



Supporting Information

for

One-pot synthesis of substituted pyrrolo[3,4-*b*]pyridine-4,5-diones based on the reaction of *N*-(1-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-oxo-2-arylethyl)acetamide with amines

Valeriya G. Melekhina, Andrey N. Komogortsev, Boris V. Lichitsky, Vitaly S. Mityanov, Artem N. Fakhrutdinov, Arkady A. Dudinov, Vasily A. Migulin, Yulia V. Nelyubina, Elizaveta K. Melnikova and Michail M. Krayushkin

Beilstein J. Org. Chem. **2019**, *15*, 2840–2846. doi:10.3762/bjoc.15.277

Experimental procedures, characterization data of all products, copies of ^1H , ^{13}C , 2D NMR, and HRMS spectra of all compounds, and X-ray data for compound 1e

Table of contents

1. General information	S2
2. General procedure for the synthesis of all compounds.....	S2
3. Characterization data of all products	S3
4. Copies of ^1H and ^{13}C NMR spectra for all compounds	S11
5. Copies of HRMS for all compounds.....	S32
6. 2D NMR spectra for compounds 7e and 1e	S44
7. X-Ray analysis of compounds 1e	S46

1. General information

Unless otherwise stated, all starting chemicals were commercially available and used as received. All reactions were performed without inert gas atmosphere. NMR spectra were recorded with Bruker AM 300 (300 MHz), Bruker AV 400 (400 MHz), Bruker DRX 500 (500 MHz), and Bruker AV 600 (600 MHz) spectrometers in DMSO-*d*₆. Chemical shifts (ppm) are given relative to solvent signals (2.50 ppm for ¹H NMR and 39.52 ppm for ¹³C NMR). High-resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF II instrument using electrospray ionization (ESI). IR spectra were registered on a Bruker ALPHA spectrophotometer as KBr pellets. The melting points were determined on a Kofler hot stage. Crystallographic data for the structure reported in this paper have been deposited in the Cambridge Crystallographic Data Centre as CCDC [1921613](#).

2. General procedure for the synthesis of compounds 2, 7 and 1.

Experimental procedure for the preparation of compounds 2.

A mixture of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**4**, 3 mmol), the corresponding arylglyoxal **5** (3 mmol) and acetamide (**6**, 9 mmol) in MeCN was refluxed for 6 h. The reaction mixture was cooled to room temperature and the precipitate formed was collected by filtration and washed with MeCN (3 × 5 mL).

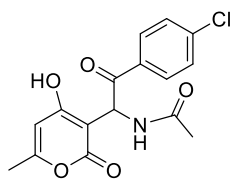
Experimental procedure for the preparation of compounds 7.

A mixture of the corresponding acetamide derivatives **2** (3 mmol), amines **3** (9 mmol) and AcOH (9 mmol) in EtOH was refluxed for 4 h. The reaction mixture was cooled to room temperature and the precipitate formed was collected by filtration and washed with EtOH (3 × 5 mL). In the case of using ammonium acetate as the source of ammonia, we used 6 equivalents of this substance.

*Experimental one-pot procedure for the preparation of pyrrolo[3,4-*b*]pyridin-5-one derivatives 1.*

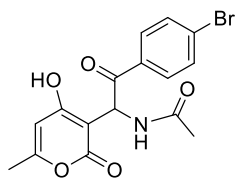
A mixture of the corresponding acetamide derivatives **2** (3 mmol), amines **3** (9 mmol) and AcOH (9 mmol) in EtOH was refluxed for 4 h. The solvent was removed under reduced pressure. Then, a mixture of hydrochloric acid and acetic acid (5 mL:5 mL) was added to the residue and the mixture refluxed for 1 h. After completion of the reaction, the solvent was evaporated under reduced pressure and water (10 mL) and NaOAc (0.5 g) were added and left overnight. The obtained solid product was filtered and recrystallized from 50% EtOH.

3. Characterization data of all products



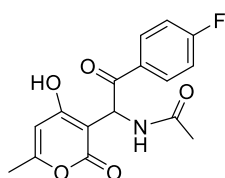
N-(2-(4-Chlorophenyl)-1-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-oxoethyl)acetamide (**2a**)

White powder; yield 42%; mp 249-250°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.25 (s, 1H), 8.13 (d, $J = 7.3$ Hz, 1H), 7.74 (d, $J = 8.5$ Hz, 2H), 7.52 (d, $J = 8.5$ Hz, 2H), 6.23 (d, $J = 7.6$ Hz, 1H), 6.00 (s, 1H), 2.12 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 193.91, 169.38, 167.40, 163.18, 162.90, 137.64, 134.20, 129.11, 128.67, 99.85, 98.40, 50.51, 22.31, 19.37. IR spectrum, ν , cm^{-1} : 3300, 3105, 3043, 2959, 2931, 2874, 2860, 2628, 2368, 1691, 1591, 1561, 1448, 1422, 1398, 1275, 1233, 1171, 1140, 1117, 1095, 1045, 997. HRMS: Calculated for $\text{C}_{16}\text{H}_{14}\text{ClNO}_5$ $[\text{M}+\text{H}]^+$: 336.0633. Found: 336.0636.



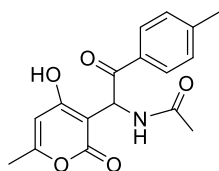
N-(2-(4-Bromophenyl)-1-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-oxoethyl)acetamide (**2b**)

White powder; yield 45%; mp 251-252°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.24 (s, 1H), 8.13 (d, $J = 7.6$ Hz, 1H), 7.66 (s, 4H), 6.22 (d, $J = 7.6$ Hz, 1H), 6.00 (s, 1H), 2.12 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 194.09, 169.34, 167.35, 163.14, 162.87, 134.52, 131.57, 129.19, 126.70, 99.81, 98.35, 50.44, 22.28, 19.33. IR spectrum, ν , cm^{-1} : 3368, 3297, 3097, 2959, 2933, 2874, 2860, 1712, 1693, 1618, 1590, 1561, 1528, 1448, 1422, 1395, 1275, 1234, 1173, 1139, 1120, 1072, 1042, 996. HRMS: Calculated for $\text{C}_{16}\text{H}_{14}\text{BrNO}_5$ $[\text{M}+\text{H}]^+$: 380.0128. Found: 380.0127.



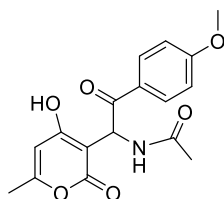
N-(2-(4-Fluorophenyl)-1-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-oxoethyl)acetamide (**2c**)

White powder; yield 46%; mp 246-247°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.21 (s, 1H), 8.11 (d, $J = 7.7$ Hz, 1H), 7.82 (dd, $J_F = 8.5, 5.5$ Hz, 2H), 7.29 (t, $J_F = 8.8$ Hz, 2H), 6.24 (d, $J = 7.7$ Hz, 1H), 6.01 (s, 1H), 2.13 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 193.36, 169.33, 167.31, 166.31, 163.07 (d, $J_{CF} = 14$ Hz), 162.82, 132.09, 130.10 (d, $J_{CF} = 9.4$ Hz), 115.57 (d, $J_{CF} = 22.0$ Hz), 99.83, 98.50, 50.42, 22.30, 19.33. IR spectrum, ν , cm^{-1} : 3301, 3087, 2959, 2922, 2875, 2629, 2457, 2345, 1898, 1691, 1599, 1561, 1508, 1448, 1411, 1396, 1302, 1276, 1233, 1159, 1140, 1117, 1106, 1047, 998. HRMS: Calculated for $\text{C}_{16}\text{H}_{14}\text{FNO}_5$ $[\text{M}+\text{H}]^+$: 320.0929. Found: 320.0932.



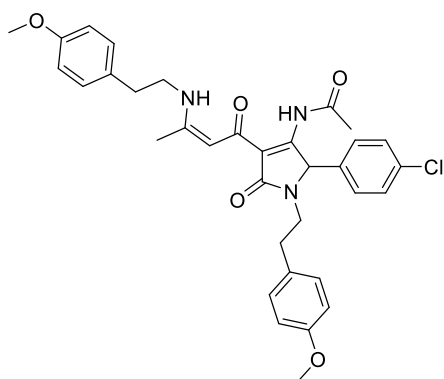
N-(1-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-oxo-2-(*p*-tolyl)ethyl)acetamide (**2d**)

White powder; yield 46%; mp 241-242°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.14 (s, 1H), 8.05 (d, $J = 7.7$ Hz, 1H), 7.66 (d, $J = 8.1$ Hz, 2H), 7.24 (d, $J = 8.0$ Hz, 2H), 6.25 (d, $J = 7.8$ Hz, 1H), 5.99 (s, 1H), 2.32 (s, 3H), 2.11 (s, 3H), 1.91 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 194.21, 169.27, 167.11, 163.16, 162.61, 143.11, 132.84, 128.99, 127.38, 99.84, 98.89, 50.33, 22.34, 21.06, 19.31. IR spectrum, ν , cm^{-1} : 3284, 3093, 3042, 2957, 2918, 2629, 2363, 2344, 1685, 1610, 1579, 1559, 1448, 1419, 1276, 1236, 1186, 1173, 1139, 1114, 1046, 997. HRMS: Calculated for $\text{C}_{17}\text{H}_{17}\text{NO}_5$ $[\text{M}+\text{H}]^+$: 316.1179. Found: 316.1184.



N-(1-(4-Hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-2-(4-methoxyphenyl)-2-oxoethyl)acetamide (**2e**)

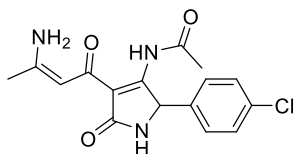
White powder; yield 47%; mp 238-239°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.10 (s, 1H), 8.02 (d, $J = 7.9$ Hz, 1H), 7.75 (d, $J = 8.7$ Hz, 2H), 6.97 (d, $J = 8.8$ Hz, 2H), 6.23 (d, $J = 7.8$ Hz, 1H), 6.00 (s, 1H), 3.80 (s, 3H), 2.12 (s, 3H), 1.90 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 192.98, 169.26, 167.11, 163.19, 162.83, 162.60, 129.58, 128.02, 113.74, 99.90, 99.06, 55.45, 50.18, 22.38, 19.34. IR spectrum, ν , cm^{-1} : 3442, 3288, 2959, 2927, 2873, 2858, 1679, 1604, 1578, 1560, 1509, 1449, 1417, 1276, 1260, 1240, 1180, 1139, 1116, 1075, 1033, 998. HRMS: Calculated for $\text{C}_{17}\text{H}_{17}\text{NO}_6$ $[\text{M}+\text{H}]^+$: 332.1129. Found: 332.1128.



N-(2-(4-Chlorophenyl)-1-(4-methoxyphenethyl)-4-(3-((4-methoxyphenethyl)amino)but-2-enoyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7a**)

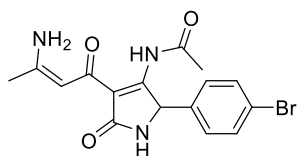
White powder; yield 60%; mp 165-166°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.14 (s, 1H), 11.16 (s, 1H), 7.50 – 7.31 (m, 2H), 7.31 – 7.16 (m, 2H), 7.16 – 7.08 (m, 2H), 7.07 – 6.94 (m, 2H), 6.94 – 6.85 (m, 2H), 6.85 – 6.74 (m, 2H), 6.35 (s, 1H), 5.71 (s, 1H), 3.85 – 3.60 (m, 6H), 3.59 – 3.48 (m, 2H), 2.88 – 2.75 (m, 2H), 2.74 – 2.57 (m, 2H), 2.53 – 2.31 (m, 2H), 1.99 (s, 6H).

^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 181.74, 167.25, 166.39, 166.17, 159.17, 157.92, 157.76, 134.71, 132.62, 130.70, 130.35, 130.00, 129.88, 129.75, 129.40, 128.52, 113.85, 113.82, 108.60, 94.35, 61.73, 54.97, 44.68, 40.89, 34.91, 32.95, 24.06, 19.01. IR spectrum, ν , cm^{-1} : 3449, 3102, 3060, 3007, 2966, 2939, 2908, 2837, 1717, 1673, 1612, 1571, 1513, 1491, 1440, 1414, 1370, 1296, 1280, 1247, 1184, 1089, 1032, 994. HRMS: Calculated for $\text{C}_{34}\text{H}_{36}\text{ClN}_3\text{O}_5$ $[\text{M}+\text{H}]^+$: 602.2416. Found: 602.2414.



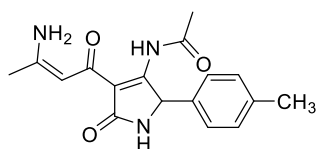
N-(4-(3-Aminobut-2-enoyl)-2-(4-chlorophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7b**)

White powder; yield 41%; mp 281-282°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.21 (s, 1H), 9.90 (s, 1H), 8.29 (s, 1H), 8.07 (s, 1H), 7.37 (d, $J = 7.6$ Hz, 2H), 7.16 (d, $J = 7.8$ Hz, 2H), 6.30 (s, 1H), 5.82 (s, 1H), 2.00 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ 183.45, 169.01, 167.51, 165.73, 161.35, 137.16, 132.12, 129.43, 128.36, 108.88, 93.62, 58.00, 24.17, 21.98. IR spectrum, ν , cm^{-1} : 3650, 3630, 3458, 3307, 3272, 1735, 1700, 1654, 163, 1625, 1596, 1561, 1542, 1508, 1491, 1438, 1421, 1375, 1363, 1301, 1226, 1194, 1129, 1087, 1040, 1015, 993. HRMS: Calculated for $\text{C}_{16}\text{H}_{16}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$: 334.0953. Found: 334.0953.



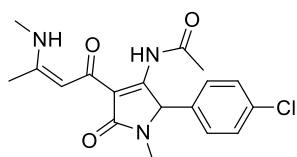
N-(4-(3-Aminobut-2-enoyl)-2-(4-bromophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7c**)

White powder; yield 42%; mp 290-291°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.21 (s, 1H), 9.89 (s, 1H), 8.30 (s, 1H), 8.07 (s, 1H), 7.50 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.4$ Hz, 2H), 6.30 (s, 1H), 5.80 (s, 1H), 2.00 (s, 3H), 1.8 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ 183.43, 169.00, 167.51, 165.74, 161.27, 137.59, 131.28, 129.77, 120.66, 108.87, 93.60, 58.07, 24.18, 21.98. IR spectrum, ν , cm^{-1} : 3630, 3442, 2923, 1735, 1702, 1655, 1637, 1625, 1561, 1490, 1458, 1438, 1375, 1293, 1220, 1193, 1179, 1128, 1107, 1073, 1035, 1012. HRMS: Calculated for $\text{C}_{16}\text{H}_{16}\text{BrN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$: 378.0448. Found: 378.0442.



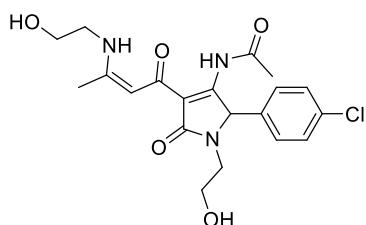
N-(4-(3-Aminobut-2-enoyl)-5-oxo-2-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7d**)

White powder; yield 30%; mp 260-261°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.17 (s, 1H), 9.88 (s, 1H), 8.21 (s, 1H), 8.03 (s, 1H), 7.10 (d, $J = 7.9$ Hz, 2H), 7.02 (d, $J = 8.0$ Hz, 2H), 6.31 (s, 1H), 5.77 (s, 1H), 2.26 (s, 3H), 1.98 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO-}d_6$) δ 183.66, 169.05, 167.36, 165.55, 161.97, 136.82, 135.09, 128.87, 127.38, 109.53, 108.81, 93.62, 58.38, 24.19, 21.97, 20.68. IR spectrum, ν , cm^{-1} : 3179, 3073, 1700, 1655, 1626, 1577, 1560, 1438, 1430, 1357, 1307, 1229, 1193, 1182, 1128, 1113, 994, 913. HRMS: Calculated for $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3$ $[\text{M}+\text{H}]^+$: 314.1499. Found: 314.1506.



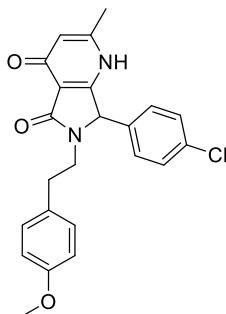
N-(2-(4-Chlorophenyl)-1-methyl-4-(3-(methylamino)but-2-enoyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7e**)

White powder; yield 59%; mp 210-211°C; ^1H NMR (300 MHz, $\text{DMSO-}d_6$) δ 12.18 (s, 1H), 10.98 (s, 1H), 7.40 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 6.39 (s, 1H), 5.82 (s, 1H), 2.99 (d, $J = 5.2$ Hz, 3H), 2.54 (s, 3H), 2.05 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (101 MHz, $\text{DMSO-}d_6$) δ 181.60, 167.33, 166.51, 158.98, 134.83, 132.56, 129.89, 128.56, 108.78, 94.09, 63.03, 29.70, 26.04, 24.07, 21.39, 19.15. IR spectrum, ν , cm^{-1} : 1719, 1692, 1626, 1573, 1519, 1489, 1445, 1418, 1388, 1305, 1275, 1190, 1156, 1103, 1077, 1013, 991, 954. HRMS: Calculated for $\text{C}_{18}\text{H}_{20}\text{ClN}_3\text{O}_3$ $[\text{M}+\text{H}]^+$: 362.1266. Found: 362.1266.



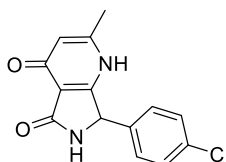
N-(2-(4-Chlorophenyl)-1-(2-hydroxyethyl)-4-(3-((2-hydroxyethyl)amino)but-2-enoyl)-5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)acetamide (**7f**)

White powder; yield 57%; mp 174-175°C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 12.15 (s, 1H), 11.14 (s, 1H), 7.40 (d, $J = 7.4$ Hz, 2H), 7.15 (d, $J = 7.8$ Hz, 2H), 6.39 (s, 1H), 6.02 (s, 1H), 4.96 (s, 1H), 4.78 (s, 1H), 3.65-3.35 (m, 4H), 3.34-3.26 (m, 4H), 2.07 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$) δ 181.79, 167.50, 166.66, 166.46, 159.54, 134.92, 132.63, 130.16, 128.57, 108.77, 94.44, 62.38, 60.12, 59.30, 45.57, 41.45, 24.20, 19.49. IR spectrum, ν , cm^{-1} : 3364, 2927, 1716, 1657, 1622, 1578, 1519, 1491, 1440, 1414, 1374, 1318, 1254, 1207, 1115, 1074, 1046, 999, 888. HRMS: Calculated for $\text{C}_{20}\text{H}_{24}\text{ClN}_3\text{O}_5$ $[\text{M}+\text{H}]^+$: 422.1477. Found: 422.1471.



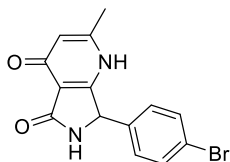
7-(4-Chlorophenyl)-6-(4-methoxyphenethyl)-2-methyl-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1a**)

White powder; yield 60%; mp 251-252°C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 7.44 (d, $J = 7.8$ Hz, 2H), 7.15 (d, $J = 8.1$ Hz, 2H), 7.04 (d, $J = 7.9$ Hz, 2H), 6.81 (d, $J = 8.2$ Hz, 2H), 6.45 (s, 1H), 5.37 (s, 1H), 3.95 – 3.77 (m, 1H), 3.70 (s, 3H), 2.85 – 2.67 (m, 2H), 2.68 – 2.55 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (75 MHz, $\text{DMSO}-d_6$) δ 165.33, 157.77, 134.96, 133.17, 130.69, 129.87, 129.47, 129.24, 128.91, 128.35, 115.25, 113.84, 112.73, 110.63, 62.54, 54.95, 40.89, 32.89, 22.42. IR spectrum, ν , cm^{-1} : 3440, 3274, 2959, 2928, 1773, 1685, 1677, 1647, 1617, 1542, 1514, 1491, 1458, 1439, 1412, 1390, 1282, 1245, 1180, 1087, 1036, 1015, 833. HRMS: Calculated for $\text{C}_{23}\text{H}_{21}\text{ClN}_2\text{O}_3$ $[\text{M}+\text{H}]^+$: 409.1313. Found: 409.1311.



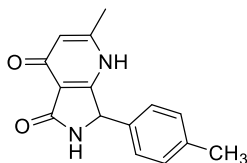
7-(4-Chlorophenyl)-2-methyl-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1b**)

White powder; yield 50%; mp >300°C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.64 (s, 1H), 7.42 (s, 2H), 7.32 (s, 2H), 6.45 (s, 1H), 5.53 (s, 1H), 2.28 (s, 3H). ¹³C NMR (75 MHz, DMSO-*d*₆) δ 167.82, 137.22, 134.65, 132.51, 129.78, 129.10, 128.48, 128.01, 126.61, 110.73, 58.77, 24.40. IR spectrum, ν, cm⁻¹: 3137, 3089, 2959, 2922, 2361, 1694, 1647, 1614, 1541, 1492, 1448, 1338, 1248, 1215, 1180, 1091, 1017, 833. HRMS: Calculated for C₁₄H₁₁ClN₂O₂ [M+H]⁺: 275.0582. Found: 275.0579.



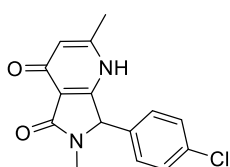
7-(4-Bromophenyl)-2-methyl-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1c**)

White powder; yield 60%; mp 190-191°C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.17 (s, 1H), 8.71 (s, 1H), 7.56 (d, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 6.59 (s, 1H), 5.50 (s, 1H), 2.30 (s, 3H). ¹³C NMR (151 MHz, DMSO-*d*₆) δ 167.76, 137.62, 131.60, 131.42, 129.80, 129.61, 129.54, 129.30, 121.17, 110.64, 58.69, 22.46. IR spectrum, ν, cm⁻¹: 3432, 3177, 3135, 3089, 3034, 2930, 2857, 1701, 1675, 1647, 1615, 1578, 1516, 1489, 1344, 1214, 1177, 1073, 1014, 859. HRMS: Calculated for C₁₄H₁₁BrN₂O₂ [M+H]⁺: 319.0077. Found: 319.0072.



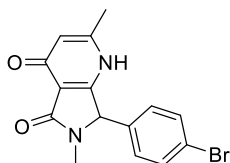
2-Methyl-7-(*p*-tolyl)-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1d**)

White powder; yield 59%; mp >300°C; a mixture of isomers. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.73 (s, 1H), 8.45 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 0.5H), 7.46-7.36 (m, 0.7H), 7.17 (d, *J* = 7.5 Hz, 1.5H), 7.13 (d, *J* = 7.3 Hz, 1.5H), 7.0 (d, *J* = 7.8 Hz, 0.3H), 6.86 (d, *J* = 7.8 Hz, 0.5H), 6.31 (s, 0.1H), 6.15 (s, 0.9H), 5.96 (s, 0.1H), 5.32 (s, 0.9H), 2.53 (s, 0.75H), 2.29 (s, 2.25H), 2.19 (s, 2.25H), 2.15 (s, 0.75H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 167.85, 160.06, 136.39, 135.21, 128.44, 127.59, 126.86, 126.67, 113.30, 110.28, 60.37, 23.27, 20.17. IR spectrum, ν, cm⁻¹: 3412, 3399, 3162, 2959, 2926, 1672, 1646, 1597, 1543, 1513, 1480, 1412, 1272, 1247, 1211, 1181, 1072, 855. HRMS: Calculated for C₁₅H₁₄N₂O₂ [M+H]⁺: 255.1128. Found: 255.1124.



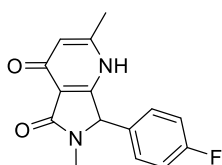
7-(4-Chlorophenyl)-2,6-dimethyl-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1e**)

White powder; yield 59%; mp 270-271°C; ^1H NMR (300 MHz, DMSO- d_6) δ 7.43 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 6.29 (s, 1H), 5.37 (s, 1H), 2.72 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, DMSO- d_6) δ 168.35, 167.38, 165.60, 158.42, 135.53, 132.88, 129.66, 128.86, 113.73, 110.72, 64.49, 26.49, 22.72. IR spectrum, ν , cm^{-1} : 3423, 3086, 3051, 2992, 2946, 2884, 2346, 1697, 1680, 1647, 1552, 1522, 1491, 1426, 1388, 1295, 1275, 1220, 1200, 1155, 1090, 1073, 1043, 1015, 948. HRMS: Calculated for $\text{C}_{15}\text{H}_{13}\text{ClN}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 289.0738. Found: 289.0740.



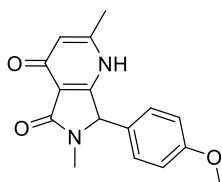
7-(4-Bromophenyl)-2,6-dimethyl-6,7-dihydro-1H-pyrrolo[3,4-b]pyridine-4,5-dione (**1f**)

White powder; yield 70%; mp 201-202°C; ^1H NMR (300 MHz, DMSO- d_6) δ 7.58 (d, J = 6.5 Hz, 2H), 7.13 (d, J = 4.5 Hz, 2H), 6.41 (s, 1H), 5.45 (s, 1H), 2.73 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 166.12, 165.02, 137.79, 135.58, 131.88, 131.42, 130.02, 128.57, 121.63, 112.84, 64.39, 26.57, 23.01. IR spectrum, ν , cm^{-1} : 3492, 3437, 3253, 3109, 2980, 2889, 2830, 2702, 1682, 1643, 1614, 1548, 1511, 1488, 1374, 1267, 1218, 1195, 1146, 1071, 1041, 1012, 934. HRMS: Calculated for $\text{C}_{15}\text{H}_{13}\text{BrN}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 333.0233 Found: 333.0239.



7-(4-Fluorophenyl)-2,6-dimethyl-6,7-dihydro-1H-pyrrolo[3,4-b]pyridine-4,5-dione (**1g**)

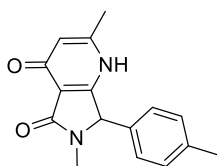
White powder; yield 54%; mp 230-231°C; ^1H NMR (300 MHz, DMSO- d_6) δ 7.29 – 7.11 (m, 4H), 6.37 (s, 1H), 5.44 (s, 1H), 2.72 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, DMSO- d_6) δ 163.67, 163.58, 160.43, 160.35, 132.30, 129.91 (d, J = 8.5 Hz), 128.45 (d, J = 8.4 Hz), 115.81 (d, J = 21.6 Hz), 115.40, 115.11, 64.42, 26.51, 22.98. IR spectrum, ν , cm^{-1} : 3492, 3439, 3255, 3111, 2980, 2891, 2830, 2701, 2346, 1681, 1646, 1611, 1551, 1510, 1473, 1425, 1386, 1265, 1217, 1156, 1080, 1040, 1015, 977. HRMS: Calculated for $\text{C}_{15}\text{H}_{13}\text{FN}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 273.1034. Found: 273.1043



7-(4-Methoxyphenyl)-2,6-dimethyl-6,7-dihydro-1H-pyrrolo[3,4-b]pyridine-4,5-dione (**1h**)

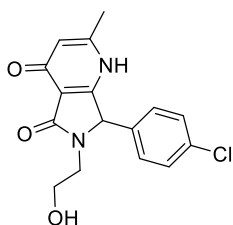
White powder; yield 55%; mp 199-200°C; ^1H NMR (300 MHz, DMSO- d_6) δ 7.05 (s, 2H), 6.92 (d, 2H), 6.23 (s, 1H), 5.30 (s, 1H), 2.70 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (151 MHz, DMSO- d_6) δ 168.75, 167.50, 165.66, 159.25, 129.03, 127.82, 114.25, 113.83, 113.69, 111.10, 64.66, 55.11, 26.33, 22.32. IR spectrum, ν , cm^{-1} : 3441, 1671, 1643, 1614, 1559, 1541, 1512, 1466, 1393, 1360,

1306, 1265, 1245, 1217, 1181, 1078, 1028, 978, 953. HRMS: Calculated for $C_{16}H_{16}ClN_2O_3$ $[M+H]^+$: 285.1234 Found: 285.1238.



2,6-Dimethyl-7-(*p*-tolyl)-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1i**)

White powder; yield 68%; mp 220-221°C; 1H NMR (300 MHz, $DMSO-d_6$) δ 7.19 (d, J = 7.5 Hz, 2H), 7.05 (d, J = 7.8 Hz, 2H), 6.41 (s, 1H), 5.39 (s, 1H), 2.69 (s, 3H), 2.29 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (75 MHz, $DMSO-d_6$) δ 165.50, 157.12, 137.87, 132.77, 129.49, 129.02, 127.75, 126.09, 113.08, 111.01, 64.40, 26.40, 21.98, 20.72. IR spectrum, ν , cm^{-1} : 3132, 3098, 2959, 2921, 2822, 1671, 1611, 1560, 1516, 1430, 1386, 1254, 1219, 1142, 1038, 851. HRMS: Calculated for $C_{16}H_{16}ClN_2O_2$ $[M+H]^+$: 269.1285. Found: 269.1294.

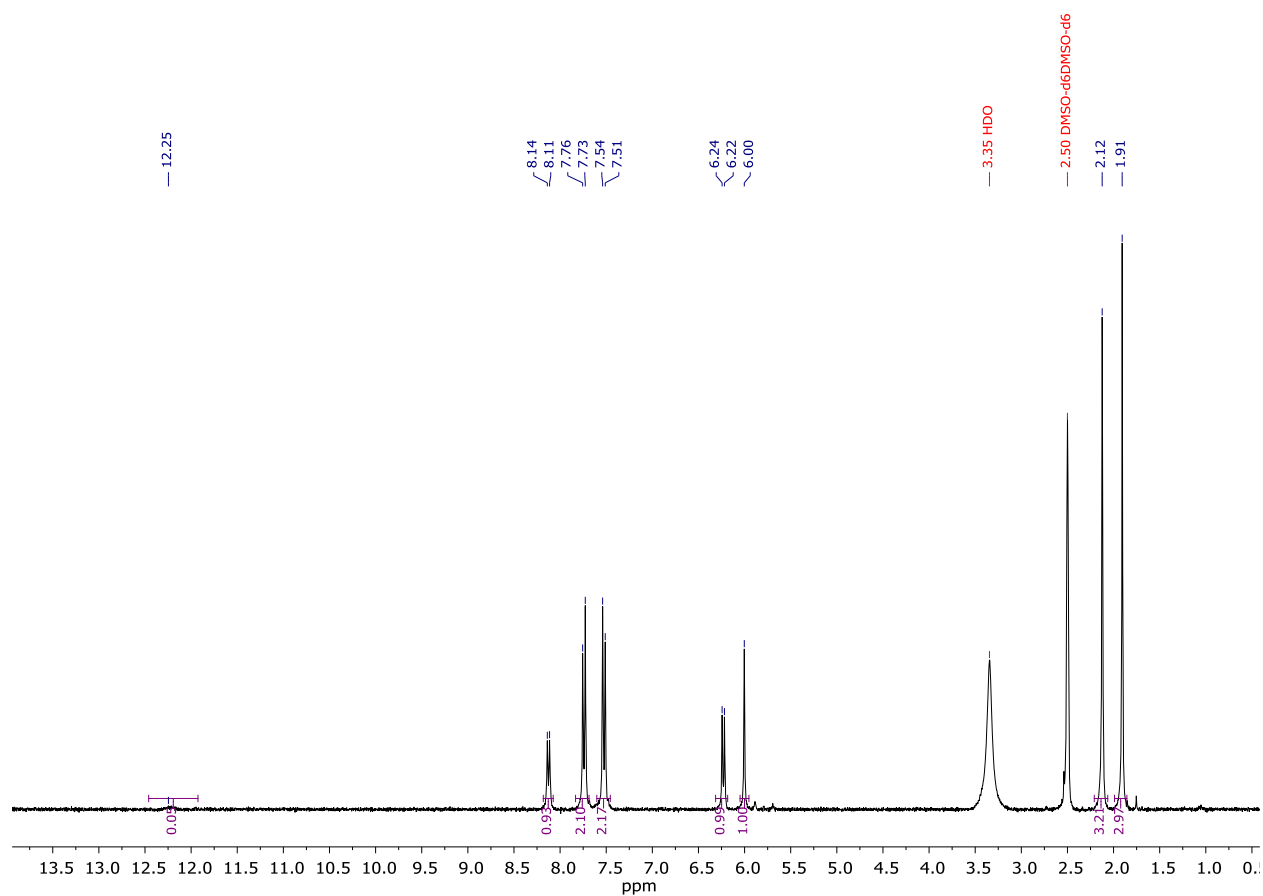


7-(4-Chlorophenyl)-6-(2-hydroxyethyl)-2-methyl-6,7-dihydro-1*H*-pyrrolo[3,4-*b*]pyridine-4,5-dione (**1j**)

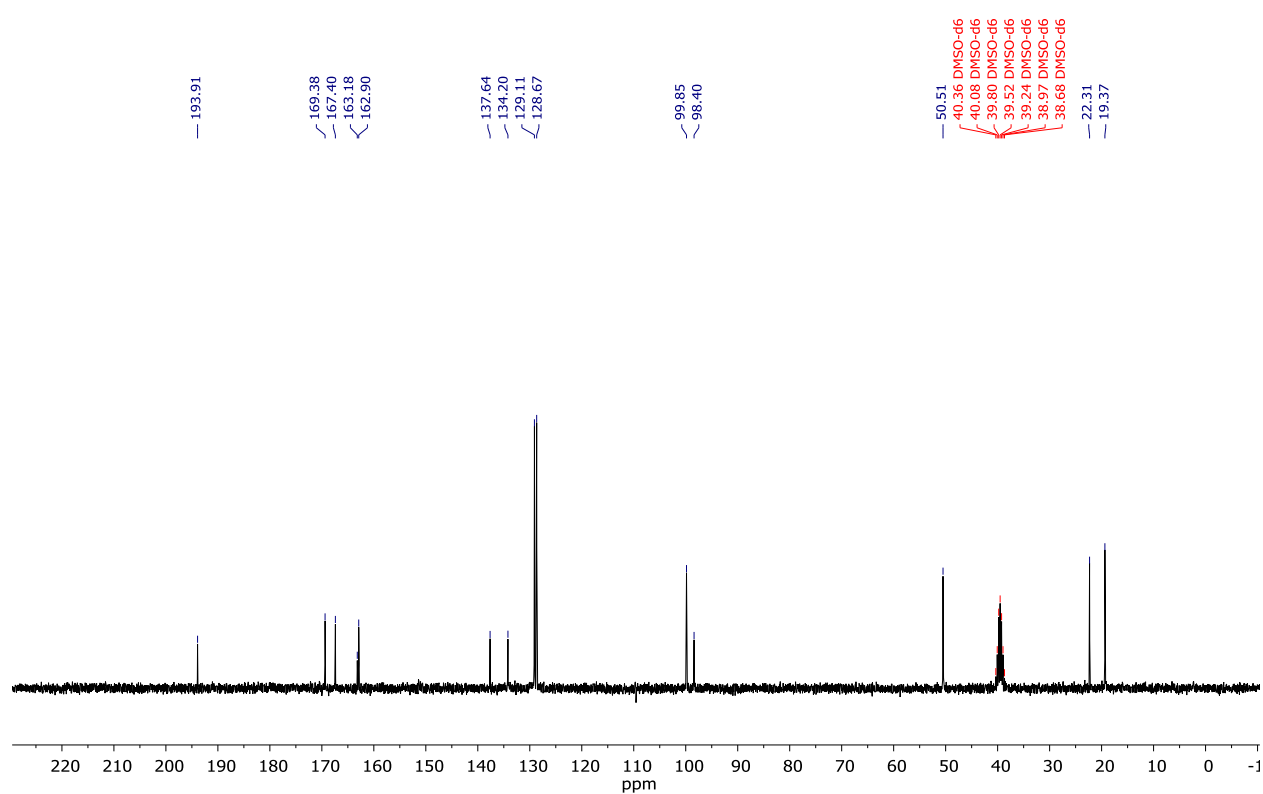
White powder; yield 50%; mp 235-236°C; 1H NMR (300 MHz, $DMSO-d_6$) δ 7.45 (d, J = 7.3 Hz, 2H), 7.20 (d, J = 7.4 Hz, 2H), 6.44 (s, 1H), 5.61 (s, 1H), 4.77 (s, 1H), 4.14 – 3.63 (m, 1H), 3.6-3.2 (m, 2H), 3.01-2.61 (m, 1H), 2.26 (s, 3H). ^{13}C NMR (126 MHz, $DMSO-d_6$) δ 170.24, 165.77, 135.24, 133.19, 133.08, 129.95, 129.90, 128.97, 128.92, 110.77, 61.71, 58.91, 41.79, 20.66. IR spectrum, ν , cm^{-1} : 3448, 3272, 3117, 2961, 2926, 2857, 1655, 1648, 1561, 1544, 1517, 1491, 1439, 1413, 1390, 1284, 1220, 1201, 1087, 1046, 1016, 845. HRMS: Calculated for $C_{16}H_{15}ClN_2O_3$ $[M+H]^+$: 319.0844. Found: 319.0842.

4. Copies of ^1H and ^{13}C NMR spectra for all compounds

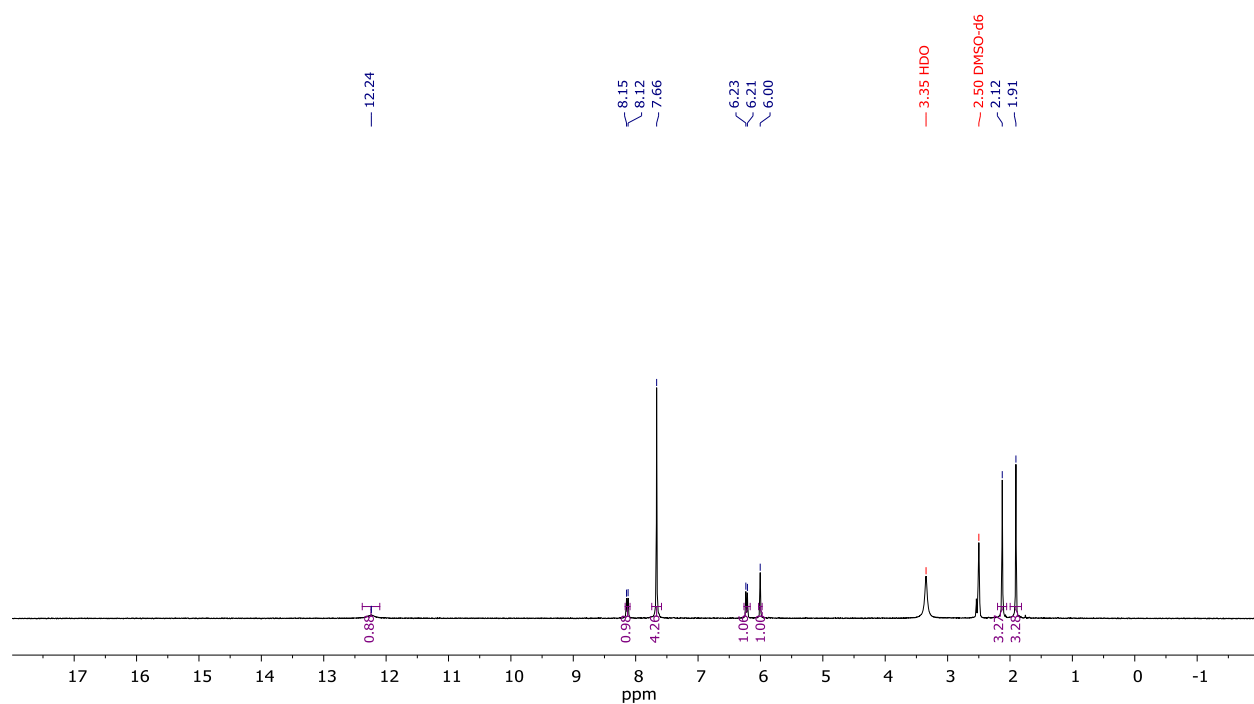
^1H NMR spectrum (300 MHz) for **2a**



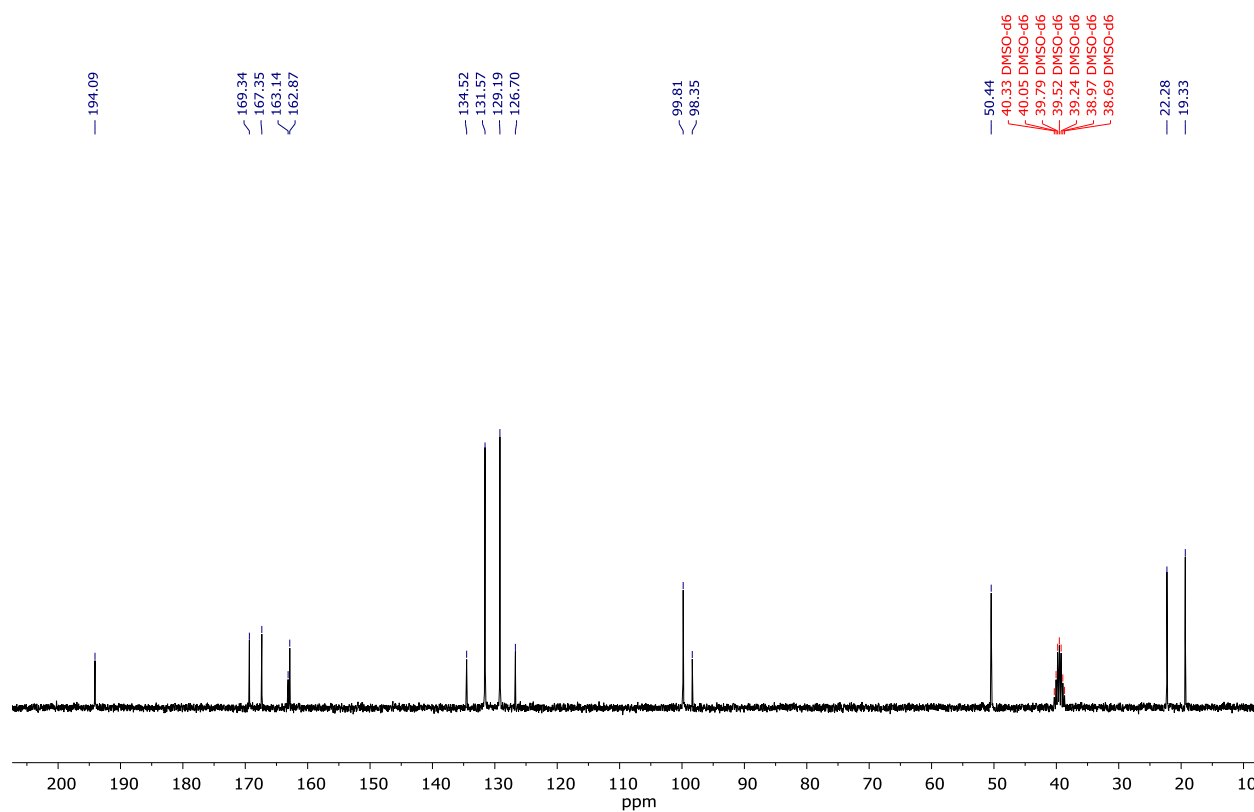
^{13}C NMR spectrum (75 MHz) for **2a**



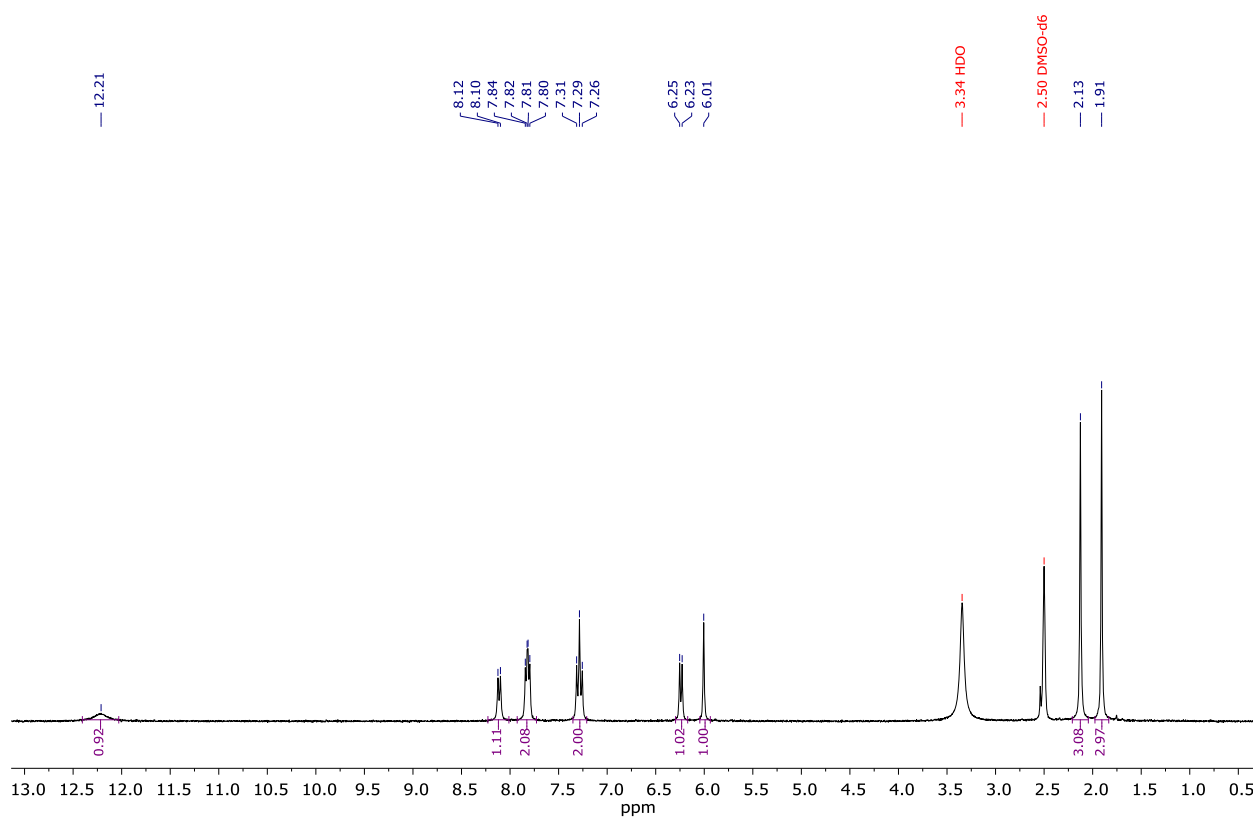
^1H NMR spectrum (300 MHz) for **2b**



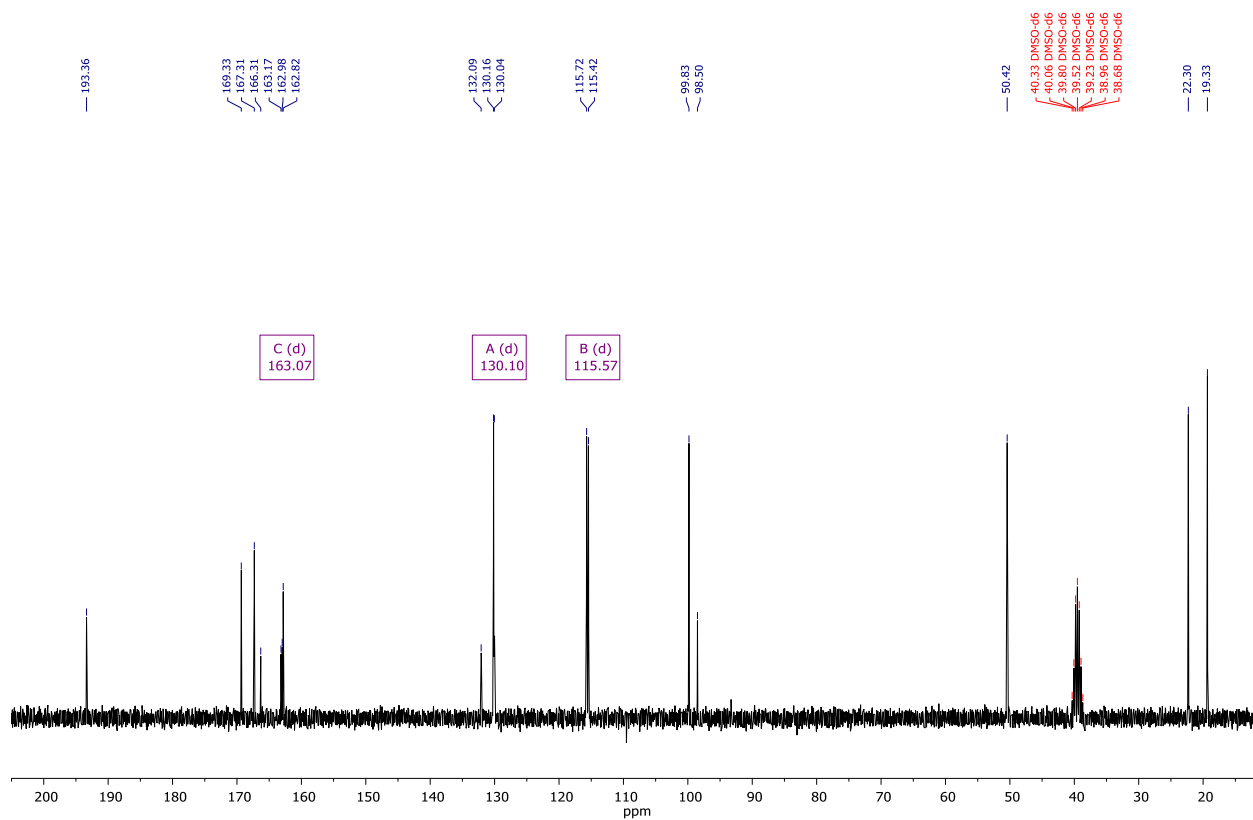
^{13}C NMR spectrum (75 MHz) for **2b**



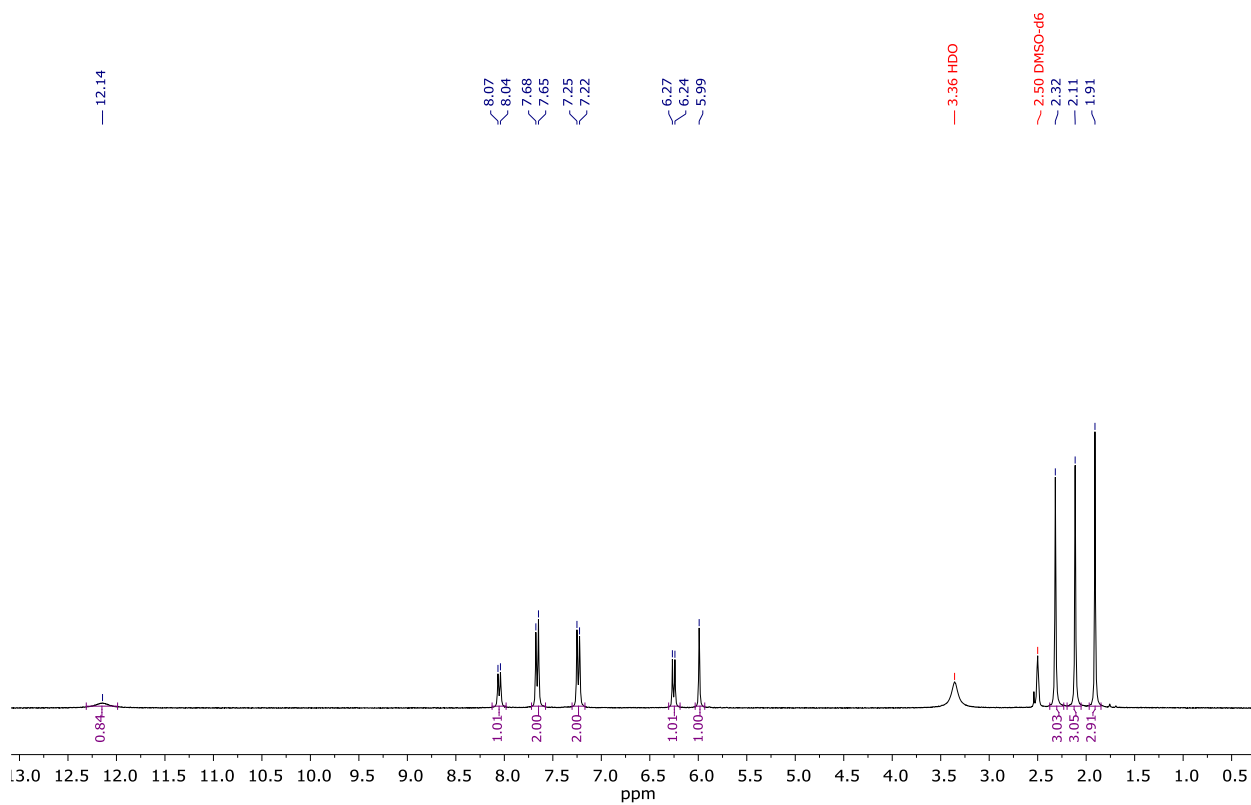
^1H NMR spectrum (300 MHz) for **2c**



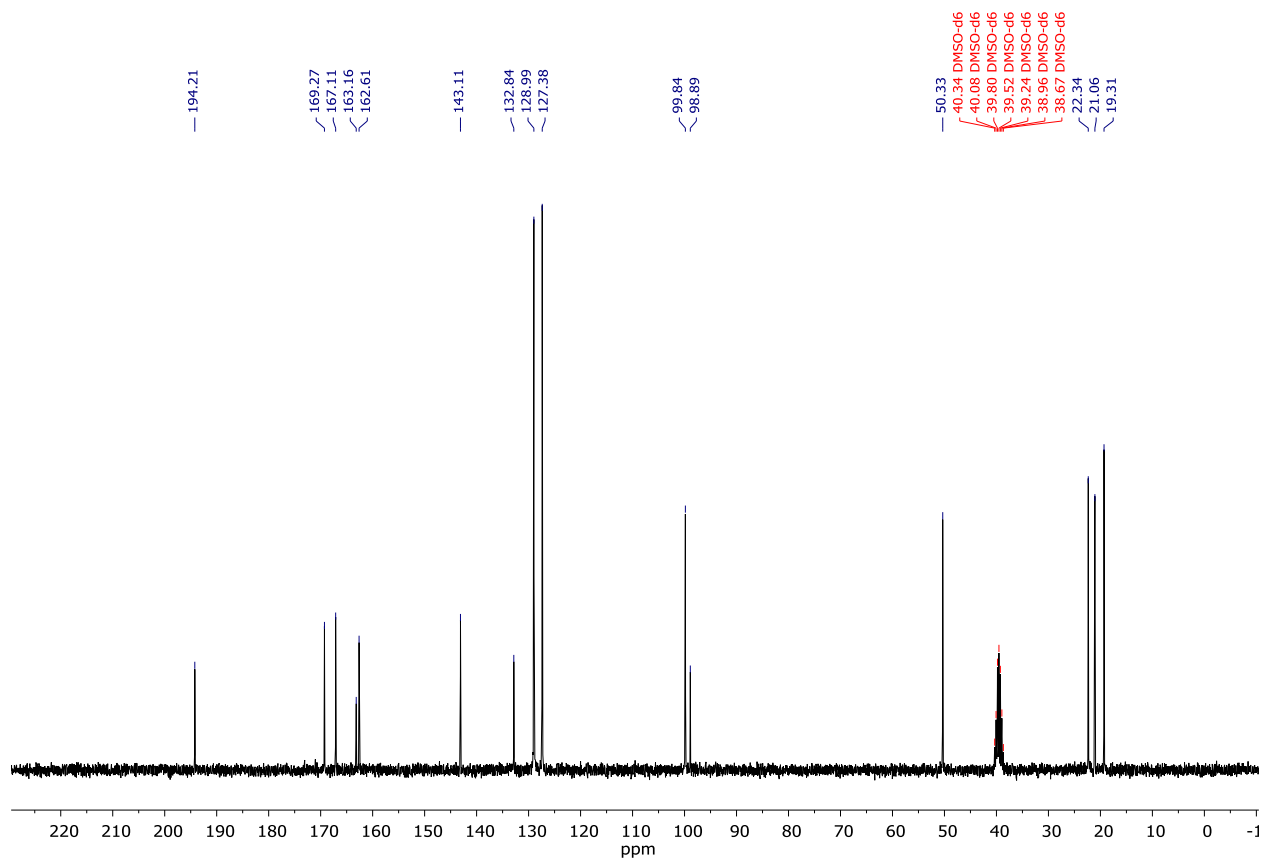
^{13}C NMR spectrum (75 MHz) for **2c**



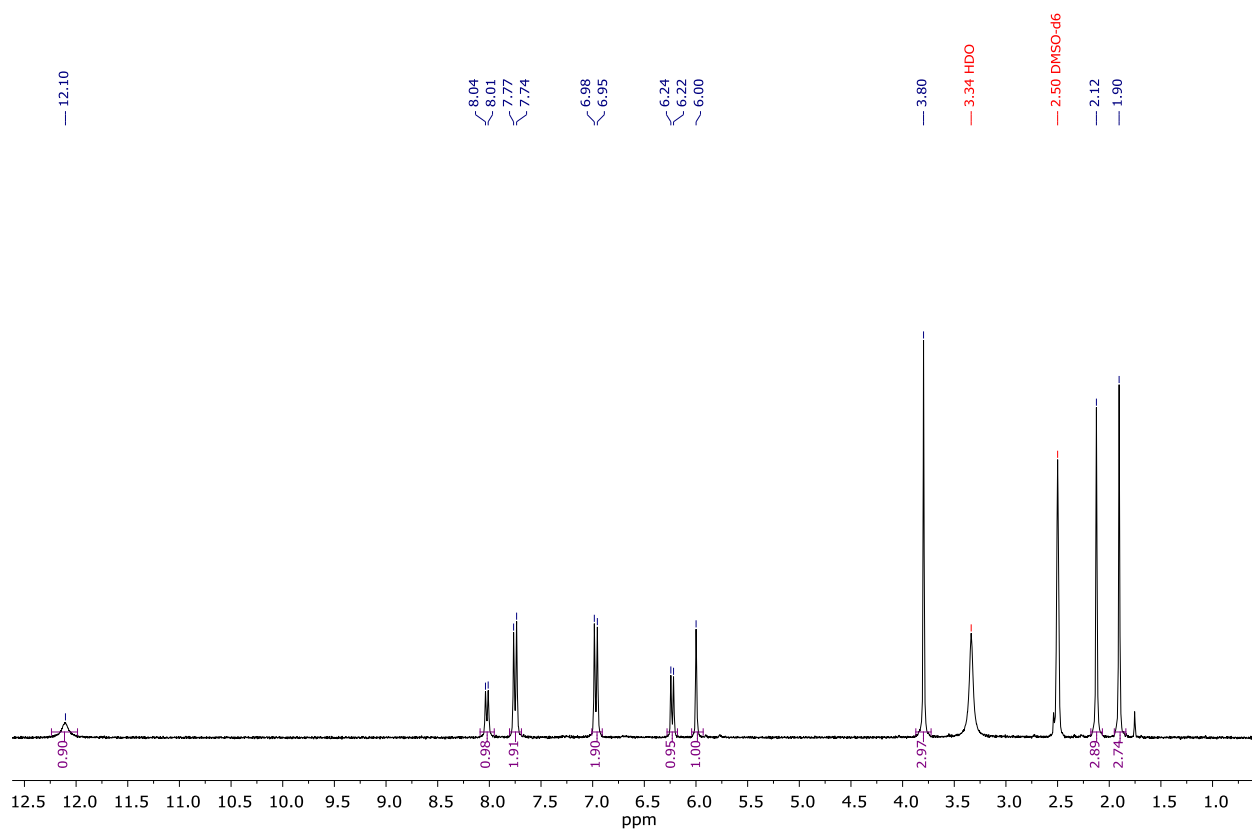
^1H NMR spectrum (300 MHz) for **2d**



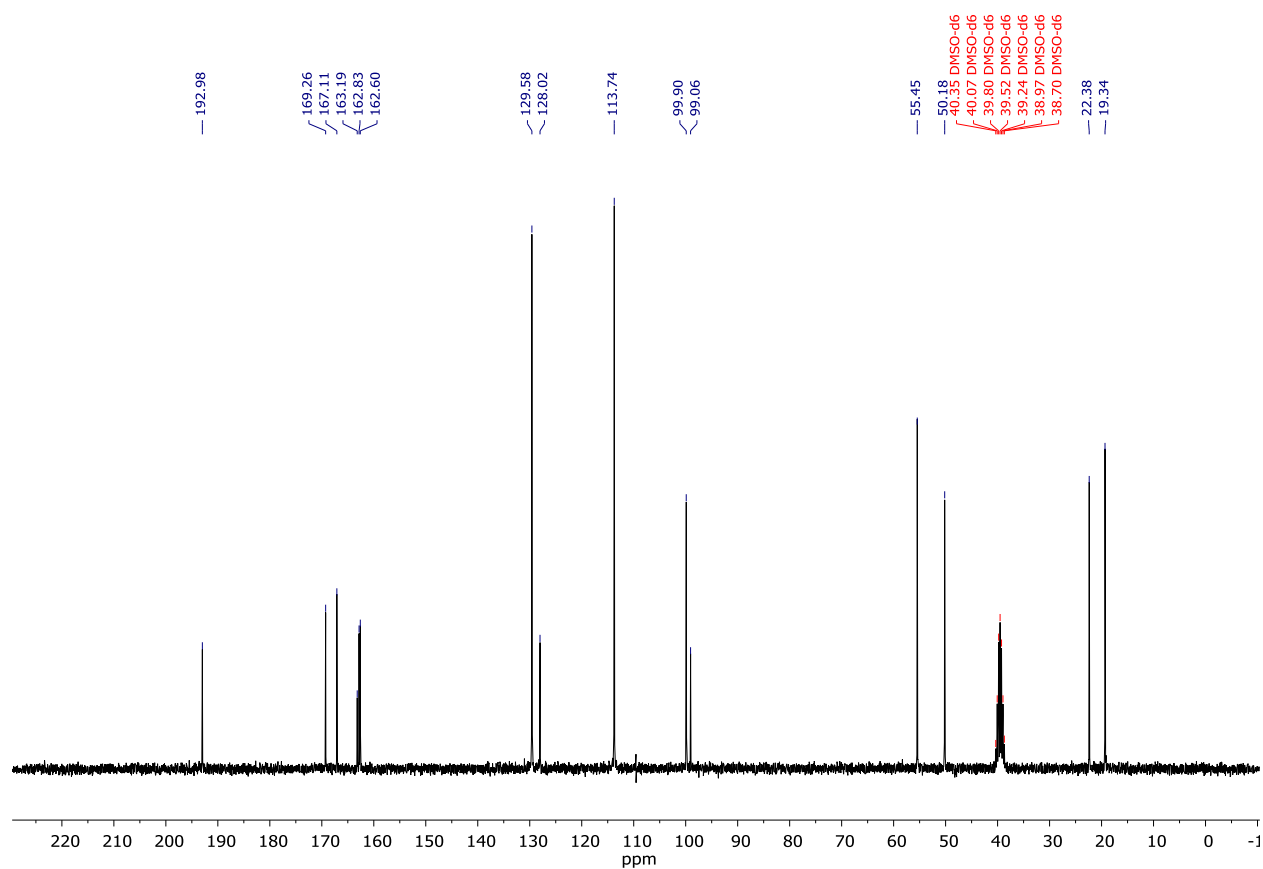
^{13}C NMR spectrum (75 MHz) for **2d**



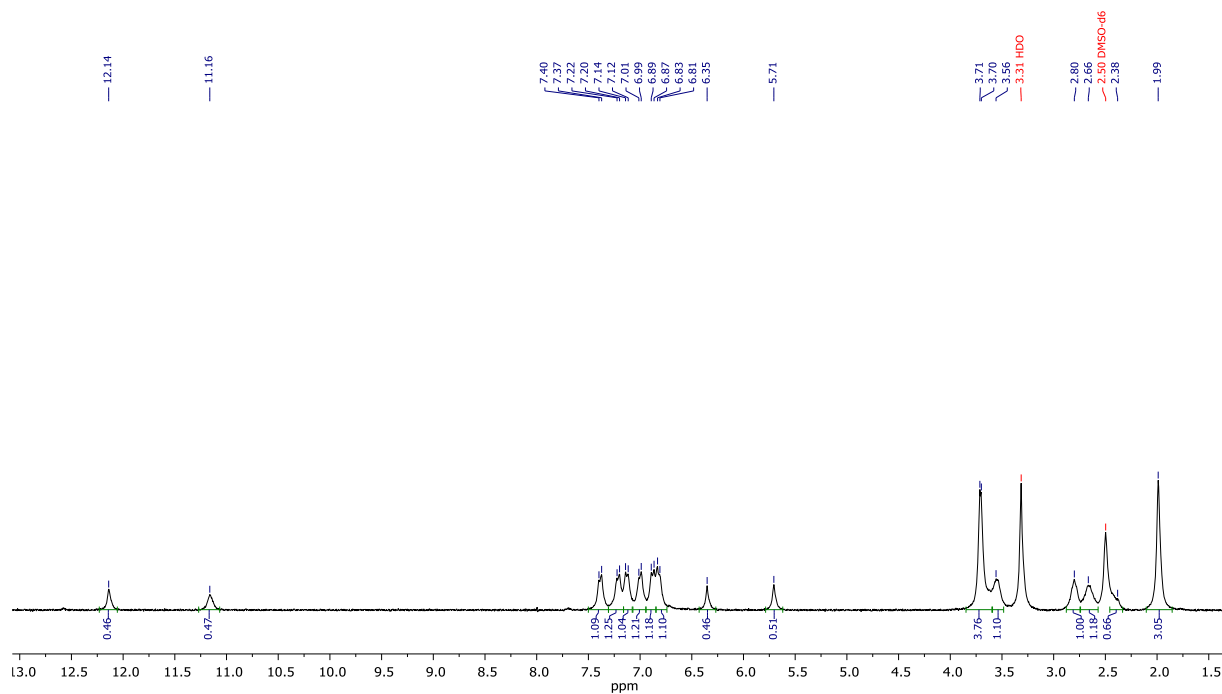
^1H NMR spectrum (300 MHz) for **2e**



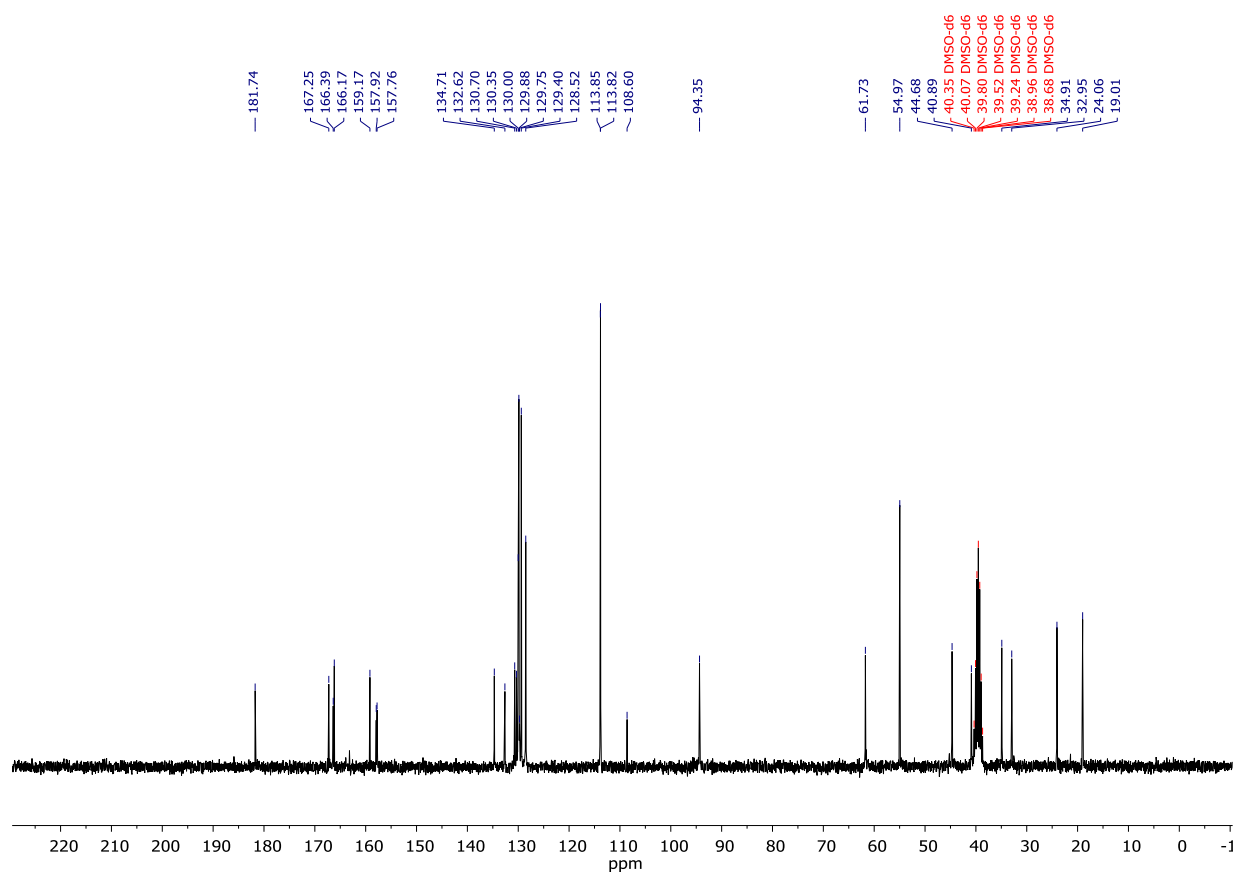
^{13}C NMR spectrum (75 MHz) for **2e**



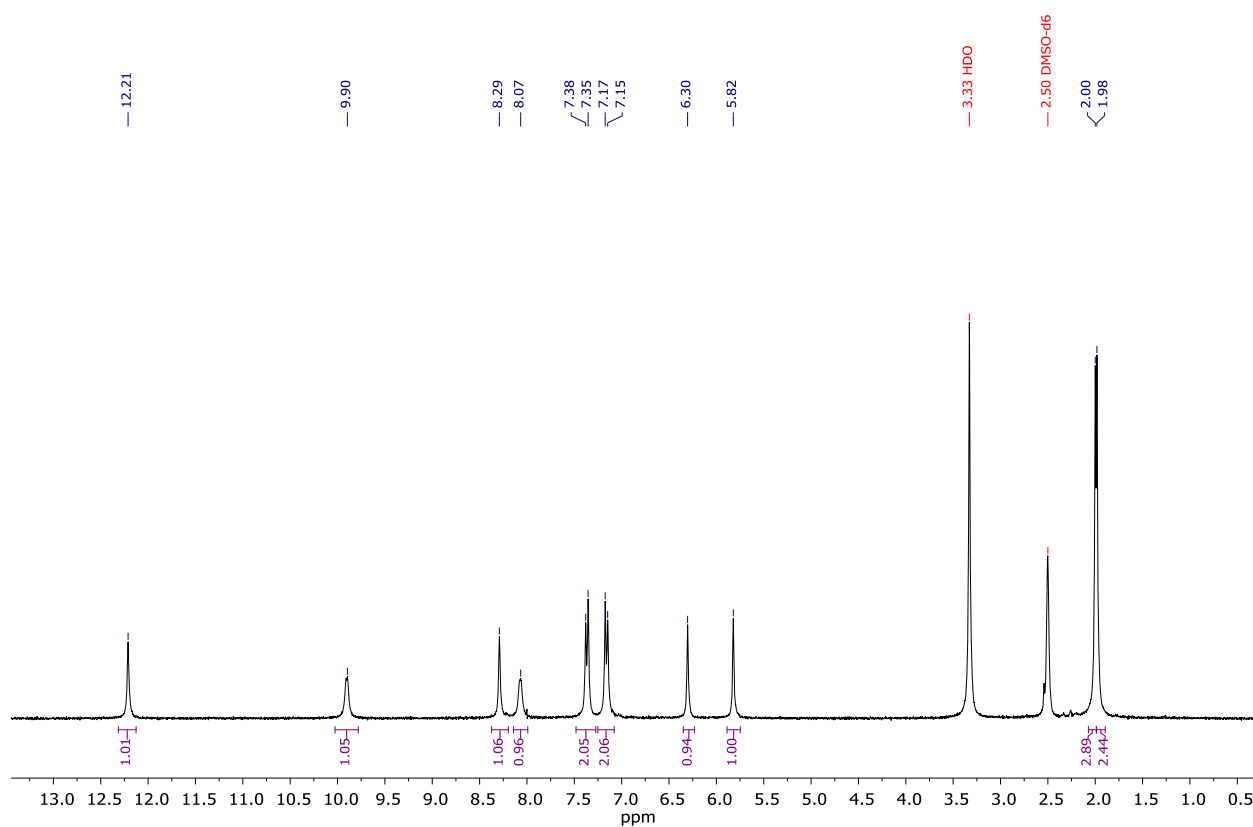
¹H NMR spectrum (300 MHz) for **7a**



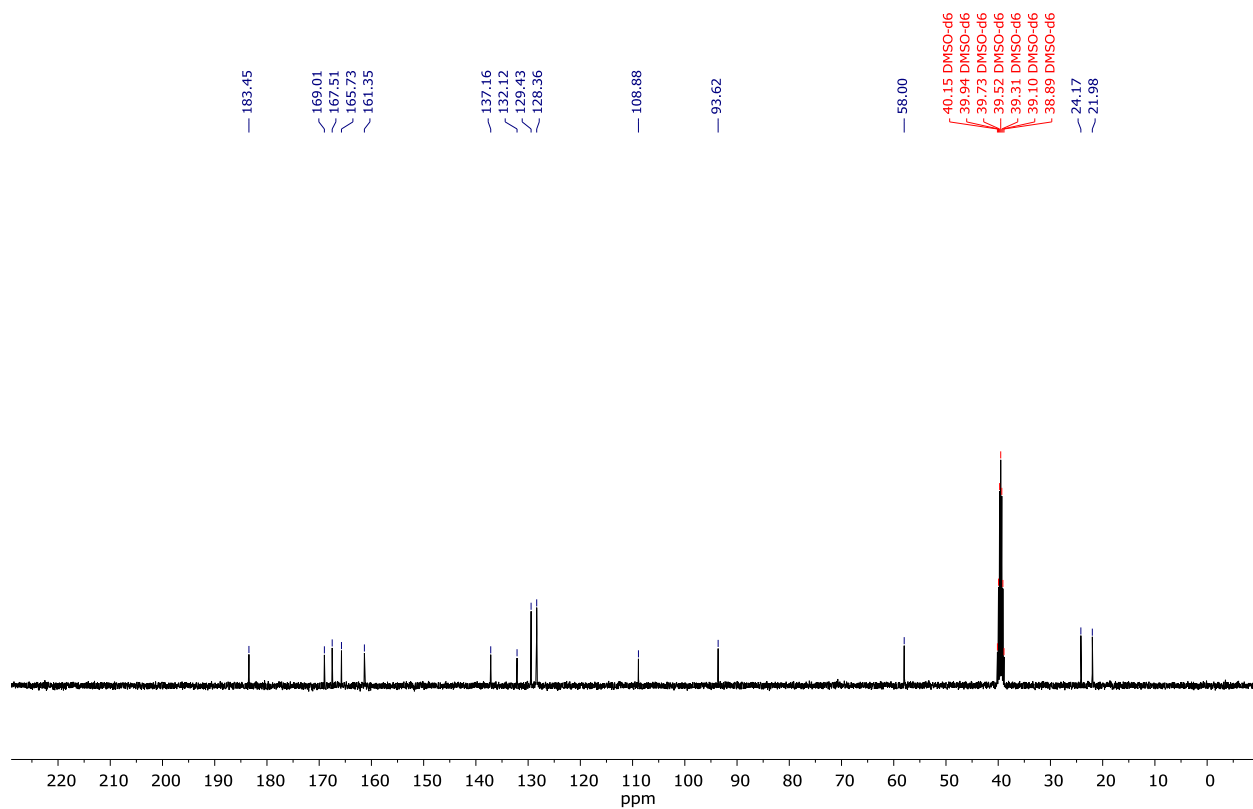
¹³C NMR spectrum (75 MHz) for **7a**



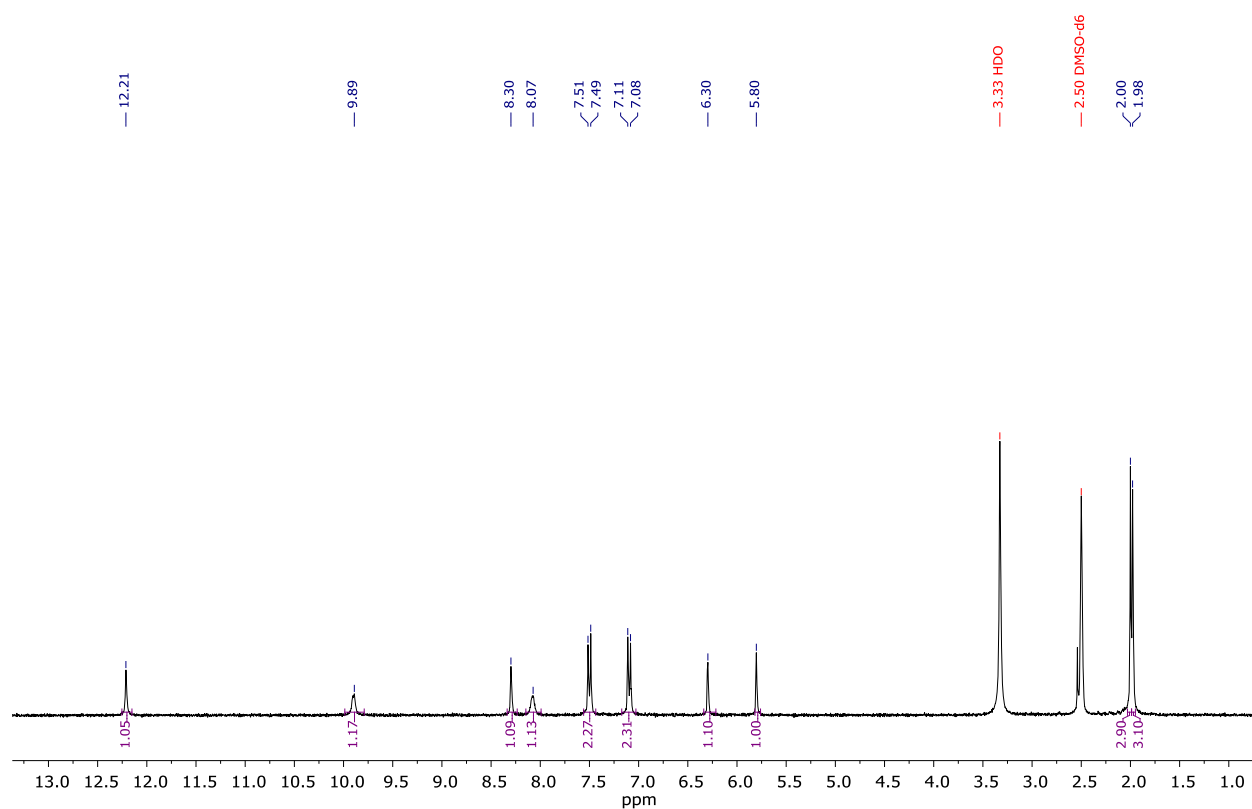
^1H NMR spectrum (300 MHz) for **7b**



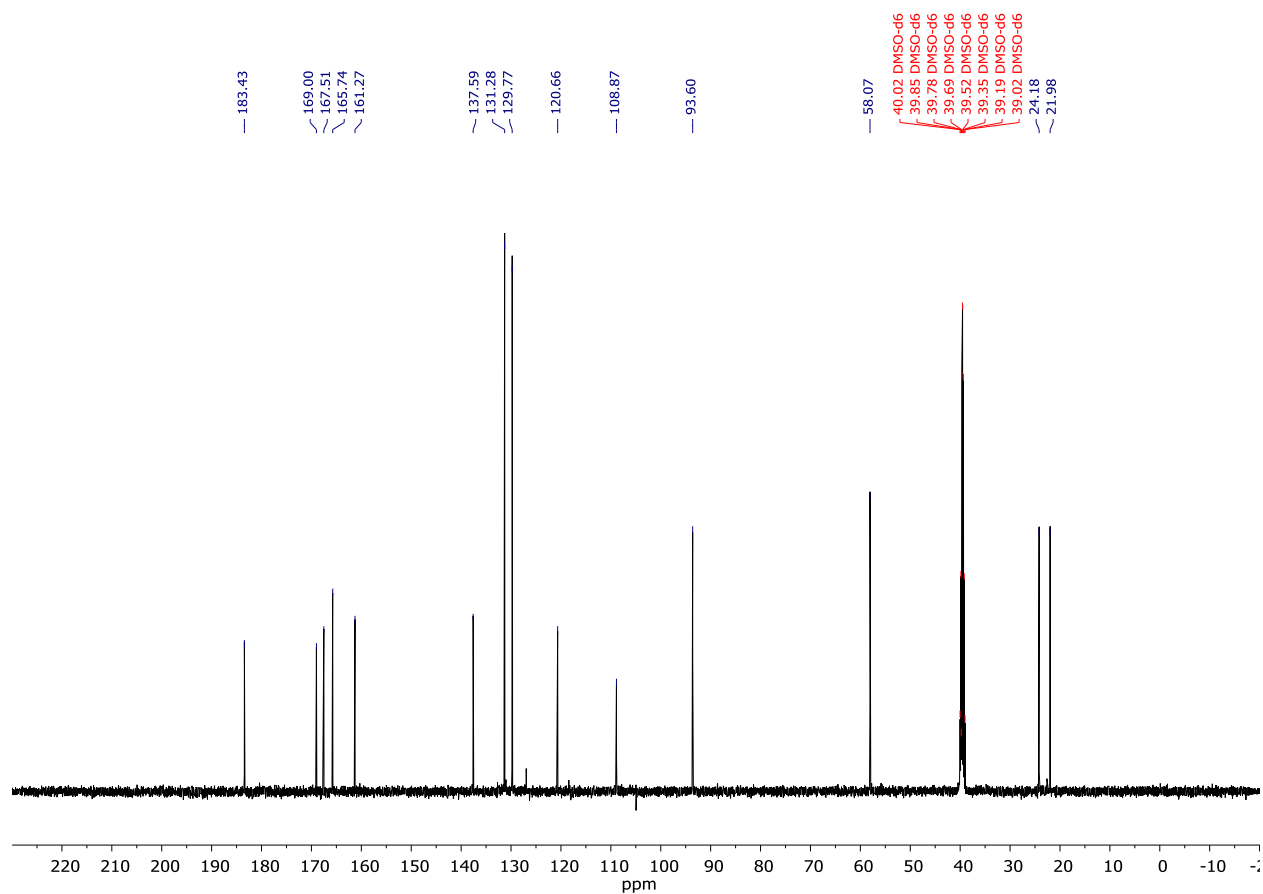
^{13}C NMR spectrum (101 MHz) for **7b**



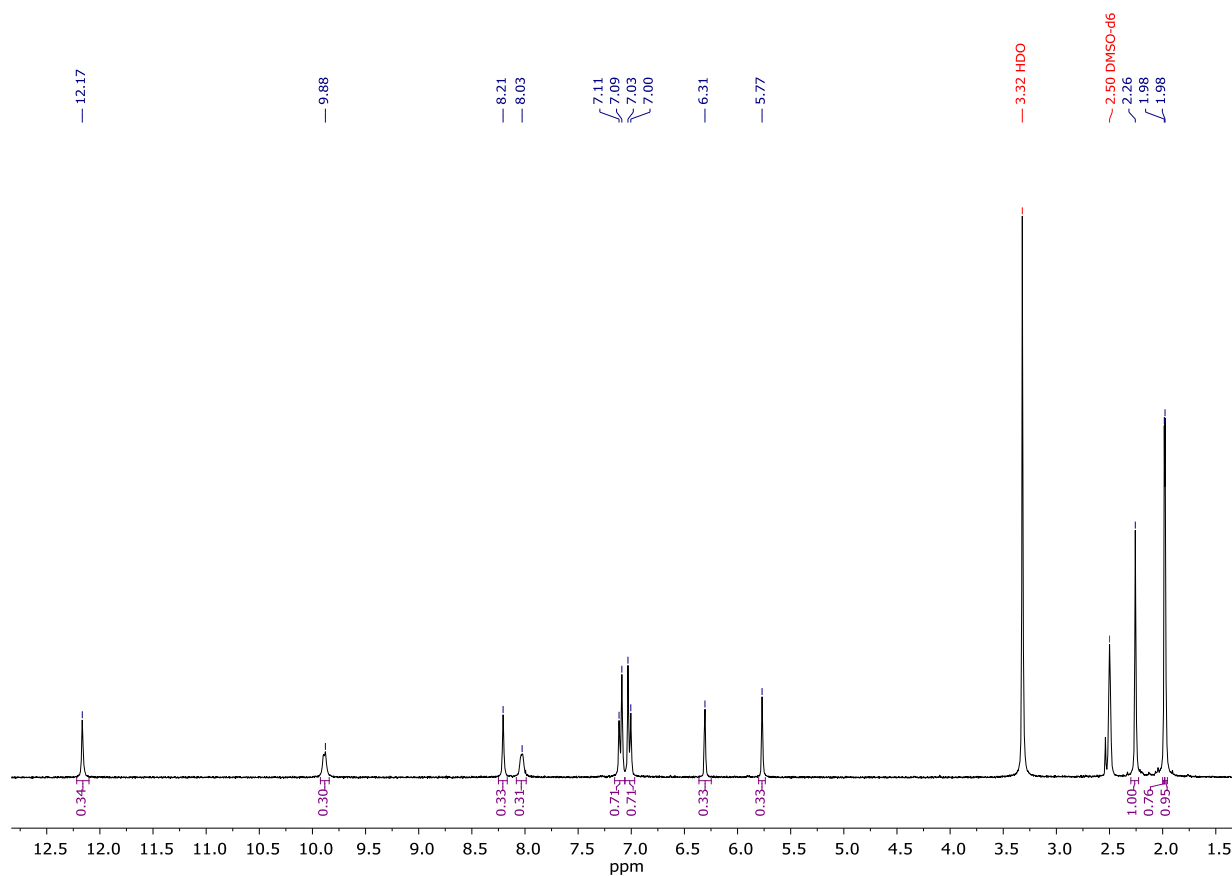
^1H NMR spectrum (300 MHz) for **7c**



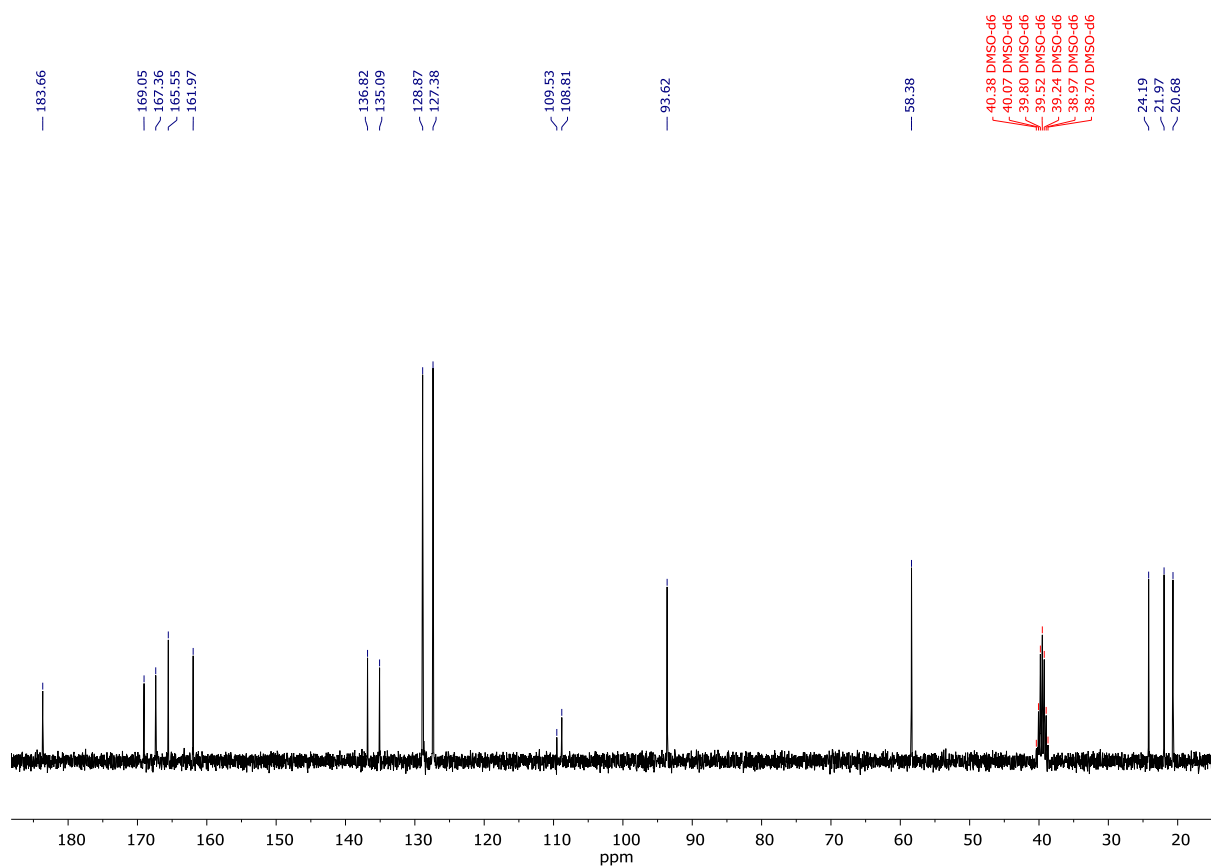
^{13}C NMR spectrum (126 MHz) for **7c**



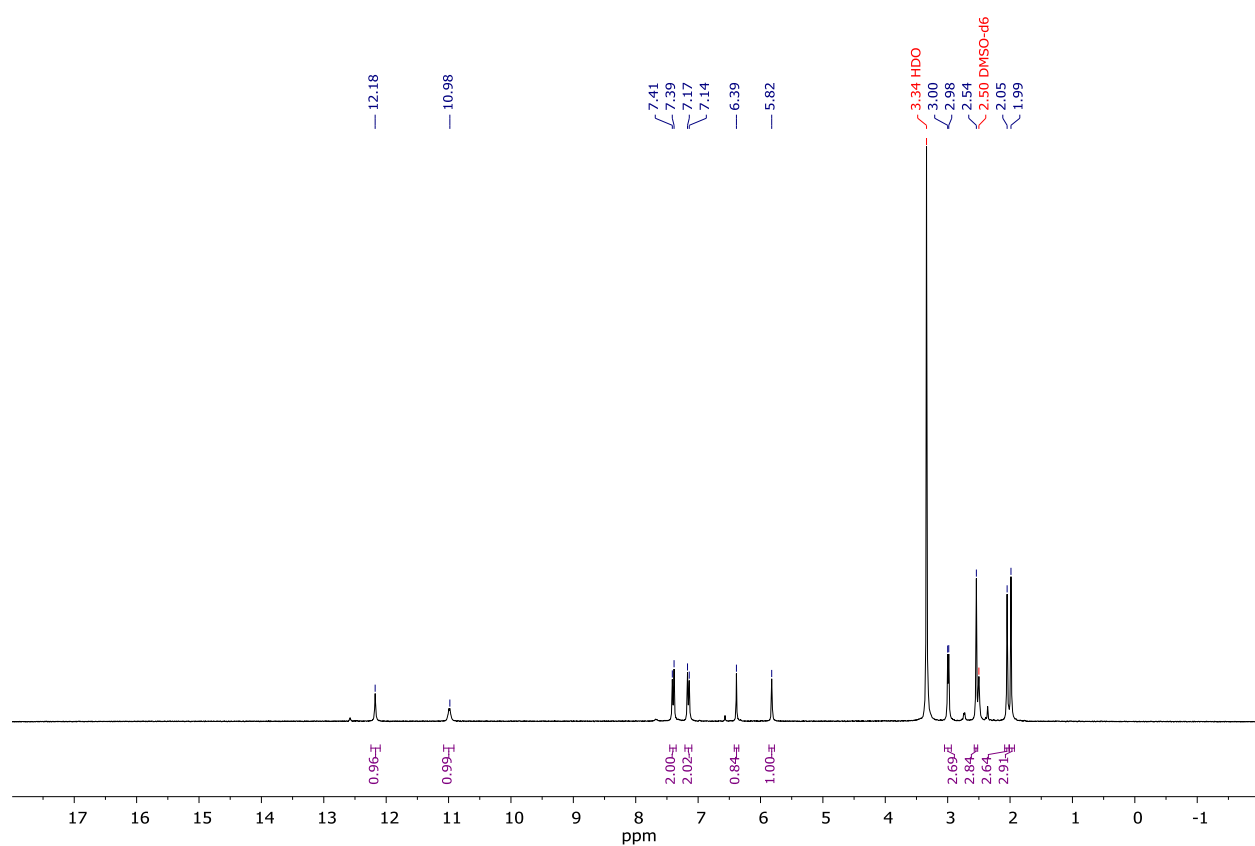
^1H NMR spectrum (300 MHz) for **7d**



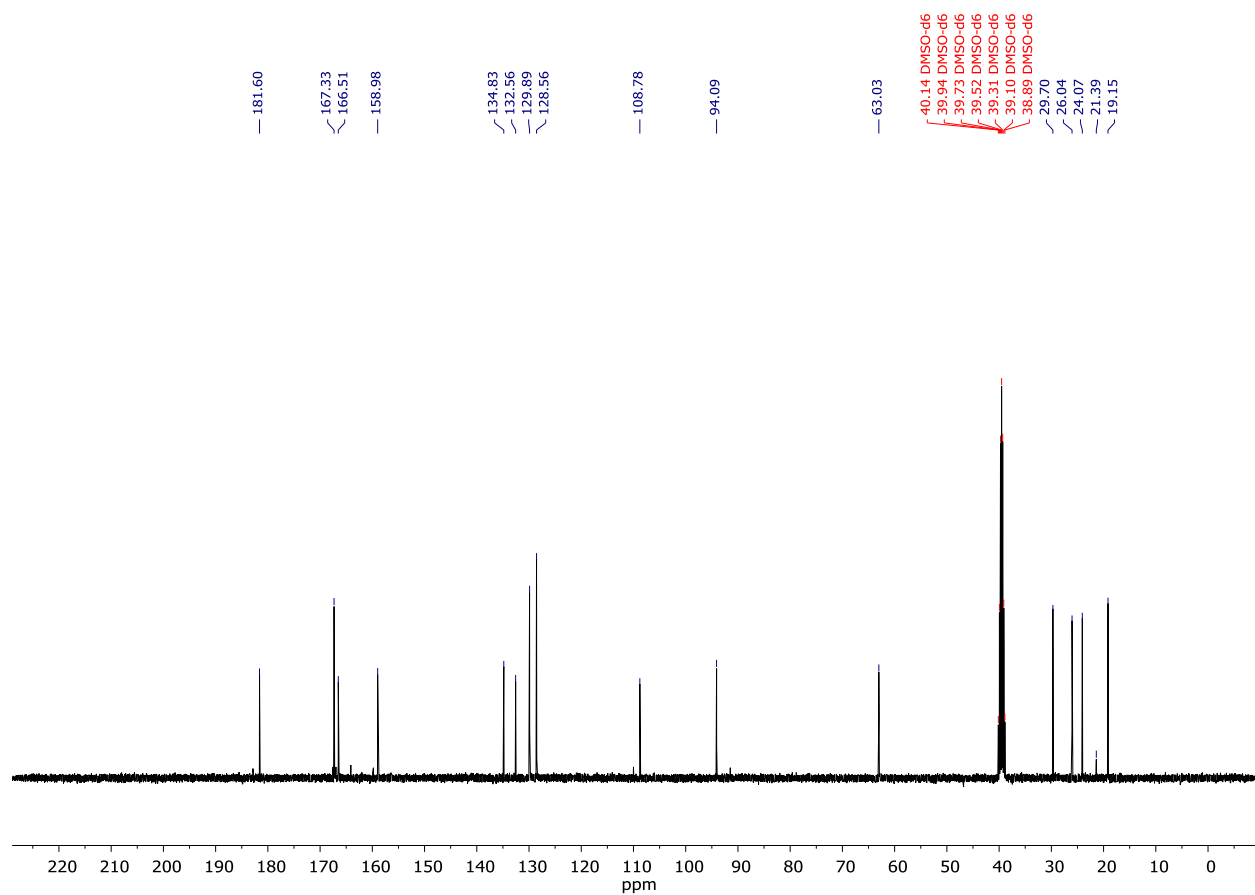
^{13}C NMR spectrum (75 MHz) for **7d**



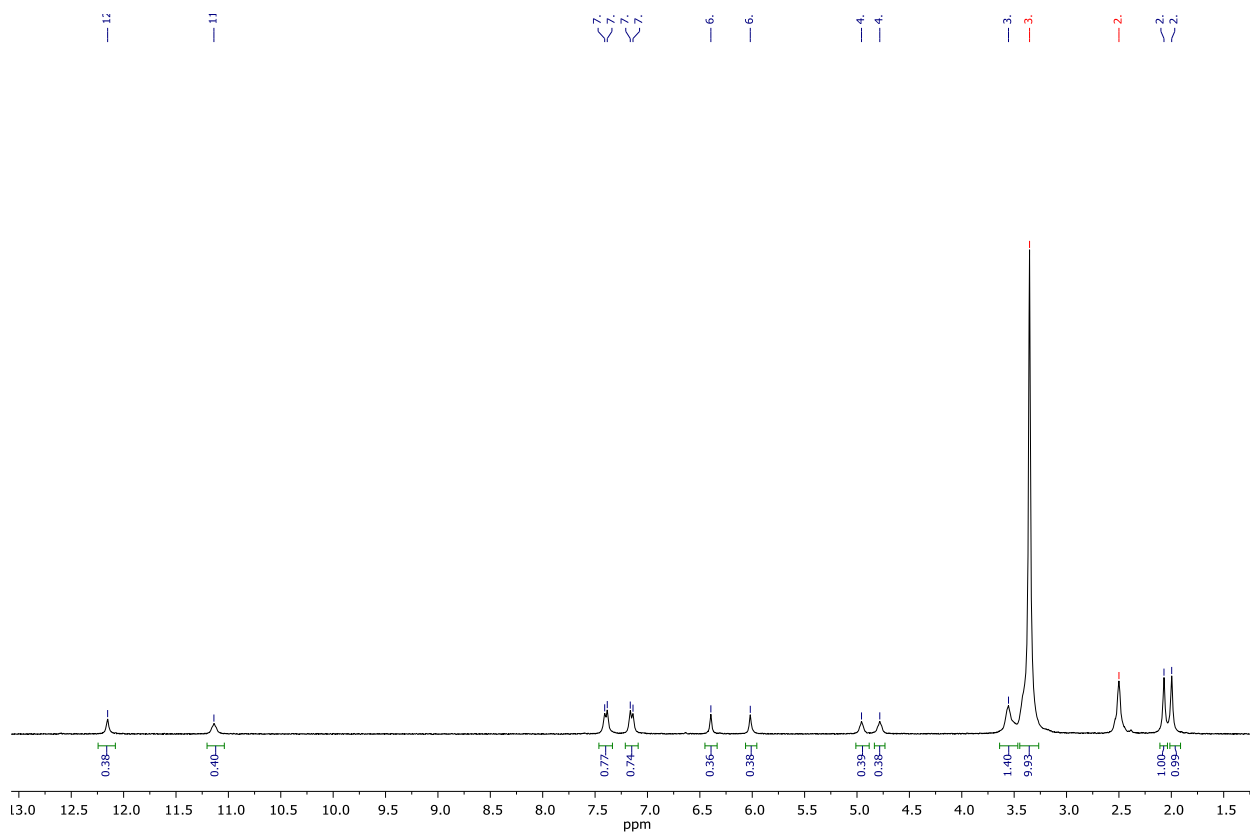
^1H NMR spectrum (300 MHz) for **7i**



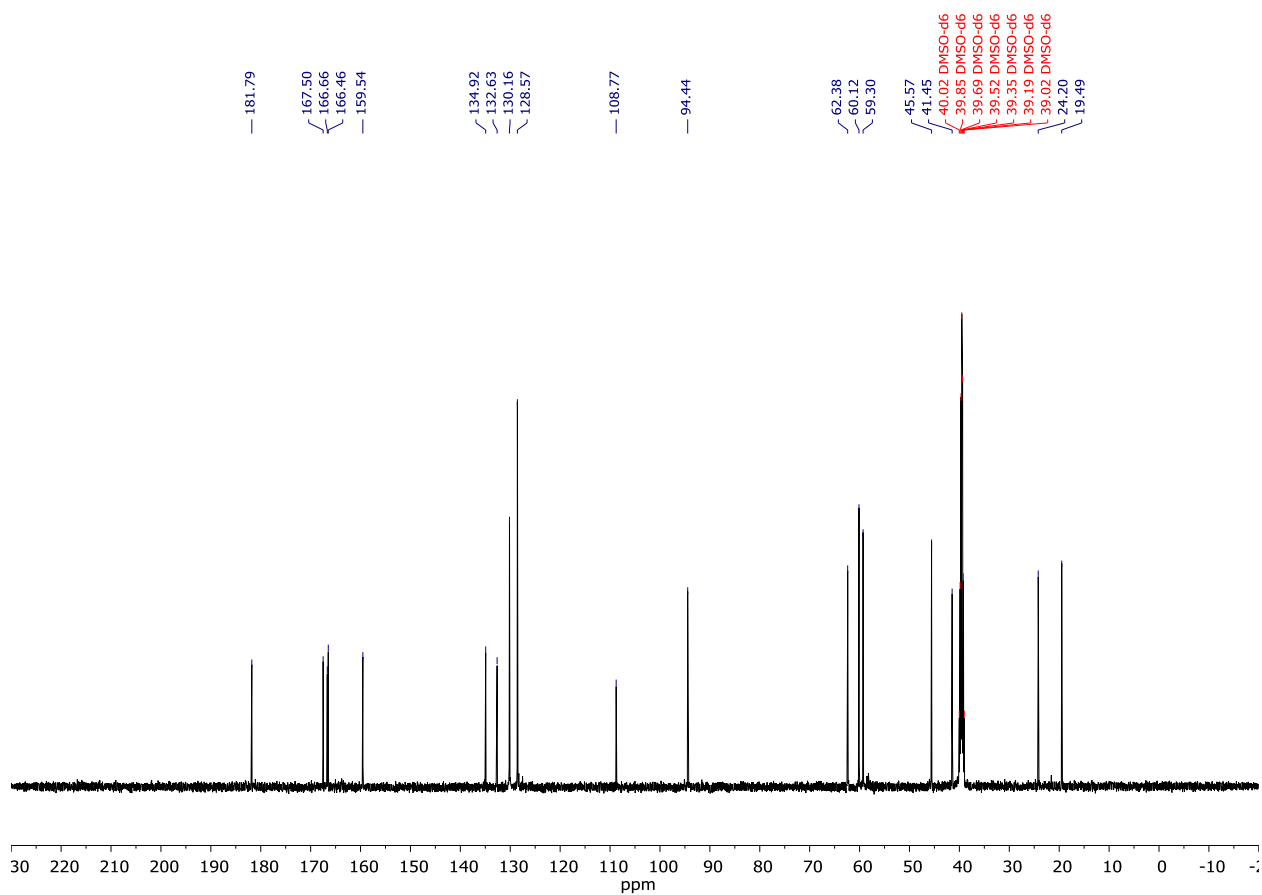
^{13}C NMR spectrum (101 MHz) for **7i**



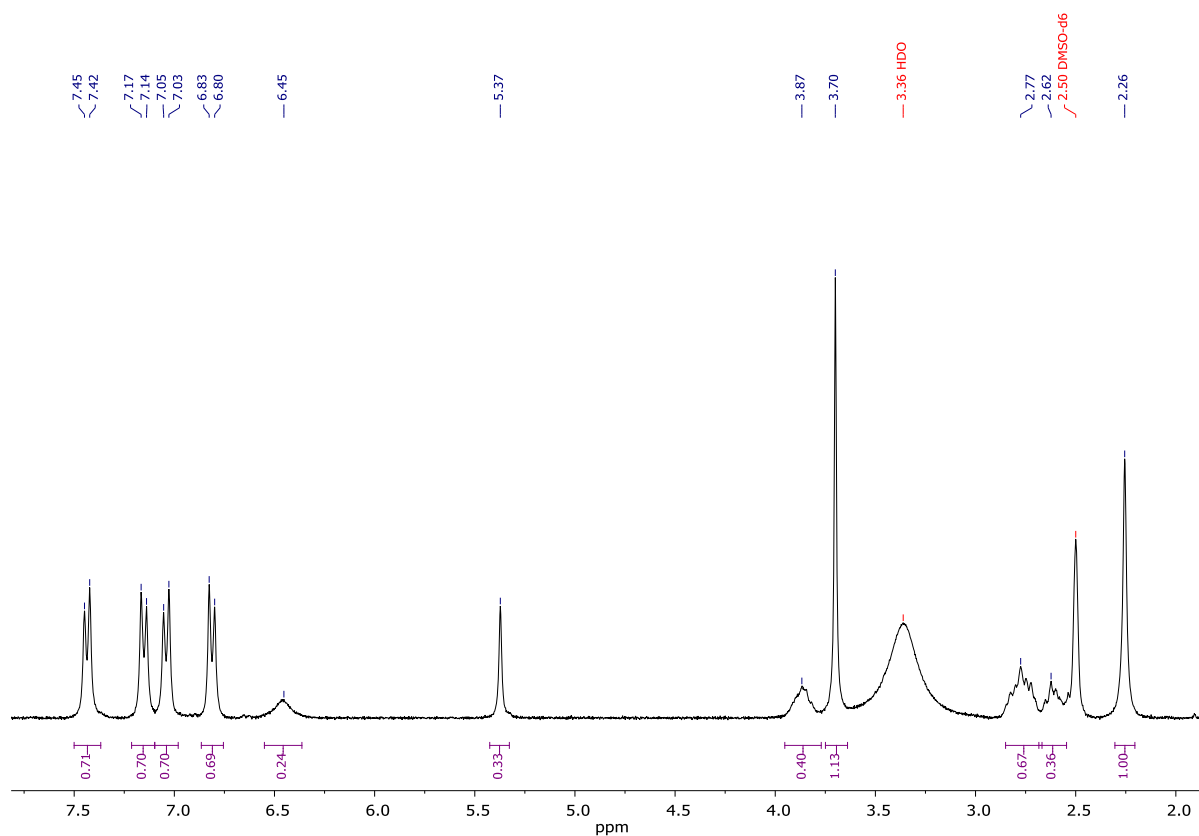
^1H NMR spectrum (300 MHz) for **7f**



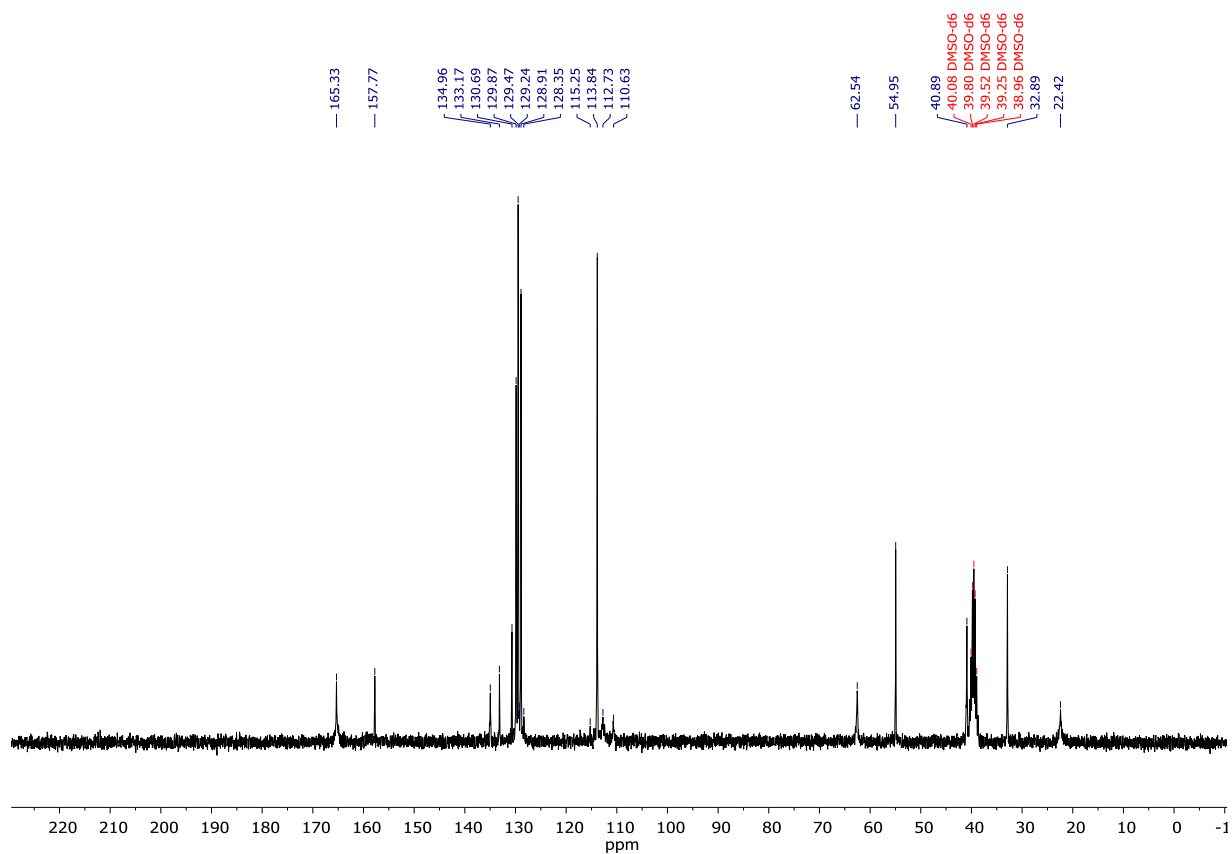
^{13}C NMR spectrum (126 MHz) for **7f**



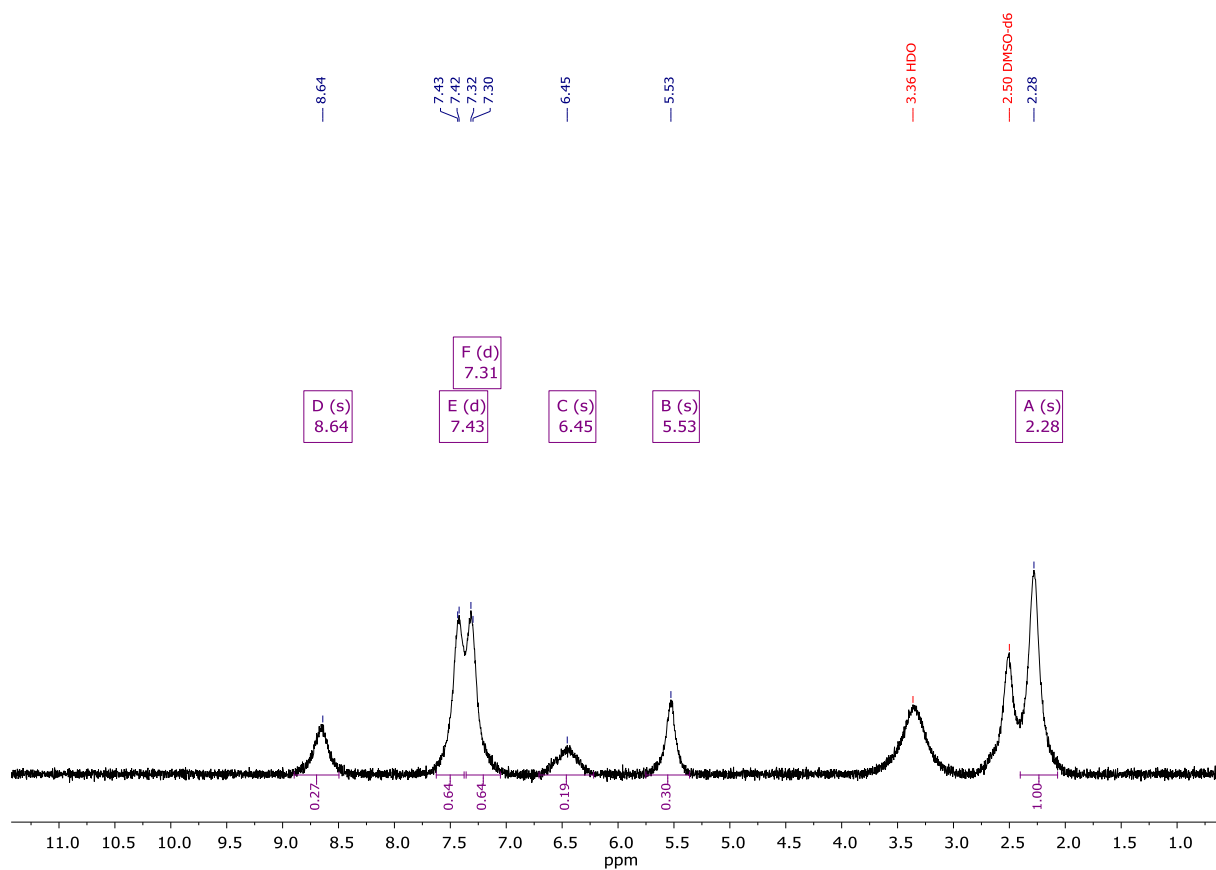
^1H NMR spectrum (300 MHz) for **1a**



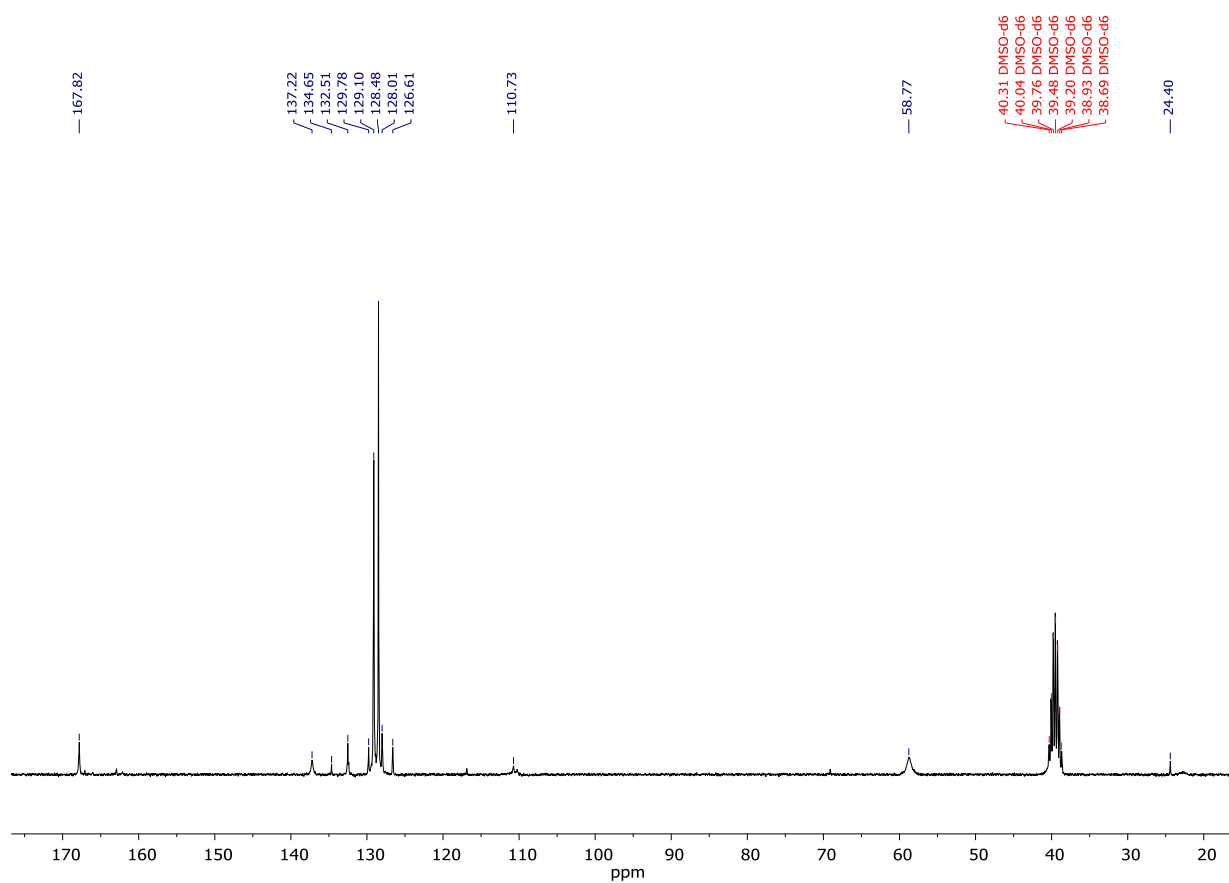
^{13}C NMR spectrum (75 MHz) for **1a**



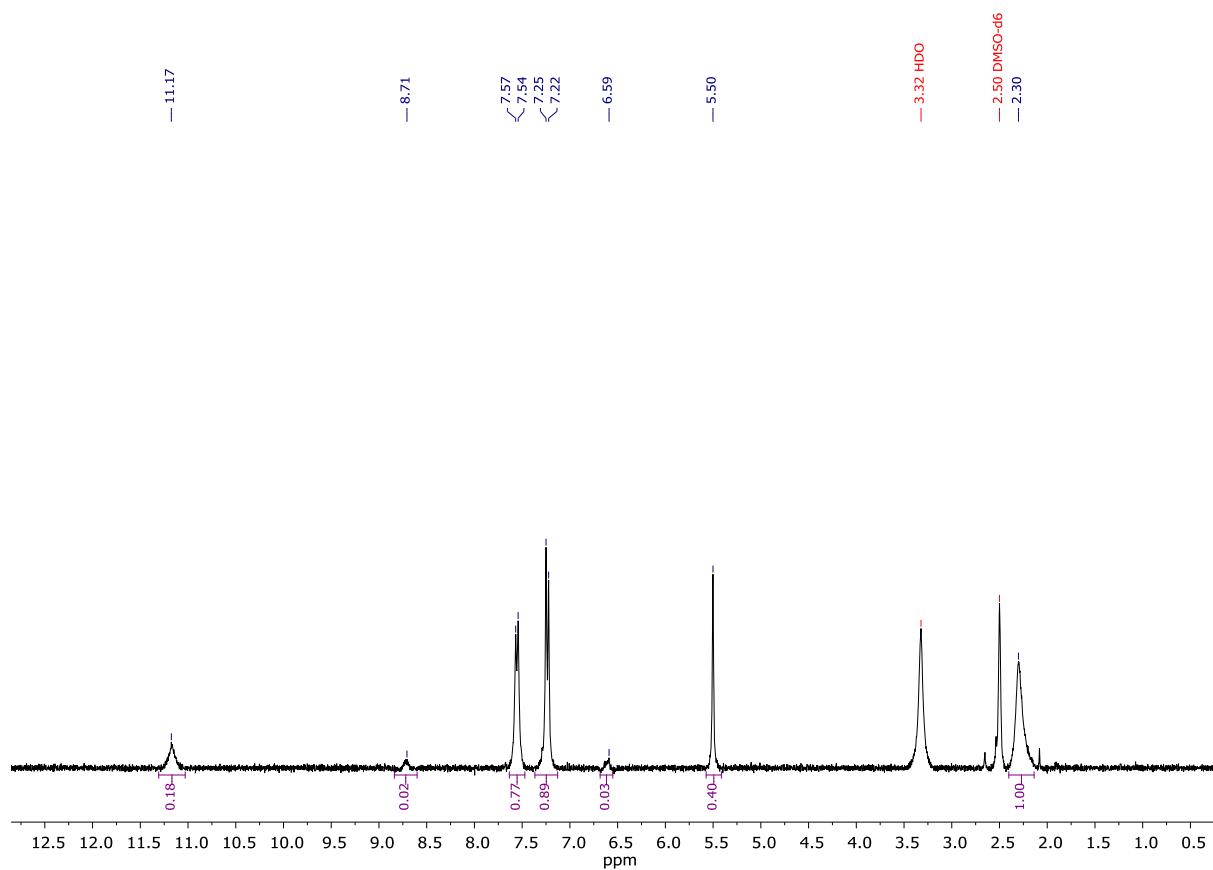
^1H NMR spectrum (300 MHz) for **1b**



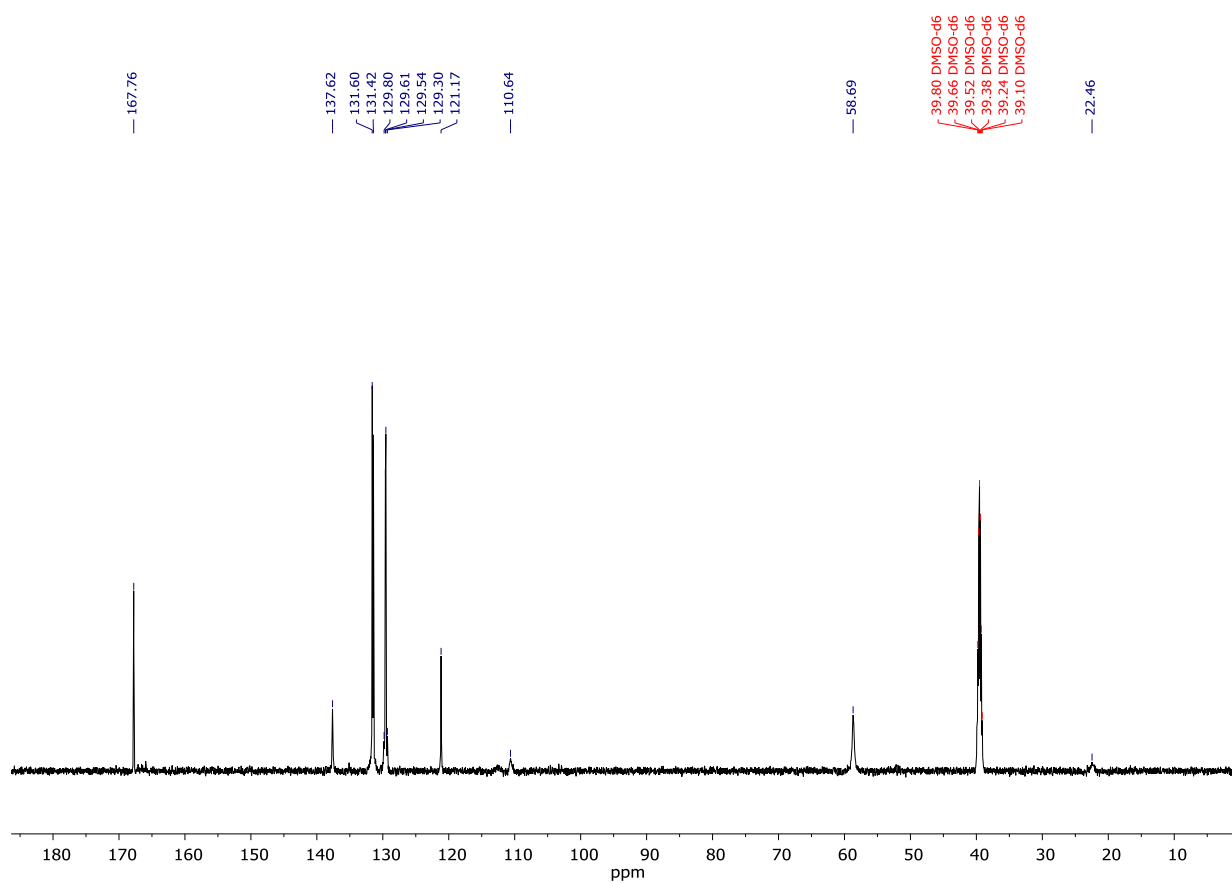
^{13}C NMR spectrum (75 MHz) for **1b**



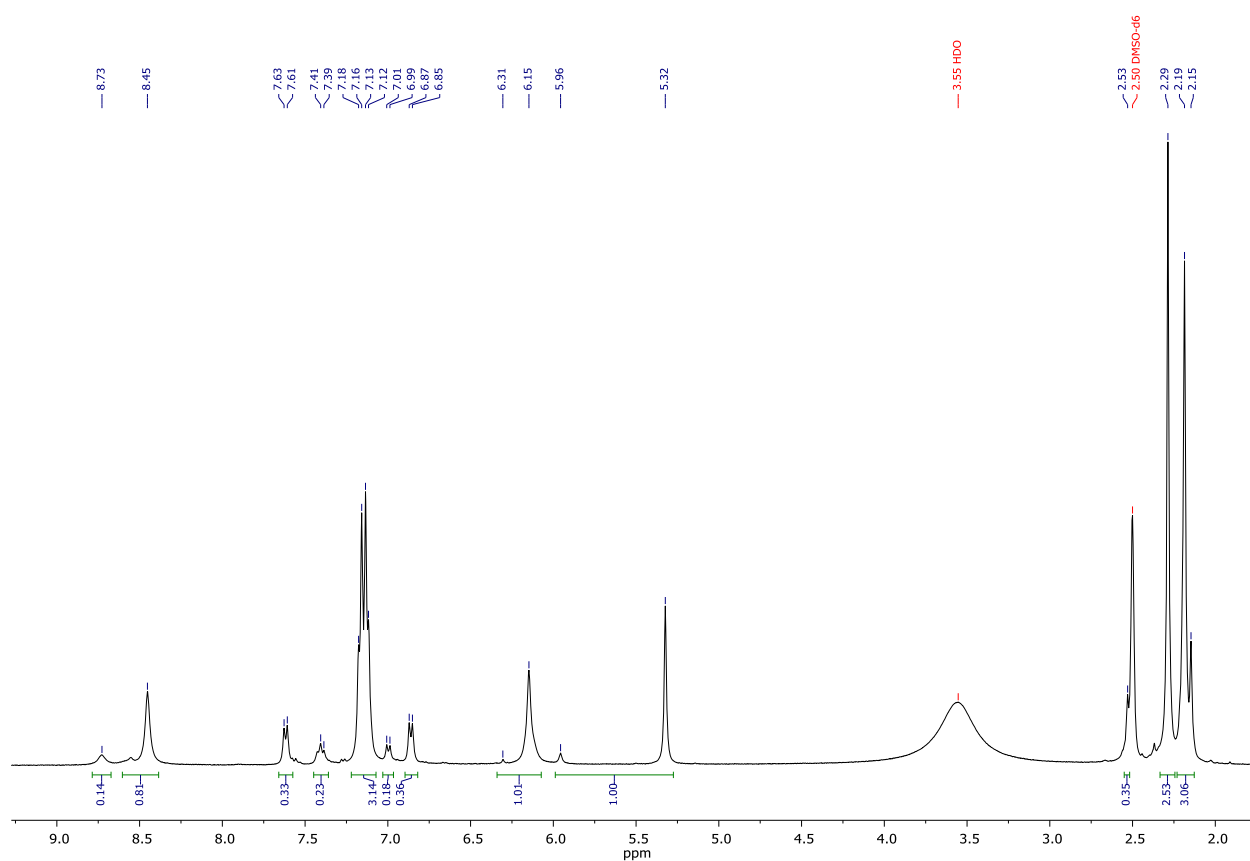
^1H NMR spectrum (300 MHz) for **1c**



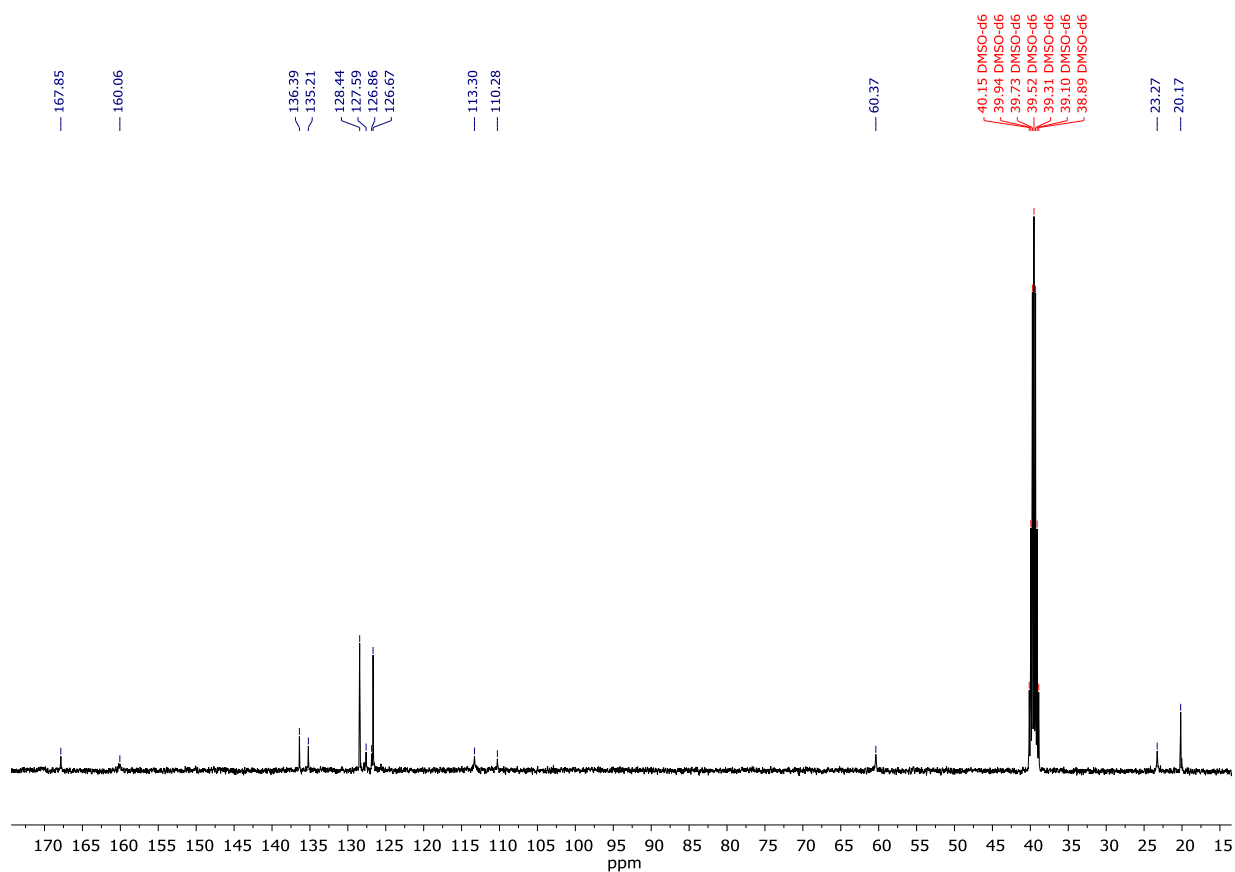
^{13}C NMR spectrum (151 MHz) for **1c**



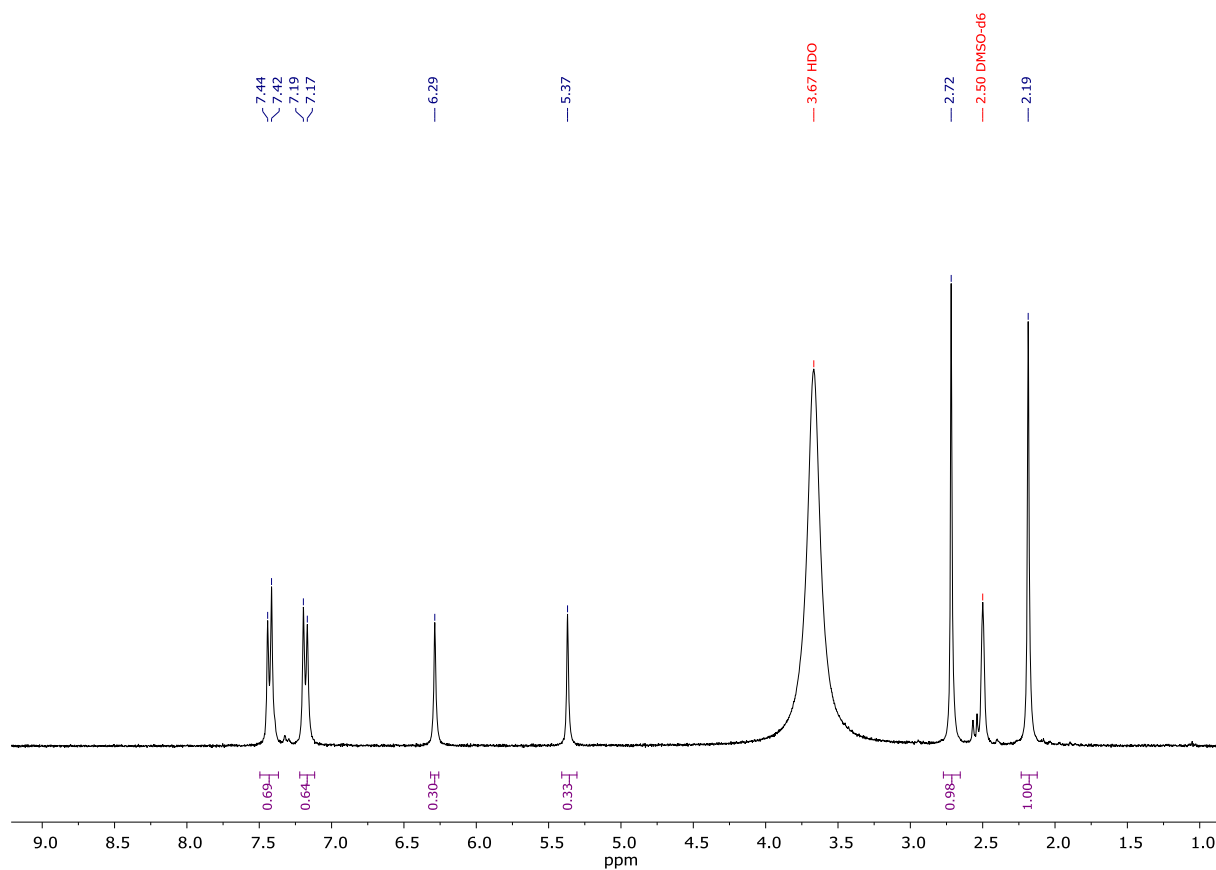
^1H NMR spectrum (400 MHz) for **1d**



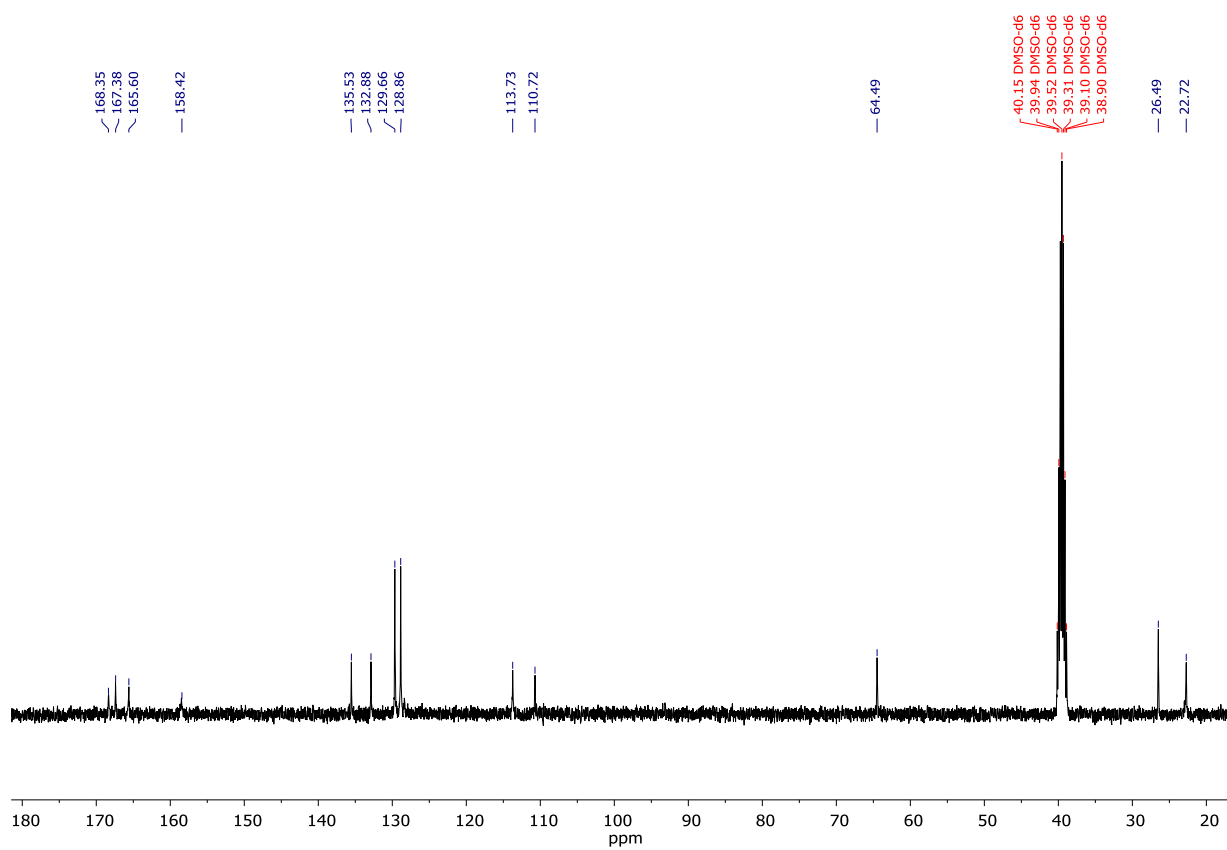
^{13}C NMR spectrum (101 MHz) for **1d**



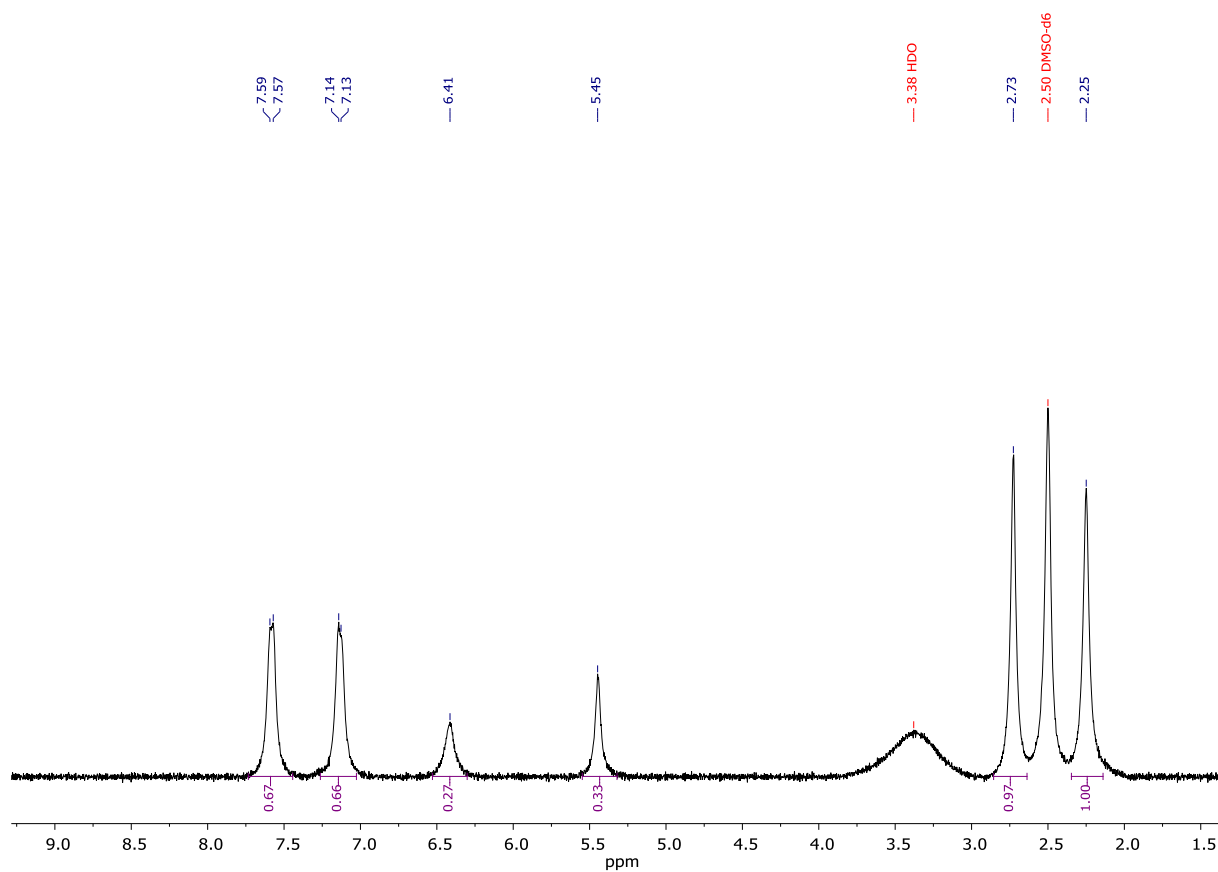
^1H NMR spectrum (300 MHz) for **1e**



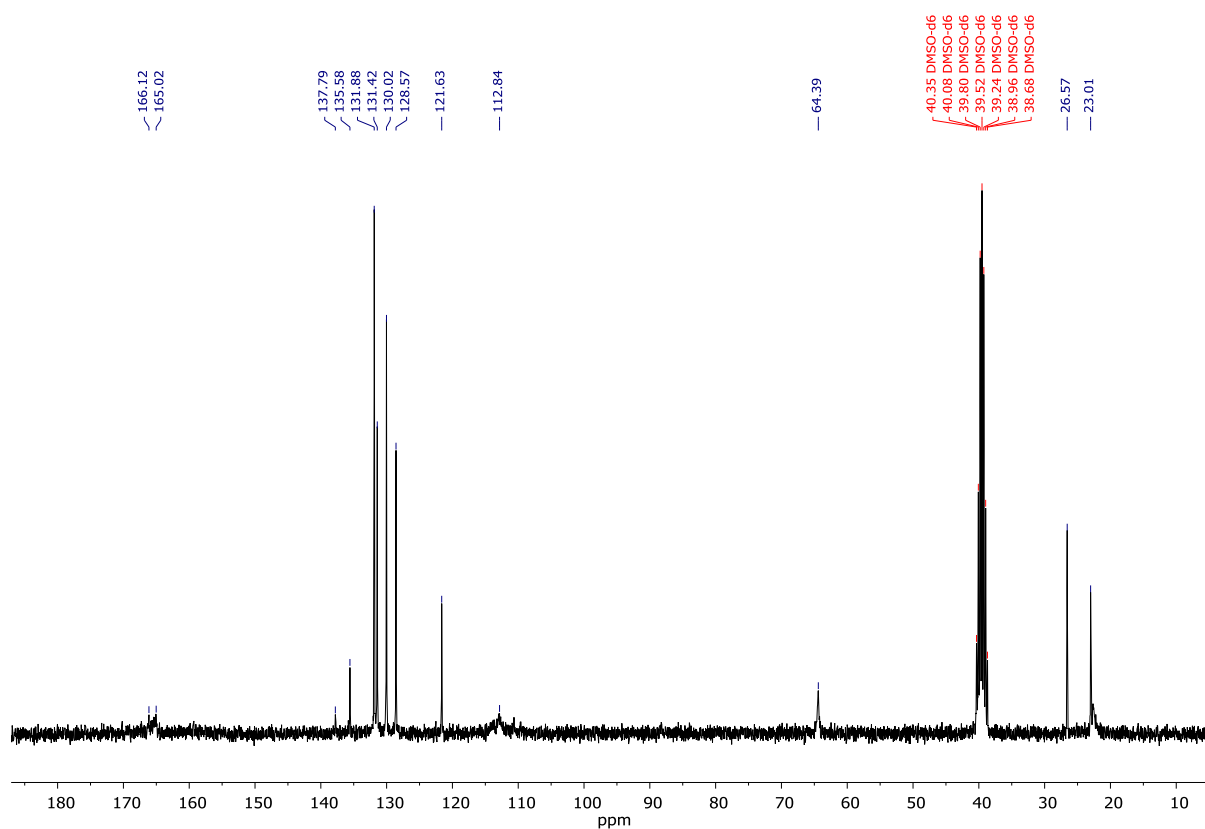
^{13}C NMR spectrum (101 MHz) for **1e**



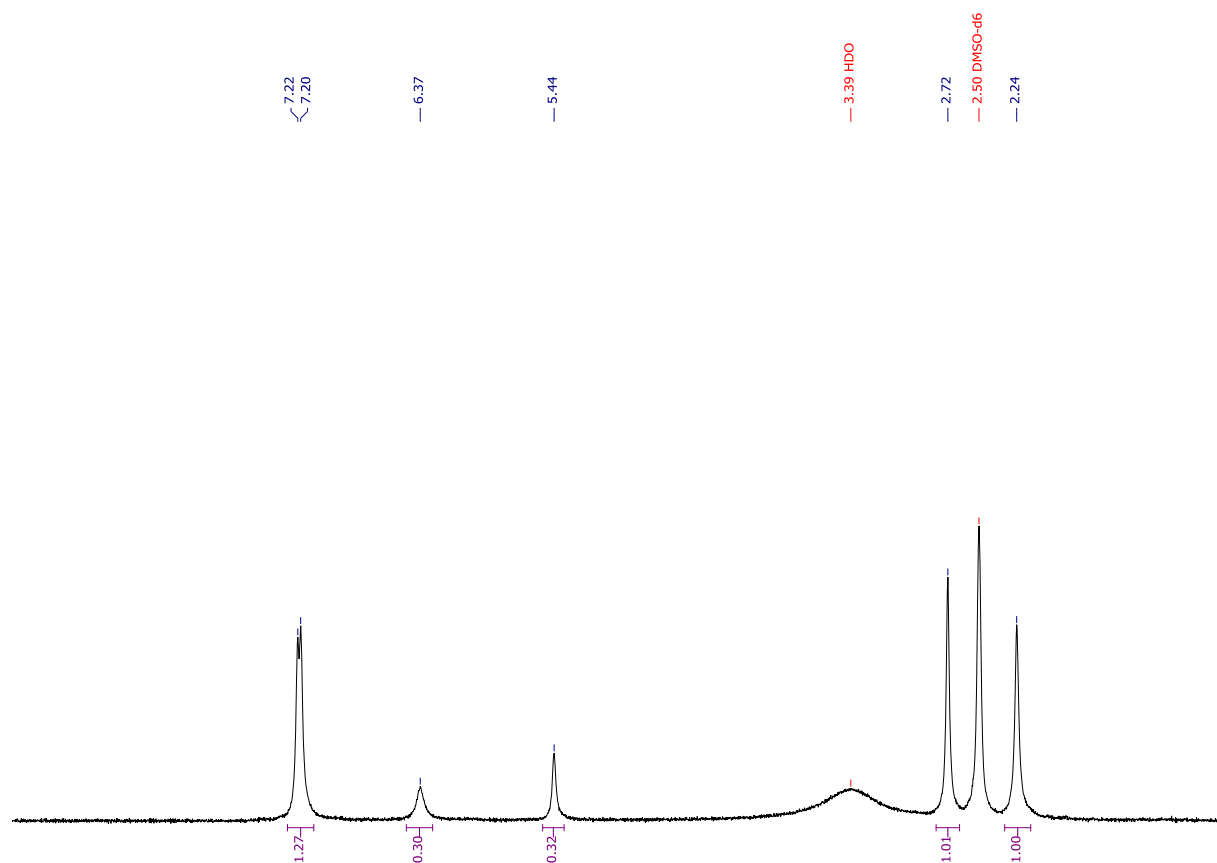
^1H NMR spectrum (300 MHz) for **1f**



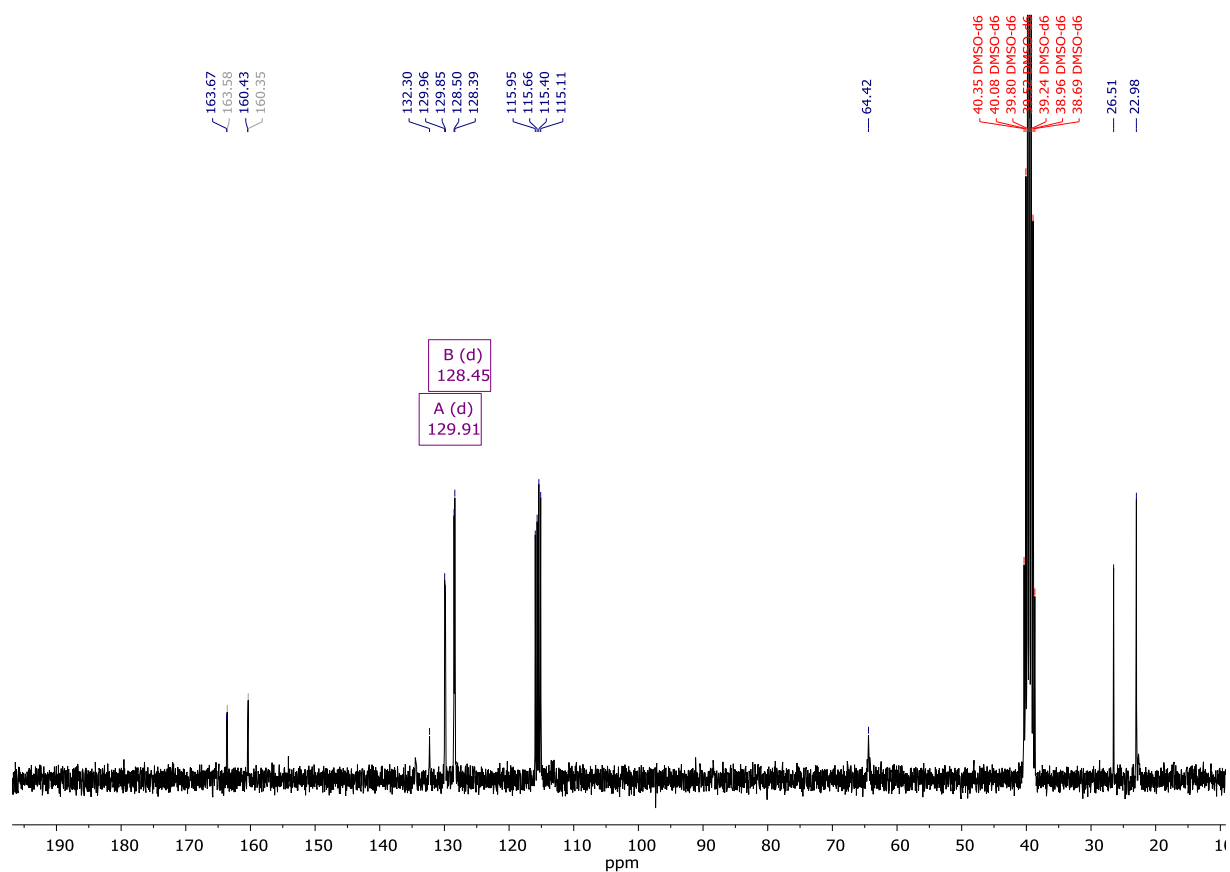
^{13}C NMR spectrum (75 MHz) for **1f**



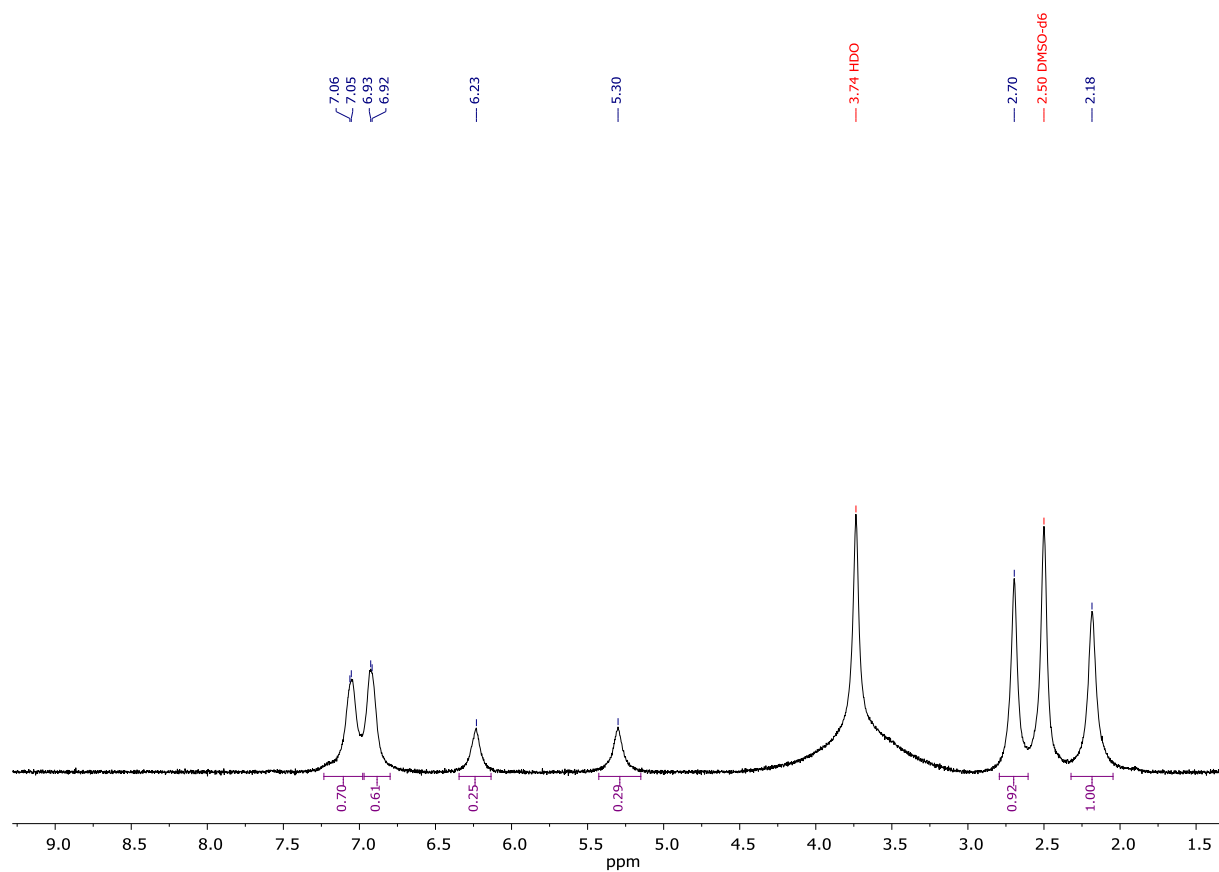
^1H NMR spectrum (300 MHz) for **1g**



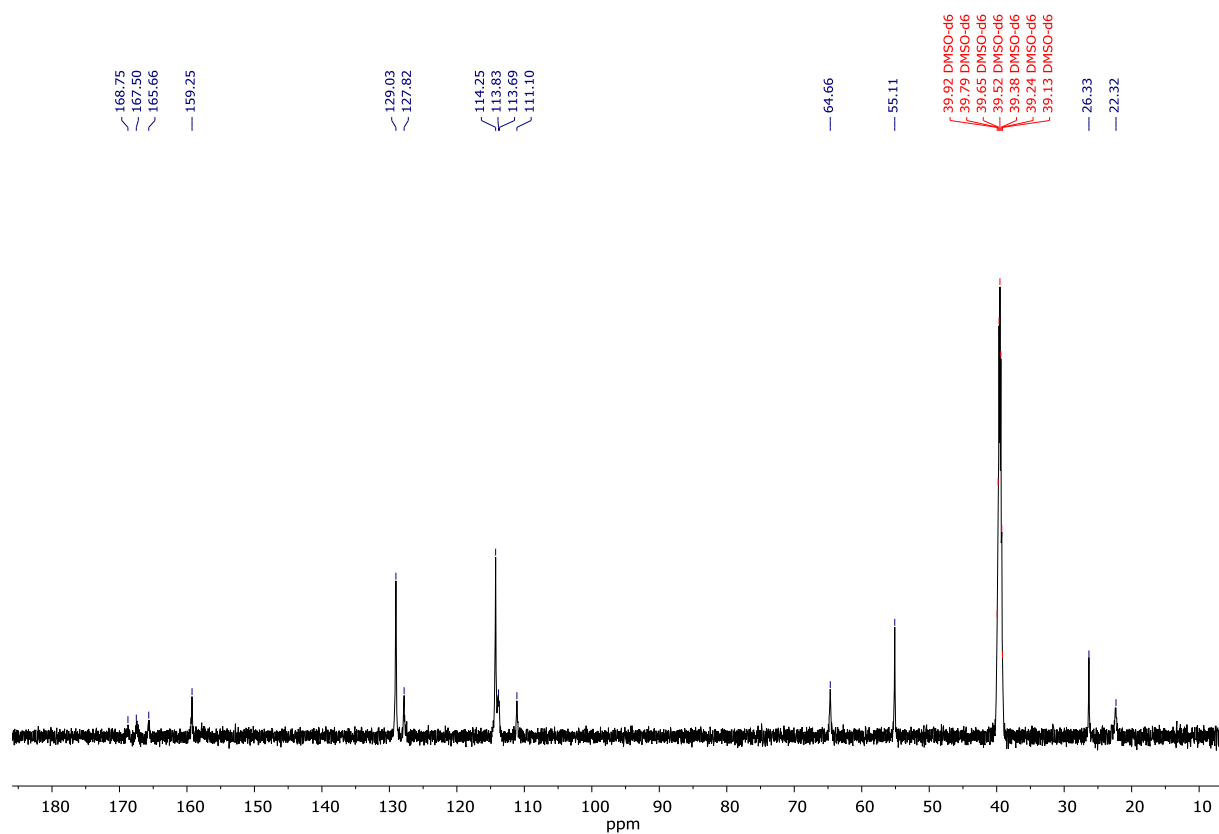
^{13}C NMR spectrum (75 MHz) for **1g**



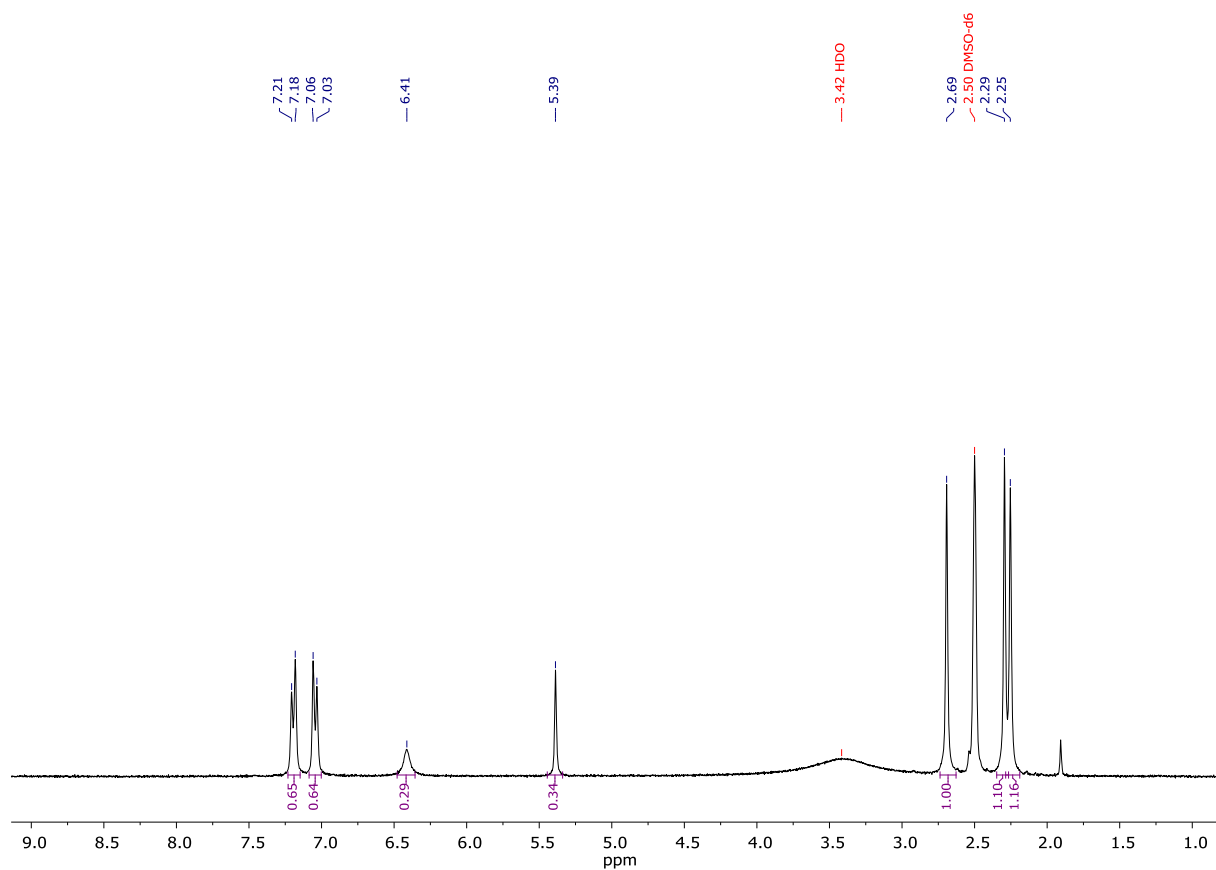
^1H NMR spectrum (300 MHz) for **1h**



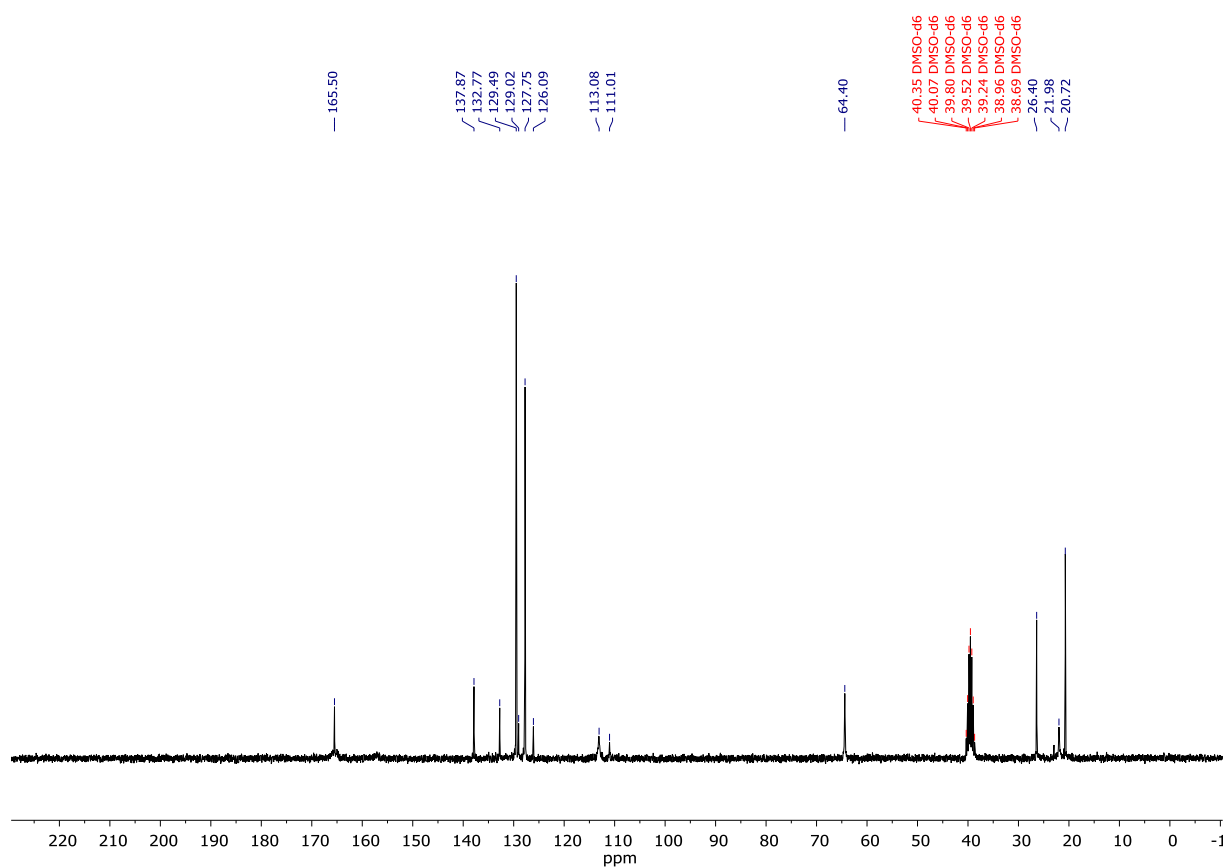
^{13}C NMR spectrum (151 MHz) for **1h**



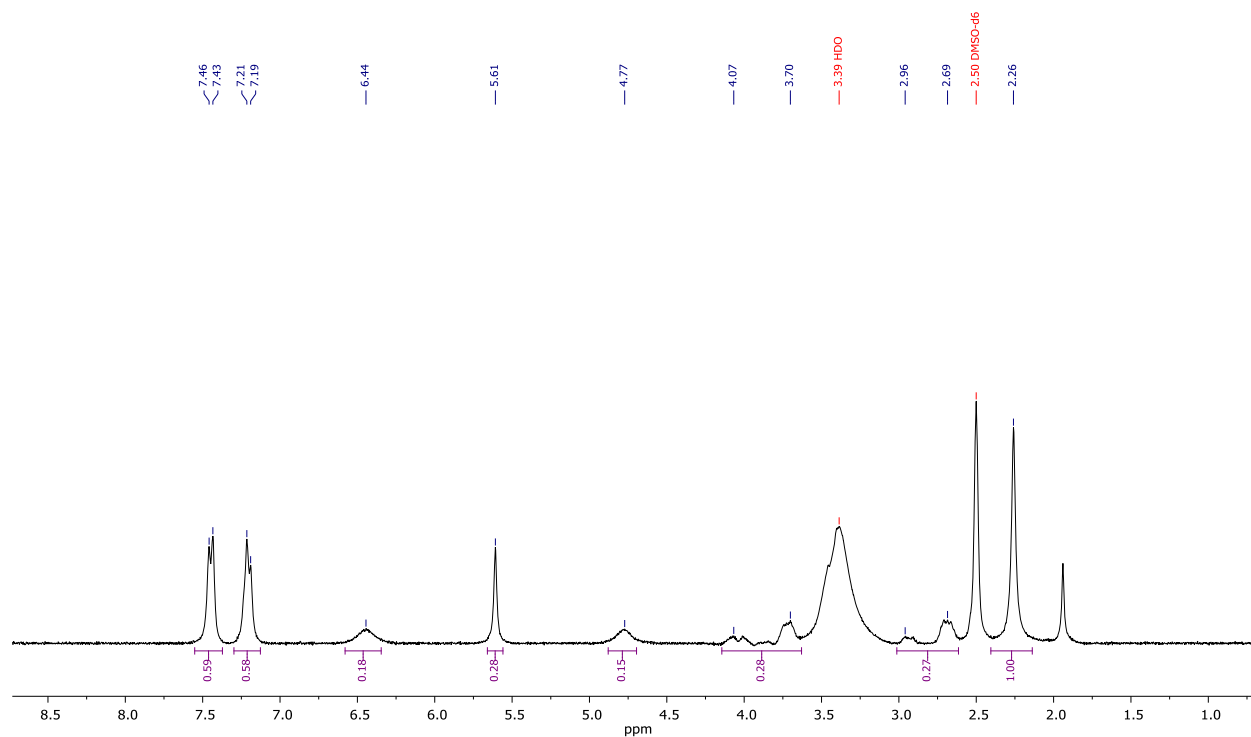
^1H NMR spectrum (300 MHz) for **1i**



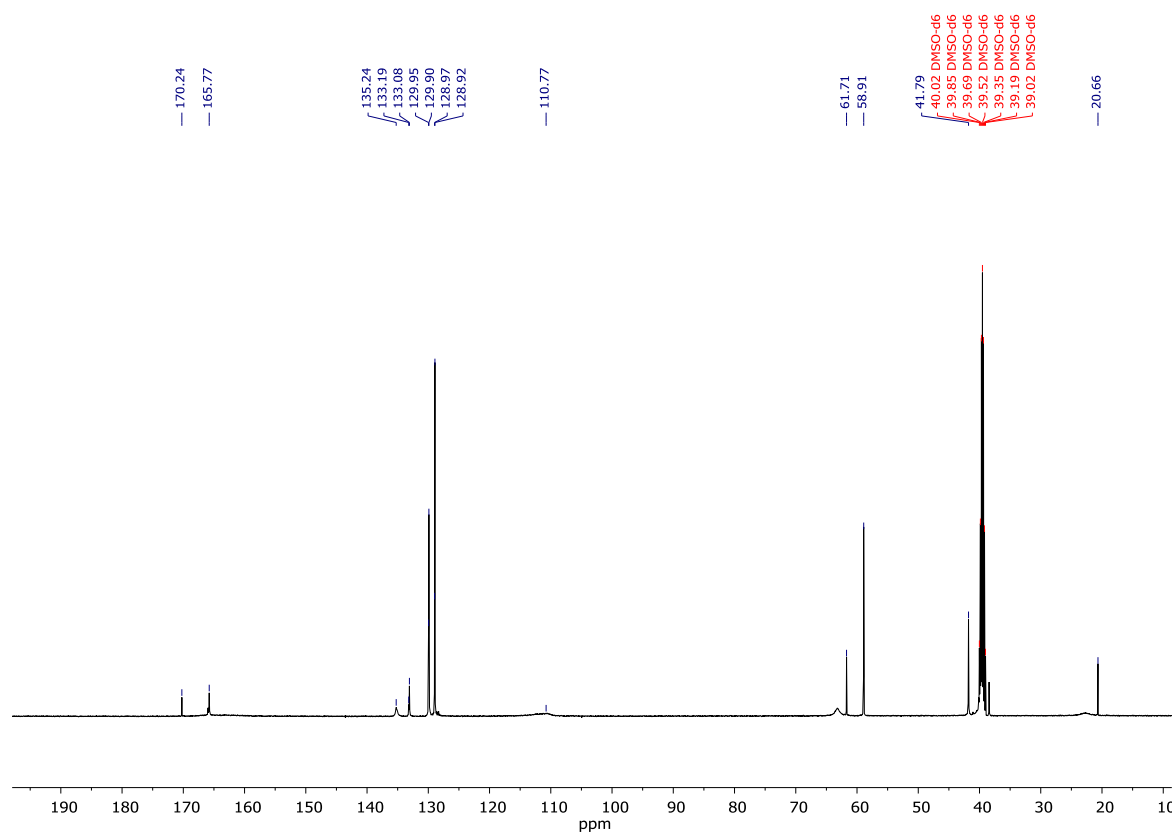
^{13}C NMR spectrum (75 MHz) for **1i**



^1H NMR spectrum (300 MHz) for **1j**

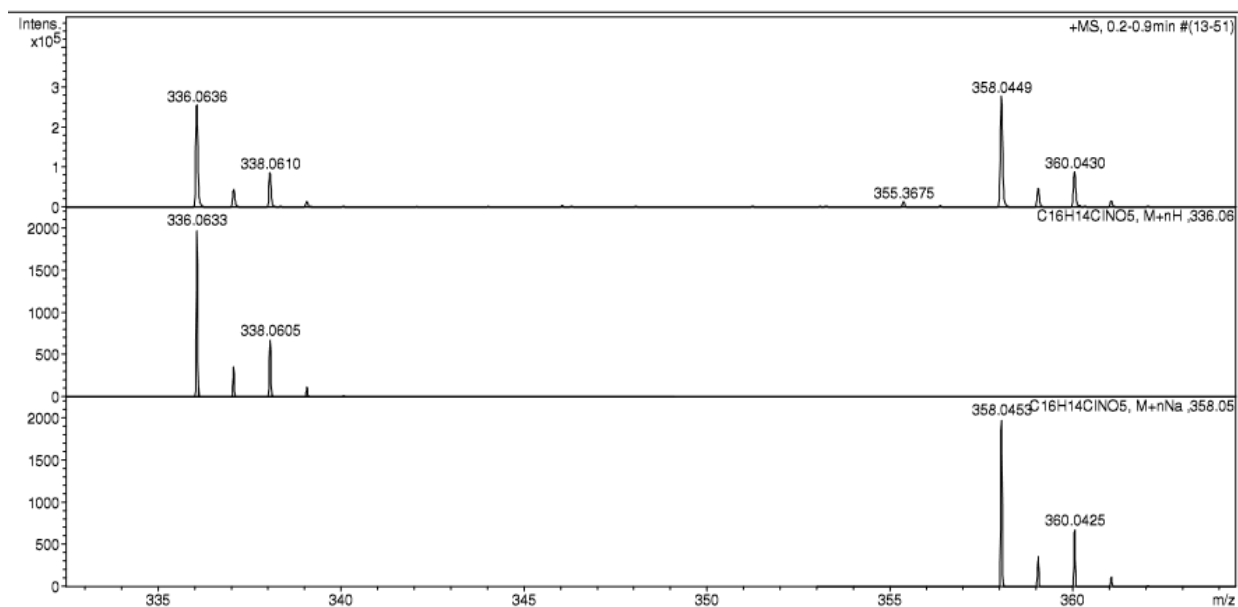


^{13}C NMR spectrum (126 MHz) for **1j**

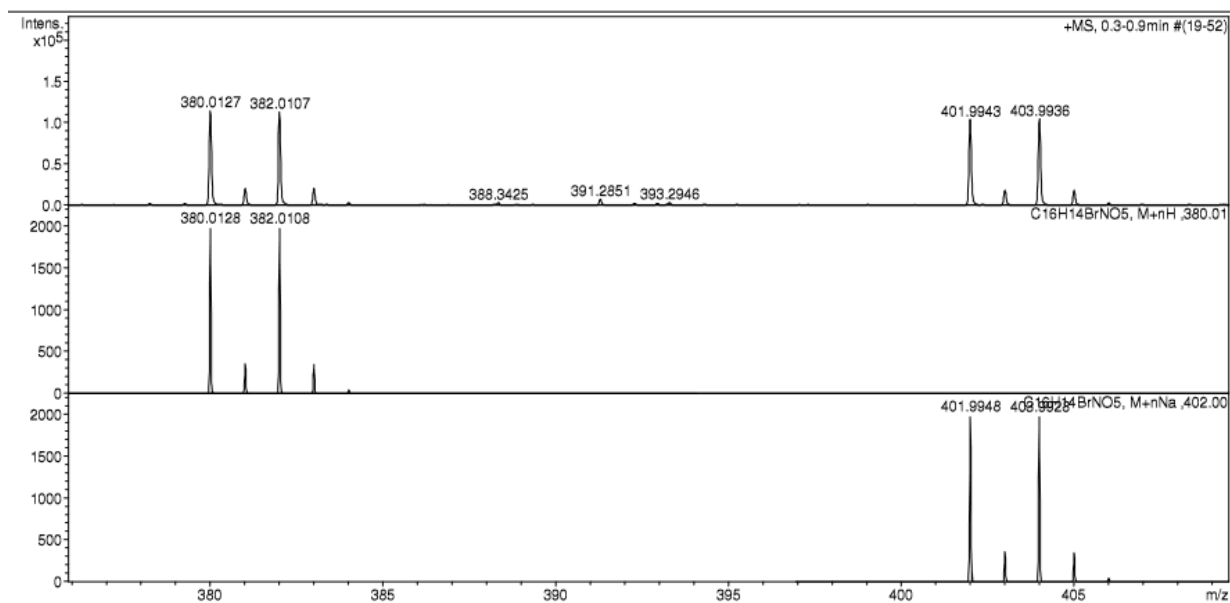


5. HRMS for all compounds.

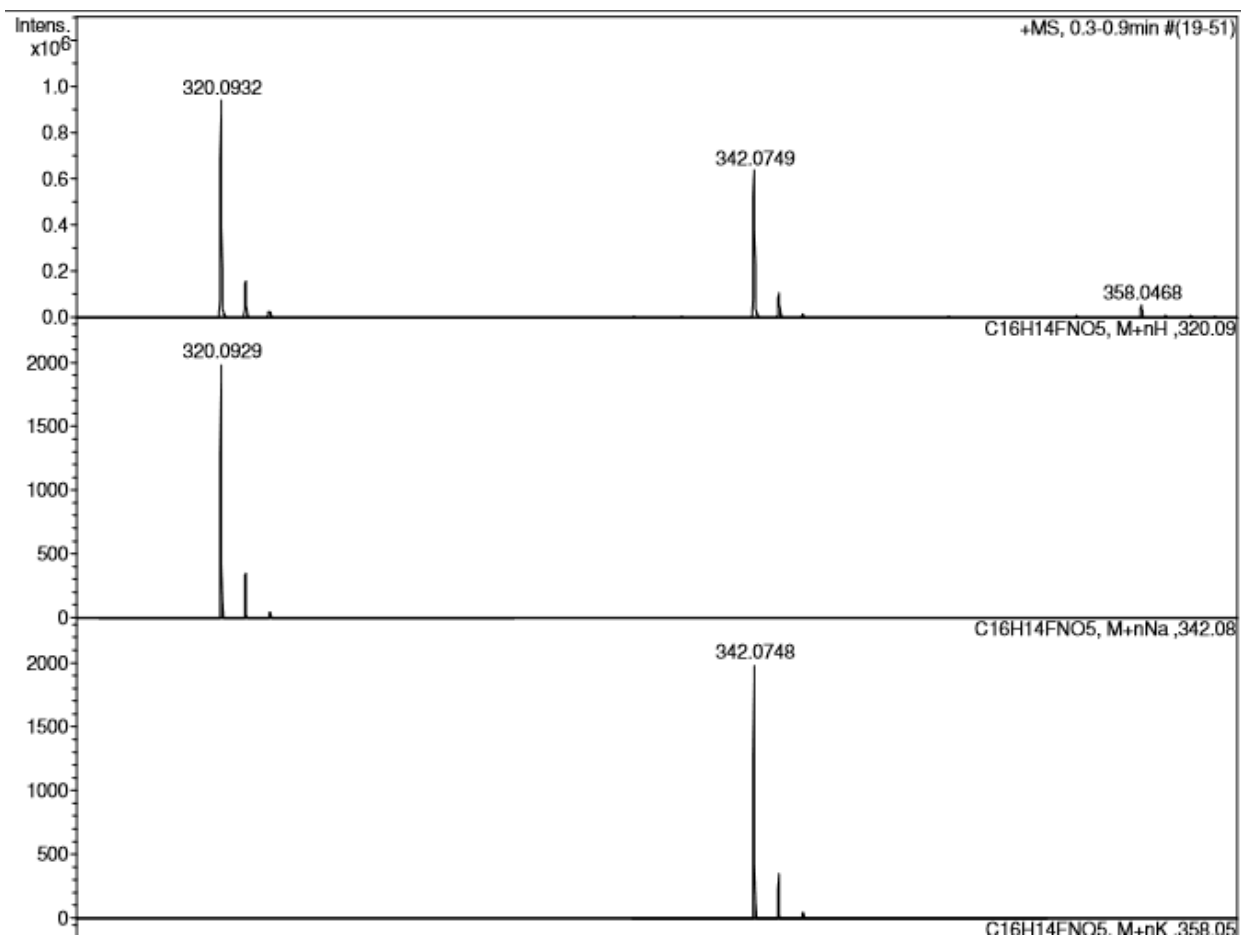
HRMS for **2a**



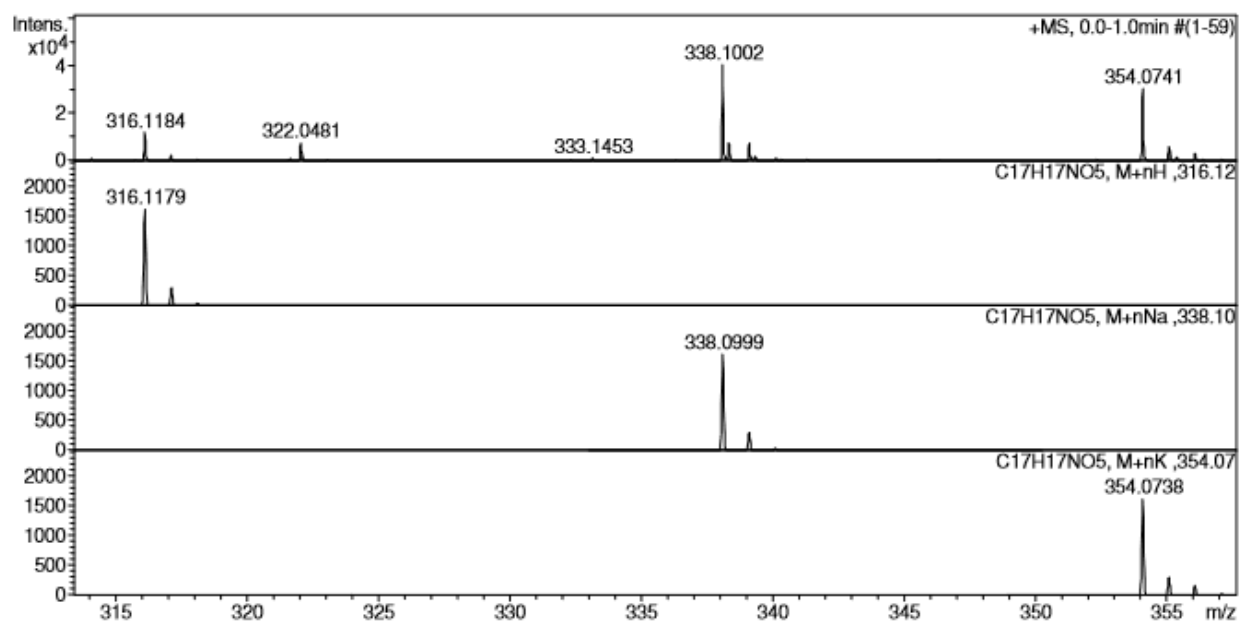
HRMS for **2b**



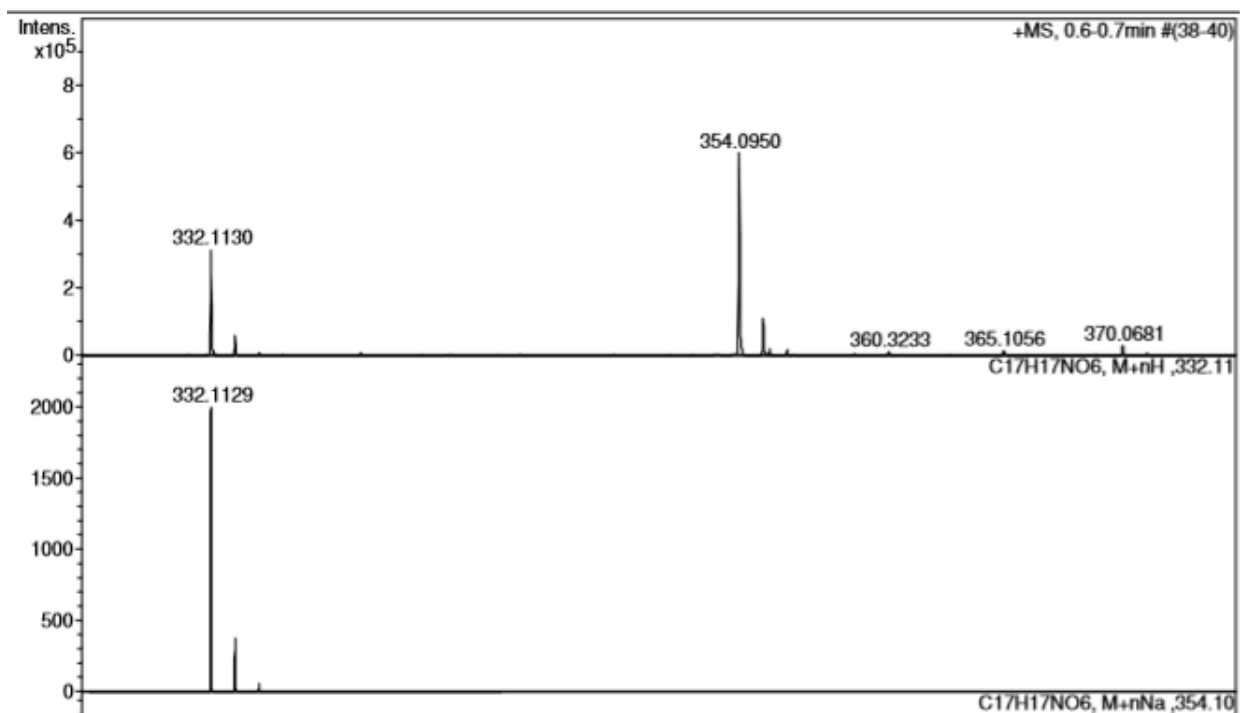
HRMS for 2c



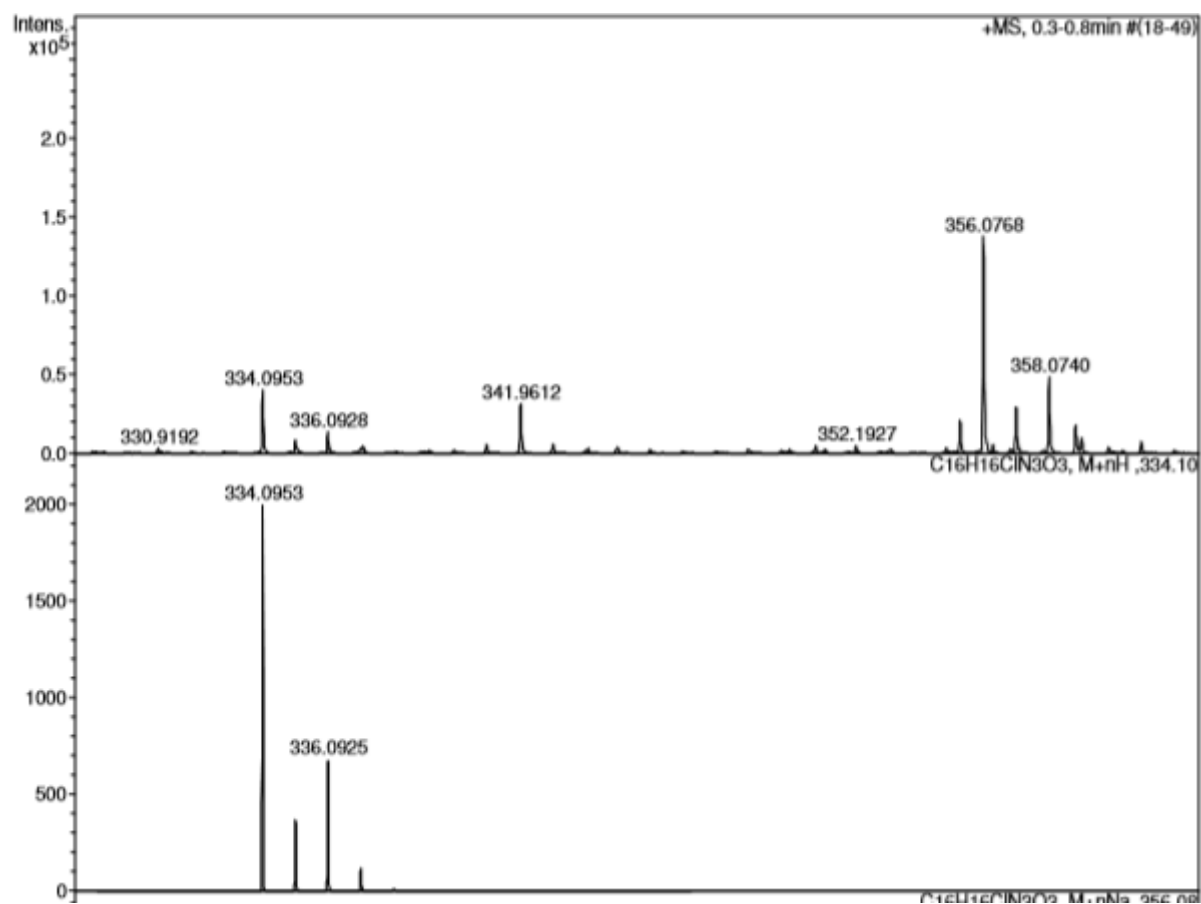
HRMS for 2d



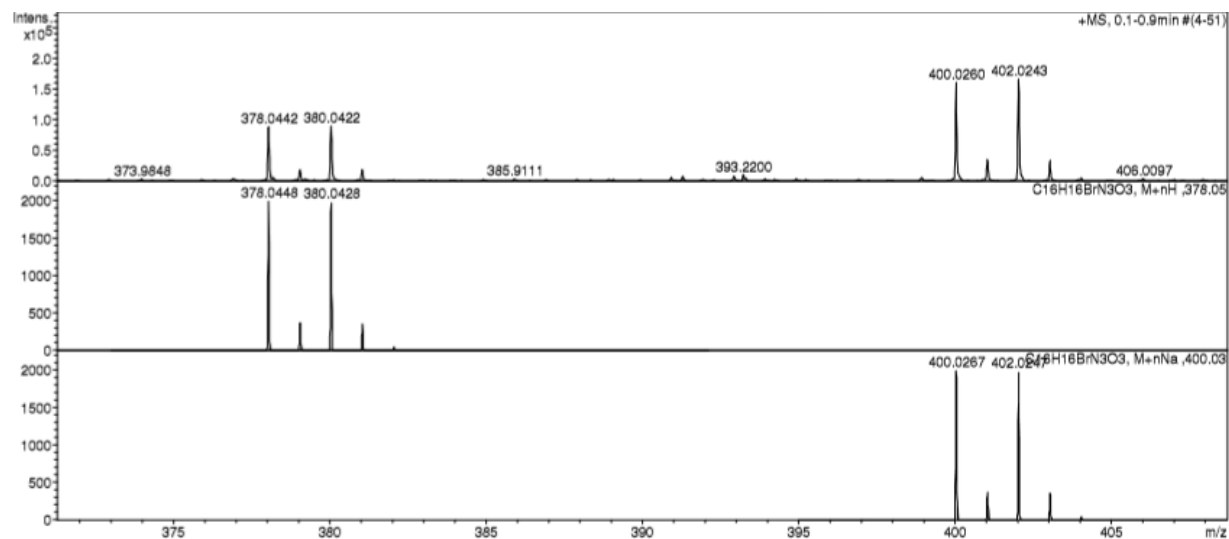
HRMS for **2e**



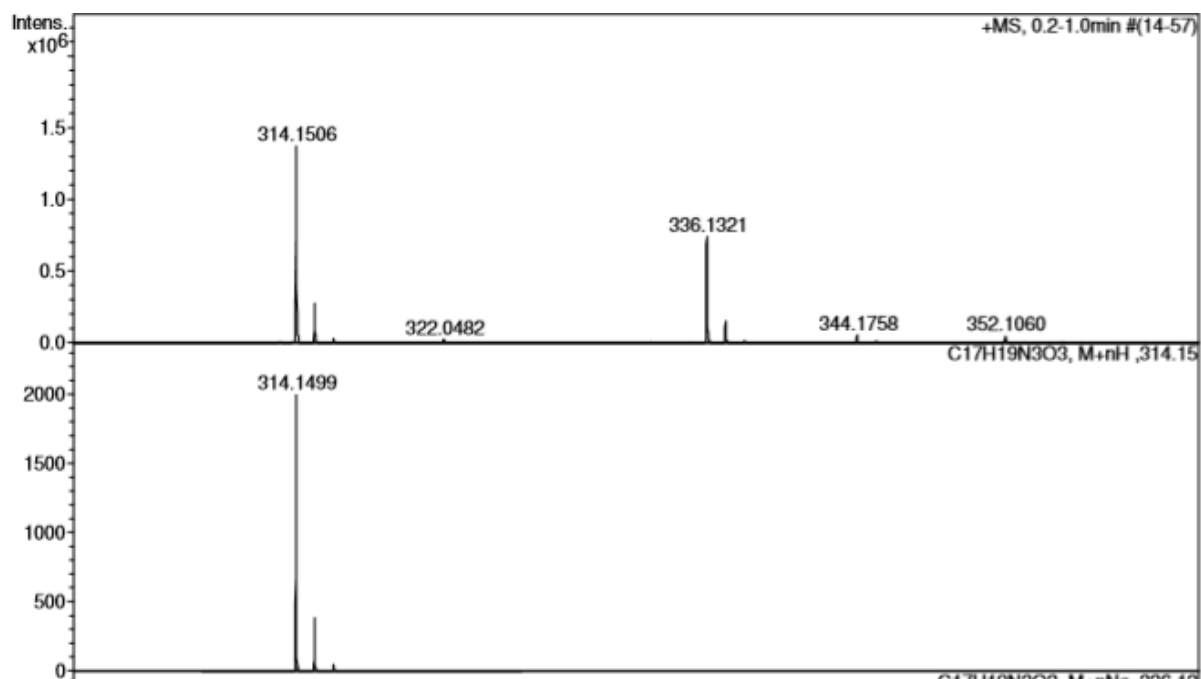
HRMS for **7b**



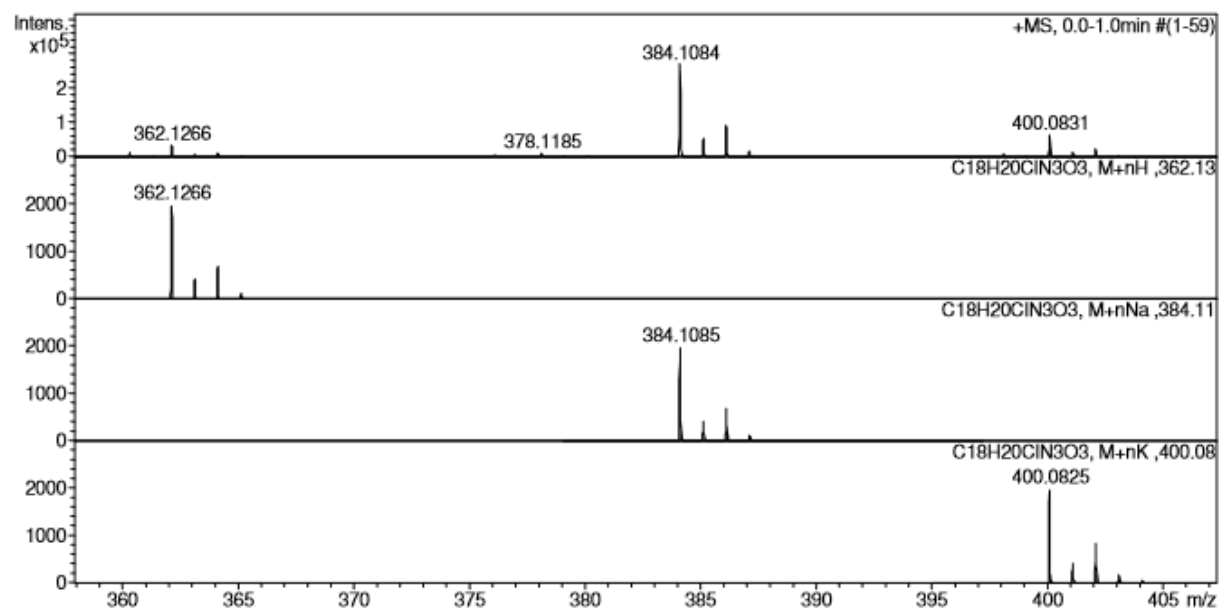
HRMS for 7c



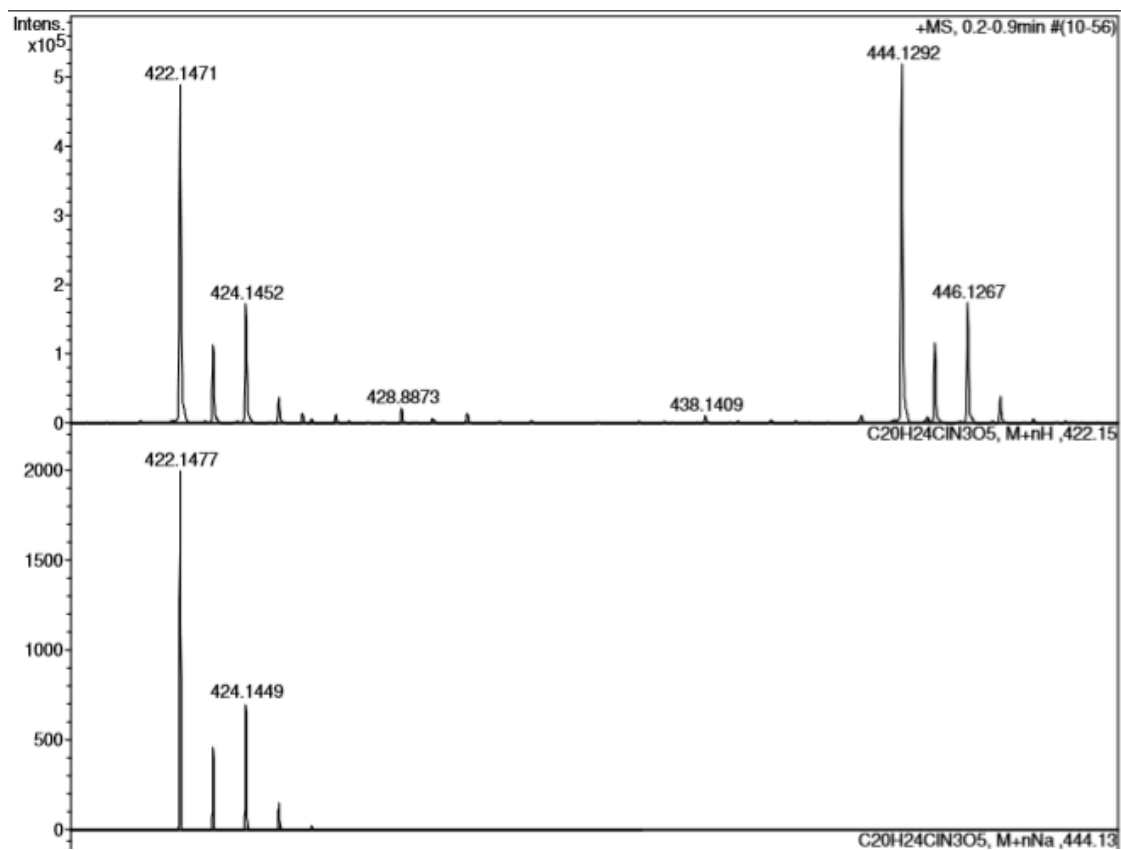
HRMS for 7d



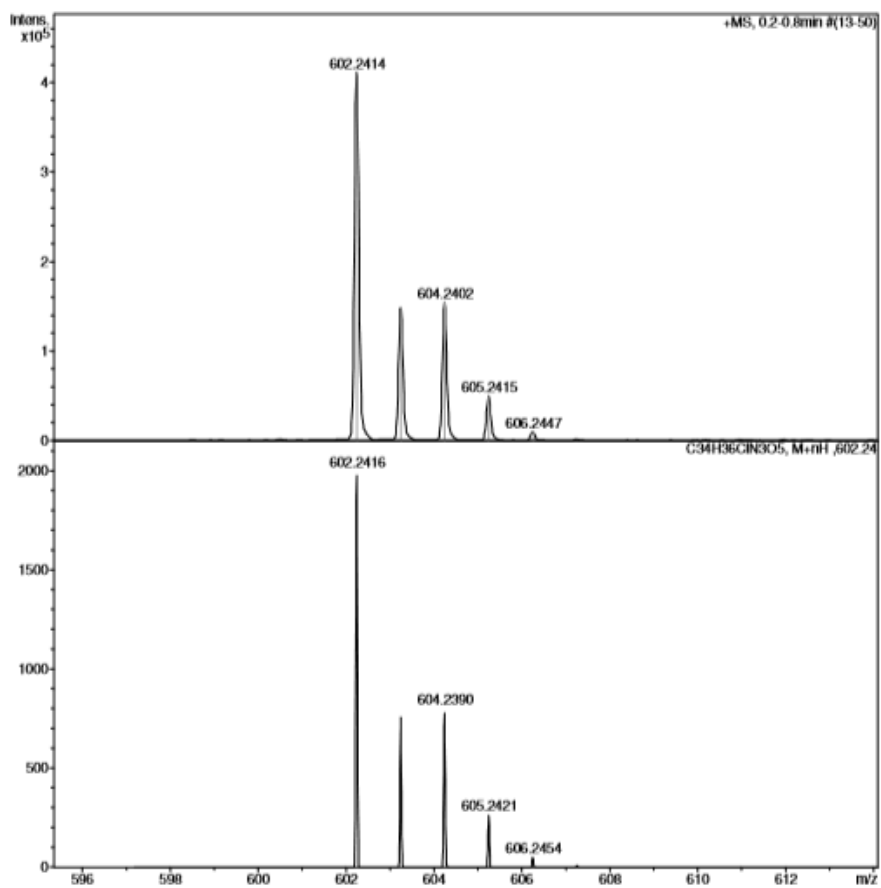
HRMS for 7e



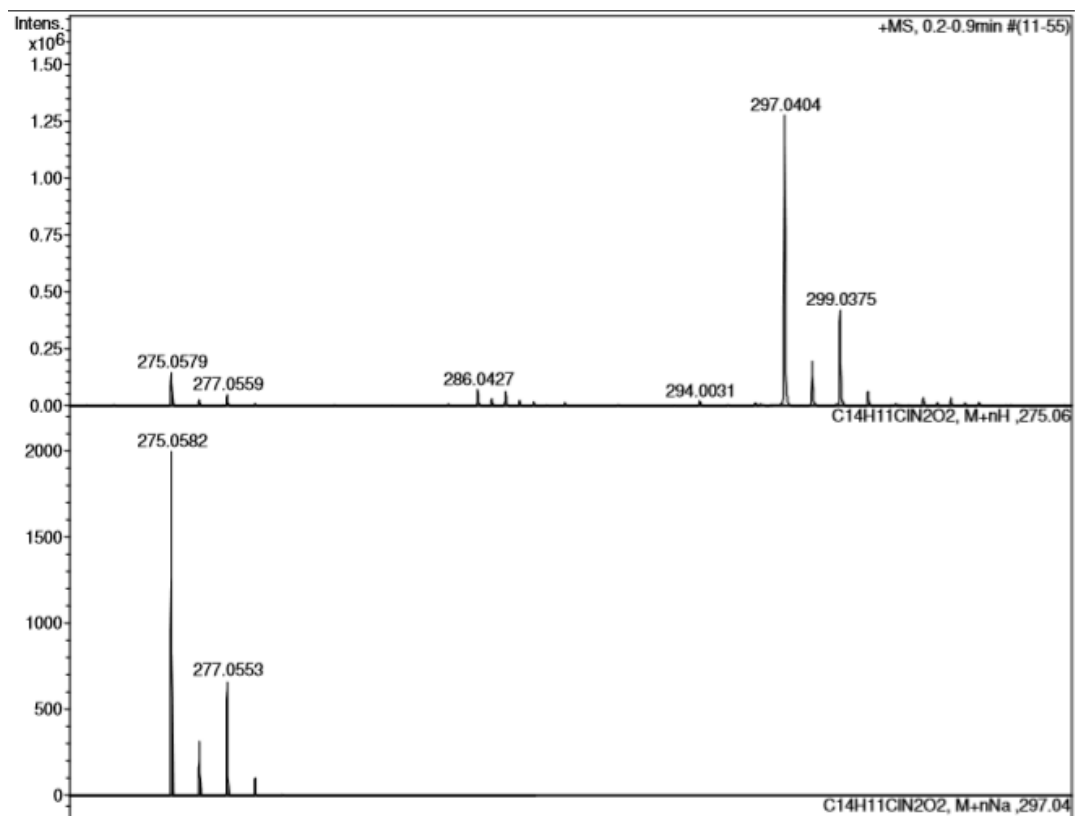
HRMS for **7f**



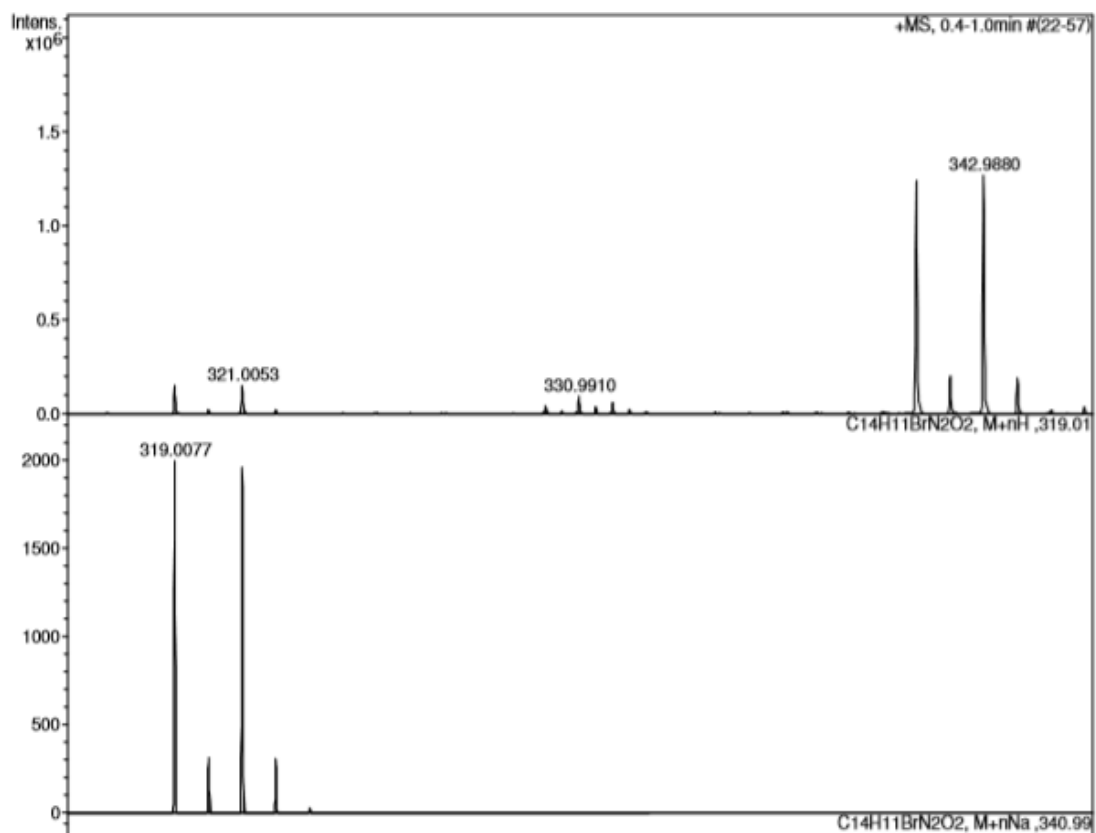
HRMS for **7a**



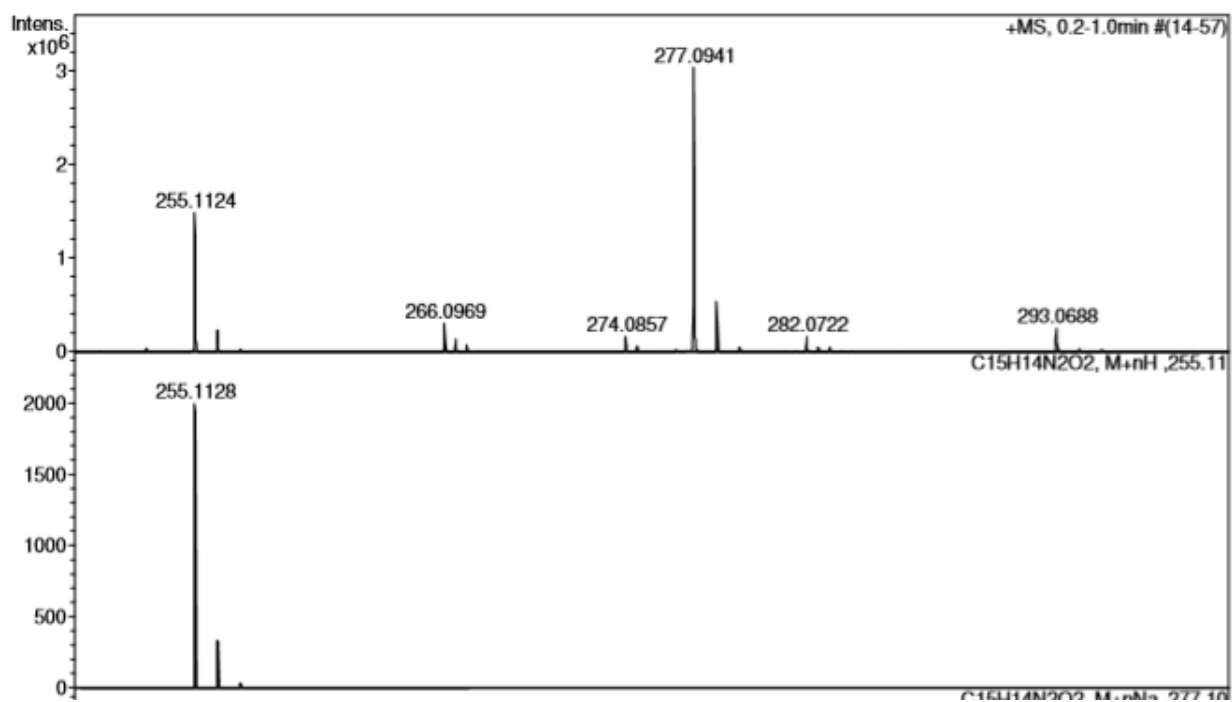
HRMS for **1b**



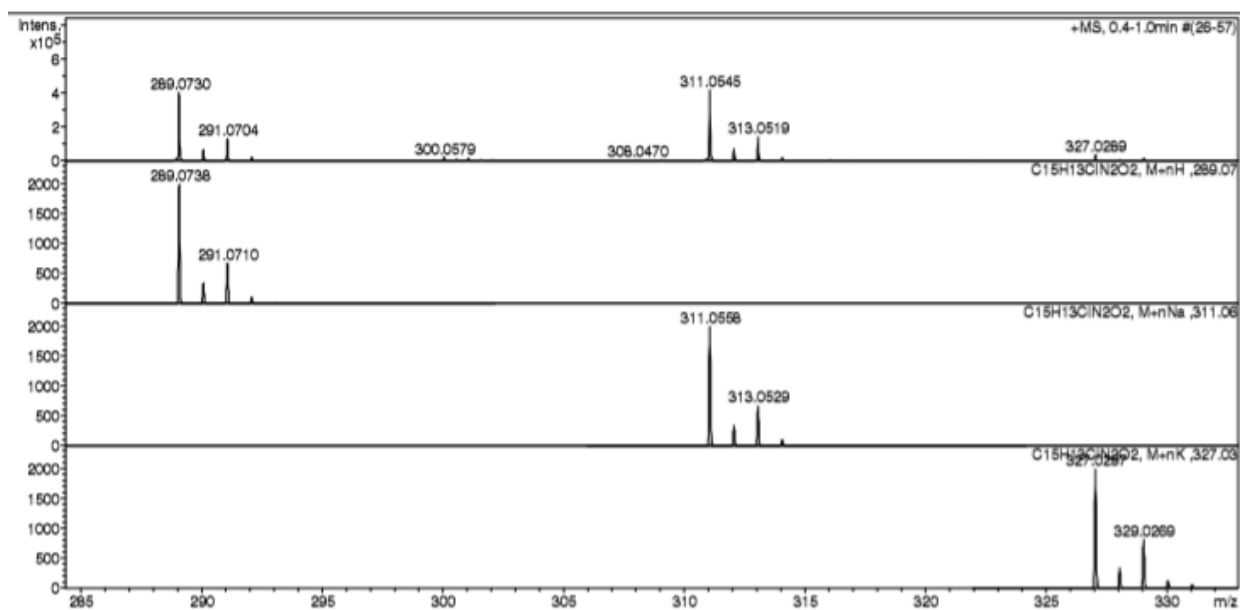
HRMS for **1c**



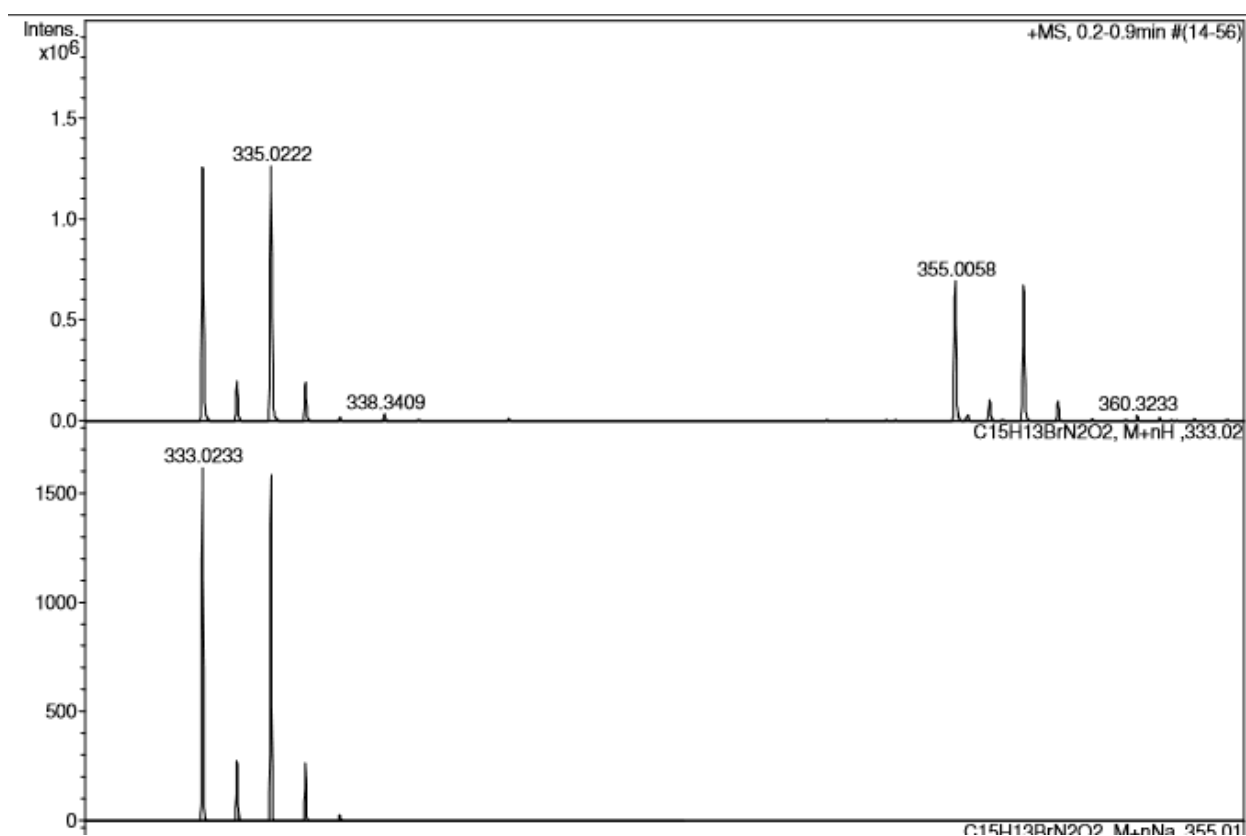
HRMS for **1d**



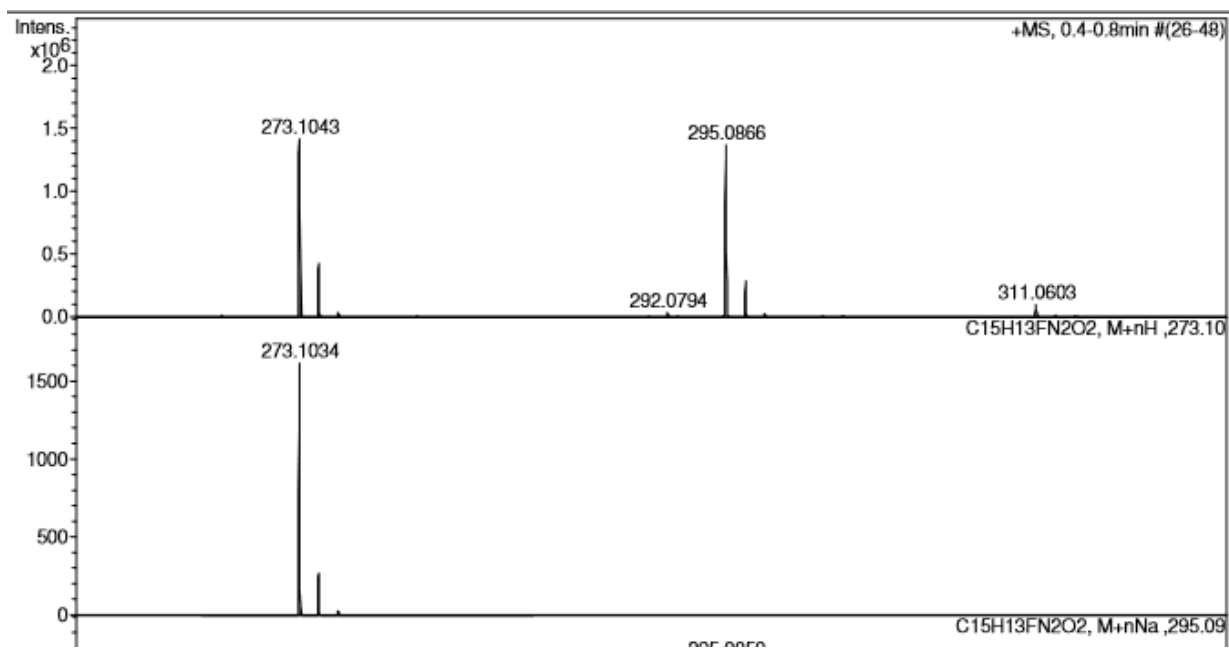
HRMS for **1e**



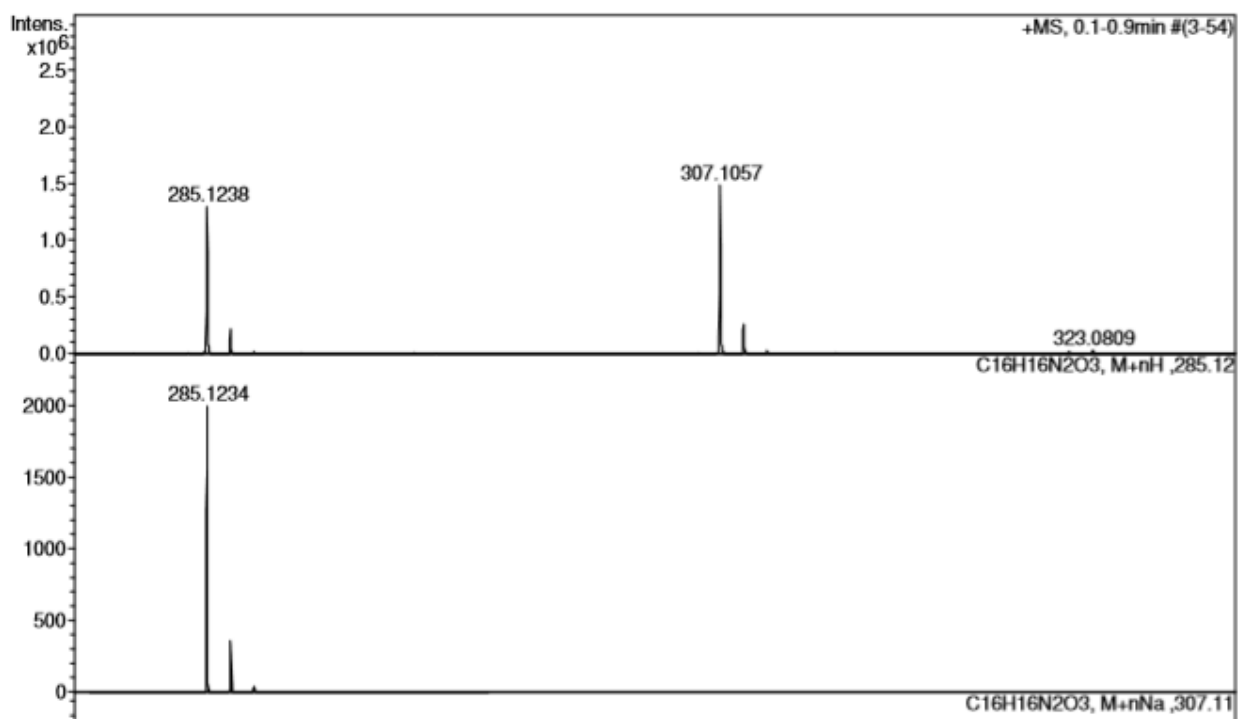
HRMS for **1f**



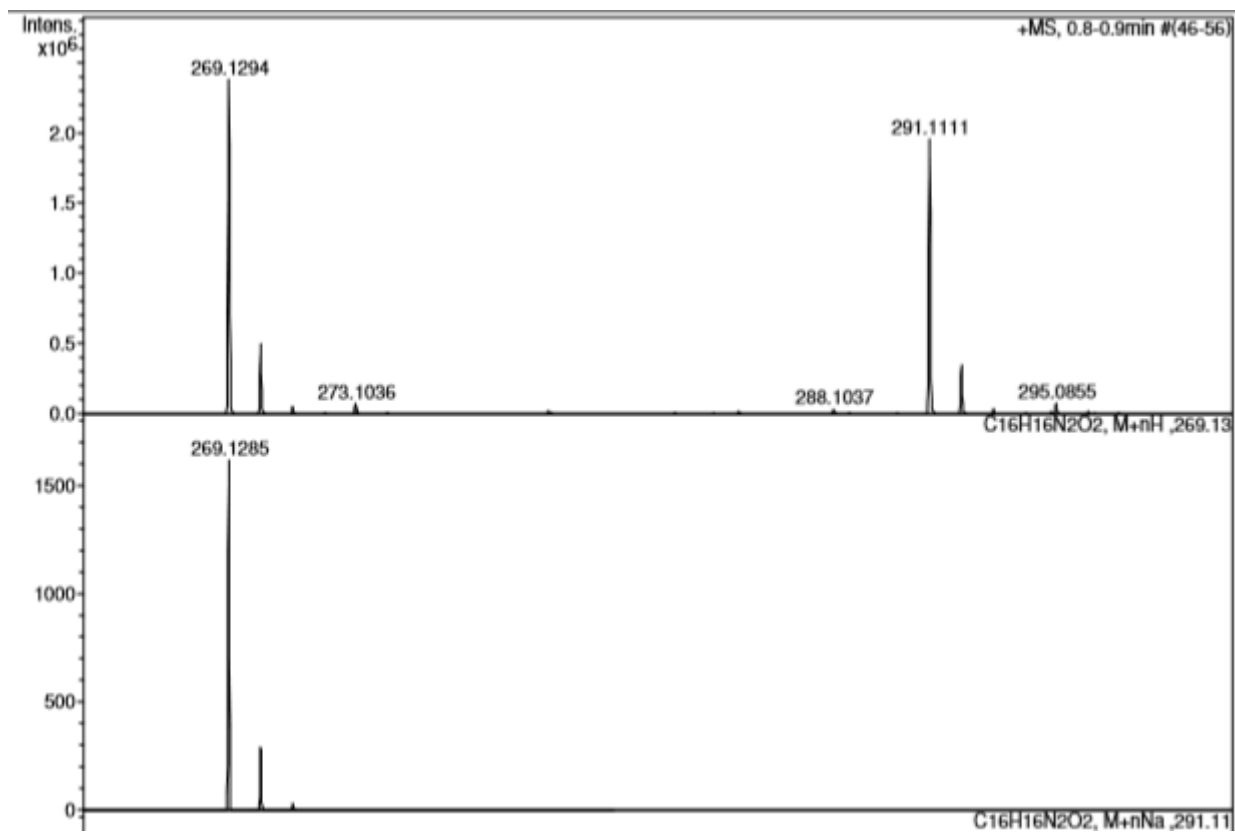
HRMS for **1g**



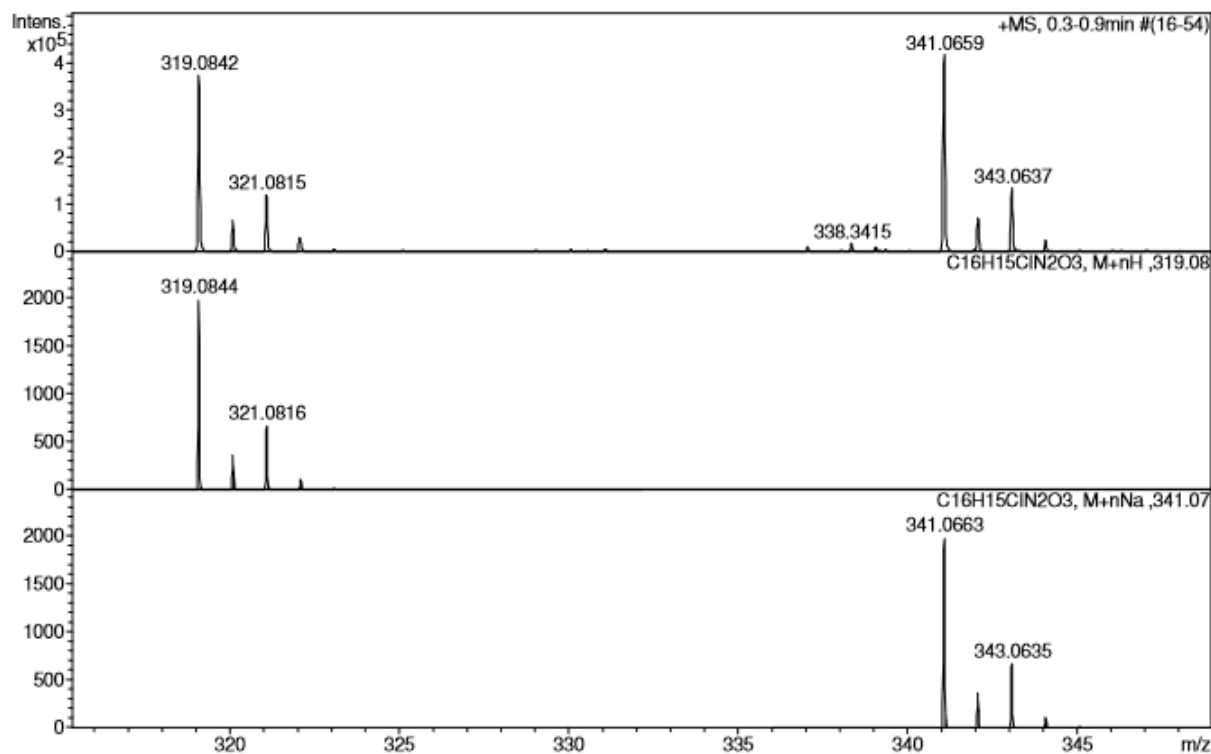
HRMS for **1h**



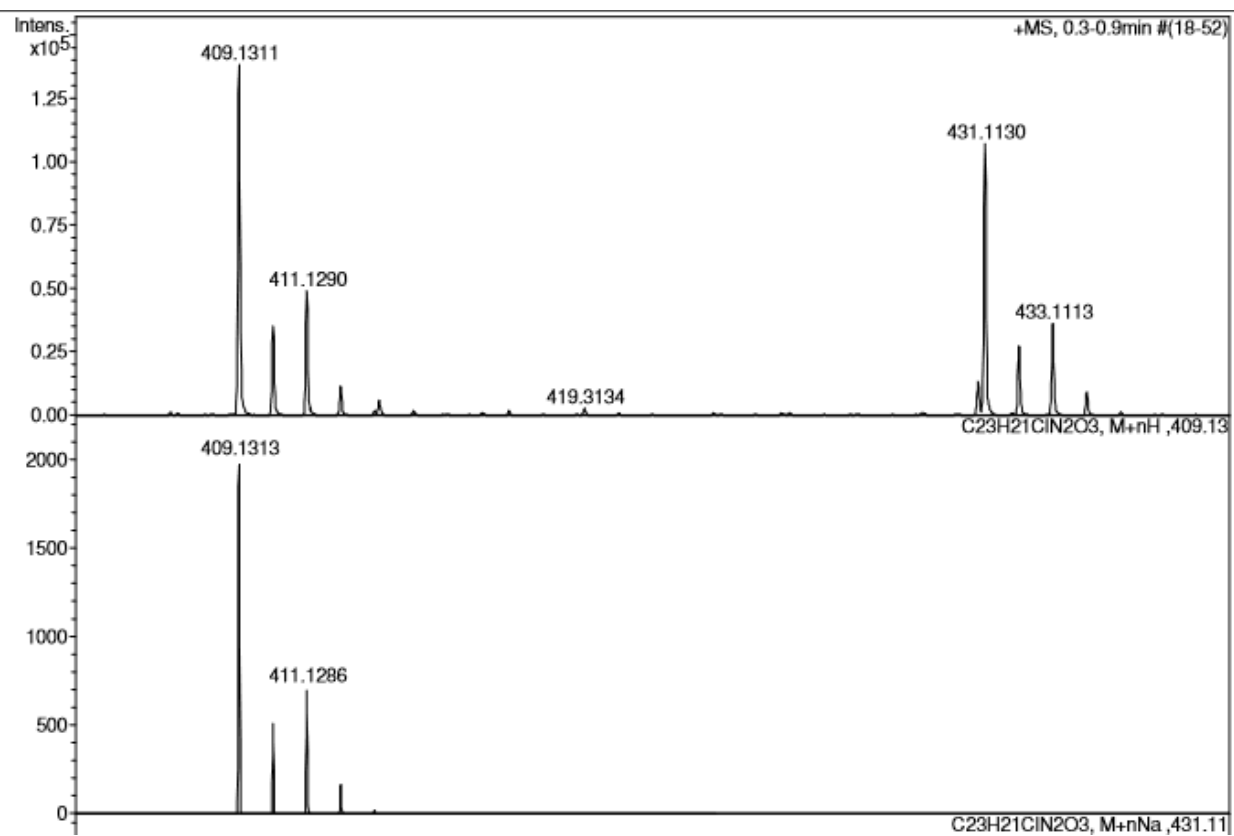
HRMS for **1i**



HRMS for **1j**

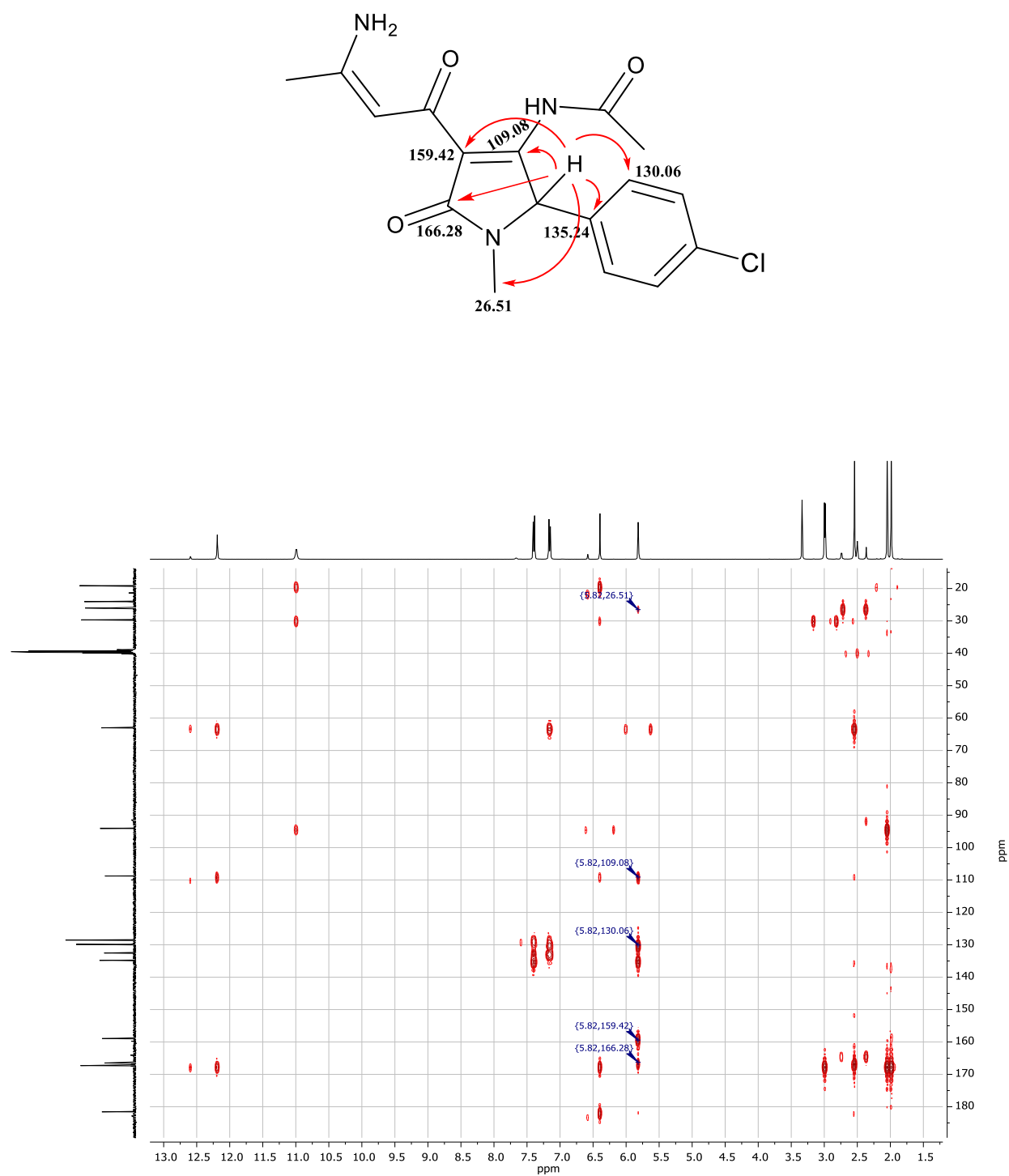


HRMS for **1a**

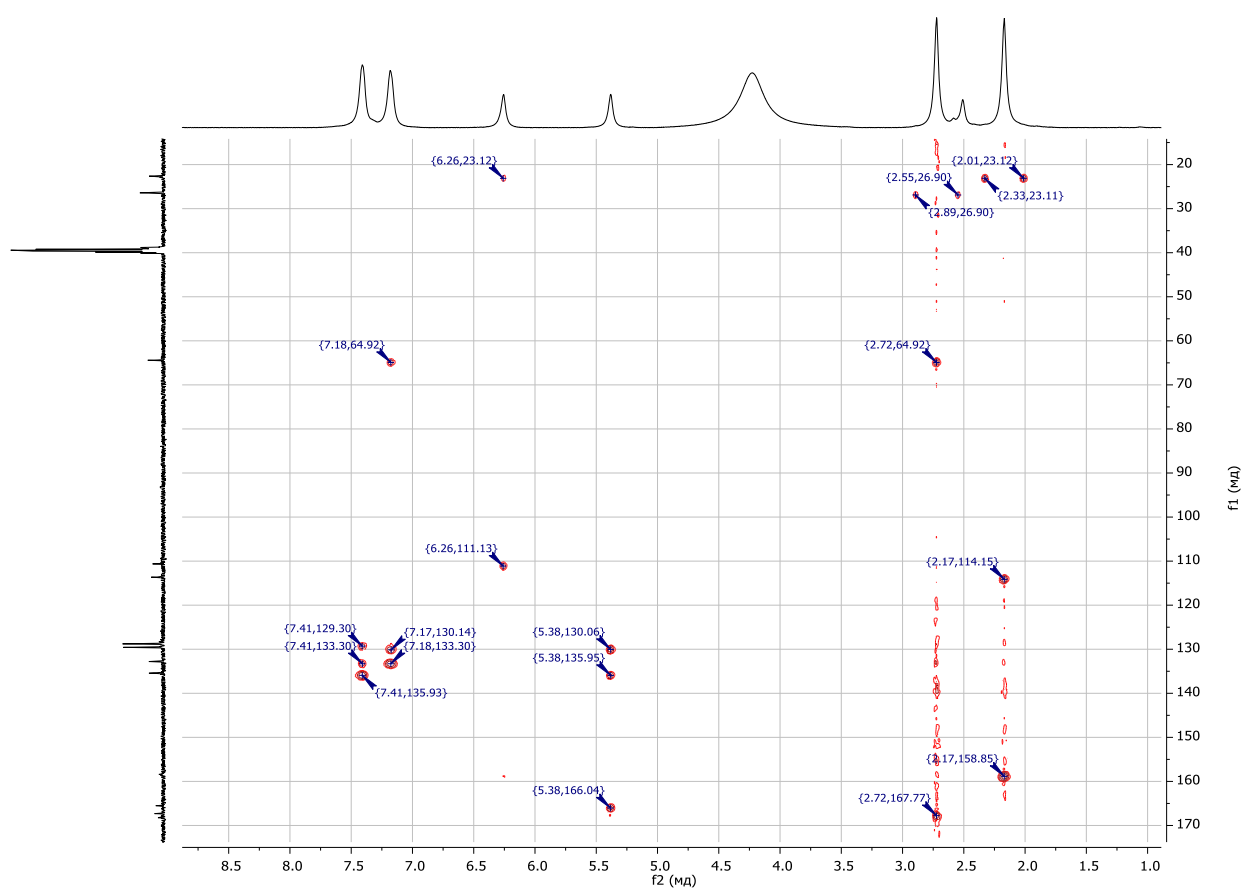
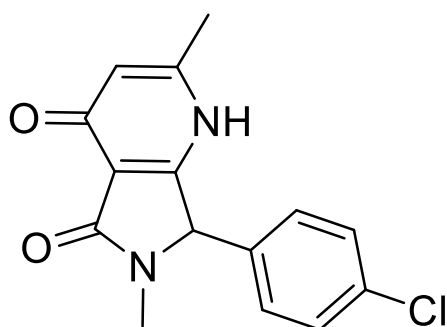


6. Copies of 2D spectra

HMBC for compound **7e**



HMBC for compound **1e**



7. X-ray analysis of compound **1e**

Crystallographic data: Crystals of **1e** ($C_{17}H_{19}ClN_2O_3$, $M = 334.79$) are orthorhombic, space group $Pbca$, at 120 K: $a = 15.8377(10)$, $b = 12.1158(7)$, $c = 17.2705(12)$ Å, $V = 3314.0(4)$ Å³, $Z = 8$ ($Z' = 1$), $d_{\text{calc}} = 1.342$ g cm⁻³, $\mu(\text{Cu K}\alpha) = 21.82$ cm⁻¹, $F(000) = 1408$. Intensities of 39379 reflections were measured with a Bruker APEX2 DUO CCD diffractometer [$\lambda(\text{Cu K}\alpha) = 1.54178$ Å, ω -scans, $2\theta < 135^\circ$], and 2914 independent reflections [$R_{\text{int}} = 0.0403$] were used in further refinement. The structure was solved by direct methods and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. Hydrogen atoms of the NH group and the OH group of the ethanol solvent molecule in **1e** were found in difference Fourier synthesis, while positions of others were calculated. All hydrogen atoms were then refined in the isotropic approximation within the riding model. The refinement converged to $wR2 = 0.1187$ and $GOF = 1.043$ for all the independent reflections ($R1 = 0.0467$ was calculated against F for 2439 observed reflections with $I > 2\sigma(I)$). All calculations were performed using SHELXTL PLUS 5.0.¹ CCDC 1921613 contains the supplementary crystallographic data for **1e**.

Reference

1. G.M. Sheldrick. A short history of SHELX. *Acta Cryst. A*, 2008, 64, 112-122