

An efficient stereoselective synthesis of 3-spirocyclopentene- and 3-spiropyrazole-2-oxindoles via 1,3-dipolar cycloaddition reaction

Kodirajan Selvakumar^a and Vadivel Vaithyanathan^a, Ponnusamy Shanmugam^{*b}

^a*Chemical Sciences and Technology Division, National Institute for Interdisciplinary Science and Technology, Trivandrum-695 019, Kerala, India*

^b*Organic Chemistry Laboratory, Central Leather Research Institute, Adyar, Chennai-600 020, India*

Contents

- (1) General remarks
- (2) General experimental procedure
- (3) Characterization data for Compounds
- (4) Scanned ¹H and ¹³C NMR's and FAB mass spectra

(1) General Considerations

All the reactions were carried out in oven-dried glassware. Progress of reactions was monitored by Thin Layer Chromatography (TLC) while purification of crude compounds was done by column chromatography using silica gel (100-200 mesh). Melting points were recorded on a Buchi melting point apparatus and are uncorrected. NMR spectra were recorded at 500 and 300 MHz (based on availability of instruments) 125 and 75 MHz (for ¹³C) respectively on Bruker Avance DPX-500 MHz. and Bruker Avance DPX-300 MHz. Chemical shifts are reported in δ (ppm) relative to TMS (¹H) or CDCl₃ (¹³C) as internal standards. Mass spectra were recorded using JEOL JMS 600H mass spectrometer. IR spectra were recorded on Bomem MB series FT-IR spectrometer, absorbencies are reported in cm⁻¹. Yields refer to quantities obtained after chromatography.

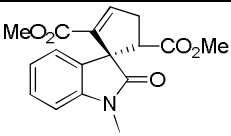
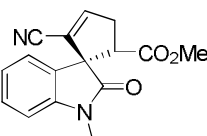
(2) General experimental procedure:

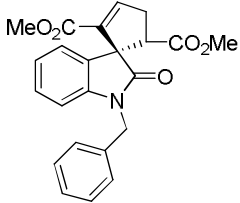
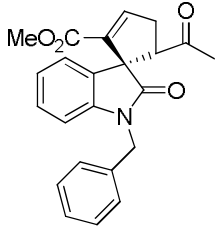
(a) *Spirocyclopentene*: Under Ar atmosphere, a solution mixture of bromo isomerized MBH adducts **1a** (100mg, 0.323 mmol) and verity of dipolarophile **2a** (1.2 equiv.) in toluene (1.0 mL) was added over with mixture of triphenylphosphine (10 % mol, 8 mg) and K₂CO₃ (1.2 equiv., 53 mg) at the indicated temperature and the reaction was continuously monitored until complete

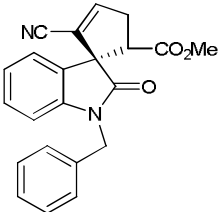
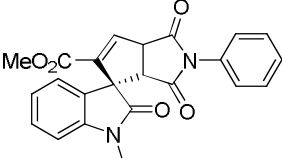
conversion of product **3a**. After the reaction (TLC), the crude mixture was filtered through a pad of celite and then purified by a silica gel column chromatography using EtOAc: hexane (20: 80) as eluent to afford products in moderate to good yields (44- 77 %).

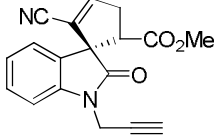
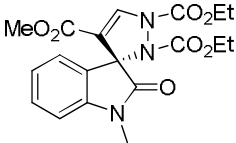
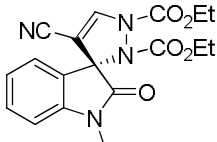
(b) *Spiropyrazole*: A mixture bromo isomerized MBH adduct **5a** (100mg, 0.323 mmol), dimethyl sulfide (1.2 equiv., 0.028 mmol), K₂CO₃ (1.2 equiv., 53 mg) in CH₃CN (1.0 mL) and diethyl azodicarboxylate **6a** (1.2 equiv.) were added successively at RT. After completion of the reaction (monitored by TLC), solvent was removed under vacuum. Water (5.0 mL) was added to the residue and extracted with ether (3×5.0 mL). Combined organic layer was dried over anhyd. Na₂SO₄ and solvent was evaporated. The crude product obtained was purified by silica gel column chromatography using EtOAc: hexane (20: 80) as eluent to afford **7a** good yields (66- 91 %).

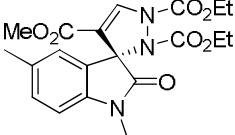
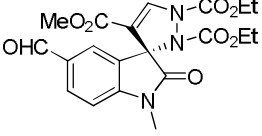
(3) Characterization data for Compounds:


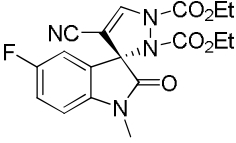
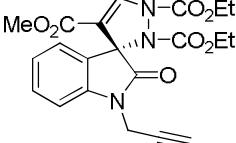
 <p>Compound 3a</p>	<p>White crystalline solid; mp: 157-159 °C. IR (KBr)_vmax: 3025, 2921, 1739, 1718, 1623, 1536, 1216, 1115, 894, 792 cm⁻¹. ¹H NMR(CDCl₃/TMS, 500.1 MHz): δ 2.88-2.94 (ddd, <i>J</i>=3, 9 and 12 Hz, 1H), 3.14 (s, 3H), 3.29-3.35 (ddd, <i>J</i>= 2.5, 9.5 and 11.5 Hz, 4H), 3.55 (s, 3H), 3.85-3.93 (dd, <i>J</i>=9.5, 9.0 Hz, 1H), 6.83-6.85 (d, <i>J</i>= 7.5 Hz, 1 H), 6.95-6.96 (m, 2H), 7.11-7.12 (dd, <i>J</i>= 2.5, 3.0 Hz, 1 H), 7.25-7.28 (m, 1H). ¹³C NMR (CDCl₃/TMS, 77.0 MHz): δ 26.72, 33.71, 51.53, 51.72, 52.80, 61.60, 107.78, 122.26, 123.22, 128.29, 129.00, 136.24, 143.98, 145.84, 162.51, 170.69, 177.92. FAB mass: Calcd. for C₁₇H₁₇NO₅ <i>m/z</i>=315.32; Found 316.54(M+1).</p>
	<p>White crystalline solid, mp: 142-144 °C IR (KBr)_vmax: 3104, 2851, 2224, 1735, 1717, 1621, 1519, 1321, 1210, 1121, 798 cm⁻¹. ¹H NMR (CDCl₃/TMS, 300.1 MHz): δ 3.01-3.05(ddd, <i>J</i>=2.8, 9.1,</p>

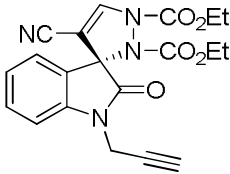
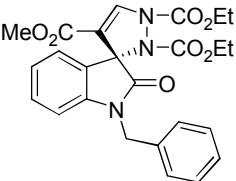
<p>Compound 3b</p>	<p>12.0 Hz, 1H), 3.19 (s, 3H), 3.32-3.42 (M, 4H), 3.89-3.95 (dd, $J=8.8, 8.8$ Hz, 1H), 6.88-6.90 (d, $J= 7.8$ Hz , 1 H), 6.96-6.98 (dd, $J=2.5, 2.6$, Hz, 1H), 6.99-7.05 (m, 2H), 7.31-7.37 (m, 1H).</p> <p>^{13}C NMR (CDCl₃/TMS, 75.3 MHz): δ 27.39, 34.74, 51.39, 51.83, 63.40, 108.3, 113.53, 115.89, 123.14, 123.89, 126.04, 130.06, 143.53, 150.20, 170.12, 175.47.</p> <p>FAB mass: Calcd. for C₁₆H₁₄N₂O₃ m/z: 282.29; Found 283.93 (M+1).</p>
<p></p> <p>Compound 3c</p>	<p>White crystalline solid, mp.: 138-140 °C</p> <p>IR (KBr) ν_{max}: 3023, 2917, 2848, 1731, 1720, 1627, 1578, 1216, 1120, 881, 796 cm⁻¹;</p> <p>^1H NMR (CDCl₃/TMS, 300.1 MHz): δ 2.97-3.01 (ddd, $J=2.9, 9.0, 12.0$ Hz, 1H), 3.05 (s, 3H), 3.33-3.37 (ddd, $J= 2.5, 9.1, 11.2$ Hz, 1H), 3.58 (s, 3H), 3.88-4.04 (dd, $J=9.1, 9.0$ Hz, 1H), 4.88-5.02(dd $J=15.20, 11.12$ Hz, 2H), 6.70-6.72 (d, $J= 7.8$ Hz , 1 H), 6.93-6.95 (m, 2H), 7.12-7.18 (m, 2H), 7.29-7.38 (m, 3H), 7.46-7.48(m, 2H);</p> <p>^{13}C NMR (CDCl₃/TMS, 77.21 MHz): δ 33.91, 44.56, 51.32, 51.59, 53.21, 61.80, 108.84, 113.75, 117.64, 119.09, 122.25, 123.50, 127.59, 127.72, 128.69, 128.88, 136.31, 136.71, 143.51, 145.66, 162.42, 170.59, 177.95.</p> <p>FAB mass: Calcd. for C₂₃H₂₁NO₅ m/z : 391.42; Found 392.23 (M+1).</p>
<p></p> <p>Compound 3d</p>	<p>White crystalline solid, mp.: 126-128 °C</p> <p>IR (KBr) ν_{max}: 3013, 2989, 1742, 1725, 1718, 1623, 1221, 1127, 879, 791 cm⁻¹;</p> <p>^1H NMR (CDCl₃/TMS, 500.1 MHz): δ 1.53(s, 3H); 2.72-2.79(ddd, $J=3, 8.5, 11.5$ Hz, 1H), 3.40-3.46 (ddd, $J= 2.5, 9.0, 11.5$ Hz, 1H), 3.53 (s, 3H), 4.01-4.05 (dd, $J=8.5, 9.0$ Hz, 1H), 4.98-5.09(dd, $J=15.5, 11.15$ Hz, 2H), 6.78-6.80 (d, $J=8.05$ Hz, 1H), 6.85-6.87(d, $J=7.5$ Hz, 1H), 6.93-6.96 (t, $J=7.5, 8.05$ Hz, 1H),</p>

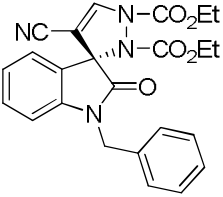
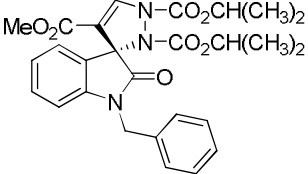
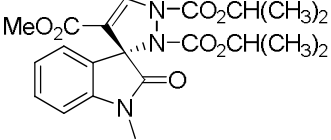
	<p>7.15-7.19 (m, 2H), 7.27-7.30 (m, 1H), 7.33-7.36 (m, 2H), 7.48-7.49 (m, 2H);</p> <p>¹³C NMR (CDCl₃/TMS, 76.9 MHz): δ 28.86, 32.77, 44.75, 51.68, 60.79, 61.08, 109.15, 122.87, 124.31, 127.75(2C), 127.85, 127.94, 128.74(2C), 129.05, 135.77, 136.01, 142.82, 146.31, 162.35, 178.35, 203.65.</p> <p>FAB mass: Calcd. for C₂₃H₂₁NO₄ <i>m/z</i>: 375.15; Found 375.85 (M+1).</p>
 <p>Compound 3e</p>	<p>White crystalline solid, mp.: 135-137 °C</p> <p>IR (KBr) ν_{\max}: 3046, 2953, 2228, 1731, 1717, 1642, 1475, 1376, 1242, 1143, 939, 785 cm⁻¹;</p> <p>¹H NMR (CDCl₃/TMS, 300.1 MHz): δ 2.99-3.05 (ddd, <i>J</i>=3.0, 9.0, 12.0 Hz, 1H), 3.08 (s, 3H), 3.42-3.45 (ddd, <i>J</i>= 2.5, 9.0, 11.0 Hz, 1H), 4.12-4.14 (m, 1H), 5.05-5.21(dd, <i>J</i>=16,15.5 Hz, 2H), 6.77-6.79 (d, <i>J</i>= 8 Hz, 1 H), 7.12-7.15 (t, <i>J</i>=7.5, 7.5 Hz 1H), 7.28-7.35(m, 8H);</p> <p>¹³C NMR (CDCl₃/TMS, 77.21 MHz): 34.76, 44.36, 51.53, 51.76, 63.45, 110.37, 115.67, 124.75, 127.02, 127.17, 127.33, 127.82, 128.80, 142.61, 170.11, 174.46.</p> <p>FAB mass: Calcd. for C₂₂H₁₈N₂O₃ <i>m/z</i> :358.13; Found 359.23 (M+1).</p>
 <p>Compound 3f</p>	<p>White crystalline solid, mp.: 161-163 °C</p> <p>IR (KBr) ν_{\max}: 3021, 2989, 1742, 1728, 1618, 1213, 1134, 879, 789 cm⁻¹;</p> <p>¹H NMR (CDCl₃/TMS, 500.1 MHz): δ 3.28(s, 3H); 3.68(s, 3H), 3.73-3.75(d, <i>J</i>=8.5 Hz, 1H), 4.37-4.39(dd, <i>J</i>= 3.5, 8.5 Hz, 1H), 6.88-6.90 (d, <i>J</i>=7.5 Hz, 1H), 7.05-7.08(m, 2H), 7.18-7.19(m, 1H), 7.32-7.37 (m, 6H); ¹³C NMR (CDCl₃/TMS, 77.0 MHz): δ 26.87, 52.12, 52.84, 53.65, 63.11, 108.77, 122.27, 122.99, 127.09, 128.89(2C), 129.20, 129.55(2C), 131.51, 131.74, 139.52, 140.61, 144.37, 161.81, 173.07, 174.26, 174.83.</p>

	<p>FAB mass: Calcd. for C₂₃H₁₈N₂O₅ <i>m/z</i>: 402.32; Found 403.85 (M+1).</p>
 <p>Compound 3g</p>	<p>White crystalline solid, mp.: 133-135 °C IR (KBr) ν_{\max}: 3269, 3016, 2923, 2226, 2135, 1742, 1712, 1676, 1612, 1467, 1102, 989, 751 cm⁻¹; ¹H NMR (CDCl₃/TMS, 300.1 MHz): δ 2.18(s, 1H), 2.92-2.95 (ddd, <i>J</i>=2.7, 9.1, 11.8 Hz, 1H), 3.11(s, 3H), 3.24-3.28(ddd, <i>J</i>=1.9, 8.7, 10.7 Hz, 1H), 3.83-3.89 (dd, <i>J</i>=8.7, 9.1 Hz, 1H), 4.71-4.78 (m, 2H), 6.88-7.02 (m, 2H), 7.14-7.19 (m, 1H), 7.26-7.36 (m, 1H), 7.63 (m, 1H); ¹³C NMR (CDCl₃/TMS, 77.0 MHz): δ 33.69, 35.30, 51.85, 58.17, 62.27, 63.31, 72.34, 109.60, 112.93, 116.16, 122.86, 123.12, 123.70, 126.09, 141.75, 149.73, 169.79, 174.56. FAB mass: Calcd. for C₁₈H₁₄N₂O₃: 306.1; Found 307.54(M⁺).</p>
 <p>Compound 7a</p>	<p>White crystalline solid, mp.: 141-143 °C IR (KBr) ν_{\max}: 2984, 1742, 1719, 1628, 1498, 1357, 1257, 1194, 1046, 915, 827, 788 cm⁻¹; ¹H NMR (CDCl₃/TMS, 500.0 MHz): δ 1.28-1.32(m, 3H), 1.36-1.39(m, 3H), 3.27(s, 3H), 3.57(s, 3H), 4.25-4.26 (m, 2H), 4.33-4.40 (m, 2H), 6.84-6.85 (d, <i>J</i>=7.5Hz, 1H); 7.03-7.06(t, <i>J</i>=7.0, 7.5Hz, 1H), 7.15-7.17(d, <i>J</i>=7.0 Hz, 1H), 7.32-7.35 (t, <i>J</i>=7.5, 7.0Hz, 1H), 7.77 (s, 1H) ; ¹³C NMR (CDCl₃/TMS, 75.3 MHz): δ 14.02, 14.43, 26.76, 51.70, 62.22, 62.88, 74.18, 107.92, 119.96, 122.20, 124.82, 130.73, 132.64, 138.39, 141.92, 153.64, 156.54, 161.24, 172.21. FAB mass: Calcd. for C₁₉H₂₁N₃O₇ <i>m/z</i>: 403.38; Found 404.28 (M+1).</p>
 <p>Compound 7b</p>	<p>White crystalline solid, mp.: 135-137 °C IR (KBr) ν_{\max}: 2984, 2234, 1745, 1718, 1613, 1487, 1346, 1265, 1021, 916, 818, 793 cm⁻¹; ¹H NMR (CDCl₃/TMS, 300.1 MHz): δ 1.25-1.30 (m, 3H), 1.31-</p>

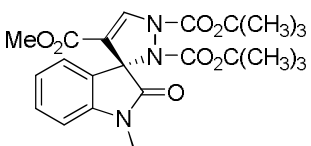
	<p>1.38 (m, 3H), 3.28 (s, 3H), 4.06-4.18 (m, 2H), 4.23-4.36 (m, 2H), 6.89-6.91(d, $J=7.8\text{Hz}$, 1H), 7.12-7.17 (t, $J=7.4, 7.5\text{Hz}$, 1H), 7.26-7.28(m, 1H), 7.38-7.44 (t, $J=8.0, 9.0\text{Hz}$, 1H), 7.64(s, 1H);</p> <p>^{13}C NMR (CDCl₃/TMS, 77.0 MHz): δ 14.13, 14.26, 26.89, 63.29, 63.98, 74.79, 108.90, 110.86, 115.36, 123.89, 124.73, 125.53, 131.35, 140.42, 142.90, 153.42, 156.69, 171.03.</p> <p>FAB mass: Calcd. for C₁₈H₁₈N₄O₅ m/z: 370.13; Found 370.51 (M+1).</p>
 <p>Compound 7c</p>	<p>White crystalline solid, mp.: 146-148 °C</p> <p>IR (KBr) ν_{max}: 3269, 2923, 1742, 1712, 1676, 1612, 1467, 1102, 989, 751cm⁻¹;</p> <p>^1H NMR (CDCl₃/TMS, 500.1 MHz): δ 1.20-1.26(m, 3H), 1.31-1.34(m, 3H), 2.44(s, 3H), 3.18 (s, 3H), 3.51(s, 3H), 4.12-4.16 (m, 2H), 4.27-4.32 (m, 2H), 6.65-6.67 (d, $J=7.5\text{Hz}$, 1H); 6.90(s, 1H), 7.05-7.06(d, $J=7.0\text{ Hz}$, 1H), 7.70 (s, 1H) ;</p> <p>^{13}C NMR (CDCl₃/TMS, 77.0 MHz): δ 14.23, 14.33, 21.03, 26.77, 51.74, 62.91, 63.39, 74.20, 108.00, 124.75, 127.46, 130.77, 132.75, 133.36, 138.49, 141.35, 151.85, 153.76, 163.60, 172.30.</p> <p>FAB mass: Calcd. for C₂₀H₂₃N₃O₇ m/z: 417.15; Found 418.56 (M+1).</p>
 <p>Compound 7d</p>	<p>White crystalline solid, mp.: 130-132 °C</p> <p>IR (KBr) ν_{max}: 3023, 2923, 2846, 2754, 1734, 1716, 1654, 1635, 1457, 1124, 992, 784 cm⁻¹;</p> <p>^1H NMR (CDCl₃/TMS, 500.1 MHz): δ 1.30-1.38(m, 3H), 1.40-1.41(m, 3H), 3.32(s, 3H), 3.58 (s, 3H), 4.19-4.37 (m, 2H), 4.39-4.40 (m, 2H), 6.97-6.99 (d, $J=8.0\text{Hz}$, 1H); 7.72-7.77 (m, 2H), 7.87-7.88 (d, $J=8.0\text{Hz}$, 1H), 9.86 (s, 1H) ;</p> <p>^{13}C NMR (CDCl₃/TMS, 77.0 MHz): δ 12.54, 12.82, 25.57, 50.38, 61.77, 63.01, 71.85, 107.43, 117.18, 122.70, 127.07, 130.83, 132.47, 137.57, 147.56, 152.30, 154.73, 161.27, 171.82, 189.05.</p> <p>FAB mass: Calcd. for C₂₀H₂₁N₃O₈ m/z: 431.13; Found 432.56</p>

 <p>Compound 7e</p>	<p>(M+1).</p> <p>White crystalline solid, mp.: 139-141 °C IR (KBr) ν_{\max}: 3011, 2956, 2845, 1746, 1718, 1628, 1619, 1437, 1254, 1132, 1102, 982, 793 cm^{-1}; ¹H NMR (CDCl_3/TMS, 500.1 MHz): δ 1.19-1.19(m, 3H), 1.36-1.39(m, 3H), 3.27(s, 3H), 3.59(s, 3H), 4.20-4.24 (m, 2H), 4.36-4.39 (m, 2H), 6.78-6.81 (m, 1H); 6.93-6.94 (m, 1H), 7.03-7.07 (m, 1H), 7.79 (s, 1H) ; ¹³C NMR (CDCl_3/TMS, 77.0 MHz): δ 13.95, 14.26, 26.85, 51.80, 63.60, 64.35, 73.94, 108.84, 112.13, 112.33, 116.57, 116.76, 128.85, 138.86, 139.61, 153.47, 158.49, 160.41, 172.18. FAB mass: Calcd. for $\text{C}_{19}\text{H}_{20}\text{FN}_3\text{O}_7$ m/z: 421.13; Found 422.14 (M+1).</p>
 <p>Compound 7f</p>	<p>White crystalline solid, mp.: 128-130 °C IR (KBr) ν_{\max}: 3054, 2986, 2232, 1742, 1715, 1631, 1616, 1265, 1112, 1106, 982, cm^{-1}; ¹H NMR (CDCl_3/TMS, 500.1 MHz): δ 1.12-1.13(m, 3H), 1.25-1.27(m, 3H), 3.27(s, 3H), 4.18-4.21 (m, 2H), 4.36-4.39 (m, 2H), 6.84-6.87 (m, 1H); 7.03-7.05 (m, 1H), 7.10-7.17 (m, 1H), 7.66 (s, 1H) ; ¹³C NMR (CDCl_3/TMS, 77.0 MHz): δ 14.20, 14.35, 26.82, 63.60, 64.84, 74.79, 110.00, 113.04, 115.30, 122.64, 123.88, 128.63, 131.73, 138.81, 141.43, 158.79, 160.73, 171.01. FAB mass: Calcd. for $\text{C}_{18}\text{H}_{17}\text{FN}_4\text{O}_5$ m/z: 388.12; Found 389.56 (M+1).</p>
 <p>Compound 7g</p>	<p>White crystalline solid, mp.: 120-122 °C IR (KBr) ν_{\max}: 3272, 3010, 2923, 2146, 1730, 1712, 1676, 1612, 1467, 1102, 989, 751 cm^{-1}; ¹H NMR (CDCl_3/TMS, 500.1 MHz): δ 1.27-1.27 (m, 3H), 1.36-1.39 (m, 3H), 2.26-2.27 (m, 1H), 3.55(s, 3H), 4.17-4.22 (m, 2H), 4.34-4.39 (m, 4H), 7.06-7.09 (m, 2H) 7.16-7.18 (d, $J=7.0$ Hz, 1H),</p>

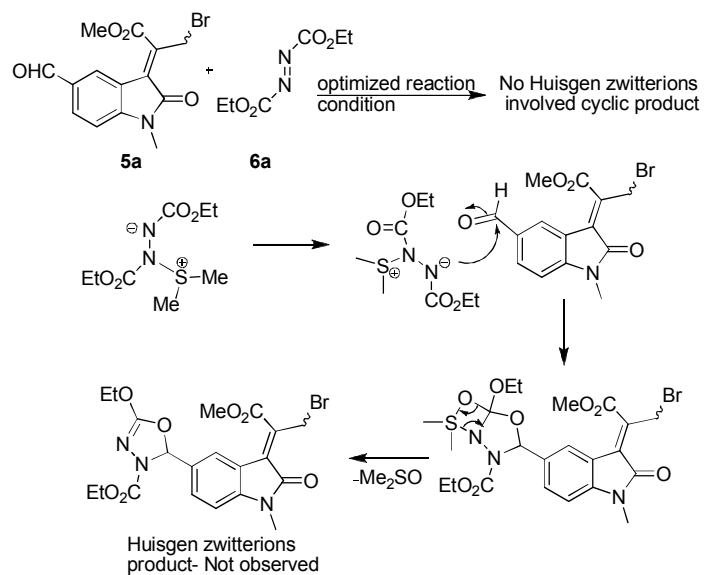
	<p>7.34-7.37 (m, 1H), 7.79 (s, 1H);</p> <p>¹³C NMR (CDCl₃/TMS, 77.00 MHz): δ 14.04, 14.37, 29.82, 51.75, 62.19, 63.11, 64.18, 72.60, 73.79, 109.30, 120.82, 123.52, 124.01, 127.43, 130.34, 138.77, 141.79, 153.43, 157.75, 161.18, 171.36.</p> <p>FAB mass: Calcd. for C₂₁H₂₁N₃O₇ <i>m/z</i>: 427.14; Found 428.51 (M+1).</p>
 <p>Compound 7h</p>	<p>White crystalline solid, mp.: 122-124 °C</p> <p>IR (KBr) ν_{max}: 3293, 3023, 2911, 2231, 2143, 1738, 1716, 1654, 1435, 1116, 989 cm⁻¹;</p> <p>¹H NMR (CDCl₃/TMS, 300.1 MHz): δ 1.21-1.34 (m, 6H), 2.22 (s, 1H), 4.02-4.45 (m, 6H), 7.04-7.14 (m, 2H) 7.21-7.23 (m, 1H), 7.35-7.40 (m, 1H), 7.57 (s, 1H);</p> <p>¹³C NMR (CDCl₃/TMS, 77.0 MHz): δ 14.20, 14.32, 29.73, 63.56, 64.06, 64.63, 73.22, 76.00, 110.12, 110.68, 118.19, 124.28, 124.79, 125.61, 131.31, 132.19, 140.19, 152.15, 155.11, 170.24.</p> <p>FAB mass: Calcd. for C₂₀H₁₈N₄O₅ <i>m/z</i>: 394.13; Found 395.51 (M+1).</p>
 <p>Compound 7i</p>	<p>White crystalline solid, mp.: 149-151 °C</p> <p>IR (KBr) ν_{max}: 3059, 2958, 1734, 1713, 1628, 1484, 1367, 1257, 1156, 927, 788 cm⁻¹.</p> <p>¹H NMR (CDCl₃/TMS, 500.1 MHz): δ 1.28-1.33 (m, 3H), 1.34-1.39 (m, 3H), 3.57 (s, 3H), 4.16-4.22 (m, 2H), 4.27-4.31 (m, 2H), 4.35-4.37 (m, 2H), 6.98-7.01 (m, 2H), 7.14-7.25 (m, 3H), 7.30-7.33 (m, 2H), 7.43-7.44 (m, 2H), 7.81 (s, 1H);</p> <p>¹³C NMR (CDCl₃/TMS, 77.00 MHz): δ 14.32, 14.42, 44.65, 51.65, 63.01, 63.98, 73.88, 109.39, 120.66, 123.10, 123.81, 127.44, 127.55 (2C), 128.66(2C), 130.22, 132.20, 135.41, 138.85, 142.97, 152.16, 156.68, 161.19, 172.35.</p> <p>FAB mass: Calcd. for C₂₅H₂₅N₃O₇ <i>m/z</i>: 479.17; Found 480.36 (M+1).</p>
	<p>White crystalline solid, mp.: 156-158 °C</p>

 <p>Compound 7j</p>	<p>IR (KBr) ν_{\max}: 3046, 2954, 2240, 1732, 1716, 1632, 1485, 1376, 1232, 1145, 937, 787 cm^{-1};</p> <p>^1H NMR (CDCl_3/TMS, 500.1 MHz): δ 0.99-1.00 (m, 3H), 1.31-1.31 (m, 3H), 4.02-4.05 (m, 2H), 4.28-4.35 (m, 2H), 4.79(m, 1H), 5.01-5.04(m, 1H), 6.64-6.65 (d, $J=7.0$ Hz, 1H), 7.01-7.04 (t, $J=7.0,7.5$ Hz, 1H), 7.18-7.21 (m, 3H), 7.22 -7.31 (m, 4H),7.51 (s, 1H);</p> <p>^{13}C NMR (CDCl_3/TMS, 77.00 MHz): δ 14.26, 14.39, 44.63, 62.90, 63.59, 74.87, 110.22, 111.18, 123.95, 124.68, 125.54, 127.18 (2C), 127.87, 128.69 (2C), 128.89, 131.28, 134.58, 141.13, 142.05, 153.57, 155.23, 171.21.</p> <p>FAB mass: Calcd. for $\text{C}_{24}\text{H}_{22}\text{N}_4\text{O}_5$ m/z: 446.17; Found 447.36 (M+1).</p>
 <p>Compound 7k</p>	<p>White crystalline solid, mp.: 146-148 $^{\circ}\text{C}$</p> <p>IR (KBr) ν_{\max}: 3039, 2945, 1742, 1712, 1623, 1474, 1357, 1264, 1135, 947, 765 cm^{-1};</p> <p>^1H NMR (CDCl_3/TMS, 300.1 MHz): δ 1.04-1.07 (m, 6H), 1.25-1.37 (m, 6H), 3.49 (s, 3H), 4.93-5.13 (s, 4H) 6.66-6.69 (d, $J=7.41\text{Hz}$, 1H), 7.00-7.02 (d, $J=7.41\text{Hz}$, 1H), 7.14-7.48 (m, 7H), 7.82 (s, 1H);</p> <p>^{13}C NMR (CDCl_3/TMS, 75.3 MHz): δ 21.84, 21.94, 29.69, 29.99, 44.74, 51.69, 72.28, 72.72, 73.81, 109.34, 121.84, 121.99, 123.10, 123.83, 127.58(2C), 128.70(2C), 130.20, 135.46, 138.70, 139.26, 140.99, 153.3, 156.33, 161.43, 174.61.</p> <p>FAB mass: Calcd. for $\text{C}_{27}\text{H}_{29}\text{N}_3\text{O}_7$ m/z: 507.2; Found 508.36 (M+1).</p>
 <p>Compound 7l</p>	<p>White crystalline solid, mp.: 153-155 $^{\circ}\text{C}$</p> <p>IR (KBr) ν_{\max}: 3269, 2923, 1737, 1712, 1666, 1612, 1487, 1102, 989, 791 cm^{-1};</p> <p>^1H NMR (CDCl_3/TMS, 300.1 MHz): δ 1.11-1.12 (m, 6H), 1.37-1.37 (m, 6H), 3.27 (s, 3H), 3.57 (s, 3H), 4.92-4.94 (m, 1H), 5.08-</p>

S10

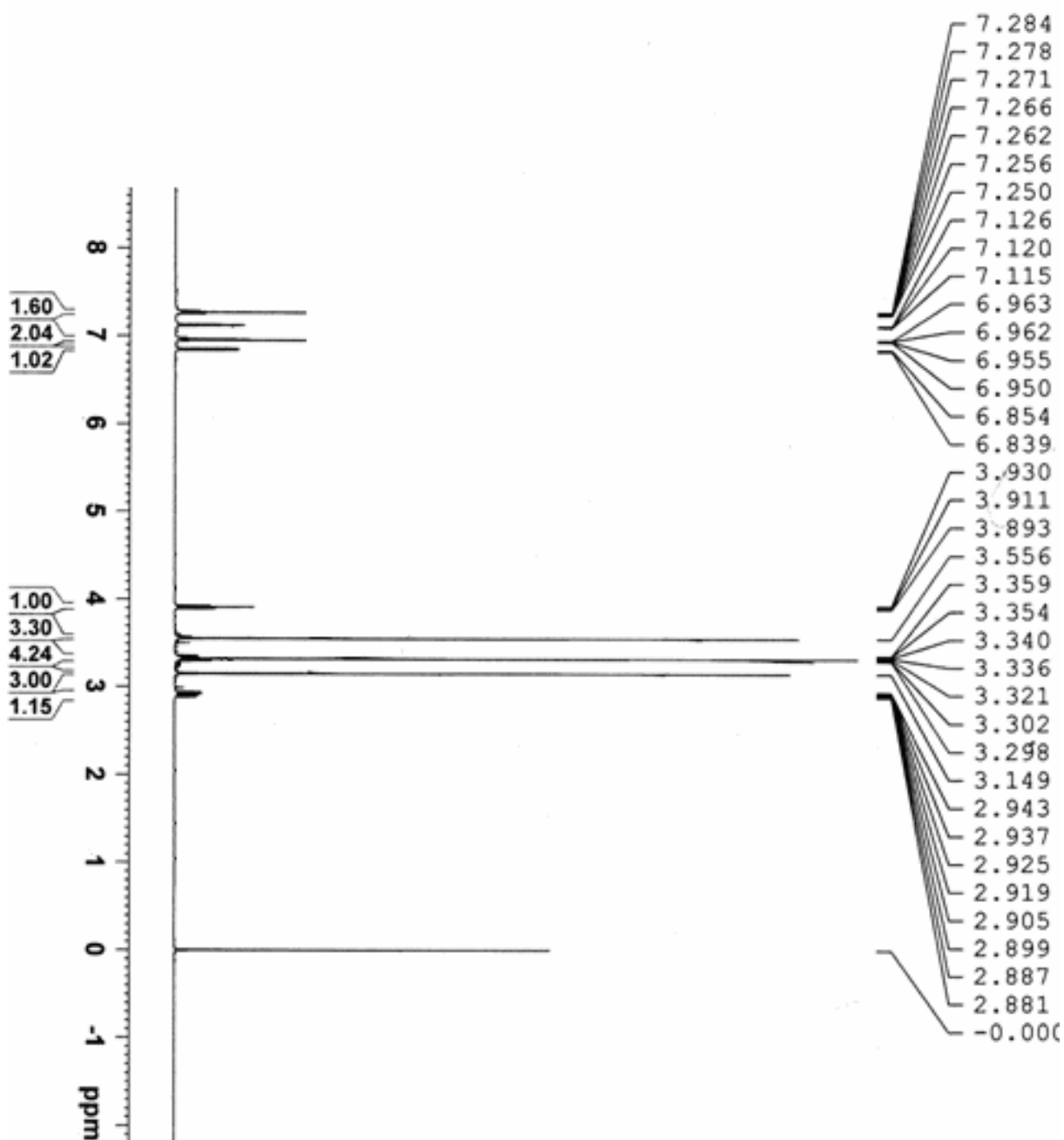
	<p>5.12 (m, 1H) 6.82-6.84 (d, $J= 8.0\text{Hz}$, 1H), 7.02-7.05 (t, $J= 7.5,7.0\text{Hz}$, 1H), 7.14-7.16 (d, $J= 7.0\text{Hz}$, 1H), 7.31-7.34 (m, 1H) 7.72 (s, 1H);</p> <p>$^{13}\text{C NMR}$ (CDCl_3/TMS, 76.07 MHz): δ 20.62, 20.89, 25.76, 28.73, 28.95, 50.73, 70.36, 71.72, 72.91, 107.15, 111.65, 122.12, 122.95, 126.74, 129.39, 137.90, 142.80, 150.31, 152.12, 160.49, 171.46.</p> <p>FAB mass: Calcd. for $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_7$ m/z: 431.17; Found 432.94 (M+1).</p>
 <p>Compound 7m</p>	<p>White crystalline solid, mp.: 192-194 °C</p> <p>IR (KBr) ν_{max}: 3011, 2986, 1741, 1719, 1624, 1471, 1363, 1248, 1165, 931, 798 cm^{-1};</p> <p>$^1\text{H NMR}$ (CDCl_3/TMS, 500.1 MHz): δ 1.42-1.43 (m, 9H), 1.56 (m, 9H), 3.27 (s, 3H), 3.56 (s, 3H), 6.81-6.82 (d, $J= 7.5\text{Hz}$, 1H), 7.03-7.06 (t, $J= 7.0, 7.5\text{Hz}$, 1H), 7.15-7.16 (d, $J= 9.5\text{Hz}$, 1H), 7.30-7.34 (t, $J= 9.5, 7.5\text{Hz}$, 1H), 7.39 (s, 1H);</p> <p>$^{13}\text{C NMR}$ (CDCl_3/TMS, 75.3 MHz): δ 12.03, 18.77, 24.42, 25.43(2C), 25.83, 49.31, 58.06, 71.64, 80.45, 82.25, 105.58, 120.75, 121.64, 126.00, 126.08, 127.89, 137.02, 141.54, 137.02, 141.54, 150.26, 159.29, 168.60, 170.36.</p> <p>FAB mass: Calcd. for $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_7$ m/z: 459.29; Found 460.65 (M+1).</p>

Scheme 5 plausible reaction mechanism



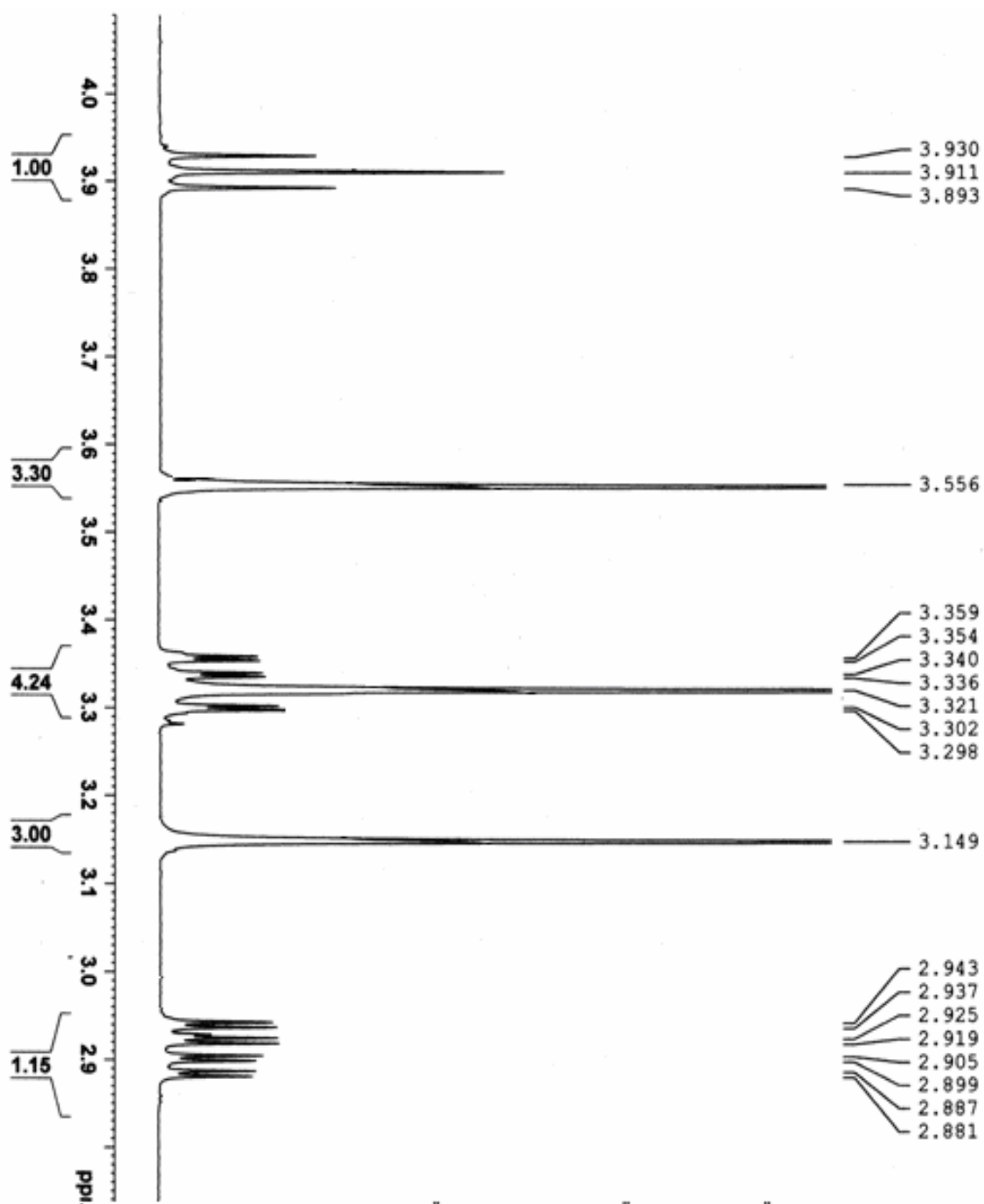
S12

Compound 3a – ^1H NMR (500 MHz)



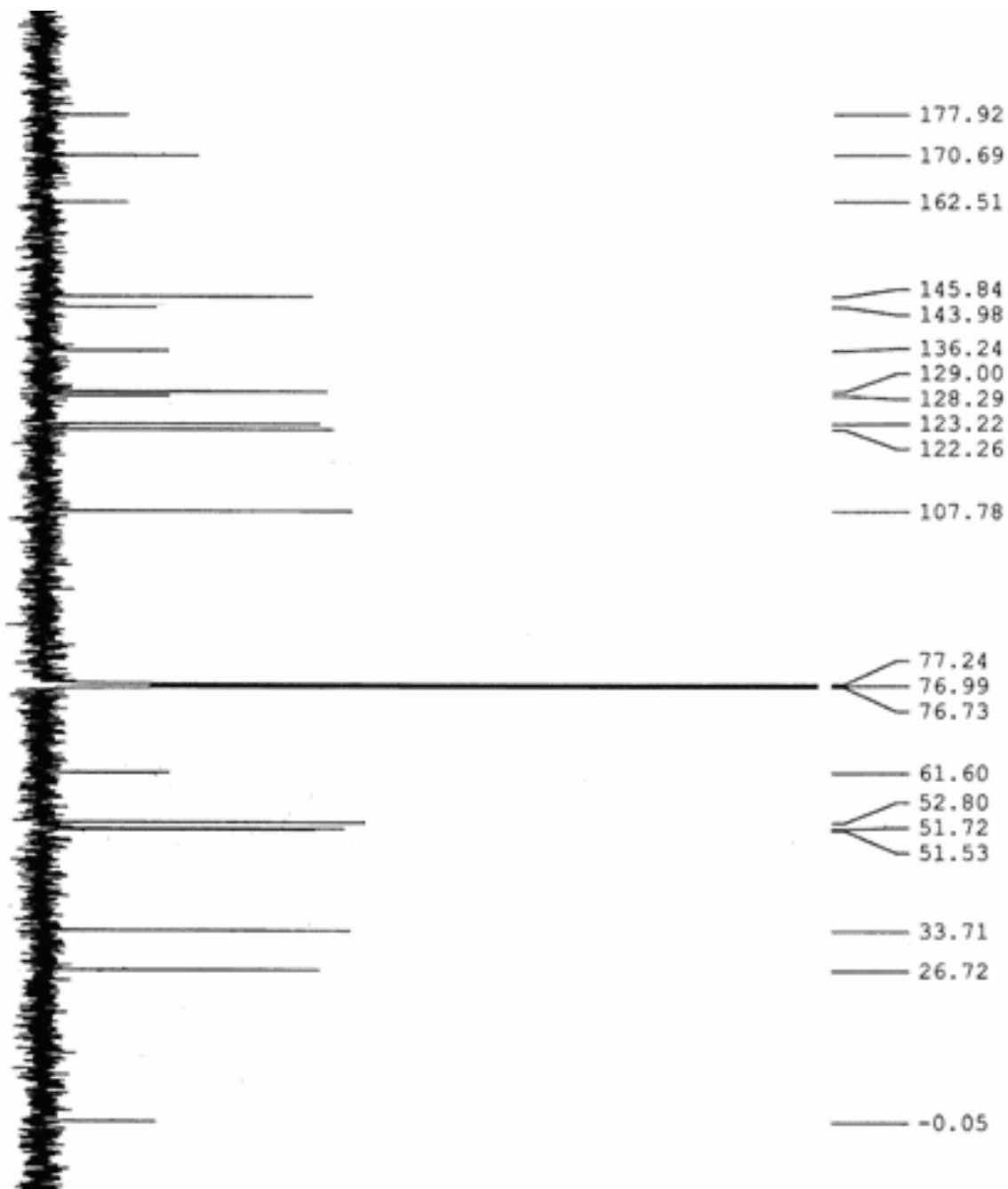
S13

Compound 3a (Expanded region) – ^1H NMR (500 MHz)



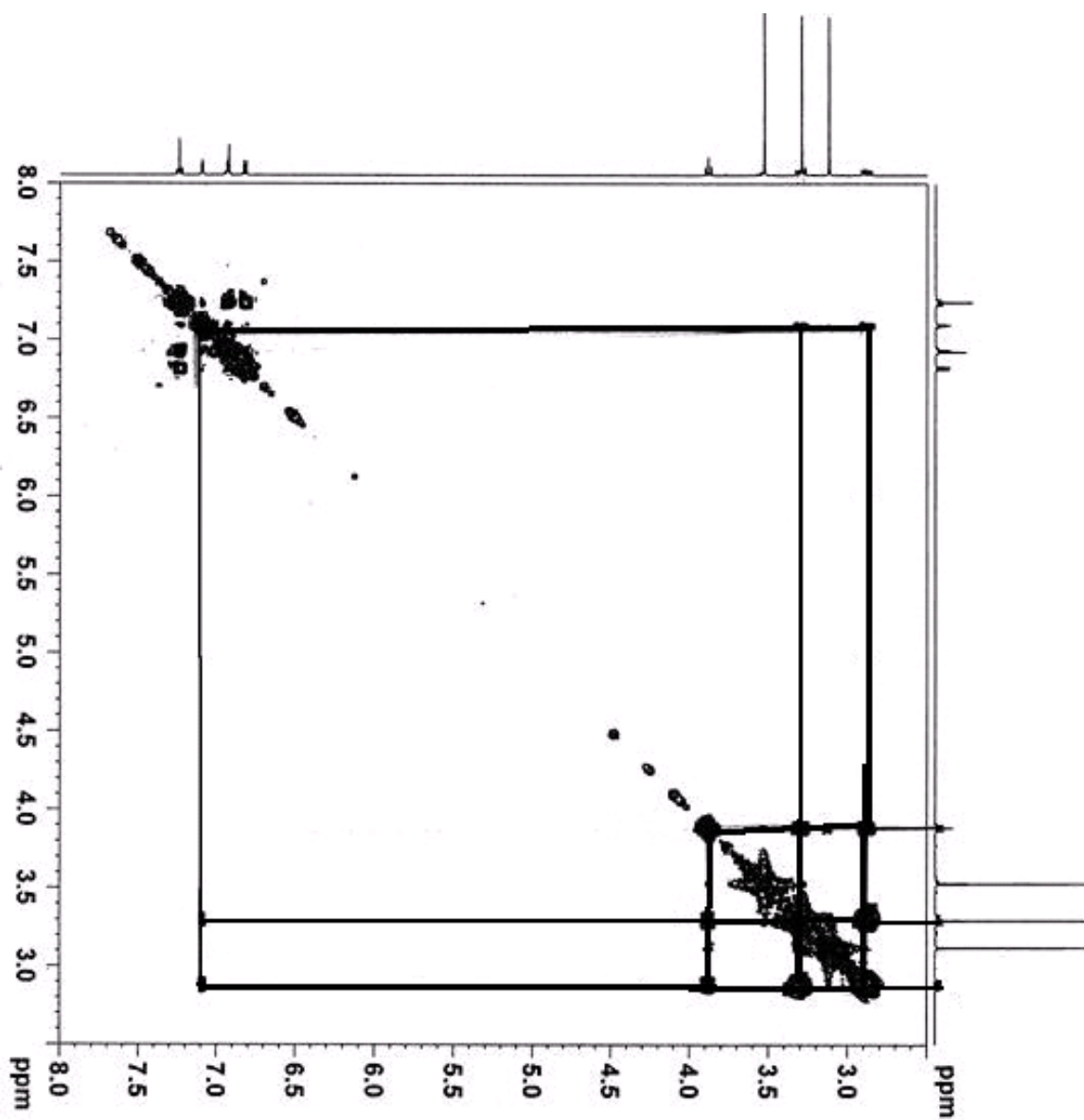
S14

Compound 3a – ^{13}C NMR (500 MHz)



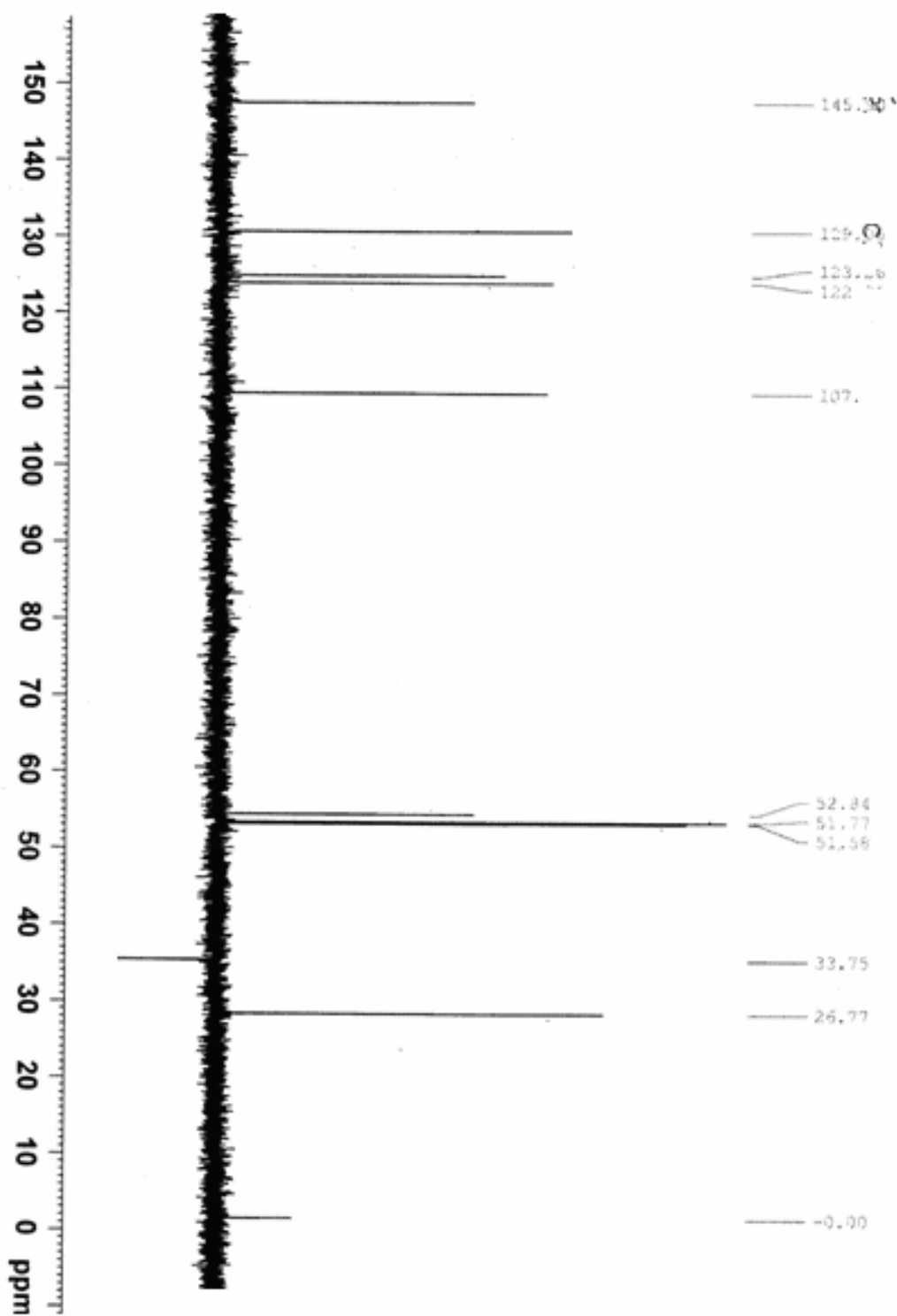
S15

Compound 3a – ^1H - ^1H COSY NMR (500 MHz)



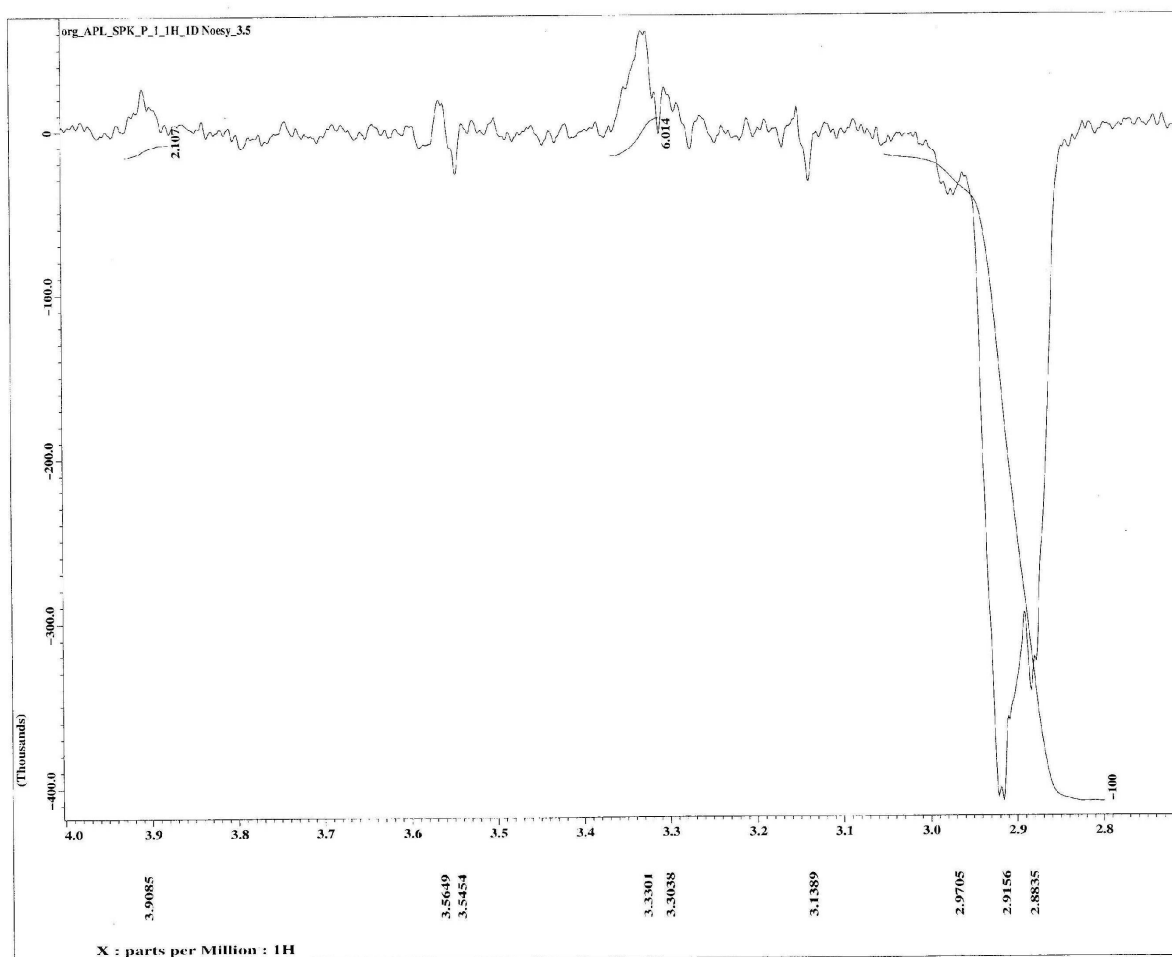
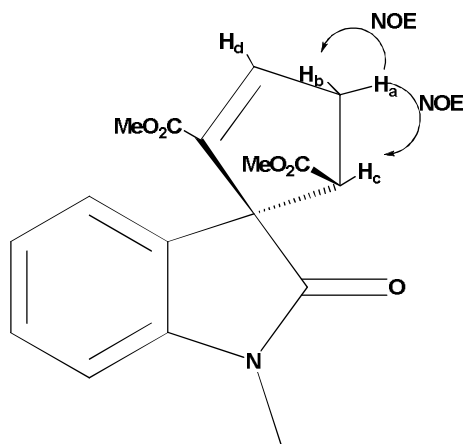
S16

Compound 3a – DEPT¹³⁵ NMR (500 MHz)



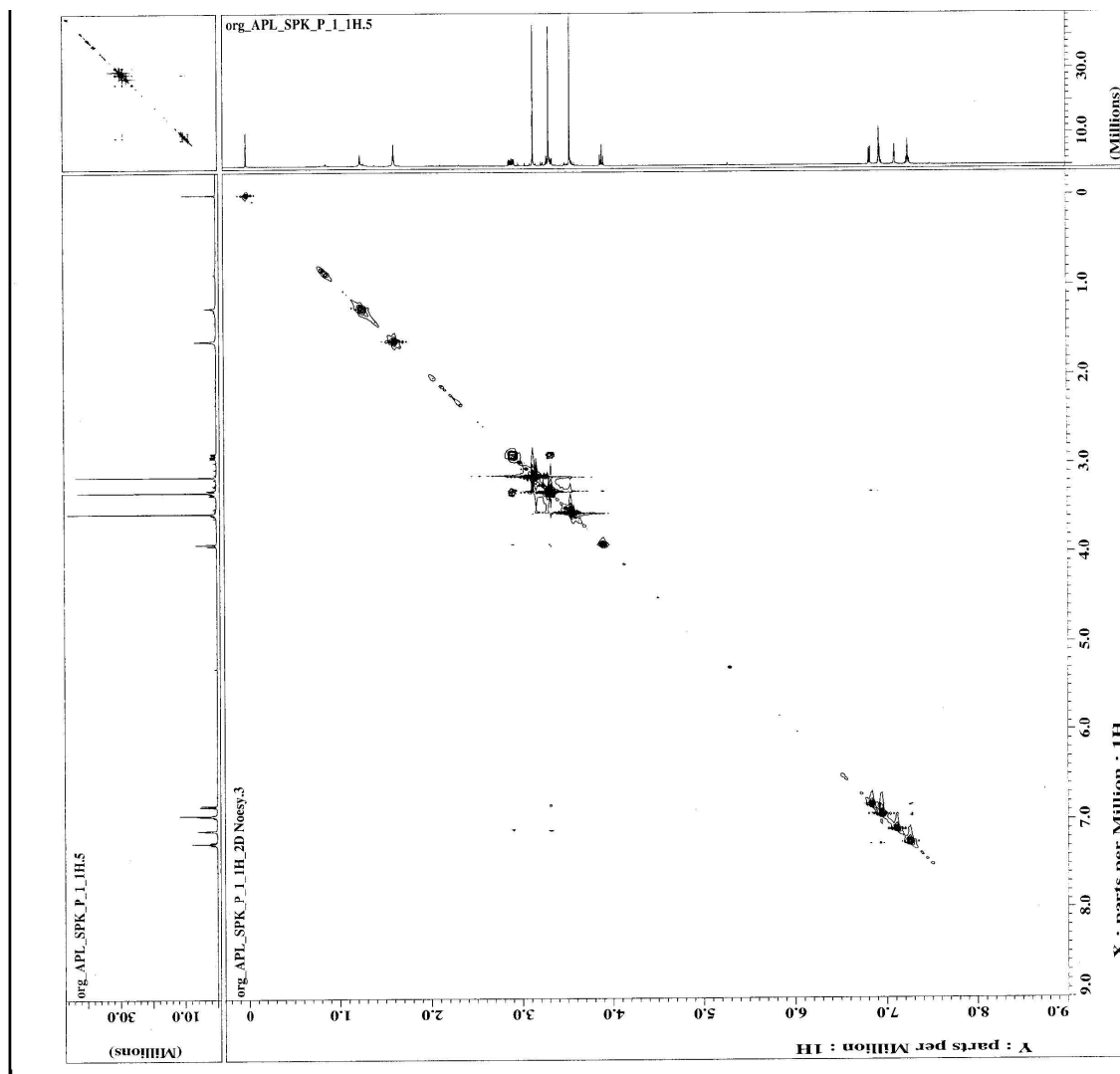
S17

DIFFNOE of Compound 3a



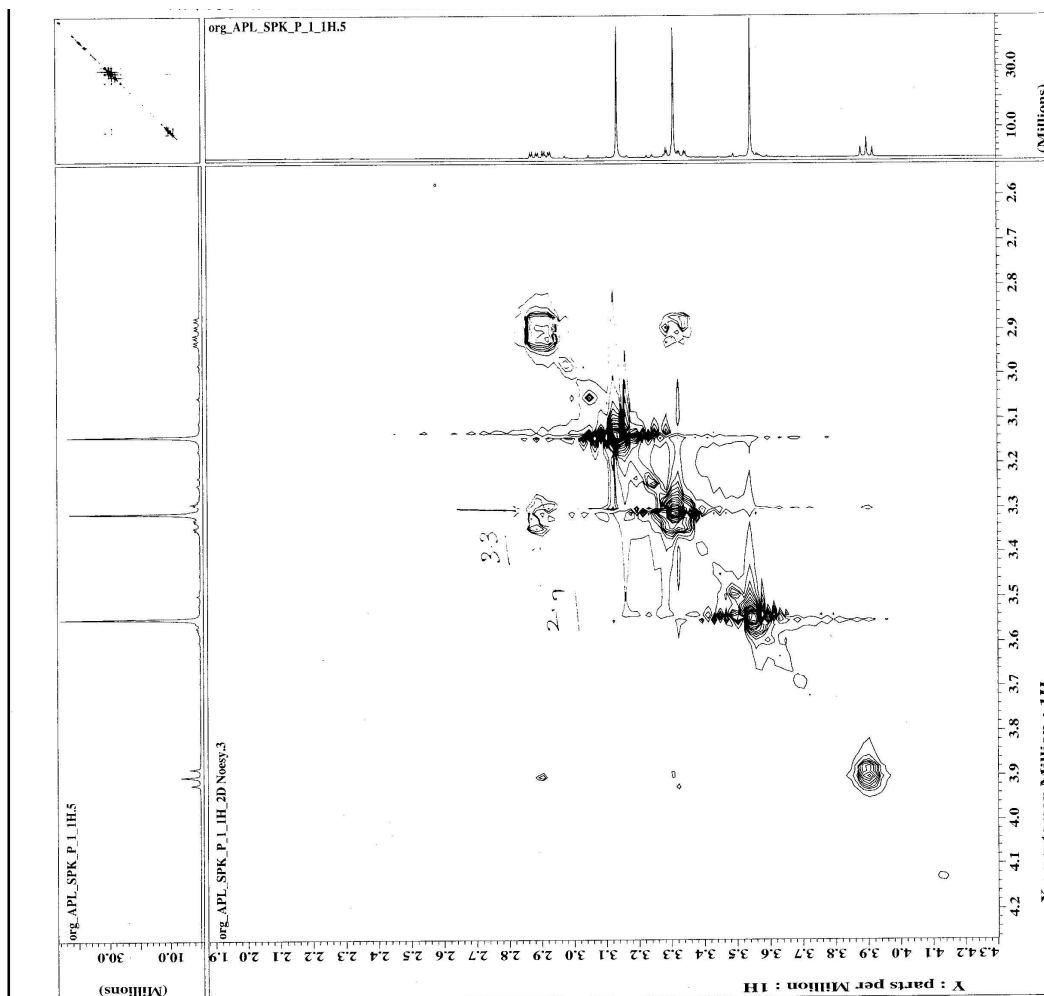
S18

2D NOESY of Compound 3a



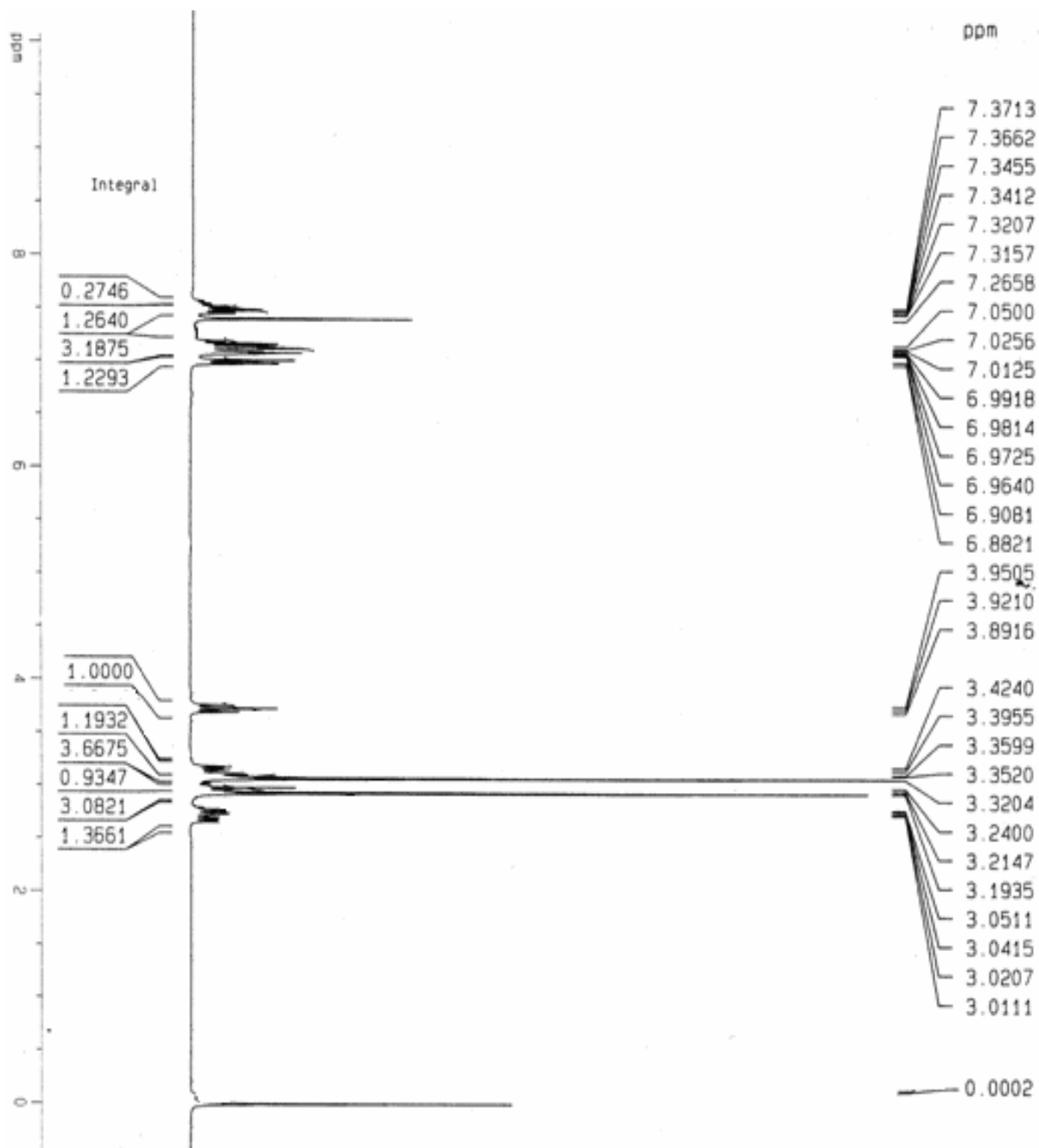
S19

2D NOESY of Compound 3a- expanded



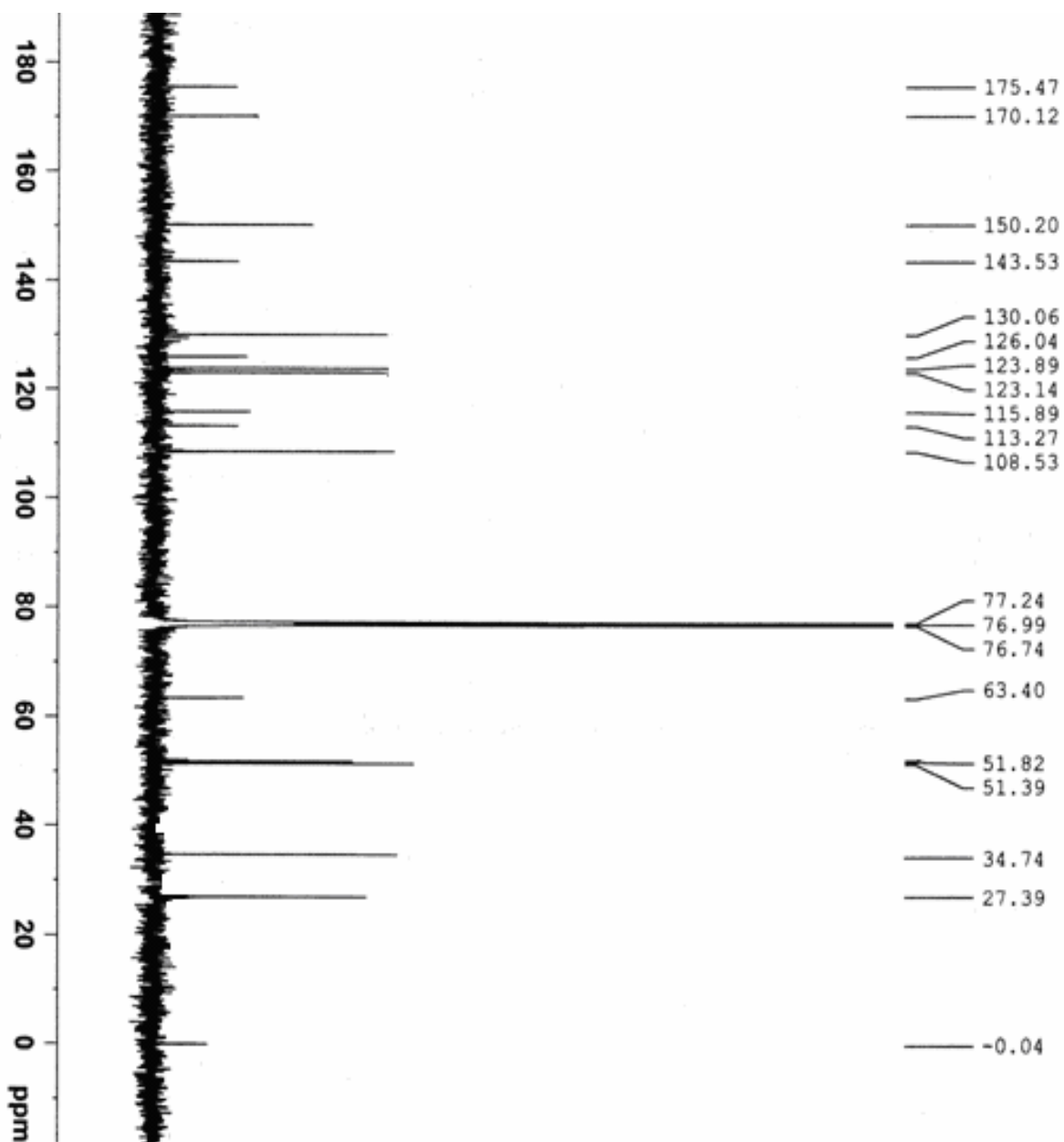
S20

Compound 3b- ¹H NMR (300 MHz)



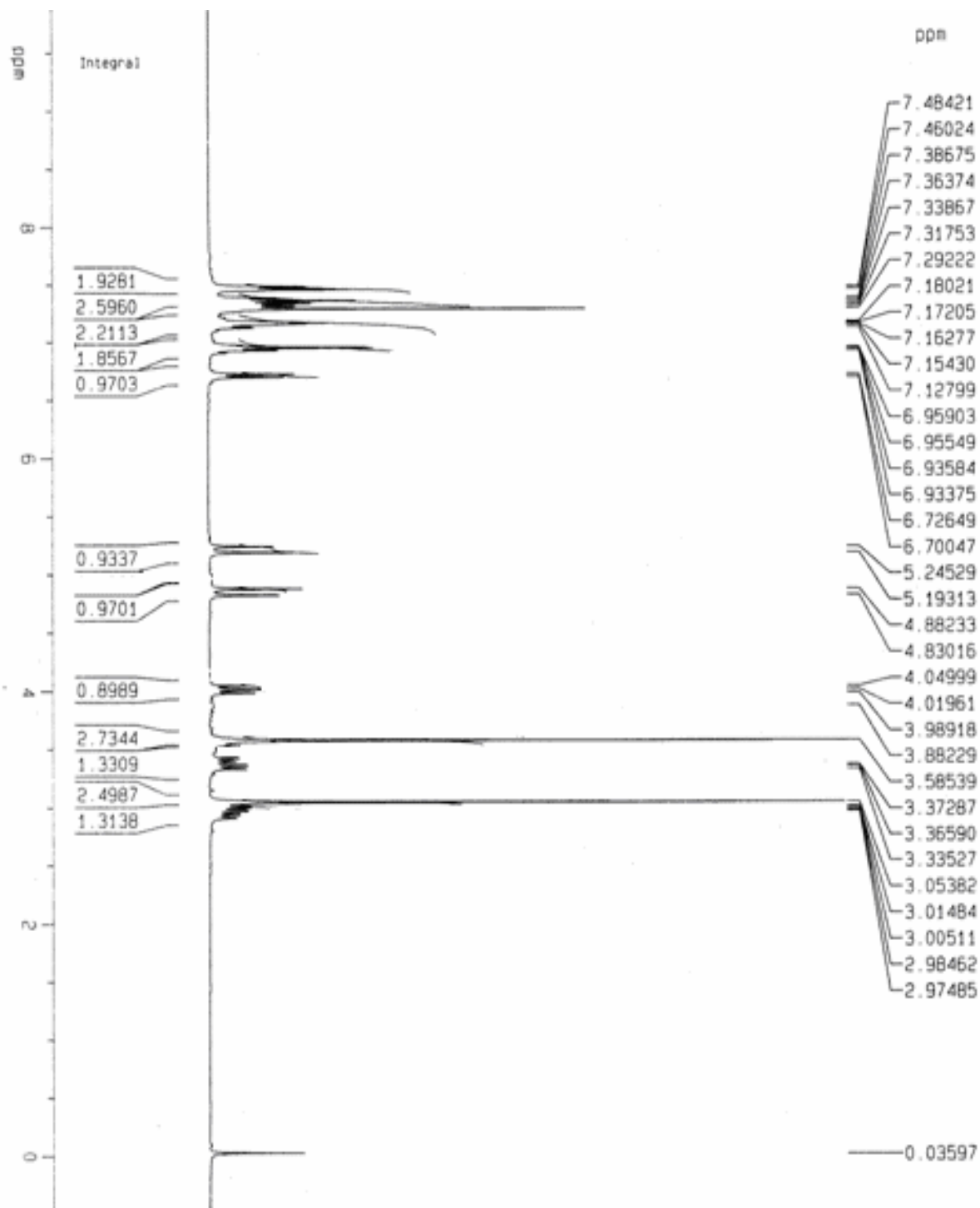
S21

Compound 3b- ^{13}C NMR (500 MHz)



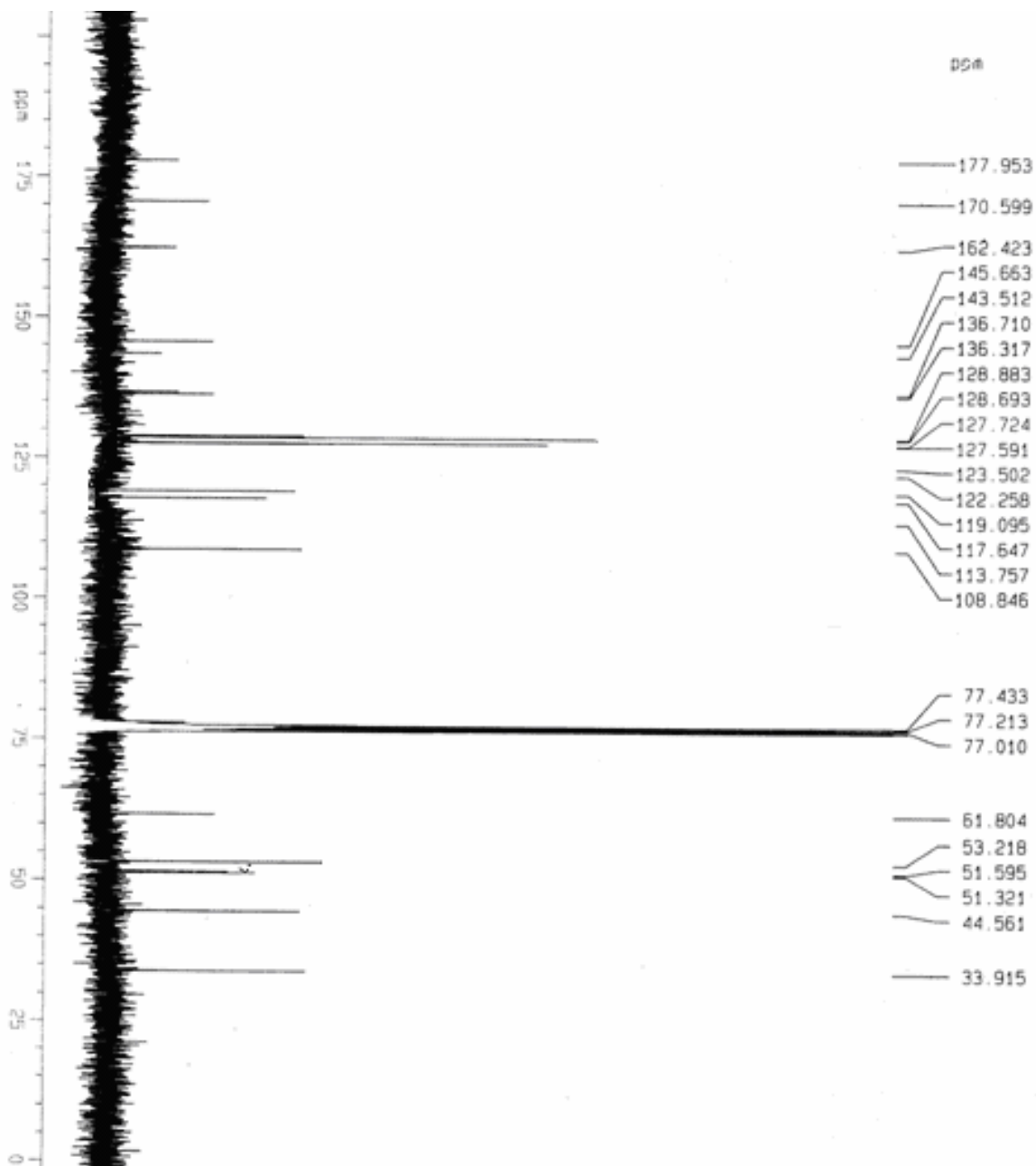
S22

Compound 3c- ^1H NMR (300 MHz)



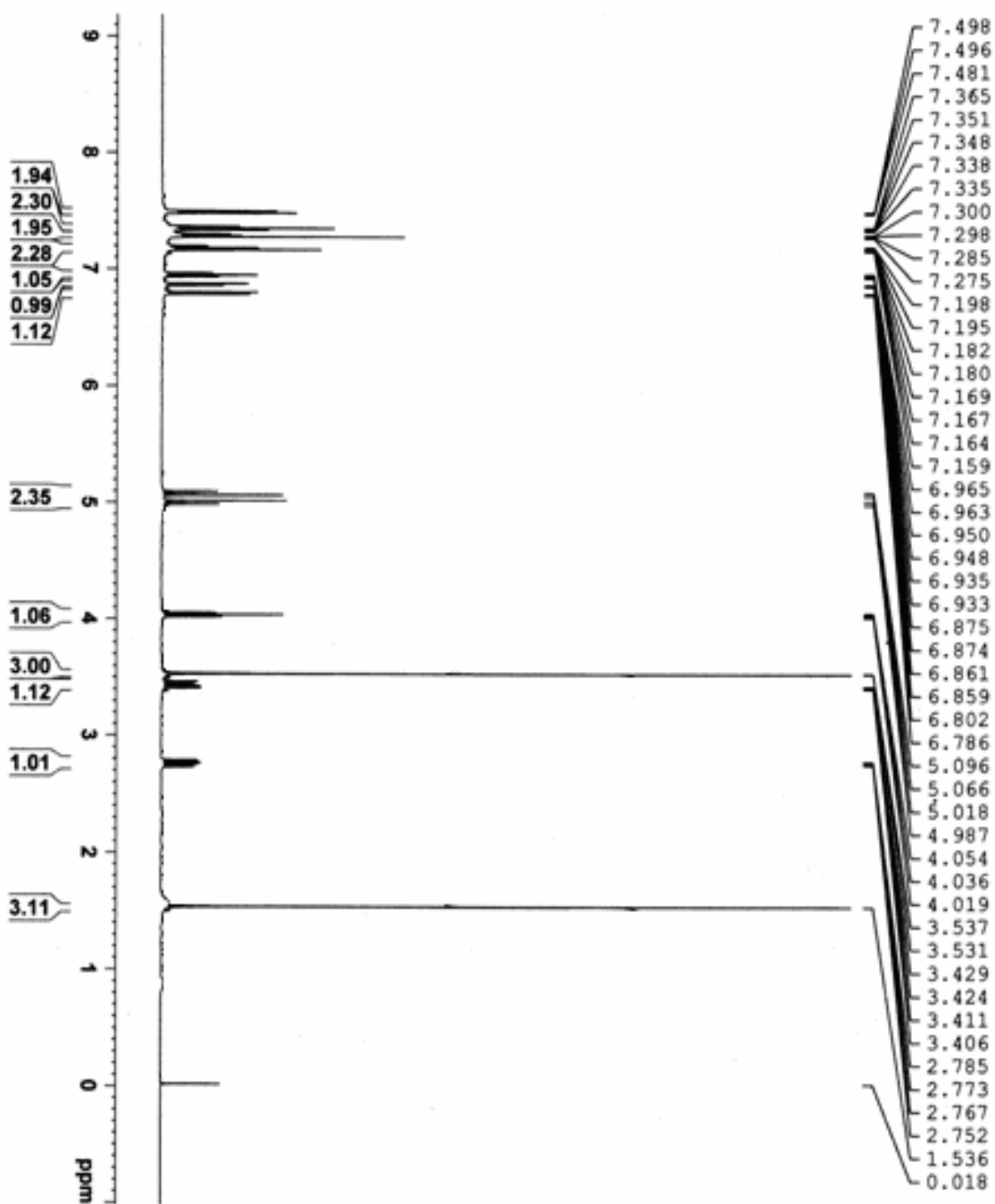
S23

Compound 3c- ^{13}C NMR (300 MHz)



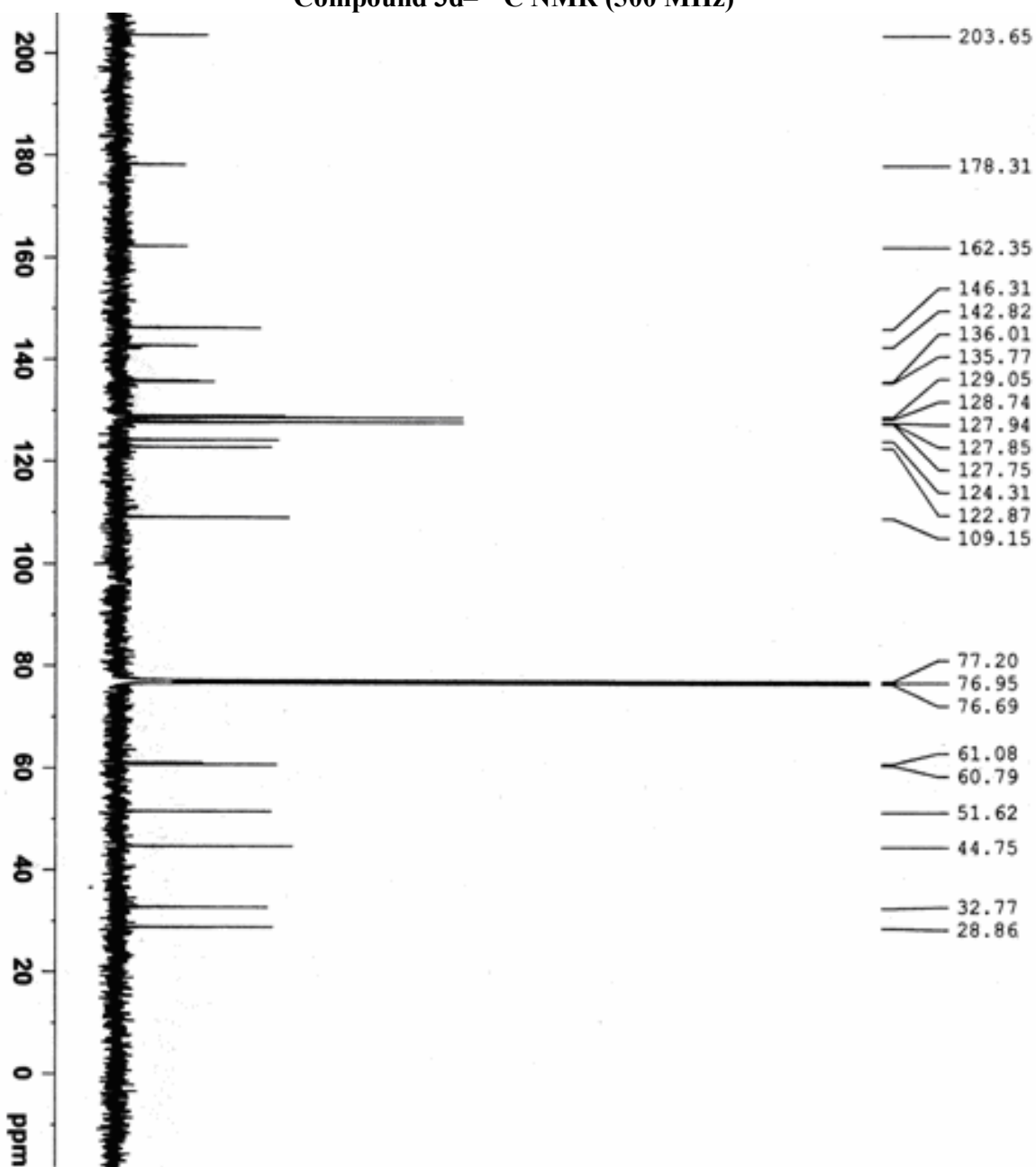
S24

Compound 3d- ^1H NMR (500 MHz)



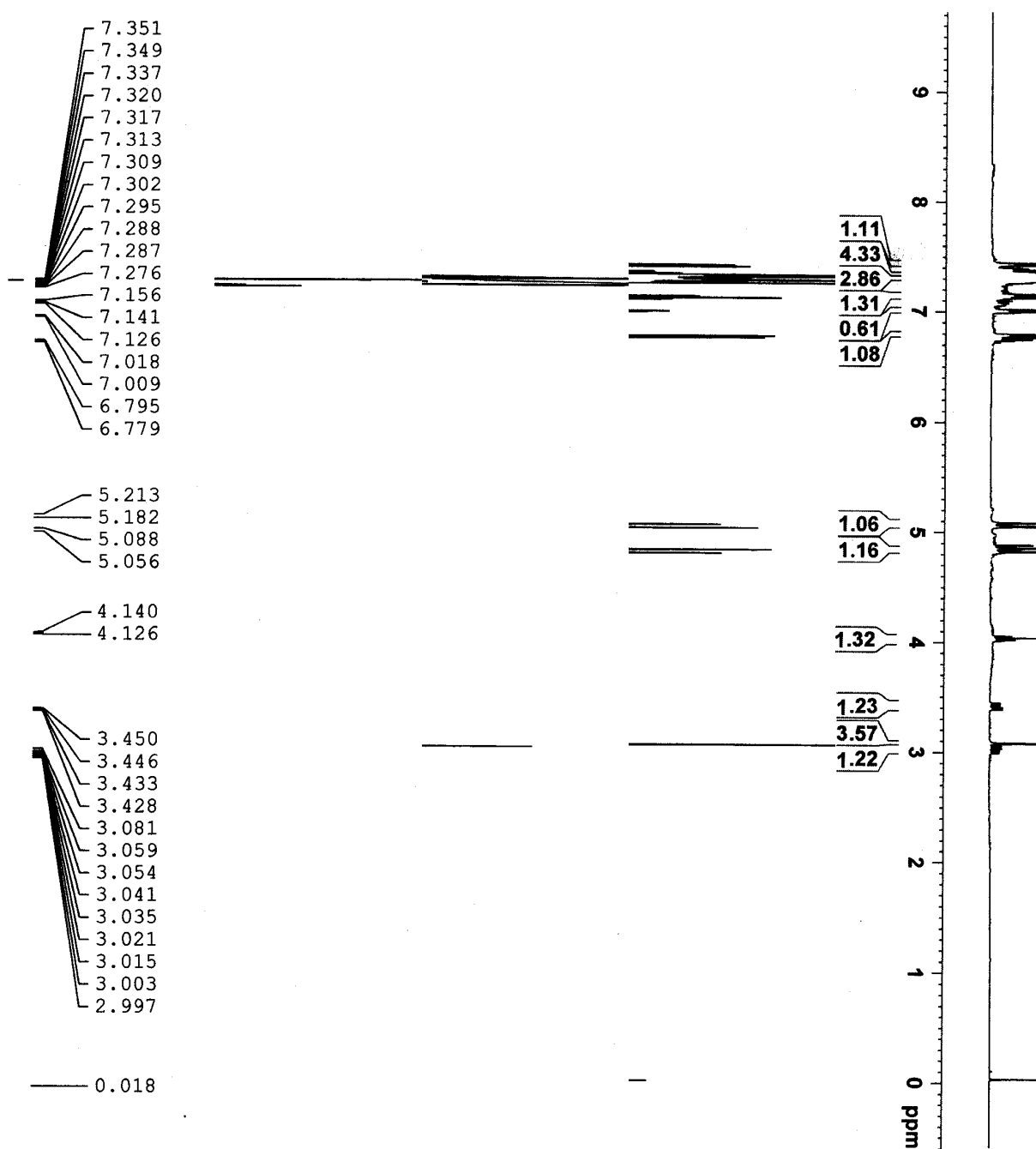
S25

Compound 3d- ^{13}C NMR (500 MHz)



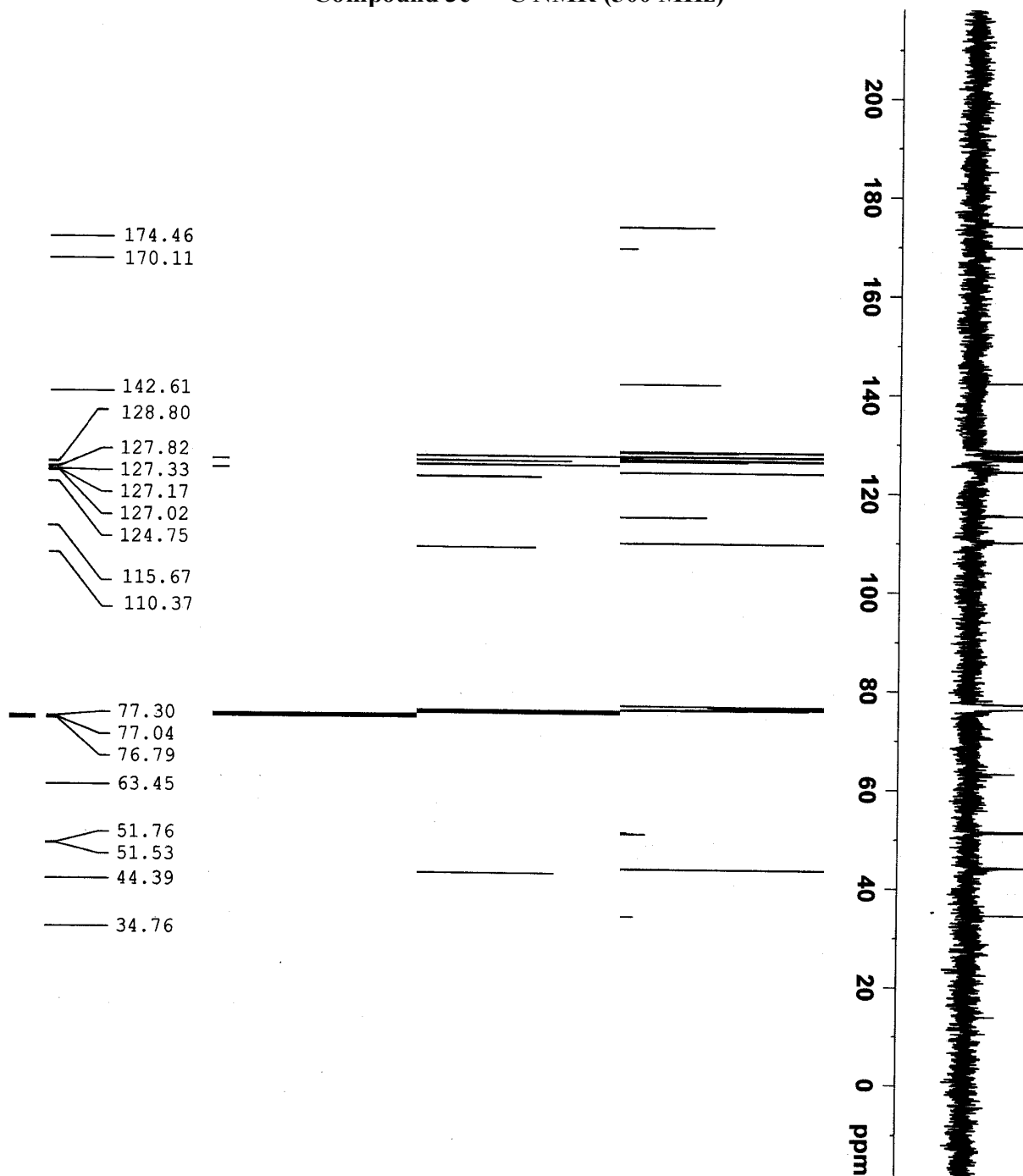
S26

Compound 3e- ^1H NMR (500 MHz)



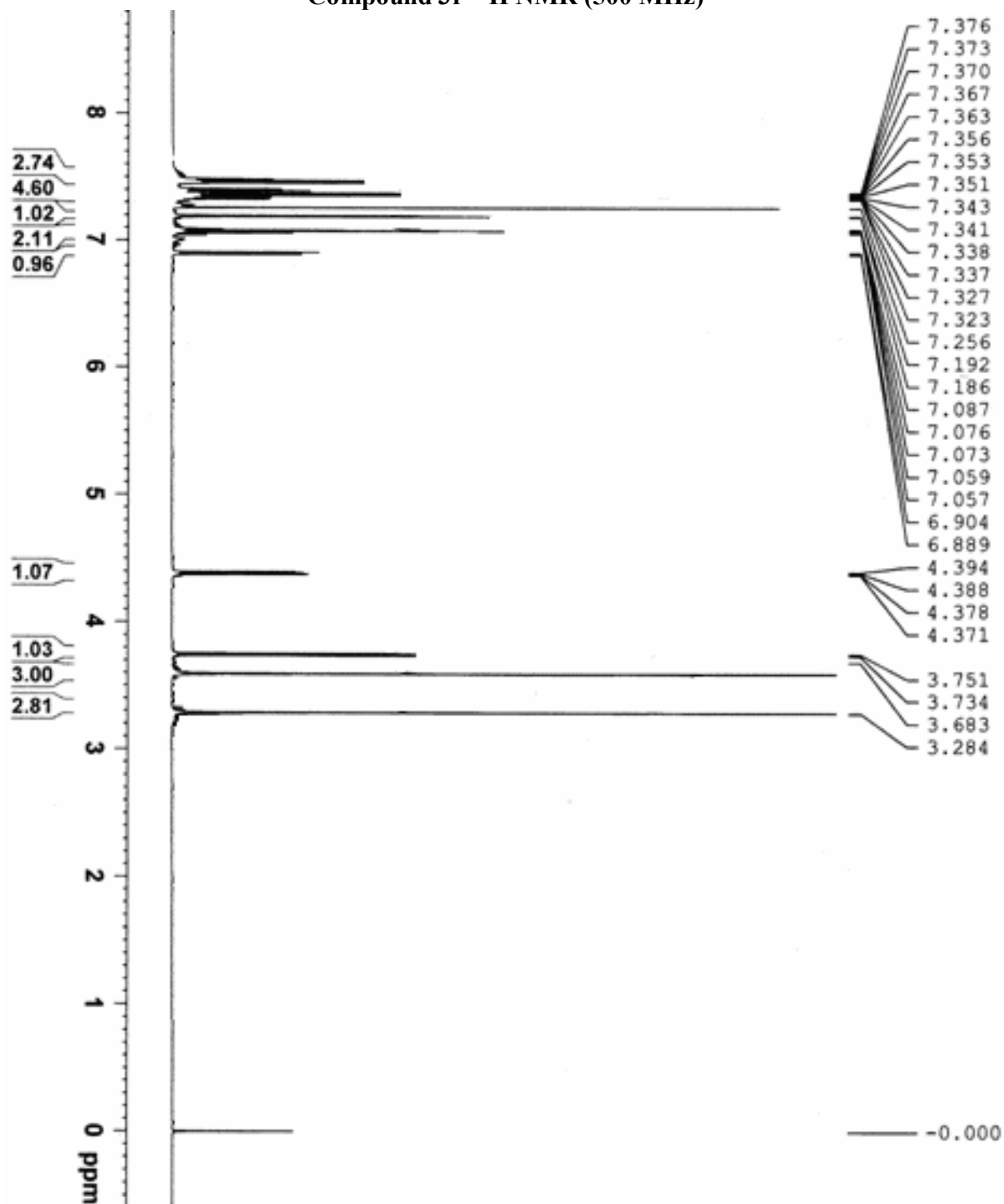
S27

Compound 3e- ^{13}C NMR (500 MHz)



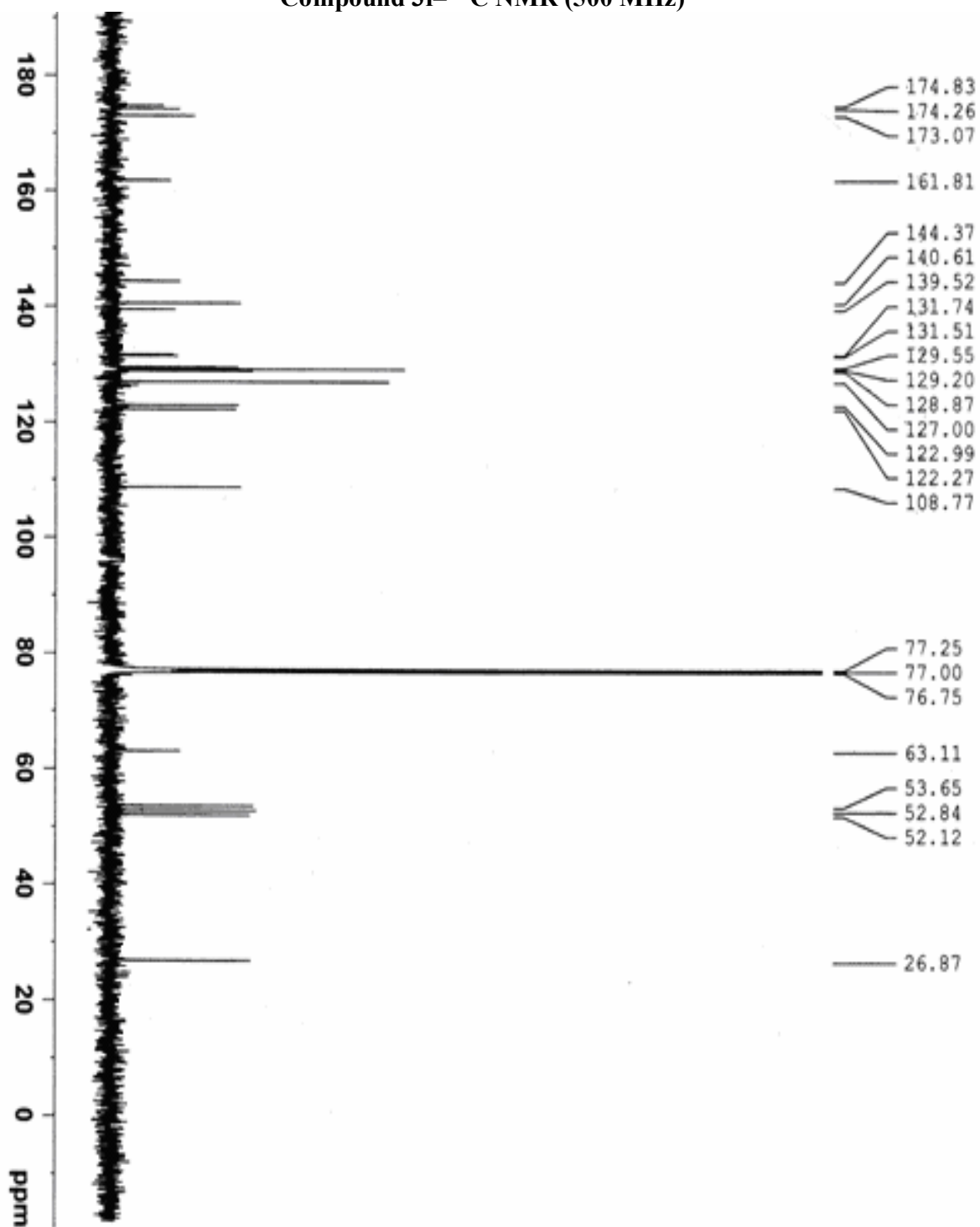
S28

Compound 3f- ^1H NMR (500 MHz)

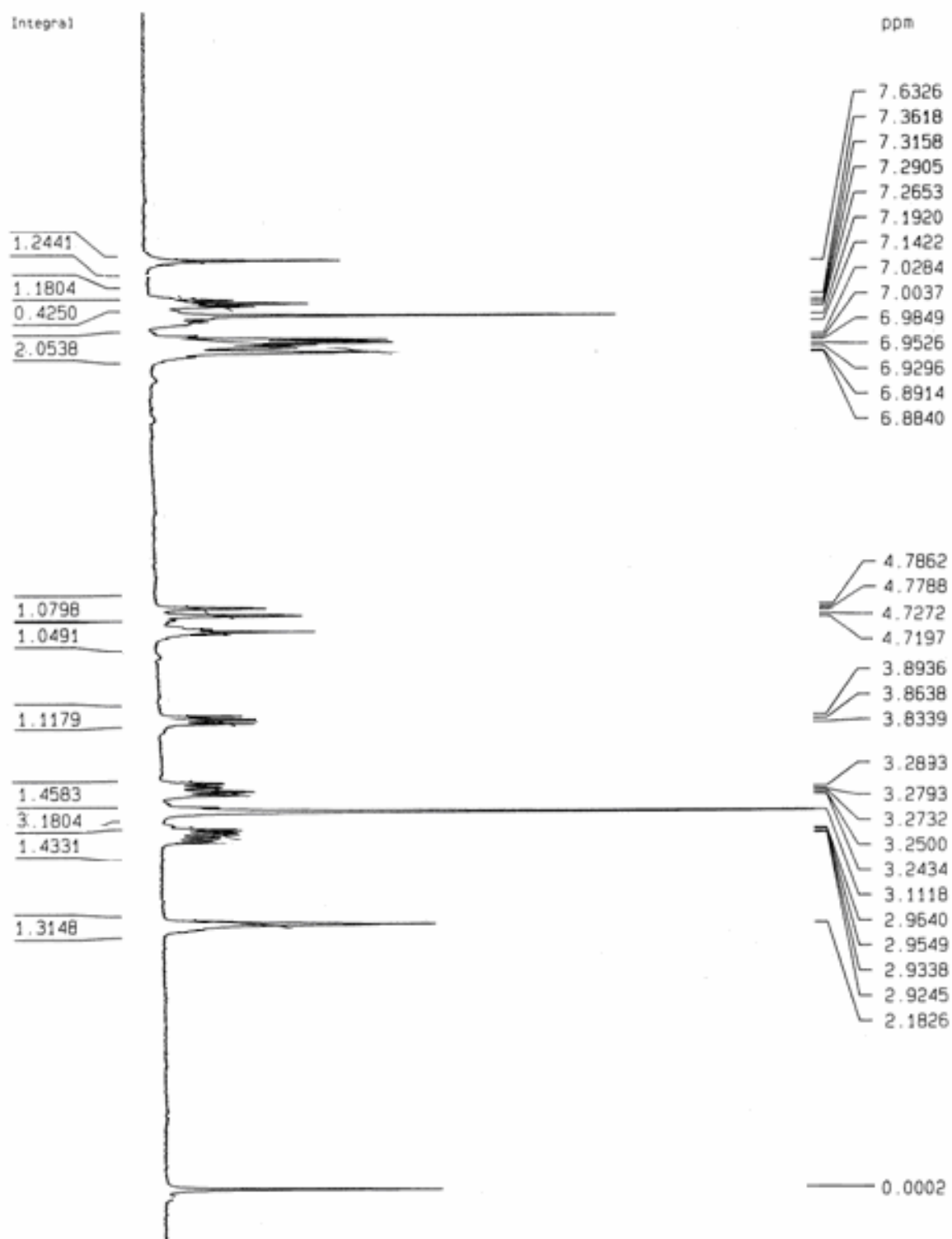


S29

Compound 3f- ^{13}C NMR (500 MHz)

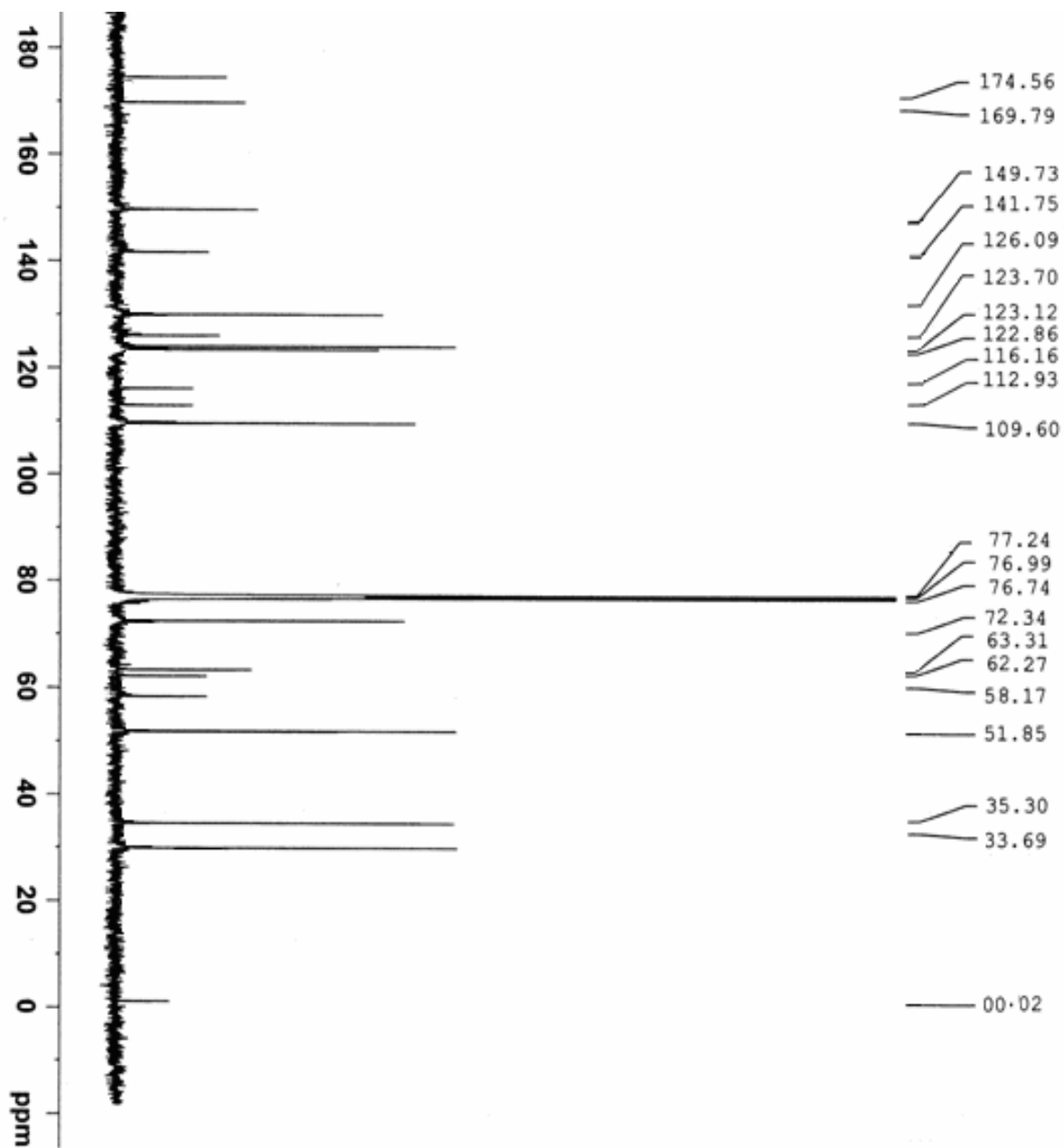


Compound 3g- ^1H NMR (300 MHz)

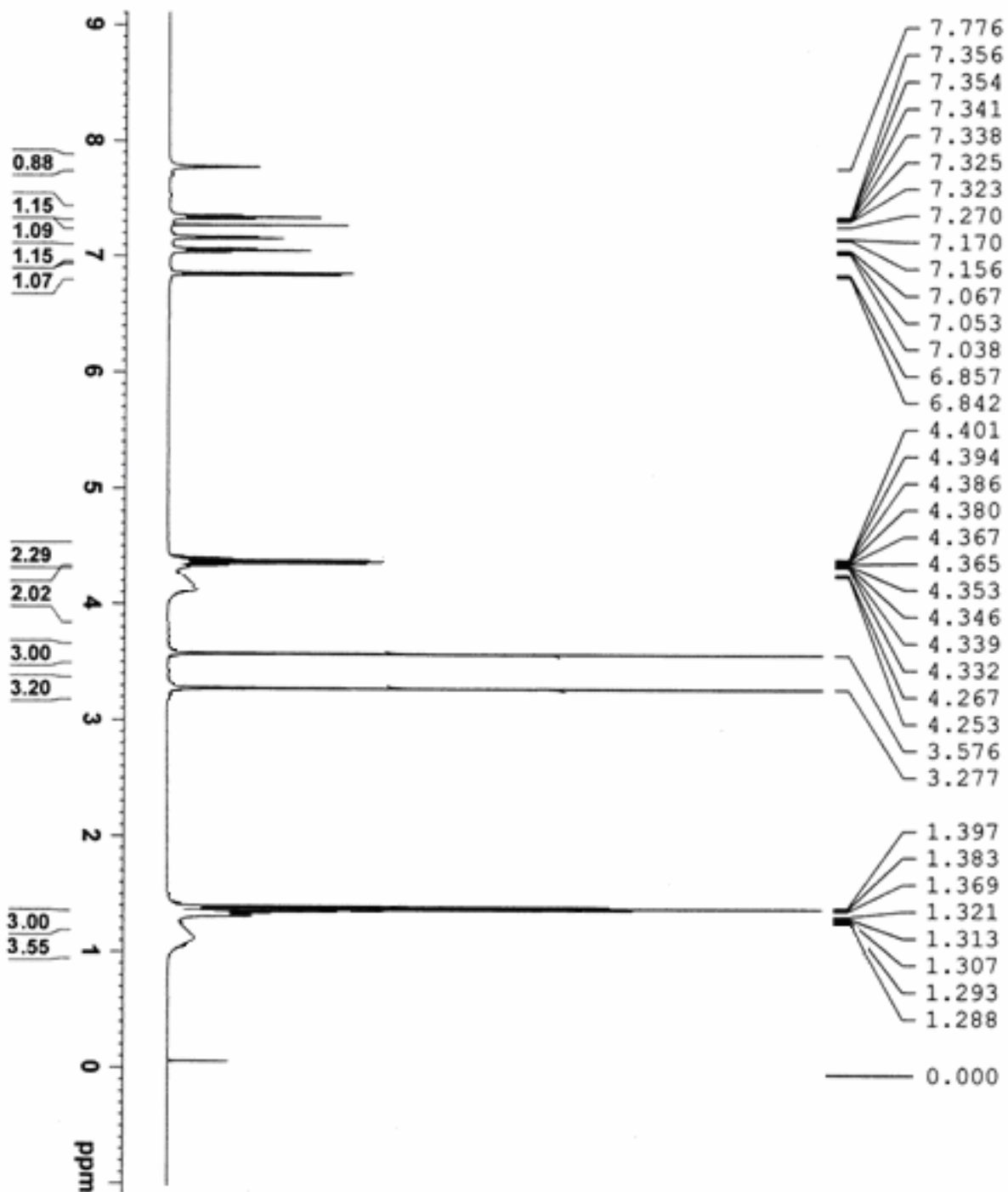


S31

Compound 3g- ^{13}C NMR (500 MHz)

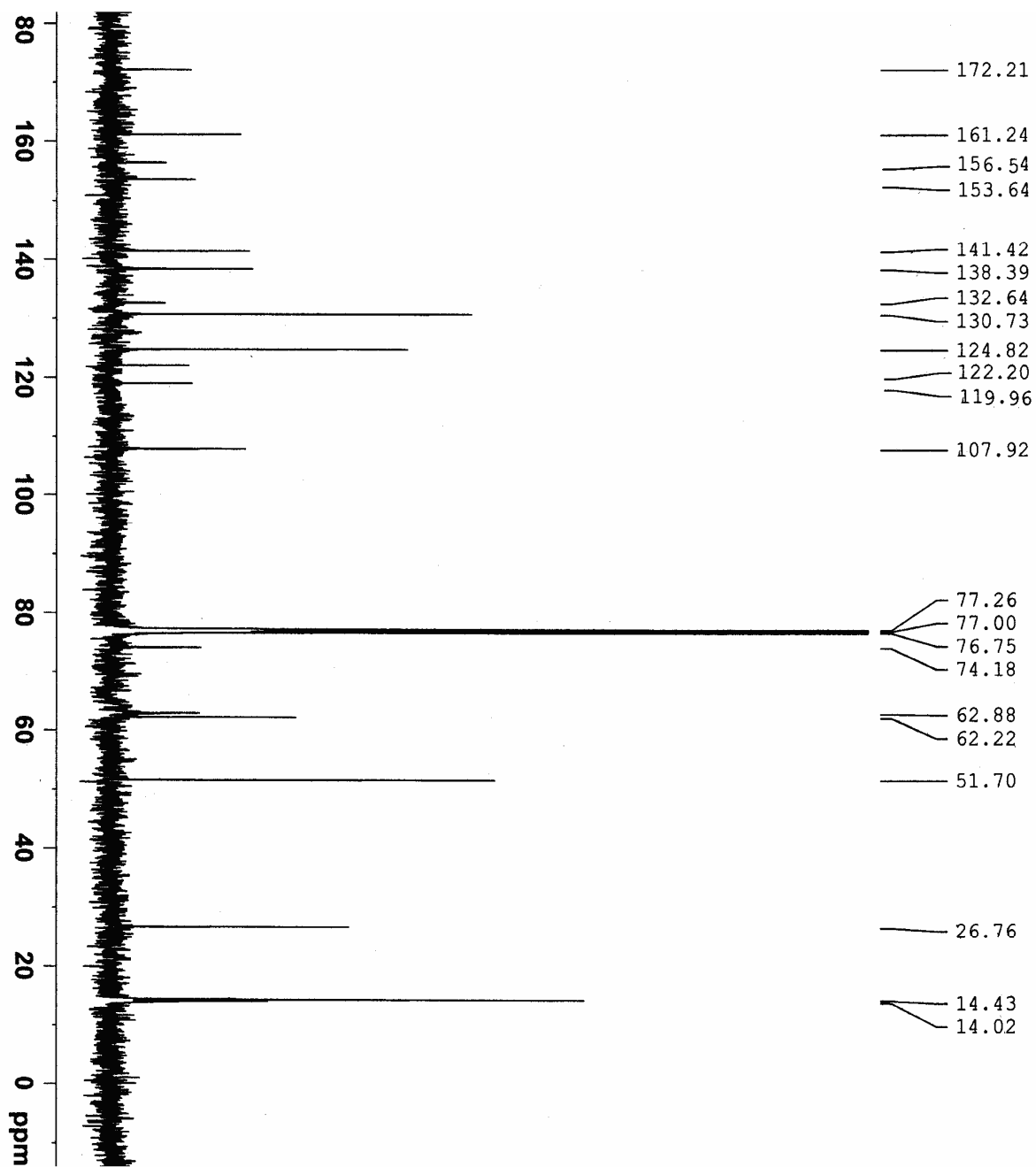


Compound 7a- ^1H NMR (500 MHz)

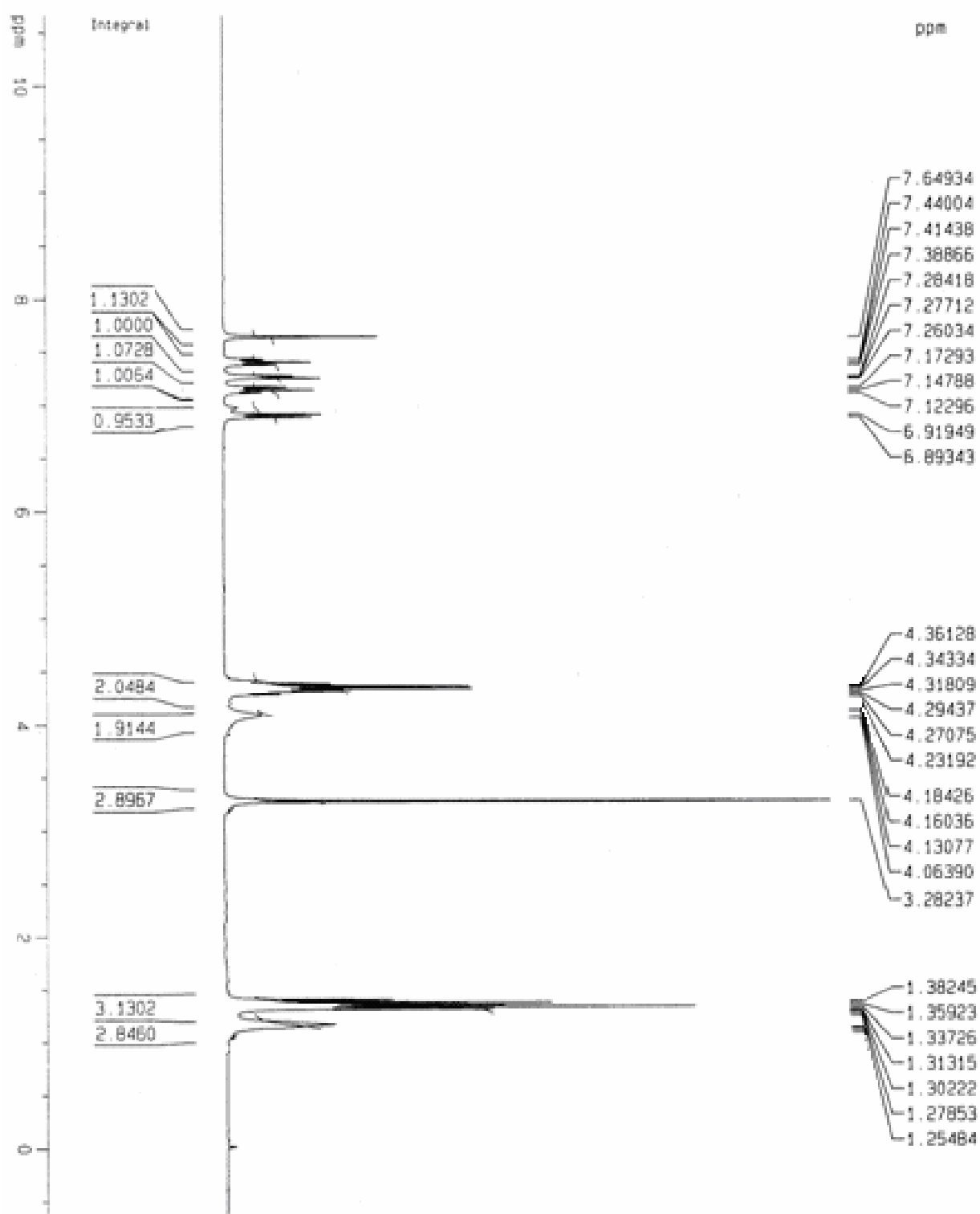


S33

Compound 7a- ^{13}C NMR (500 MHz)

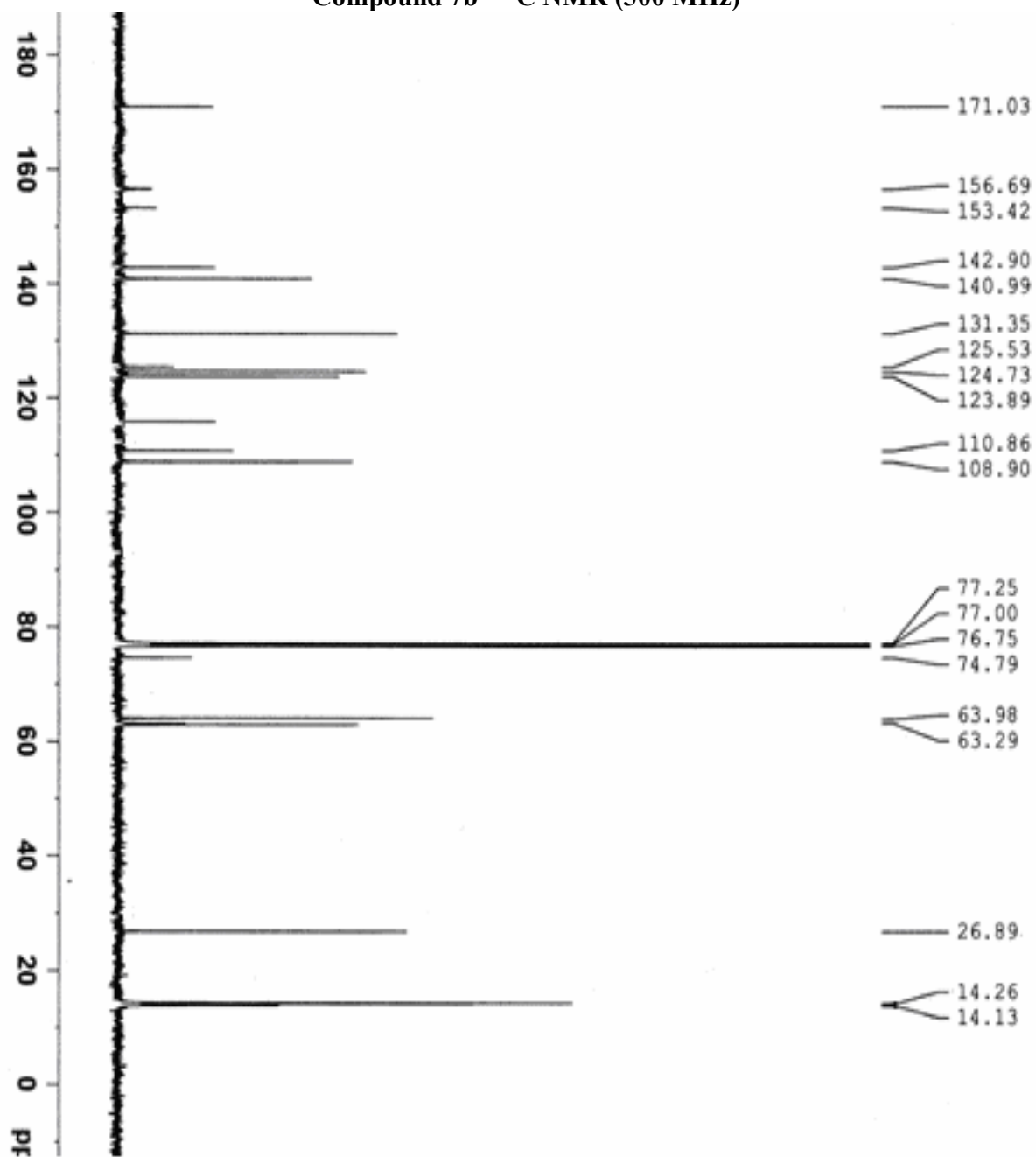


Compound 7b- ¹H NMR (300 MHz)



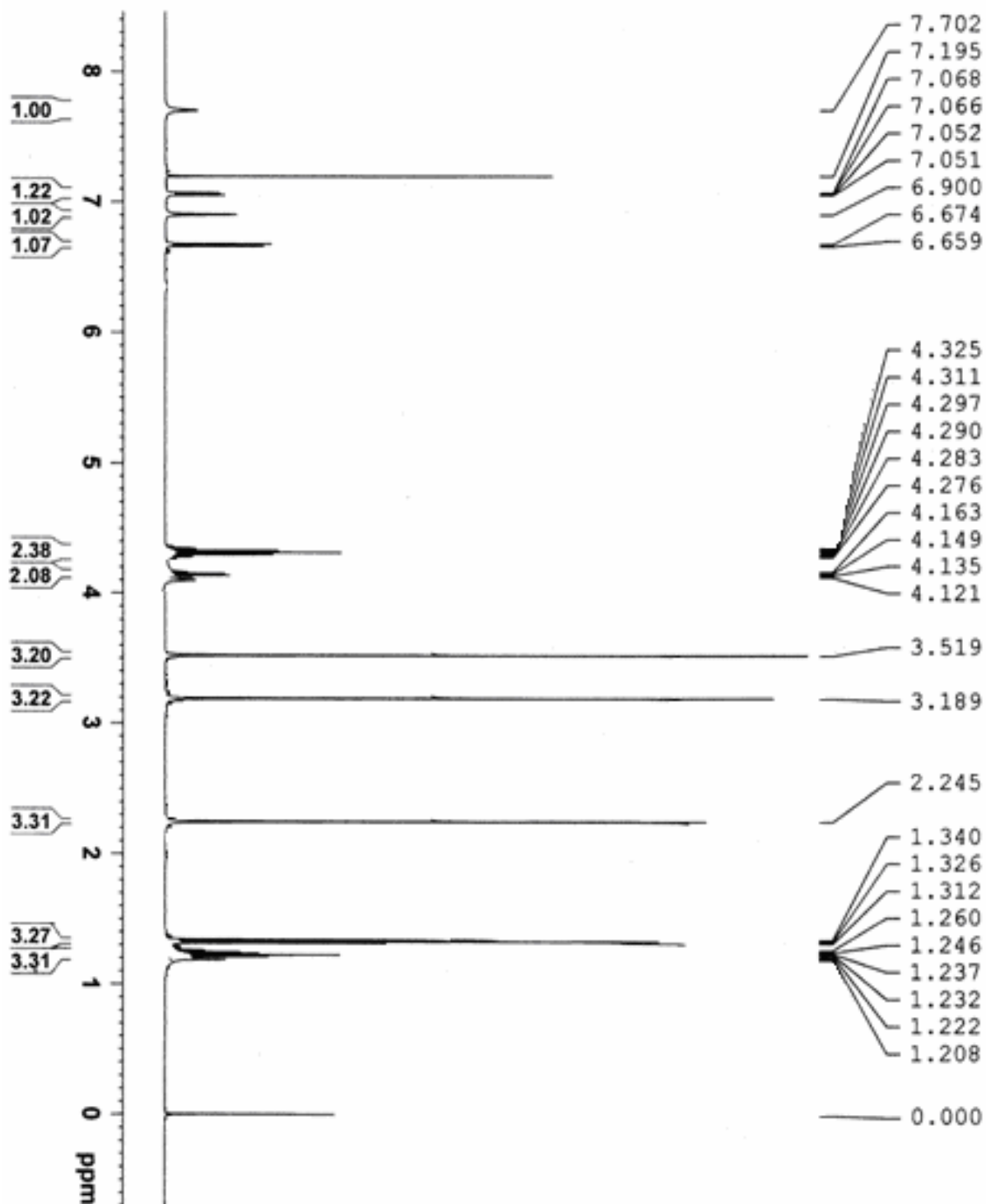
S35

Compound 7b- ^{13}C NMR (500 MHz)



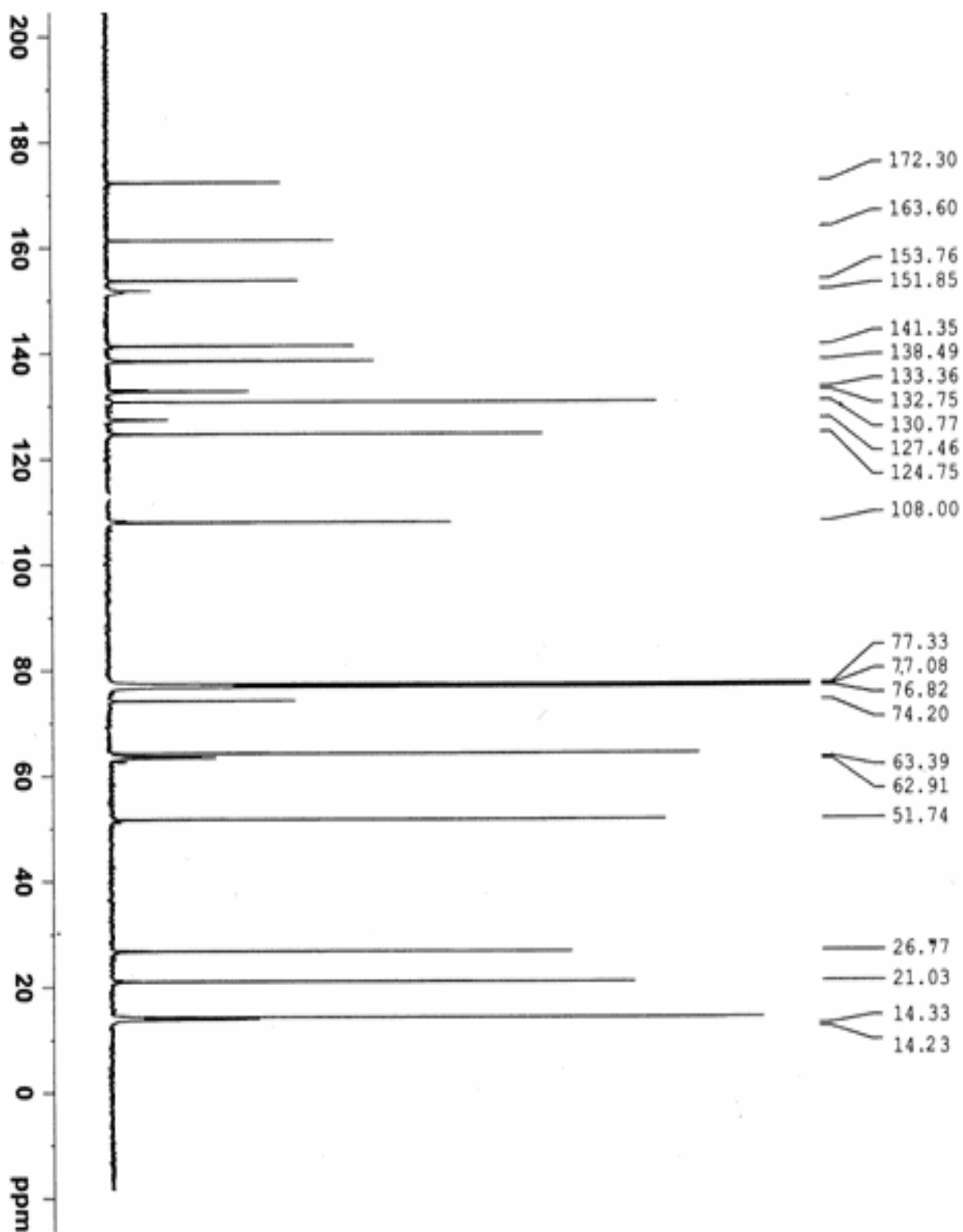
S36

Compound 7c- ^1H NMR (500 MHz)



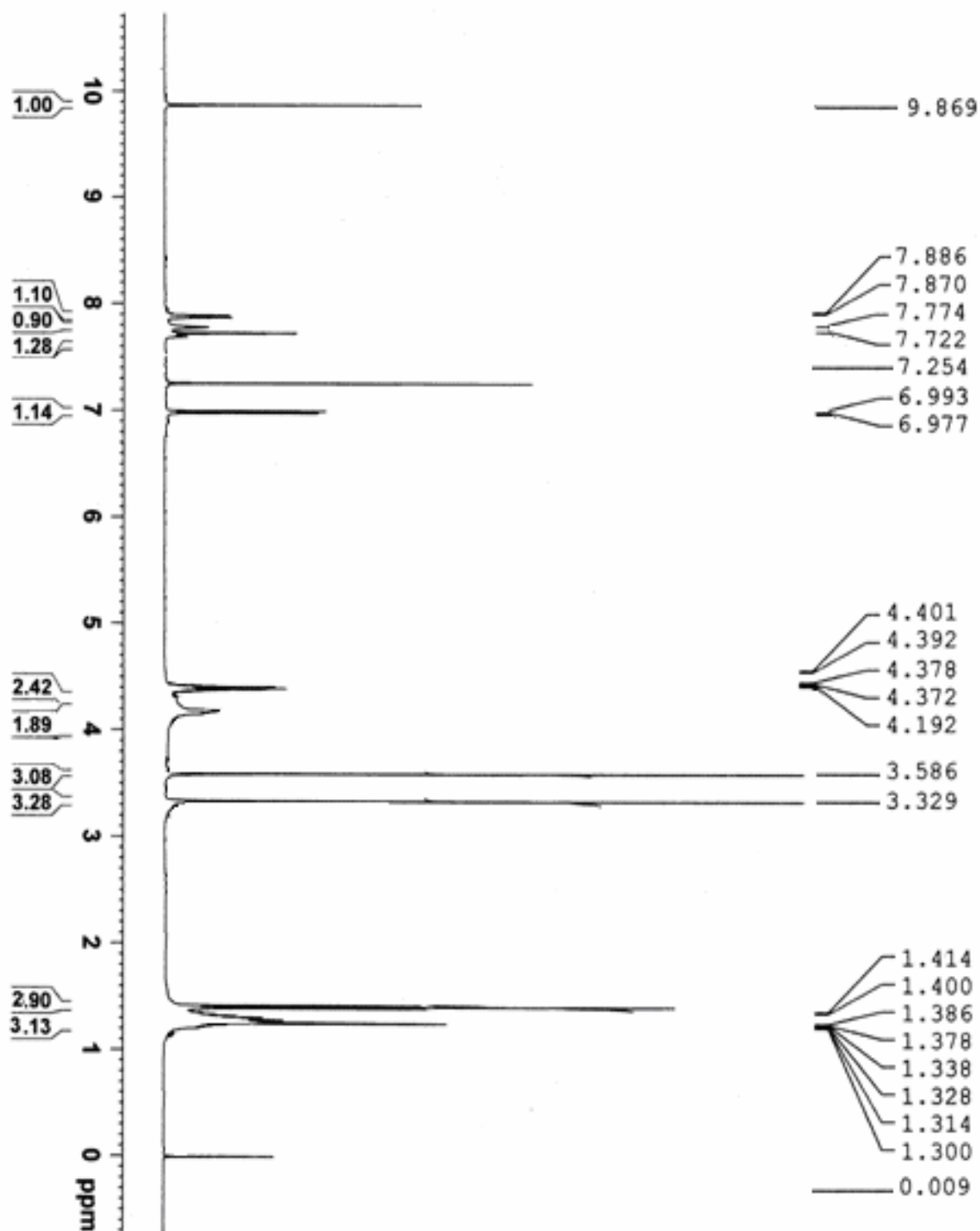
S37

Compound 7c- ^{13}C NMR (500 MHz)

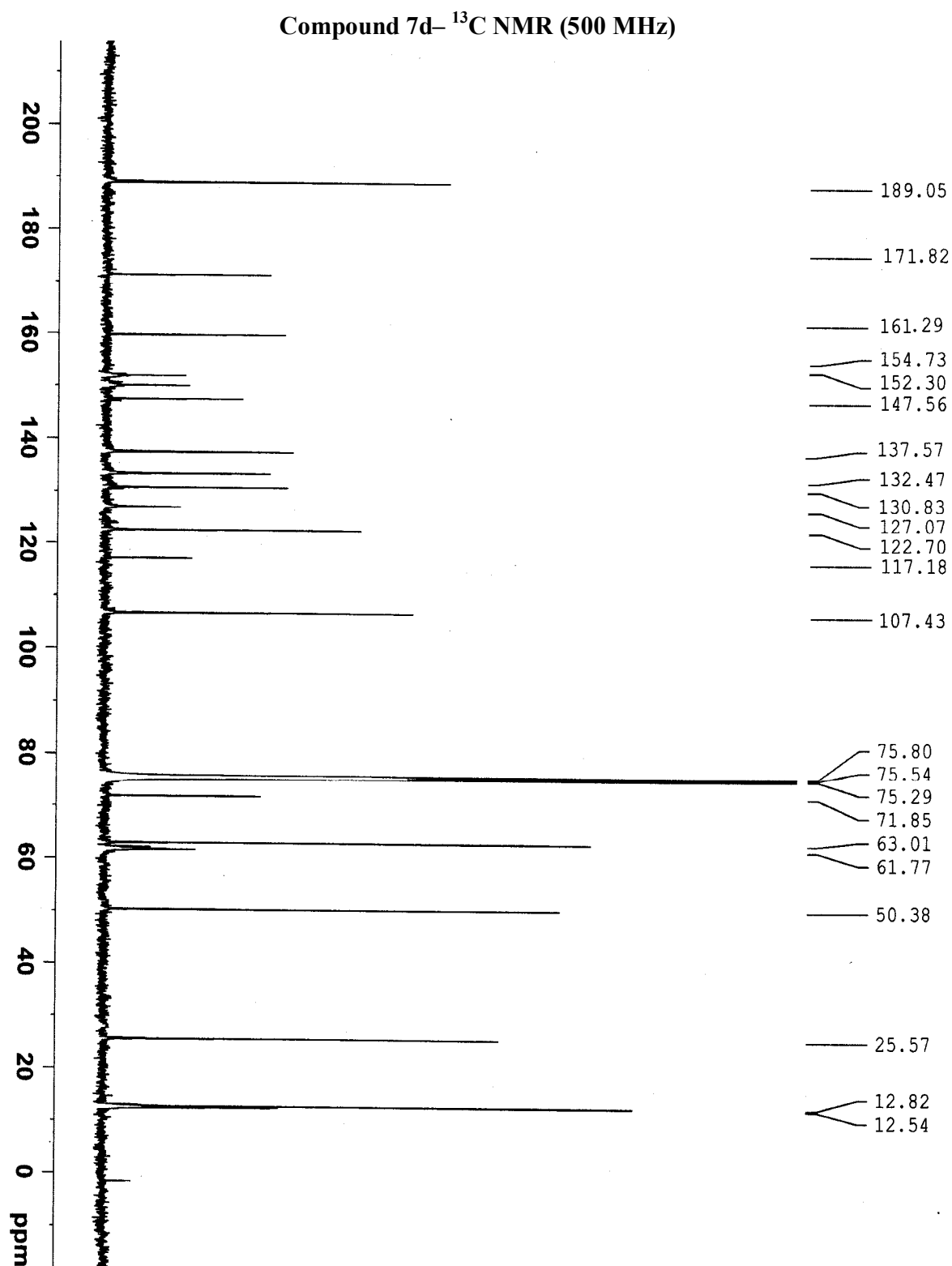


S38

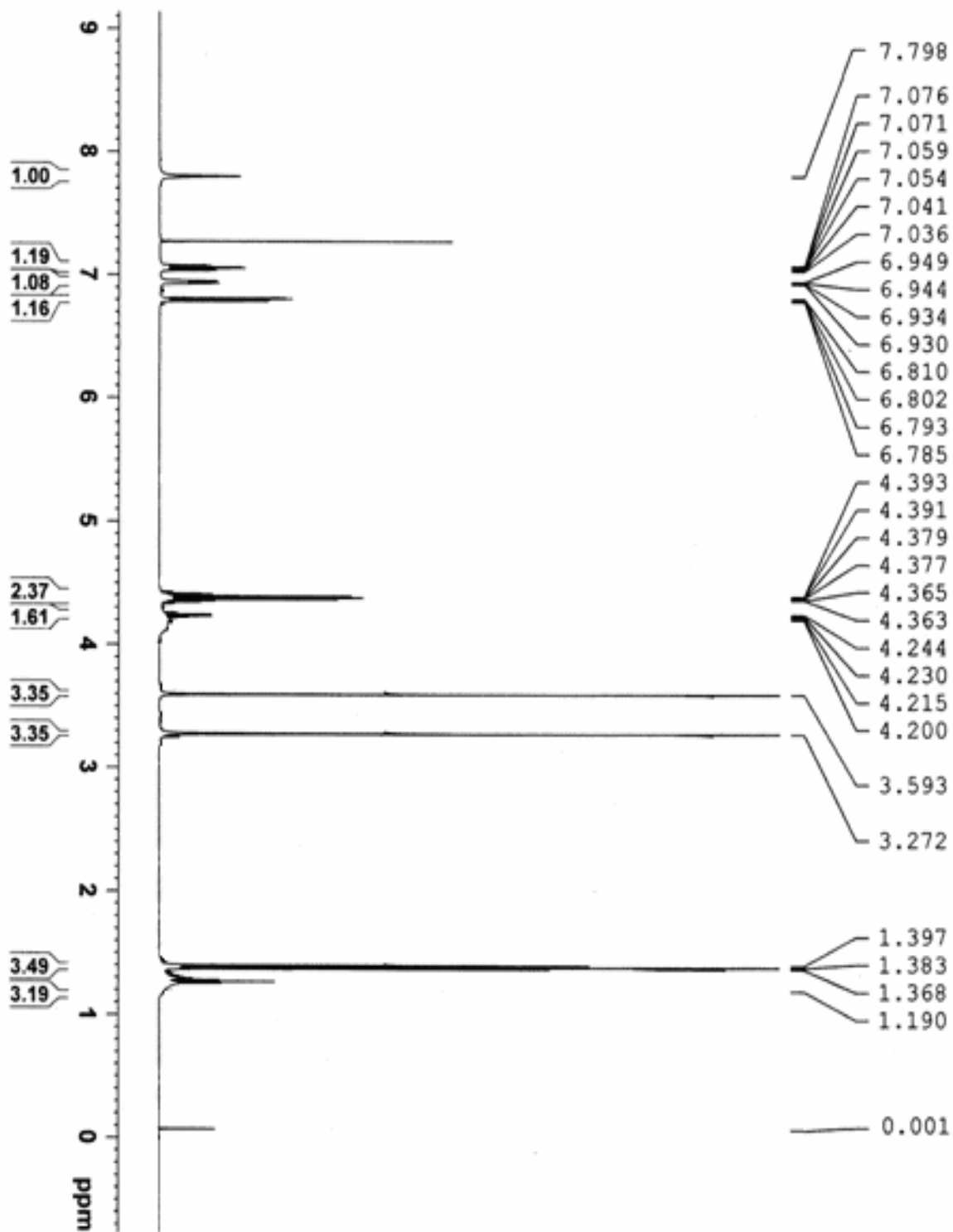
Compound 7d- ^1H NMR (500 MHz)



S39

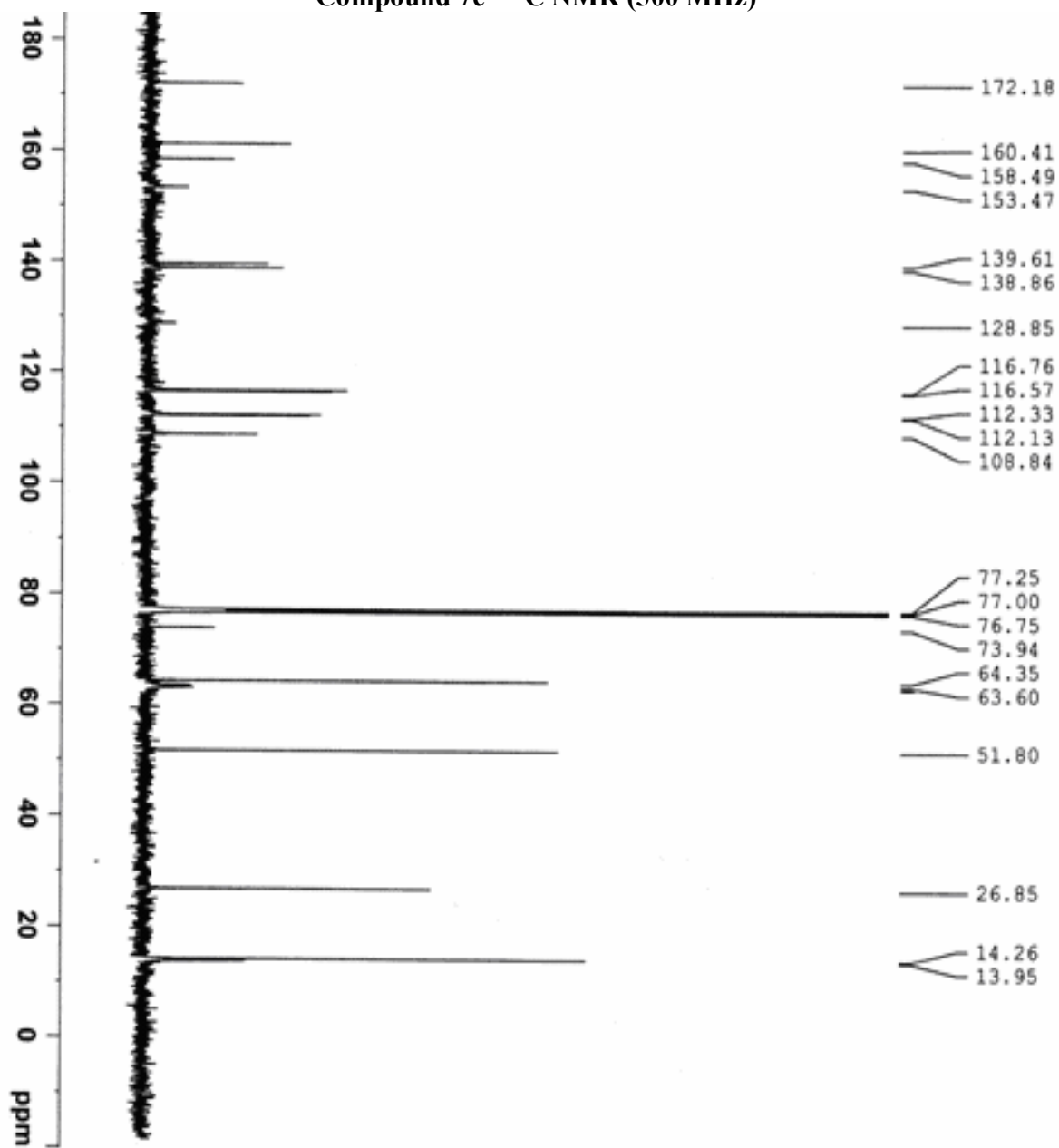


Compound 7e- ^1H NMR (500 MHz)

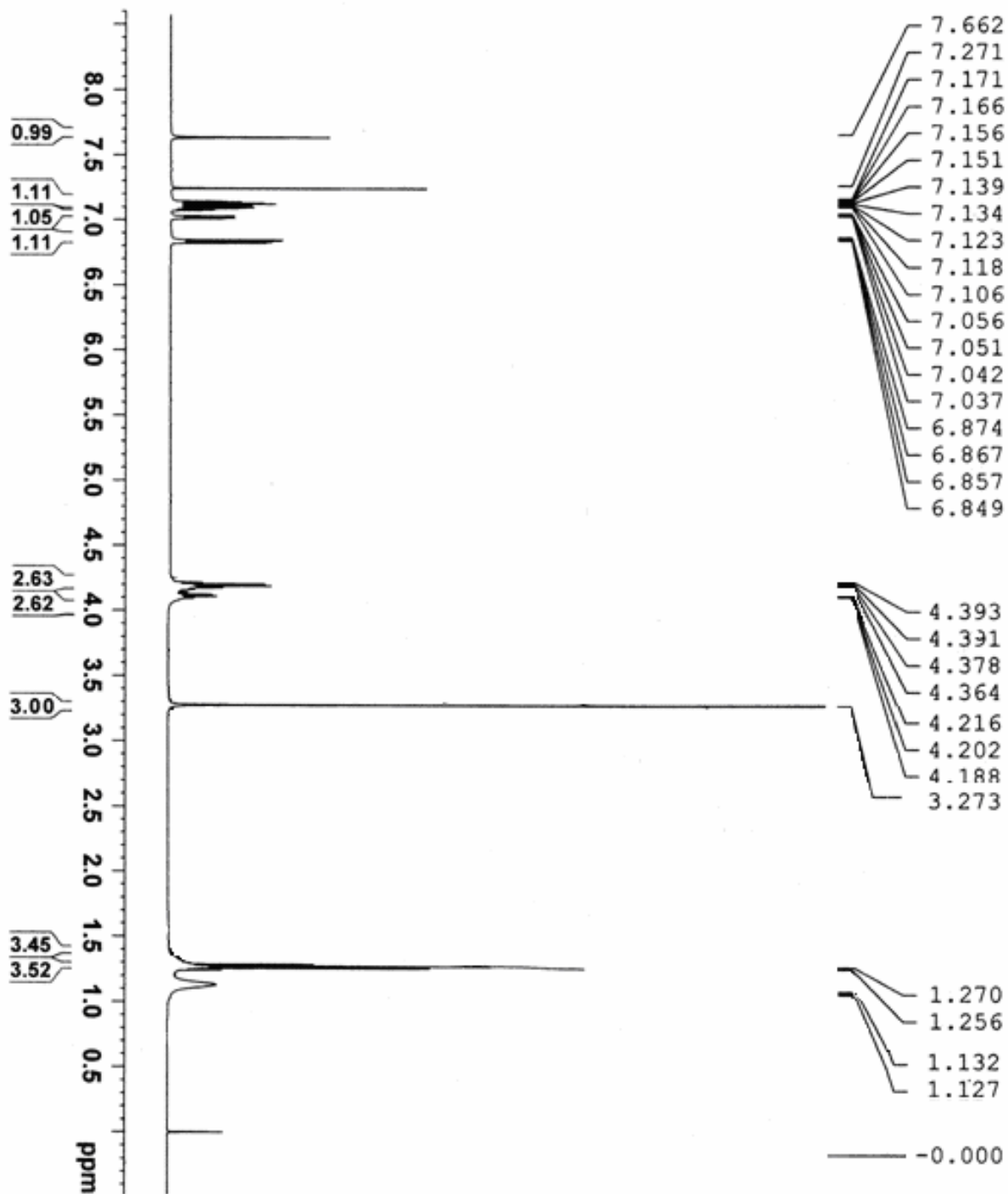


S41

Compound 7e- ^{13}C NMR (500 MHz)

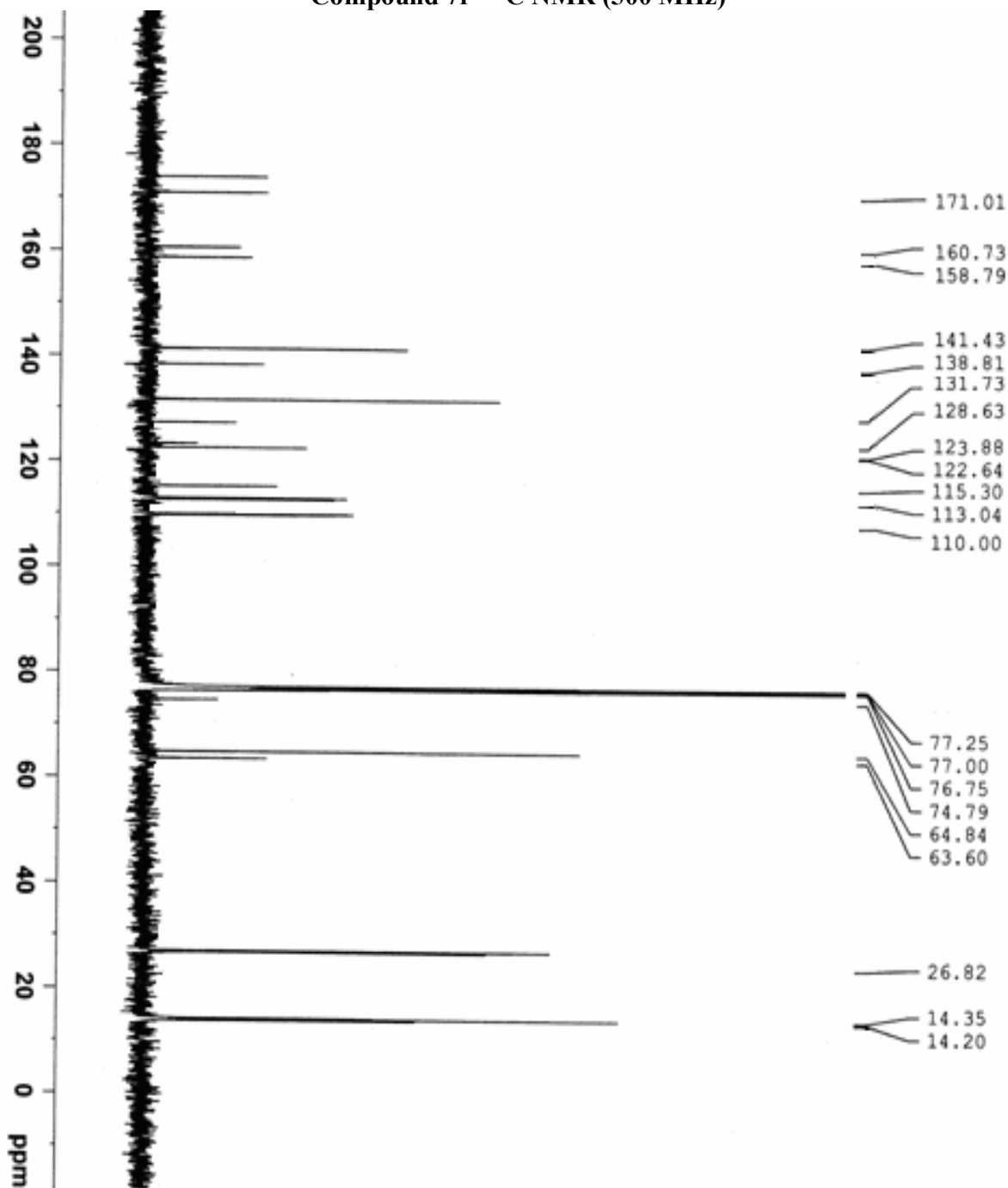


Compound 7f- ^1H NMR (500 MHz)



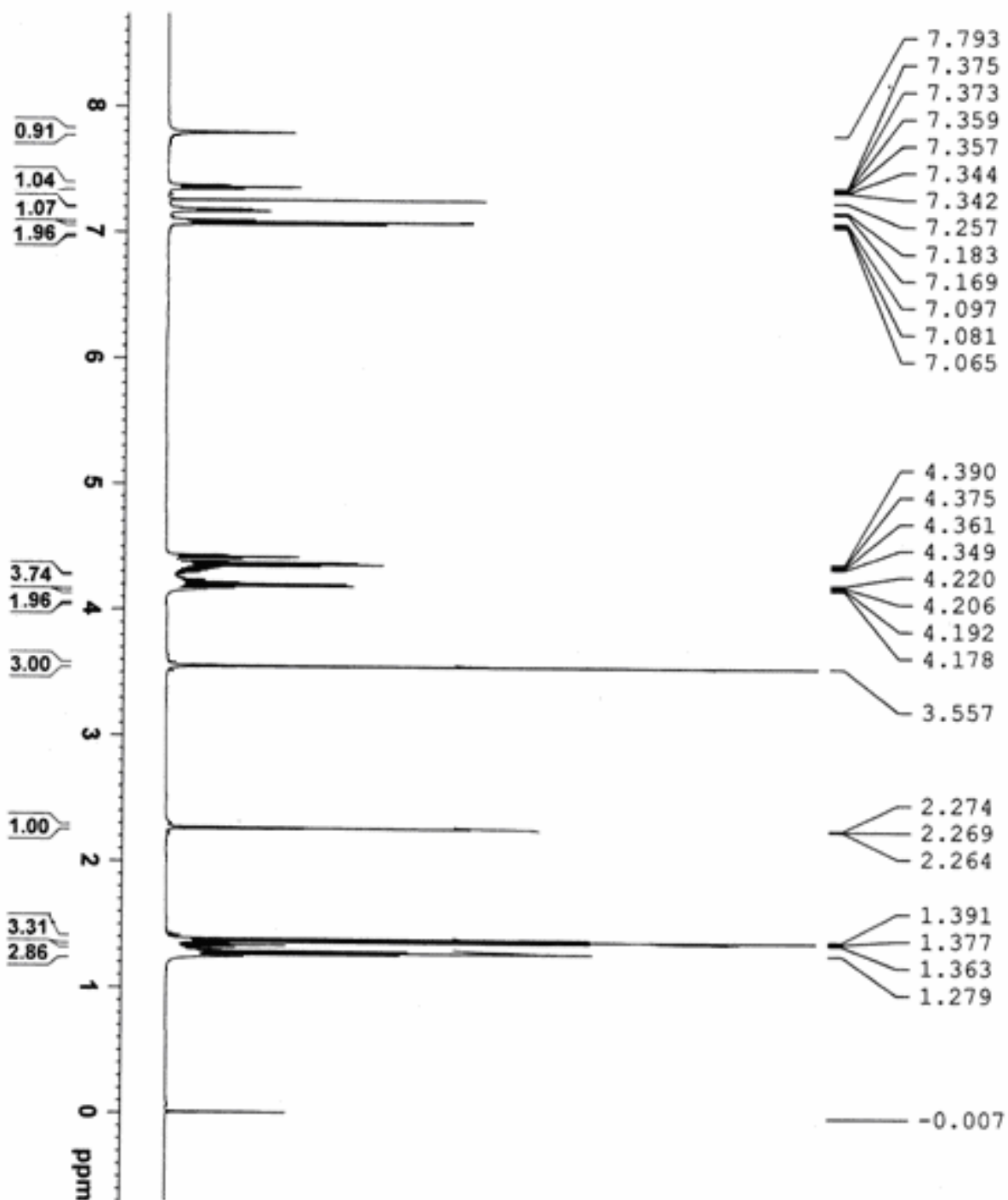
S43

Compound 7f- ^{13}C NMR (500 MHz)



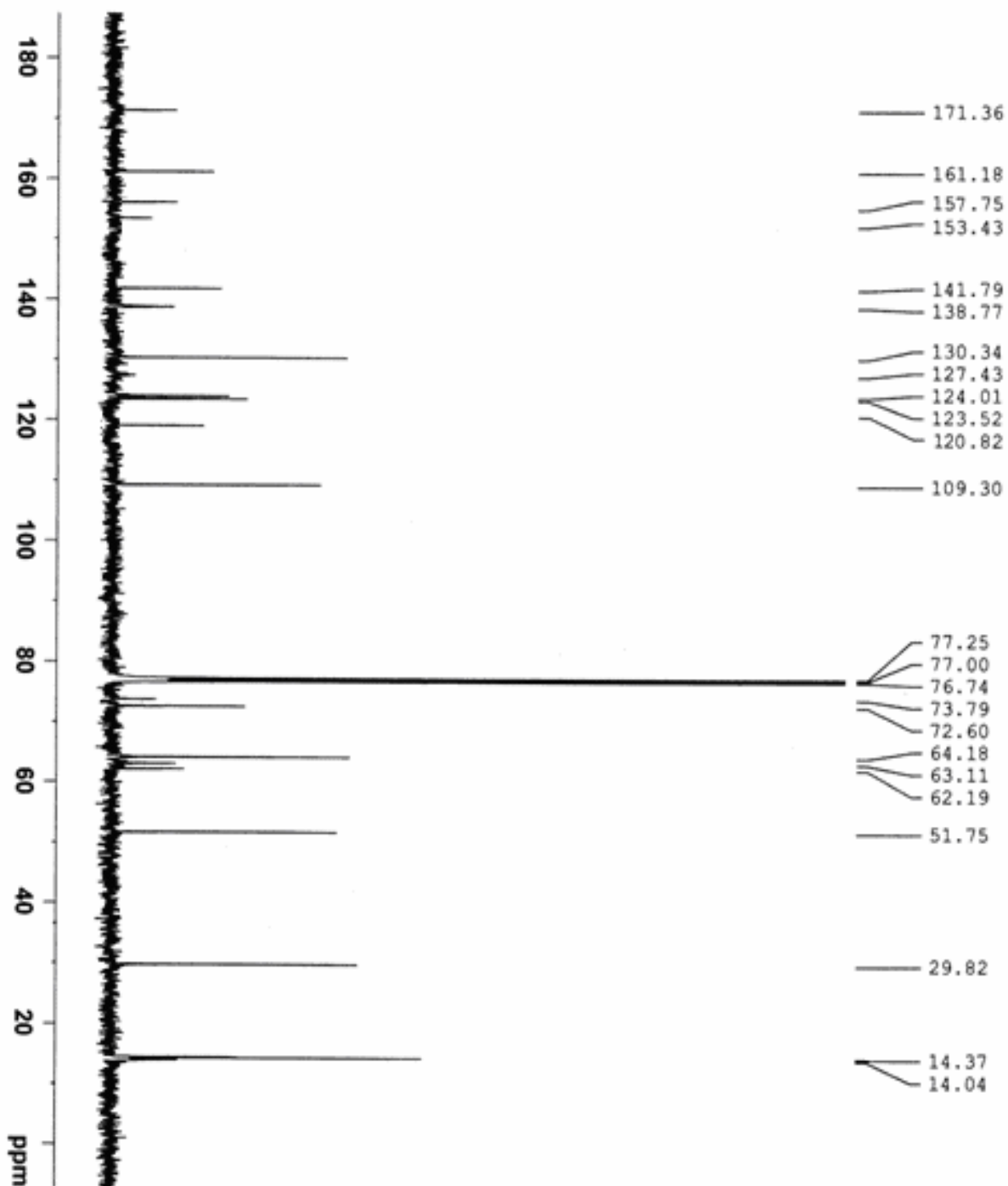
S44

Compound 7g- ^1H NMR (500 MHz)



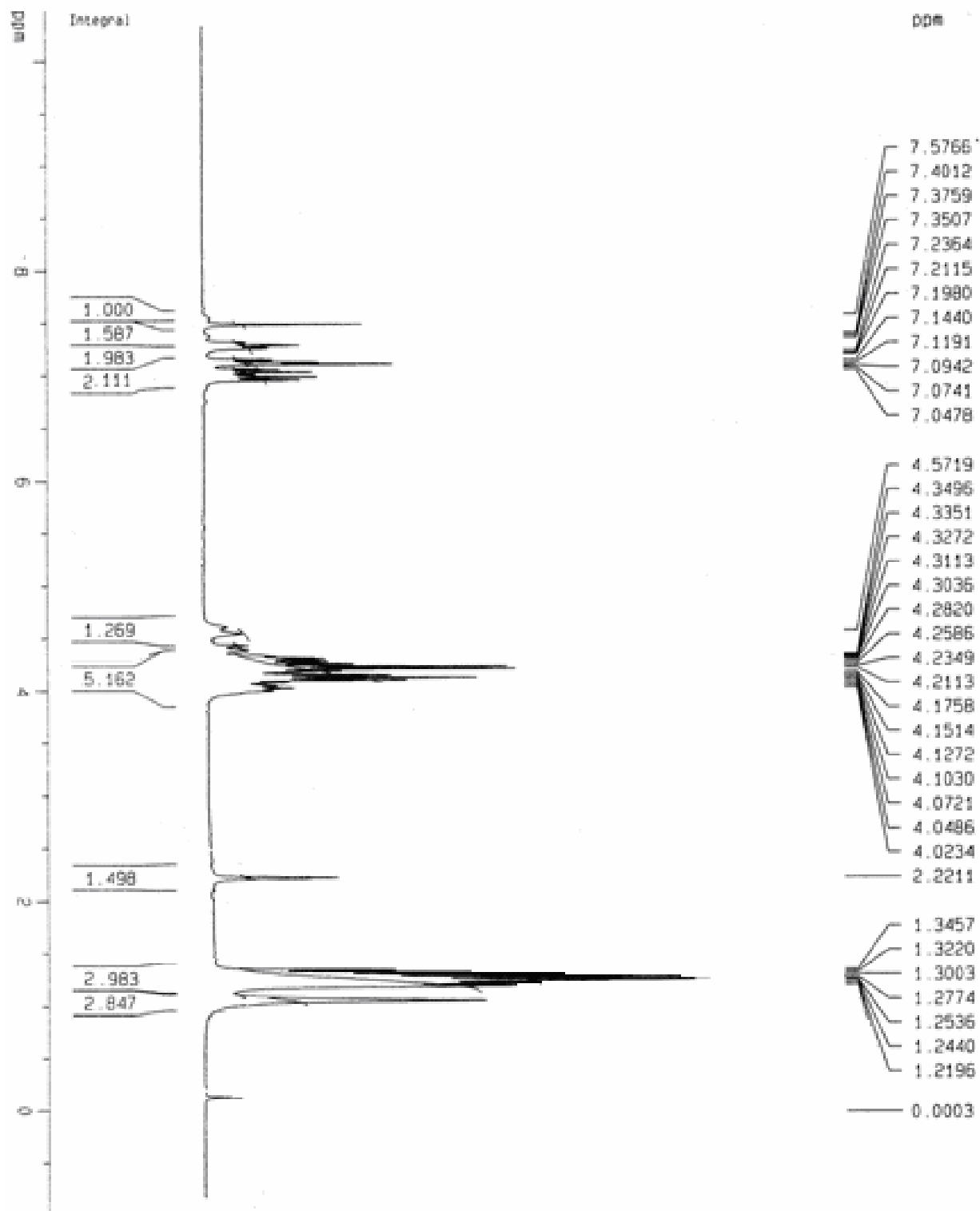
S45

Compound 7g- ^{13}C NMR (500 MHz)



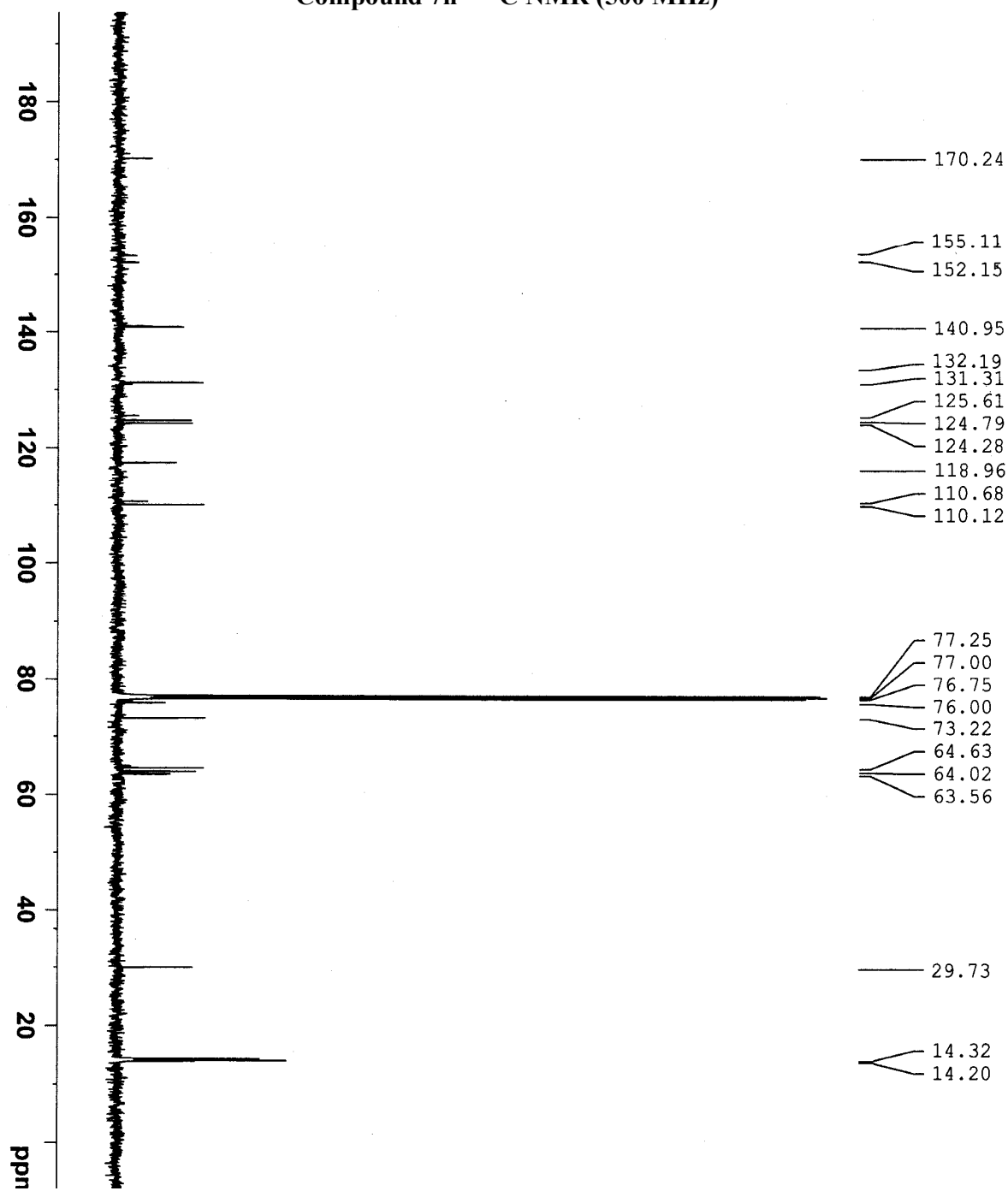
S46

Compound 7h- ¹H NMR (300 MHz)



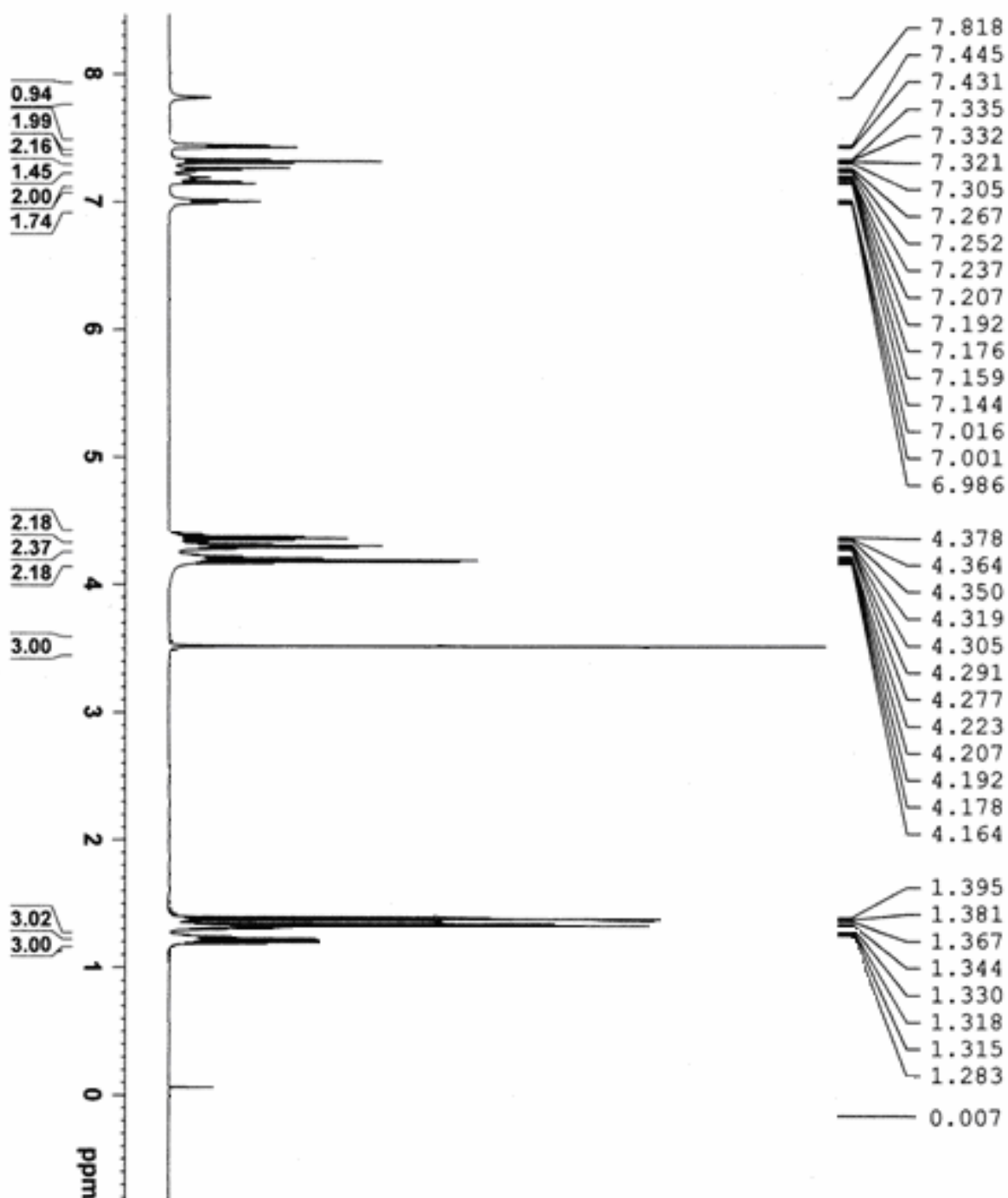
S47

Compound 7h- ^{13}C NMR (500 MHz)

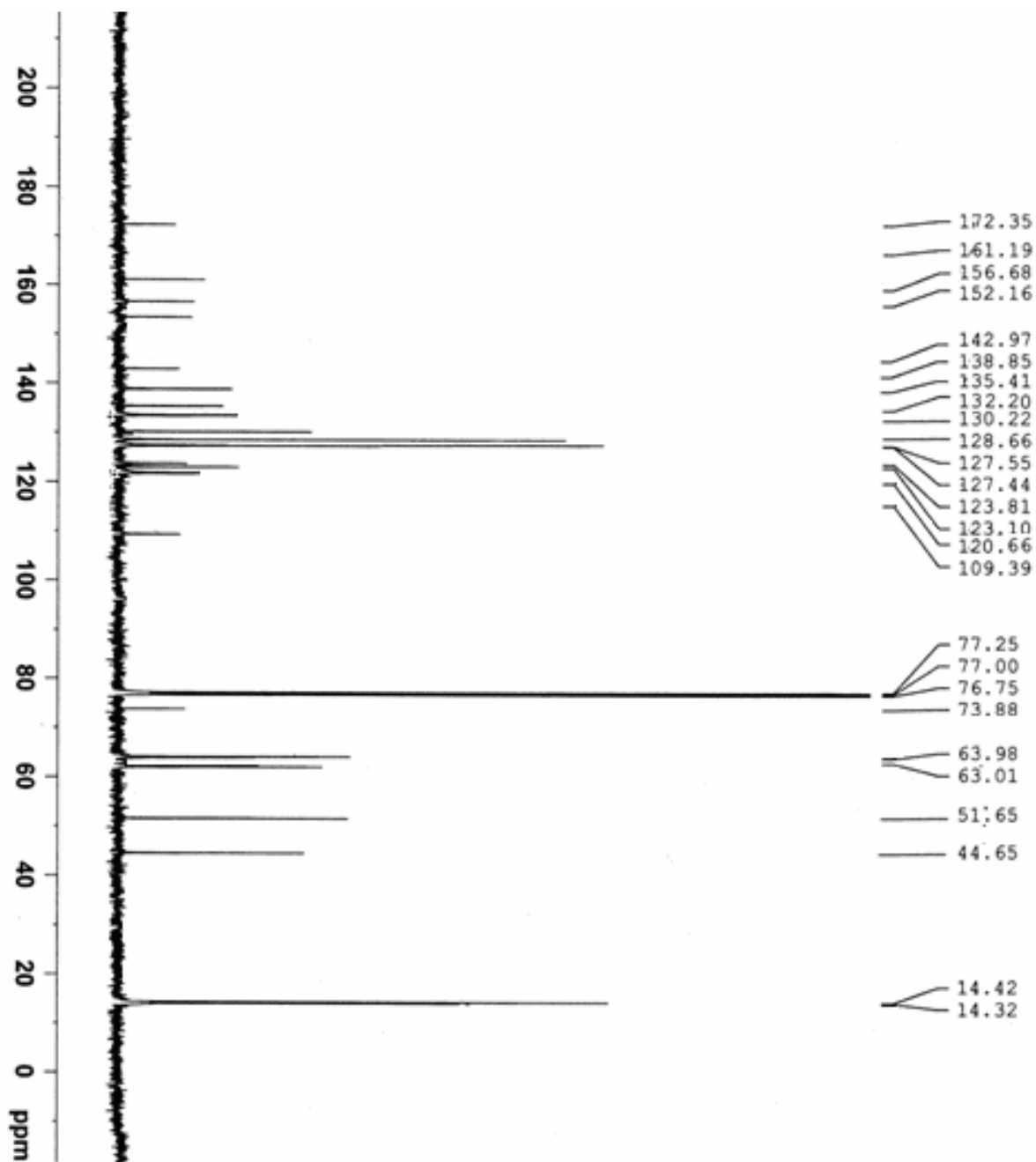


S48

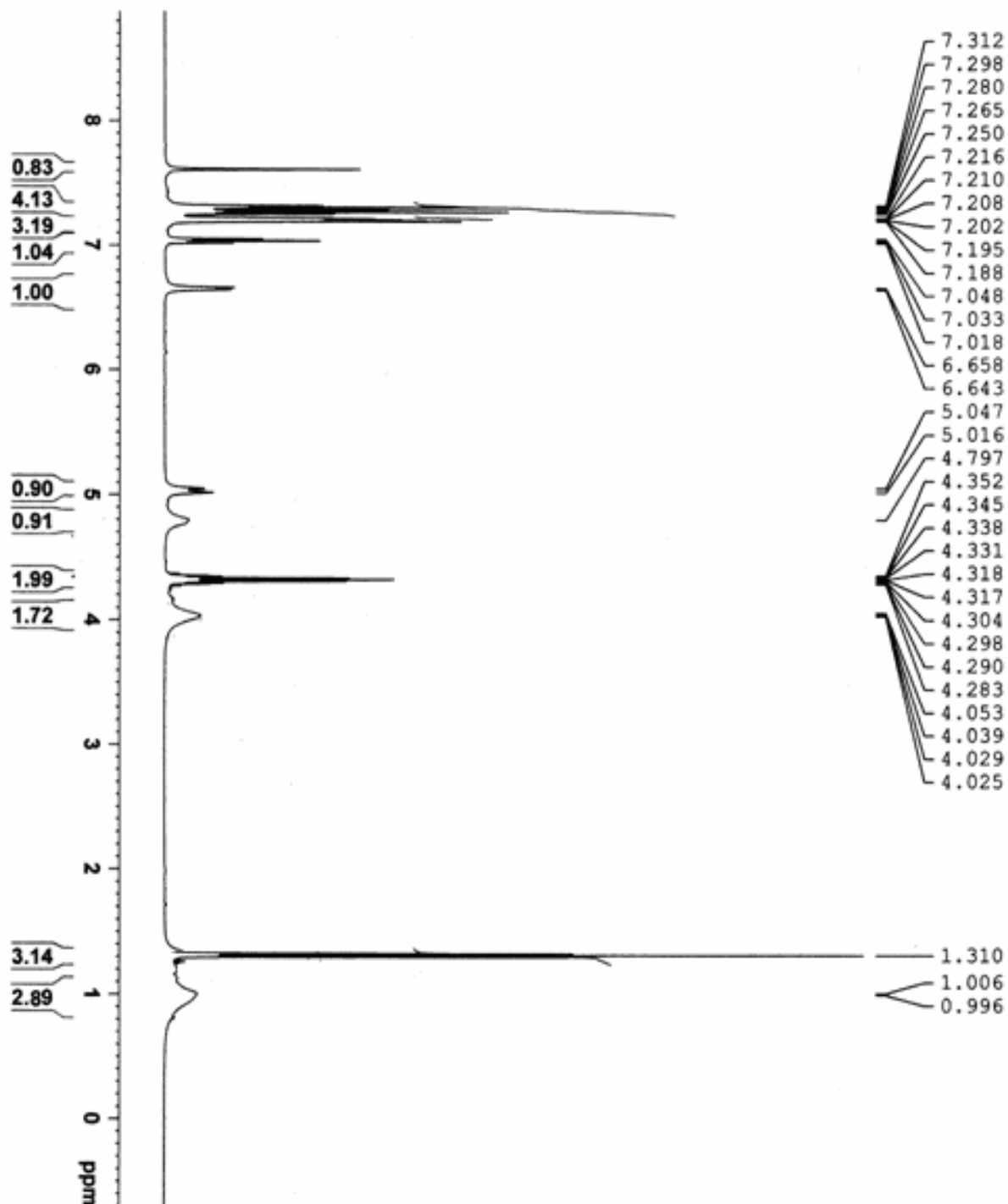
Compound 7i ^1H NMR (500 MHz)

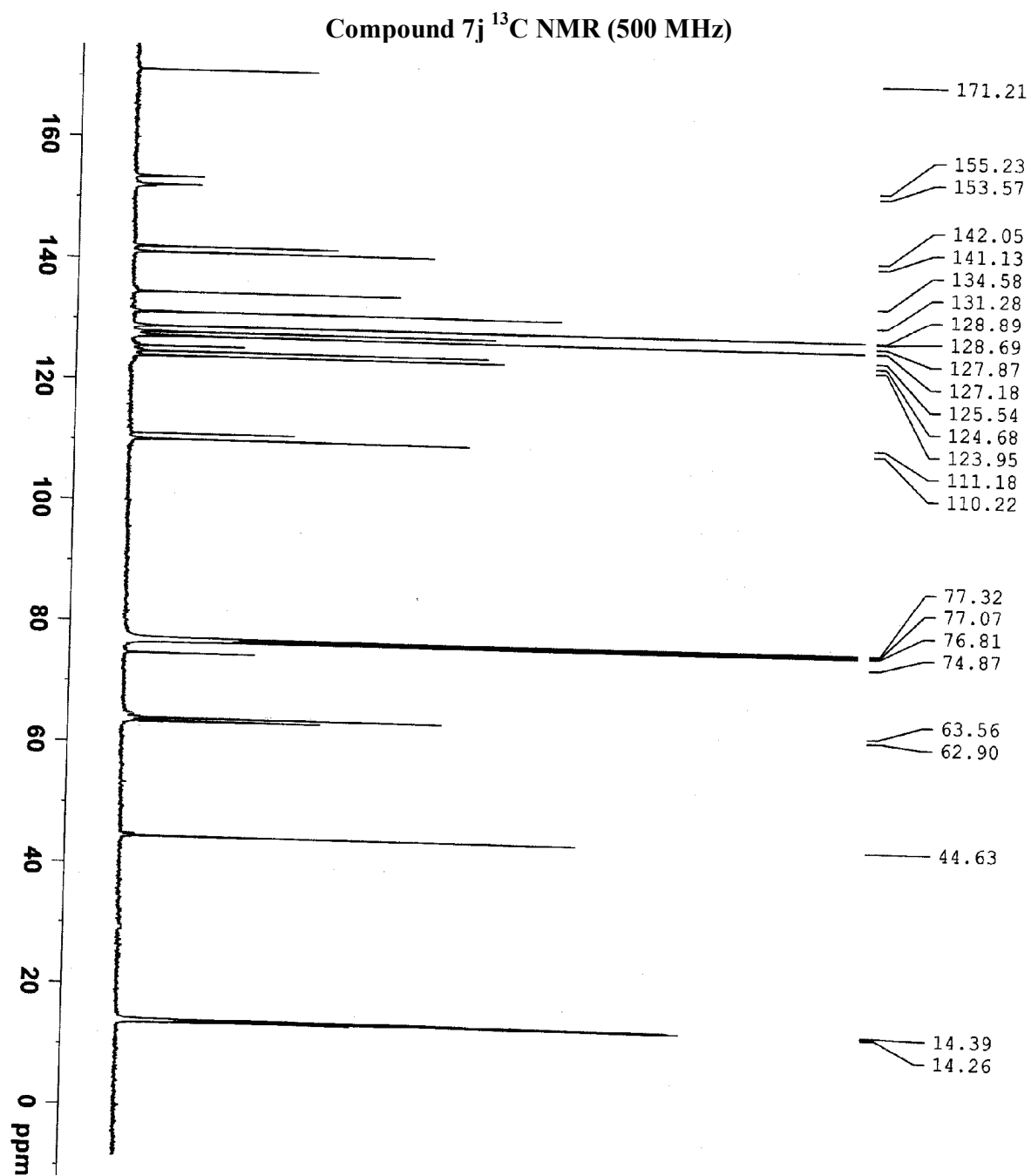


Compound 7i ^{13}C NMR (500 MHz)

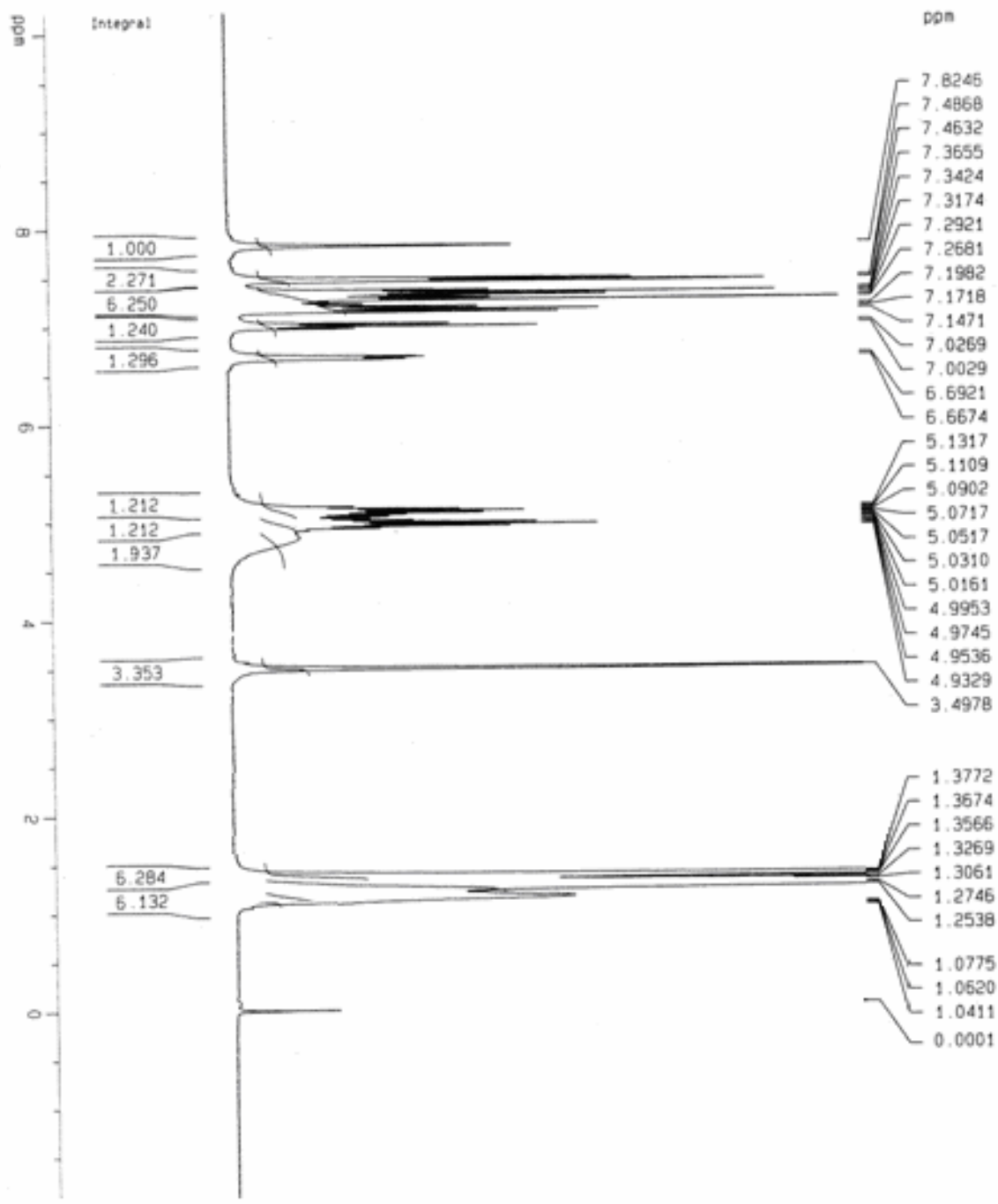


Compound 7j ^1H NMR (500 MHz)

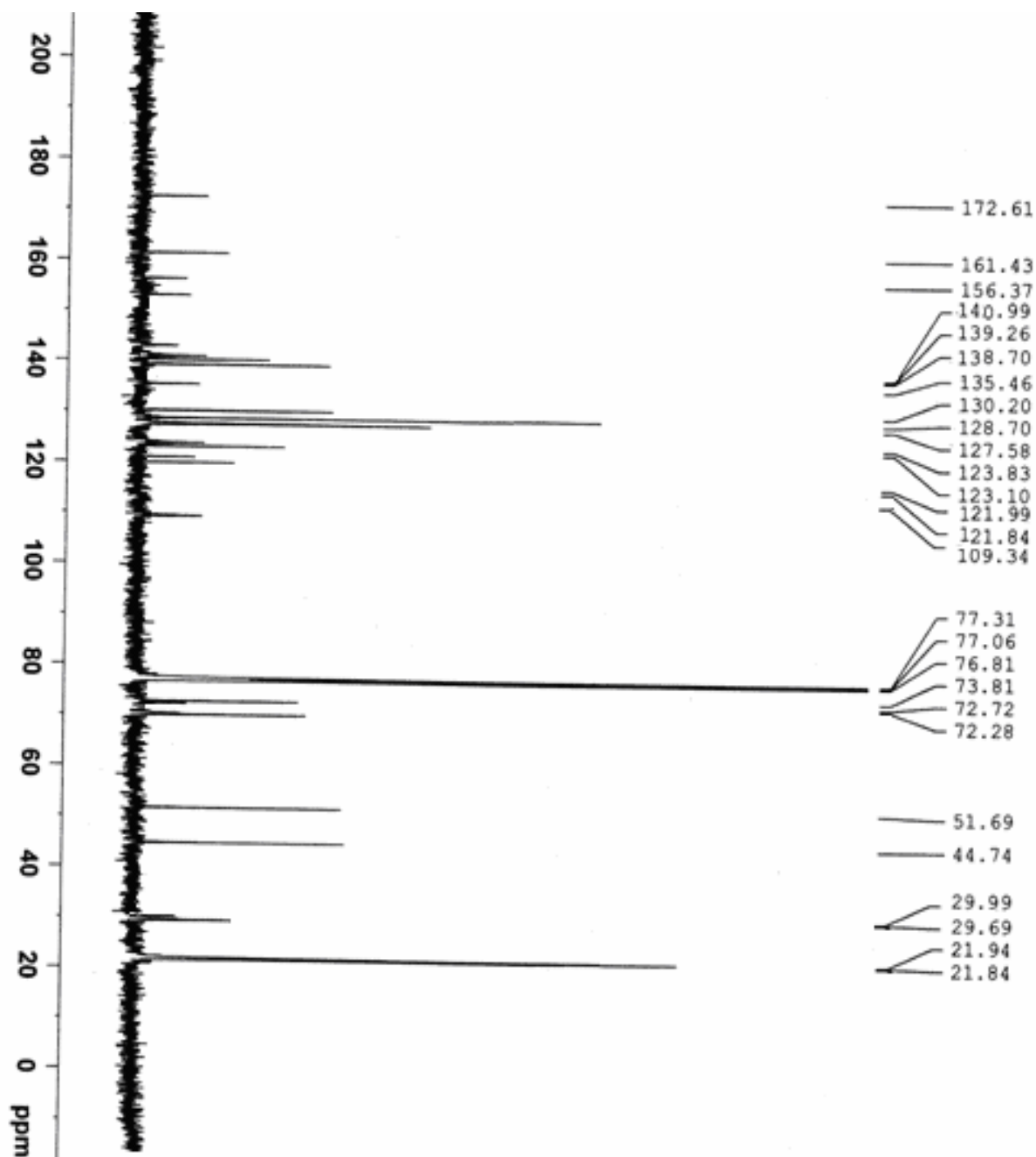




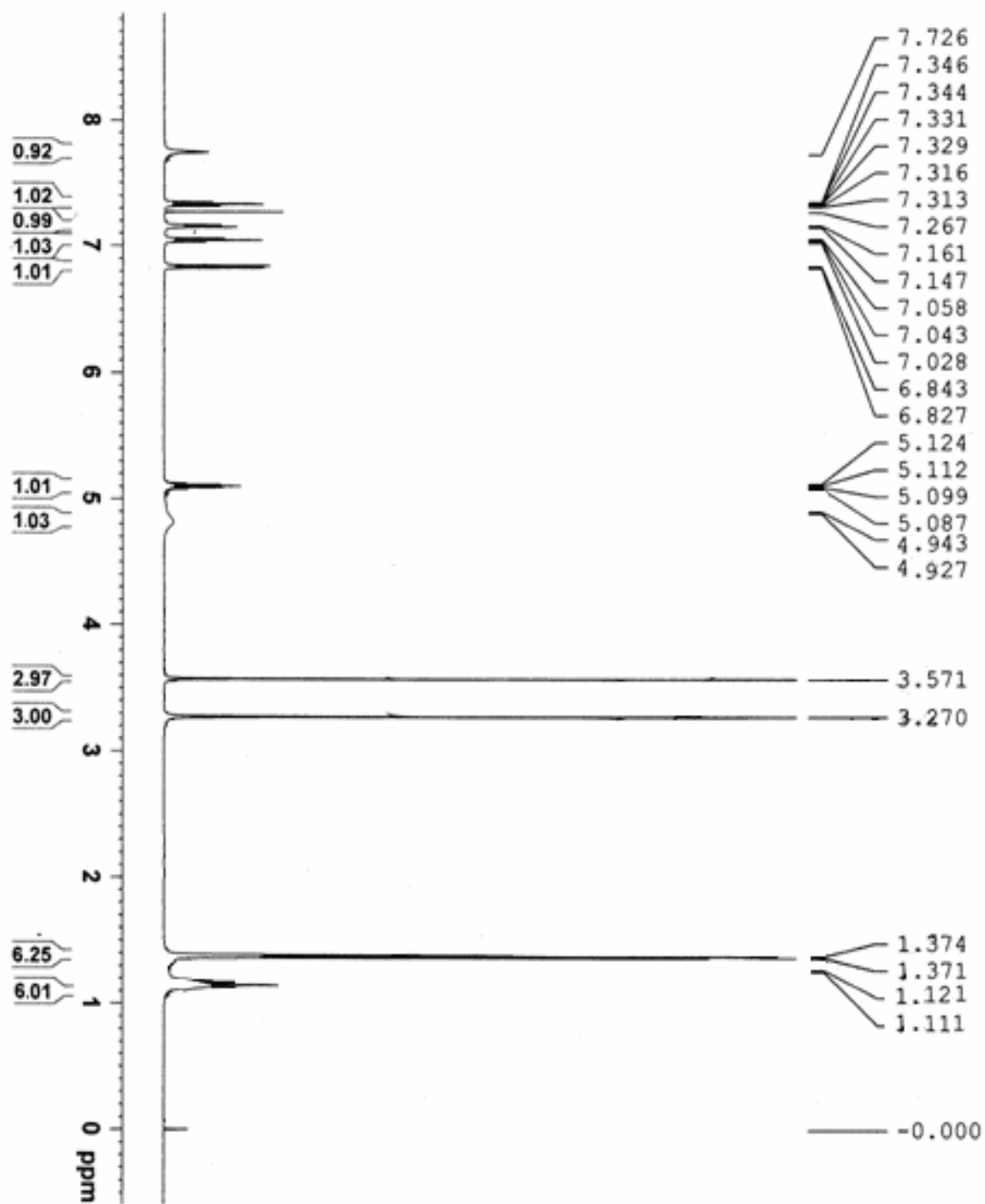
Compound 7k ^1H NMR (300 MHz)



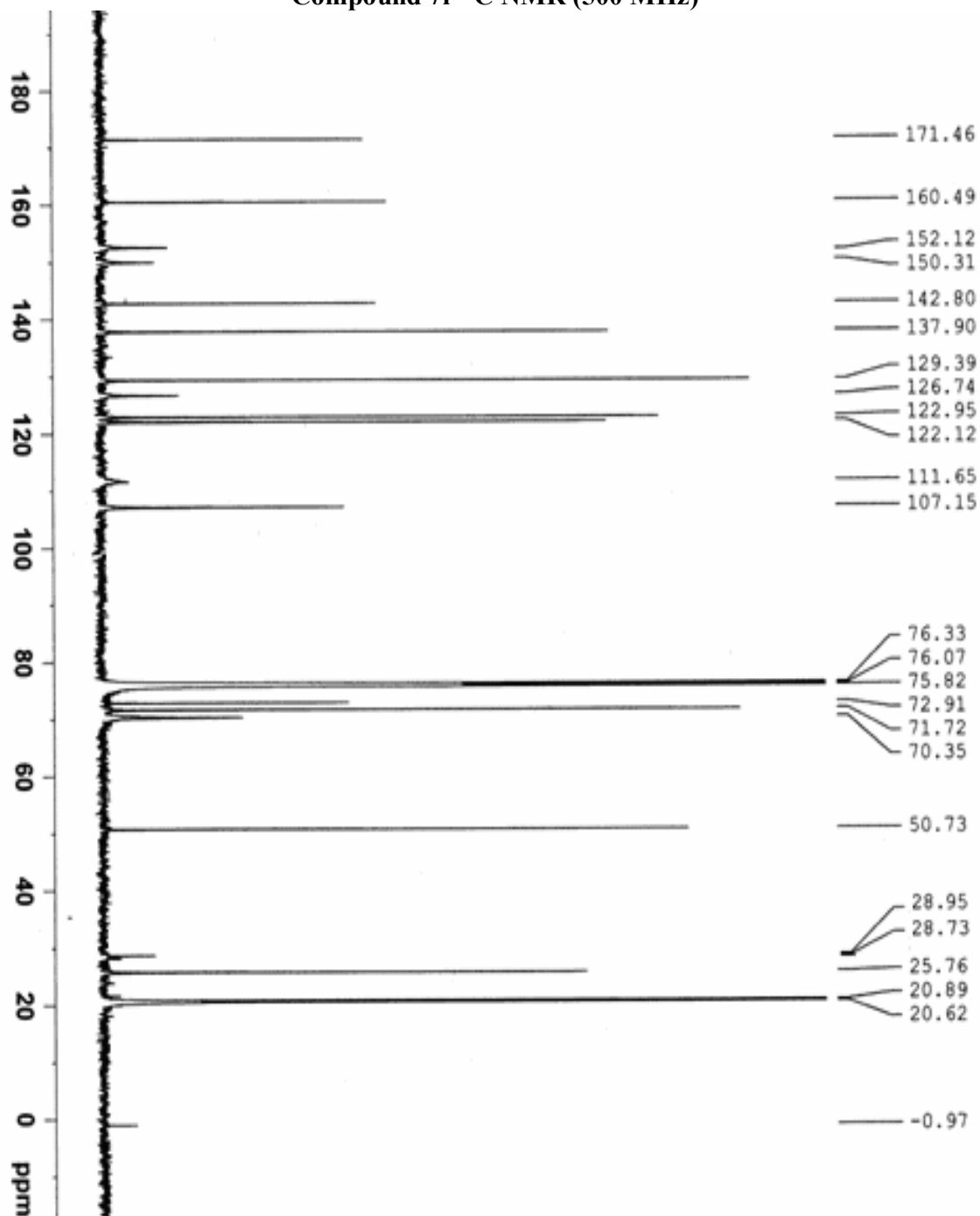
Compound 7k ^{13}C NMR (500 MHz)



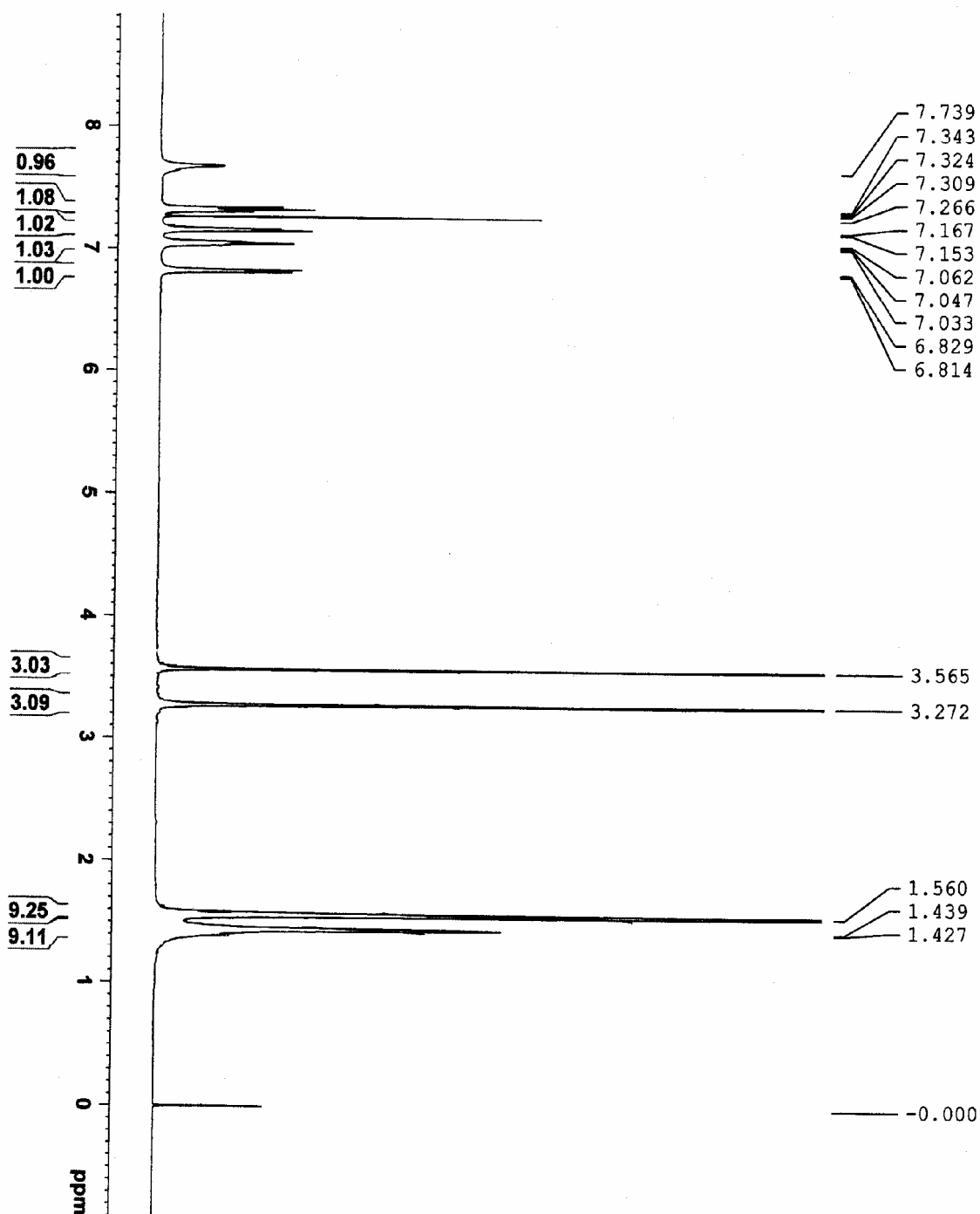
Compound 71 ^1H NMR (500 MHz)



Compound 71 ^{13}C NMR (500 MHz)



Compound 7m ^1H NMR (500 MHz)



S57

Compound 7m ^1H NMR (500 MHz)

