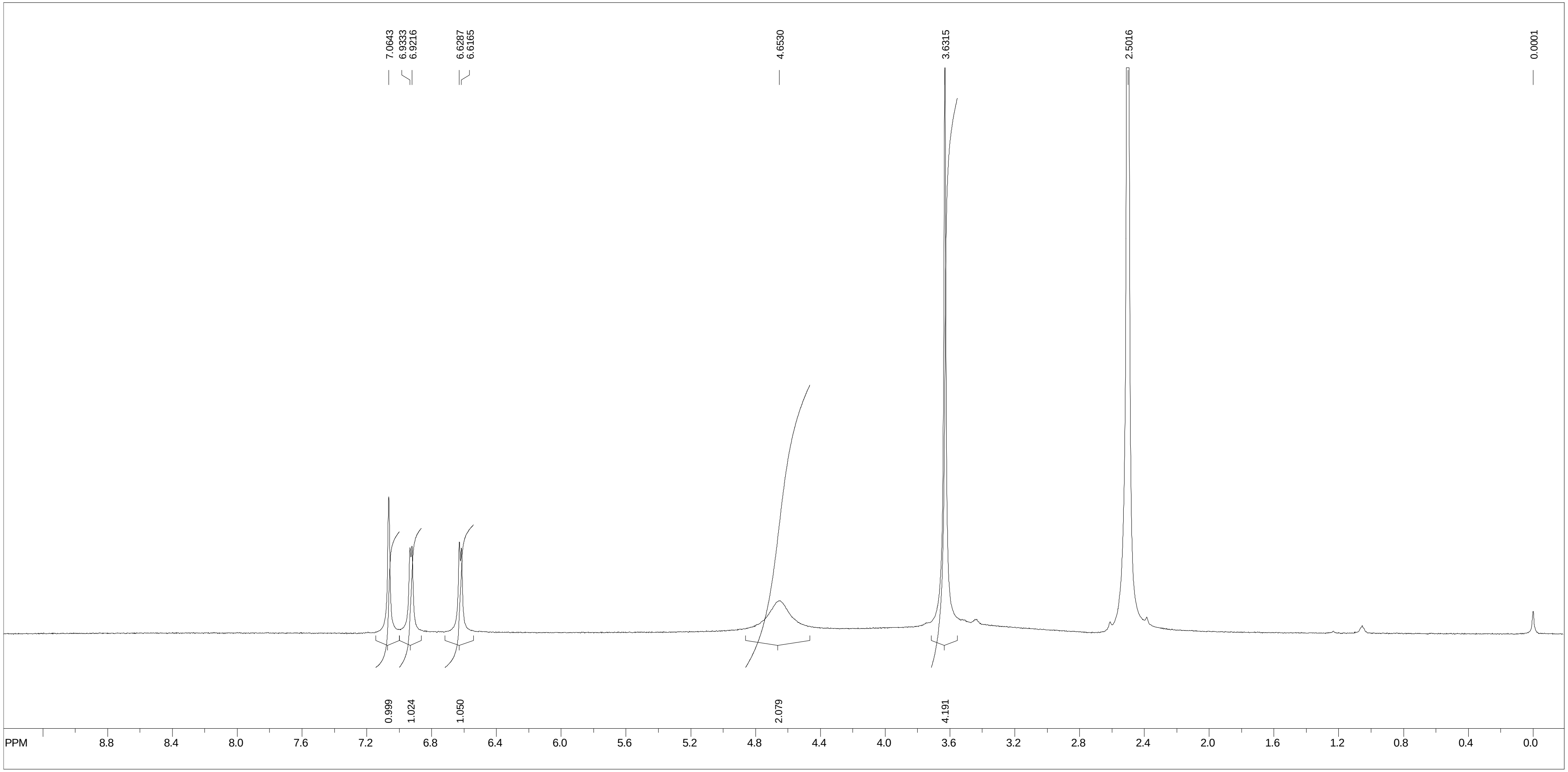

Figure S25. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-amino-4-(4,5-dihydro-1*H*-imidazol-3-ium-2-yl)phenolate hemihydrochloride dihydrate **8b**

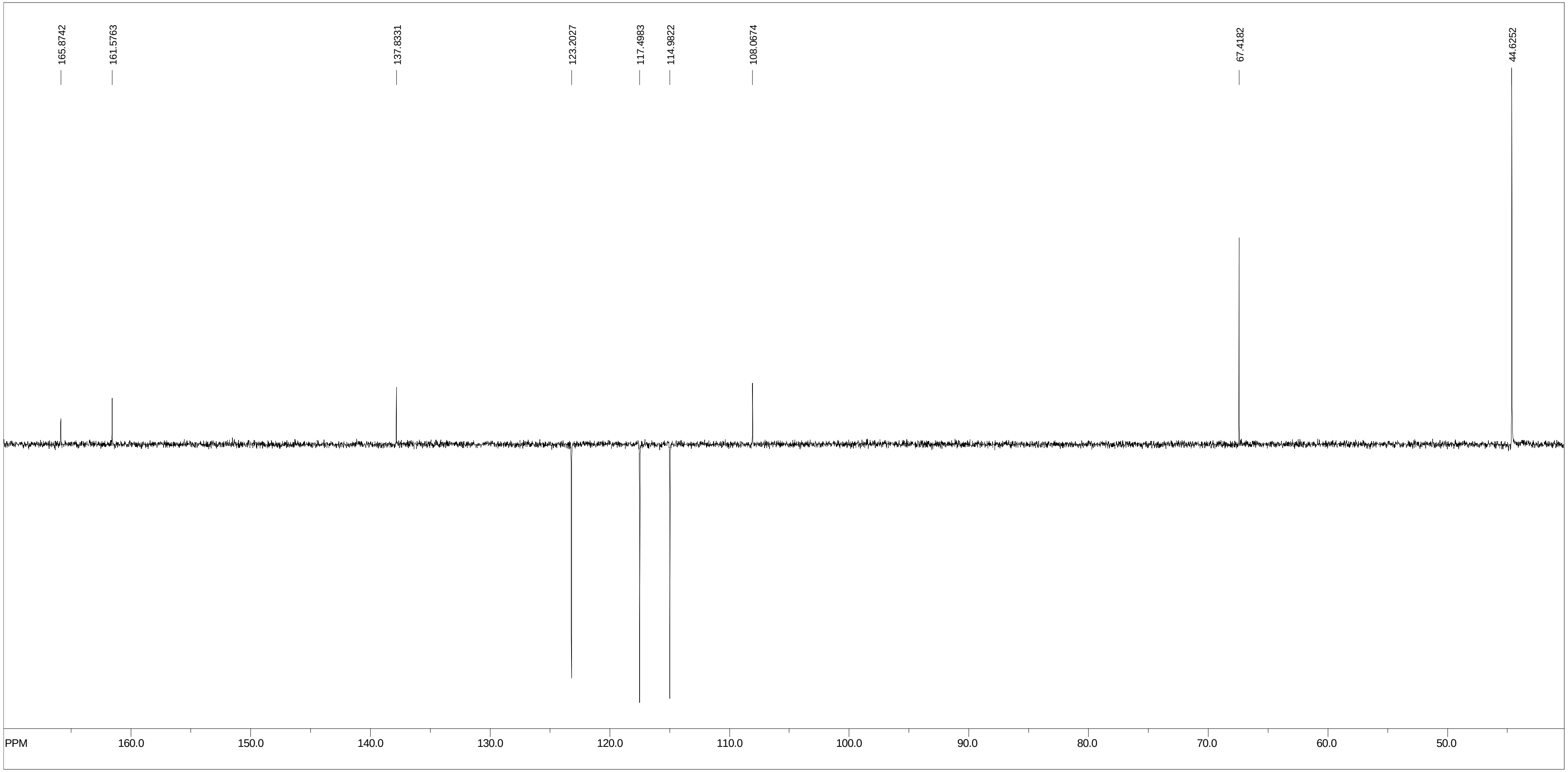

Figure S26. ^{13}C NMR (150 MHz, D_2O) of 2-amino-4-(4,5-dihydro-1*H*-imidazol-3-ium-2-yl)phenolate hemihydrochloride dihydrate **8b**

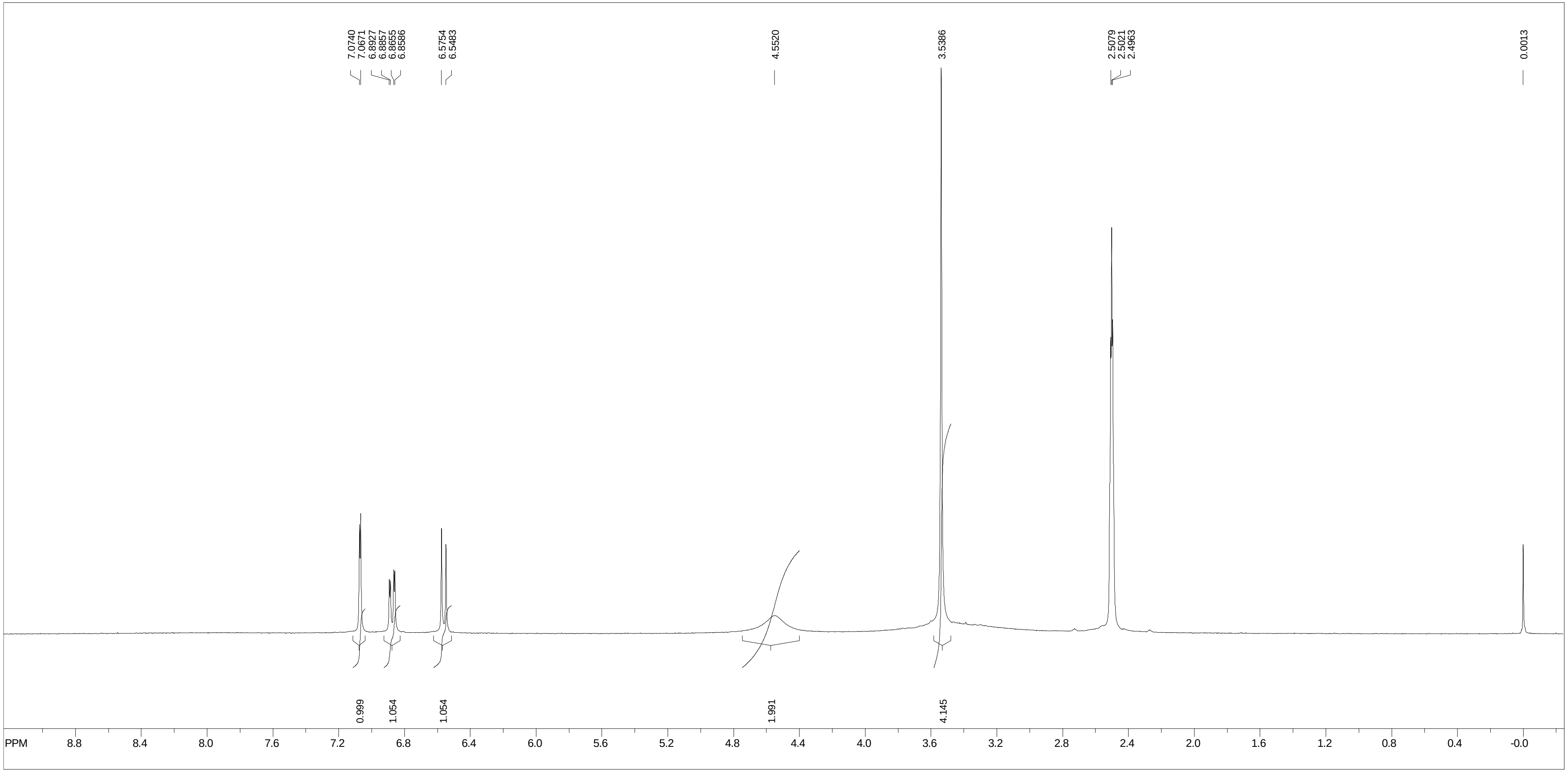

Figure S27. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate hydrate **8b'**

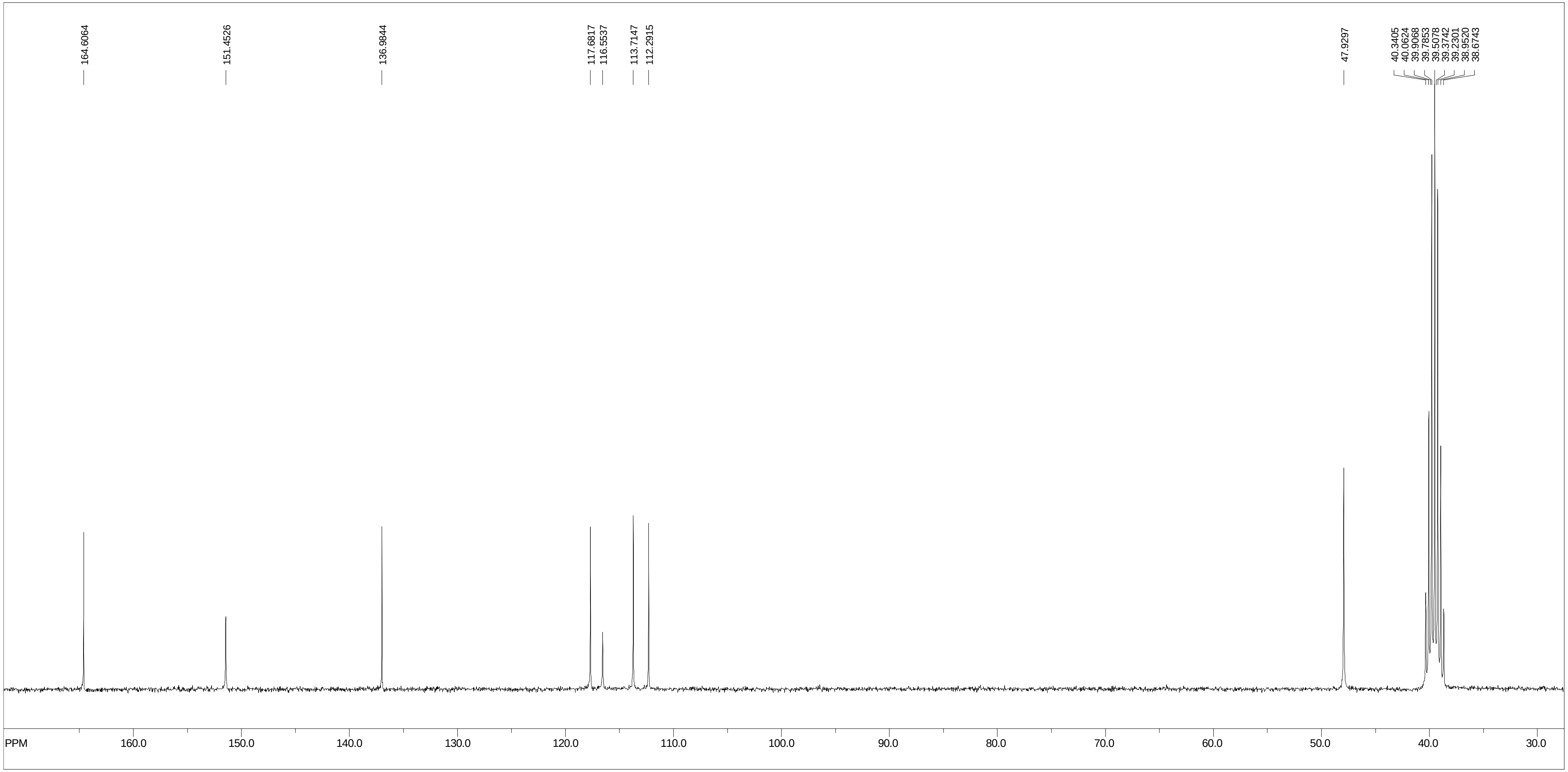

Figure S28. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-4-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate hydrate **8b'**

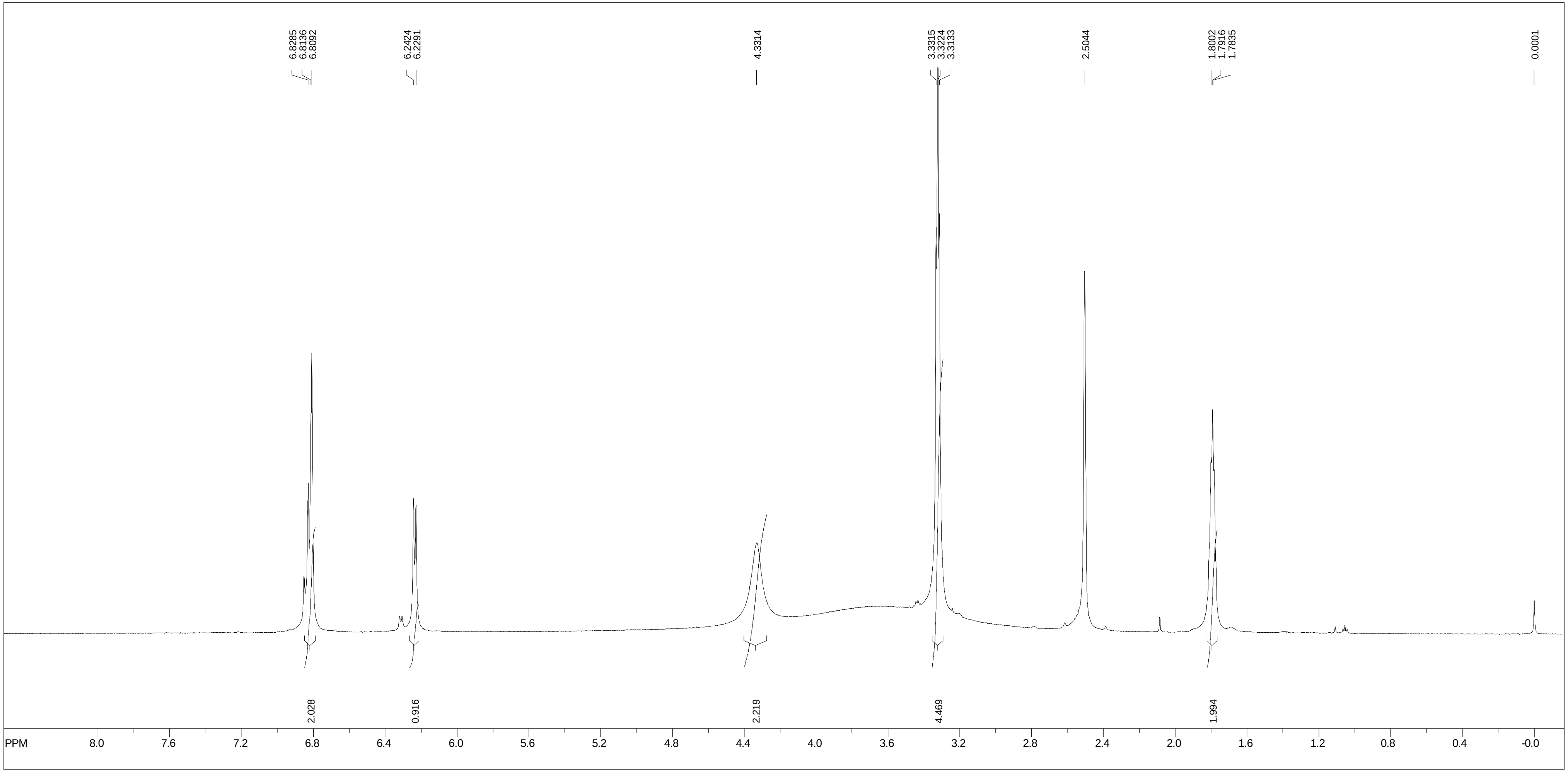

Figure S29. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-amino-4-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate **8c'**

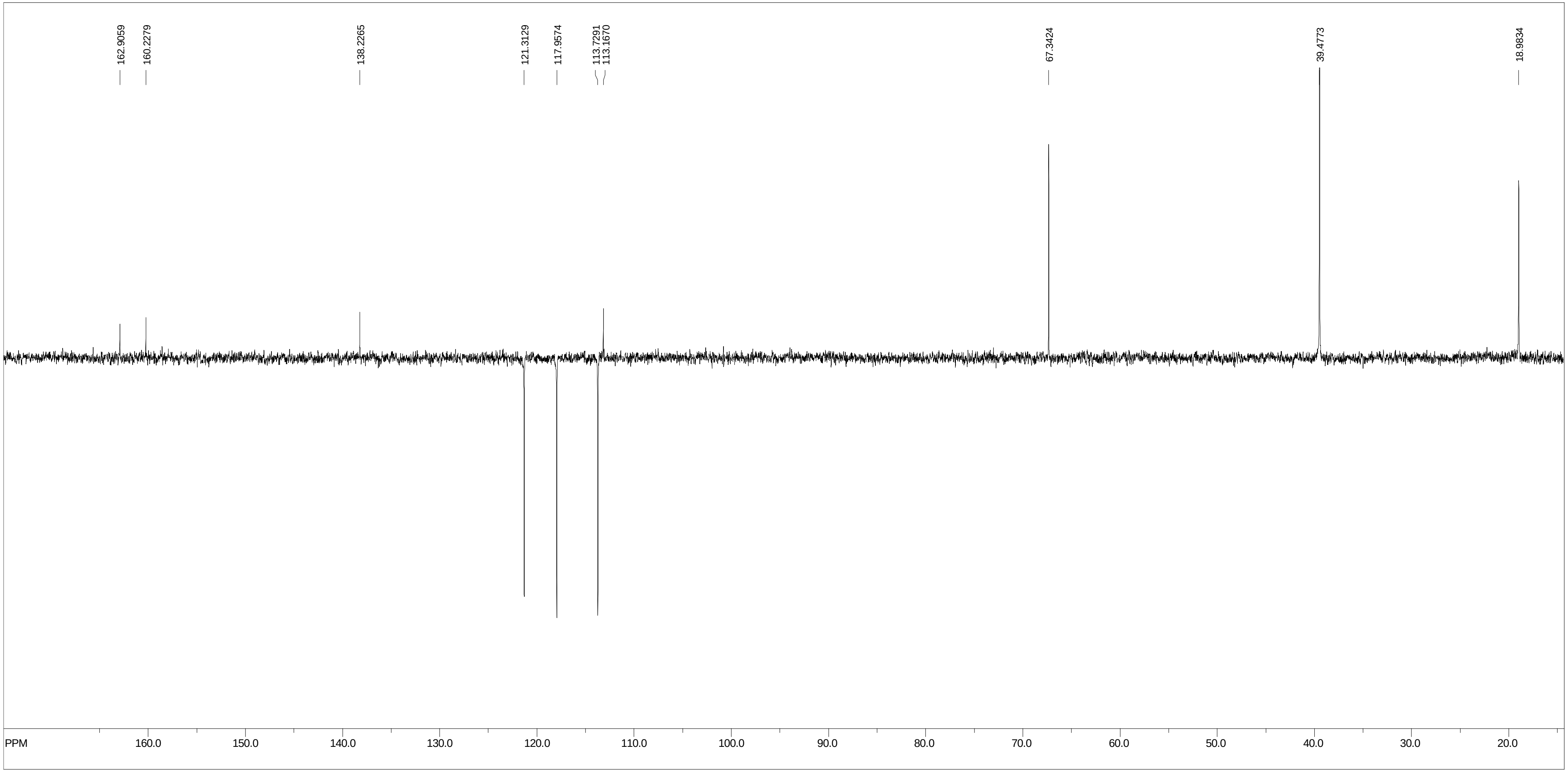

Figure S30. ^{13}C NMR spectrum (75 MHz, D_2O) of 2-amino-4-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate **8c'**

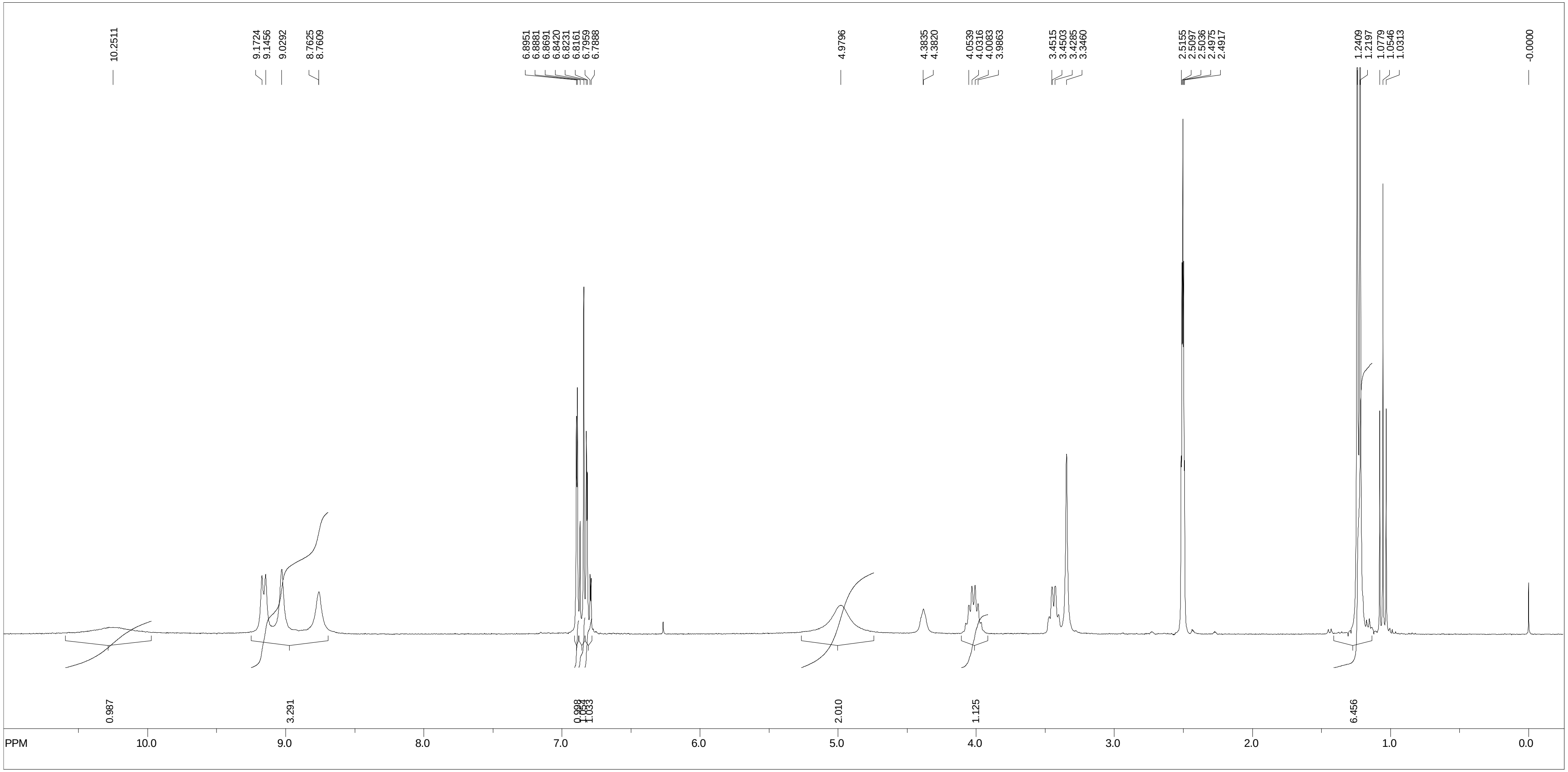

Figure S31. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-(*N*-isopropylamidino)phenol hydrochloride ethanol solvate **8d**

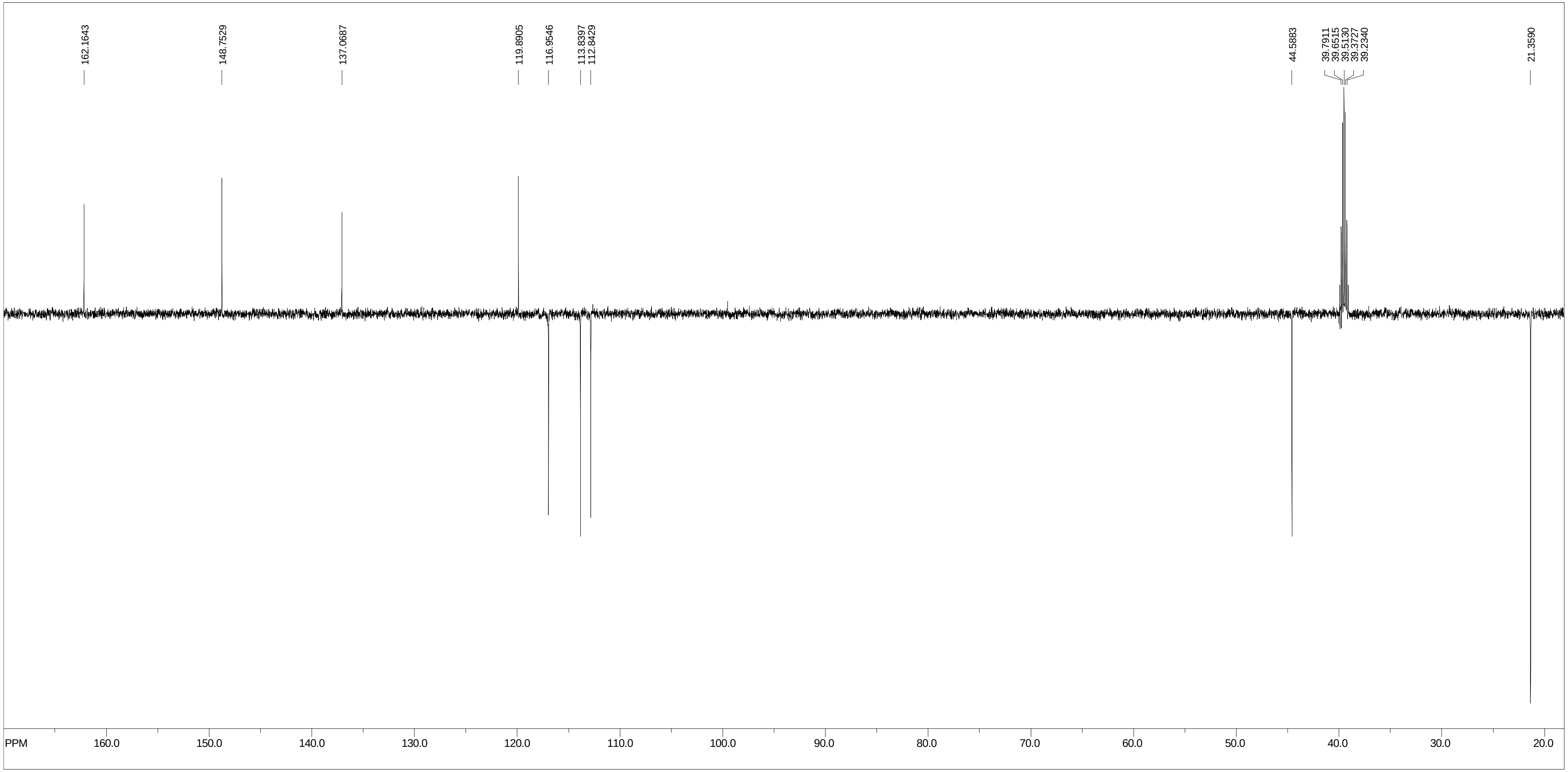

Figure S32. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2-amino-4-(*N*-isopropylamidino)phenol hydrochloride **8d**

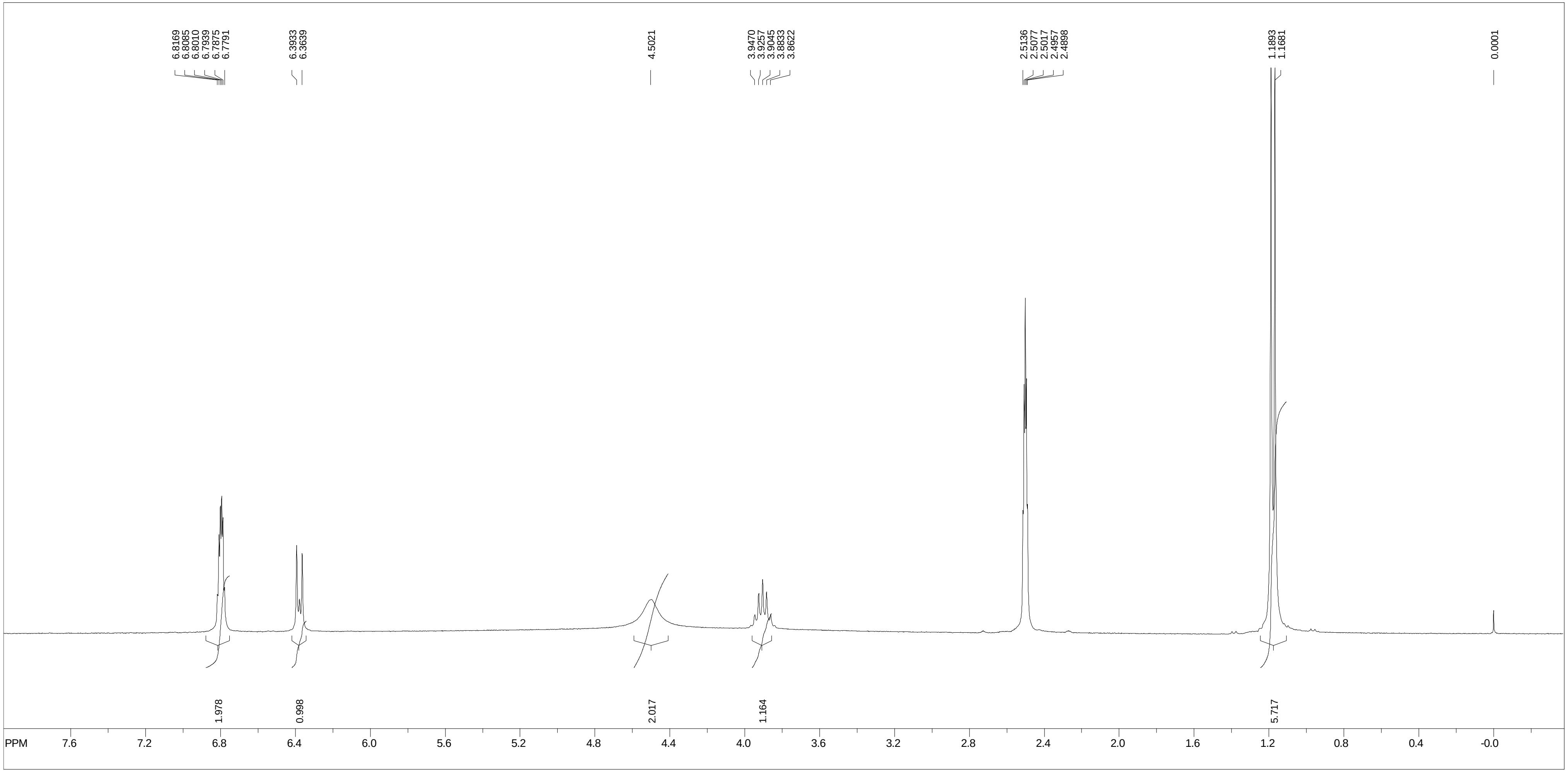

Figure S33. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-(*N*-isopropylamidinium)phenolate **8d'**

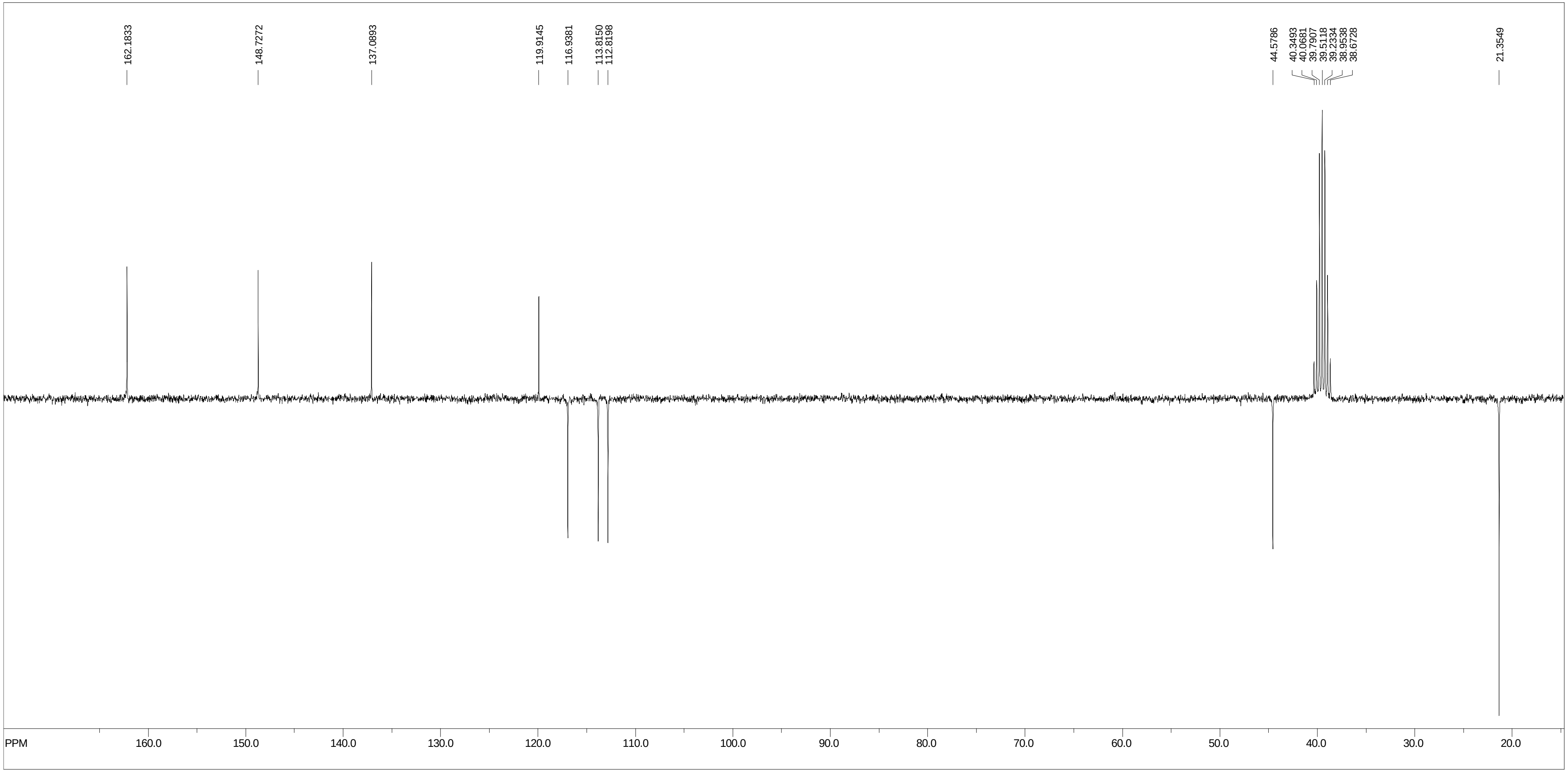

Figure S34. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-4-(*N*-isopropylamidinium)phenolate **8d'**

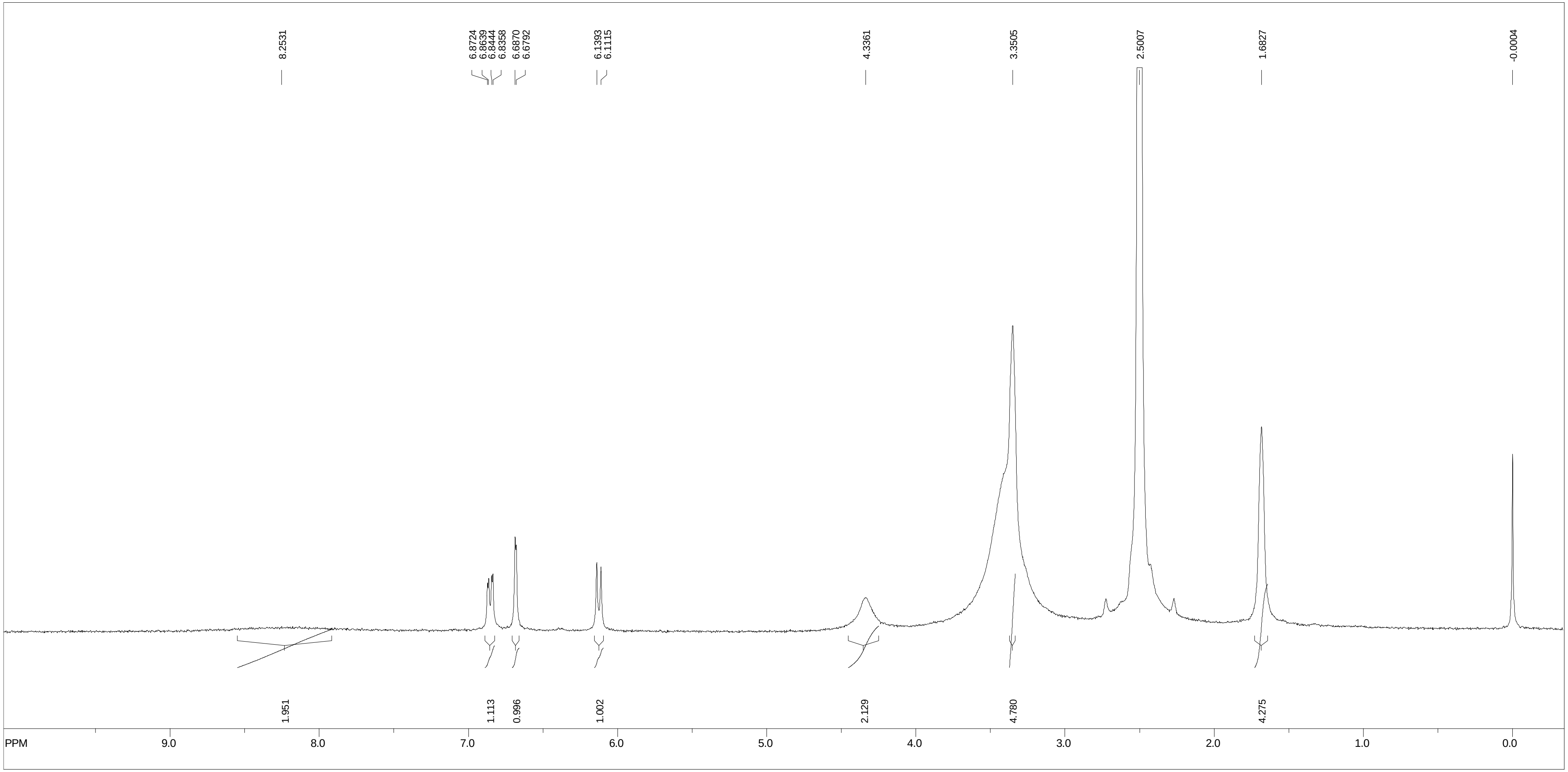

Figure S35. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-(4,5,6,7-tetrahydro-1*H*-1,3-diazepinium-2-yl)phenolate (**8e'**)

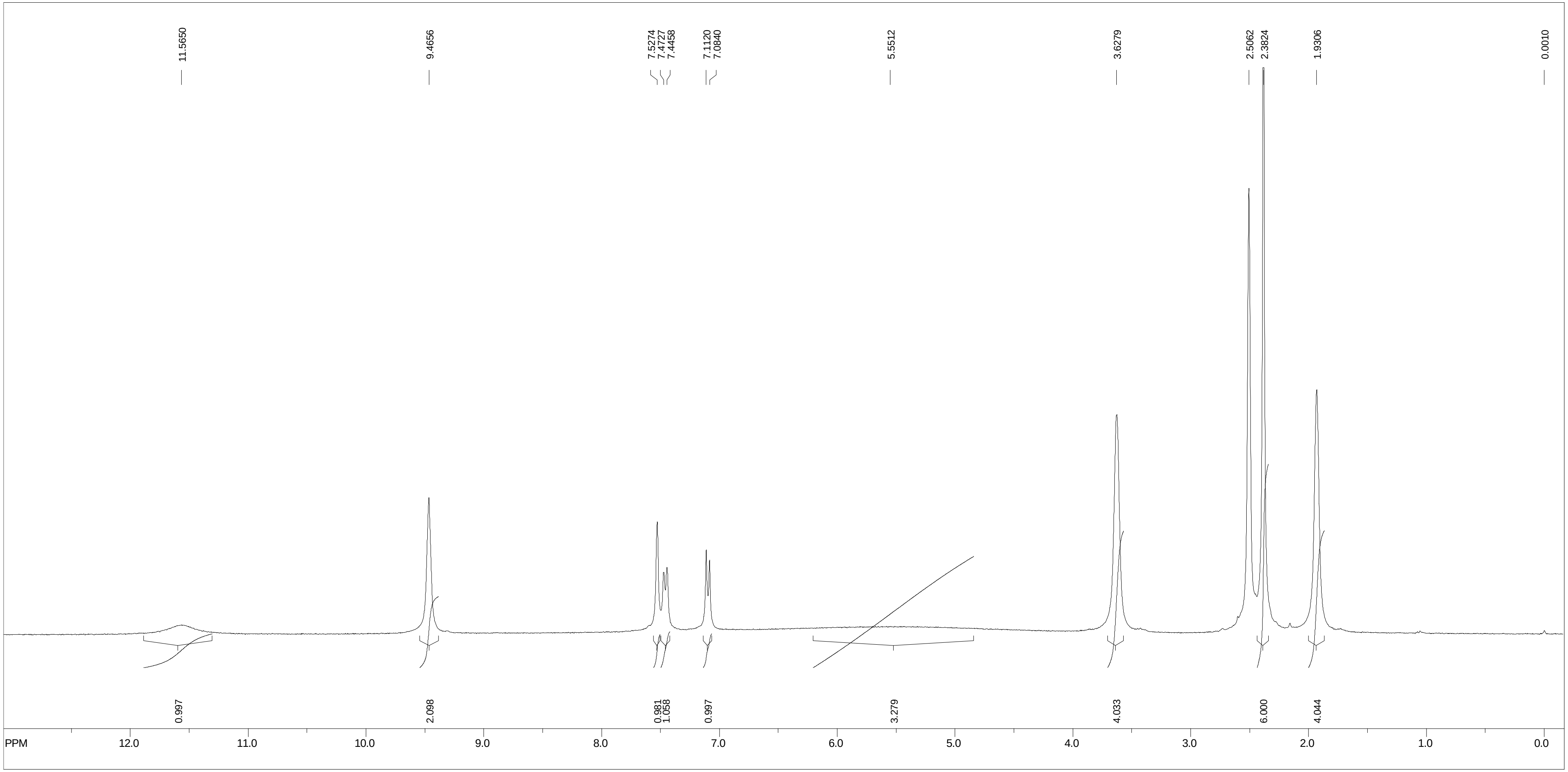

Figure S36. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-4-(4,5,6,7-tetrahydro-1*H*-1,3-diazepinium-2-yl)phenolate dimethanesulphonate dihydrate (**8e**)

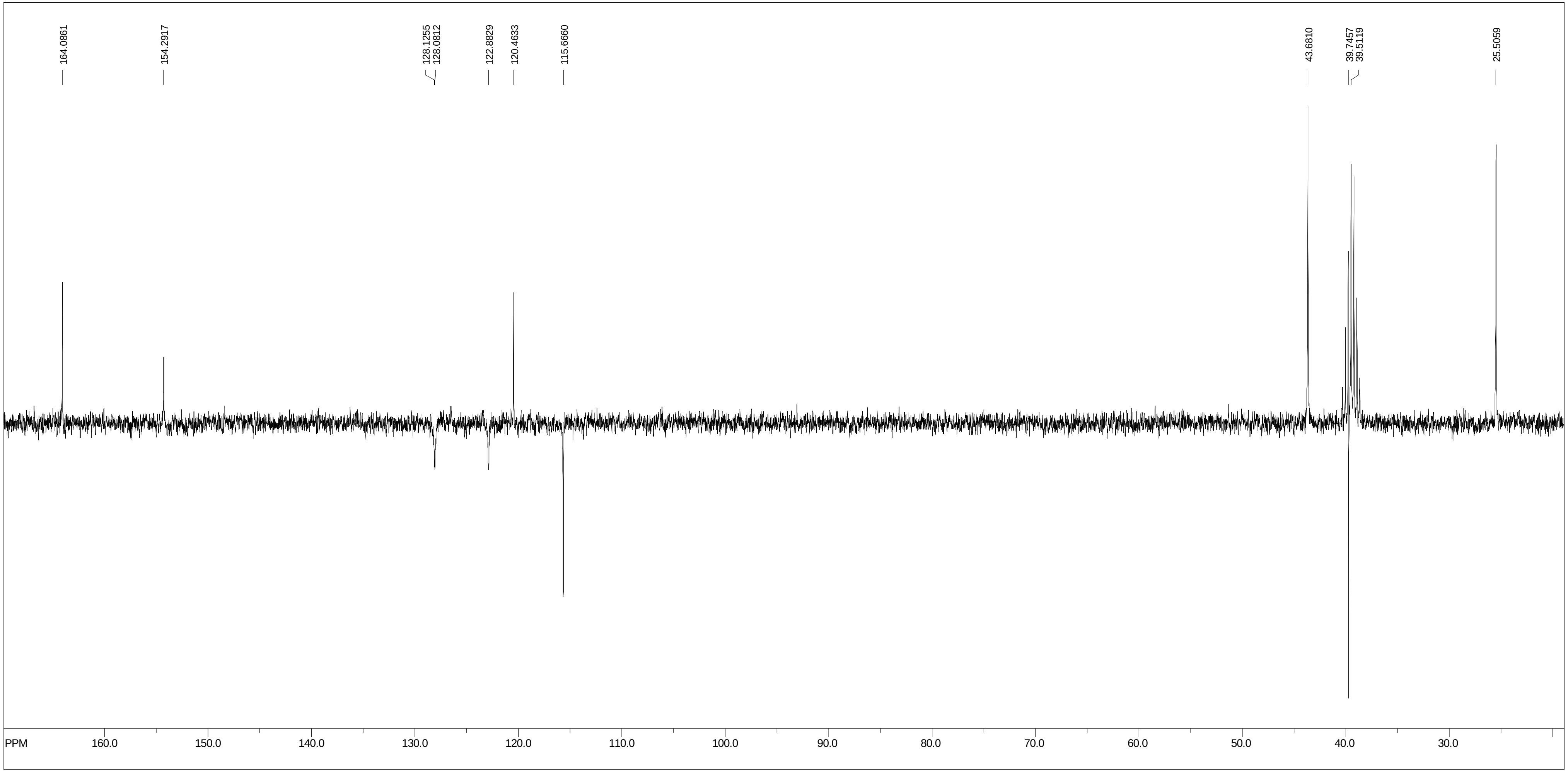

Figure S37. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-4-(4,5,6,7-tetrahydro-1*H*-1,3-diazepinium-2-yl)phenolate dimethanesulphonate hydrate (**8e**)

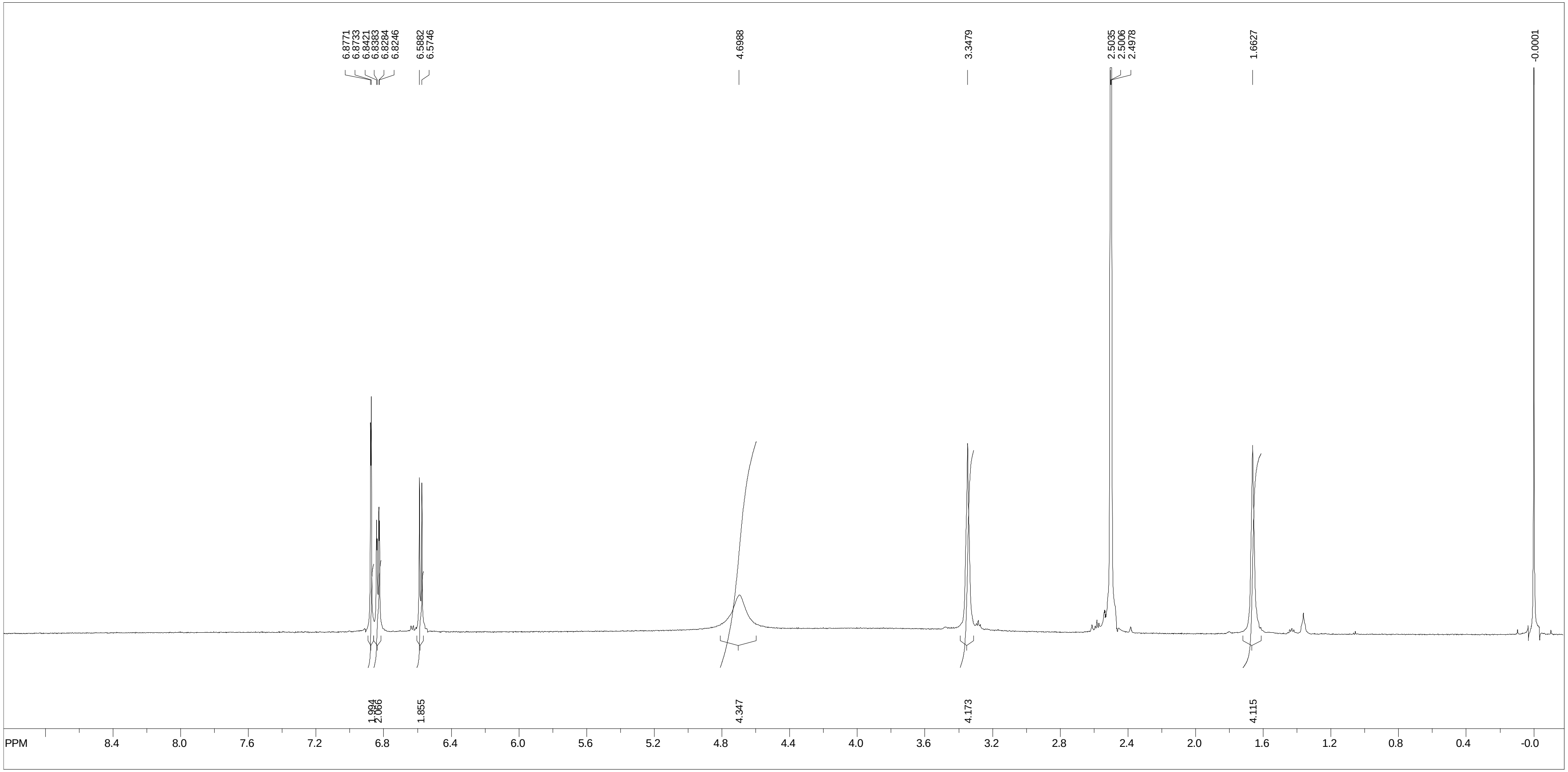

Figure S38. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2,2'-bis(3-amino-4-phenolate)butane-1,4-diimidamide (**8f'**)

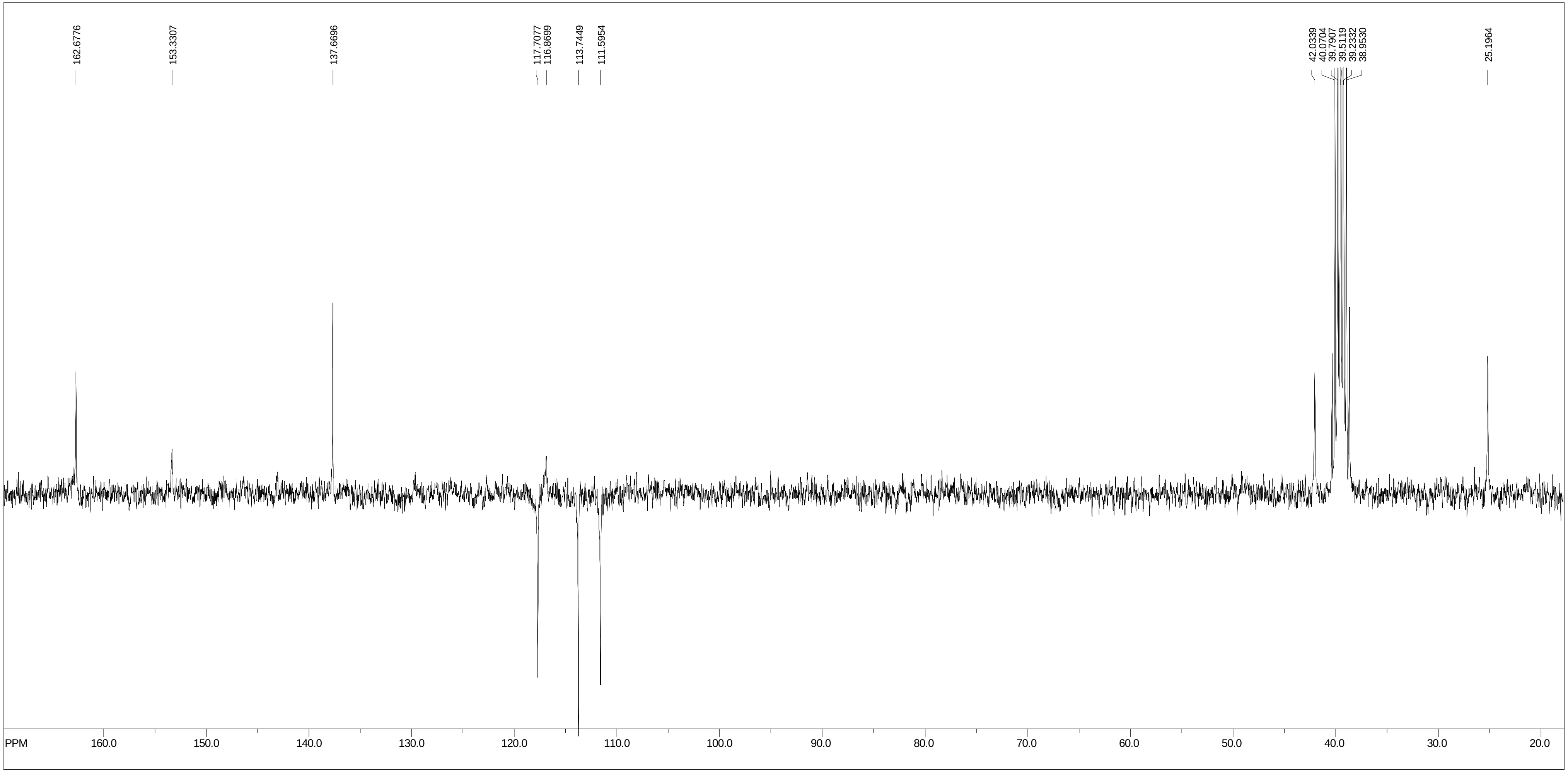

Figure S39. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2,2'-bis(3-amino-4-phenolate)butane-1,4-diimidamide (**8f'**)

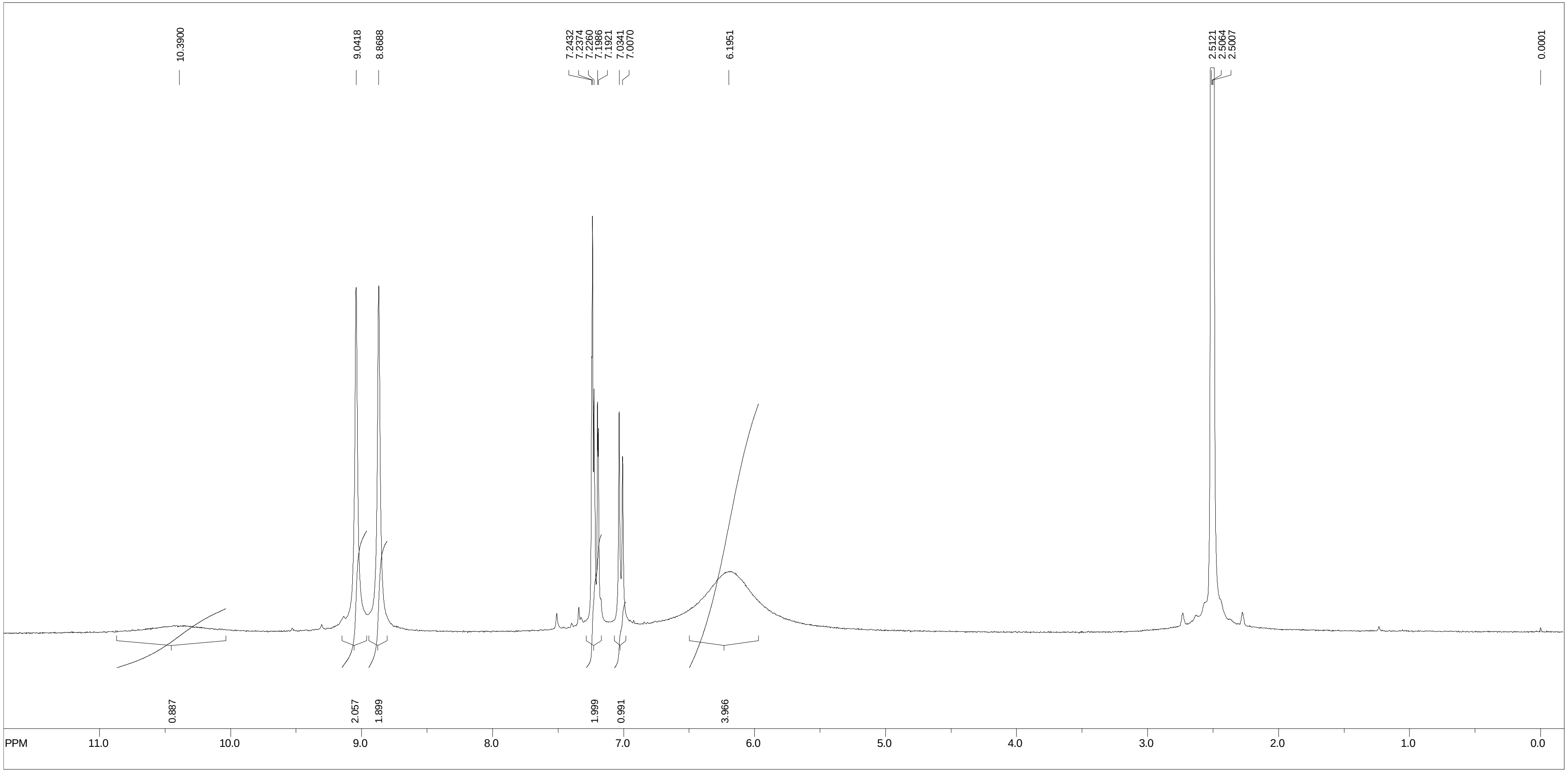

Figure S40. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-5-amidinophenol dihydrochloride **8g**

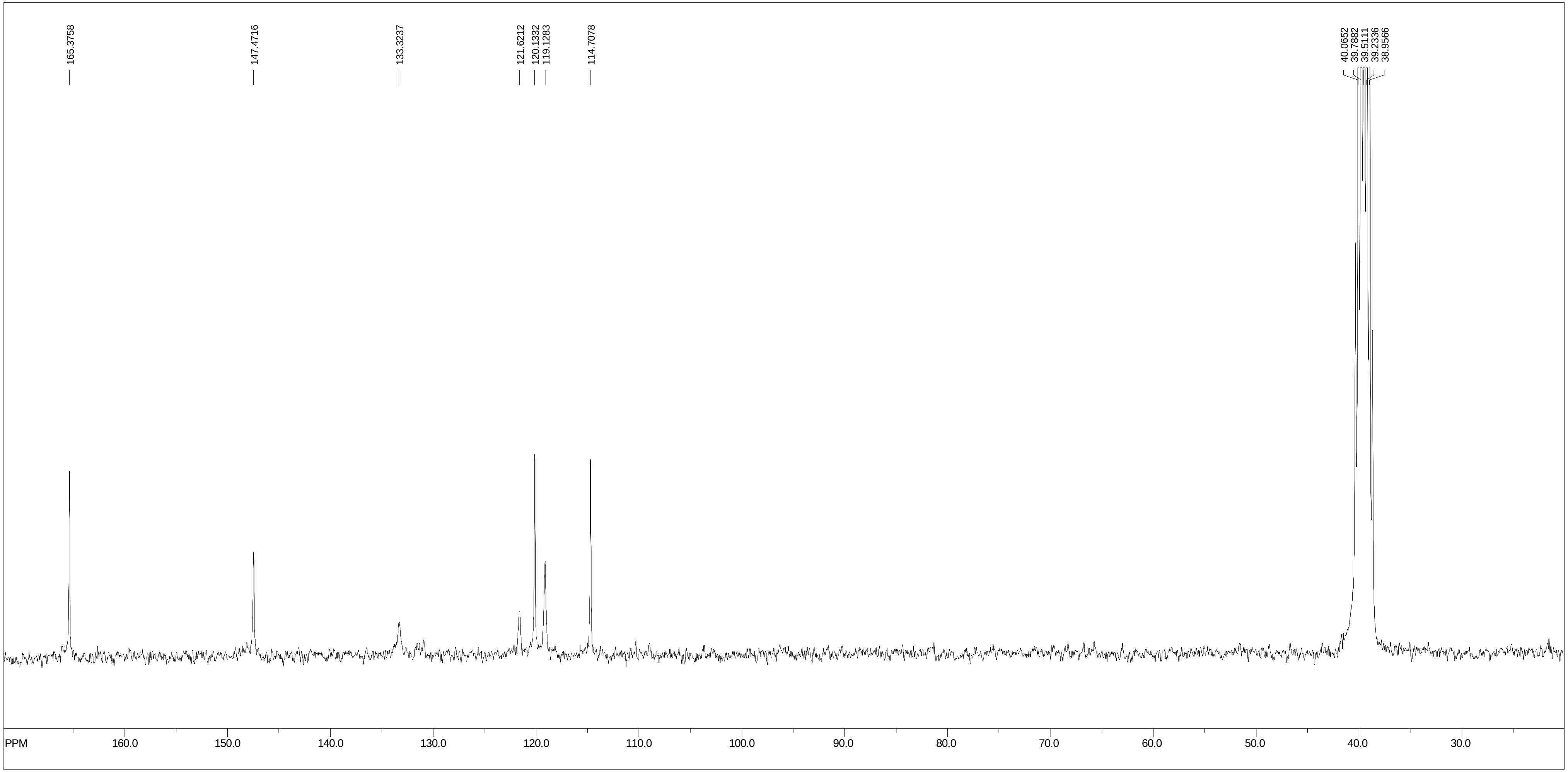

Figure S41. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-5-amidinophenol dihydrochloride **8g**

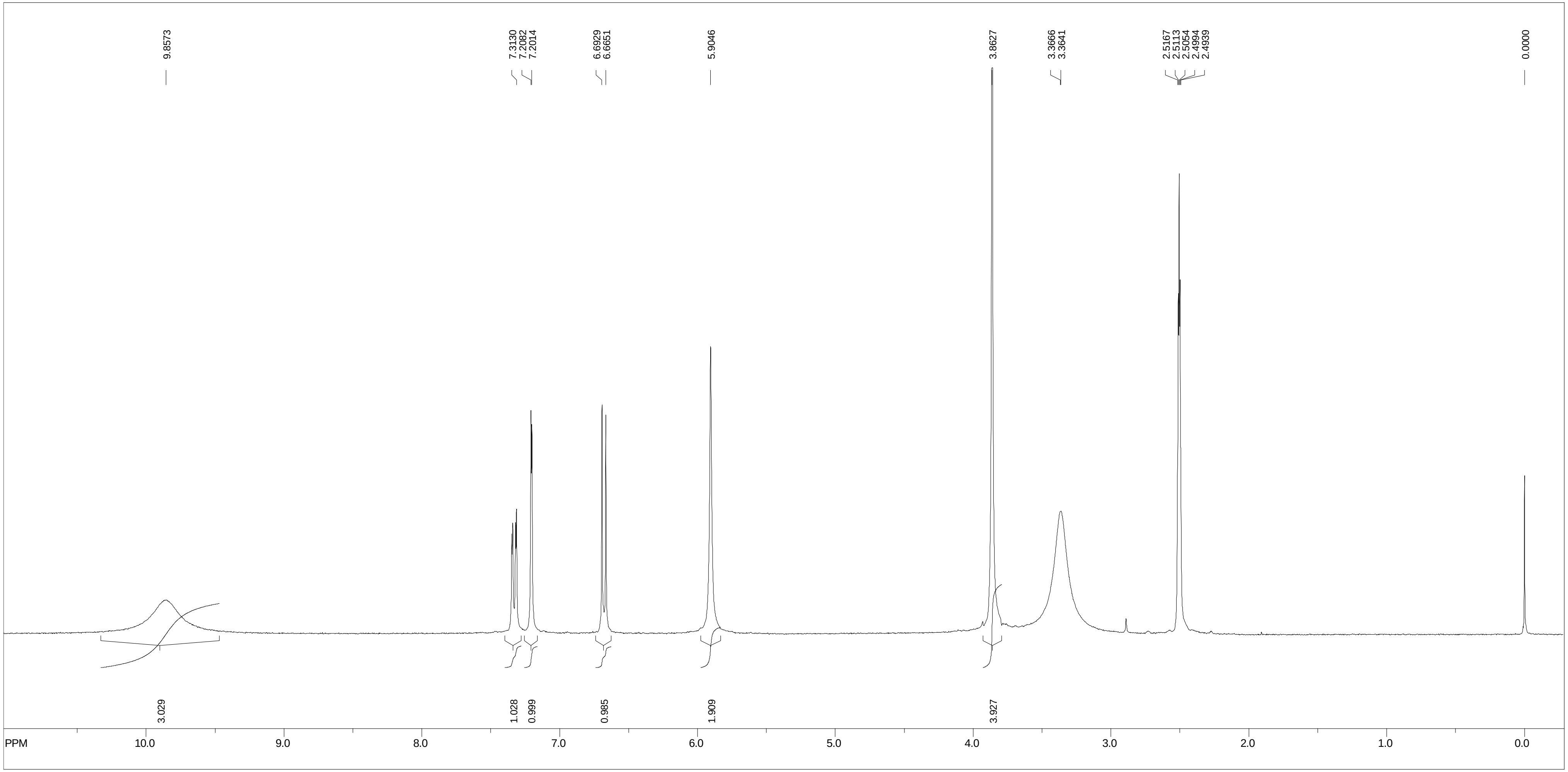

Figure S42. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-5-(4,5-dihydro-1*H*-imidazol-2-yl)phenol hydrochloride dihydrate **8h**

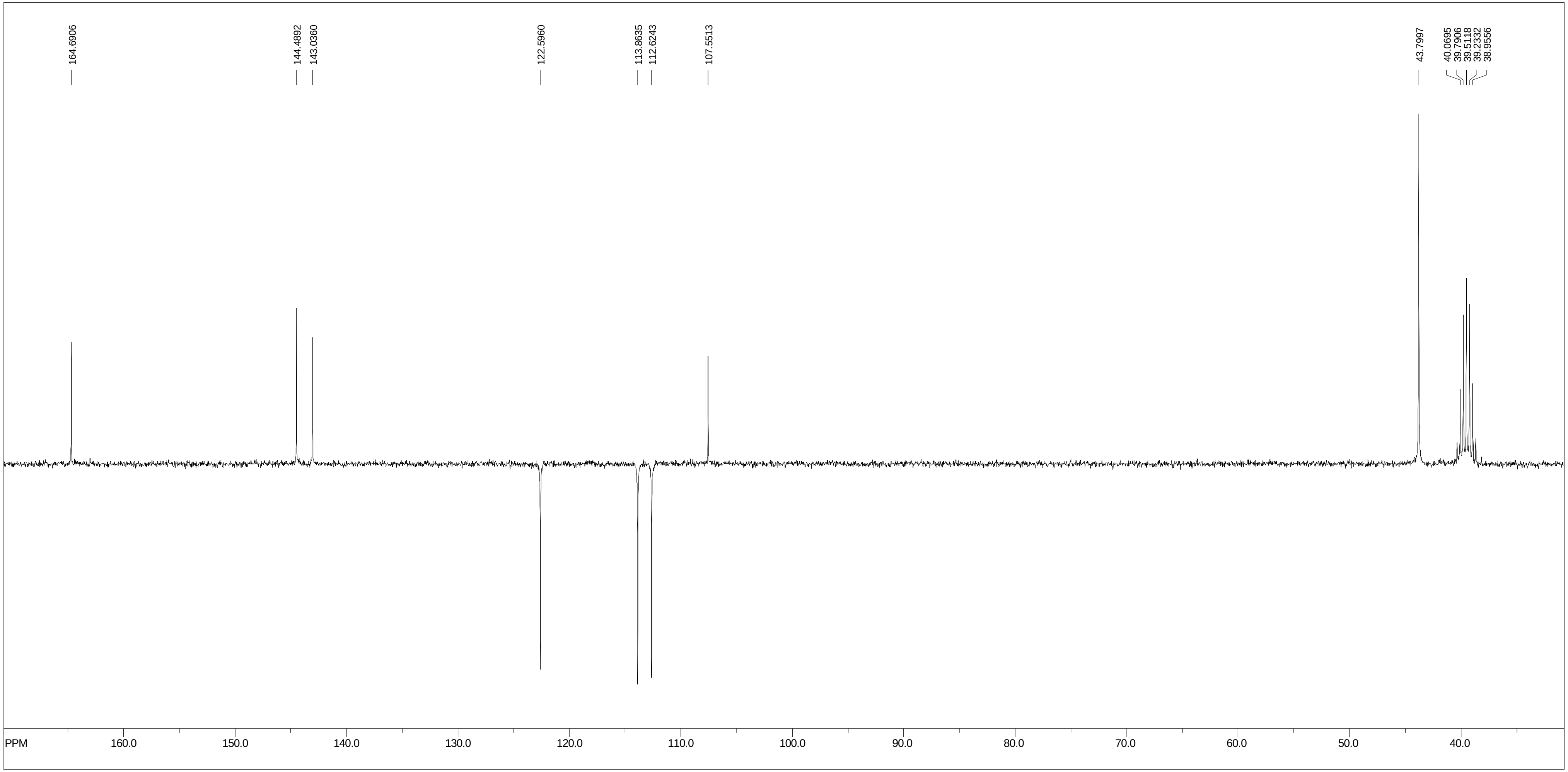

Figure S43. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 2-amino-5-(4,5-dihydro-1*H*-imidazol-2-yl)phenol hydrochloride dihydrate **8h**

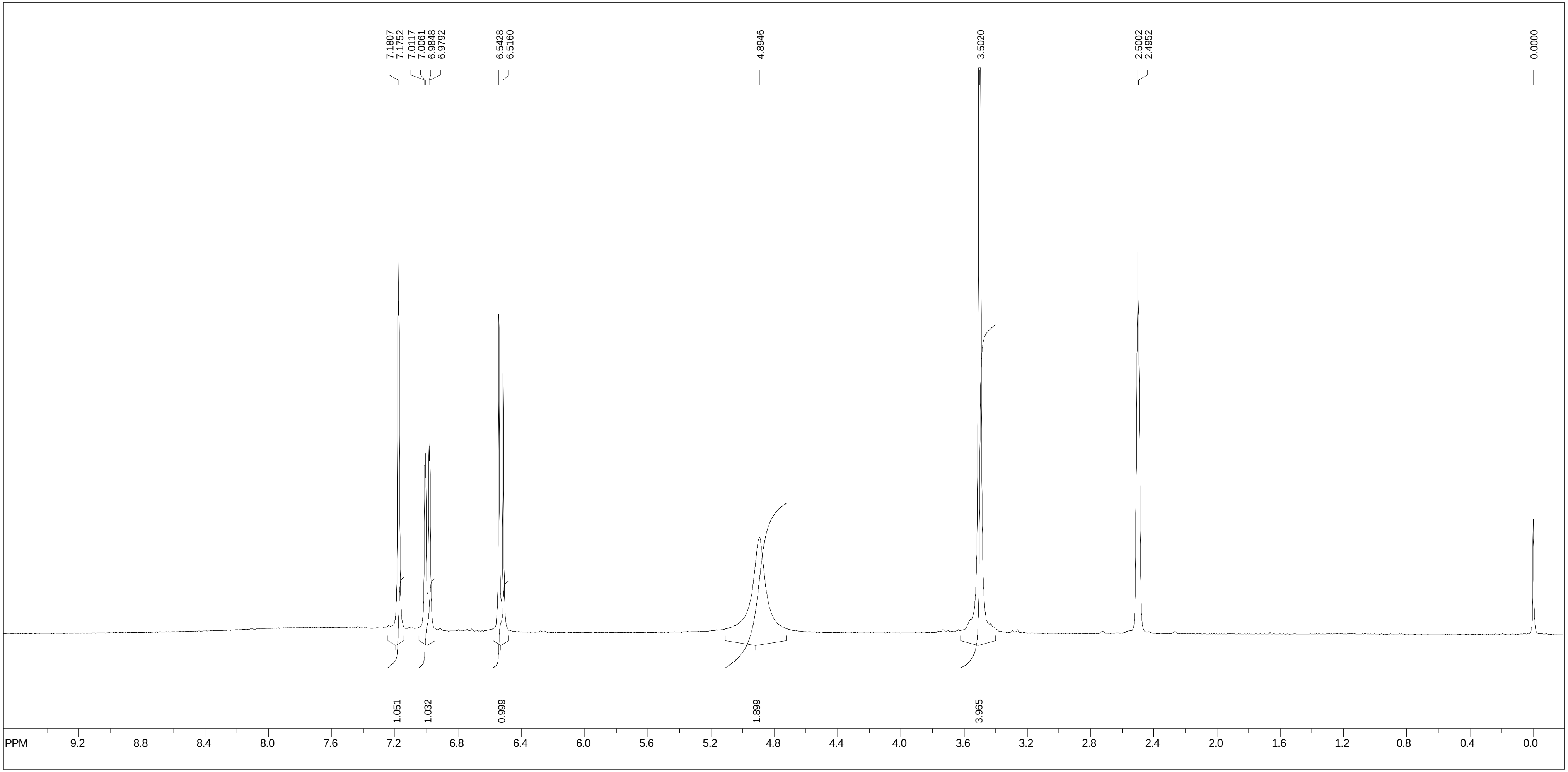

Figure S44. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 2-amino-5-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate **8h'**

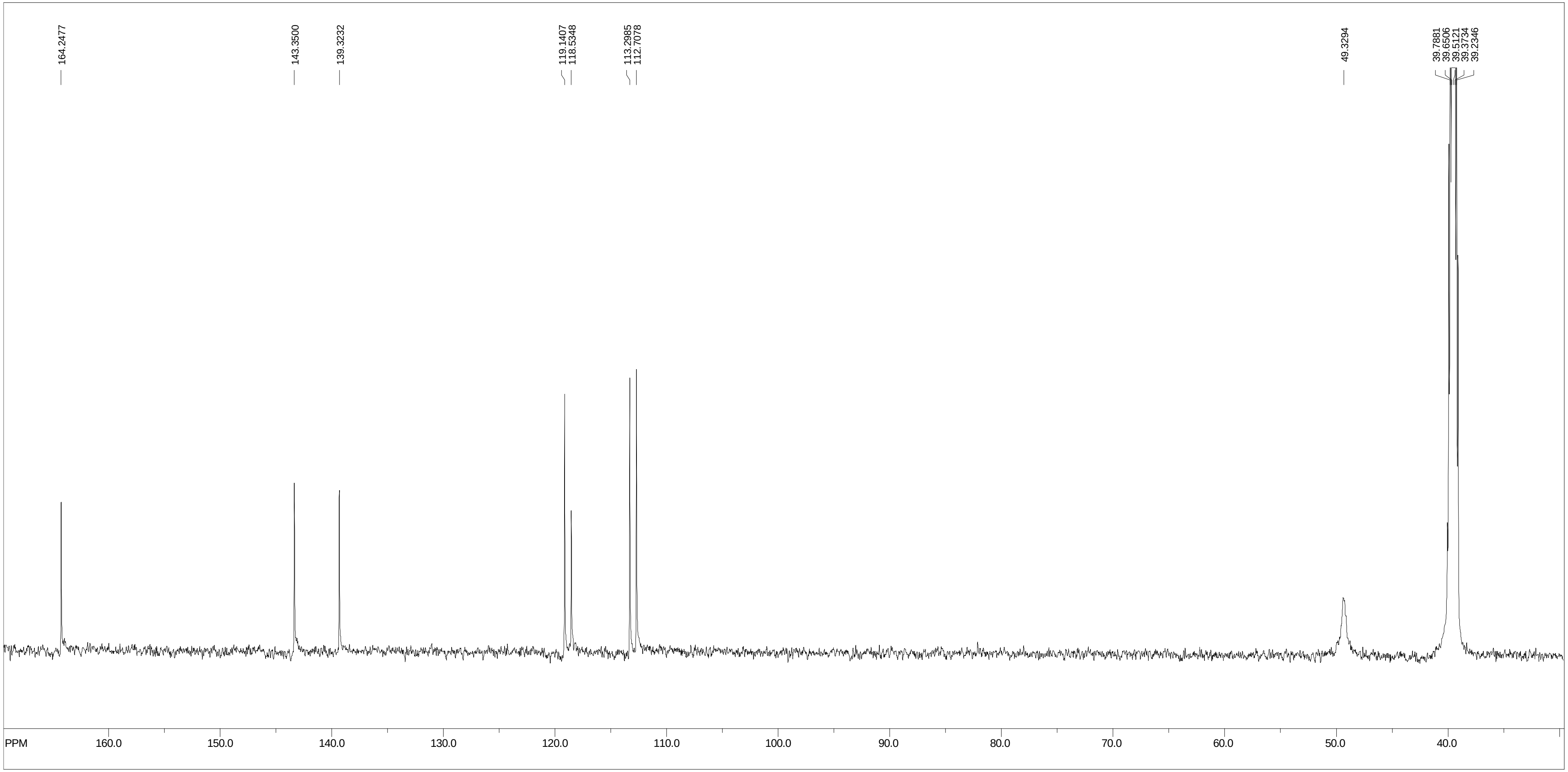

Figure S45. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2-amino-5-(4,5-dihydro-1*H*-imidazolium-2-yl)phenolate **8h'**

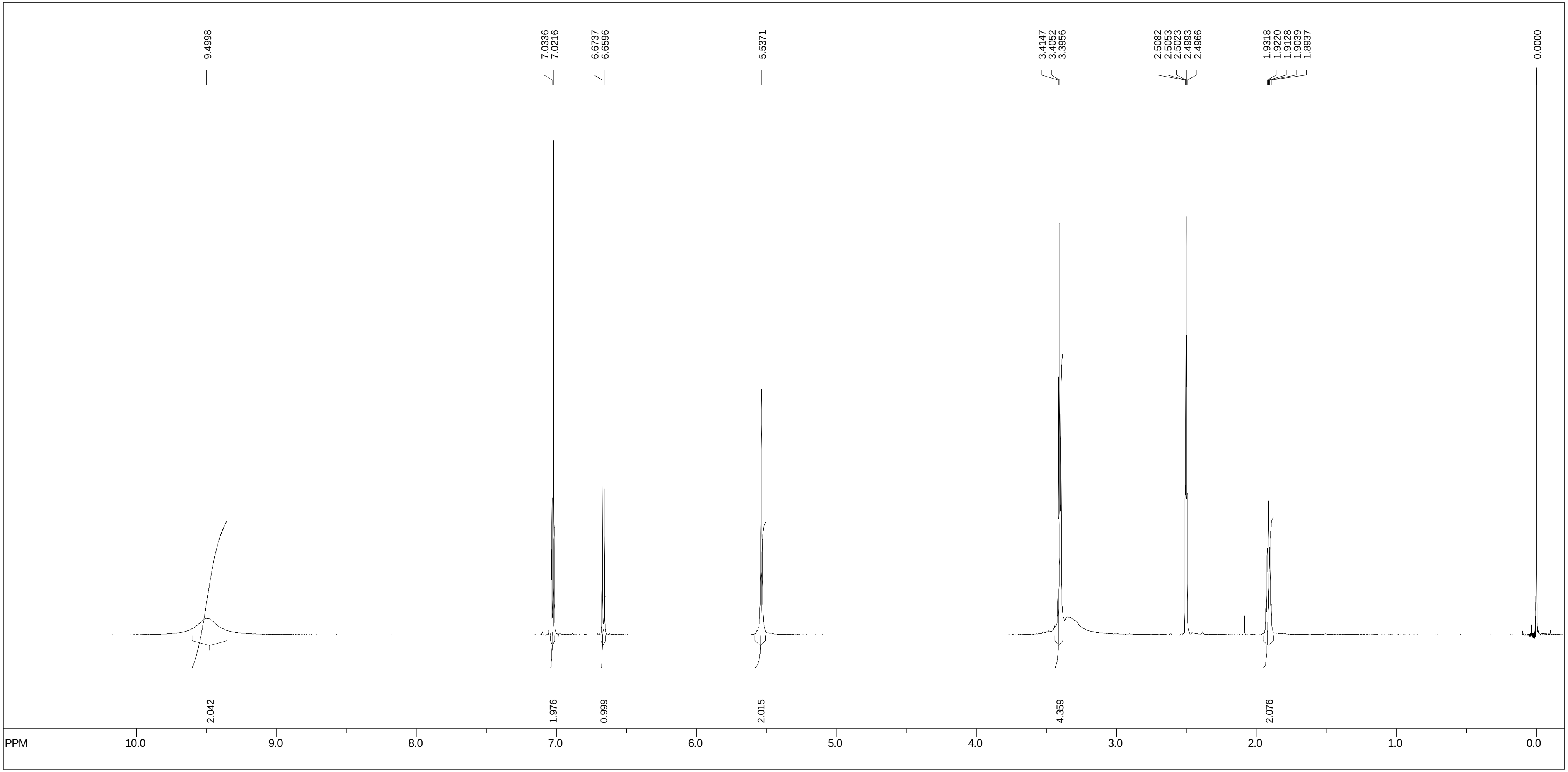

Figure S46. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-amino-5-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate **8i'**

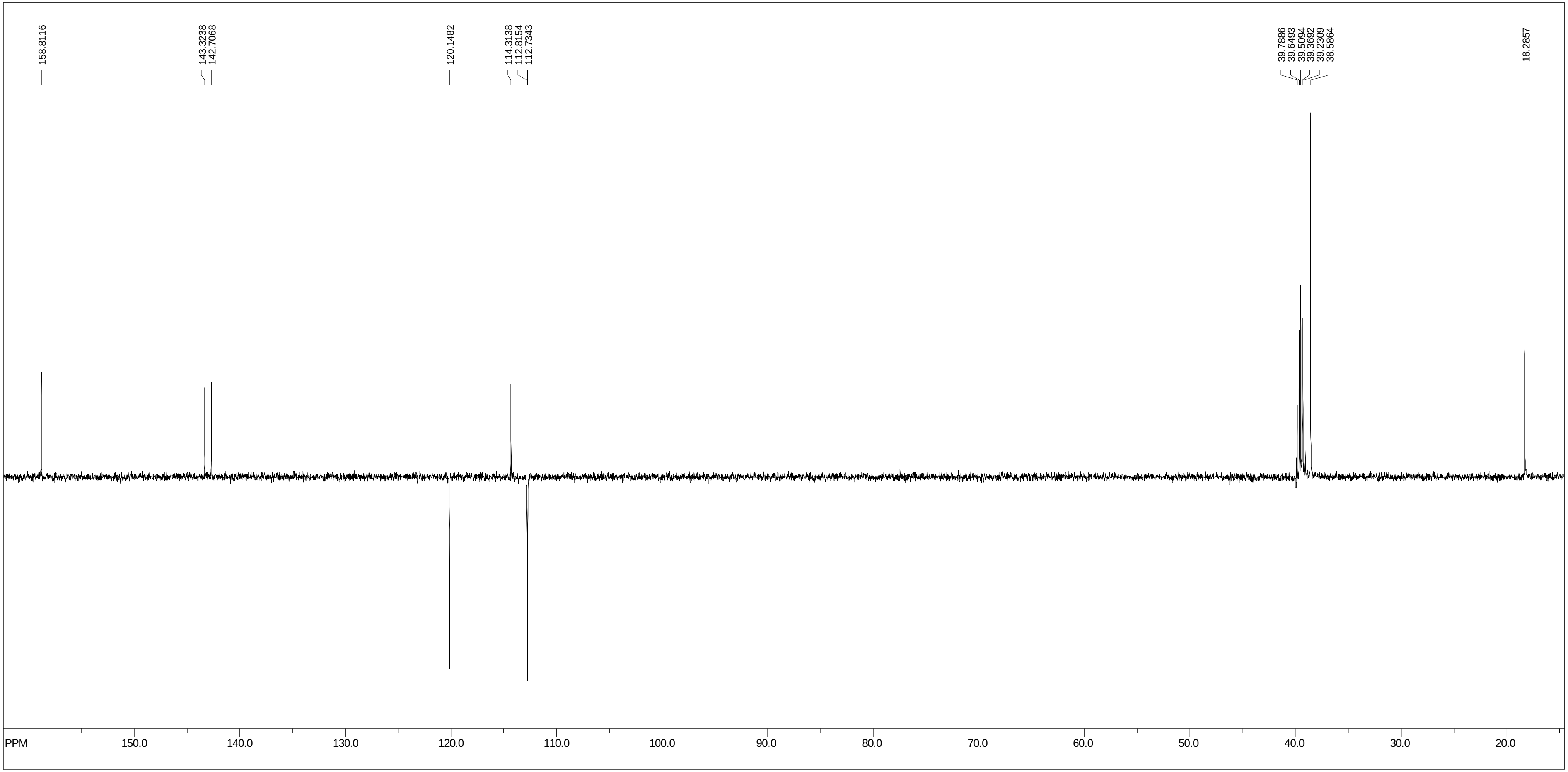

Figure S47. ^{13}C NMR spectrum of 2-amino-5-(3,4,5,6-tetrahydropyrimidinium-2-yl)phenolate **8i'**

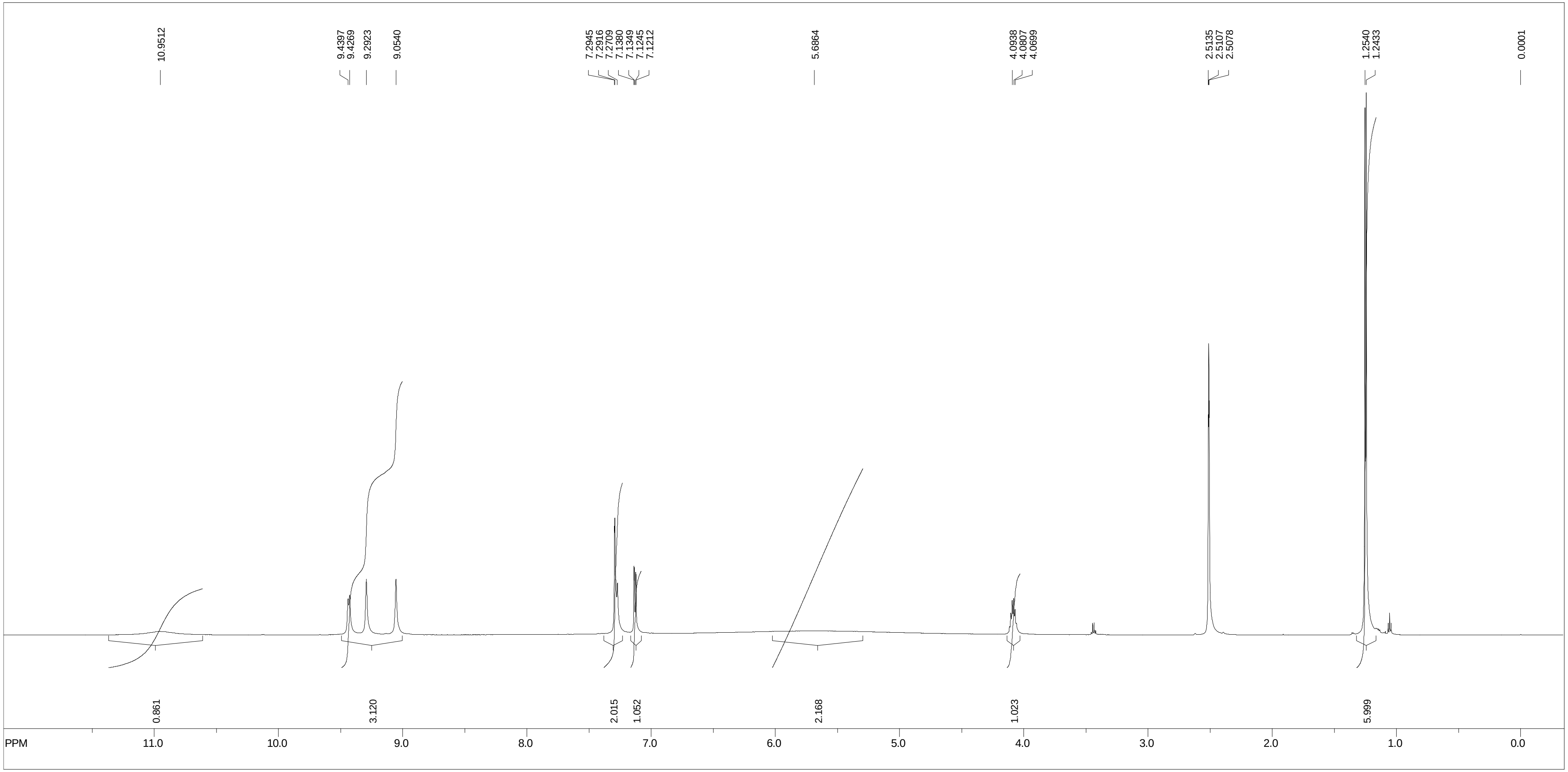

Figure S48. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 2-amino-5-(*N*-isopropylamidino)phenol hydrochloride **8j**

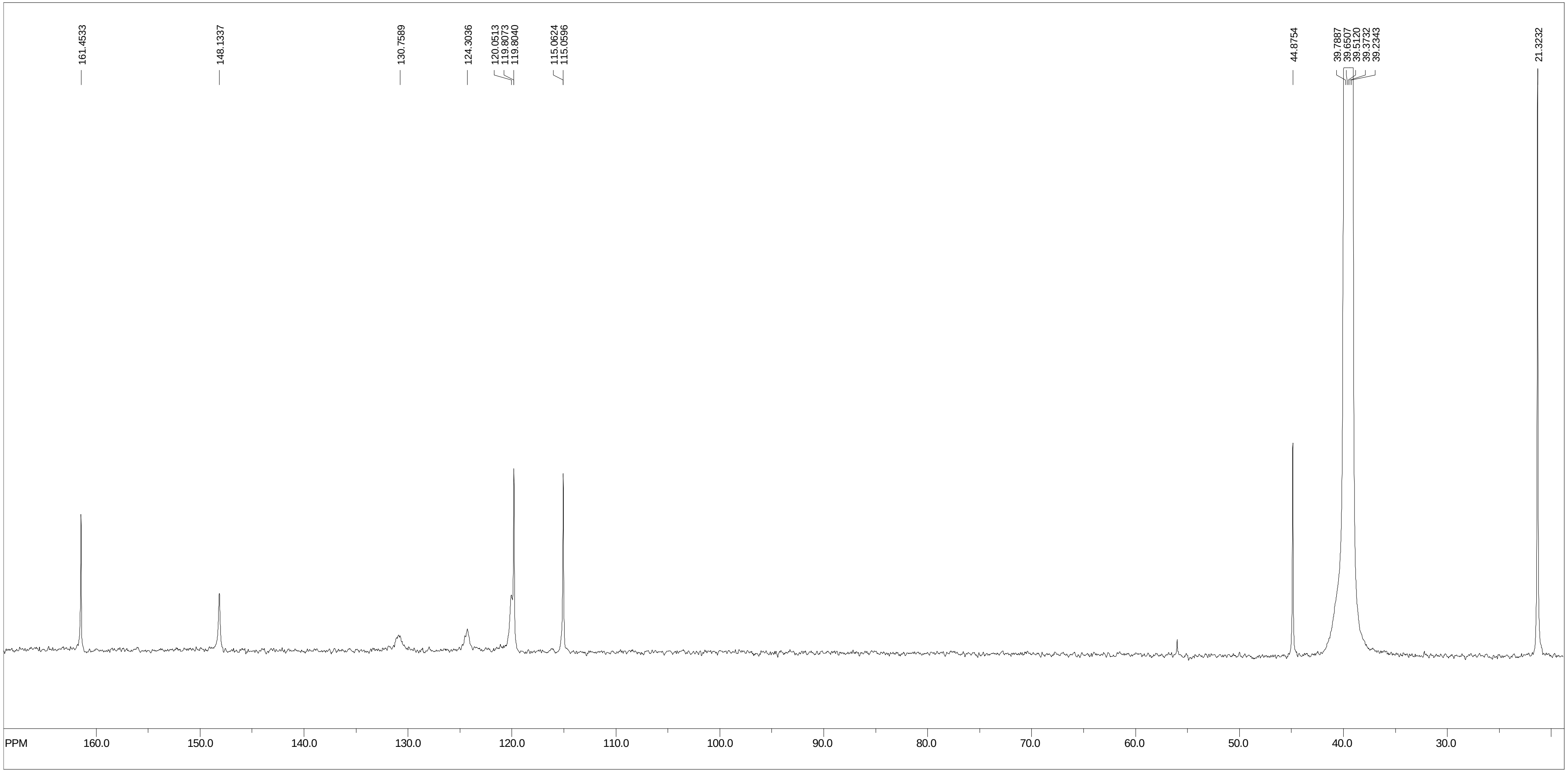

Figure S49. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 2-amino-5-(*N*-isopropylamidino)phenol hydrochloride **8j**

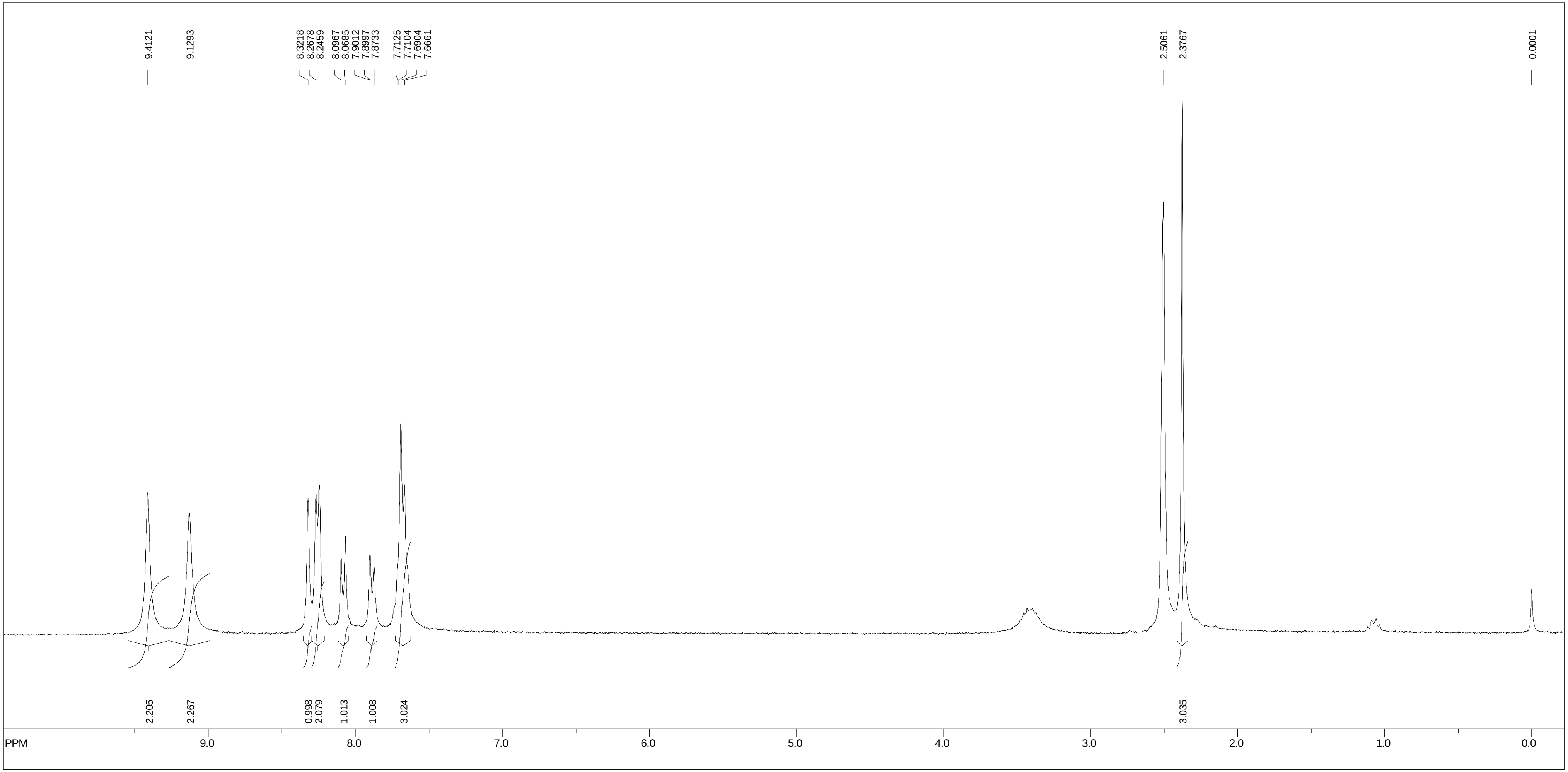

Figure S50. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 5-amidinium-2-phenylbenzoxazole methansulfonate (**10a**)

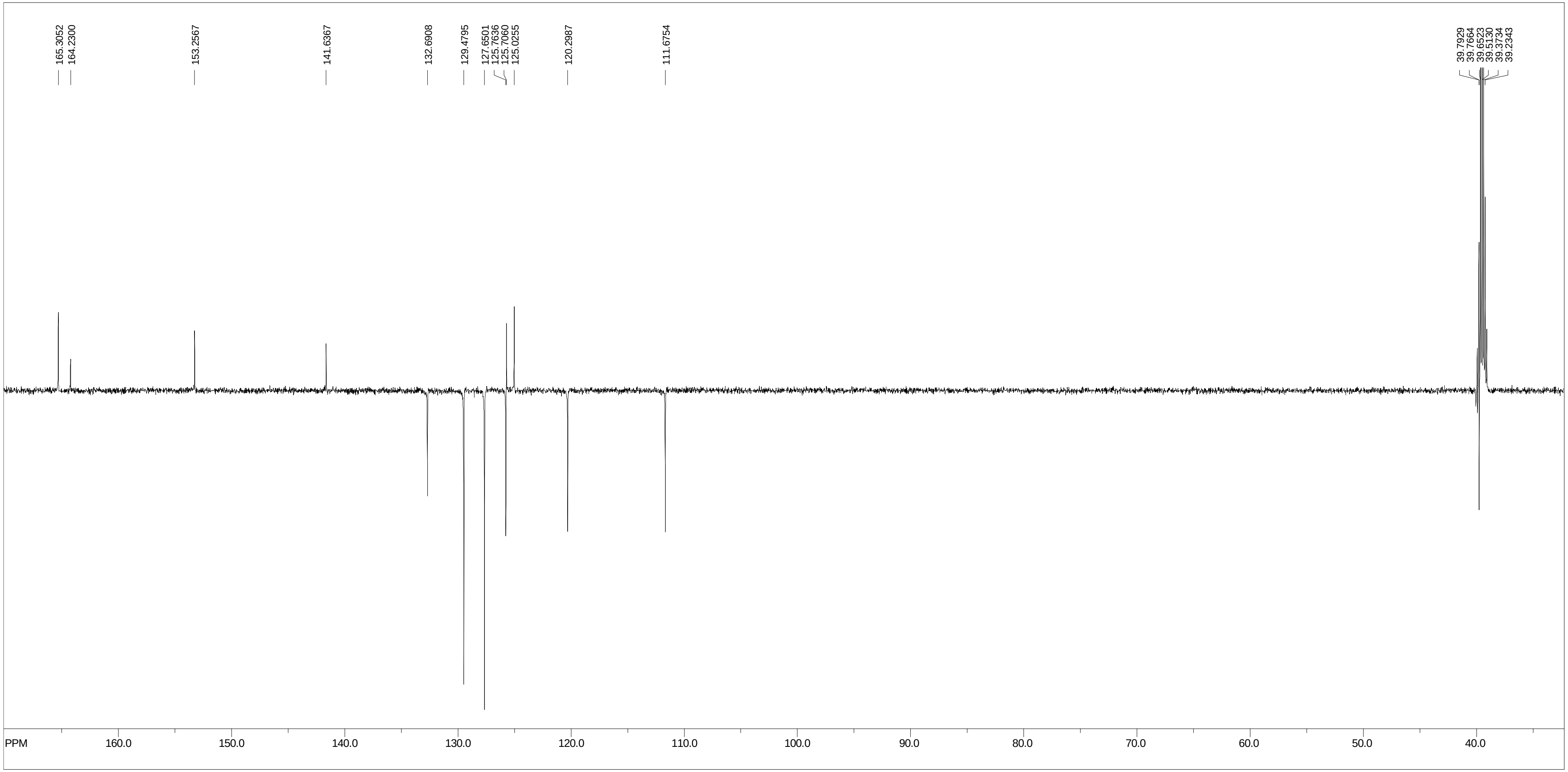

Figure S51. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 5-amidinium-2-phenylbenzoxazole methansulfonate (**10a**)

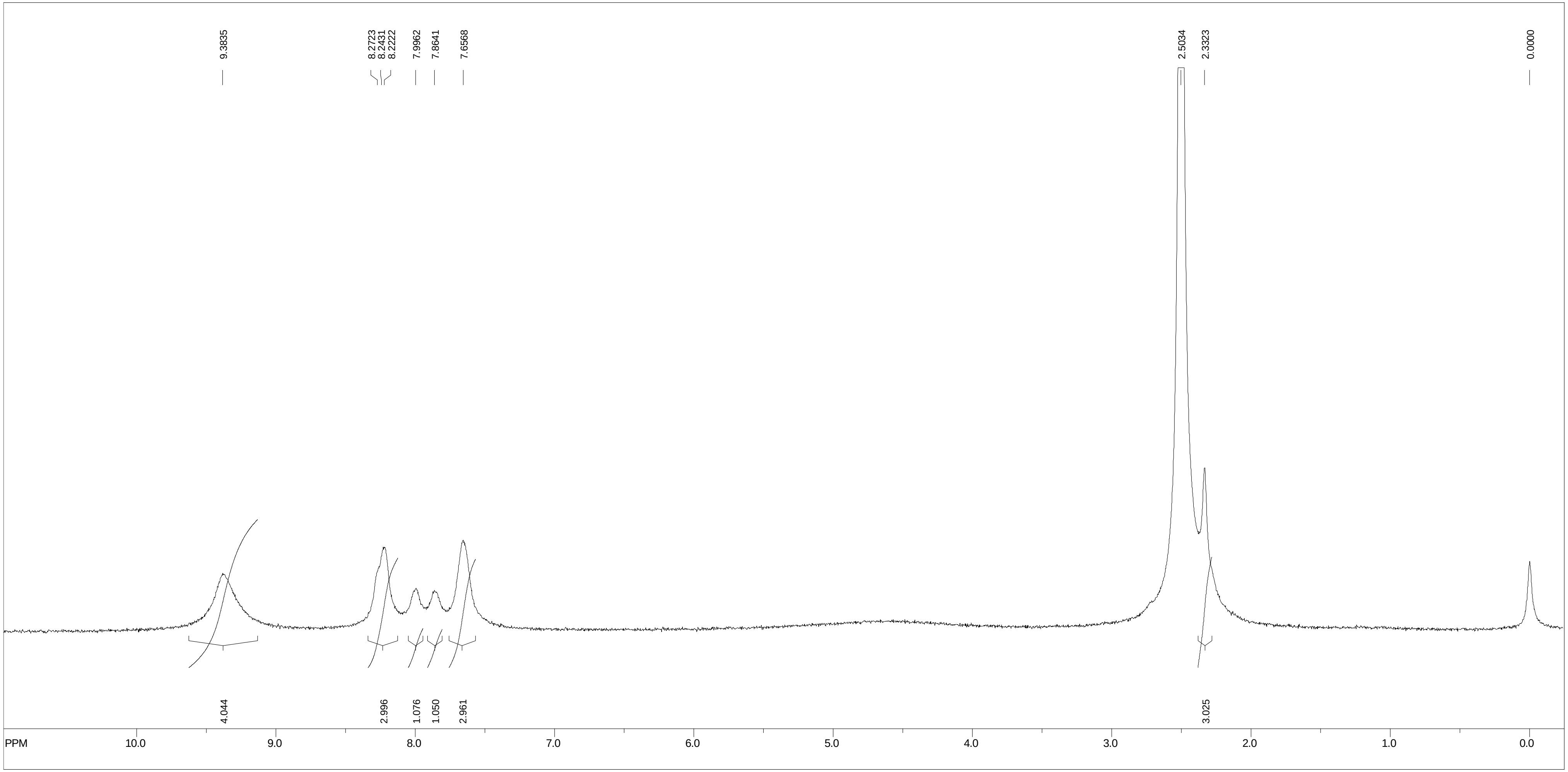

Figure S52. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 6-amidinium-2-phenylbenzoxazole methansulfonate dihydrate (**10b**)

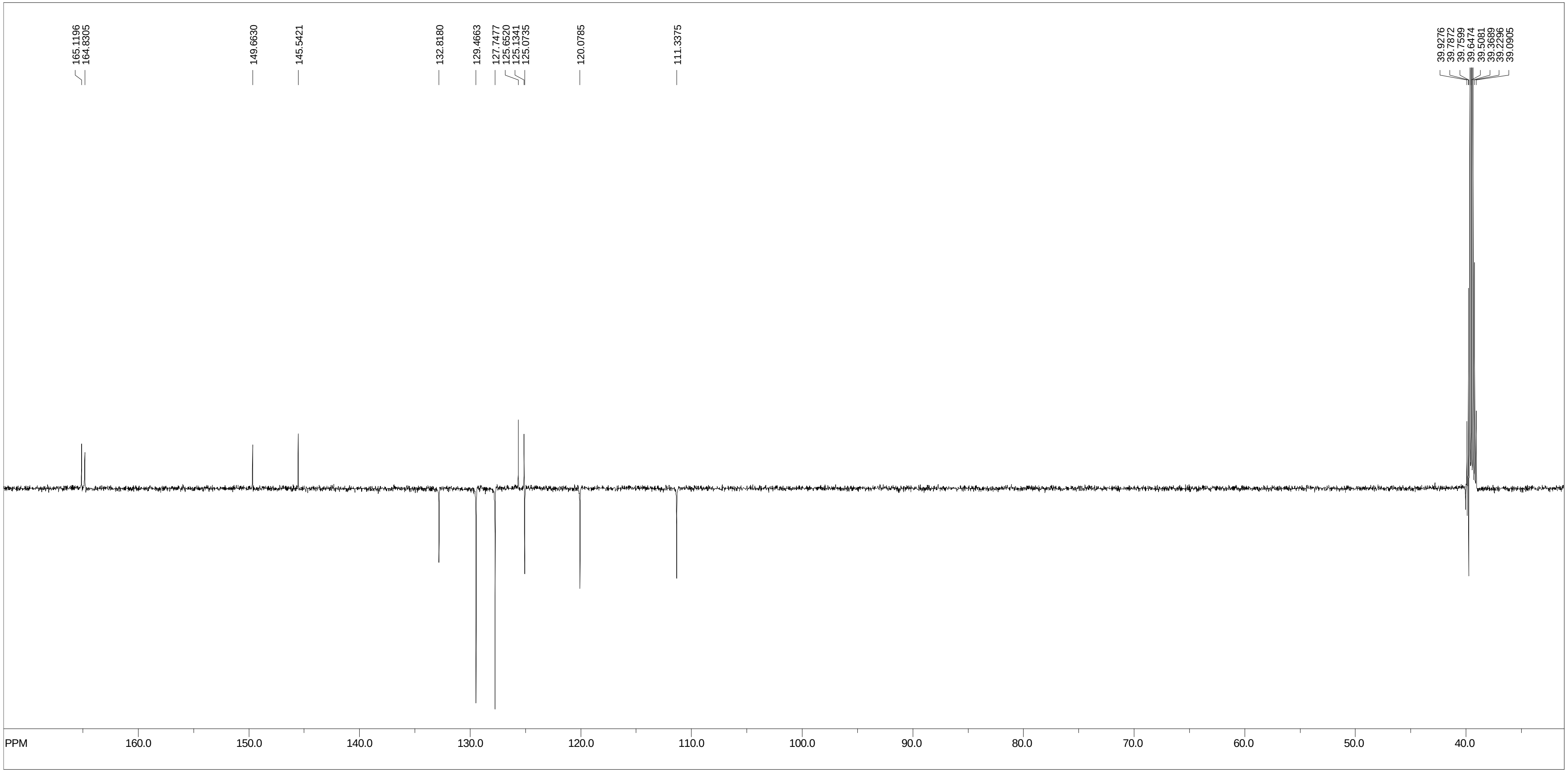

Figure S53. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-amidinium-2-phenylbenzoxazole methansulfonate dihydrate (**10b**)

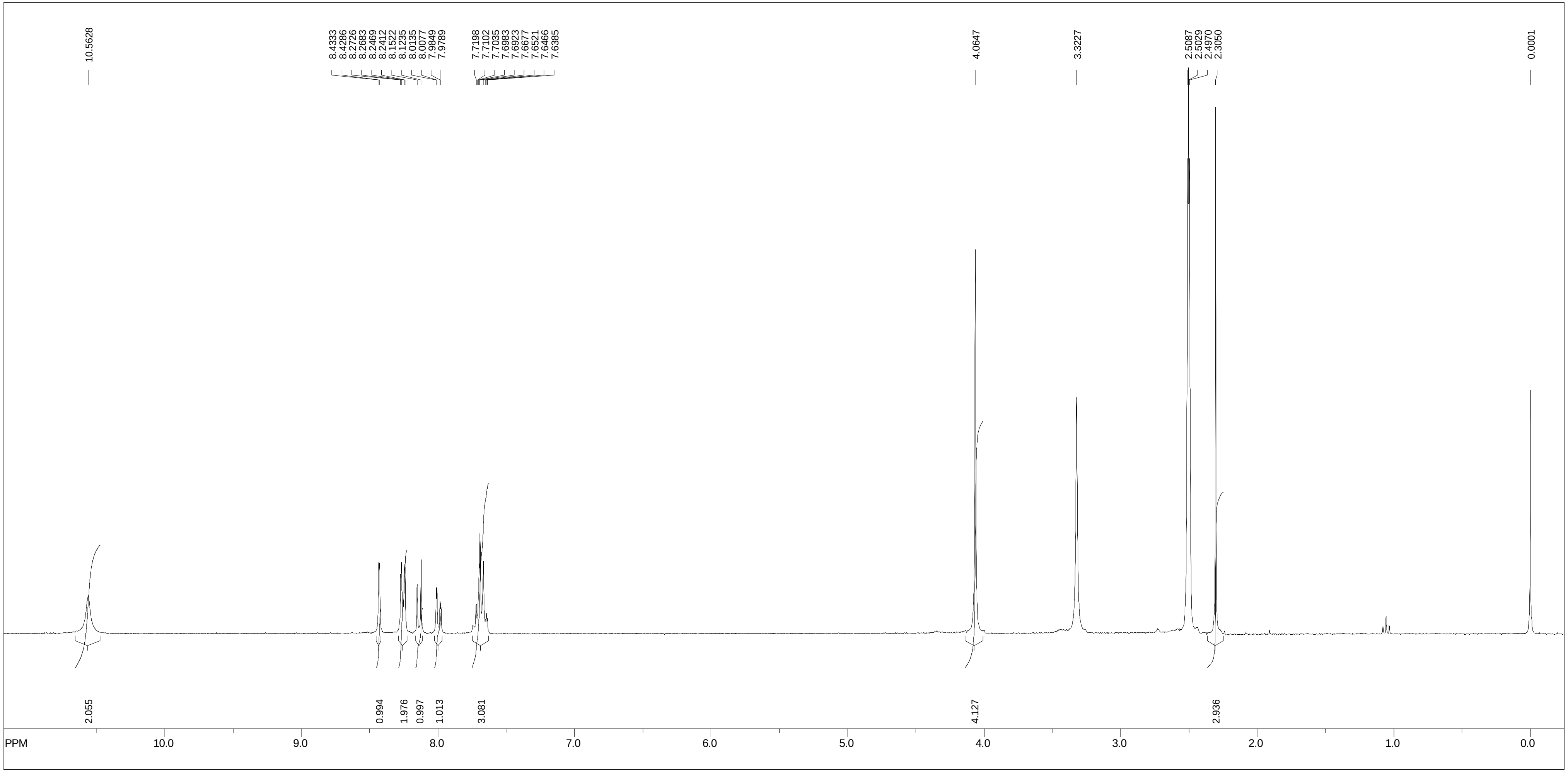

Figure S54. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 5-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (**10c**)

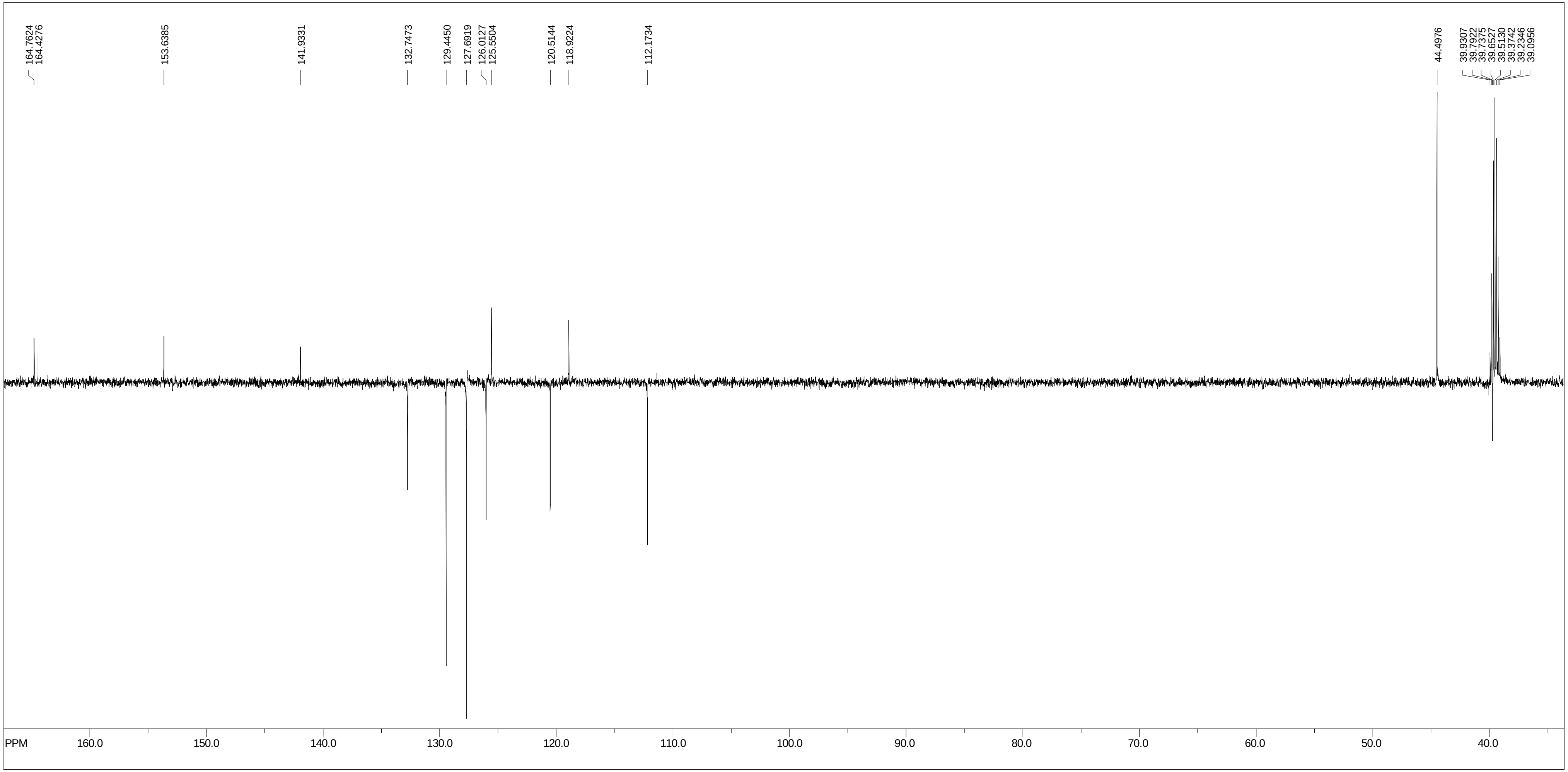

Figure S55. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 5-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (**10c**)

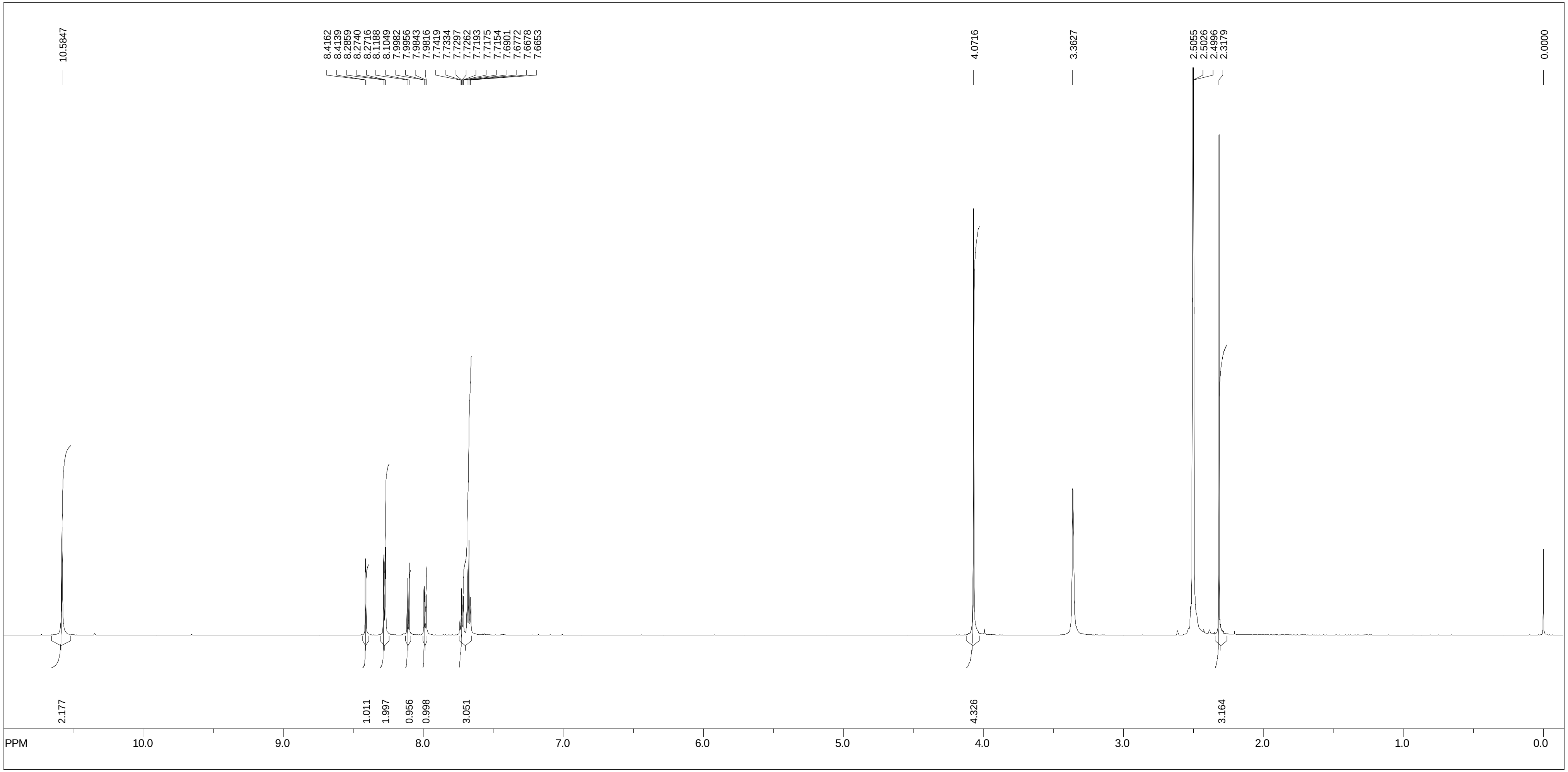

Figure S56. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (**10d**)

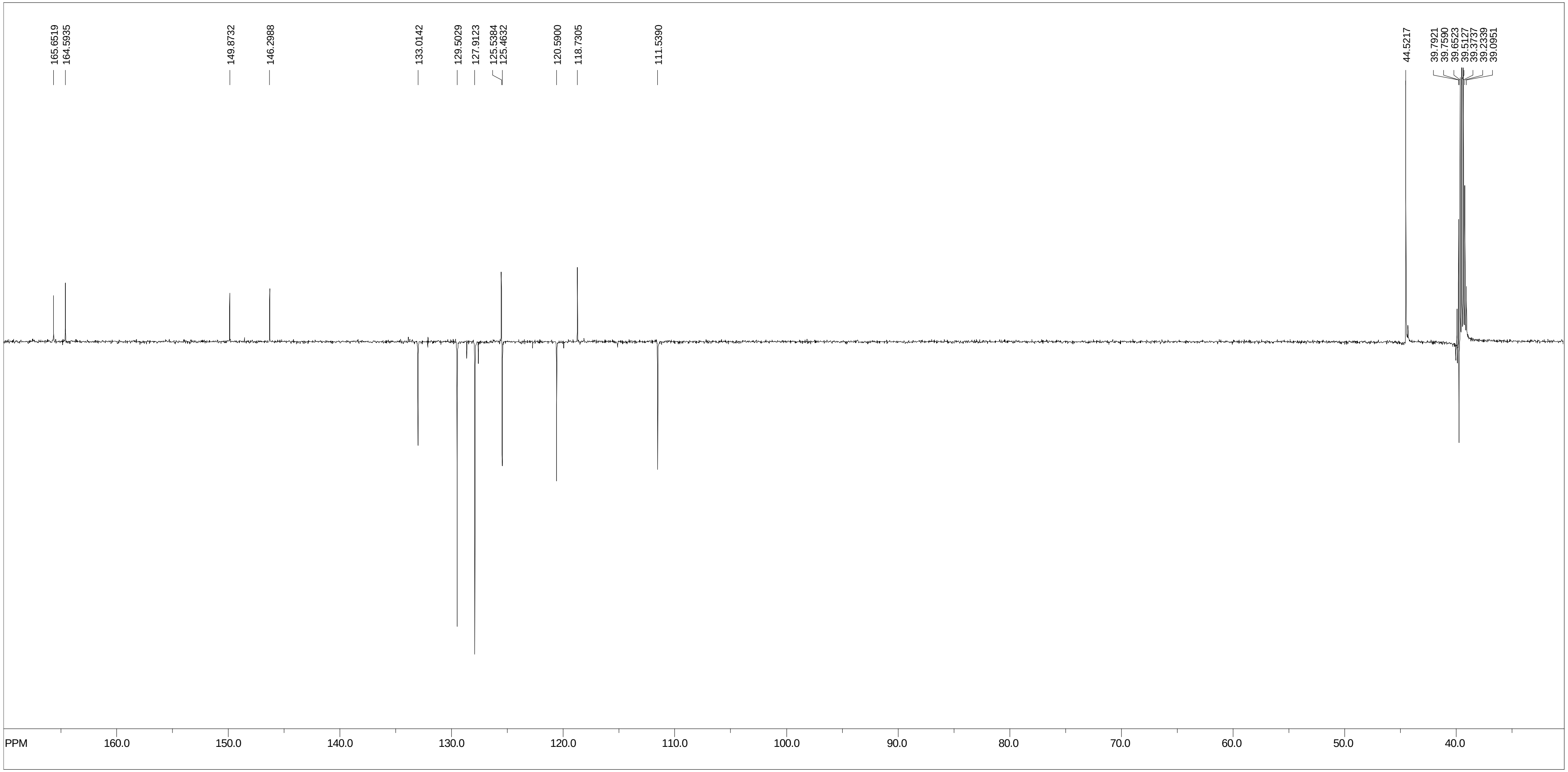

Figure S57. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-phenylbenzoxazole methansulfonate (**10d**)

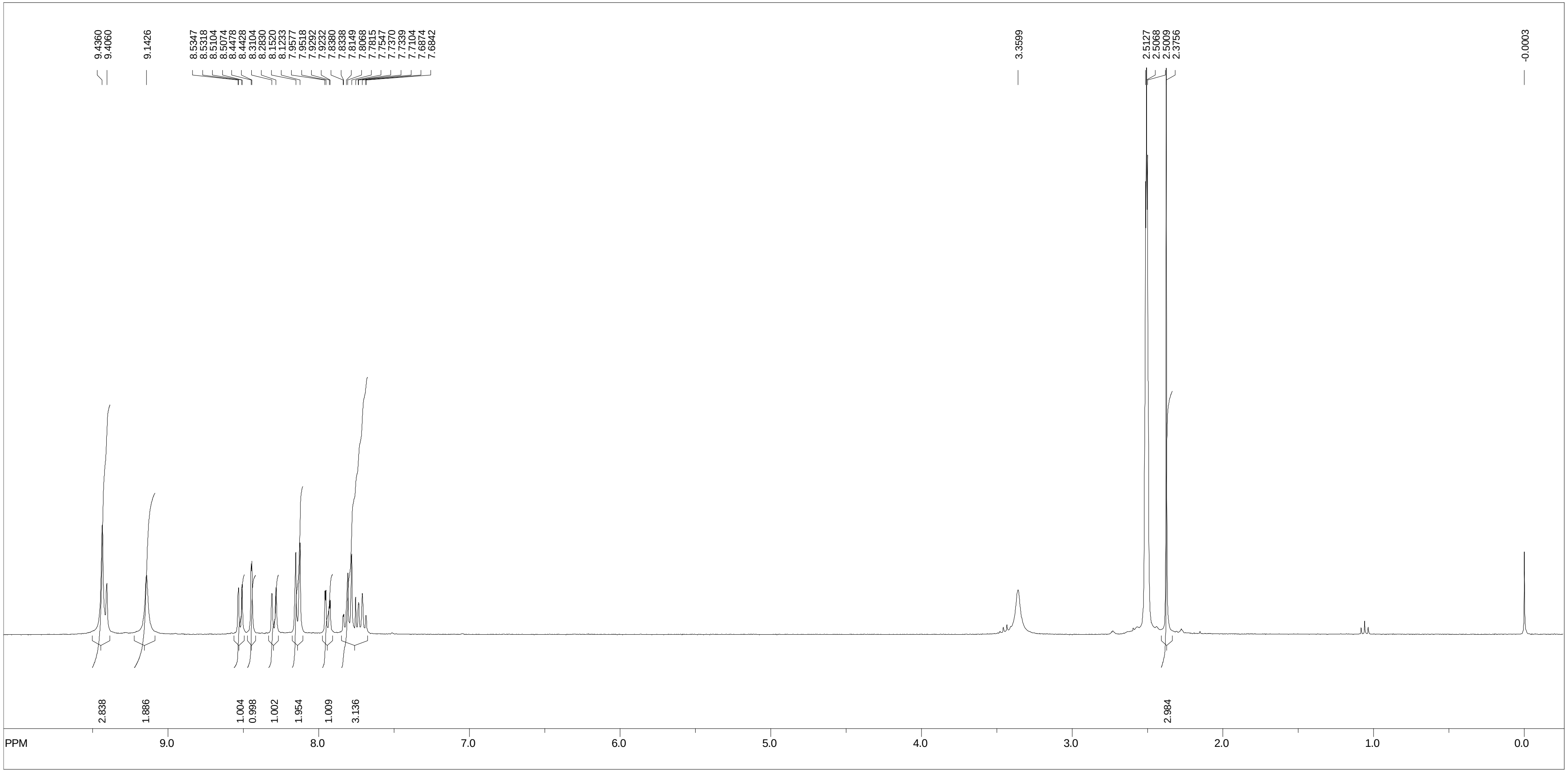

Figure S58. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 5-amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10e**)

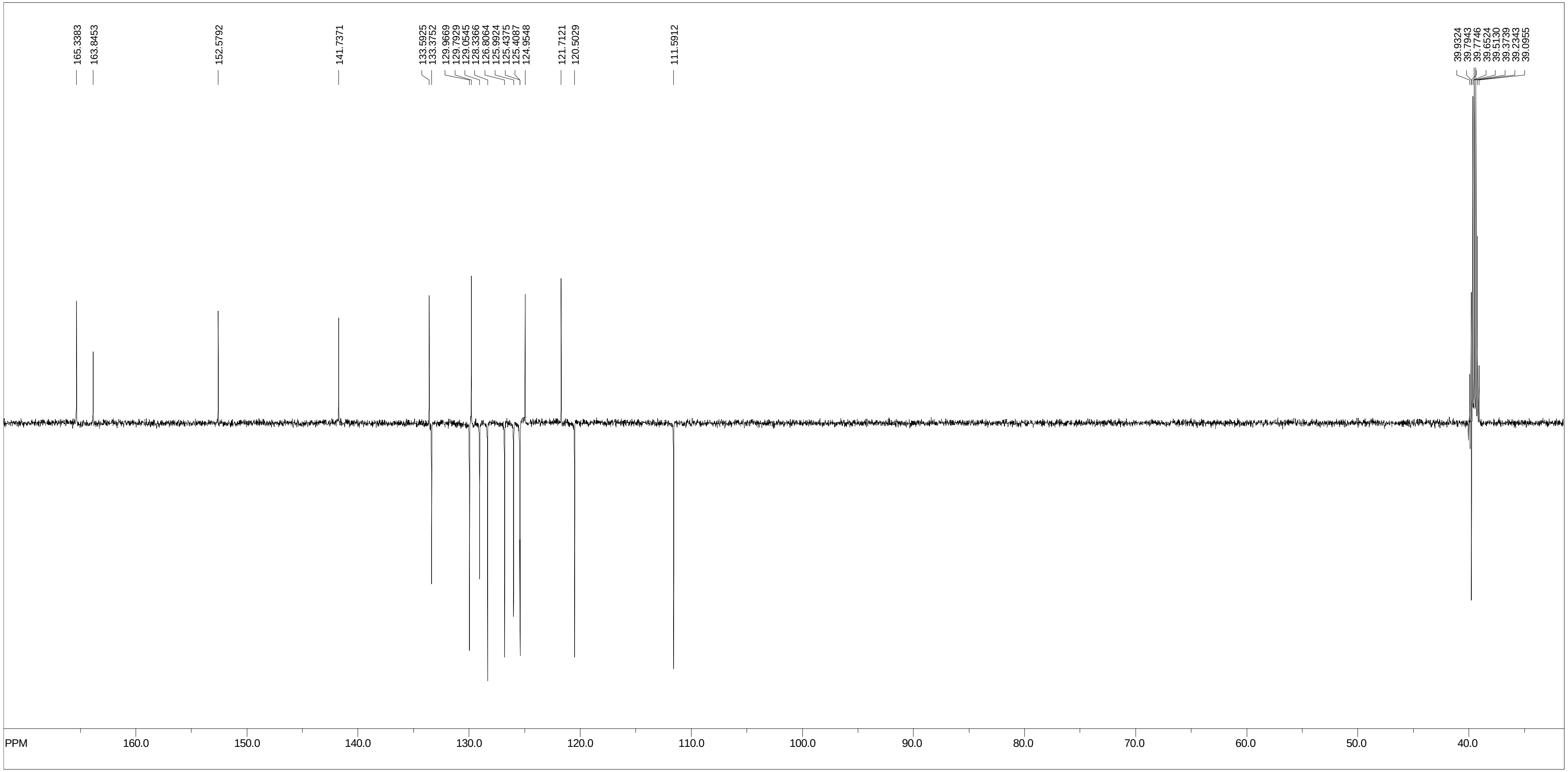

Figure S59. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 5-amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10e**)

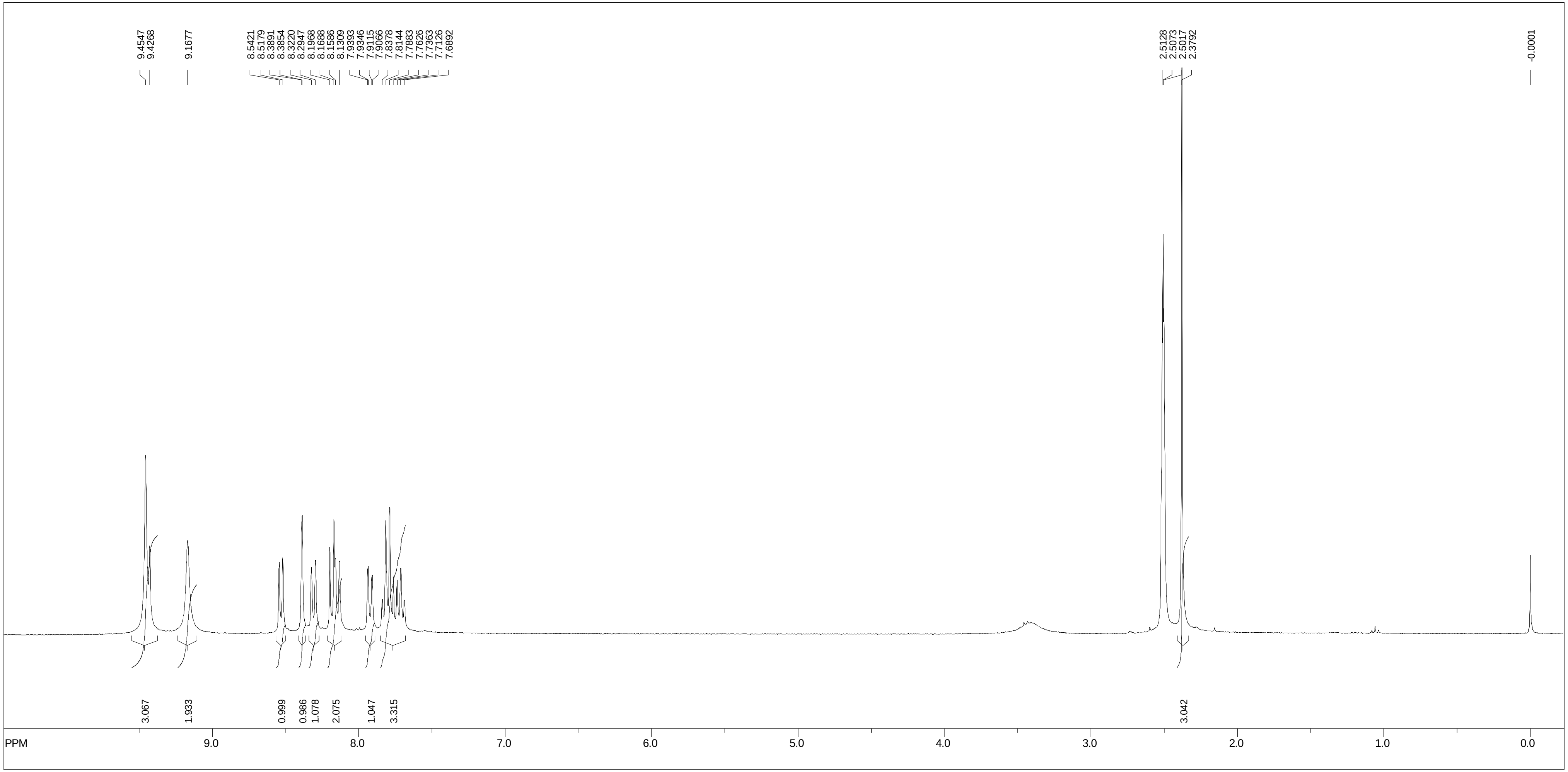

Figure S60. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 6-amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10f**)

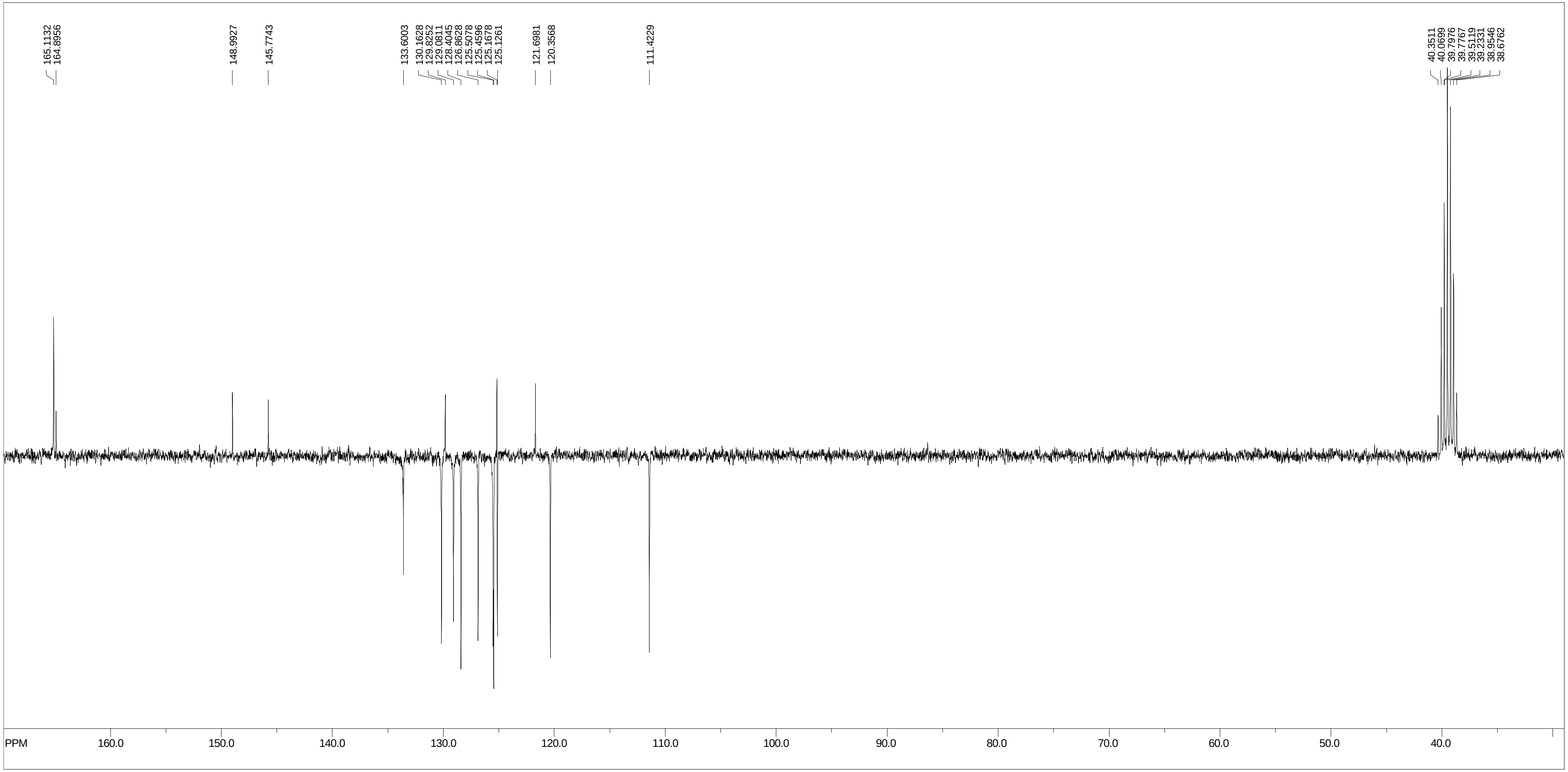

Figure S61. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 6-amidinium-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10f**)

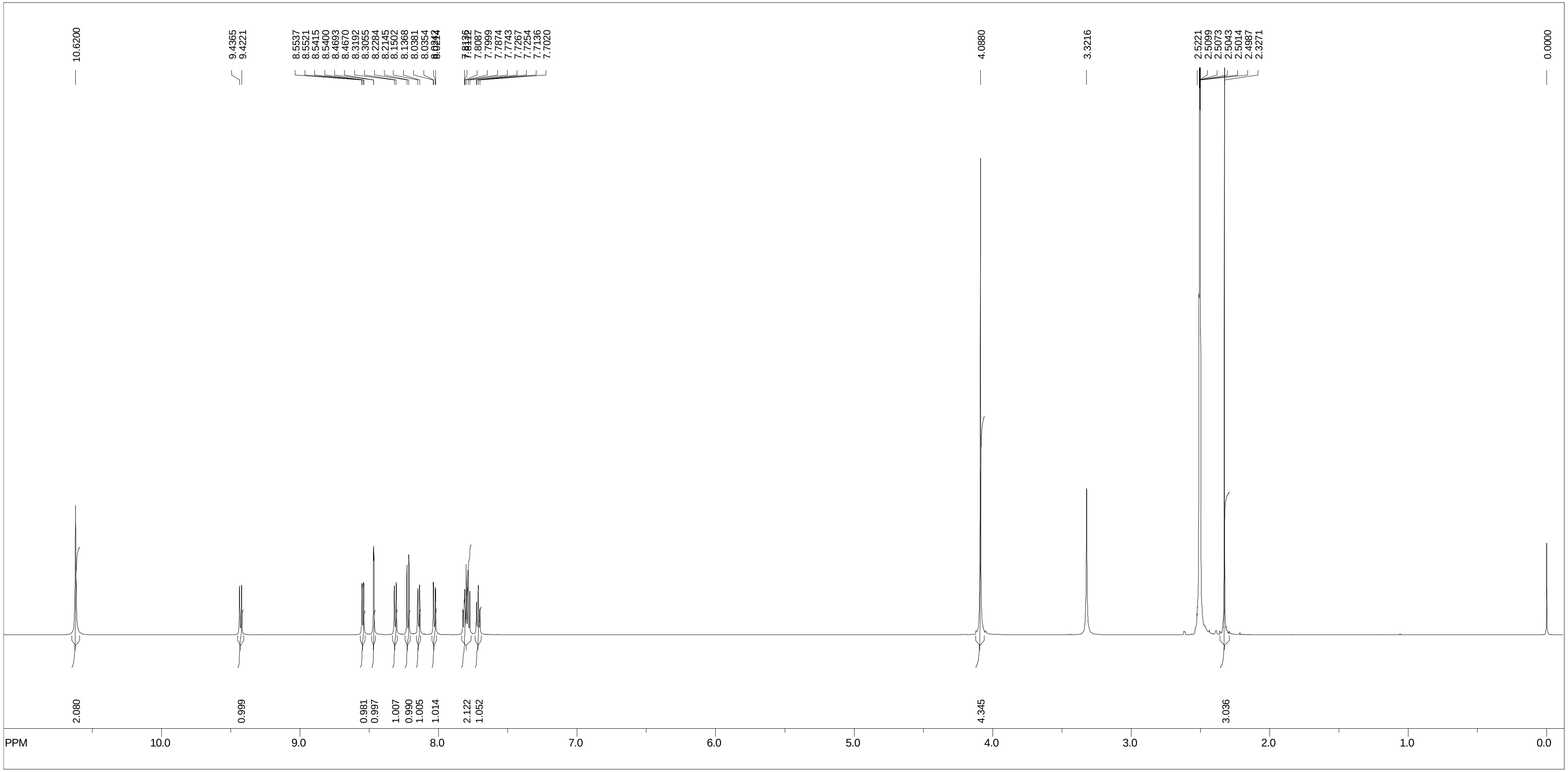

Figure S62. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10g**)

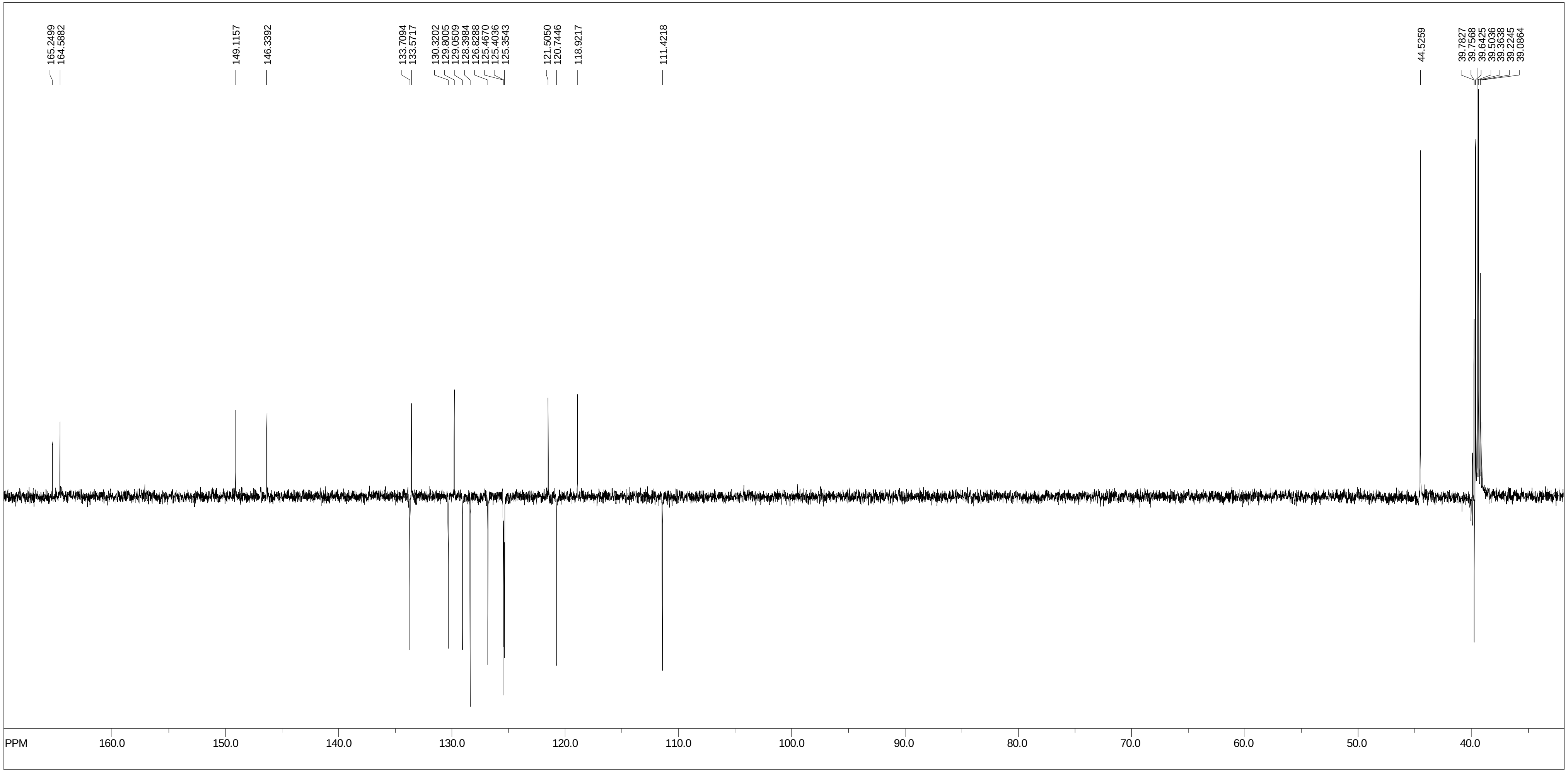

Figure S63. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10g**)

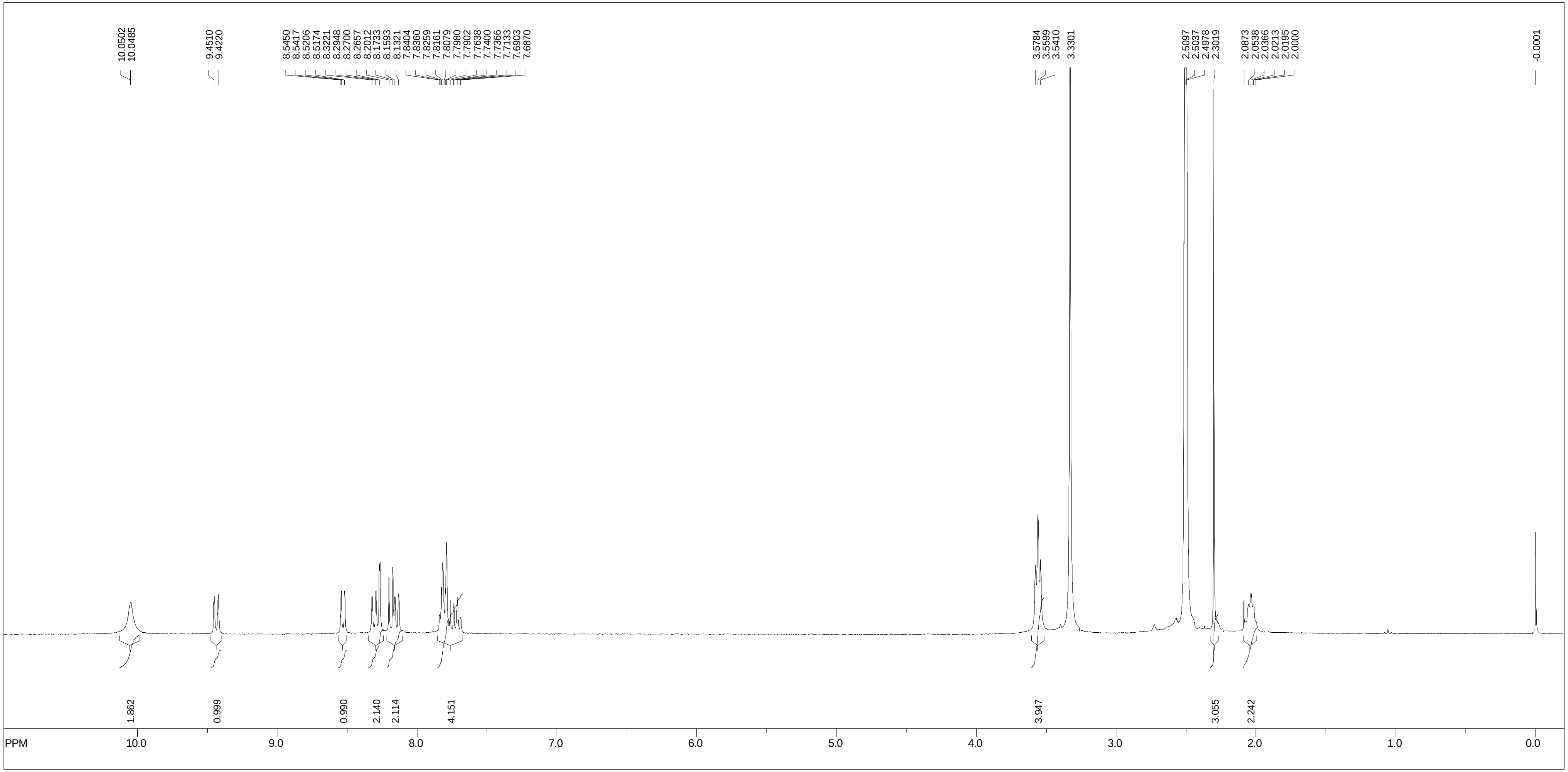

Figure S64. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 6-(3,4,5,6-tetrahydropyrimidinium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10h**)

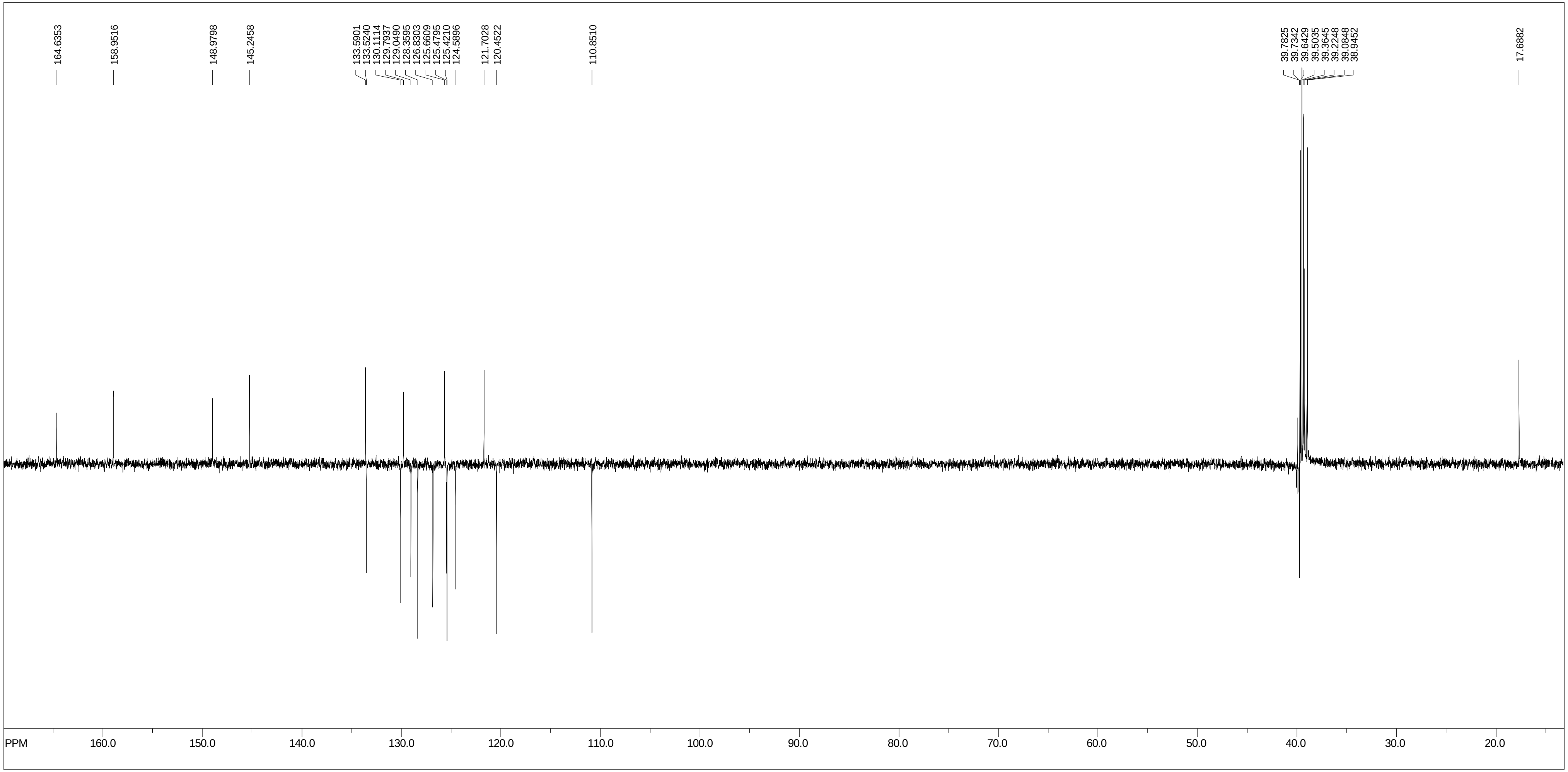

Figure S65. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-(3,4,5,6-tetrahydropyrimidinium-2-yl)-2-(naphthalene-1-yl)benzoxazole methansulfonate (**10h**)

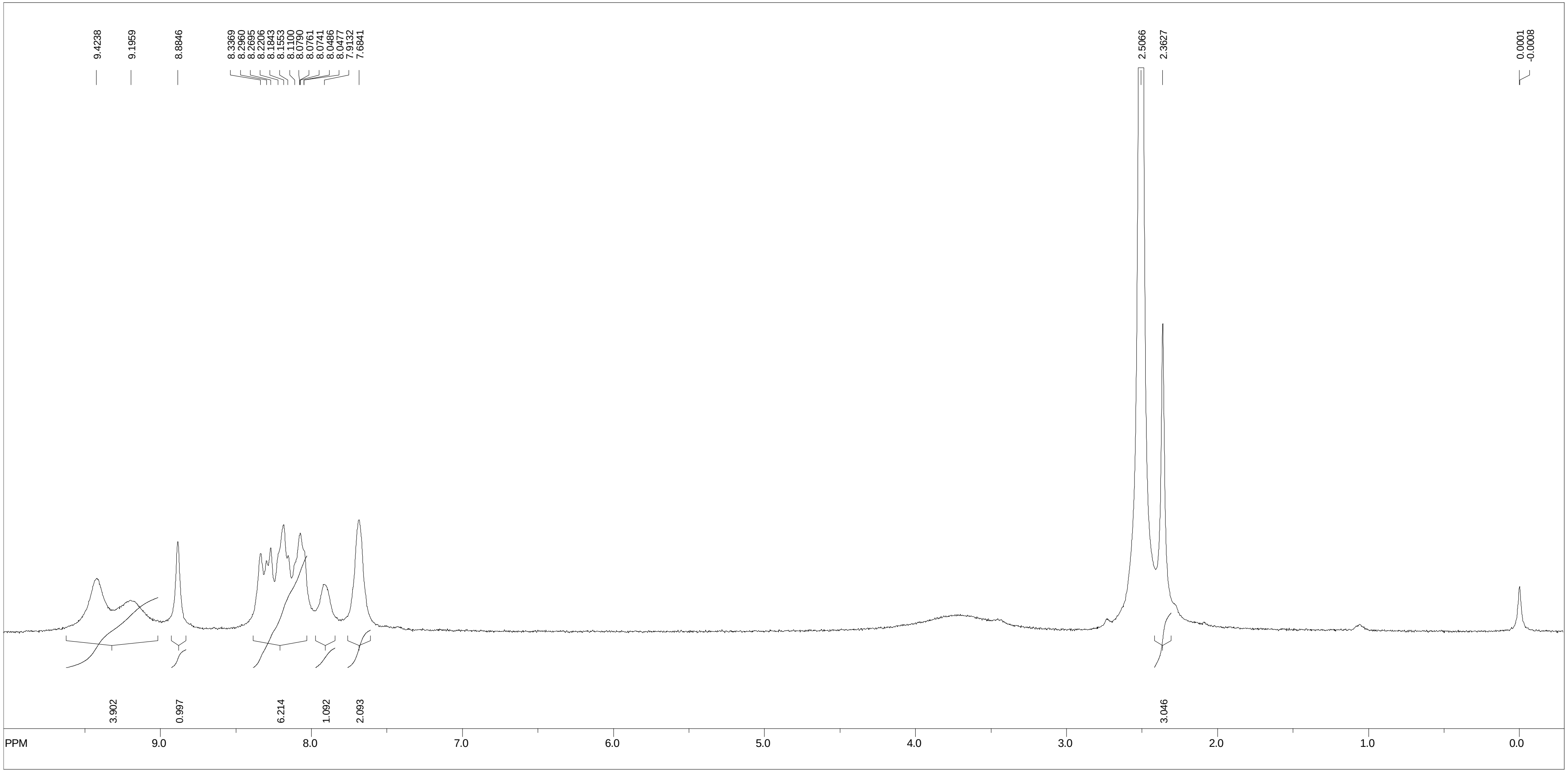

Figure S66. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 5-amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (**10i**)

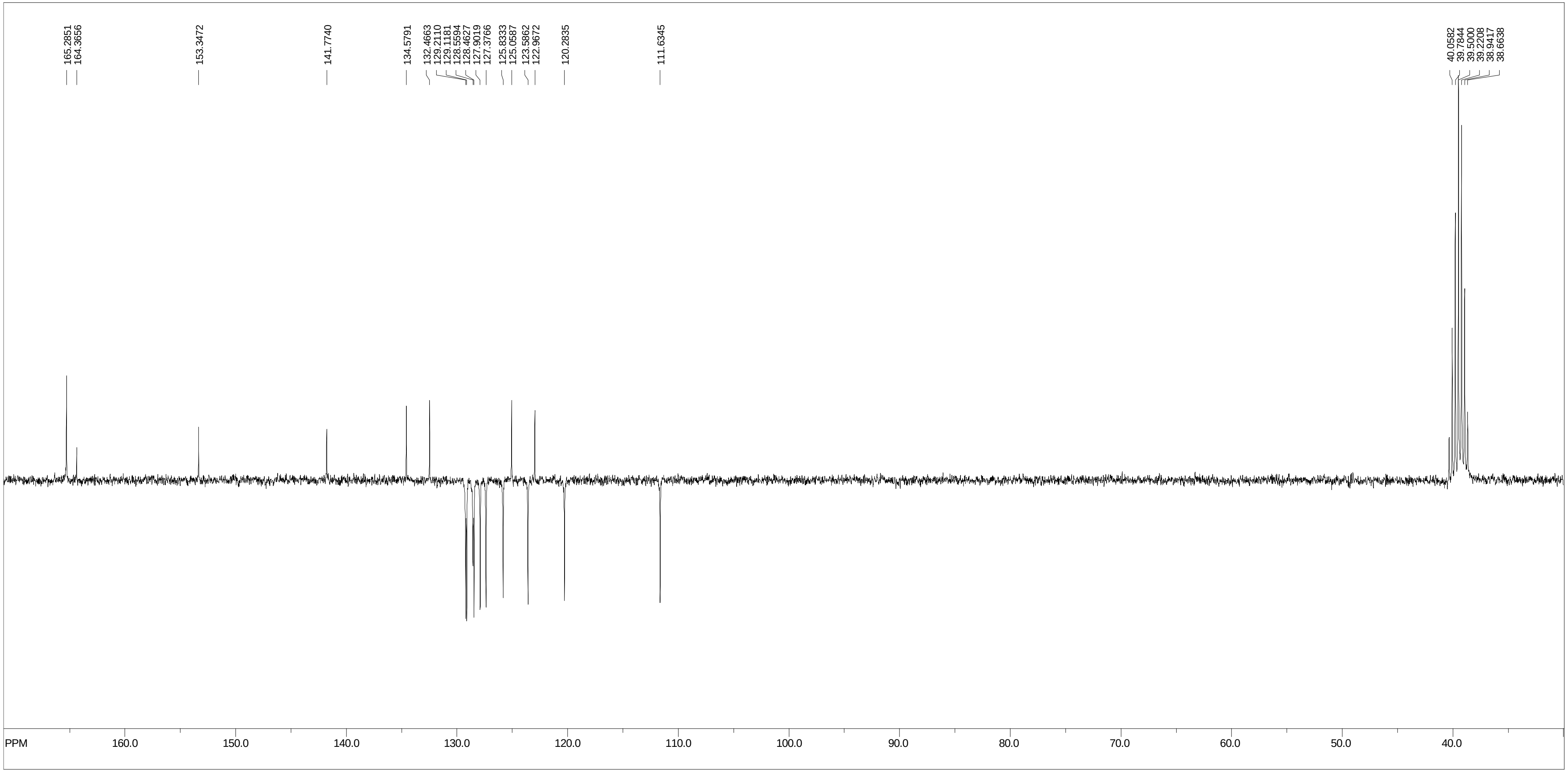

Figure S67. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 5-amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (**10i**)

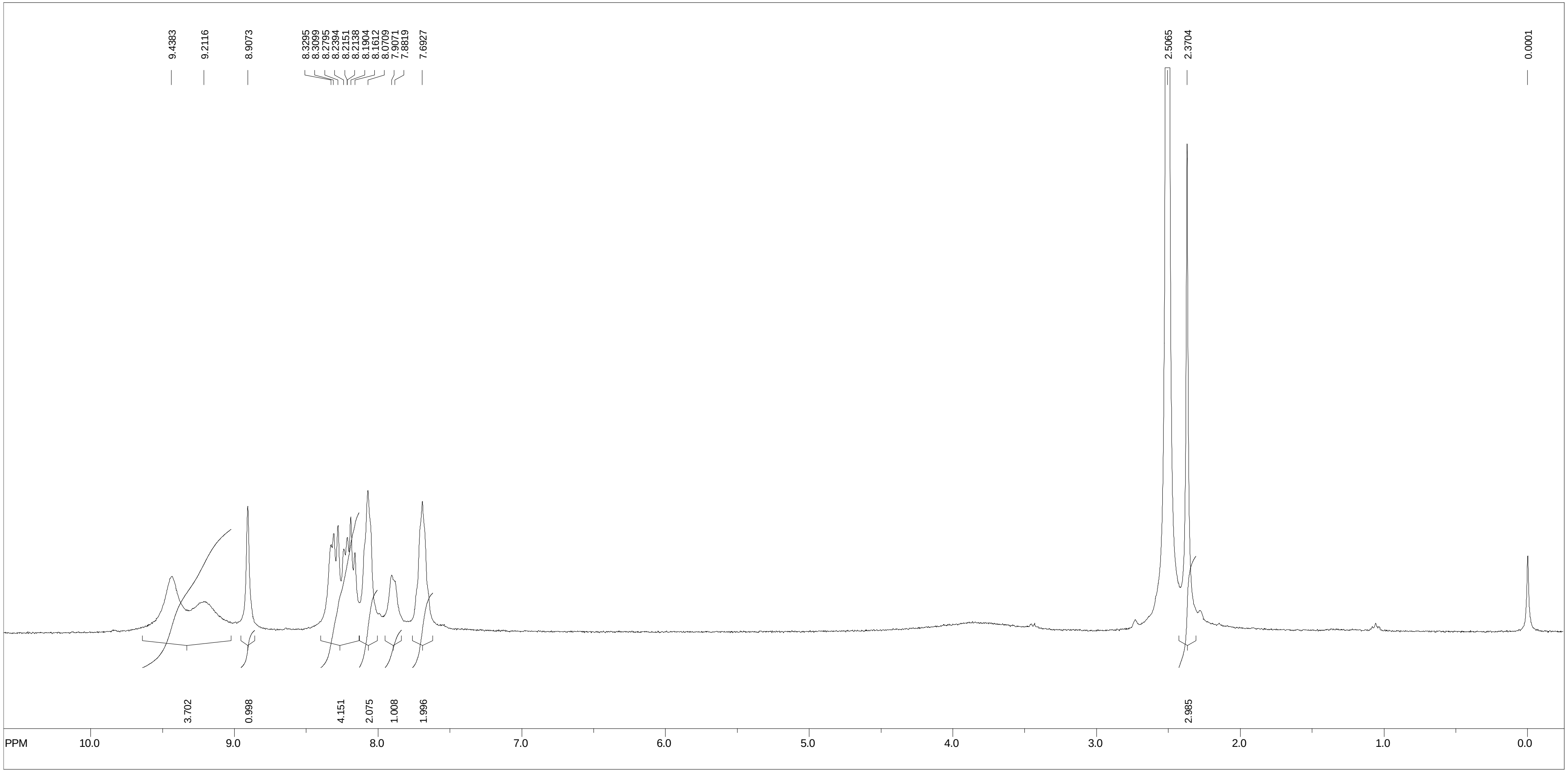

Figure S68. ^{1}H NMR spectrum (300 MHz, DMSO-d_6) of 6-amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (**10j**)

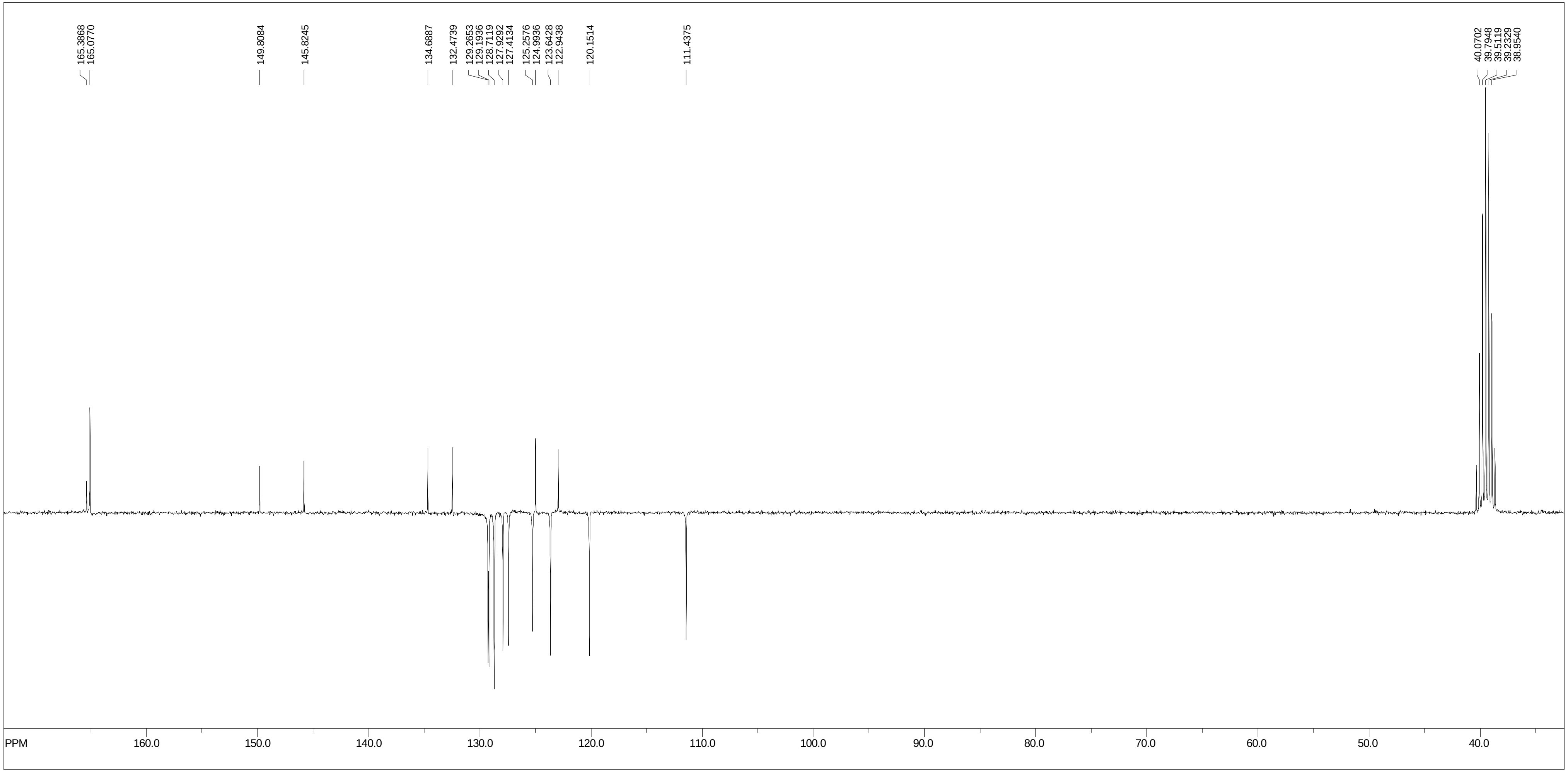

Figure S69. ^{13}C NMR spectrum (75 MHz, DMSO-d_6) of 6-amidinium-2-(naphthalene-2-yl)benzoxazole methansulfonate dihydrate (**10j**)

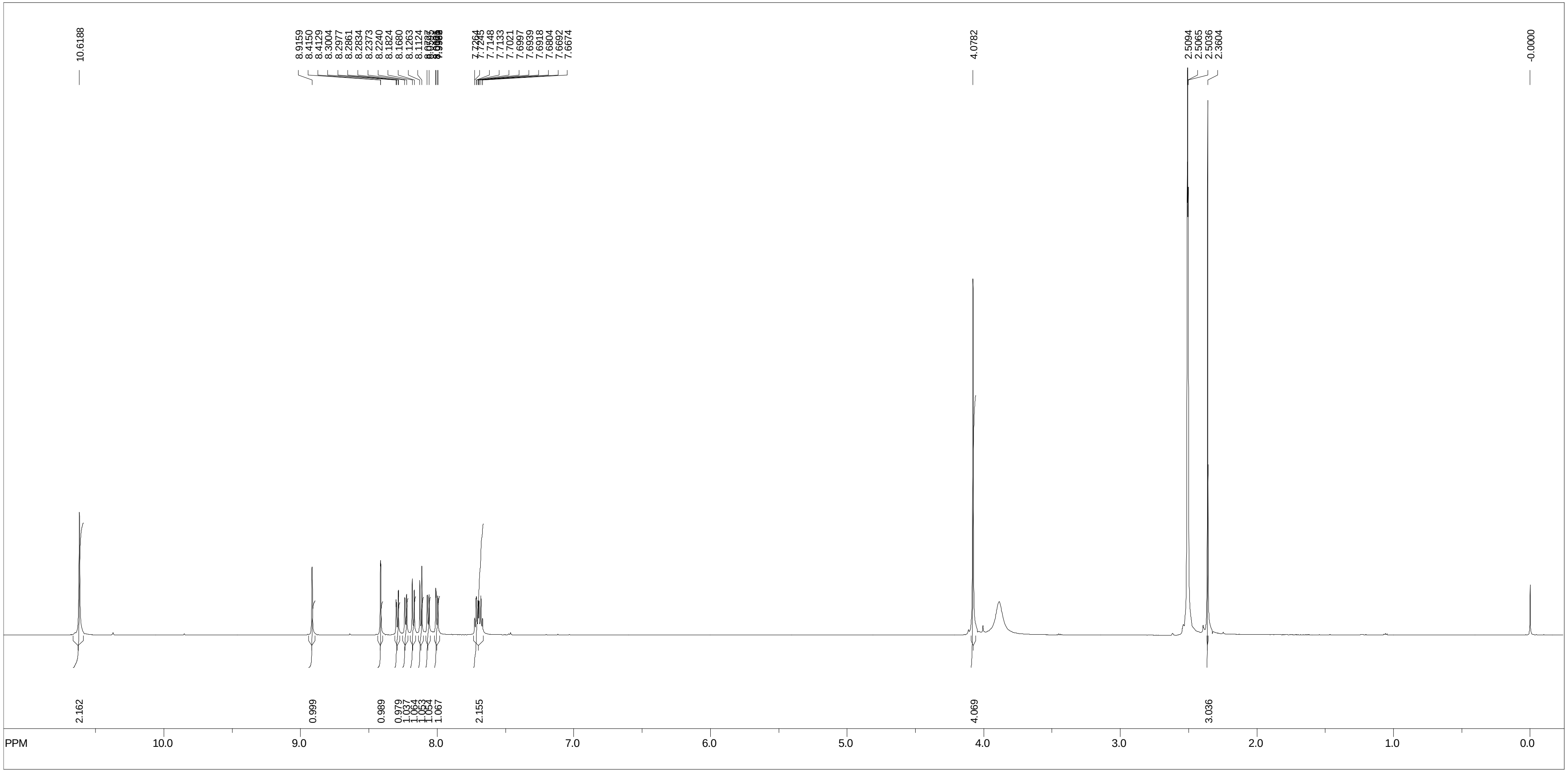

Figure S70. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (**10k**)

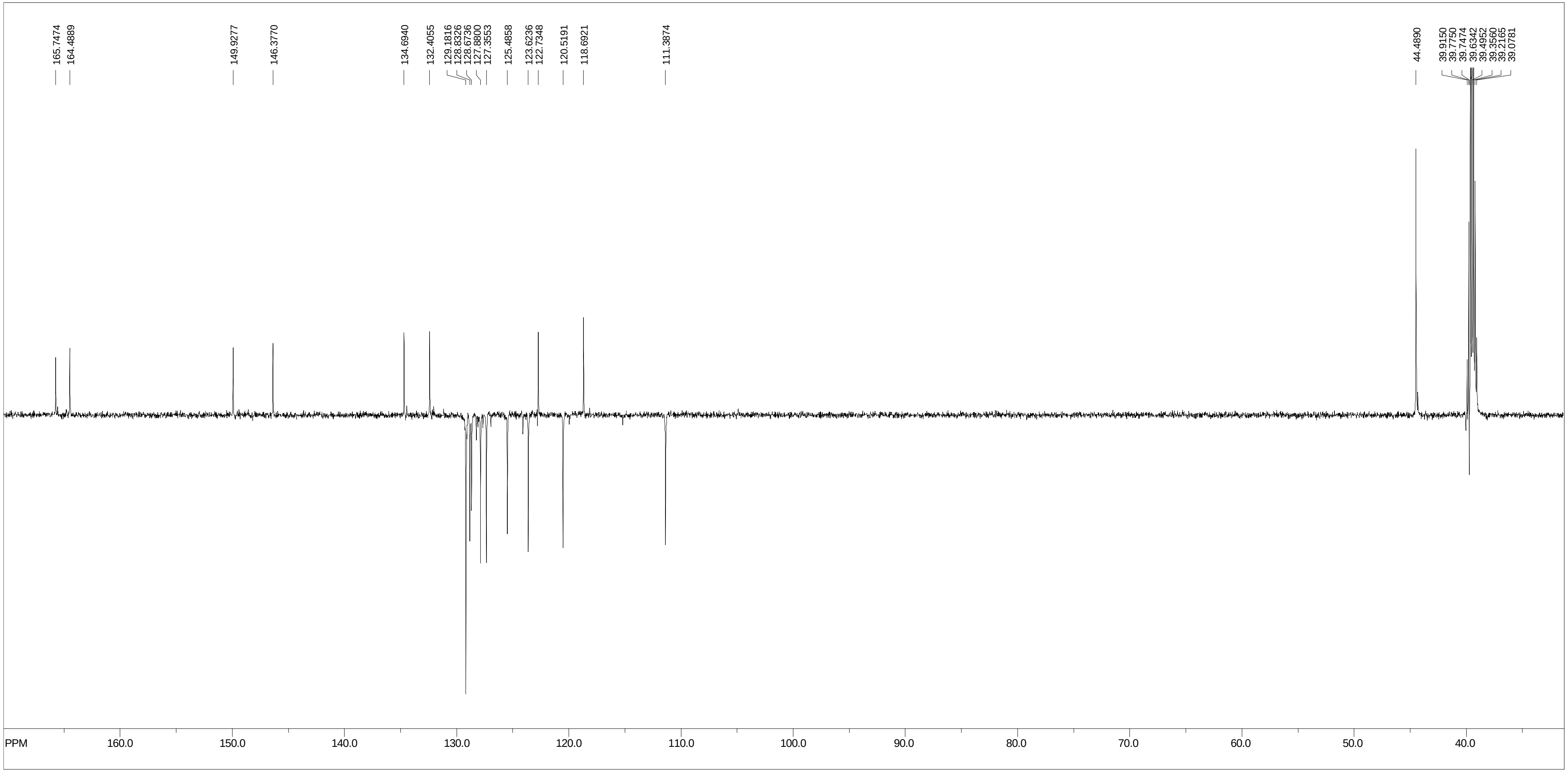

Figure S71. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-(4,5-dihydro-1*H*-imidazolium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (**10k**)

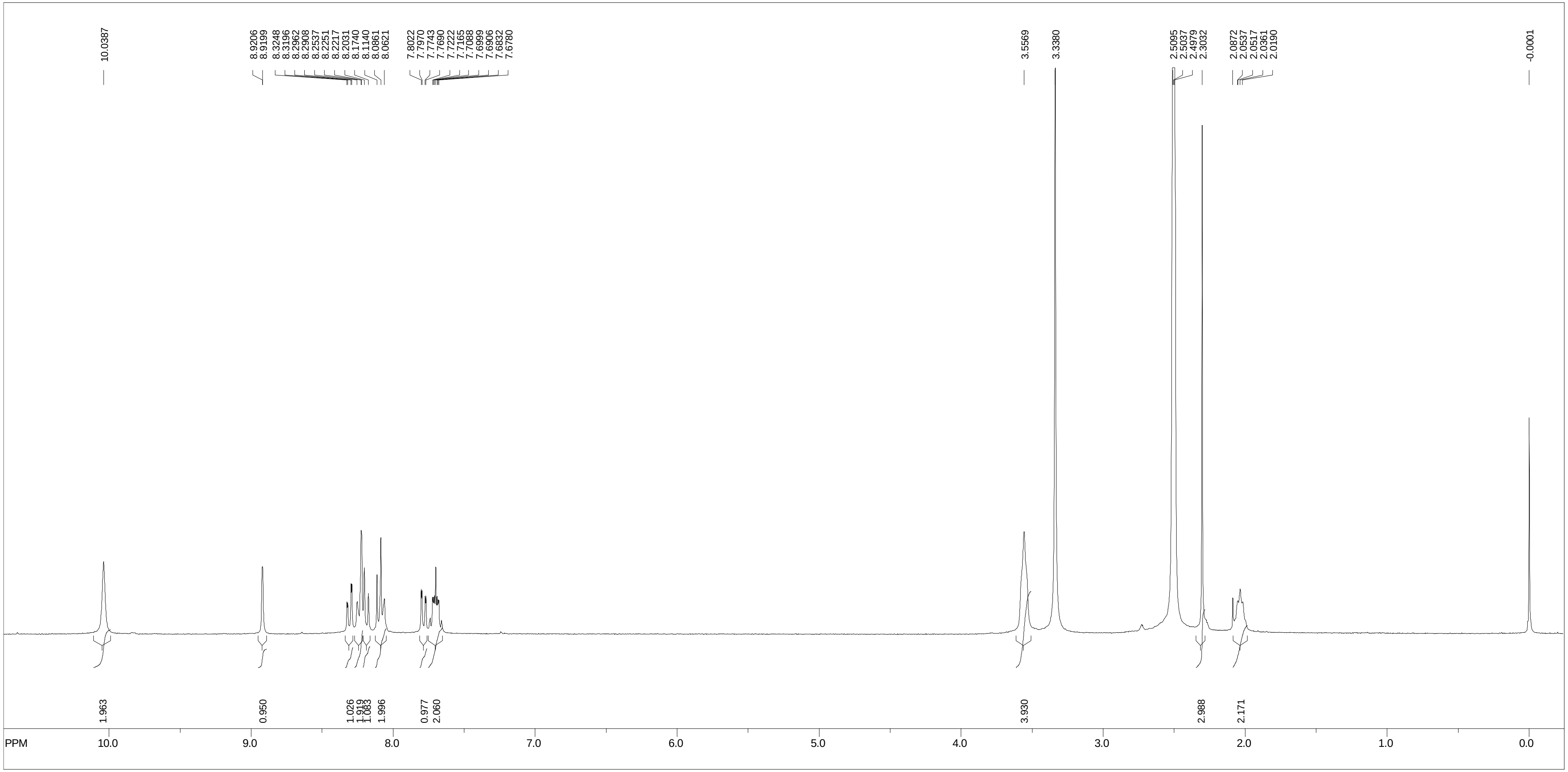

Figure S72. ^{1}H NMR spectrum (600 MHz, DMSO-d_6) of 6-(3,4,5,6-tetrahydropyrimidinium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (**10l**)

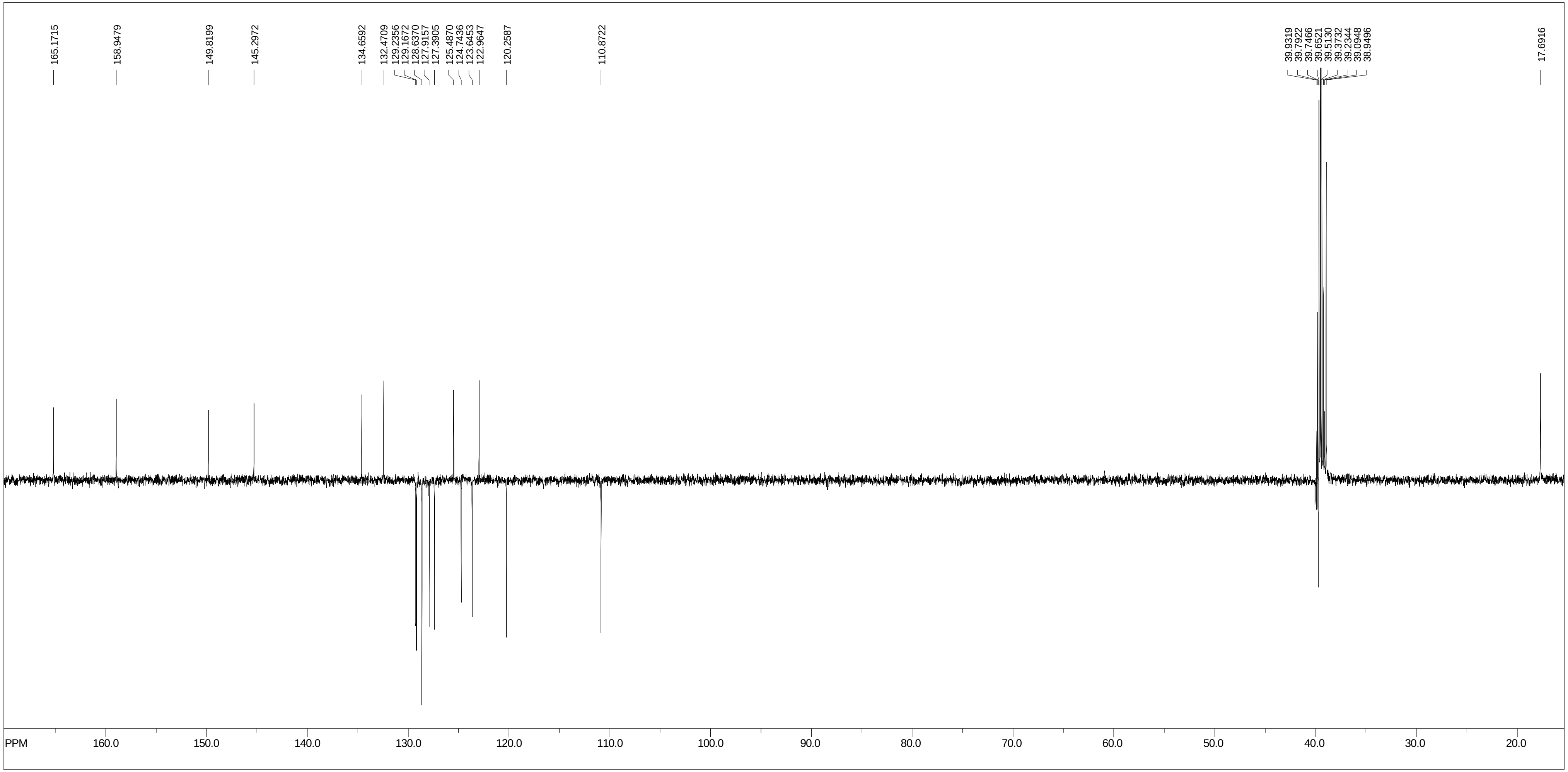

Figure S73. ^{13}C NMR spectrum (150 MHz, DMSO-d_6) of 6-(3,4,5,6-tetrahydropyrimidinium-2-yl)-2-(naphthalene-2-yl)benzoxazole methansulfonate (**10l**)

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