Divergent synthesis of a thiolate-based α-hydroxytropolone library with a dynamic bioactivity profile

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Supporting Information

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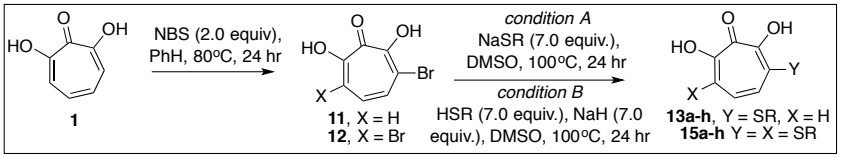
I. General Information

All starting materials and reagents were purchased from commercially available sources and used without further purification with exception of *N*-Bromosuccinimide which was recrystallized from de-ionized water. All reactions were performed in a sealed microwave vial. ^{1}H NMR shifts are measured using the solvent residual peak as the internal standard ($CDCl_3$ δ 7.26), and reported as follows: chemical shift, multiplicity (s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = doublet of doublet, td = triplet of doublet, q = quartet, m = multiplet), coupling constant (Hz), and integration. ^{13}C NMR shifts are measured using the solvent residual peak as the internal standard ($CDCl_3$ δ 77.16) and reported as chemical shifts. Infrared (IR) spectral bands are characterized as broad (br), strong (s), medium (m), and weak (w). Purification via column chromatography was performed on the Biotage Isolera Prime, with Biotage SNAP 30g C_{18} cartridges, in a solvent system of acetonitrile (MeCN) and de-ionized water (H_2O), with each containing 0.05% trifluoroacetic acid (TFA). Column gradients are measured in terms of column volumes (CV). Mass spectra were recorded on a spectrometer by the electrospray ionization (ESI) technique with a time-of-flight (TOF) mass analyzer.

II. Synthesis and characterization of α-hydroxytropolone thioethers



General Procedure: Recrystallized *N*-Bromosuccinimide (2 equiv, 1.24 mmol, 221.4 mg) was added to a solution of **1** (1 equiv, 0.62mmol, 86.0 mg) in benzene (0.2 M, 3 mL) and stirred at 80 °C for 24 hours. After cooling the reaction mixture to room temperature, the mixture was concentrated *en vacuo* to remove benzene, which gave crude solid compounds **11** and **12** as a mixture. Without purification *condition A* or *B* was applied to obtain compounds **13a-h and 15a-h**.

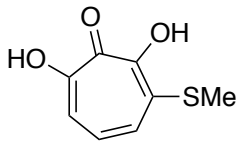
Condition A: From the thiolate salt

Crude solid mixture compounds **11** and **12** were dissolved in DMSO (6 mL) and the appropriate thiolate salt (7.0 equiv) was added to the reaction mixture and stirred at 100 °C for 24 hours.

Condition B: From the thiol

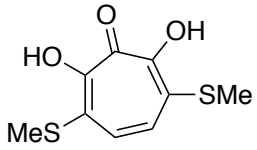
In a separate screw cap vial the appropriate thiol compound (7 equiv) was dissolved in DMSO (6 mL), NaH (7 equiv, 13.06 mmol, 313.35 mg) was added, venting off gas formation, and the resulting mixture was stirred at 80 °C for 1 hour. After cooling the reaction mixture to room temperature, crude solid mixture compounds **11** and **12**, dissolved in DMSO (~1 mL), was added to the cooled reaction mixture and stirred at 100 °C for 24 hours.

After 24 hours the cooled reaction mixture was directly loaded to C18 reverse-phase column chromatography conditions with solvent gradient: 10% - 90% MeCN in H_2O (15 CV); 90% - 100% MeCN in H_2O (2 CV). Product fractions were concentrated *en vacuo* to remove MeCN, and the remaining aqueous solution was extracted with CH_2Cl_2 (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *en vacuo* to yield the respective product(s).



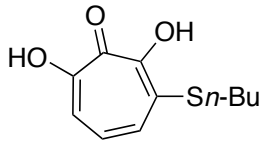
2,7-dihydroxy-3-(methylthio) cyclohepta-2,4,6-trien-1-one (13a)

Prepared following general procedure and *condition A* using sodium thiomethoxide (13.06 mmol, 915.38 mg). Product was obtained as a brown solid (35.6 mg, 31 % yield over 2 steps). **MP**: 141 – 142 °C. **IR (thin film, KBr)** 3209 (br), 2929 (w), 1609 (w), 1573 (m) 1525 (m), 1491 (m), 1407 (s), 1374 (s), 1304 (s), 1235 (m), 1182 (s), 1069 (m), 899 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 (dd, *J* = 7.5, 3.6 Hz, 1H), 7.14 – 7.10 (m, 2H), 2.56 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.05, 158.80, 156.37, 138.91, 127.52, 125.73, 117.81, 15.44. **HRMS (ESI+)** *m/z* calc'd for $C_8H_9O_3S^+$: 185.0267. Found: 185.0264



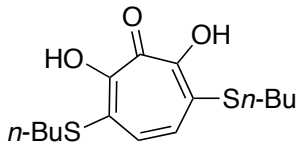
2,7-dihydroxy-3,6-bis(methylthio)cyclohepta-2,4,6-trien-1-one (15a)

Prepared following general procedure and *condition A* using sodium thiomethoxide (13.06 mmol, 915.38 mg). Product was obtained as a brown solid (34.4 mg, 24 % yield over 2 steps). **MP**: decomposed at 195 °C. **IR (thin film, KBr)** 3152 (br), 2911 (w), 1502 (m), 1481b (m), 1303 (s), 1168 (s), 1114 (m), 1081 (m), 880 (s), 765 (w), (721 (m), 681 (m), 662 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.07 (s, 2H), 2.55 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 159.31, 155.42, 134.26, 124.40, 15.51. **HRMS (ESI+)** *m/z* calc'd for $C_9H_{11}O_3S_2^+$: 231.0280. Found: 231.0280.



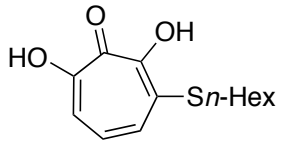
3-(butylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (13b)

Prepared following general procedure and *condition A* using sodium 1-butanethiolate (13.06 mmol, 1.46 g). Product was obtained as a brown solid (21.2 mg, 15 % yield over 2 steps). **MP**: 89 – 90 °C. **IR (thin film, KBr))** 3221 (br), 2958 (s), 2925 (s), 2853 (m), 1569 (m), 1507 (m), 1457 (m), 1435 (m), 1417 (s), 1339 (s), 1233 (m), 1185 (s), 1071 (m), 1045 (m), 901 (s), 793 (m), 740 (m), 669 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (dd, *J* = 10.1, 0.8 Hz, 1H), 7.19 (d, *J* = 10.9 Hz, 1H), 7.06 (dd, *J* = 11.2, 10.1 Hz, 1H), 3.13 – 2.90 (m, 2H), 1.73 (ddd, *J* = 15.0, 8.5, 6.3 Hz, 2H), 1.52 (dq, *J* = 14.5, 7.3 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.80, 158.86, 156.50, 137.84, 127.35, 127.07, 117.89, 31.81, 30.56, 22.22, 13.75. **HRMS (ESI+)** *m/z* calc'd for $C_{11}H_{15}O_3S^+$: 227.0736. Found: 227.0741.



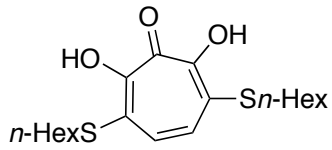
3,6-bis(butylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (15b)

Prepared following general procedure using sodium 1-butanethiolate (13.06 mmol, 1.46 g). Product was obtained as a brown solid (28.7 mg, 15 % yield over 2 steps). **MP**: 88 – 89 °C. **IR (thin film, KBr)** 3421 (br), 3189 (br), 2945 (s), 2926b (s), 2857 (w), 1647 (m), 1406 (s), 1424 (w), 1376 (s), 1295 (s), 1185 (s), 1120 (s), 1081 (w), 885 (s), 733 (m), 692 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.10 (s, 2H), 3.08 – 2.94 (m, 4H), 1.70 (ddd, *J* = 15.0, 8.5, 6.3 Hz, 4H), 1.50 (dq, *J* = 14.5, 7.3 Hz, 4H), 1.05 – 0.82 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.58, 155.71, 133.23, 125.83, 31.96, 30.78, 22.15, 13.72. **HRMS (ESI+)** *m/z* calc'd for $C_{15}H_{23}O_3S_2^+$: 315.1083. Found: 315.1087.



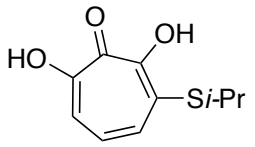
3-(hexylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (13c)

Prepared following general procedure and *condition B* using 1-hexanethiol (13.06 mmol, 1.5 g). Product was obtained as a brown solid (29.9 mg, 19 % yield over 2 steps). **MP**: 77 – 78 °C. **IR (thin film, KBr)** 3446 (br), 3239 (br), 2954 (m), 2923 (s), 2852 (s), 1471 (m), 1404 (m), 1304 (s), 1239 (w), 1184 (s), 1067 (s), 1045 (s), 896 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 (dd, *J* = 10.1, 0.5 Hz, 1H), 7.18 (d, *J* = 11.0 Hz, 1H), 7.06 (dd, *J* = 11.1, 10.2 Hz, 1H), 3.05 – 2.96 (m, 2H), 1.74 (dt, *J* = 15.0, 7.5 Hz, 2H), 1.49 (ddd, *J* = 15.1, 8.5, 6.2 Hz, 2H), 1.32 (td, *J* = 7.0, 3.4 Hz, 4H), 0.93 – 0.83 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 163.81 (s), 158.83 (s), 156.48 (s), 137.84 (s), 127.33 (s), 127.05 (s), 117.86 (s), 32.13 (s), 31.45 (s), 28.76 (s), 28.50 (s), 22.62 (s), 14.12 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{19}O_3S^+$: 255.1050. Found 255.1152.



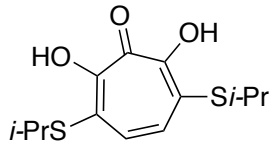
3,6-bis(hexylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (15c)

Prepared following general procedure and *condition B* using 1-hexanethiol (13.06 mmol, 1.5 g). Product was obtained as a brown solid (72.5 mg, 32 % yield over 2 steps). **MP**: 89 – 90 °C. **IR (thin film, KBr)** 3424 (br) 3186 (br), 2954 (s), 2926 (s), 1565 (w), 1422 (m), 1367 (m), 1317 (s), 1185 (s), 1120 (w), 1065 (m), 833 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.09 (s, 2H), 3.05 – 2.96 (m, 4H), 1.71 (dt, *J* = 15.0, 7.4 Hz, 4H), 1.53 – 1.43 (m, 4H), 1.36 – 1.25 (m, 8H), 0.93 – 0.83 (m, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 160.71 (s), 155.72 (s), 133.19 (s), 125.88 (s), 32.33 (s), 31.45 (s), 28.74 (s), 22.63 (s), 14.13 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{19}H_{31}O_3S^+$: 371.1710. Found 371.1799



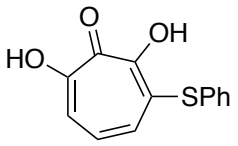
2,7-dihydroxy-3-(isopropylthio)cyclohepta-2,4,6-trien-1-one (13d)

Prepared following general procedure and *condition A* using sodium 2-propanethiolate (13.06 mmol, 1.28 g). Product was obtained as a brown solid (18.2 mg, 14 % yield over 2 steps). **MP**: 74 – 75 °C. **IR (thin film, KBr)** 3400 (br), 29310 (m), 2920 (s), 2840 (m), 1500 (m), 1442 (m), 1367 (m), 1298 (m), 1245 (m) 1168 (m), 1034 (s), 932 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (dd, *J* = 10.2, 0.7 Hz, 1H), 7.28 (d, *J* = 11.1 Hz, 1H), 7.05 (dd, *J* = 11.2, 10.2 Hz, 1H), 3.76 – 3.65 (m, 1H), 1.40 (d, *J* = 6.7 Hz, 6H**).** **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.88, 158.86, 157.06, 136.04, 129.36, 127.15, 118.32, 36.19, 22.91. **HRMS (ESI+)** *m/z* calc'd for $C_{10}H_{13}O_3S^+$: 212.0579. Found: 213.0578.



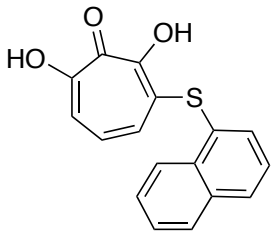
2,7-dihydroxy-3,6-bis(isopropylthio)cyclohepta-2,4,6-trien-1-one (15d)

Prepared following general procedure and *condition A* using sodium 2-propanethiolate (13.06 mmol, 1.28 g). Product was obtained as a brown solid (118.5 mg, 67 % yield over 2 steps). **MP**: 109 – 110 °C. **IR (thin film, KBr)** 3406 (br), 2960 (m), 2923 (s), 2853 (m), 1503 (m), 1461 (m), 1381 (m), 1302 (m), 1239 (m) 1198 (m), 1047 (s), 910 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.17 (s, 2H), 3.72 (hept, *J* = 6.7 Hz, 2H), 1.38 (d, *J* = 6.7 Hz, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.14, 156.40, 132.32, 127.86, 36.43, 22.99. **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{19}O_3S_2^+$: 287.0770. Found: 287.0770.



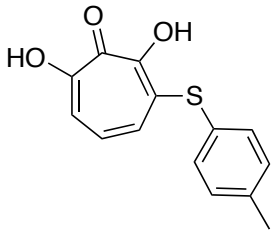
2,7-dihydroxy-3-(phenylthio)cyclohepta-2,4,6-trien-1-one (13e)

Prepared following general procedure and *condition A* using sodium thiophenolate (13.06 mmol, 1.72 g). Product was obtained as as a brown solid (41.8 mg, 27 % yield over 2 steps). **MP**: 92 – 93 °C. **IR (thin film, KBr)** 3219 (br), 3058 (w), 2926 (w), 2853 (w), 1570 (m), 1524 (m), 1498 (m), 1141 (m), 1372 (m), 1303 (s), 1241 (m), 1187 (s), 891 (s), 751 (m), 690 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.65 – 7.58 (m, 2H), 7.57 – 7.47 (m, 3H), 7.29 (d, *J* = 2.7 Hz, 1H), 6.92 – 6.82 (m, 1H), 6.72 (d, *J* = 11.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.37 (s), 158.69 (s), 154.99 (s), 138.67 (s), 136.05 (s), 130.23 (d, *J* = 8.3 Hz), 129.94 (s), 127.67 (s), 127.18 (s), 118.11 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{11}O_3S^+$: 247.0423. Found: 247.0423



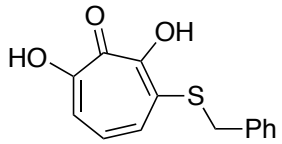
2,7-dihydroxy-3-(naphthalen-1-ylthio)cyclohepta-2,4,6-trien-1-one (13f)

Prepared by adding 1-Naphthalenethiol (1 equiv, 13.72 mmol, 2.2 g) to a solution of sodium hydroxide (1.3 M, 10 mL) and benzene (25 mL) and stirred at reflux for 1 hour. The resulting solution was concentrated *en vacuo* to obtain yellowish solid (2.4 g, 96 % yield), which was used without further purification. The obtained sodium salt of the 1-Naphthalenethiol was then added to a solution of compound **2a** and **2b**, dissolved in DMSO (6 mL), and stirred at 100 ^{o}C for 24 hours. Purification of the thioether was then performed just as described in the general procedure. Product was obtained as a brown solid (35.5 mg, 19 % yield over 2 steps). **MP**: 184 – 185 °C. **IR (thin film, KBr)** 3445 (br), 3055 (w), 2958 (w), 2924 (m), 2853 (m), 1634 (m), 1572 (m), 1502 (s), 1410 (s), 1375 (s), 1301 (s), 1254 (m), 1186 (s), 1066 (m), 1045 (m), 914 (s), 799 (s), 771 (s), 735 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.26 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.05 (d, *J* = 8.3 Hz, 1H), 7.98 – 7.92 (m, 2H), 7.62 – 7.48 (m, 3H), 7.17 (dd, *J* = 10.2, 0.6 Hz, 1H), 6.65 (dd, *J* = 11.2, 10.3 Hz, 1H), 6.39 (dd, *J* = 11.3, 0.6 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.19 (s), 158.68 (s), 155.03 (s), 138.60 (s), 136.78 (s), 134.86 (s), 134.63 (s), 131.92 (s), 129.05 (s), 128.07 (s), 127.57 (s) 127.01 (s), 126.51 (s), 126.29 (s), 125.76 (s), 117.94 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{17}H_{13}O_3S^+$: 297.0580. Found 297.0601.



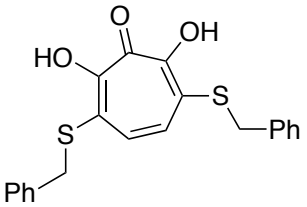
2,7-dihydroxy-3-(*p*-tolylthio)cyclohepta-2,4,6-trien-1-one (13g)

Prepared following general procedure and *condition A* using 4-methylbenzenethiol sodium salt (13.06 mmol, 1.9 g). Product was obtained as a brown solid (25.6 mg, 16 % yield over 2 steps). **MP**: 96 – 97 °C. **IR (thin film, KBr)** 3223 (br), 2956 (w), 2921 (m), 2853 (m), 1570 (m), 1525 (m), 1489 (s), 1401 (m), 1306 (s), 1236 (m), 1187 (s), 1178 (s), 1068 (m), 1045 (m), 891 (s), 809 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.49 – 7.45 (m, 2H), 7.29 (dd, *J* = 8.4, 0.5 Hz, 2H), 7.23 (dd, *J* = 10.2, 0.8 Hz, 1H), 6.83 (dd, *J* = 11.3, 10.2 Hz, 1H), 6.67 (dd, *J* = 11.3, 0.7 Hz, 1H), 2.43 (s, 3H) **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.25 (s), 158.69 (s), 154.72 (s), 140.75 (s), 139.38 (s), 136.24 (s), 131.12 (s), 127.36 (s), 127.13 (s), 117.91 (s), 87.45 (s), 21.54 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{14}H_{13}O_3S^+$: 261.0589. Found 262.0632.



3-(benzylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (13h)

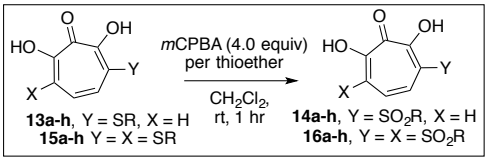
Prepared following general procedure and *condition B* using benzyl mercaptan (13.06 mmol, 1.6 g). Product was obtained as a brown solid (21.5 mg, 13 % yield over 2 steps). **MP**: 98 – 99 °C. **IR (thin film, KBr)** 3198 (br), 3060 (w), 3027 (w), 2957 (m), 2923 (s), 2852 (m), 1571 (w), 1494 (m), 1403 (s), 1305 (s), 1238 (m), 1186 (s), 1068 (m), 1046 (m), 895 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, *J* = 6.8 Hz, 2H), 7.35 – 7.27 (m, 4H), 7.22 (d, *J* = 11.1 Hz, 1H), 7.00 (dd, *J* = 11.0, 10.3 Hz, 1H), 4.28 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 164.19, 158.78, 156.85, 136.61, 135.47, 129.07, 128.91, 128.28, 127.86, 127.36, 118.47, 37.05. **HRMS (ESI+)** *m/z* calc'd for $C_{14}H_{13}O_3S^+$: 261.0579. Found: 261.0575.



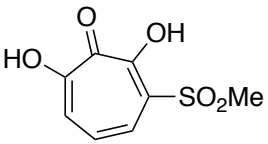
3,6-bis(benzylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (15h)

Prepared following general procedure and *condition B* using benzyl mercaptan (13.06 mmol, 1.6 g). Product was obtained as a brown solid (73.4 mg, 31 % yield over 2 steps). **MP**: 154 – 155 °C. **IR (thin film, KBr)** 3425 (br), 2924 (w), 2853 (w), 1635 (s), 1494 (w), 1396 (w), 1307 (w), 1186 (m), 1069 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 – 7.27 (m, 10H), 7.02 (s, 2H), 4.24 (s, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 161.19, 156.09, 135.75, 132.74, 129.04, 128.89, 127.82, 126.97, 37.14. **HRMS (ESI+)** *m/z* calc'd for $C_{21}H_{19}O_3S_2^+$: 383.0770. Found: 383.0770.

III. Synthesis and characterization of α-hydroxytropolone sulfones

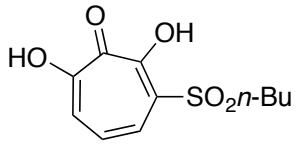


General Procedure: *meta*-Chloroperoxybenzoic acid (70% - 75% balance 3-chlorobenzoic acid and water) (4.0 equiv per thioether group) was added to a solution of **13a-h** or **15a-h** in chloroform (0.02 M) and stirred at room temperature for 1 hour, at which point proton NMR indicated complete oxidation. Excess *m*CPBA was quenched by adding aqueous solution of sodium sulfite (30 mL) to the reaction mixture and then extracted with dichloromethane (3 X 10 mL). The combined organic extractions were concentrated *en vacuo*, dissolved in 1 mL of DMSO, and subjected to reverse-phase C_{18} column chromatography conditions with solvent gradient: 10% - 90% MeCN in H_2O (15 CV); 90% - 100% MeCN in H_2O (2 CV). Product fractions were concentrated *en vacuo* to remove MeCN, and the remaining aqueous solution was extracted with CH_2Cl_2 (3 x 15 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated *en vacuo* to yield the respective product(s).



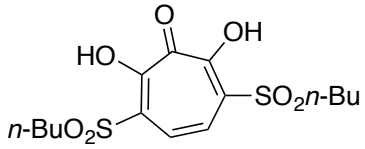
2,7-dihydroxy-3-(methylsulfonyl)cyclohepta-2,4,6-trien-1-one (14a)

Prepared following general procedure using **3b** (1 equiv, 0.129 mmol, 23.7 mg), *m*CPBA (4 equiv, 0.515 mmol, 88.9 mg). Product was obtained as a brown solid (32.8 mg, 72 % yield). **MP**: 178 – 179 °C. **IR (thin film, KBr)** 3264 (br), 2923 (w), 1602 (w), 1541 (m), 1306 (s), 1136 (m), 1060 (w), 967 (w), 798 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.03 (dd, *J* = 11.1, 0.8 Hz, 1H), 7.68 (dd, *J* = 10.3, 0.8 Hz, 1H), 7.36 (dd, *J* = 11.1, 10.3 Hz, 1H), 3.39 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.83 (s), 158.87 (s), 157.67 (s), 132.99 (s), 128.17 (s), 127.75 (s), 124.59 (s), 43.01 (s). **HRMS (ESI+)** *m/z* calc'd for $C_8H_9O_5S^+$: 217.0165. Found: 217.1039.



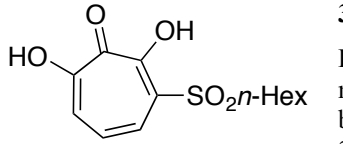
3-(butylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (14b)

Prepared following general procedure using **3d** (1 equiv, 0.093 mmol, 21.2 mg), *m*CPBA (4 equiv, 0.374 mmol, 64.6 mg). Product was obtained as a brown solid (15.2 mg, 63 % yield). **MP**: 70 -71 °C **IR (thin film, KBr)** 3441 (br), 1635 (br) 1542 (w), 1465 (m) 1375 (m), 1298 (m), 1198 (m), 1133 (m), 1068 (w) 783 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 – 7.95 (m, 1H), 7.72 – 7.62 (m, 1H), 7.35 (dd, *J* = 11.0, 10.3 Hz, 1H), 3.81 – 3.21 (m, 2H), 1.83 – 1.61 (m, 2H), 1.57 – 1.33 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.66 (s), 158.88 (s), 157.80 (s), 131.84 (s), 128.52 (s), 128.05 (s), 124.63 (s), 54.34 (s), 24.57 (s), 21.73 (s), 13.63 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{11}H_{14}O_5SNa^+$: 281.0454. Found: 281.0456



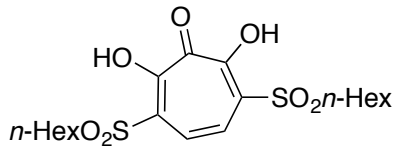
3,6-bis(butylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (16b)

Prepared following general procedure using **3e** (1 equiv, 0.091 mmol, 28.7 mg), *m*CPBA (8 equiv, 0.730 mmol, 125.9 mg). Product was obtained as a brown solid (10.4 mg, 30 % yield). **MP**: 155 -156 °C **IR (thin film, KBr)** 3452 (br), 2958 (w), 2923 (M), 2853 (w), 1636 (br), 1463 (w), 1377 (w), 1298 (w), 1238 (w), 1131 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.11 (s, 2H), 3.62 – 3.46 (m, 4H), 1.72 (ddd, *J* = 12.1, 10.3, 6.5 Hz, 4H), 1.56 – 1.36 (m, 4H), 0.93 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.61 (s), 156.50 (s), 133.61 (s), 126.57 (s), 54.57 (s), 24.51 (s), 21.73 (s), 13.62 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{15}H_{23}O_7S_2^+$: 379.0880. Found: 379.0877.



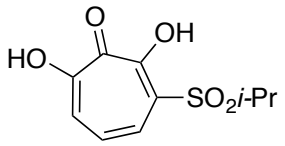
3-(hexylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (14c)

Prepared following general procedure using **3k** (1 equiv, 0.186 mmol, 47.5 mg), *m*CPBA (4 equiv, 0.746 mmol, 128.8 mg). Product was obtained as a brown solid (34.7 mg, 62 % yield). **MP**: 86 – 87 °C **IR (thin film, KBr)** 3223 (br), 3073 (w), 2959 (m), 2920 (m), 2865 (m), 1587 (s), 1354 (w), 1333 (m), 1316 (s), 1284 (s), 1138 (s), 1100 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.00 (dd, *J* = 11.1, 0.8 Hz, 1H), 7.67 (dd, *J* = 10.2, 0.8 Hz, 1H), 7.35 (dd, *J* = 11.1, 10.3 Hz, 1H), 3.83 – 3.15 (m, 2H), 1.78 – 1.64 (m, 2H), 1.39 (dt, *J* = 14.7, 7.3 Hz, 2H), 1.31 – 1.19 (m, 4H), 0.85 (dd, *J* = 8.7, 5.2 Hz, 3H**).** **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.52 (s), 158.89 (s), 157.87 (s), 131.87 (s), 128.56 (s), 128.07 (s), 124.76 (s), 54.56 (s), 31.23 (s), 28.07 (s), 22.45 (d, *J* = 15.6 Hz), 14.00 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{18}O_5SNa^+$: 309.0767. Found: 309.0765.



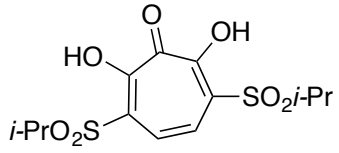
3,6-bis(hexylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (16c)

Prepared following general procedure using **3l** (1 equiv, 0.195 mmol, 72.5 mg), *m*CPBA (8 equiv, 1.56 mmol, 270 mg). Product was obtained as a brown solid (82.4 mg, 97 % yield). **MP**: 177 – 178 °C **IR (thin film, KBr)** 3242 (br), 3077 (w), 2955 (m), 2925 (m), 2855 (m), 1541 (s), 1395 (m), 1362 (m), 1316 (s), 1284 (s), 1134 (s), 1101 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.09 (s, 2H), 3.74 – 3.23 (m, 4H), 1.71 (ddd, *J* = 12.1, 10.2, 6.5 Hz, 4H), 1.45 – 1.35 (m, 4H), 1.32 – 1.22 (m, 8H), 0.86 (t, *J* = 6.9 Hz, 6H**).** **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.57 (s), 156.52 (s), 133.58 (s), 126.53 (s), 54.78 (s), 31.21 (s), 28.08 (s), 22.42 (d, *J* = 12.0 Hz), 14.00 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{19}H_{31}O_7S_2^+$: 435.1506. Found: 435.1506.



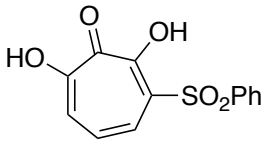
2,7-dihydroxy-3-(isopropylsulfonyl)cyclohepta-2,4,6-trien-1-one (14d)

Prepared following general procedure using **3f** (1 equiv, 0.085 mmol, 18.2 mg), *m*CPBA (4 equiv, 0.342 mmol, 58.1 mg). Product was obtained a as a brown solid (10.3 mg, 49 % yield). **MP**: 109 – 110 °C **IR (thin film, KBr)** 3421 (br), 2984 (w), 2921 (m), 2824 (m), 1732 (m), 1716 (m), 1656(m), 1445 (m), 1355 (m), 1133 (m), 1022 (m), 1011 (w), 932 (w), 821 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.05 – 7.95 (m, 1H), 7.72 – 7.62 (m, 1H), 7.35 (dd, *J* = 11.0, 10.3 Hz, 1H), 3.81 – 3.21 (m, 2H), 1.83 – 1.61 (m, 2H), 1.57 – 1.33 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.60 (s), 158.86 (s), 157.79 (s), 130.72 (s), 129.04 (s), 127.92 (s), 124.51 (s), 53.87 (s), 15.22 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{10}H_{12}O_5SNa^+$: 267.0297. Found: 267.0297.



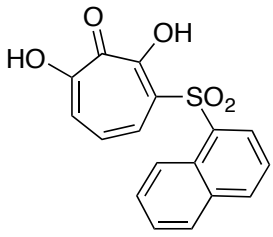
2,7-dihydroxy-3,6-bis(isopropylsulfonyl)cyclohepta-2,4,6-trien-1-one (16d)

Prepared following general procedure using **3g** (1 equiv, 0.413 mmol, 118.5 mg), *m*CPBA (8 equiv, 3.31 mmol, 571.1 mg). Product was obtained as a brown solid (60.8 mg, 42 % yield). **MP**: decomposed at 230 °C. **IR (thin film, KBr)** 3439 (br), 2996 (w), 2923 (m), 2852 (m), 1778 (m), 1723 (m), 1636 (m), 1465 (m), 1305 (m), 1128 (m), 1055 (m), 1031 (w), 964 (w), 876 (w), 788 (w) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.09 (s, 2H), 4.20 – 3.72 (m, 2H), 1.36 (d, *J* = 6.8 Hz, 12H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 170.32 (s), 156.57 (s), 132.64 (s), 126.90 (s), 54.37 (s), 15.18 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{19}O_7S_2^+$: 351.0567. Found: 351.0573.



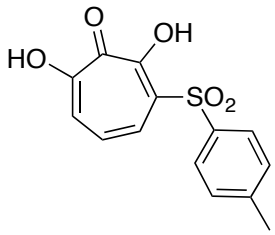
2,7-dihydroxy-3-(phenylsulfonyl)cyclohepta-2,4,6-trien-1-one (14e)

Prepared following general procedure using **3h** (1 equiv, 0.169 mmol, 41.8 mg), *m*CPBA (4 equiv, 0.678 mmol, 117.1 mg). Product was obtained as a brown solid (12.0 mg, 25 % yield). **MP**: 121 – 122 °C **IR (thin film, KBr)** 3215 (br), 3066 (w), 2925 (w), 1507 (s), 1446 (m), 1419 (m), 1319 (s), 1191 (m), 1139 (s), 1086 (m), 798 (m), 722 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.28 (dd, *J* = 11.2, 0.8 Hz, 1H), 8.03 (dd, *J* = 8.5, 1.2 Hz, 2H), 7.67 – 7.60 (m, 2H), 7.57 – 7.49 (m, 2H), 7.37 (dd, *J* = 11.2, 10.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.99 (s), 158.75 (s), 157.30 (s), 139.92 (s), 134.01 (s), 133.40 (s), 129.17 (s), 128.90 (s), 127.92 (s), 127.62 (s), 124.26 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{13}H_{11}O_5S^+$: 279.0322. Found: 279.0316



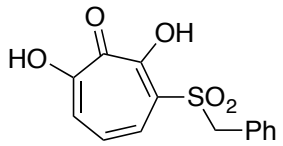
2,7-dihydroxy-3-(naphthalen-1-ylsulfonyl)cyclohepta-2,4,6-trien-1-one (14f)

Prepared following general procedure using **3j** (1 equiv, 0.069 mmol, 15.5 mg), *m*CPBA (4 equiv, 0.276 mmol, 47.7 mg). Product was obtained as a brown solid (10.9 mg, 48 % yield). **MP**: 243 -244 °C **IR (thin film, KBr)** 3451 (br), 3033 (w), 2912 (w), 2909 (m), 2878 (m), 1612 (m), 1553 (m), 1498 (s), 1445 (s), 1364 (s), 1301 (s), 1232 (m), 1145 (s), 1176 (m), 1034 (m), 934 (s), 767 (s), 712 (s) cm^{-1} . **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.68 (d, *J* = 7.5 Hz, 1H), 8.49 (d, *J* = 11.2 Hz, 1H), 8.27 (d, *J* = 5.8 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.97 – 7.87 (m, 1H), 7.75 – 7.57 (m, 2H), 7.48 (ddd, *J* = 21.4, 9.9, 3.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.22 (s), 158.81 (s), 157.26 (s), 135.60 (s), 134.65 (s), 134.13 (s), 133.68 (s), 132.73 (s), 129.42 (s), 128.53 (s), 127.67 (d, *J* = 8.3 Hz), 126.81 (s), 124.38 (s), 123.96 (s), 123.62 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{17}H_{12}O_5SNa^+$: 351.0297. Found: 351.0298.



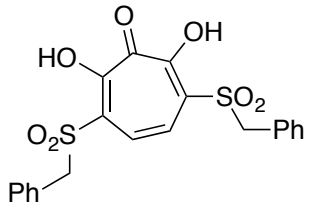
2,7-dihydroxy-3-tosylcyclohepta-2,4,6-trien-1-one (14g)

Prepared following general procedure using **3i** (1 equiv, 0.098 mmol, 25.6 mg), *m*CPBA (4 equiv, 0.393 mmol, 67.8 mg). Product was obtained as a brown solid (12.0 mg, 42 % yield). **MP**:171 – 172 °C **IR (thin film, KBr)** 3421 (br), 3189 (br), 2957 (s), 2926 (s), 2857 (m), 1486 (m), 1376 (m), 1318 (s), 1215 (m), 1185 (s), 1120 (m), 1081 (m), 885 (s), 733 (m), 692 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.27 (dd, *J* = 11.2, 0.8 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.62 (dd, *J* = 10.2, 0.8 Hz, 1H), 7.40 – 7.27 (m, 3H), 2.43 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 158.60 (s), 157.18 (s), 145.06 (s), 133.83 (s), 130.27 (s), 129.87 (s), 129.42 (s), 129.14 (s), 128.32 (s), 127.87 (s), 127.46 (s), 124.10 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{14}H_{13}O_5S^+$: 293.0478. Found: 293.0457.



3-(benzylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (14h)

Prepared following general procedure using **3m** (1 equiv, 0.082 mmol, 21.5 mg), *m*CPBA (4 equiv, 0.330 mmol, 57.0 mg). Product was obtained as a brown solid (10.8 mg, 45 % yield). **MP**: 131 -132 °C **IR (thin film, KBr)** 3201 (br), 3066 (w), 3035 (w), 2925 (m), 1603 (m), 1541 (m), 1419 (m), 1361 (m), 1315 (s), 1250 (m), 1197 (m), 1146 (m), 1121 (m) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.70 (dd, *J* = 11.1, 0.8 Hz, 4H), 7.59 (dd, *J* = 10.3, 0.8 Hz, 4H), 7.27 (s), 18H), 7.16 (dd, *J* = 11.1, 10.3 Hz, 5H), 4.82 (s, 7H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 168.20 (s), 158.61 (s), 157.77 (s), 131.21 (s), 130.81 (s), 129.265 (s), 128.959 (s), 127.76 (s), 127. 33 (s), 124. 74 (s), 60.59 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{14}H_{13}O_5S^+$: 293.0405. Found: 293.0457.



3,6-bis(benzylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one (16h)

Prepared following general procedure using **3n** (1 equiv, 0.082 mmol, 31.4 mg), *m*CPBA (8 equiv, 0.656 mmol, 113.3 mg). Product was obtained as a brown solid (21.6 mg, 59 % yield). **MP**: 220 – 221 °C. **IR (thin film, KBr)** 3214 (br), 3026 (w), 2925 (w), 1572 (m), 1525 (m), 1495 (s), 1408 (s), 1304 (s), 1254 (s), 1186 (s), 1070 (m), 1044 (m), 896 (s) cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.58 (s, 2H), 7.32 – 7.27 (m, 2H), 7.22 (ddd, *J* = 9.7, 8.6, 1.8 Hz, 8H), 4.77 (s, 4H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 169.82 (s), 156.20 (s), 132.93 (s), 130.64 (s), 129.63 (s), 129.17 (s), 126.59 (s), 126.57 (s), 50.85 (s). **HRMS (ESI+)** *m/z* calc'd for $C_{21}H_{19}O_7S_2^+$: 447.0567. Found: 447.0531.

IV. Biological Assays. Biological assays were performed consistent with previously described conditions. A full table of results can be seen in **Table S1**.

***Cryptococcus neoformans* MIC_{80} determination.** *C. neoformans* MIC_{80} values were obtained consistent with prior experiments from our labs.[1] Compounds were tested in a limiting dilution assay with a starting optical density (at 650 nm) of 0.001 in YNB-02 plus 1% DMSO. Cells were incubated without shaking for 48 h at 35°C and cell densities were measured at 650 nm. The MICs were determined using compound concentrations from 0.19 to 50 μM in YNB-02 plus 1% DMSO. Each assay was done in triplicates and all values are the averages from two or more independent assays. The data are presented as the average cell densities as percentages of DMSO-only treated cells. MICs are reported as the minimal concentration needed to inhibit 80% of *C. neoformans* growth relative to vehicle-treated controls.

Herpes simplex virus-1 antiviral assays. HSV-1 antiviral studies were carried out as previously reported.[2] Test compounds were diluted in PBS containing 2% newborn calf serum and 2 mM L–glutamine and were added to confluent Vero cell monolayers in 24-well plates. Equivalent dilutions of DMSO were used as vehicle controls. HSV-1 was diluted in supplemented PBS medium and added so that the final compound concentrations were 5 or 1 μM and the HSV MOI was 0.1. The cells were incubated at 37°C for 1 h, the virus-containing inoculum was removed, the wells were washed once in PBS, and the compound (5 or 1 μM) in supplemented DMEM was added. Cells were incubated at 37°C for an additional 23 h, and the plates were then inspected by phase-contrast microscopy for cytopathic effect (CPE) or toxicity. Cells in wells showing negligible toxicity were frozen and then harvested by scraping, along with DMSO control wells. Samples were sonicated and virus titers were determined by plaque assay on Vero cells. Each experiment was repeated at least once. The 50% effective concentrations (EC_{50}s) were determined for select compounds as described above except that serial dilutions of the compounds were employed. Values were calculated with GraphPad Prism using the three-parameter log(inhibitor)-versus-response algorithm with the bottom value set to zero.

Vero cytotoxicity assays. Vero cell cytotoxicity measurements were carried out as previously reported.[2] Vero cells ($1x10^4$ cells per well) were seeded into 96-well plates and incubated in DMEM/10% FBS plus PS. Test compounds were serially diluted in medium containing 1% DMSO and added to the cells 24 h after plating, with each concentration being tested in duplicate. Twenty-four hours after compound addition, [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS)] and phenazine ethosulfate (PES) (Promega) were added to 0.33 mg/ml, the cultures were incubated for 60 min, and the absorbance was read at 490 nm.MT. The 50% cytotoxic concentration (CC_{50}) values were calculated with GraphPad Prism using the four-parameter variable-response log(inhibitor)-versus-response algorithm with the bottom value set to zero.

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[1] Donlin, M. J.; Zunica, A.; Lipnicky, A; Garimallaprabhakaran, A. K.; Berkowitz, A. J.; Grigoryan, A.; Meyers, M. J.; Tavis, J. E.; Murelli, R. P. *Antimicrob. Agents Chemother.,* **2017**, *61,* e02574-16

[2] Tavis, J. E.; Wang, H; Tollefson, A. E..; Ying, B.; Korom, M.; Cheng, X.; Cao, F.; Davis, K. L.; Wold, W. S. W.; Morrison, L. A. *Antimicrob. Agents Chemother.* **2014,** *58*, 7451-7461.

HBV Replication Assay. This assay was conducted analogously to previous studies in the Tavis lab, using a HepDES19 cell system.[3] Cells were seeded in 12-well plates and incubated in Dulbecco's modified Eagle's medium (DMEM)/F12, 10% fetal bovine serum (FBS), and 1% penicillin and streptomycin (P/S). The test compounds (20 or 5 μM) was applied to duplicate wells 48 h later in medium containing a final DMSO concentration of 1%. Cells were harvested three days after compound addition, and nonencapsidated nucleic acids were digested with micrococcal nuclease (New England BioLabs). HBV DNA was purified from capsids using a QIAamp cador pathogen minikit (Qiagen) with proteinase K incubation overnight at 37 °C. TaqMan PCR was performed for 40 cycles at an annealing temperature of 60 °C. The primers and probe (IDT Inc.) for the plus-polarity strand were 5'CATGAACAAGAGATGATTAGGCAGAG3', 5'GGAGGCTGTAGGCATAAATTGG3', and 5'/56-FAM/CTGCGCACC/ZEN/AGCACCATGCA/3IABkFQ. The primers and probe for the minus-polarity strand were 5'GCAGATGAGAAGGCACAGA3', 5'CTTCTCCGTCTGCCGTT3', and 5'/56-FAM/AGTCCGCGT/ZEN/AAAGAGAGGTGCG/3IABkFQ.

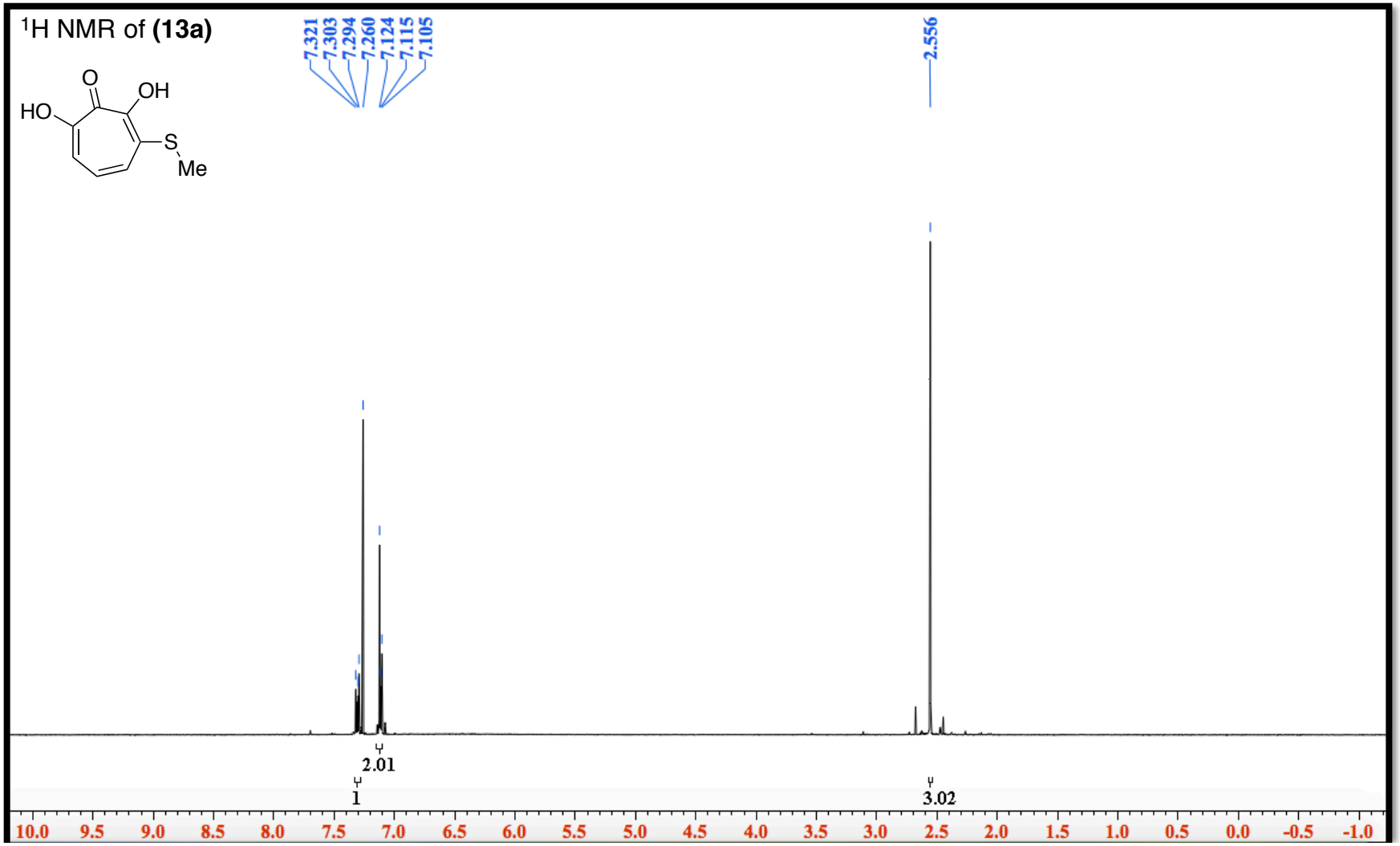
HepDES19 Cytotoxicity Assay. Cytotoxicity measurements were conducted as described previously.[3] HepDES19 cells ($1.0x10^4$ cells per well) were seeded in 96-well plates and incubated in DMEM/F12 with 10% FBS plus 1% P/S. The compounds were diluted in the medium to the indicated concentrations plus 1% DMSO and added to the cells 24 h after plating, with each concentration tested in triplicate. MTS [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] and phenazine ethosulfate (PES) (Promega). (Promega) were added to 0.33 mg/ml, the cultures were incubated for 60 min, and the absorbance was read at 490 nm. The 50% cytotoxic concentration (CC_{50}) values were calculated with GraphPad Prism using the four-parameter variable-response log(inhibitor)-versus-response algorithm with the bottom value set to zero.

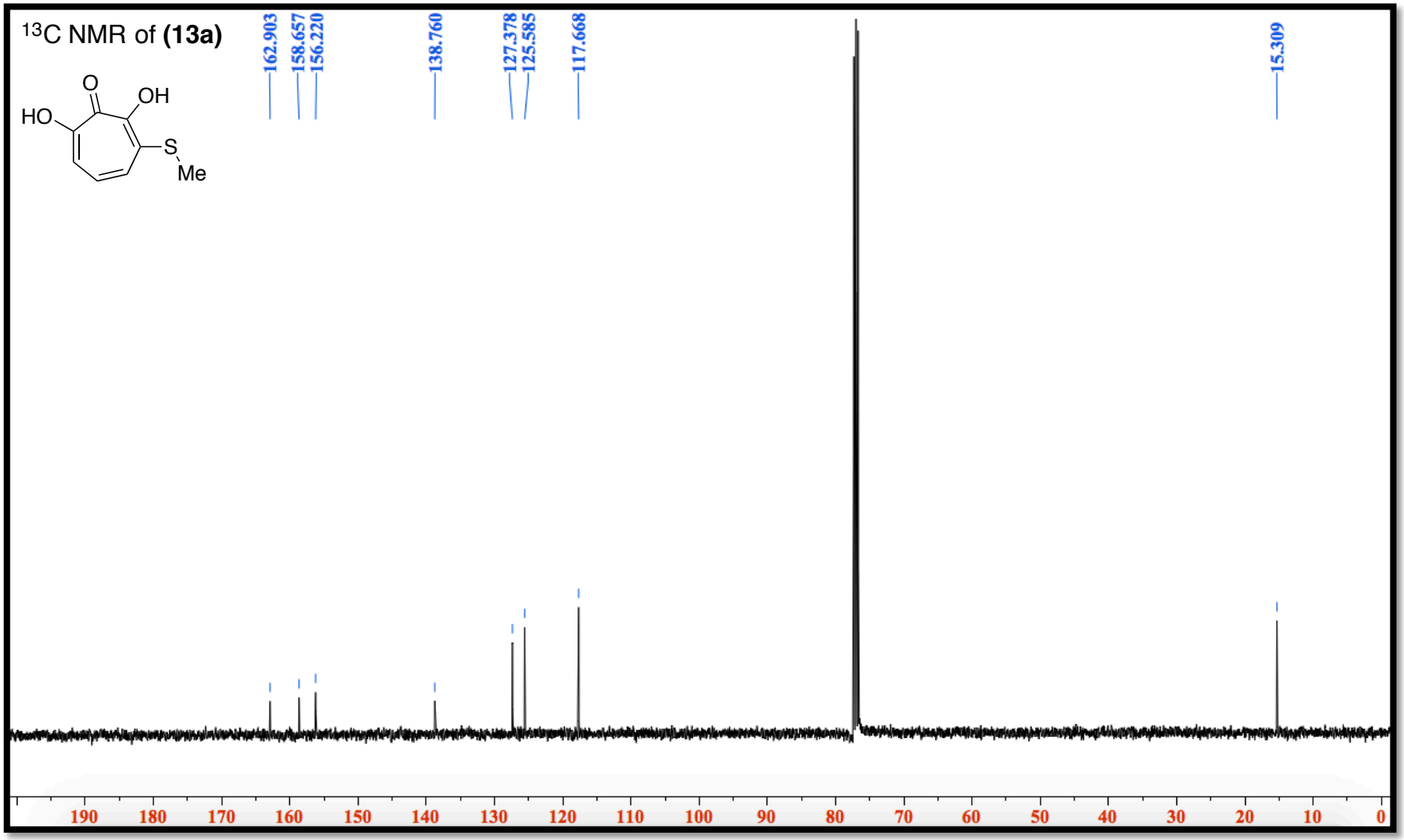
[3] (a) Cai, C.W.; Lomonosova, E.; Moran, E. A.; Cheng, X.; Patel, K. B.; Bailly, F.; Cotelle, P.; Meyers, M. J.; Tavis J. E. *Antiviral Res.* **2014**, *108*, 48–55. (b) Lu, G.; Lomonosova, E.; Cheng, X.; Moran, E. A.; Meyers, M. J.; Le Grice, S. F.; Thomas, C. J.; Jiang, J. K.; Meck, C.; Hirsch, D. R.; D'Erasmo, M. P.; Suyabatmaz, D. M.; Murelli, R. P.; Tavis, J. E. *Antimicrob. Agents. Chemother.* **2015**, *59*, 1070-9.

Table S1. Complete list of results from biological assays. HSV-1 EC_{50} measurements and Vero cell CC_{50} are reported as the average of 3 runs ± standard error. HBV EC_{50} values are shown as either a single run, or, for more potent molecules, an average of 2 runs ± standard deviation. MIC_{80} values are shown as the range for each set of triplicate experiments, performed. The average value shown is derived from these runs. HepDES19 CC_{50} values are reported as the average of 2 runs ± standard deviation.

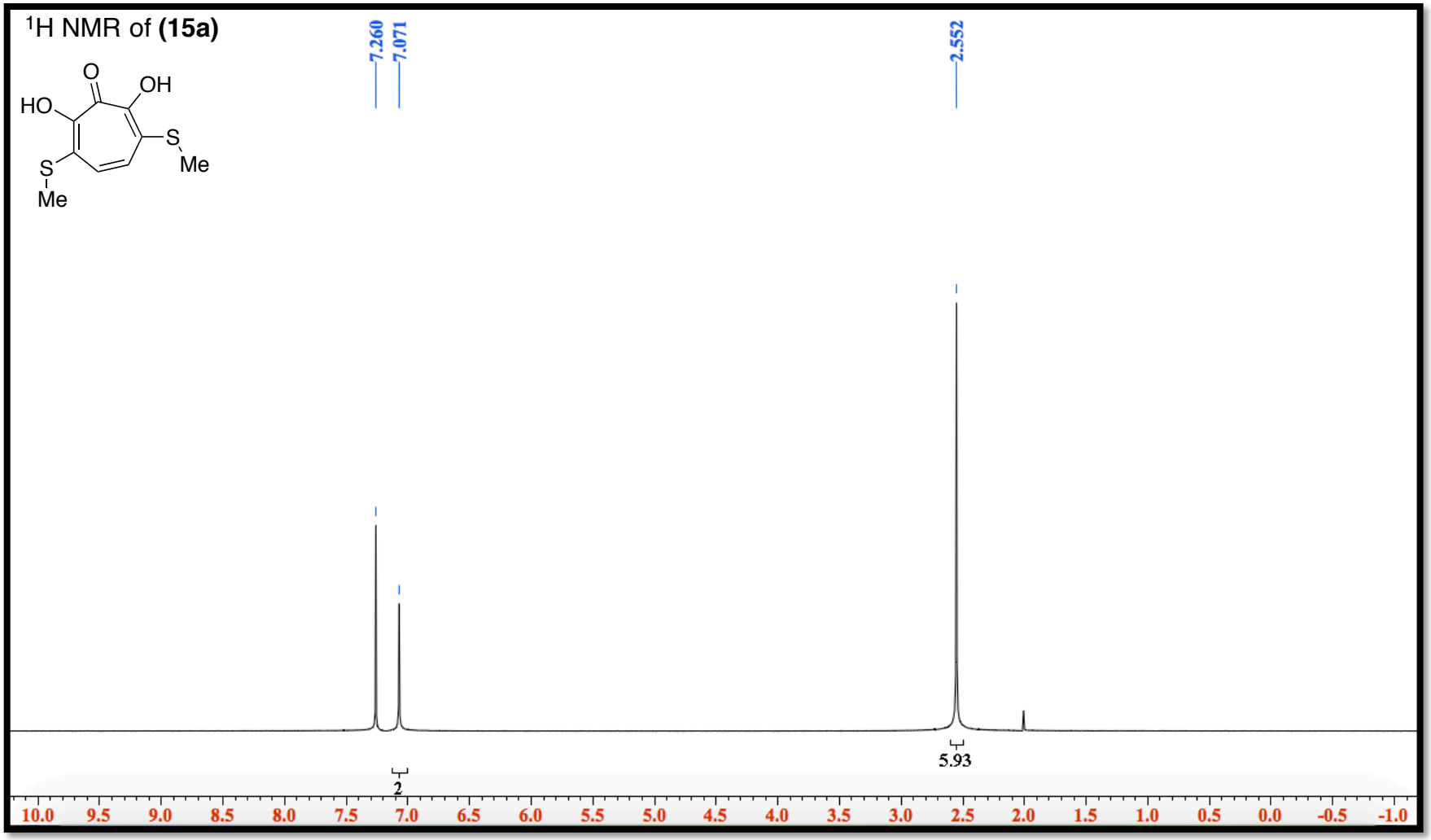
		Herpes Simplex Virus-1 Antiviral Activity					HBV antiviral	*C. neoformans*				HepDES19
		Replication Inhibition (Log_{10})			EC_{50} (μM)	Vero Cell CC_{50} (μM)	EC_{50} (μM)	MIC_{80} (μM)				CC_{50} (μM)
Cmpd #	SLU#	5 μM	1 μM	0.33 μM				Rep 1	Rep 2	Rep 3	Average	
13a	**385**	0.162/-0.007	-	-	-	-	14.3 ± 7.2	37.5	13.5	-	28	100
13b	**693**	5.64	2.7	0.07/0.22	1.01 ± 0.32	>100	47	.78-1.56	.625-1.25	-	1	14 ± 9.0
13c	**840**	3.69/4.26	1.52	0.2714	0.93 ± 0.08	>100	50	0.78-1.56	1.56-3.12	-	1.7	22 ± 9.7
13d	**695**	2.28	-0.23	-	-	-	31 ± 8	1.56-3.12	1.56-3.12	-	2.6	21 ± 1.4
13e	**691**	5.69	0.72	-	-	-	47	.78-1.56	1.25-2.5	-	1.5	20 ± 1.5
13f	**839**	3.21	-0.1	-	-	-	>50	3.12-6.25	3.12-6.25	-	4.7	35 ± 20
13g	**838**	5.33	0.05	-	-	-	17	0.78-1.56	1.56-3.12	-	1.7	19 ± 4.9
13h	**702**	5.79	3.23	0.13	0.59 ± 0.06	>100	25	0.39-0.78	.312-.625	0.39-0.78	0.55	17 ± 2.4
14a	**387**	0.02	-	-	-	-	0.55 ± 0.27	50	50	-	50	32 ± 17
14b	**535**	1.02/-0.21	0.07	-	-	-	1.9 ± 0.4	50	50	-	50	19 ± 2.8
14c	**699**	4.39	0.2/0.17	0.22/0.0147			6.6 ± 0.6	6.25-12.5	12-25	12-26	15	13 ± 6.3
14d	**537**	0.005/0.88	0.25	-	-	-	0.79 ± 0.24	50	50	-	50	21.0
14e	**408**	0.1	-	-	-	-	11.3 ± 4.0	50	50	-	50	20 ± 9.4
14f	**698**	4.85	-0.35	-0.31	-	-	5.9 ± 0.4	25-50	25-50	-	38	13.7 ± 7.1
14g	**697**	0.01	-	-	-	-	49	25-50	25-50	-	38	35 ± 11
14h	**705**	3.55	0.19/0.13	0.02/0.19	-	-	2.8 ± 0.6	>50	>50	-	50	8.4 ± 2.4
15a	**386**	0.51	-	-	-	-	8.6 ± 2.1	25-50	25-50	-	38	69 ± 9.8
15b	**694**	5.86	4.85/5.68	4.77/1.87	0.26 ± 0.06	87.2 ± 4.6	12	1.56-3.12	1.56-3.12	-	2.3	1.8 ± 1.4
15c	**841**	4.77/5.93	4.99	4.82/5.09	0.08 ± 0.00	>100	11	3.12-6.25	6.25-12.5	-	7	7.8 ± 3.0
15d	**696**	5.82	0.08	-0.06	-	-	12.7 ± 5.0	.78-1.56	.625-1.25	1.56-3.12	1.5	9.3 ± 1.0
15h	**703**	5.88	4.56/5.94	0.73/2.19	0.08 ± 0.02	>100	11	3.12-6.25	6.25-12.5	-	7	8.2 ± 0.1
16b	**536**	0.35/0.42	0.09	-	-	-	>50	50	6-12	50	36	100
16c	**700**	2.01	0.57	0.49	-	-	50	>50	>50	-	50	46 ± 4.1
16d	**538**	0.21	0.74	-	-	-	>50	50	50	-	50	100
16h	**706**	0.59	-	-	-	-	>50	25-50	25-50	-	38	73 ± 27

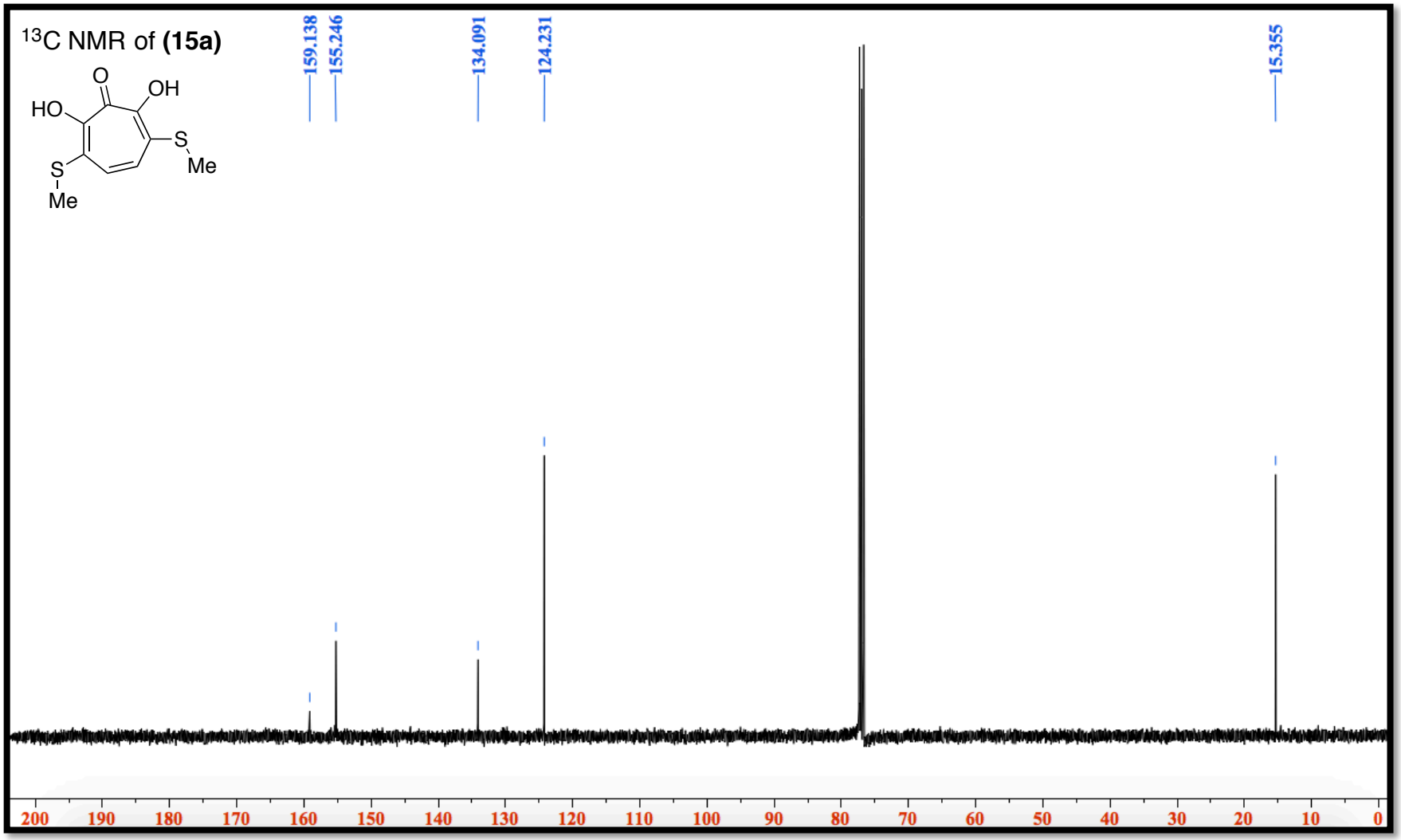
2,7-dihydroxy-3-(methylthio)cycloheptа-2,4,6-trien-1-one **(13a)**



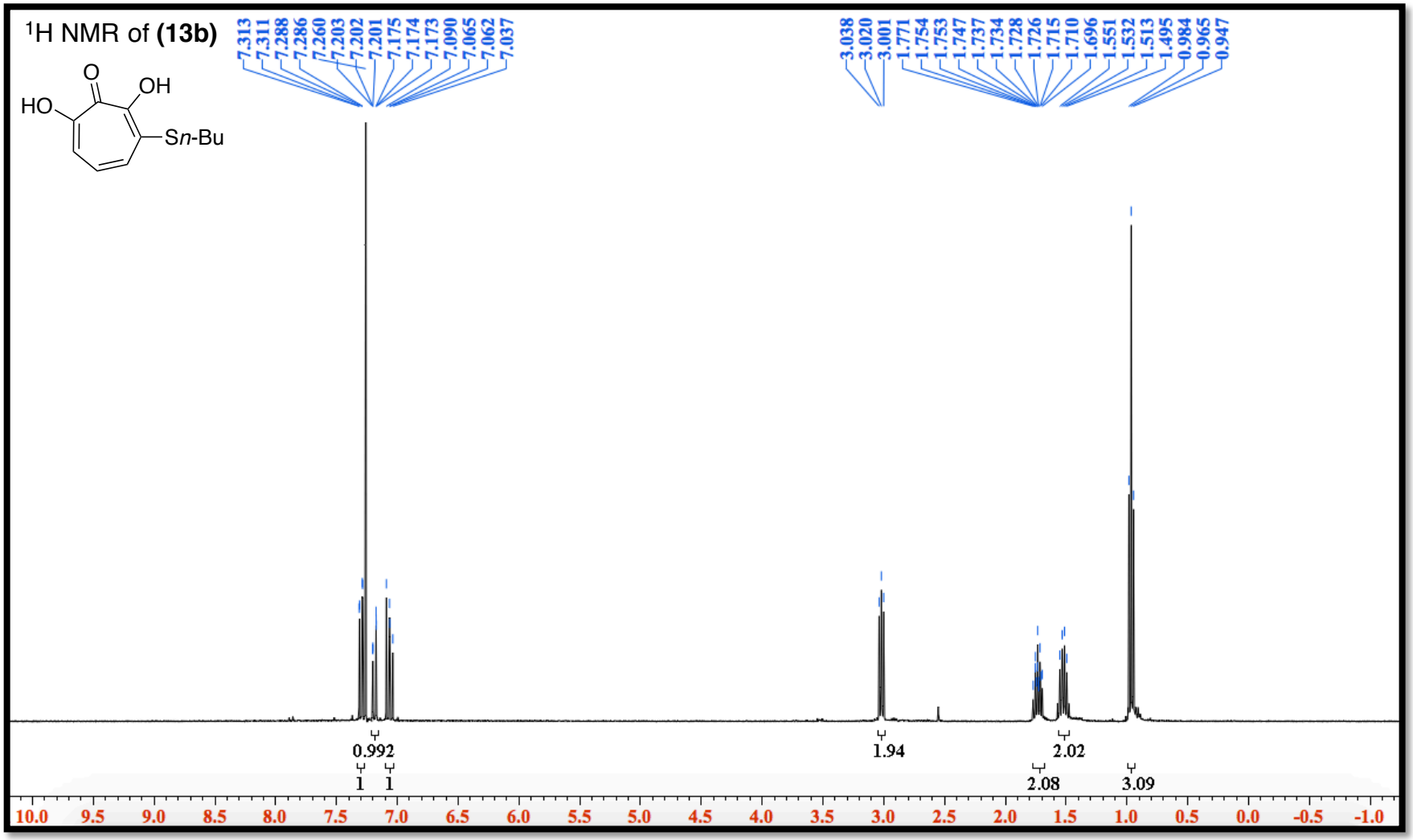

^{13}C NMR of **(13a)**
O
OH
HO
S
Me
162.903
158.657
156.220
138.760
127.378
125.585
117.668
15.309
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

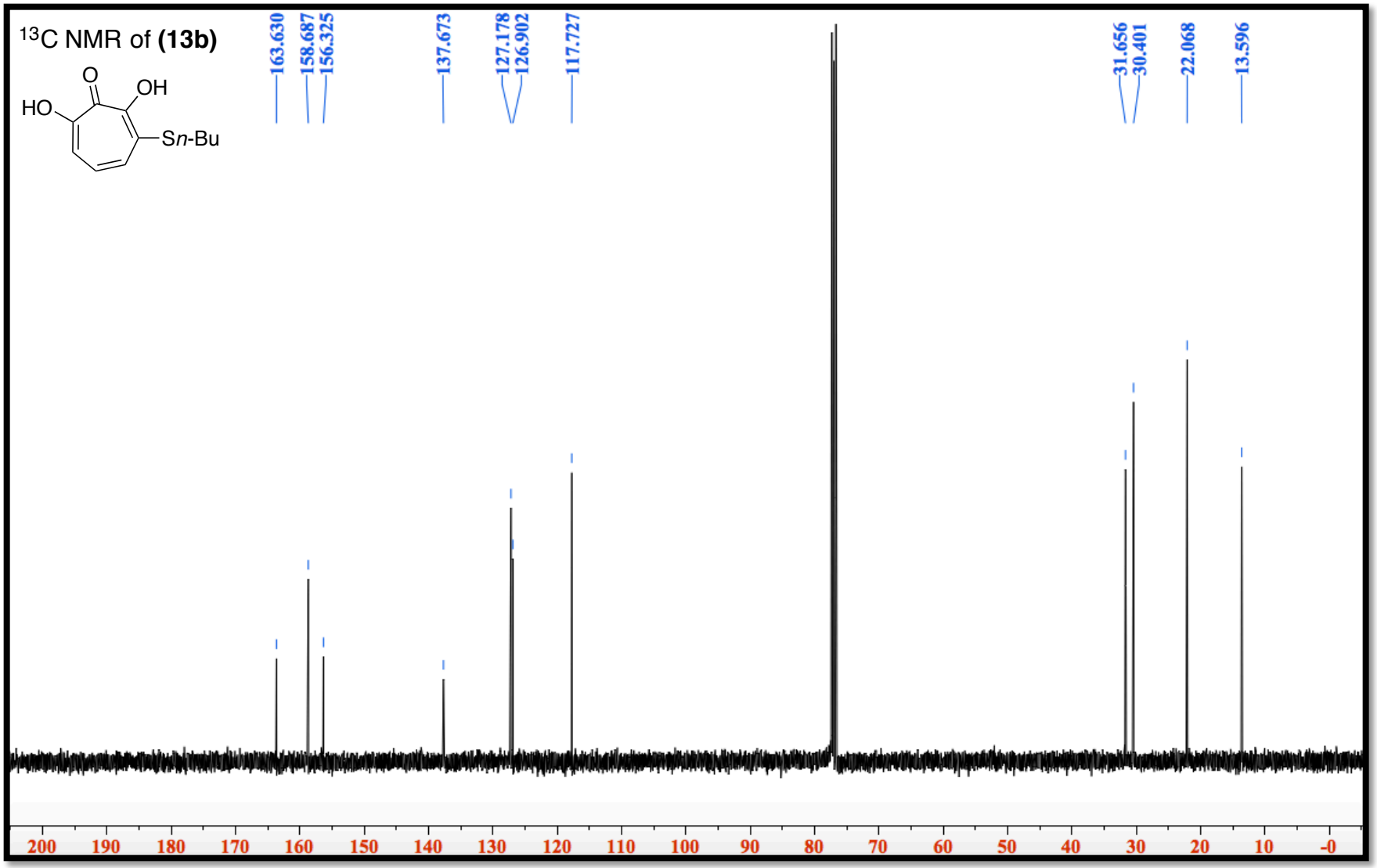
2,7-dihydroxy-3,6-bis(methylthio)cyclohepta-2,4,6-trien-1-one **(15a)**



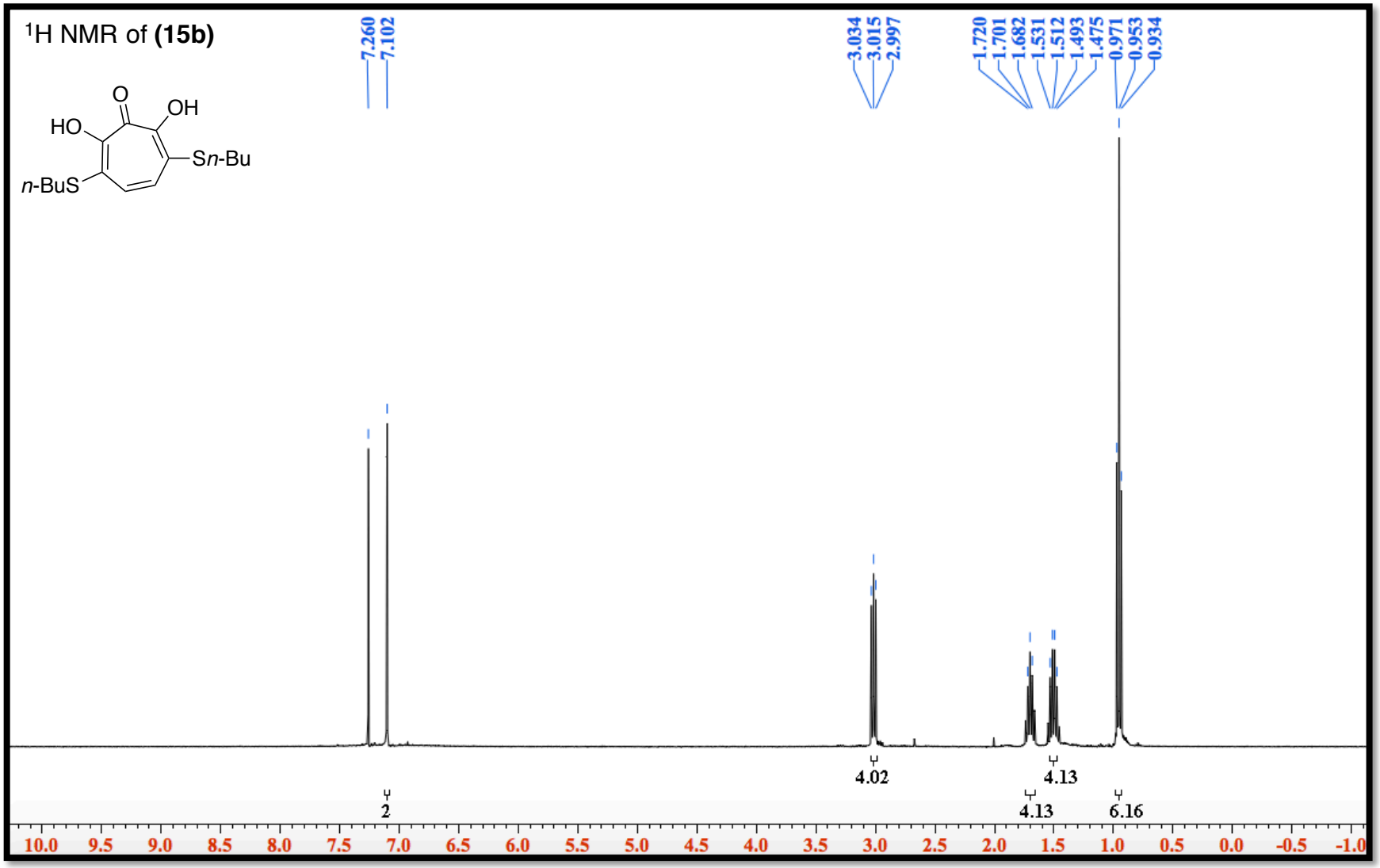

13C NMR of (15a)
O
OH
HO
S
Me
S
Me
159.138
155.246
134.091
124.231
15.355
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

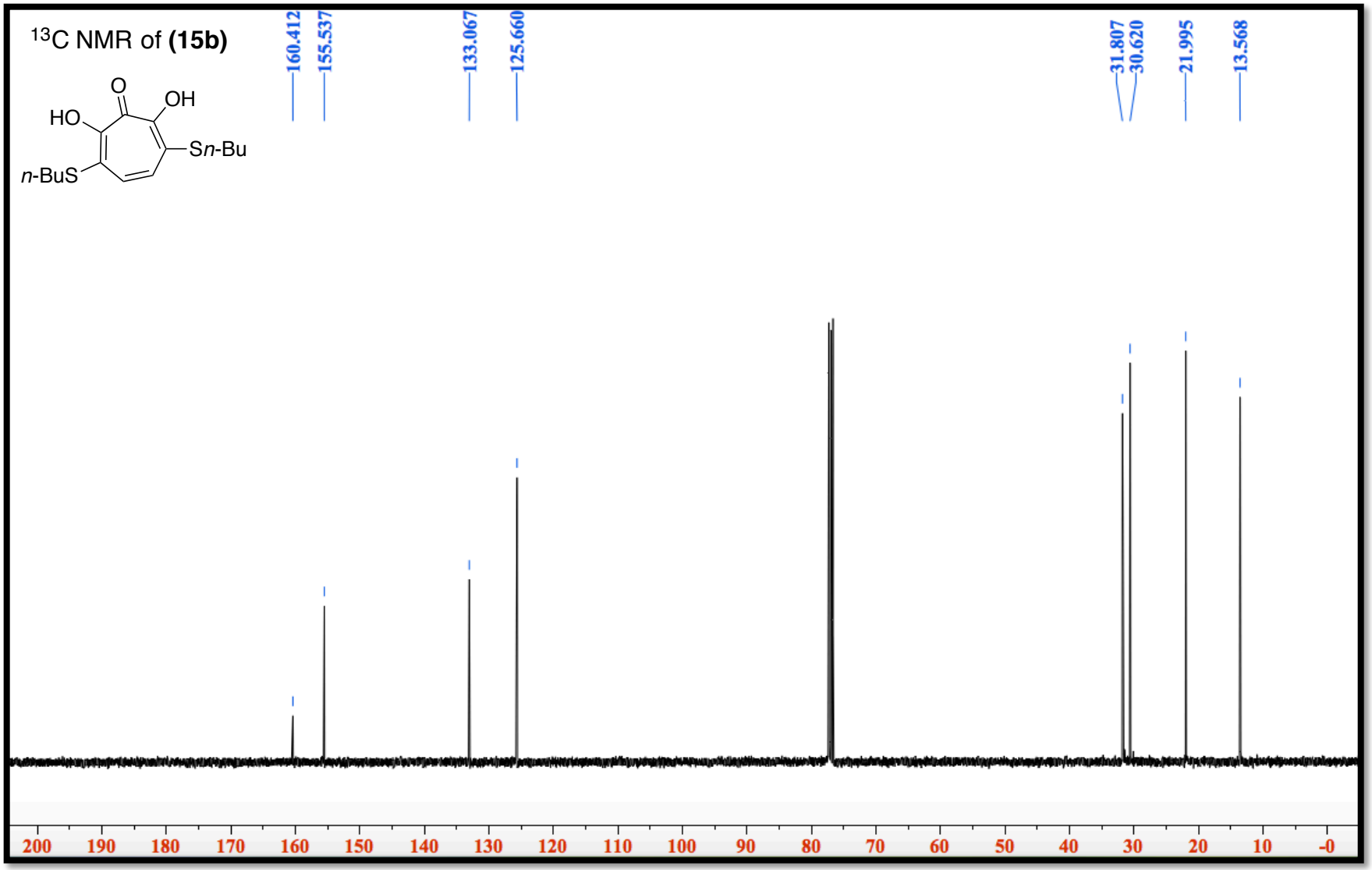
3-(butylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(13b)**



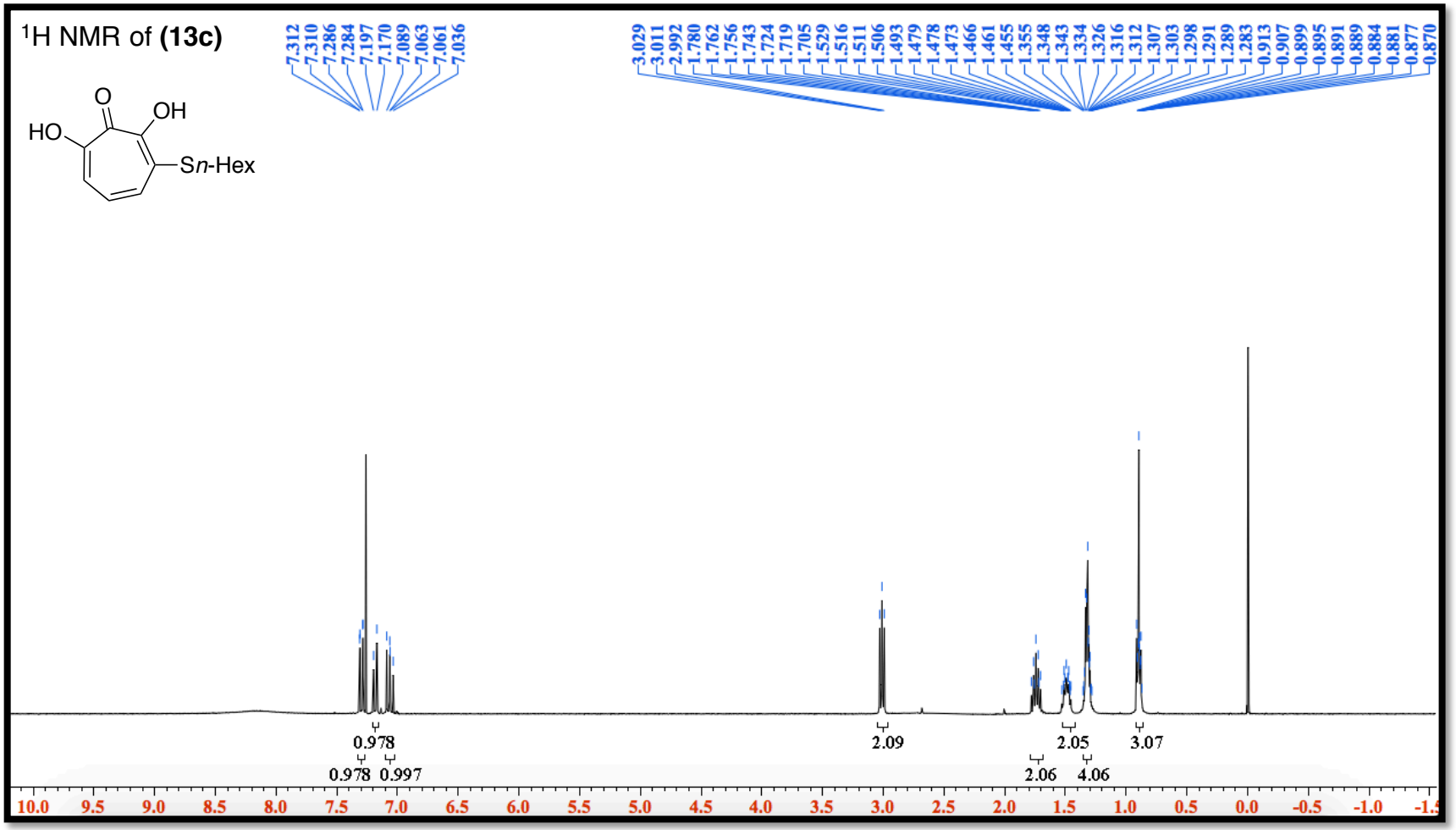

^{13}C NMR of **(13b)**
O
OH
HO
S*n*-Bu
163.630
158.687
156.325
137.673
127.178
126.902
117.727
31.656
30.401
22.068
13.596
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0

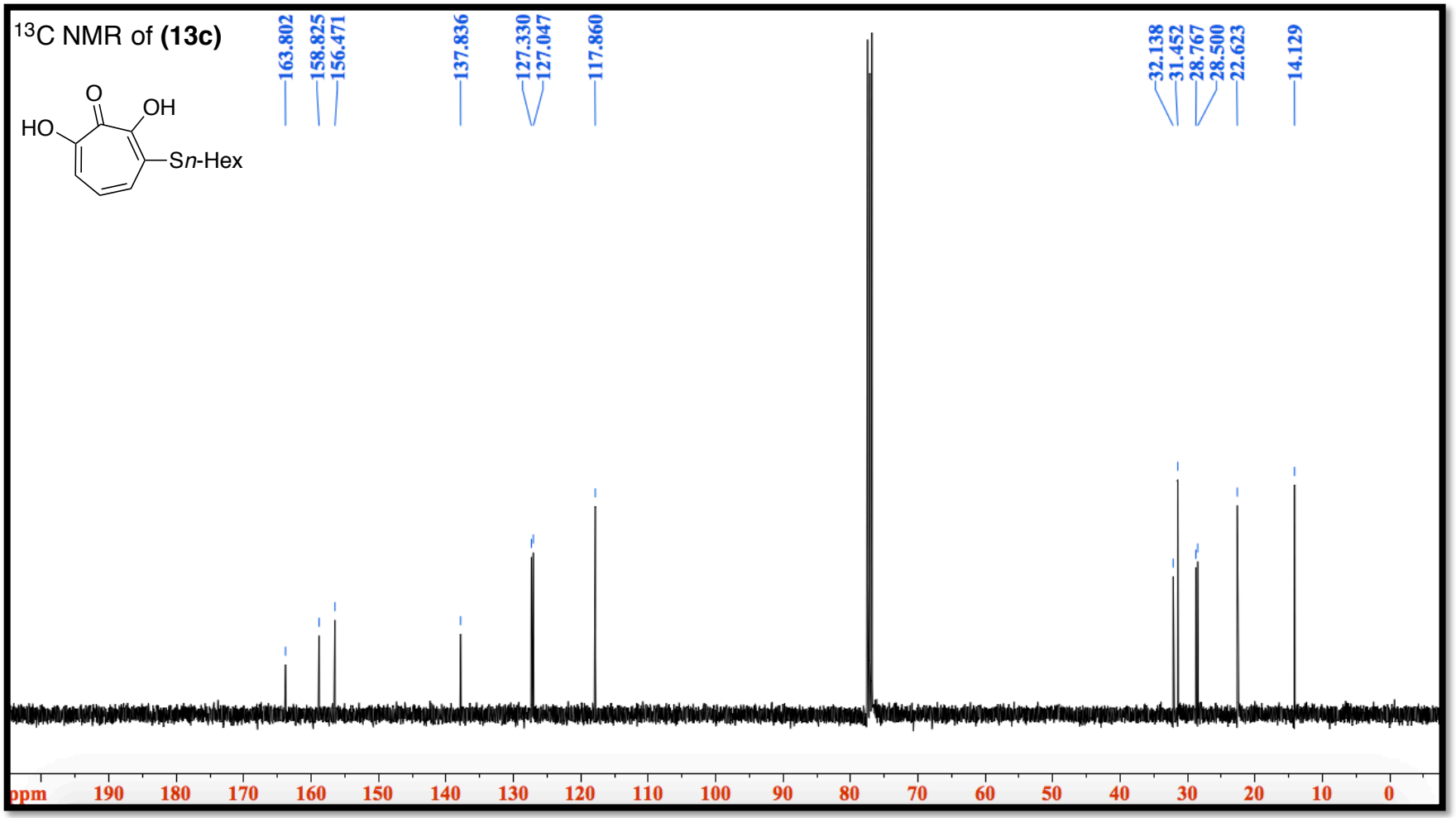
3,6-bis(butylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(15b)**



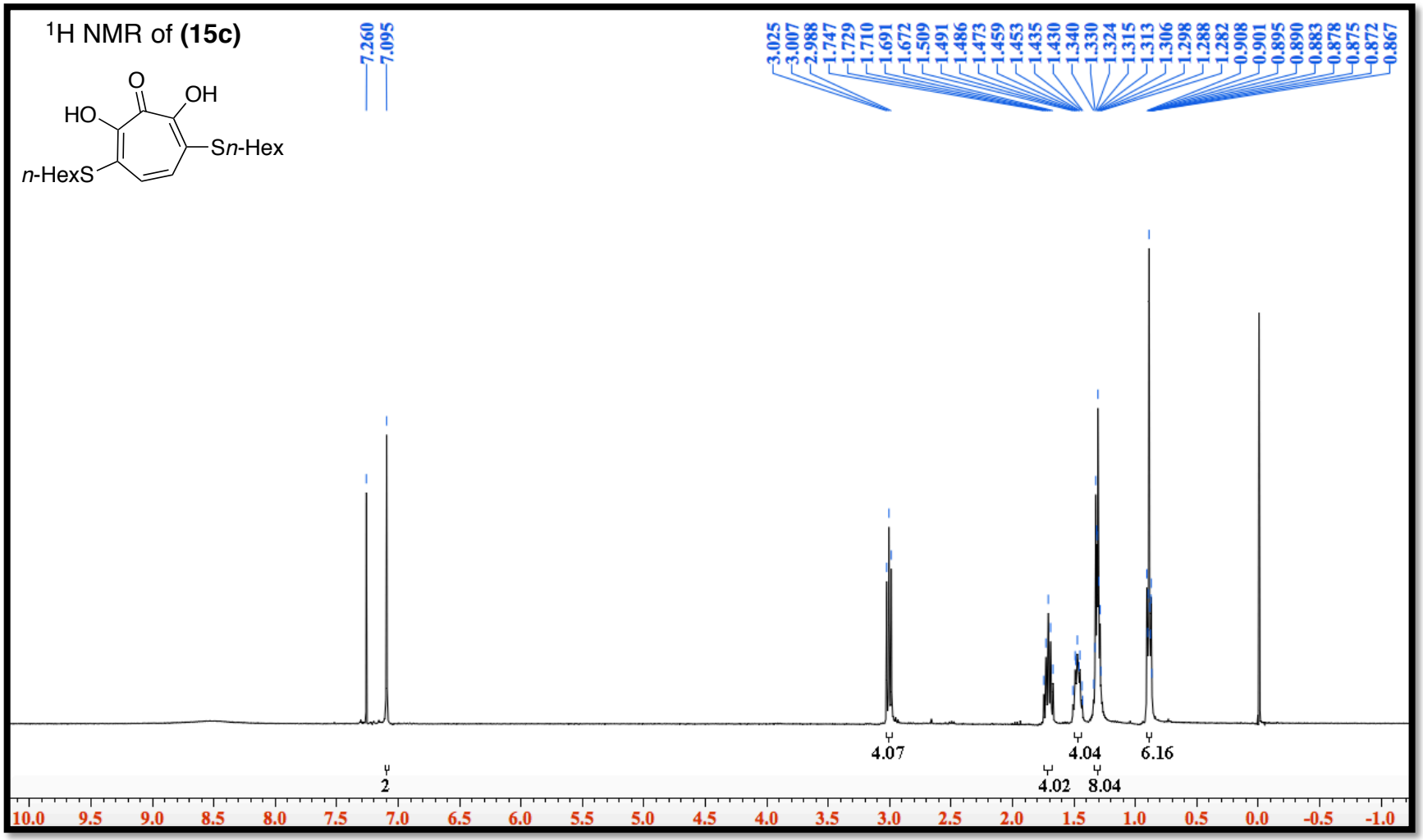

^{13}C NMR of **(15b)**
O
OH
HO
S*n*-Bu
n-BuS
160.412
155.537
133.067
125.660
31.807
30.620
21.995
13.568
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0

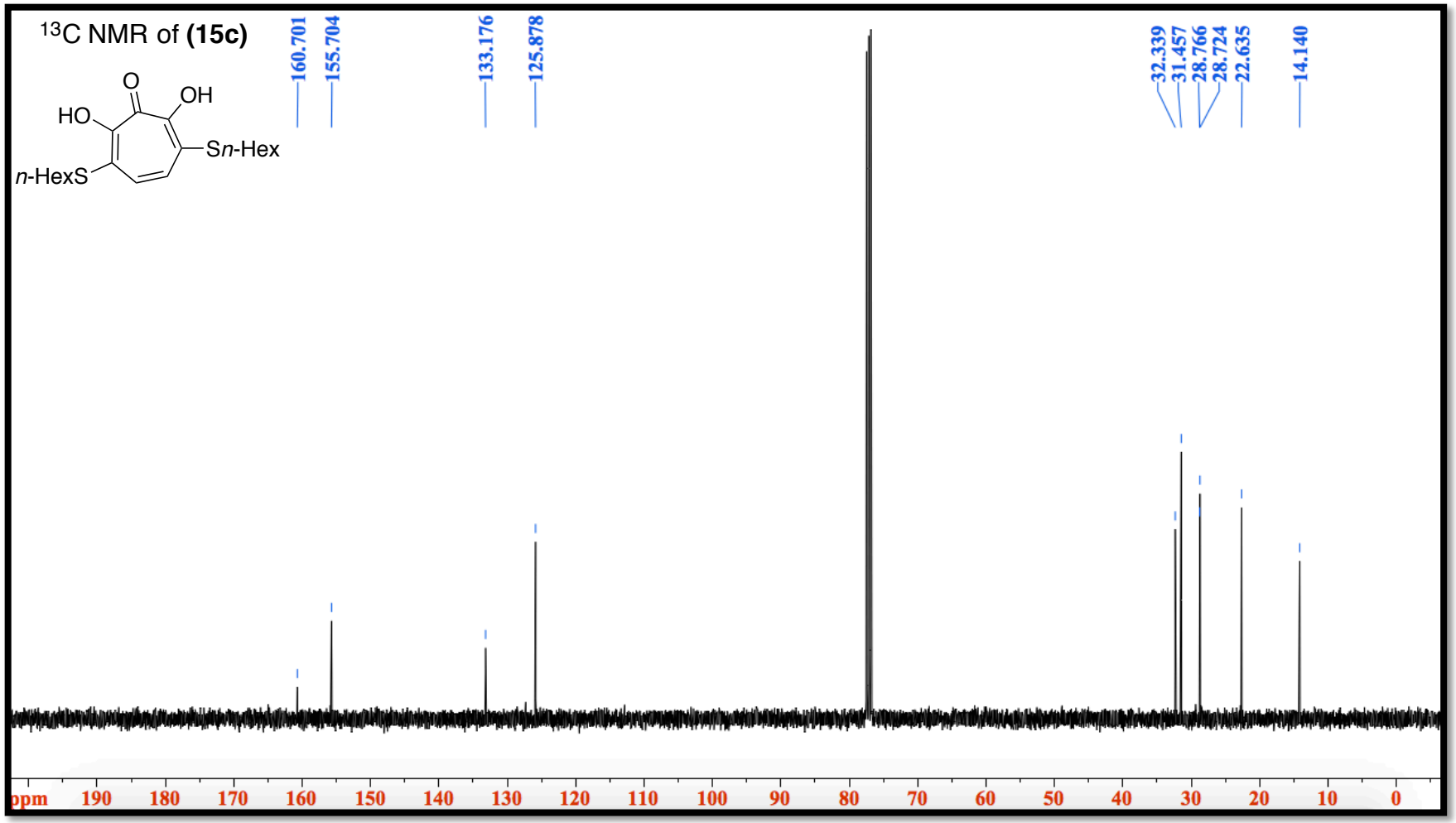
3-(hexylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(13c)**



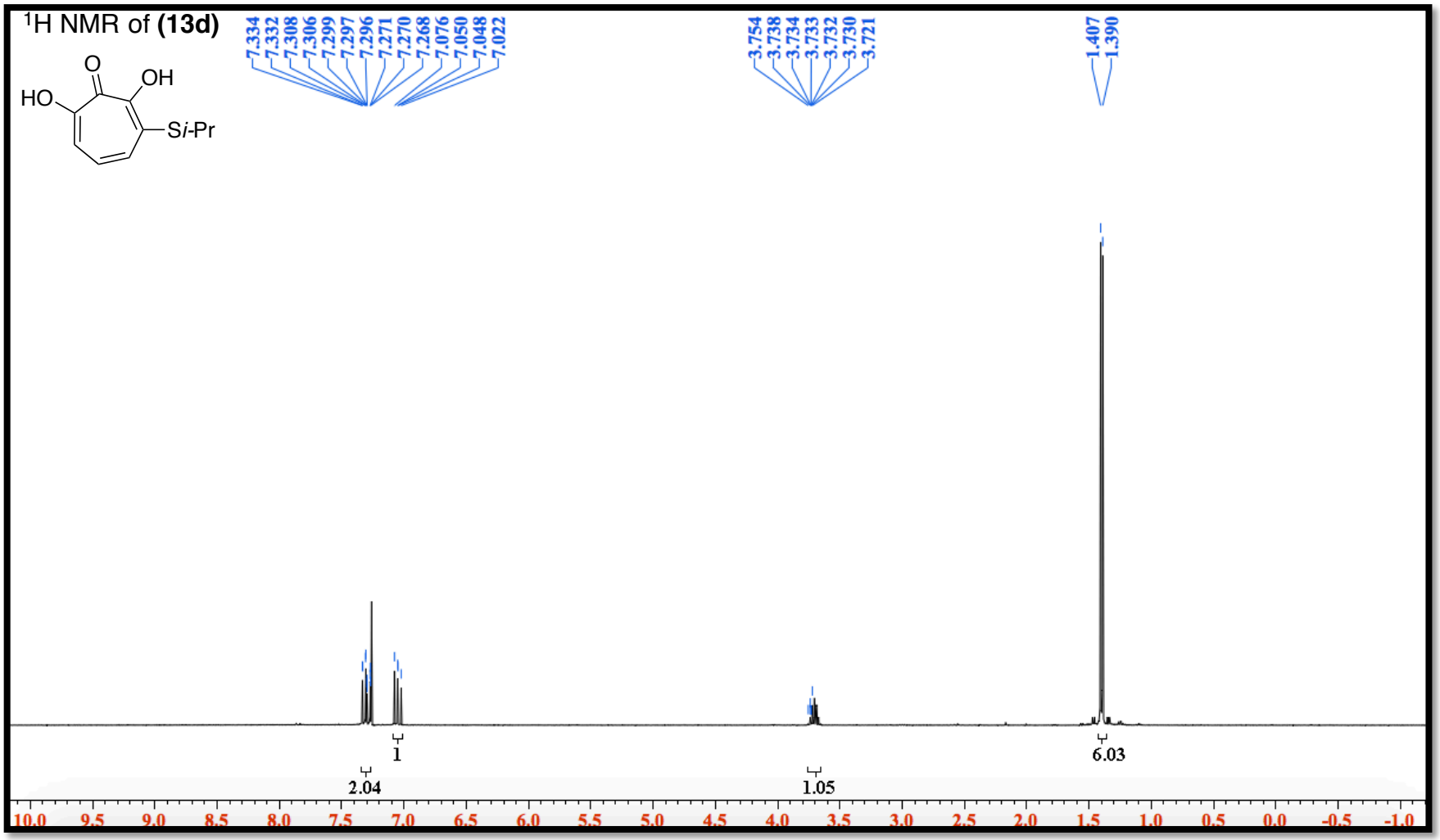

^{13}C NMR of **(13c)**
O
OH
HO
S*n*-Hex
163.802
158.825
156.471
137.836
127.330
127.047
117.860
32.138
31.452
28.767
28.500
22.623
14.129
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

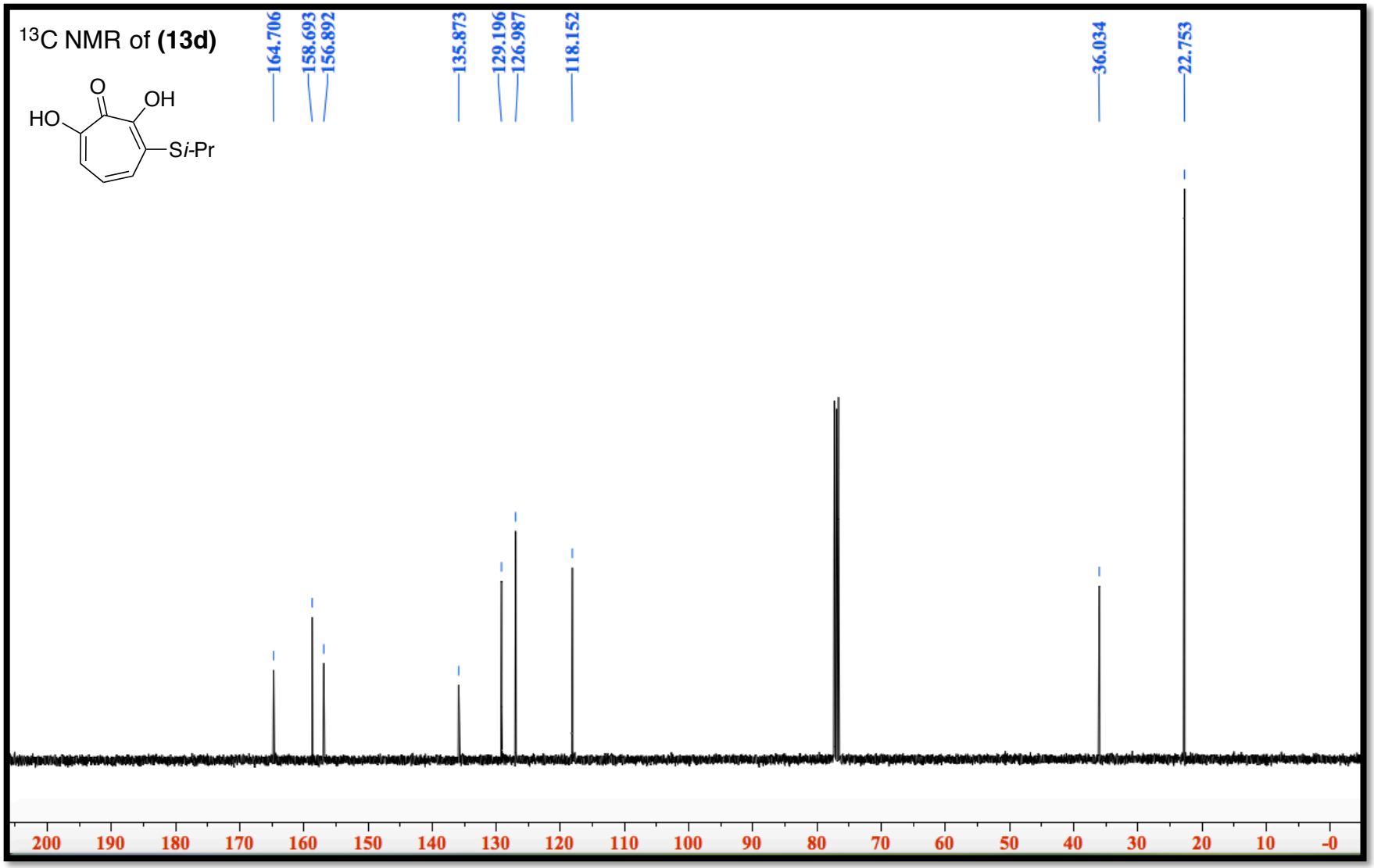
3,6-bis(hexylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(15c)**



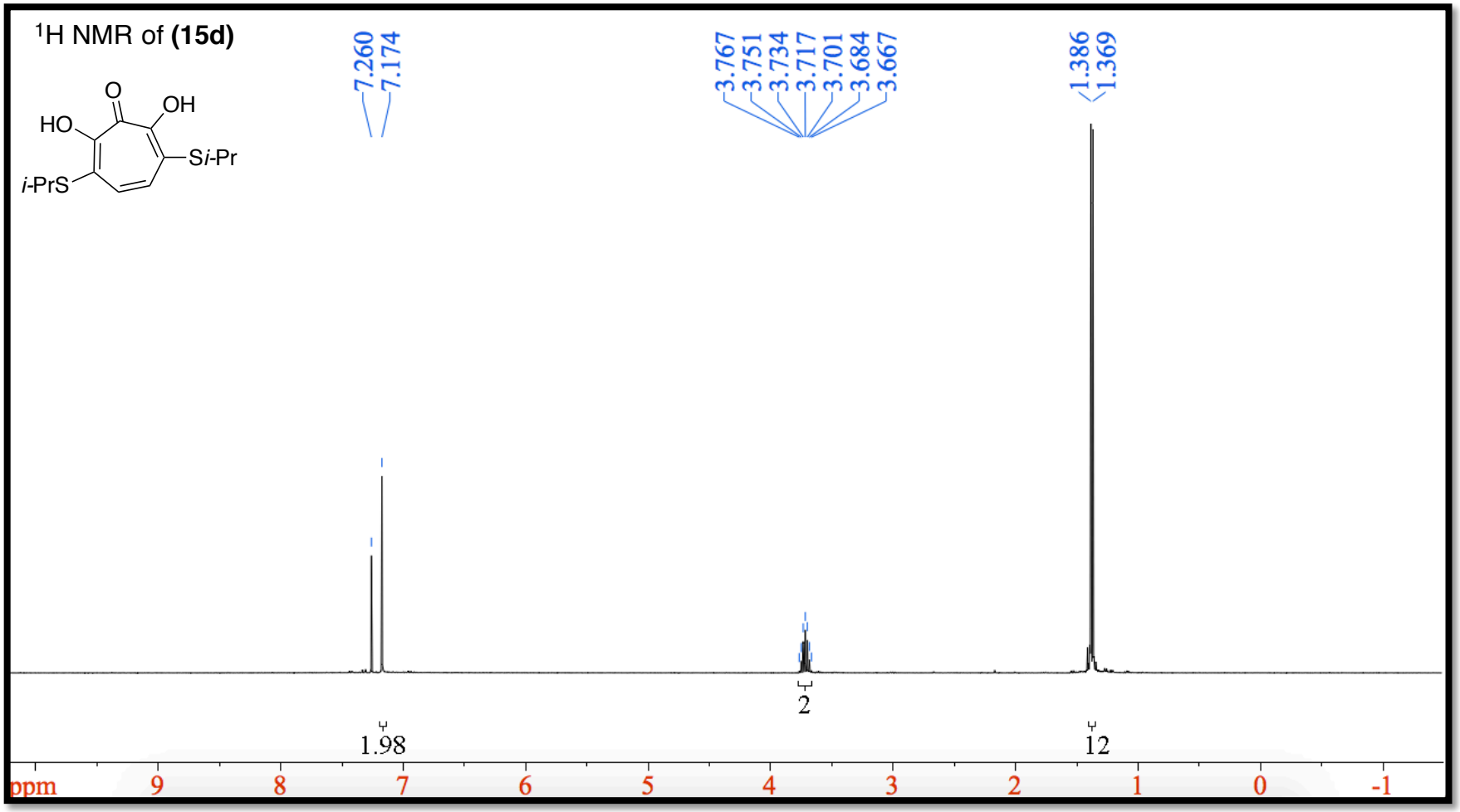

13C NMR of (15c)
O
OH
HO
Sn-Hex
n-HexS
160.701
155.704
133.176
125.878
32.339
31.457
28.766
28.724
22.635
14.140
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

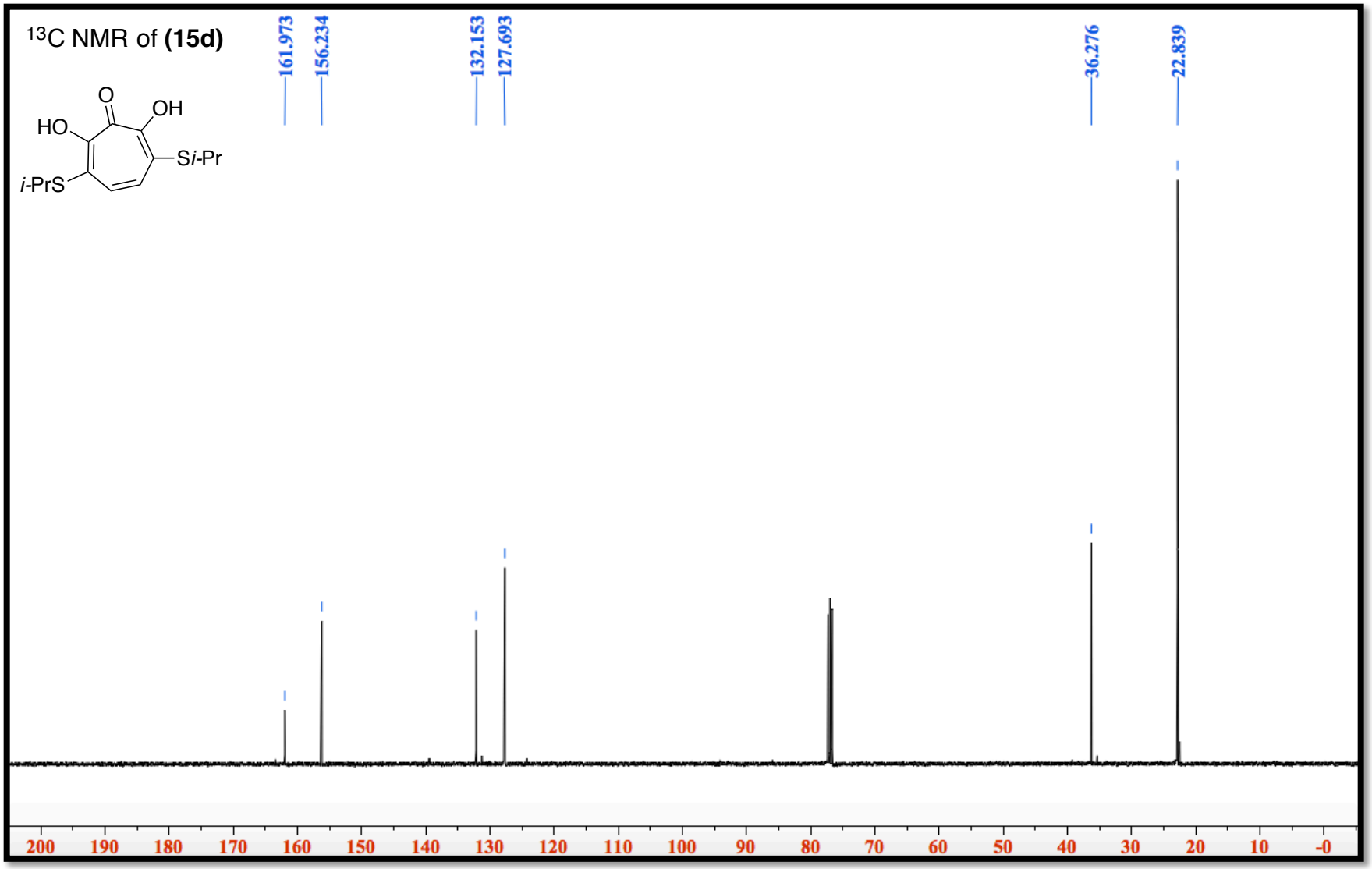
2,7-dihydroxy-3-(isopropylthio)cyclohepta-2,4,6-trien-1-one **(13d)**



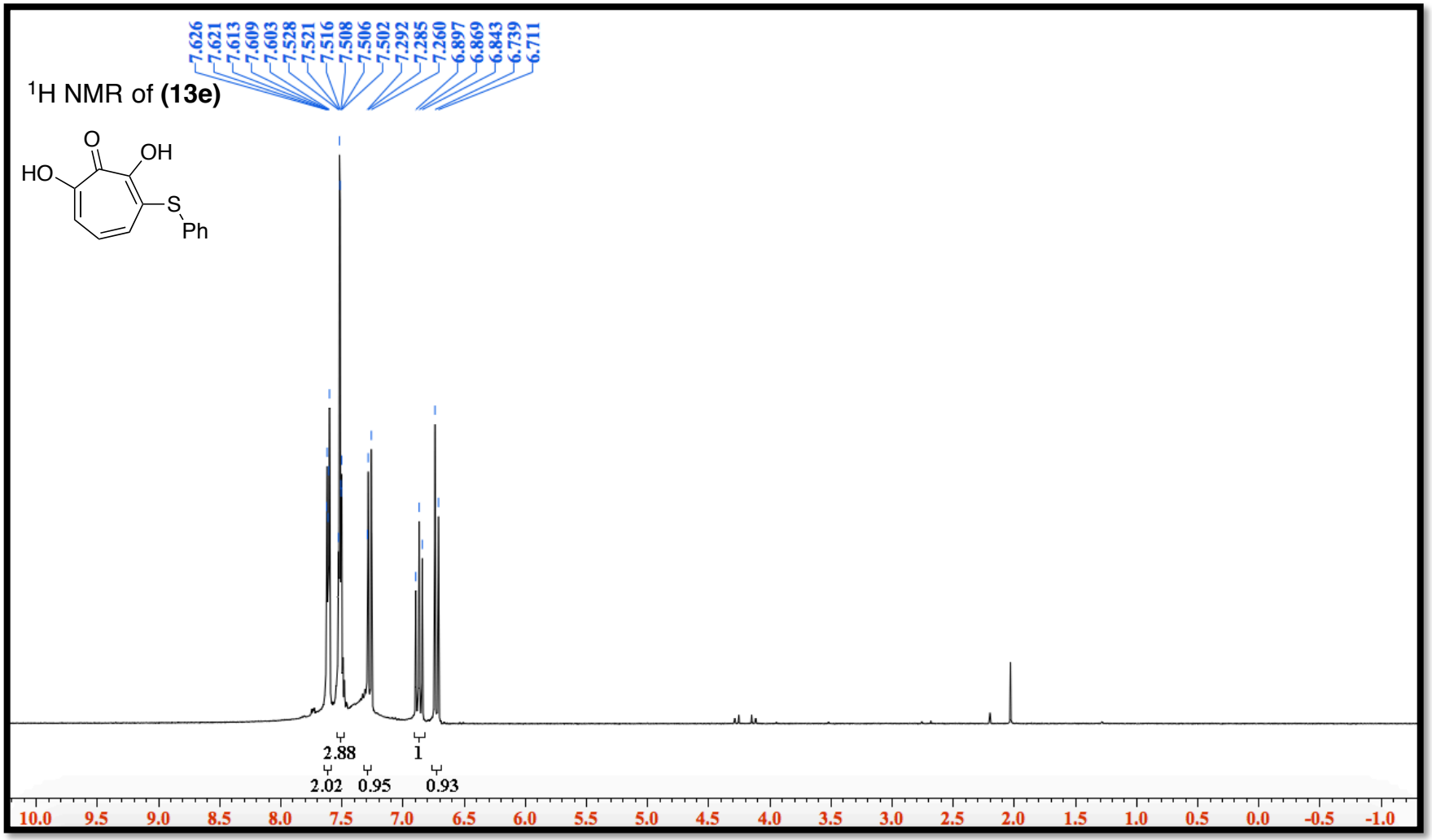

^{13}C NMR of **(13d)**
O
OH
HO
S*i*-Pr
164.706
158.693
156.892
135.873
129.196
126.987
118.152
36.034
22.753
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0

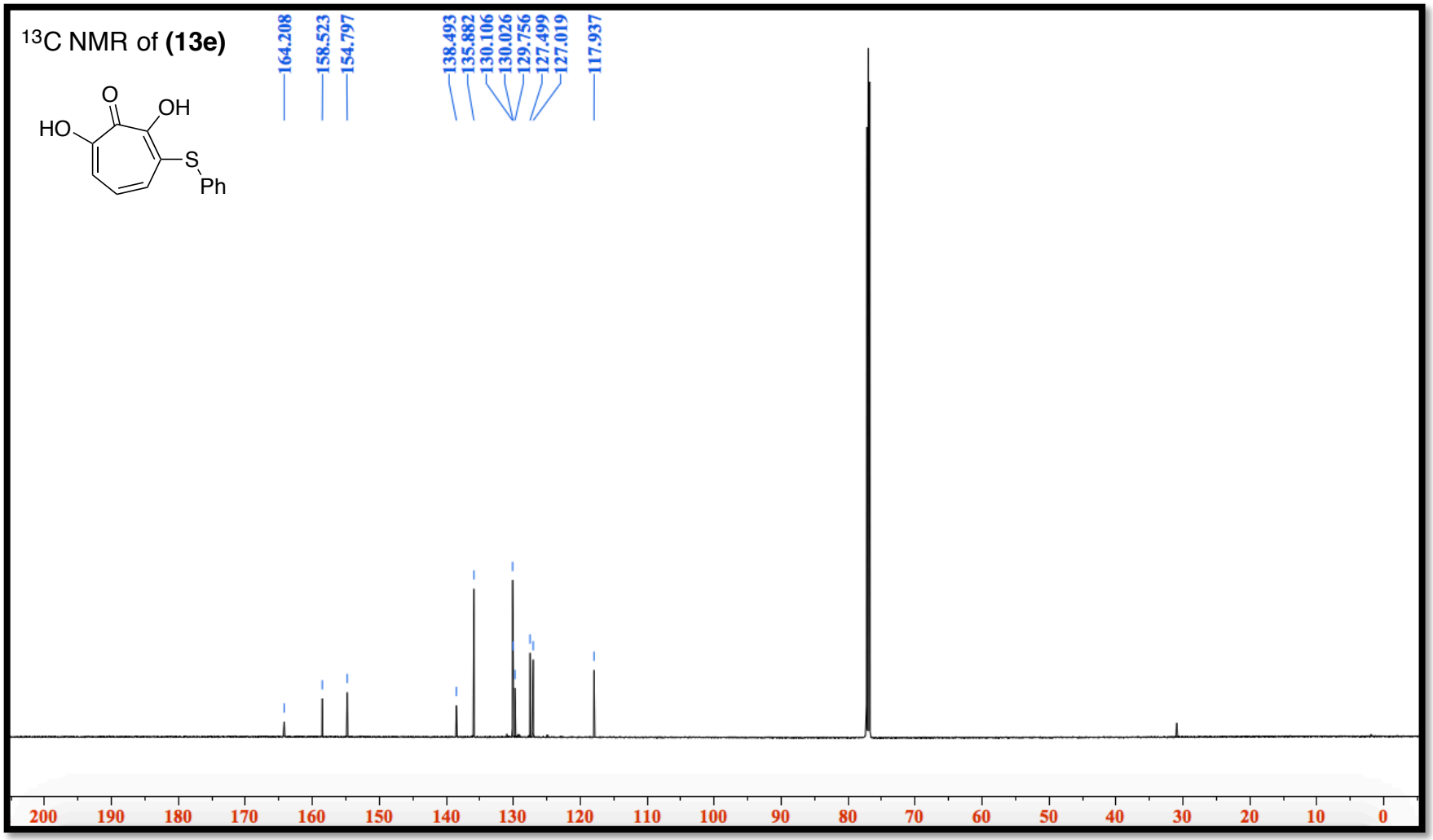
2,7-dihydroxy-3,6-bis(isopropylthio)cyclohepta-2,4,6-trien-1-one **(15d)**



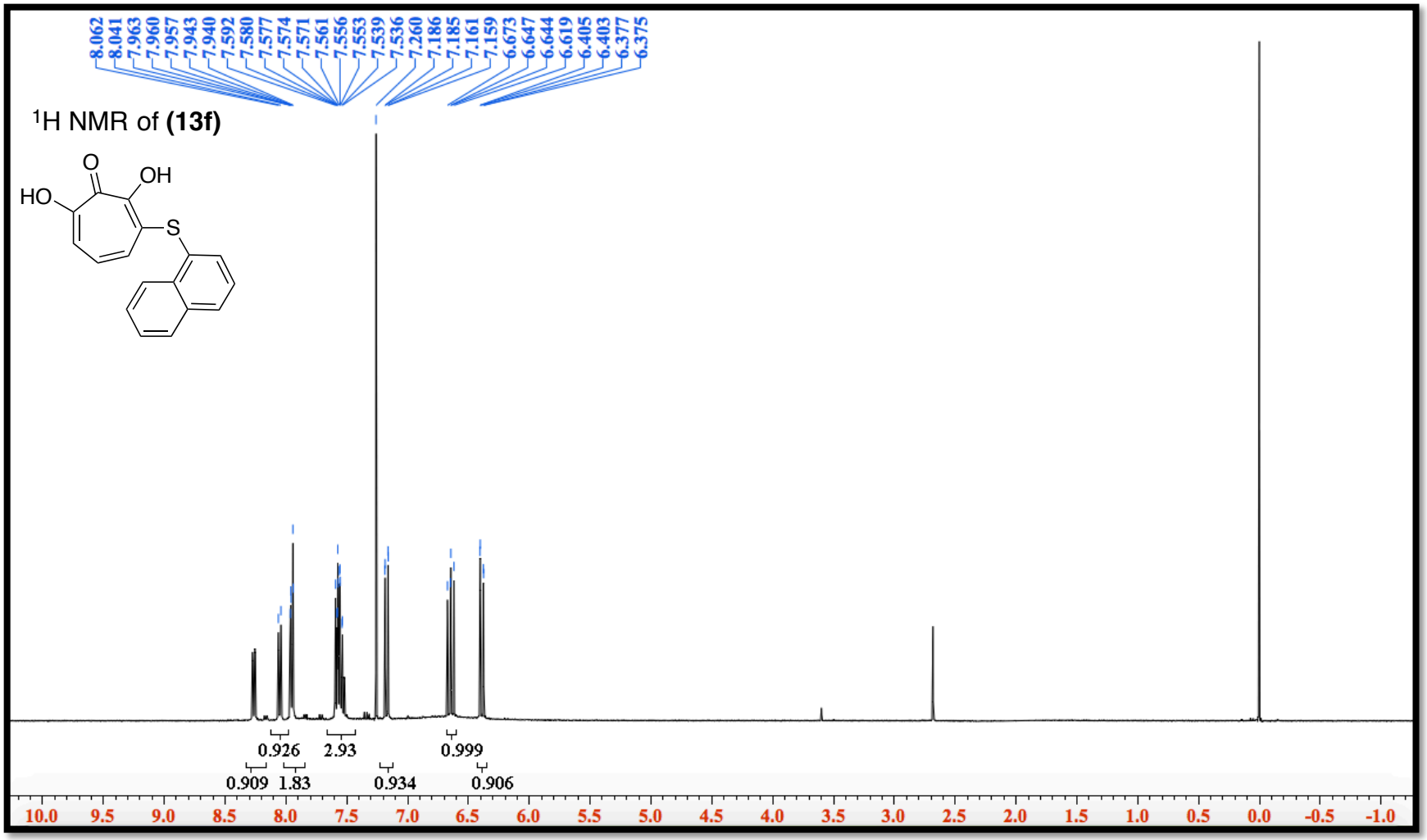

^{13}C NMR of **(15d)**
161.973
156.234
132.153
127.693
36.276
22.839
O
OH
HO
S*i*-Pr
i-PrS
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0

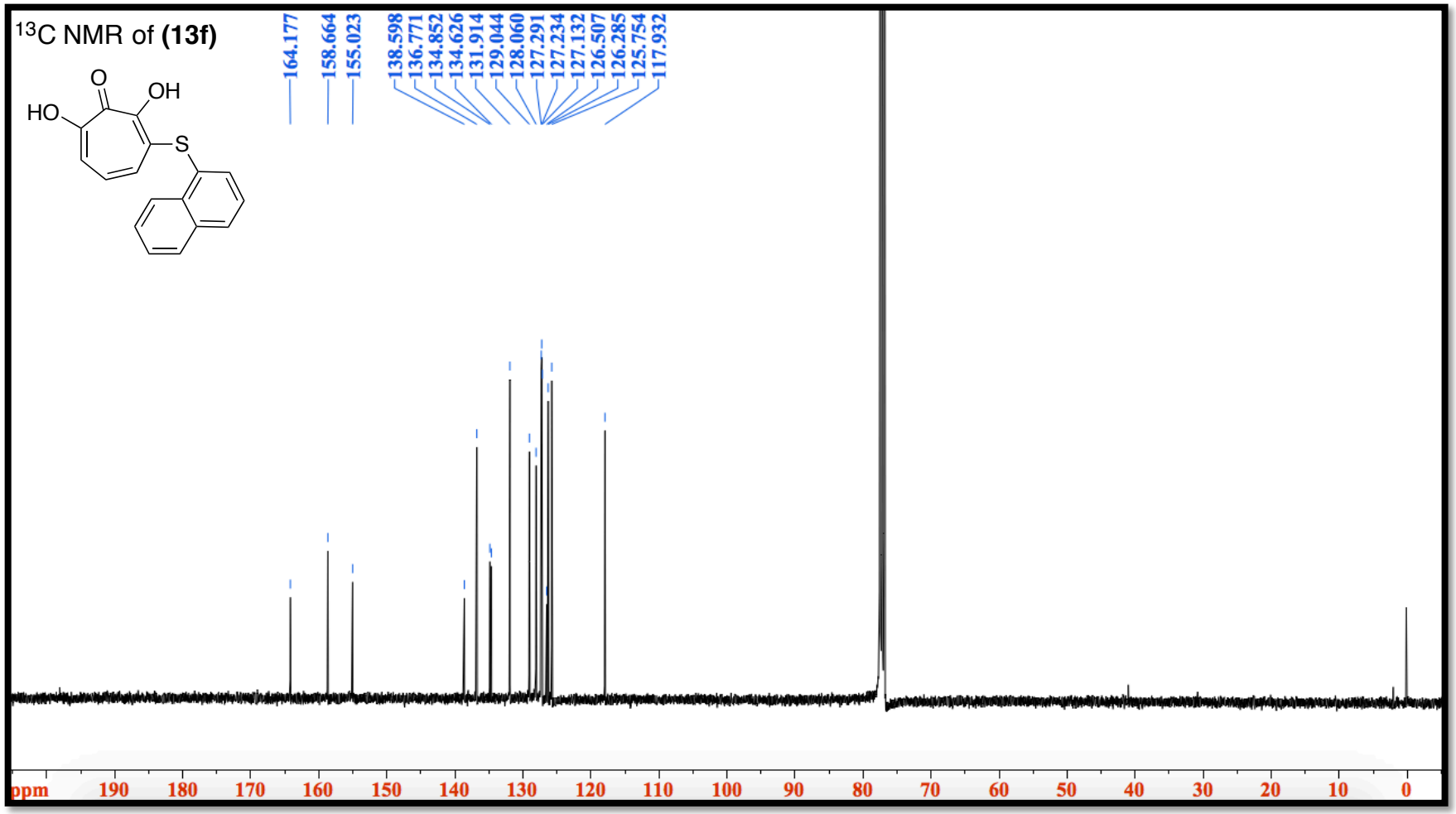
2,7-dihydroxy-3-(phenylthio)cyclohepta-2,4,6-trien-1-one **(13e)**



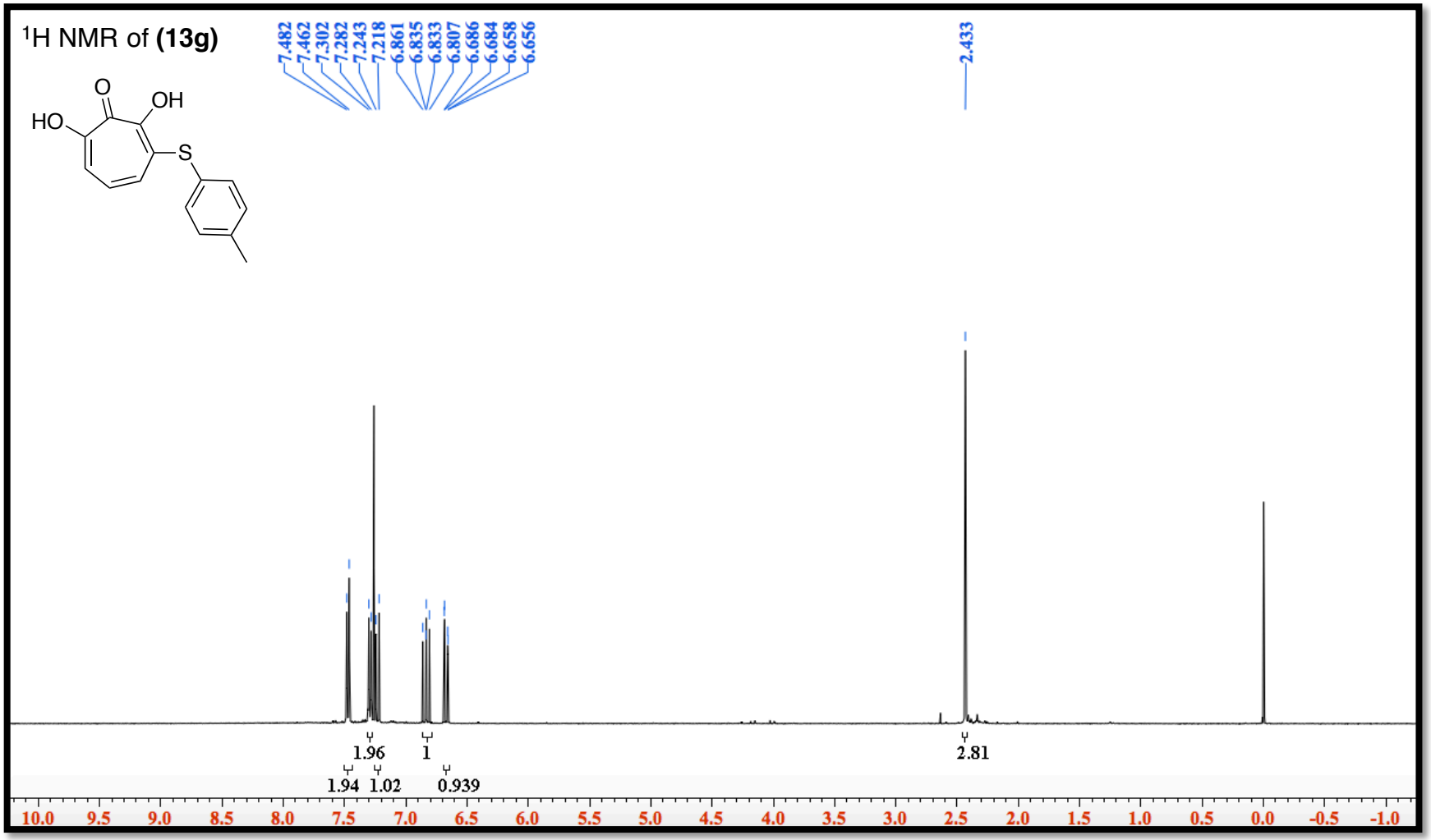

^{13}C NMR of **(13e)**
O
OH
HO
S
Ph
164.208
158.523
154.797
138.493
135.882
130.106
130.026
129.756
127.499
127.019
117.937
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

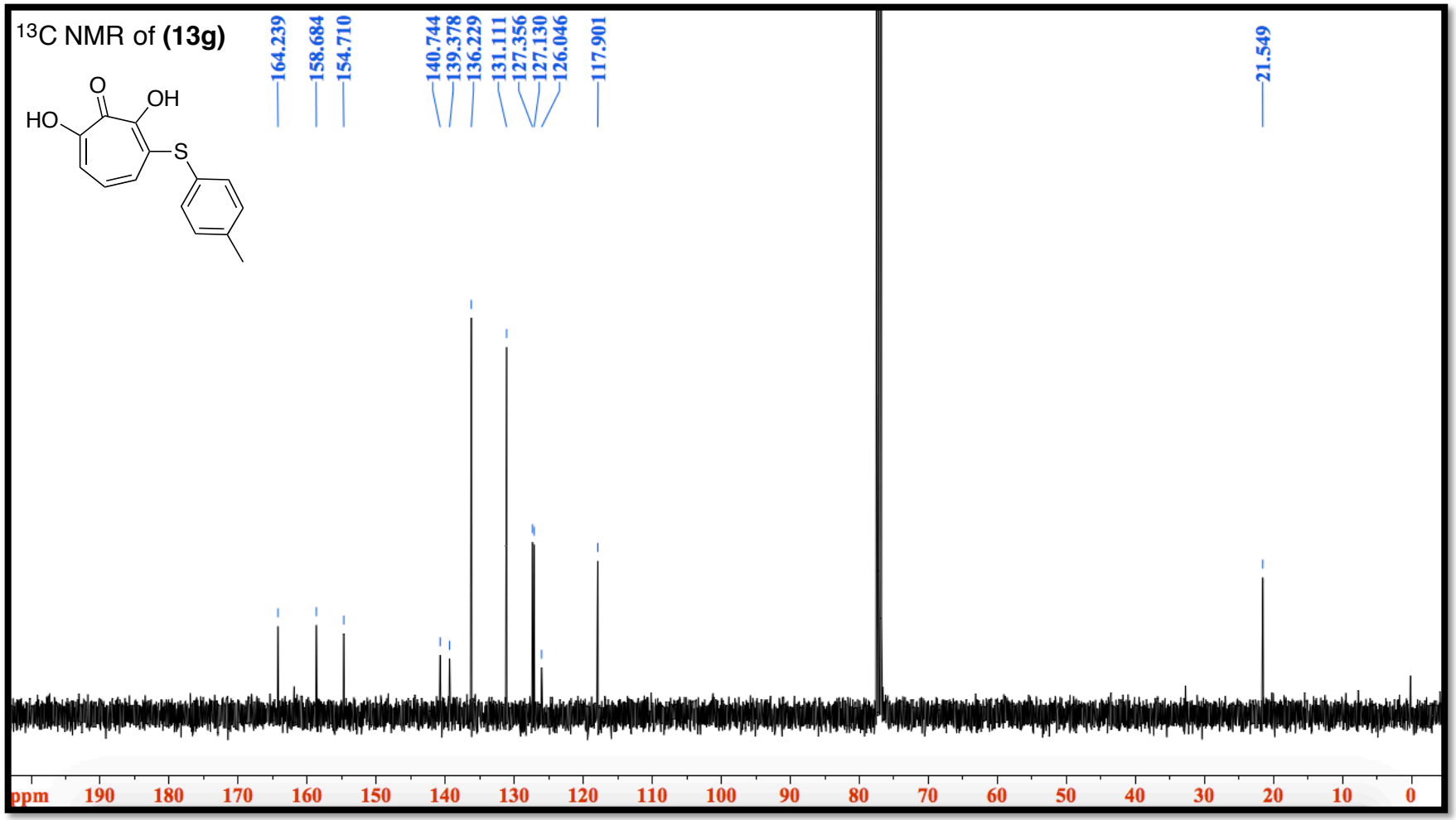
2,7-dihydroxy-3-(naphthalen-1-ylthio)cyclohepta-2,4,6-trien-1-one **(13f)**



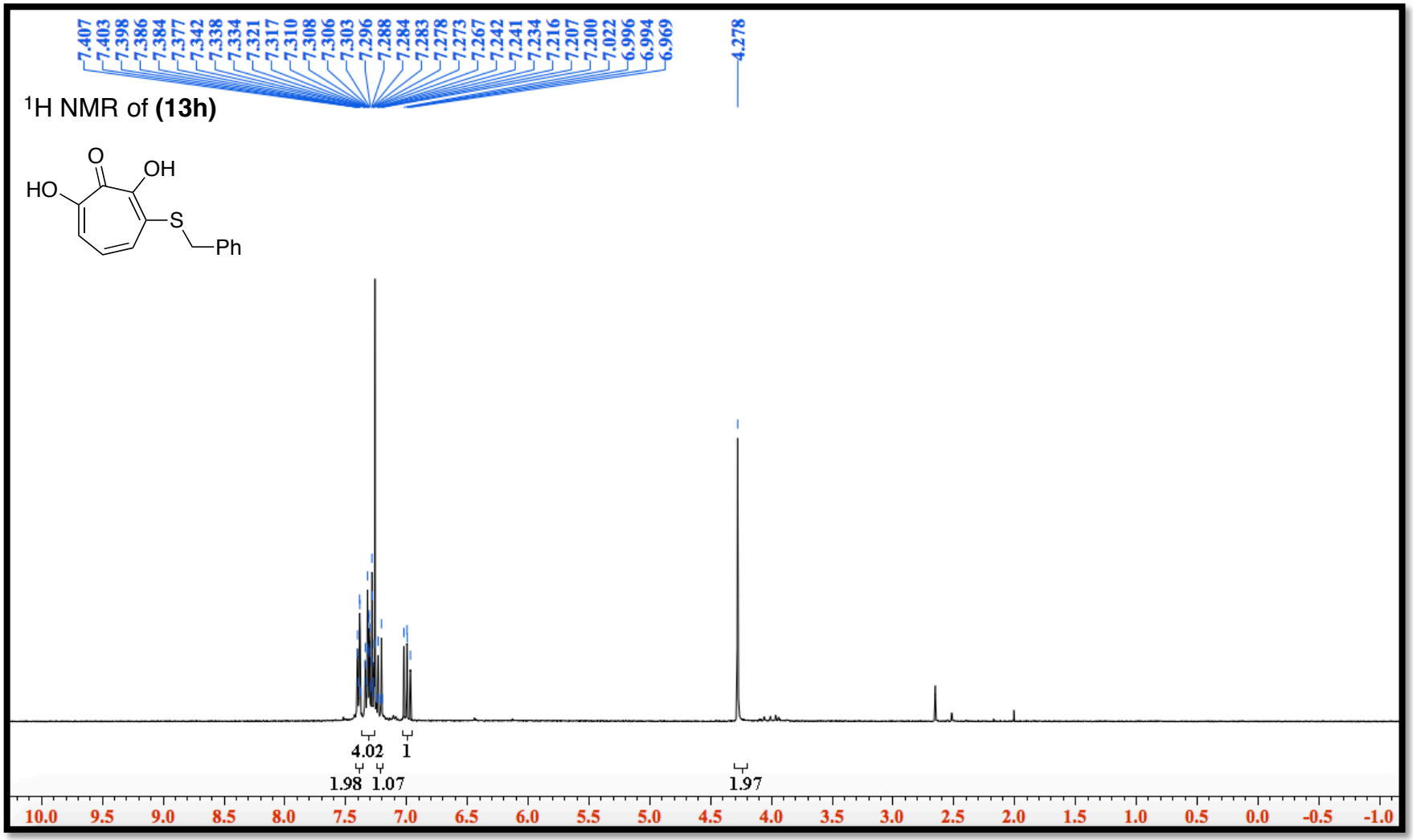

^{13}C NMR of **(13f)**
O
OH
HO
S
164.177
158.664
155.023
138.598
136.771
134.852
134.626
131.914
129.044
128.060
127.291
127.234
127.132
126.507
126.285
125.754
117.932
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

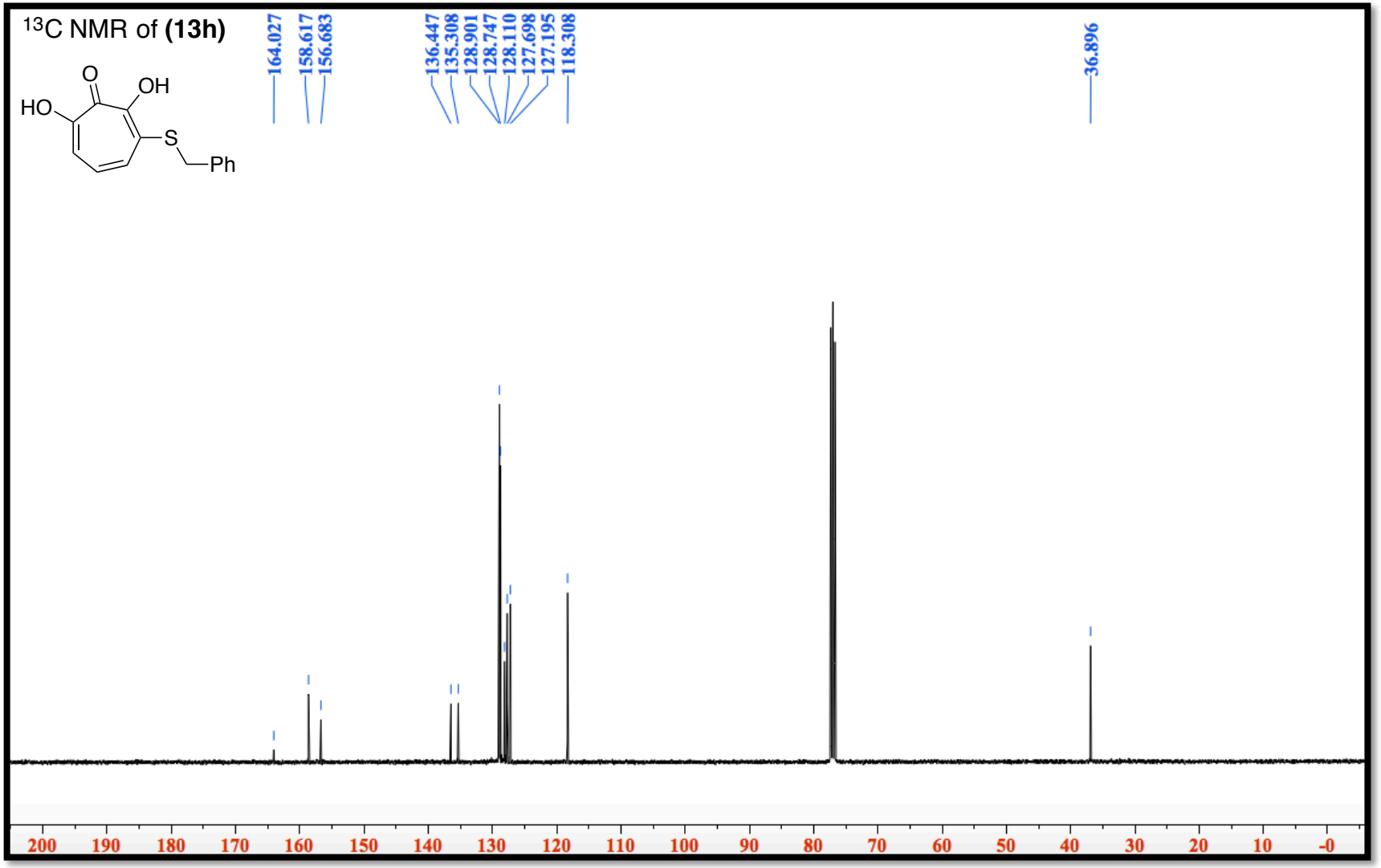
2,7-dihydroxy-3-(p-tolylthio)cyclohepta-2,4,6-trien-1-one (**13g**)



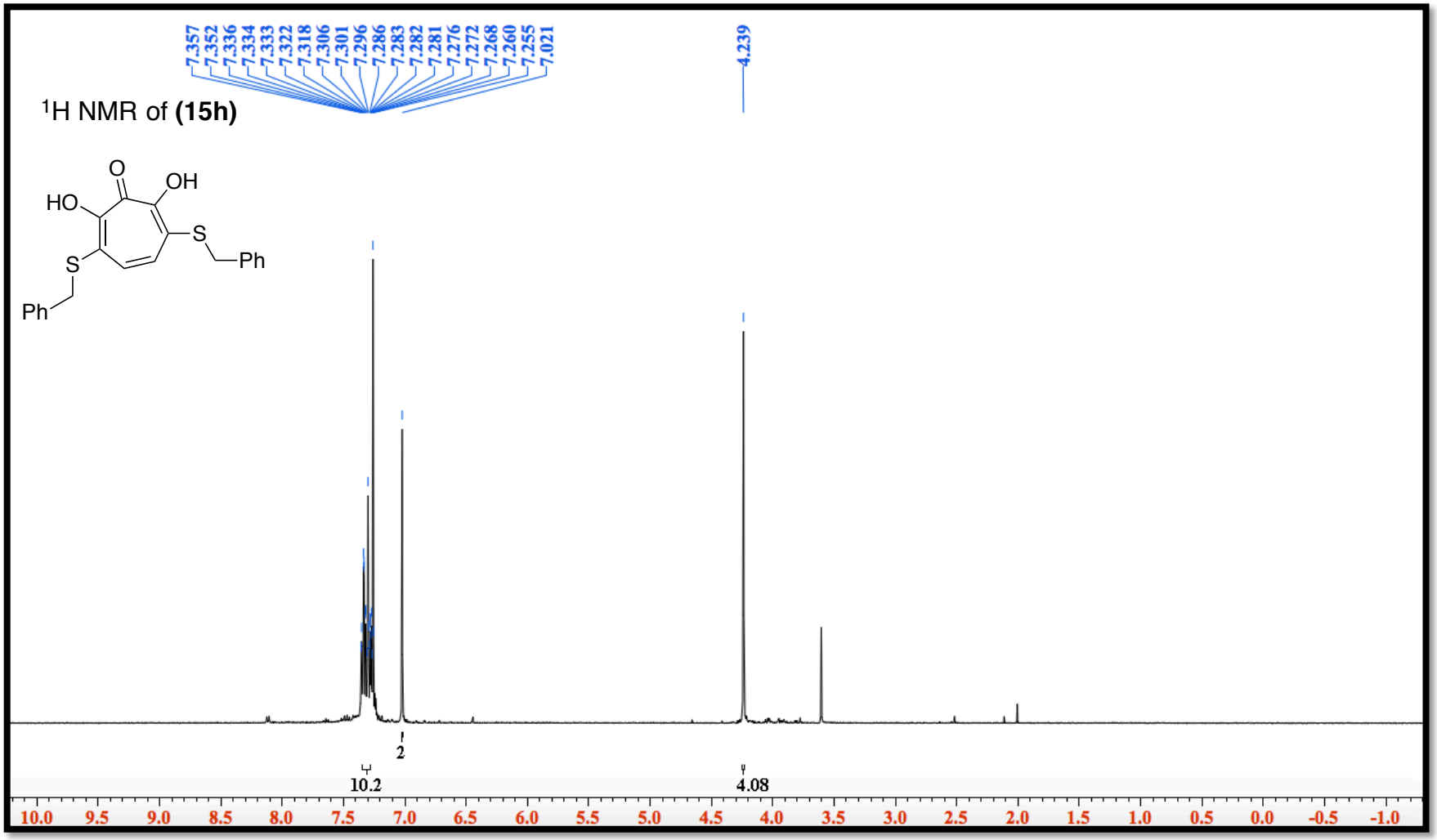

^{13}C NMR of **(13g)**
O
OH
HO
S
164.239
158.684
154.710
140.744
139.378
136.229
131.111
127.356
127.130
126.046
117.901
21.549
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

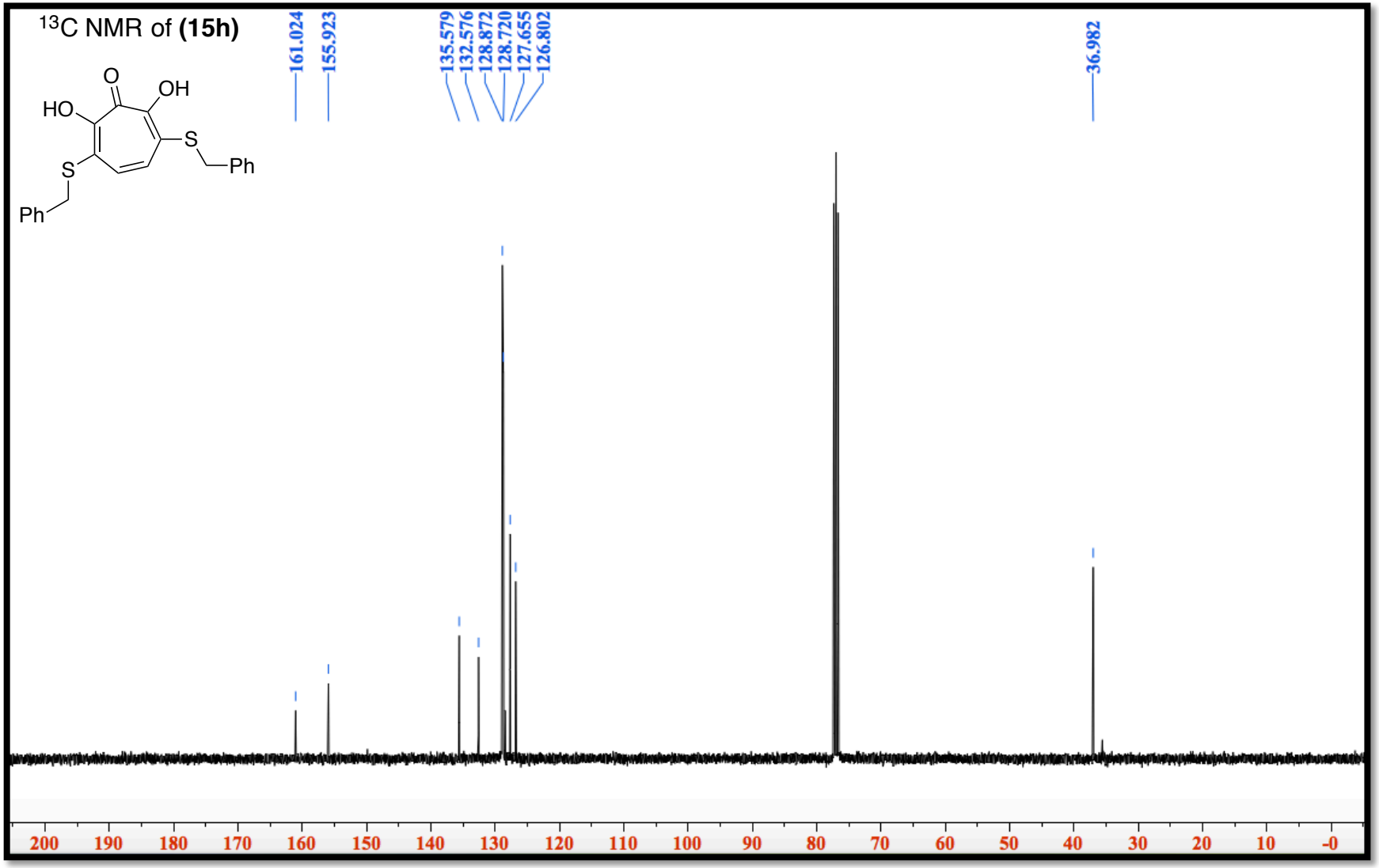
3-(benzylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(13h)**



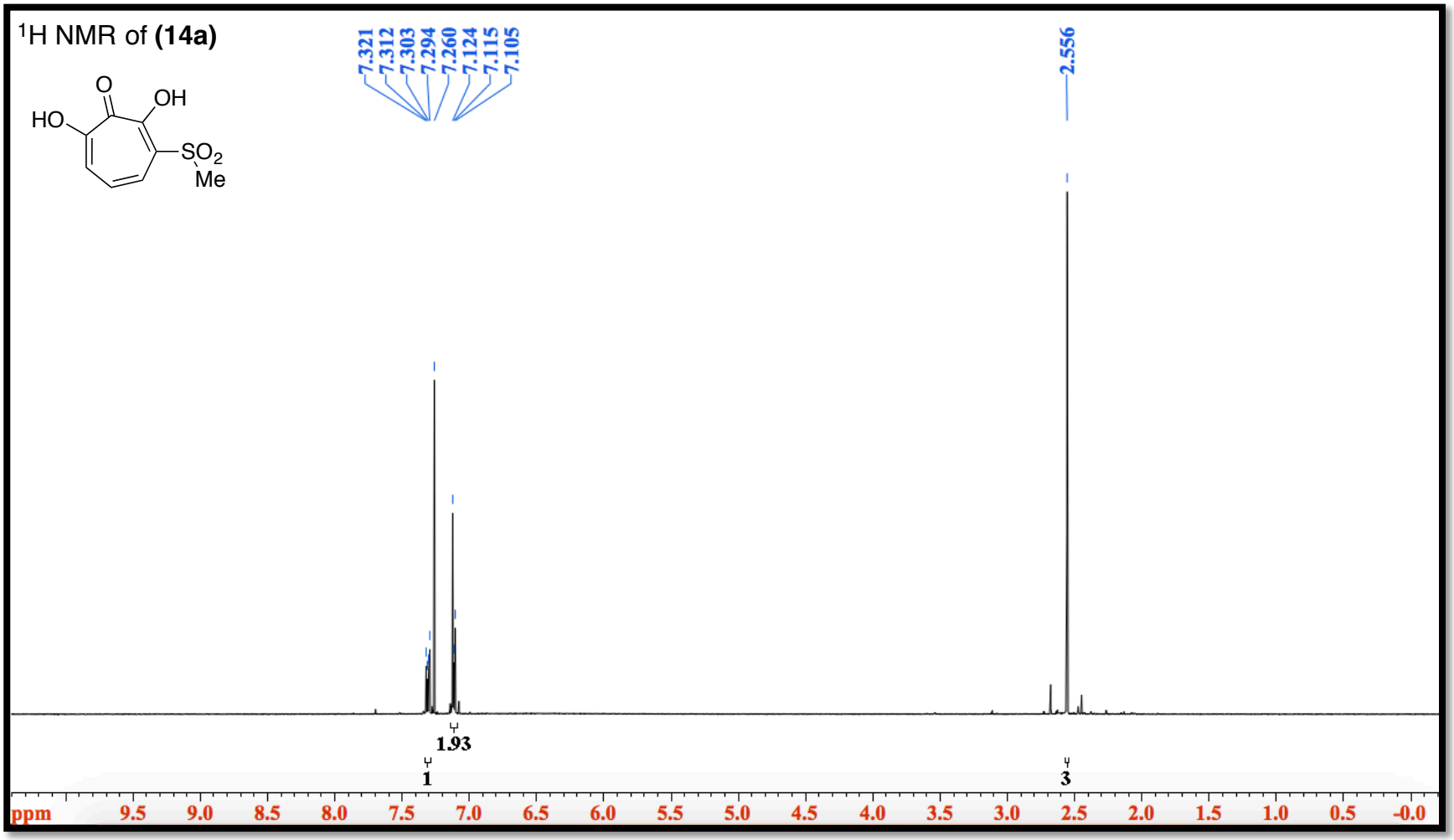

^{13}C NMR of **(13h)**
O
OH
HO
S
Ph
164.027
158.617
156.683
136.447
135.308
128.901
128.747
128.110
127.698
127.195
118.308
36.896
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0

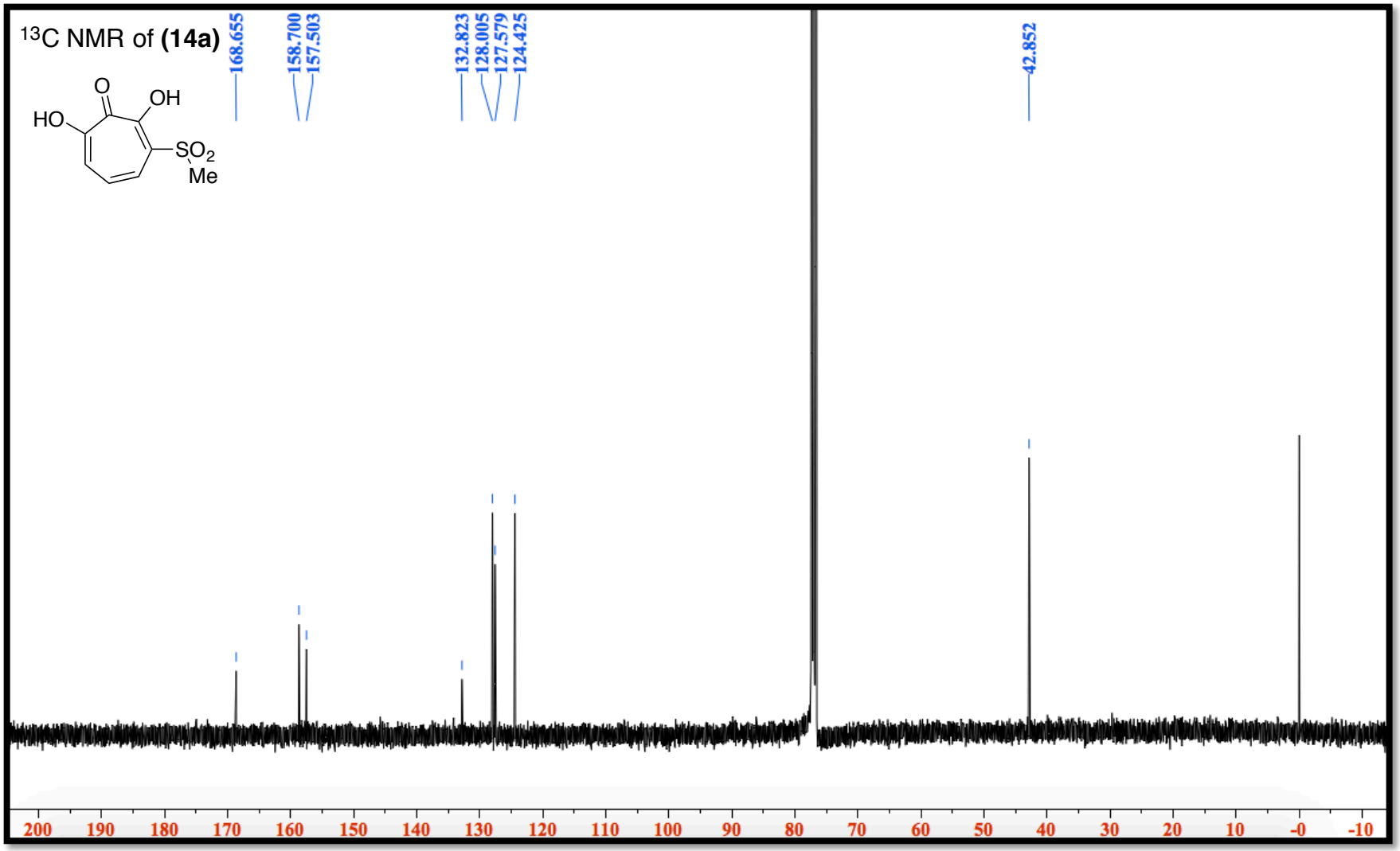
3,6-bis(benzylthio)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(15h)**



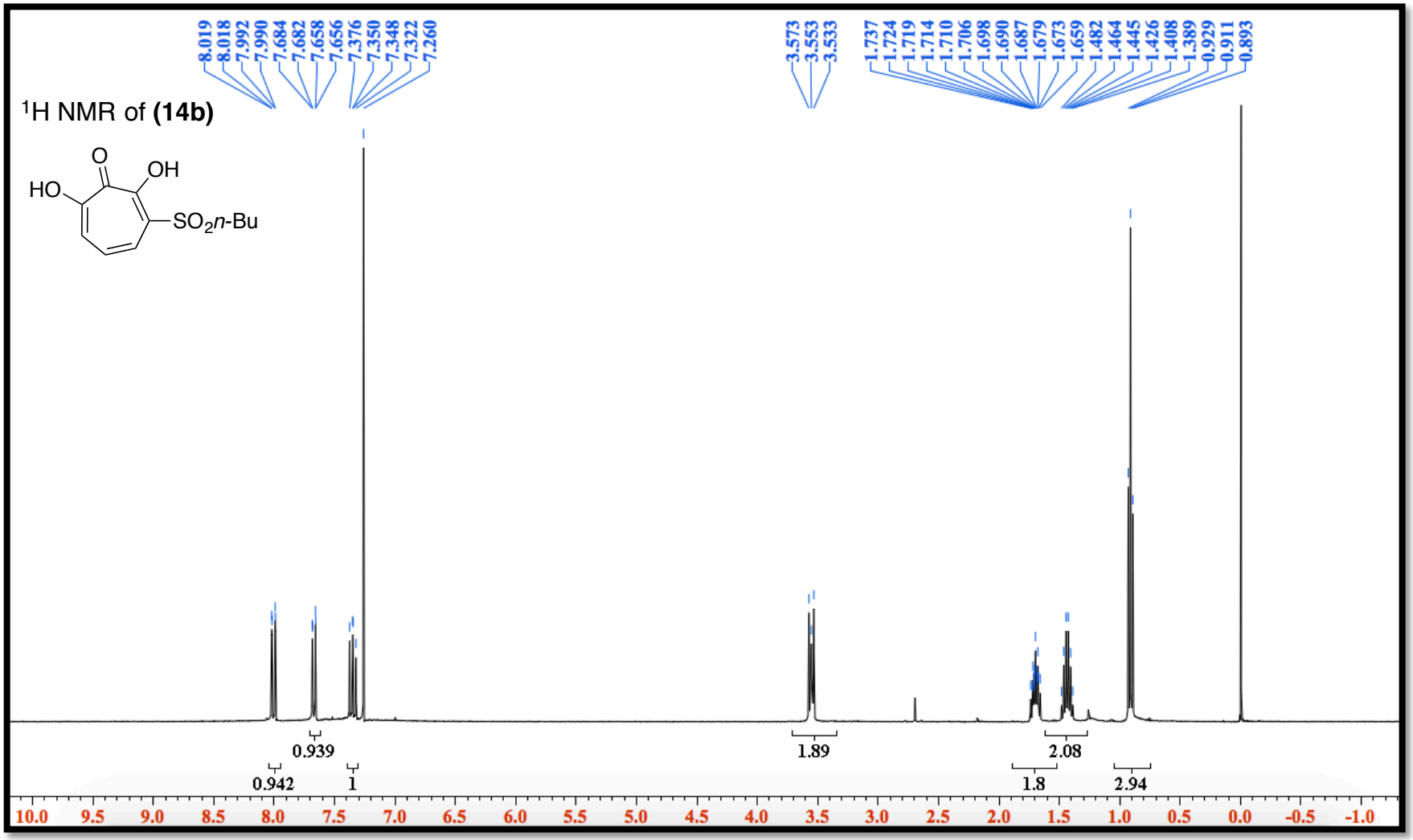

^{13}C NMR of **(15h)**
O
OH
HO
S
Ph
S
Ph
161.024
155.923
135.579
132.576
128.872
128.720
127.655
126.802
36.982
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0

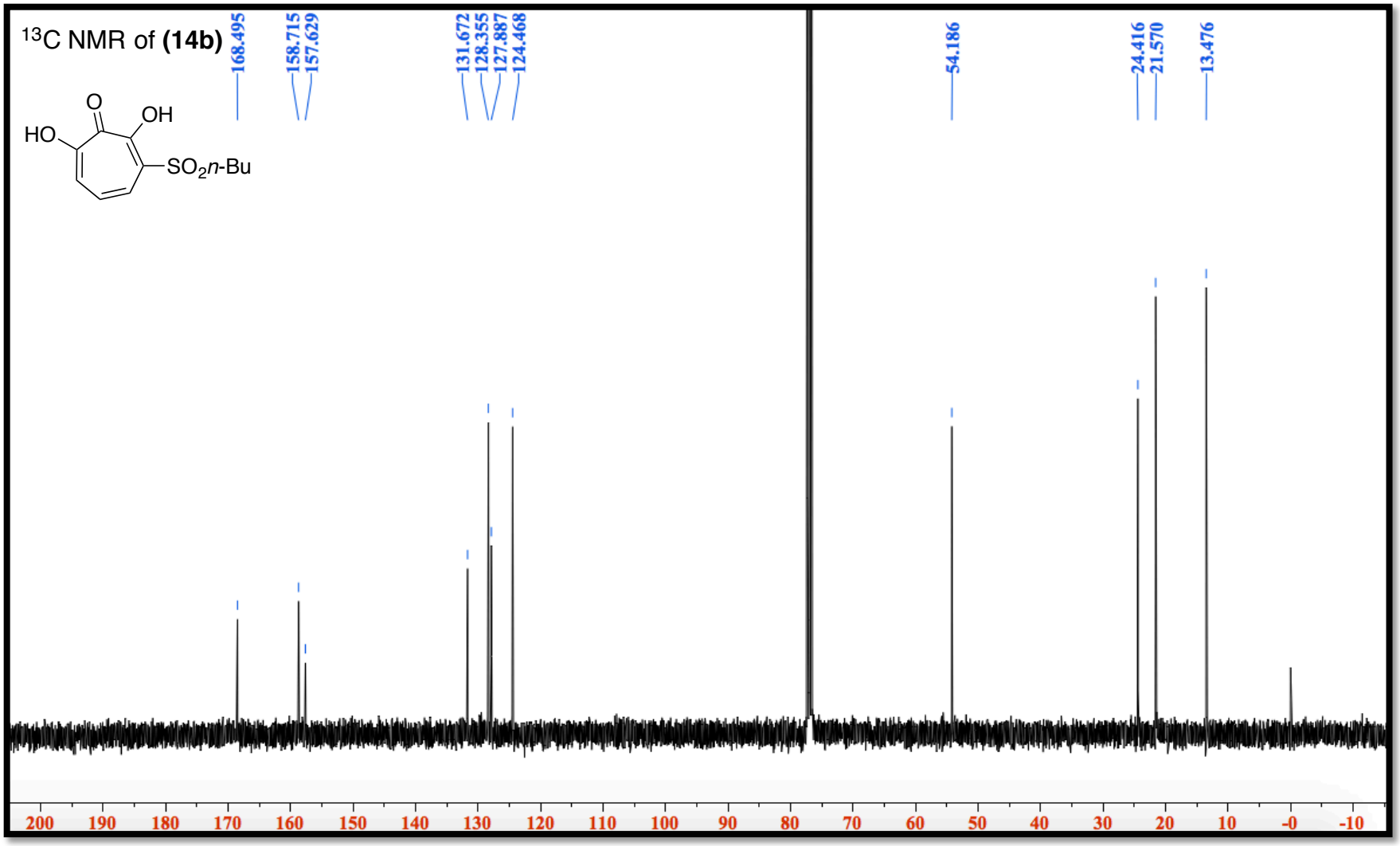
2,7-dihydroxy-3-(methylsulfonyl)cyclohepta-2,4,6-trien-1-one **(14a)**



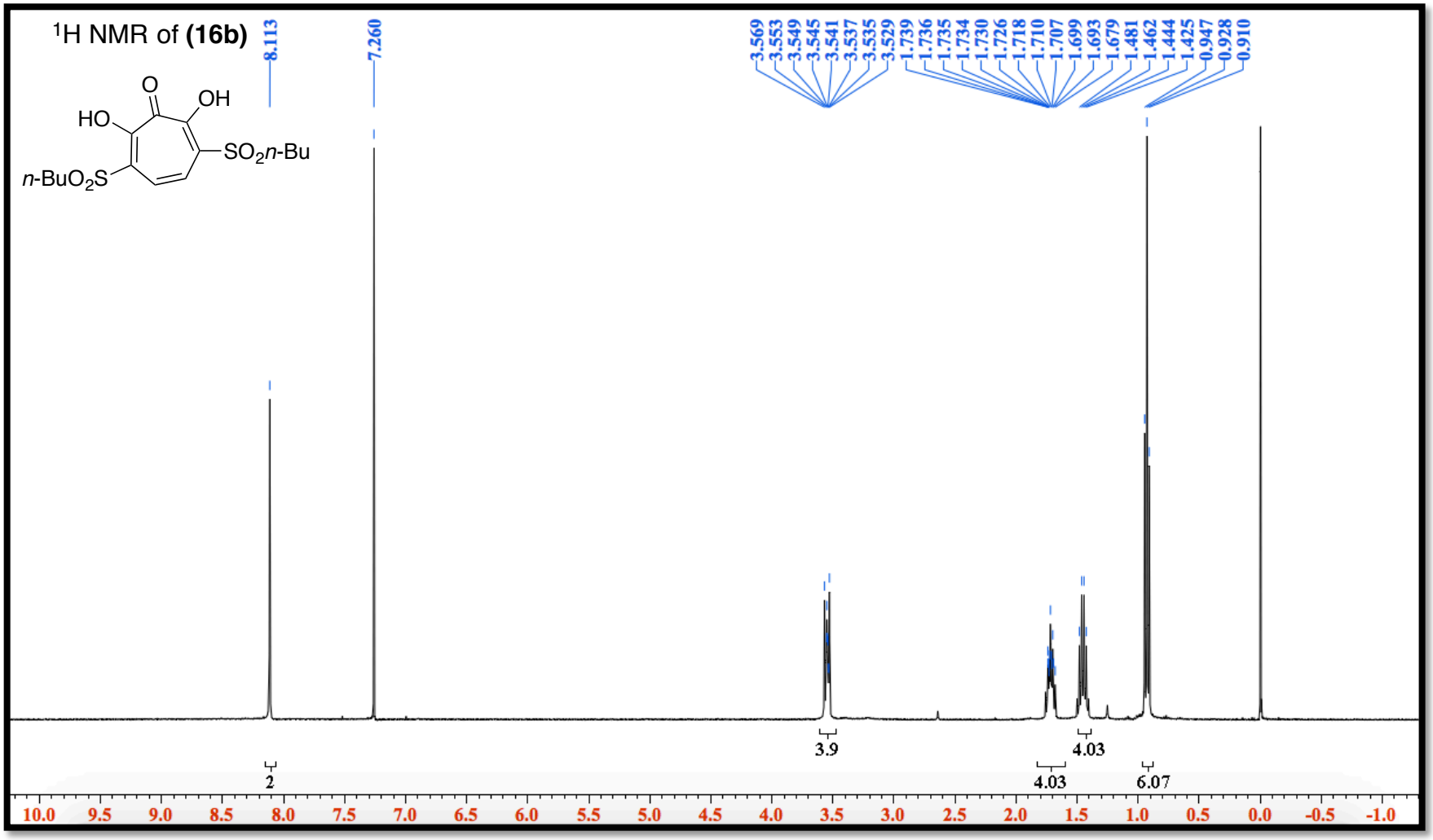

^{13}C NMR of **(14a)**
O
OH
HO
SO_2
Me
168.655
158.700
157.503
132.823
128.005
127.579
124.425
42.852
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0 -10

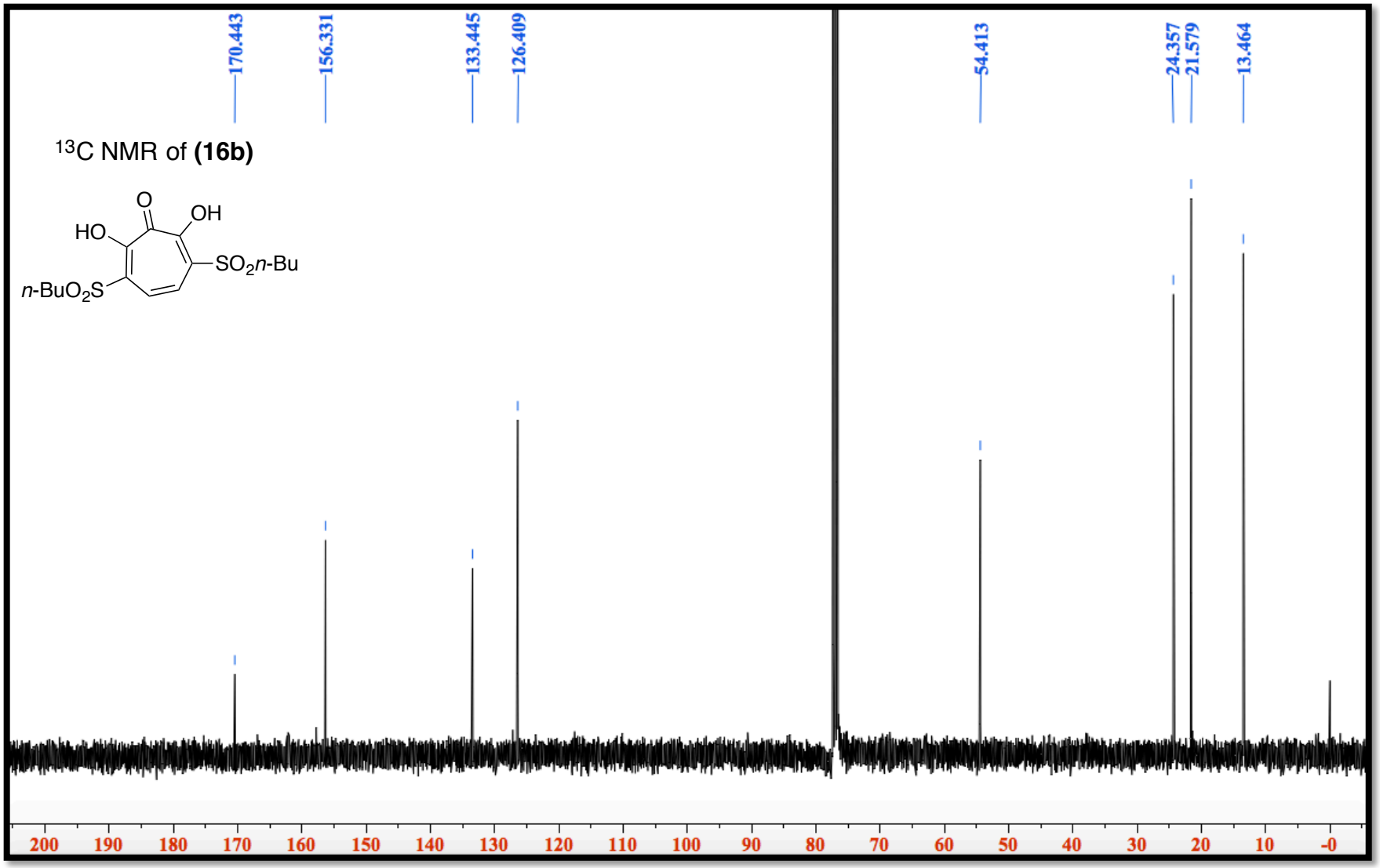
3-(butylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(14b)**



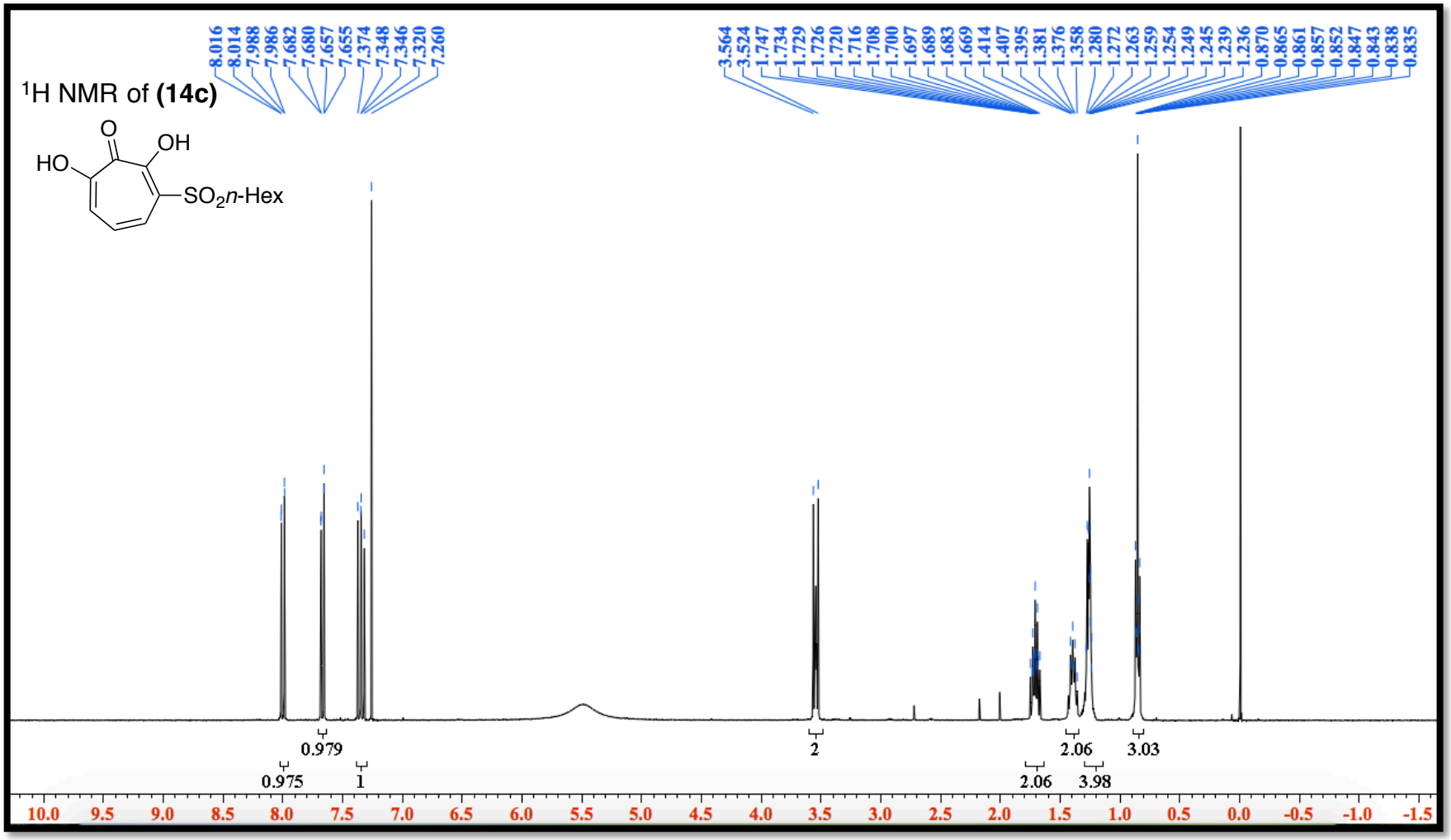

^{13}C NMR of **(14b)**
168.495
158.715
157.629
131.672
128.355
127.887
124.468
54.186
24.416
21.570
13.476
HO
O
OH
SO$_2$*n*-Bu
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0 -10

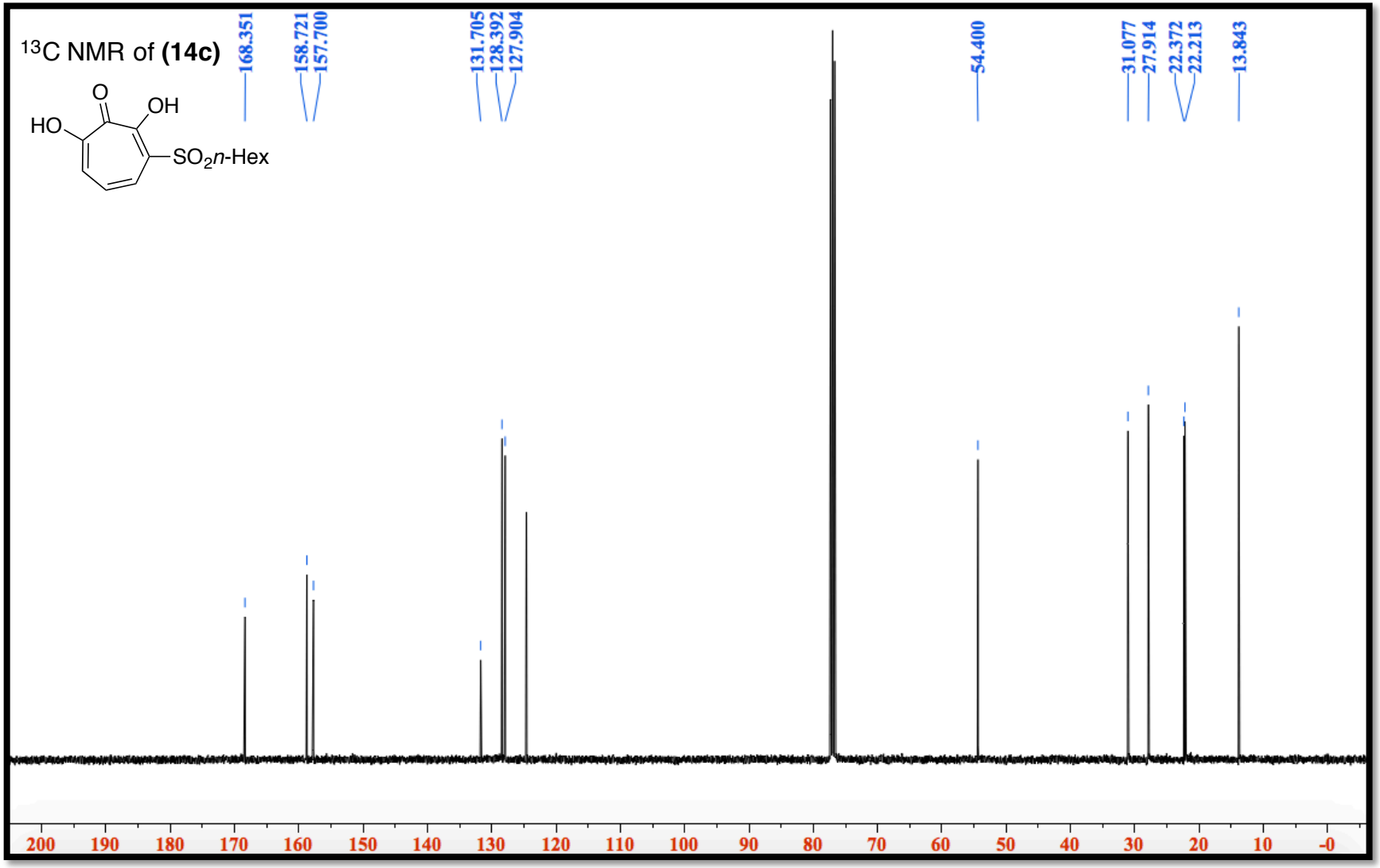
3,6-bis(butylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(16b)**



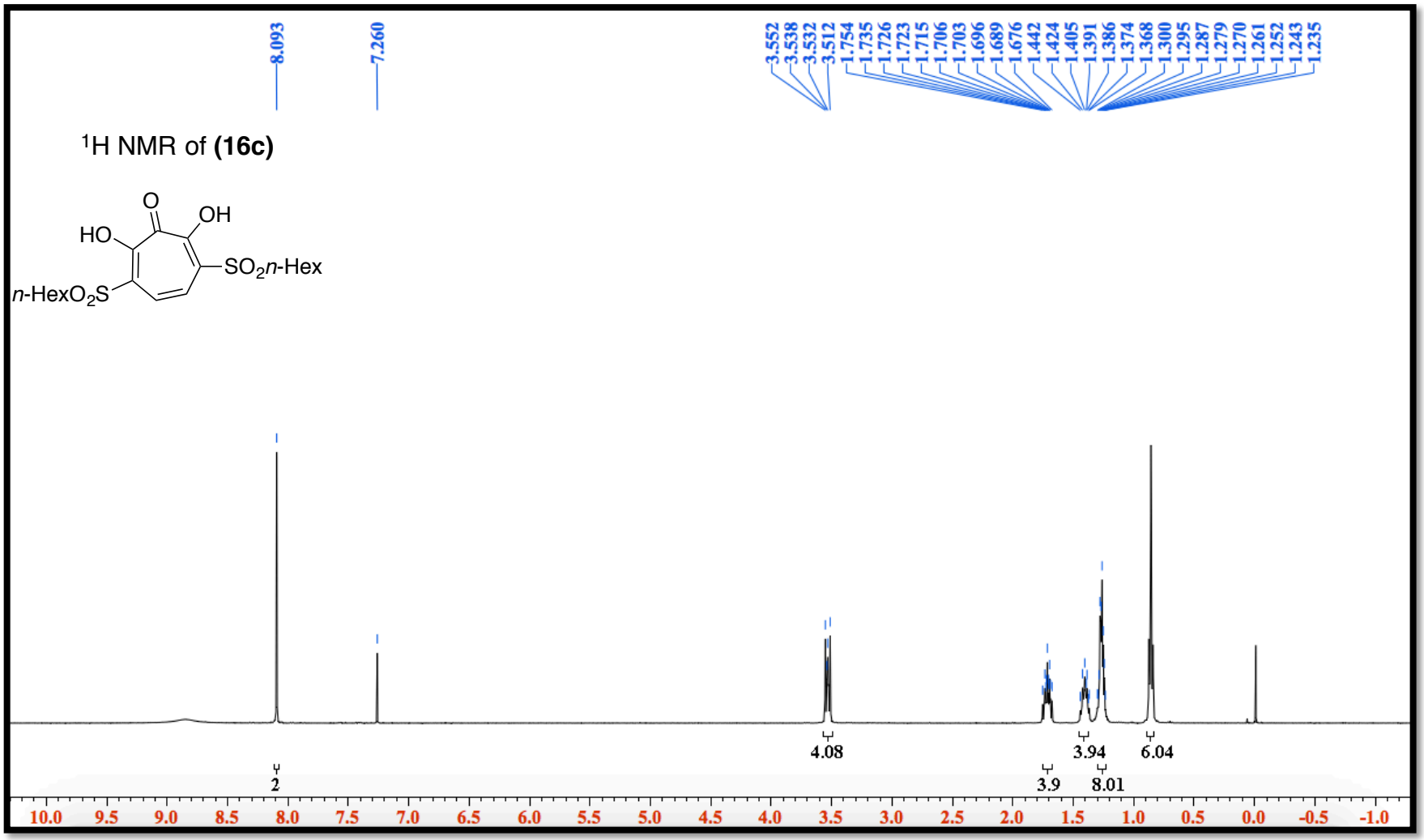

170.443
156.331
133.445
126.409
54.413
24.357
21.579
13.464
^{13}C NMR of **(16b)**
O
OH
HO
SO_2n-Bu
n-BuO_2S
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0

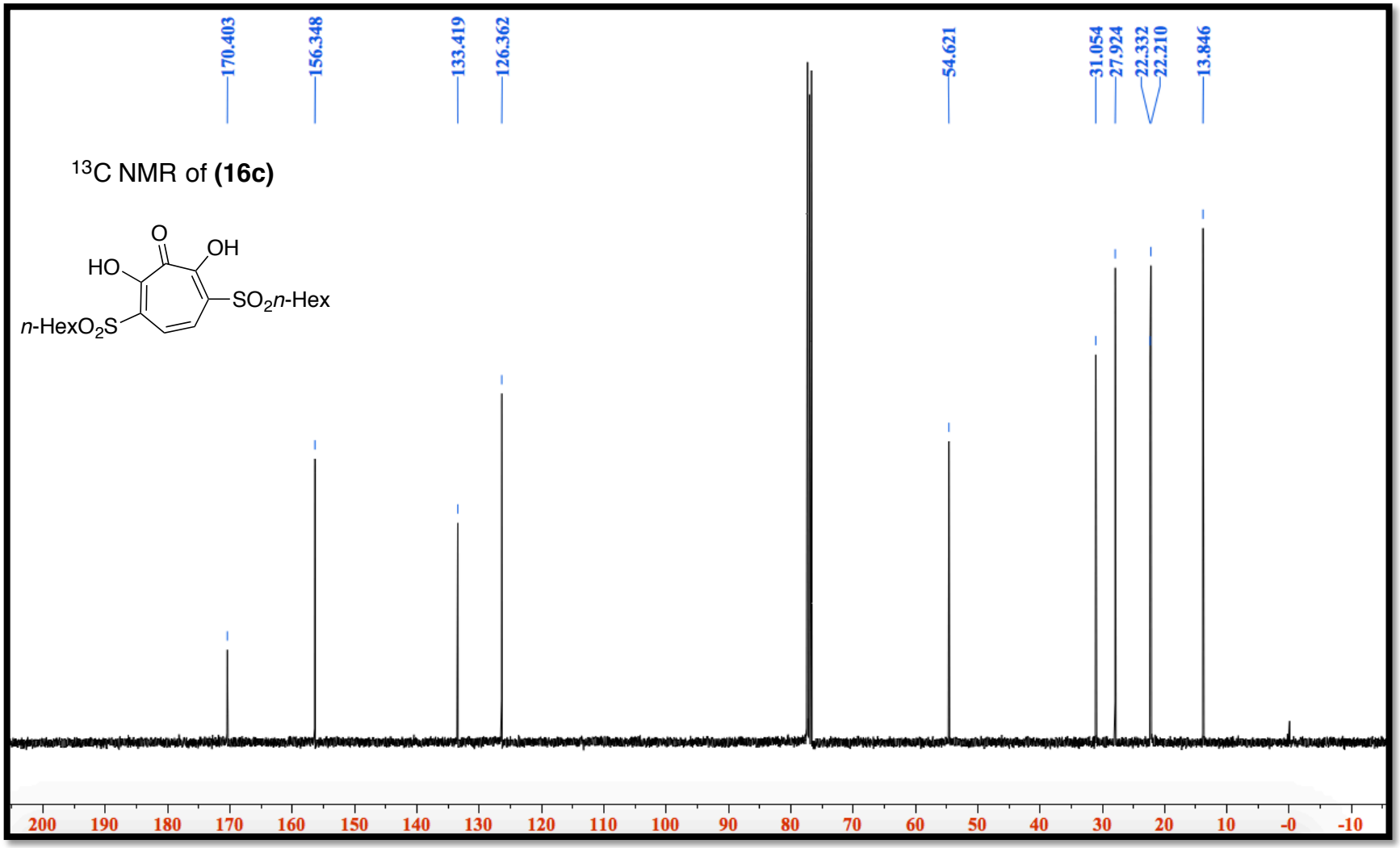
3-(hexylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(14c)**



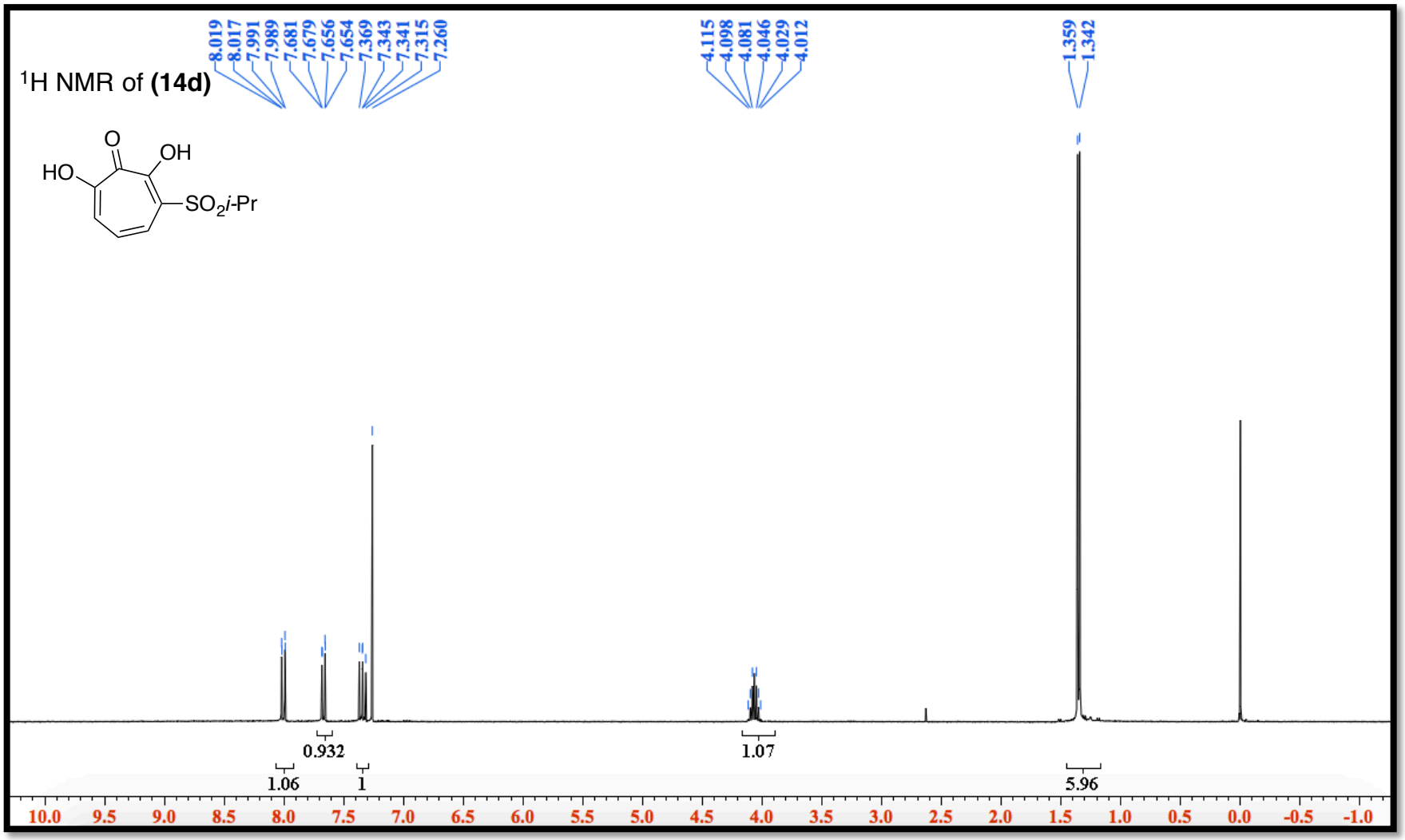

^{13}C NMR of **(14c)**
O
OH
HO
SO$_2$*n*-Hex
168.351
158.721
157.700
131.705
128.392
127.904
54.400
31.077
27.914
22.372
22.213
13.843
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0

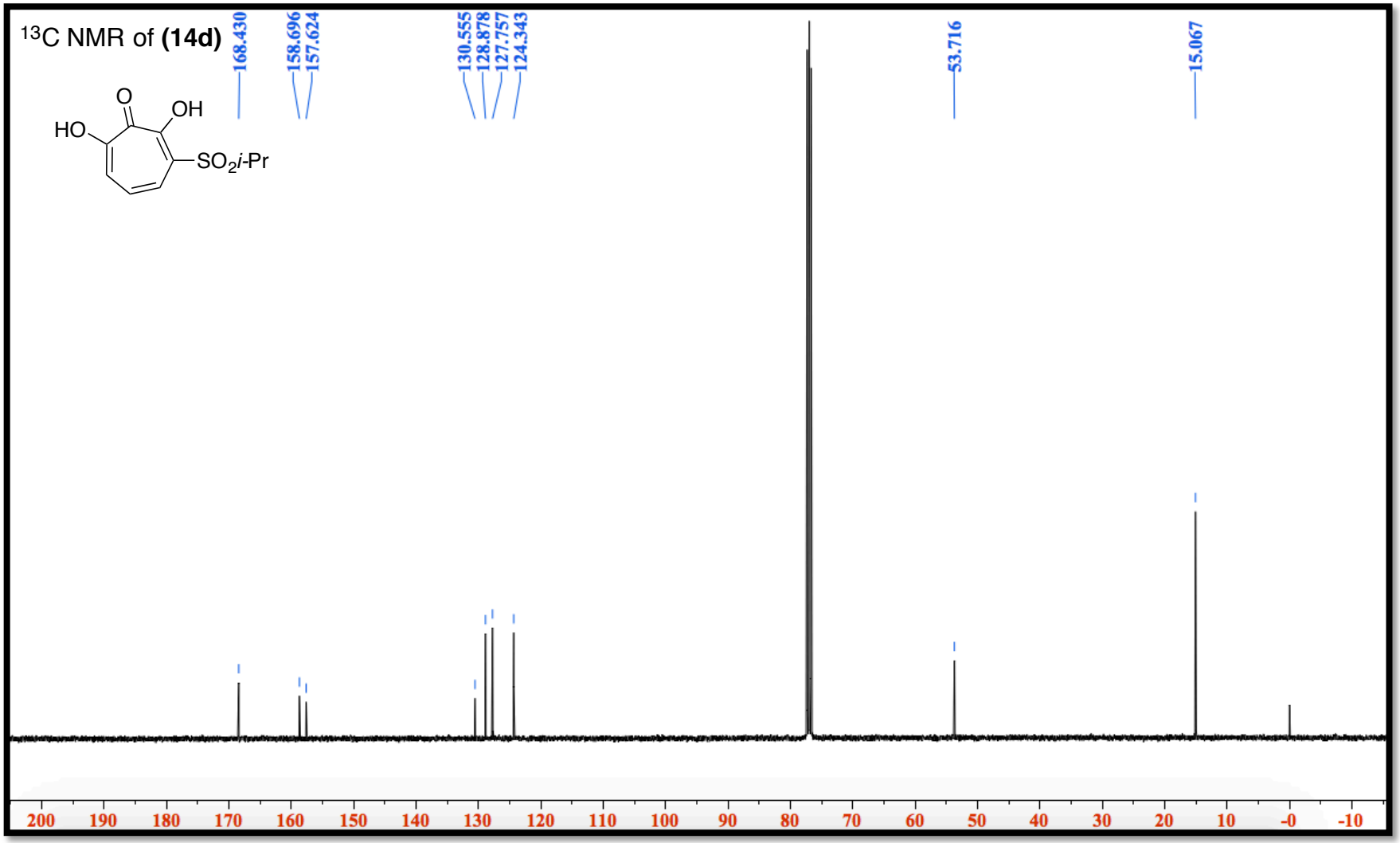
3,6-bis(hexylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(16c)**



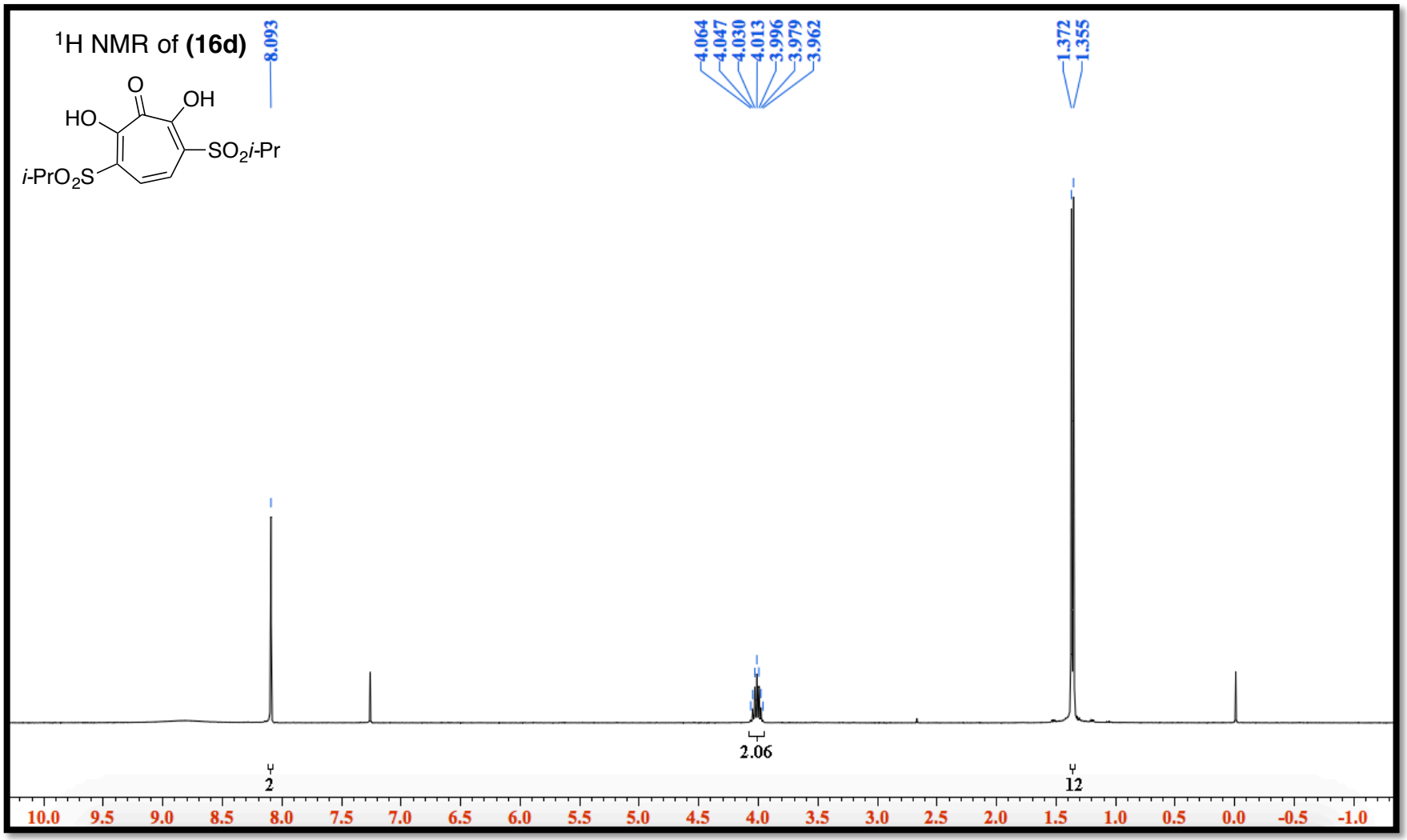

170.403
156.348
133.419
126.362
54.621
31.054
27.924
22.332
22.210
13.846
^{13}C NMR of **(16c)**
O
OH
HO
SO_2*n*-Hex
n-HexO_2S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0
-10

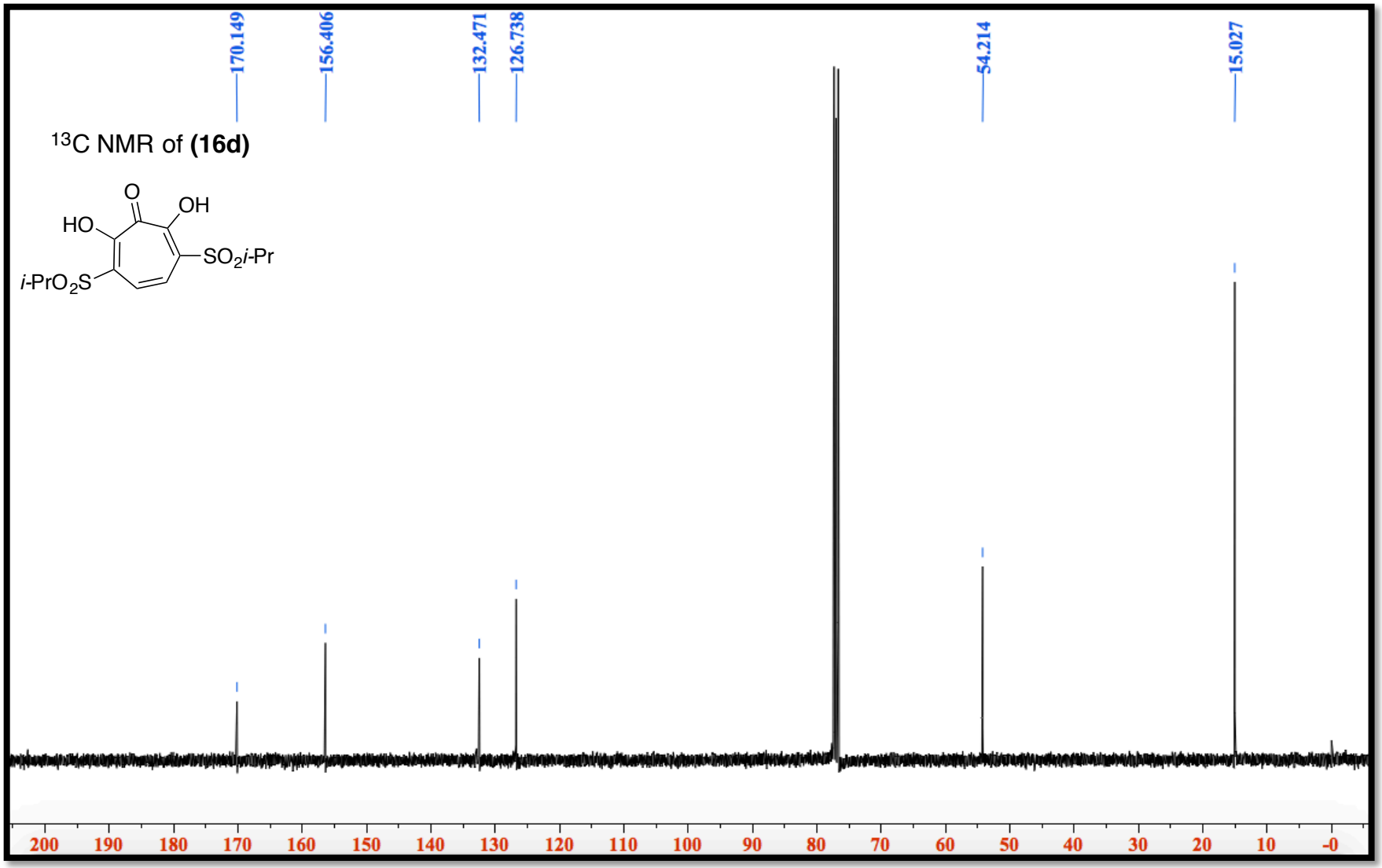
2,7-dihydroxy-3-(isopropylsulfonyl)cyclohepta-2,4,6-trien-1-one **(14d)**



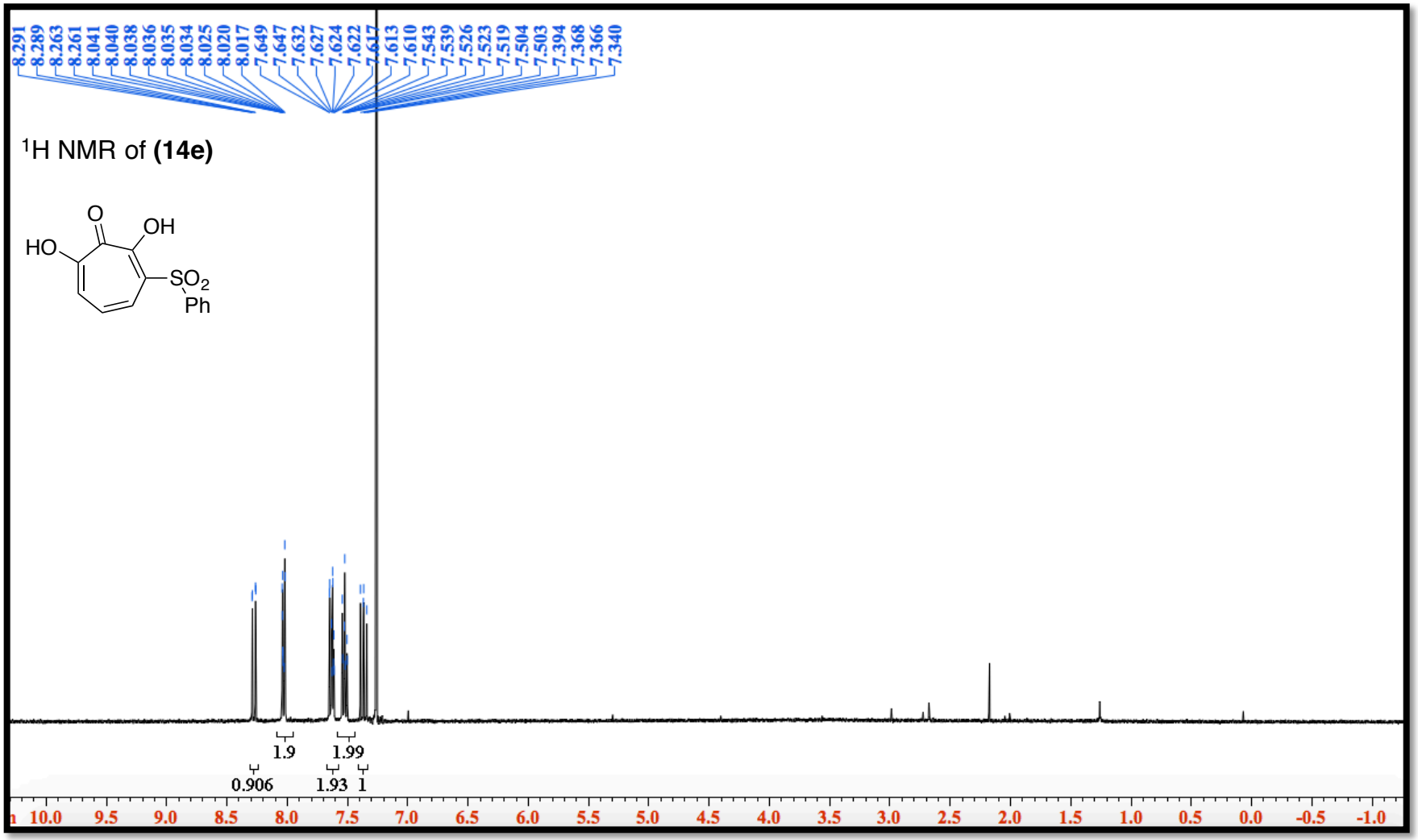

^{13}C NMR of **(14d)**
168.430
158.696
157.624
130.555
128.878
127.757
124.343
53.716
15.067
O
OH
HO
SO$_2$*i*-Pr
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0 -10

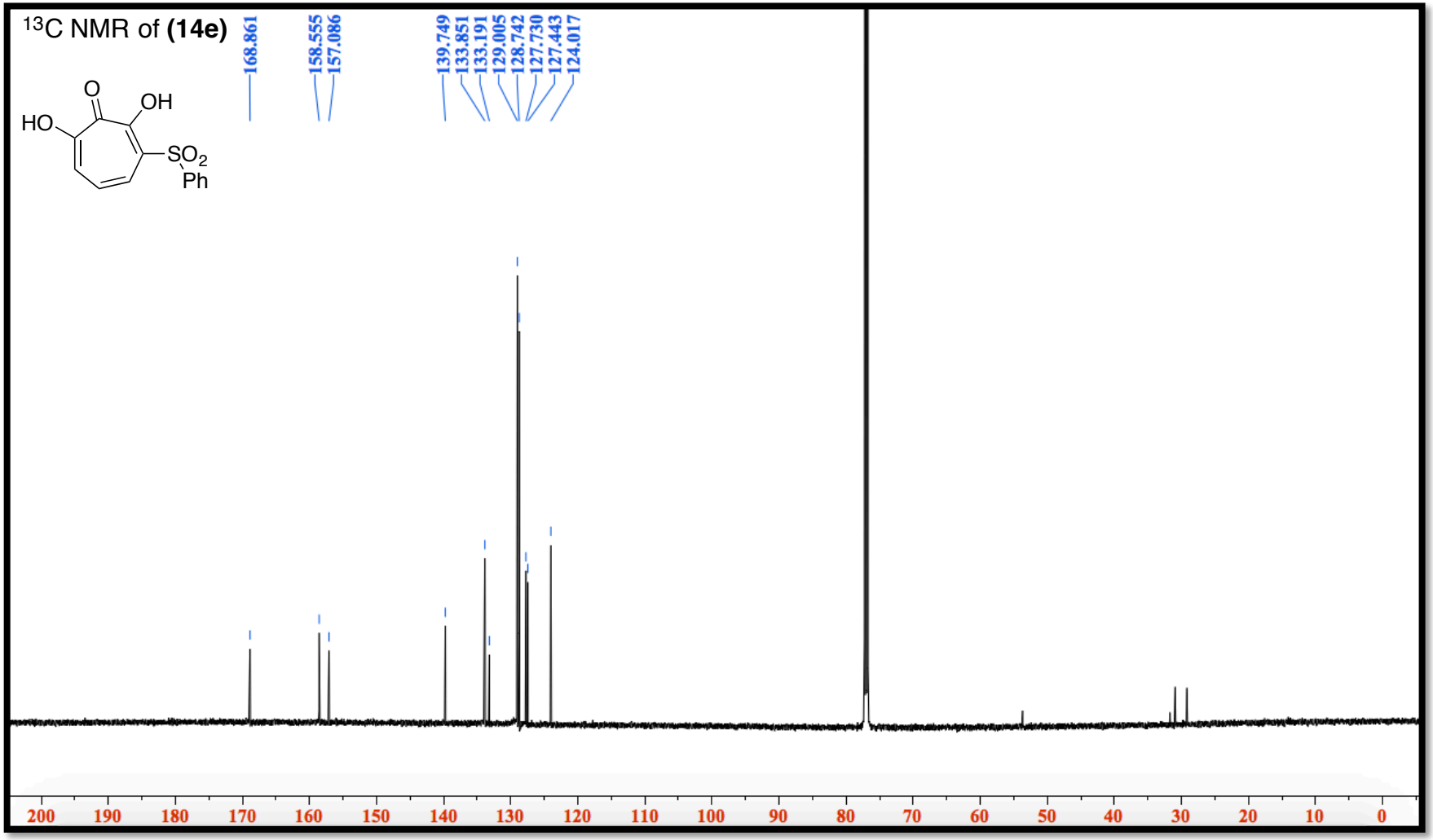
2,7-dihydroxy-3,6-bis(isopropylsulfonyl)cyclohepta-2,4,6-trien-1-one **(16d)**



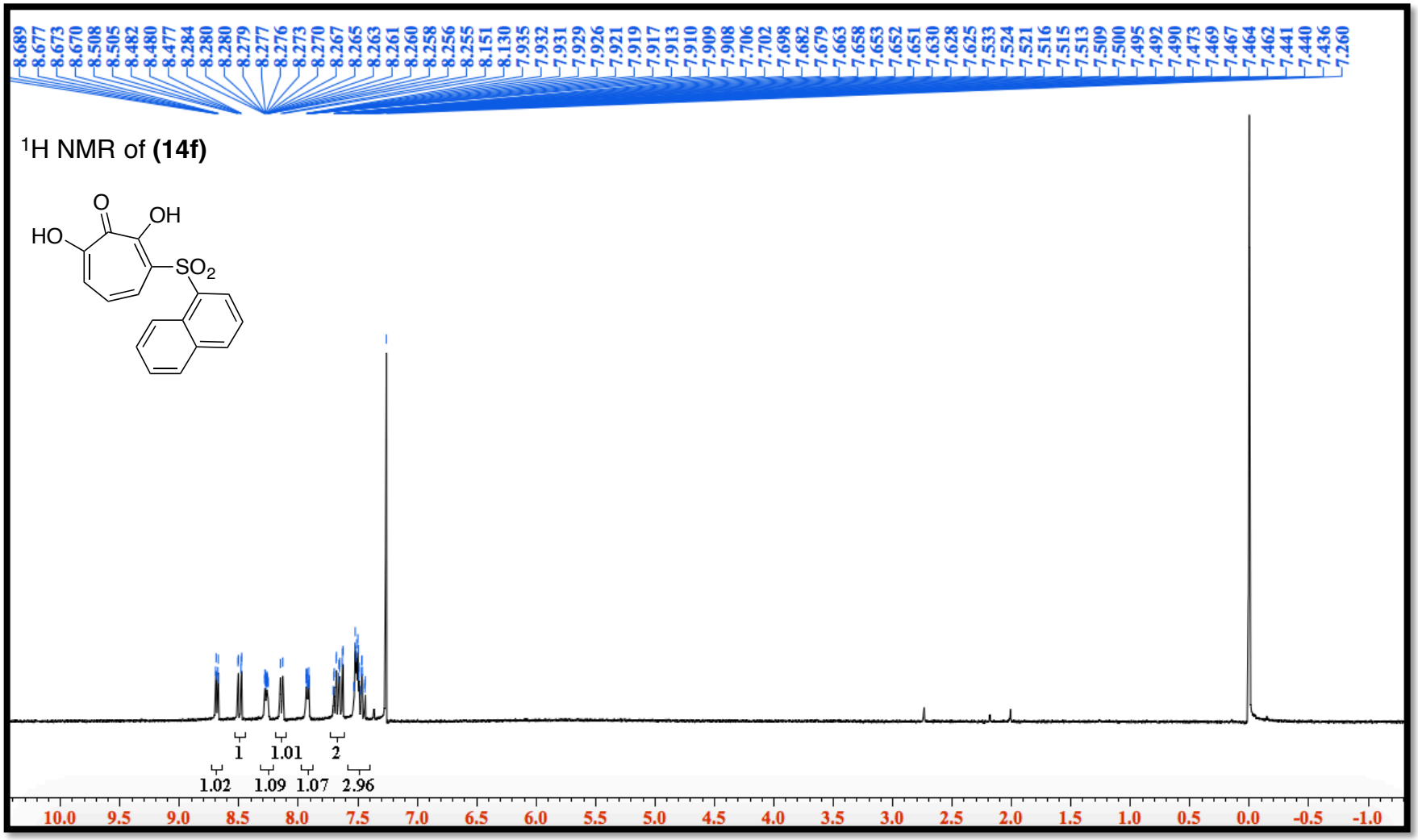

170.149
156.406
132.471
126.738
54.214
15.027
^{13}C NMR of **(16d)**
O
OH
HO
SO_2i-Pr
i-PrO_2S
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
-0

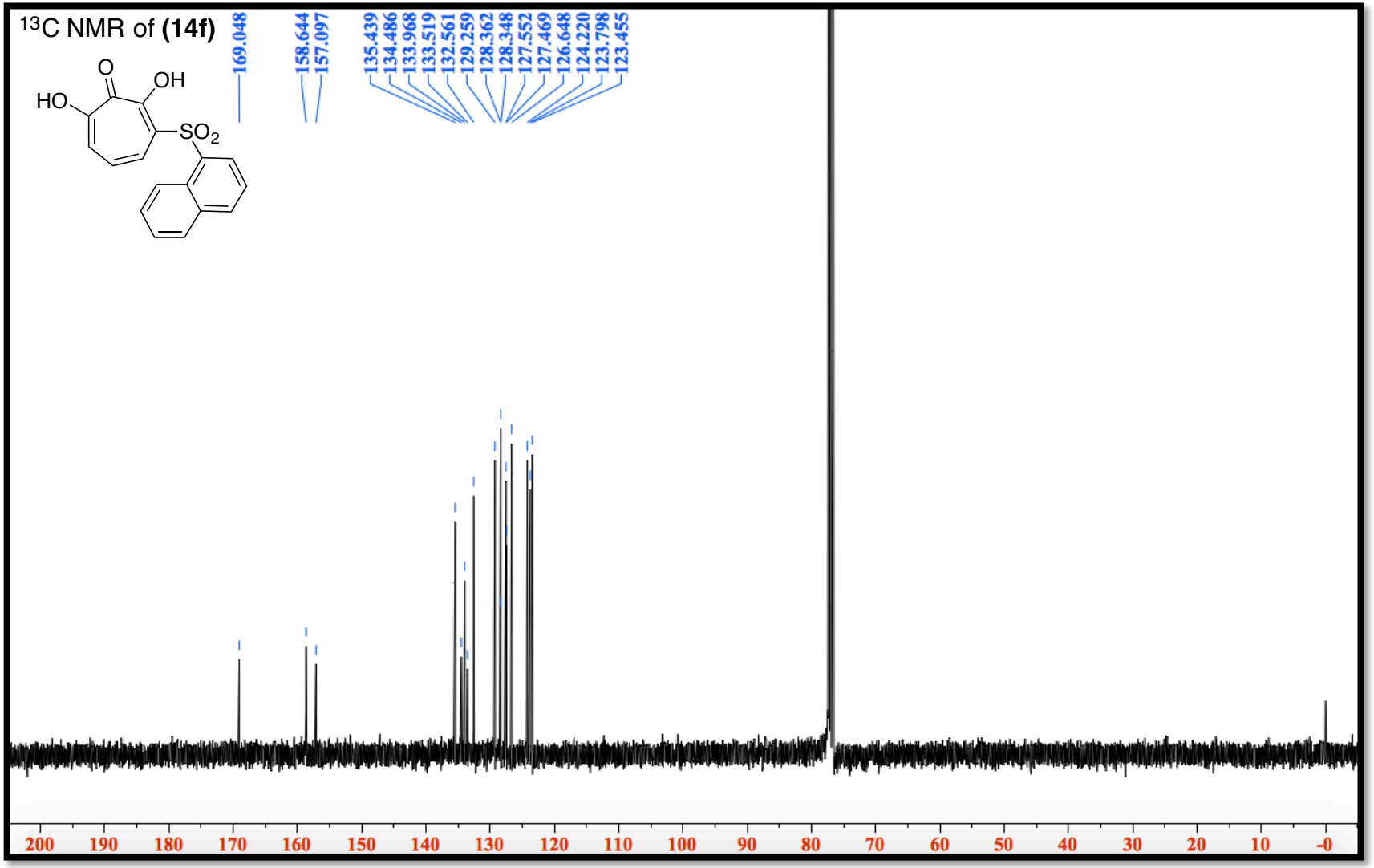
2,7-dihydroxy-3-(phenylsulfonyl)cyclohepta-2,4,6-trien-1-one **(14e)**



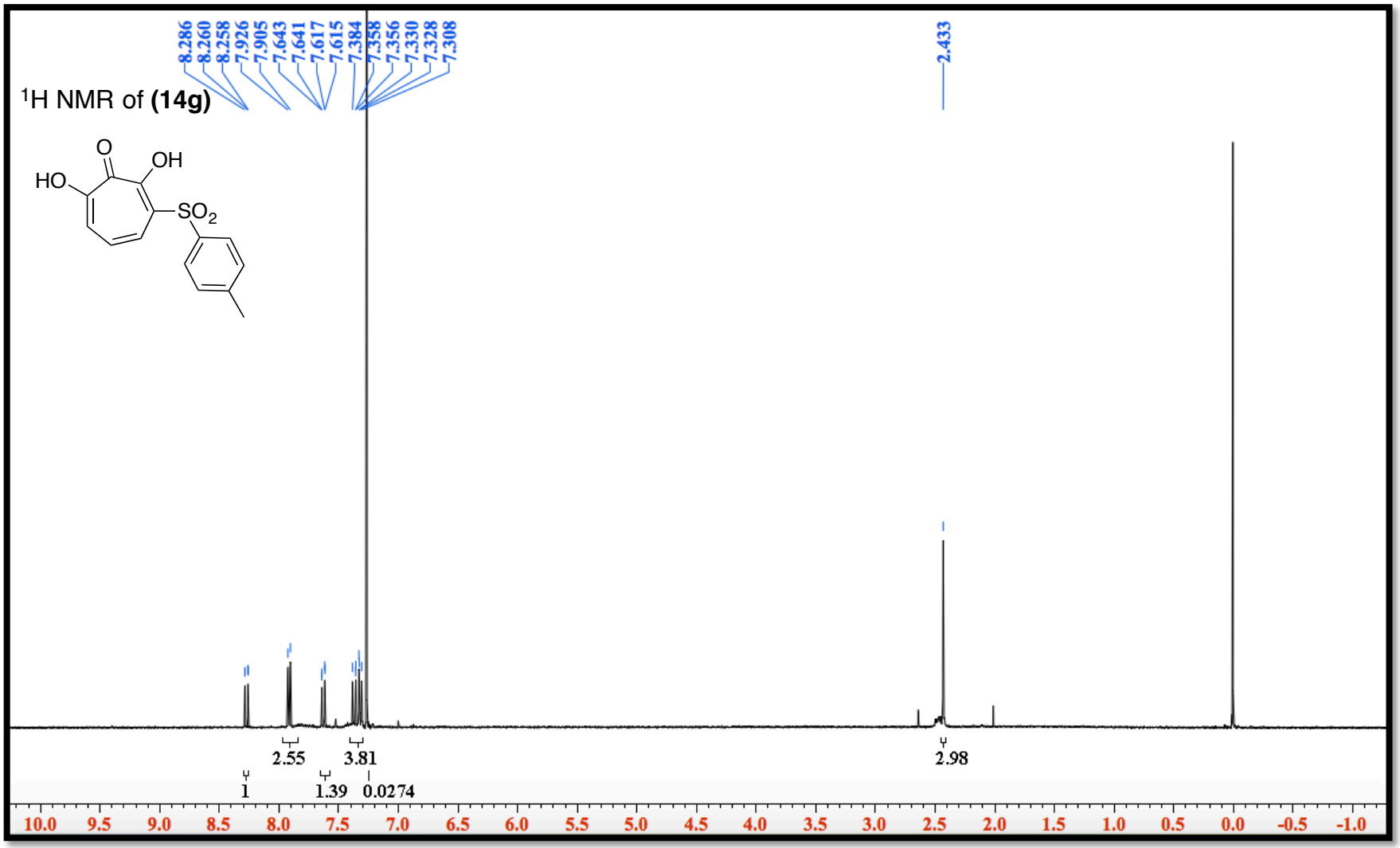

^{13}C NMR of **(14e)**
168.861
158.555
157.086
139.749
133.851
133.191
129.005
128.742
127.730
127.443
124.017
O
OH
HO
SO_2
Ph
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

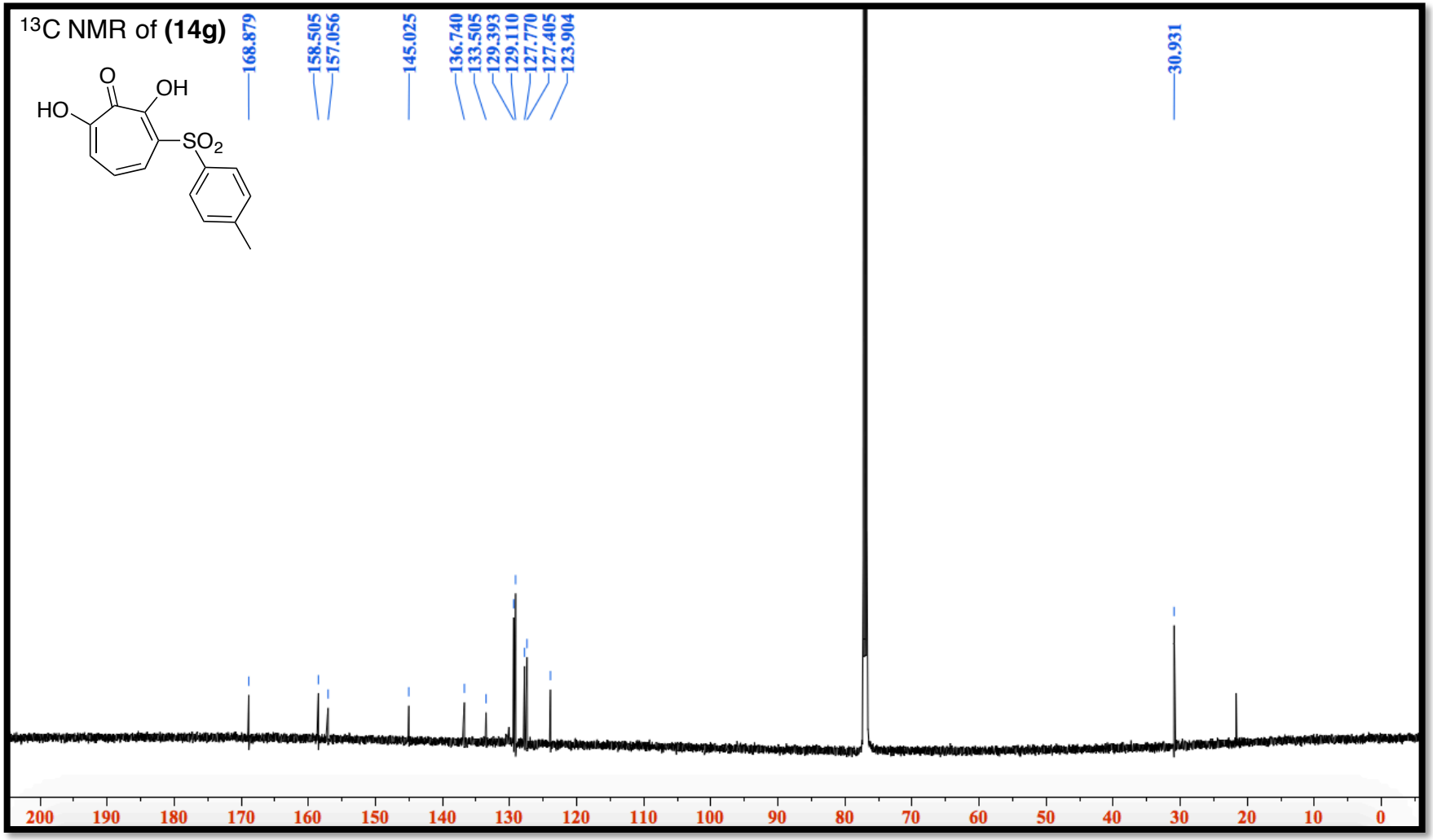
2,7-dihydroxy-3-(naphthalen-1-ylsulfonyl)cyclohepta-2,4,6-trien-1-one **(14f)**



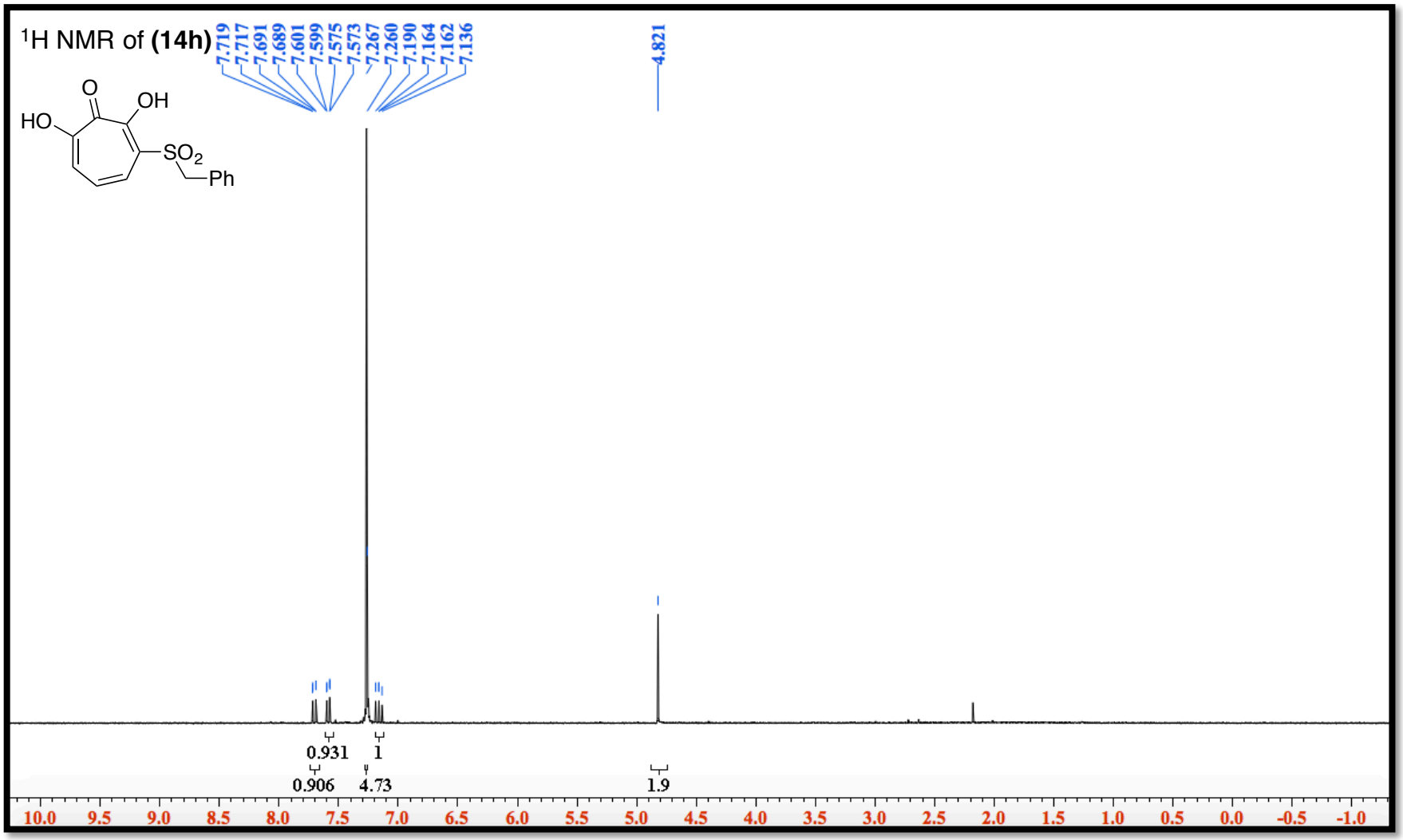

^{13}C NMR of **(14f)**
O
OH
HO
SO_2
169.048
158.644
157.097
135.439
134.486
133.968
133.519
132.561
129.259
128.362
128.348
127.552
127.469
126.648
124.220
123.798
123.455
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 -0

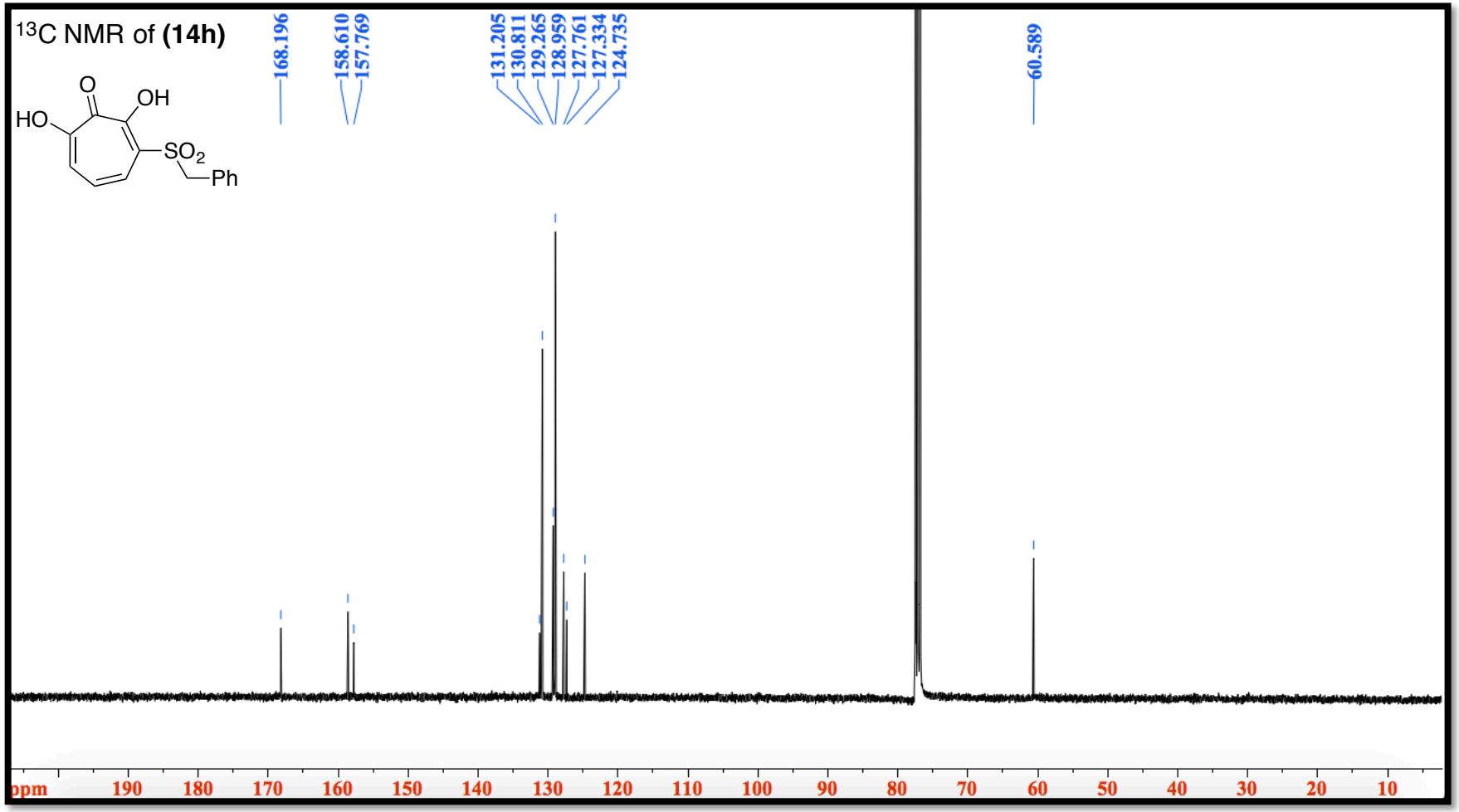
2,7-dihydroxy-3-tosylcyclohepta-2,4,6-trien-1-one **(14g)**



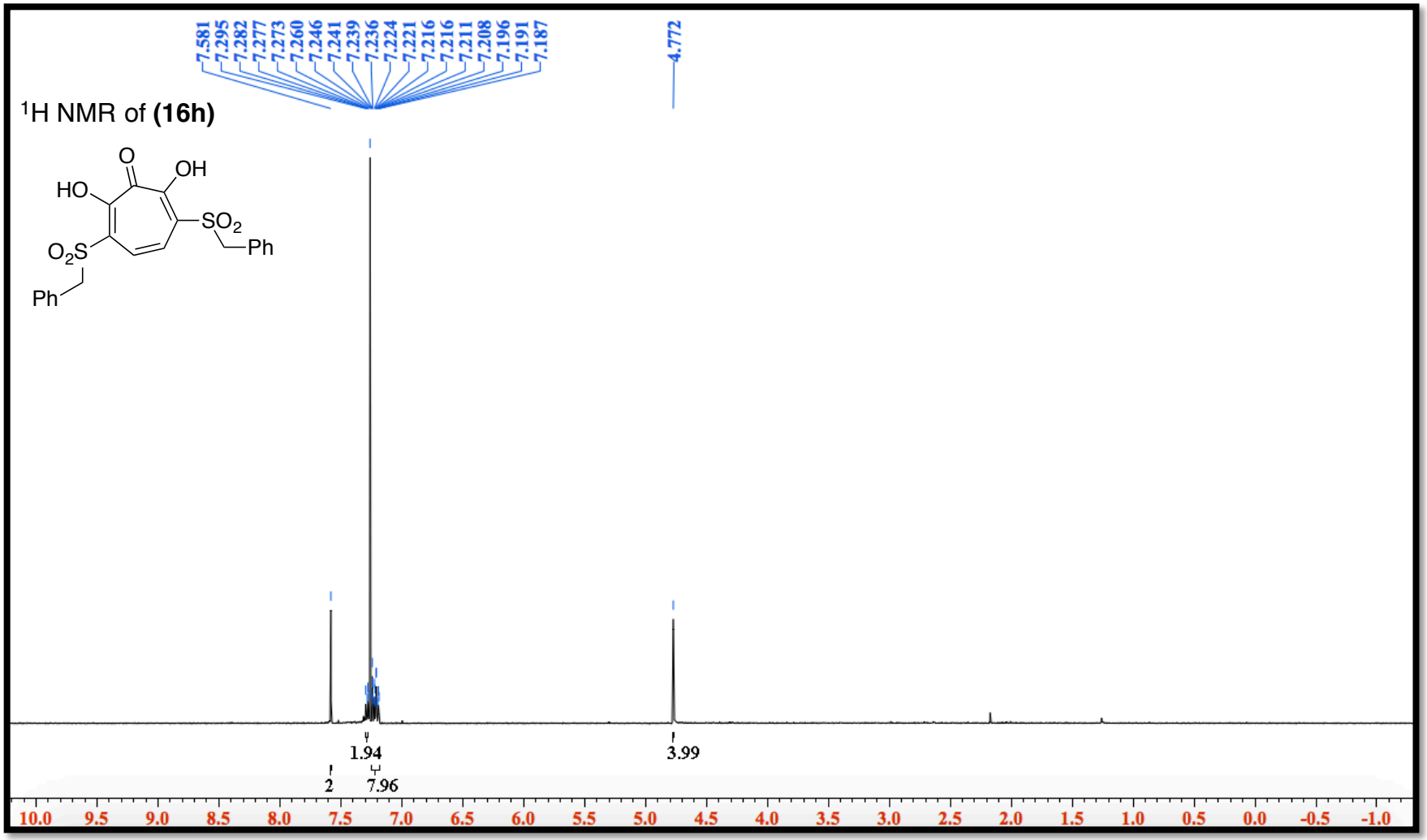

^{13}C NMR of **(14g)**
O
OH
HO
SO_2
168.879
158.505
157.056
145.025
136.740
133.505
129.393
129.110
127.770
127.405
123.904
30.931
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

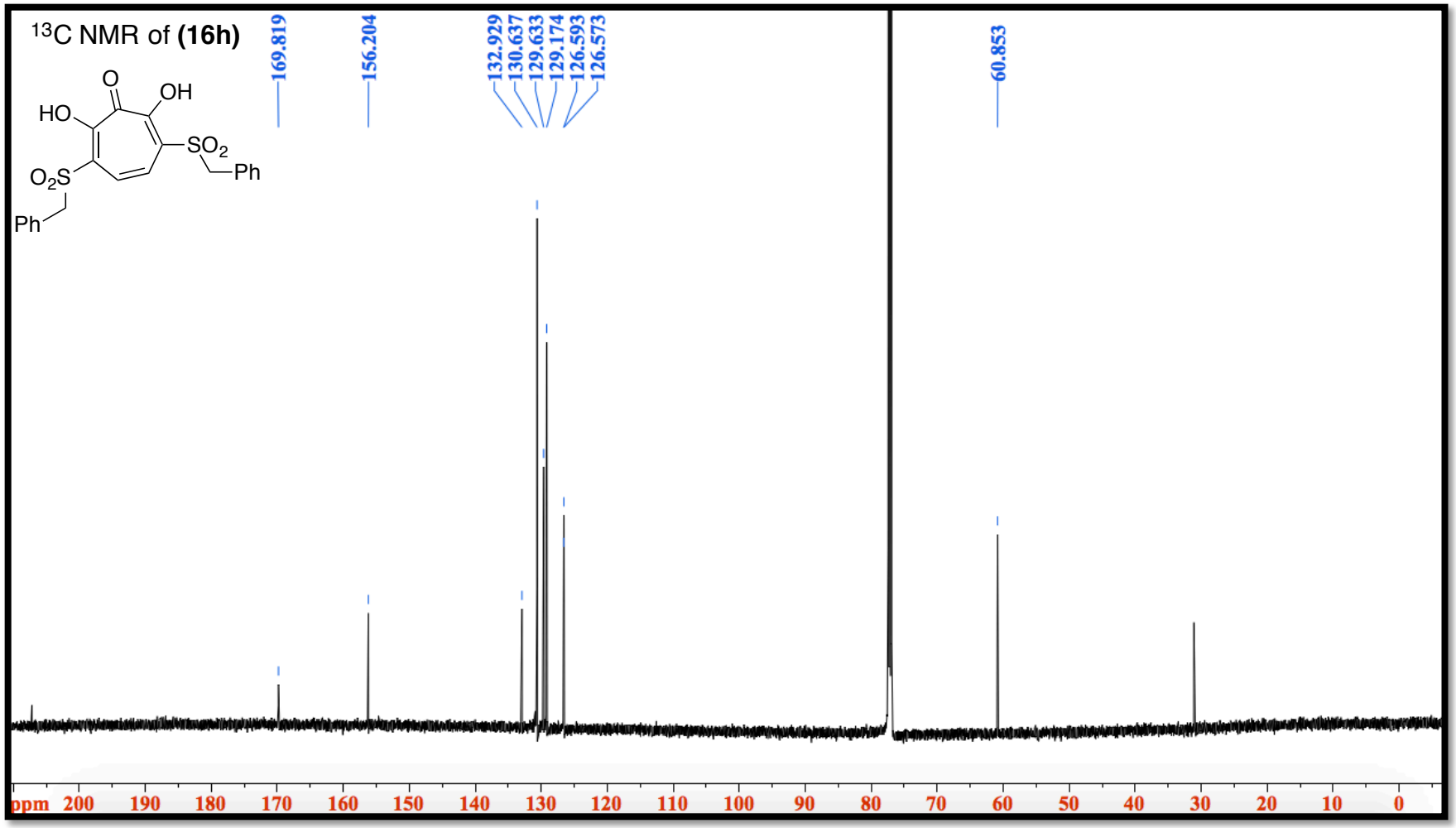
3-(benzylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(14h)**




13C NMR of (14h)
O
OH
HO
SO2
Ph
168.196
158.610
157.769
131.205
130.811
129.265
128.959
127.761
127.334
124.735
60.589
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

3,6-bis(benzylsulfonyl)-2,7-dihydroxycyclohepta-2,4,6-trien-1-one **(16h)**




^{13}C NMR of **(16h)**
169.819
156.204
132.929
130.637
129.633
129.174
126.593
126.573
60.853
HO
O
OH
SO_2
Ph
O_2S
Ph
ppm 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0