Supplementary Information

Enantioselective Total Synthesis of a Novel Polyketide Natural Product (+)-Integrasone, an HIV-1 Integrase Inhibitor

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Selected spectral data:

(-)-**8**: $[\alpha]^{26}_{D}$ –133.9 (*c* 2.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.91 (d, *J* = 12.6 Hz, 1H), 4.73 (d, *J* = 15 Hz, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 4.52 (d, *J* = 15.3 Hz, 1H), 3.84-3.82 (dd, *J* = 1.5, 3.6 Hz, 1H), 3.70 (d, *J* = 3.0 Hz, 1H), 3.55 (d, *J* = 3.0, 1.0 Hz, 1H), 2.01 (s, 3H), 0.99 (t, *J* = 7.8 Hz, 9H), 0.68 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.4, 170.6, 154.6, 126.4, 64.6, 62.9, 56.2, 55.7, 52.6, 20.7, 6.6, 4.1; HRMS (ES) m/z calcd for $C_{16}H_{26}O_6SiNa$ $[M + Na]^+$ 365.1396, found 365.1410.

(-)-**9**: $[\alpha]^{24}_{D}$ –23.1 (*c* 0.91, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.74 (d, *J* = 12.3 Hz, 1H), 4.69 (d, *J* = 12.3 Hz, 1H), 4.60 (br s, 2H), 4.56 (s, 1H), 4.21 (d, *J* = 12.2 Hz, 1H), 3.70 (d, *J* = 1.8 Hz, 1H), 3.56 (t, *J* = 3,6 Hz, 1H), 3.50 (dd, *J* = 4.2, 1.5 Hz, 1H), 2.03 (s, 3H), 0.95 (t, *J* = 8.1 Hz, 9H), 0.64 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 135.5, 127.6, 65.4, 65.1, 62.6, 59.2, 54.6, 53.9, 20.7, 6.5, 4.0; HRMS (ES) m/z calcd for $C_{16}H_{28}O_6SiNa$ $[M + Na]^+$ 367.1563, found 367.1563.

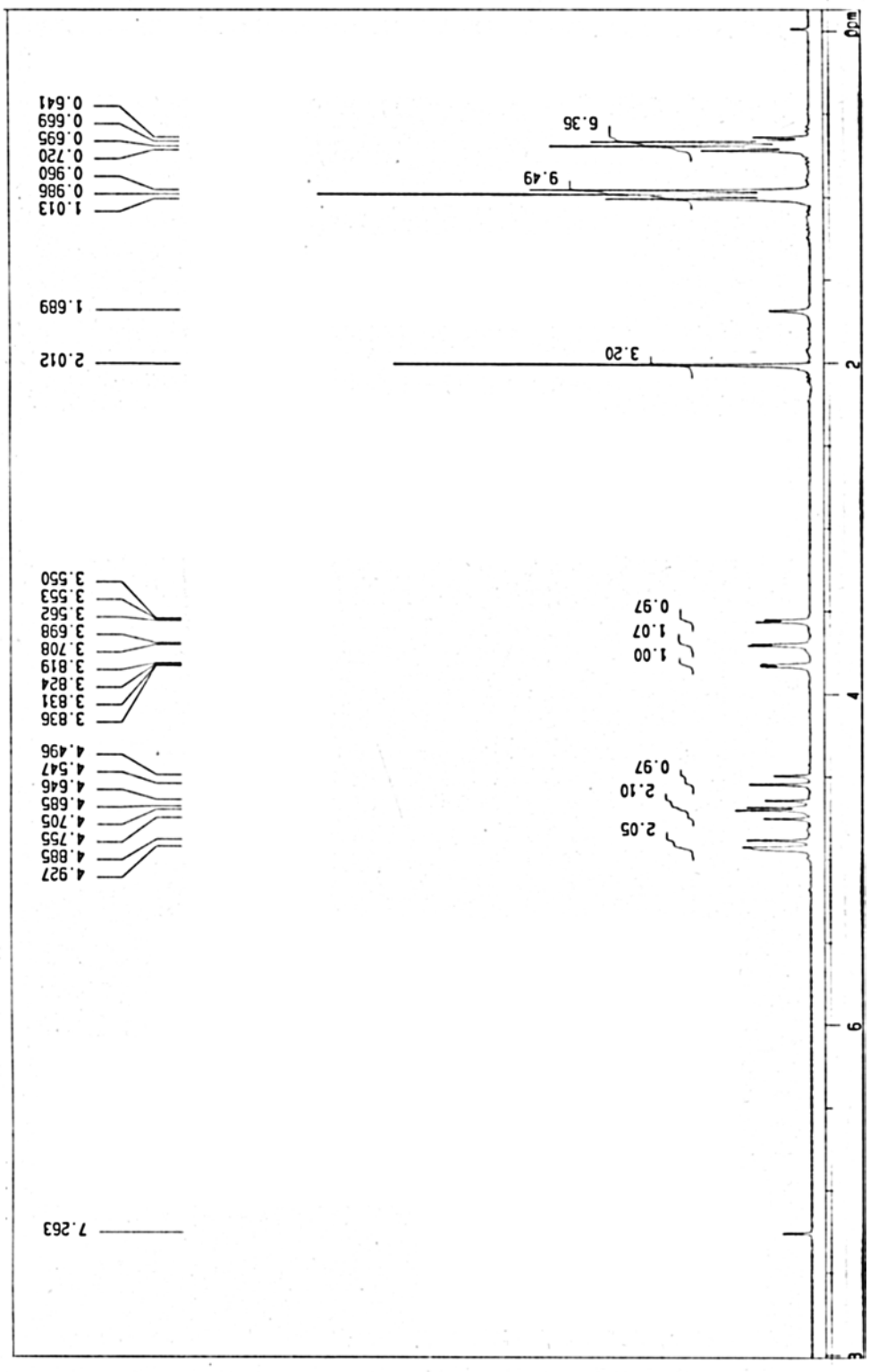
(-)-**10**: $[\alpha]^{24}_{D}$ –21.9 (*c* 1.96, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91 (br s, 1H), 5.89 (br s, 1H), 4.77 (d, *J* = 12.3 Hz, 1H), 4.65 (d, *J* = 12.9 Hz, 1H), 4.32 (d, *J* = 12.9 Hz, 1H), 4.17 (d, *J* = 12.9 Hz, 1H), 3.55 (t, *J* = 3.3 Hz, 1H), 3.43 (dd, *J* = 3.9, 1.8 Hz, 1H), 2.14 (s, 3H), 2.09 (s, 3H), 2.02 (s, 3H), 0.93 (t, *J* = 7.5 Hz, 9H), 0.58 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.4, 170.0, 134.7, 127.7, 67.3, 65.1, 59.6, 58.9, 51.4, 51.0, 20.9, 20.8, 20.6, 6.6, 4.1; HRMS (ES) m/z calcd for $C_{20}H_{32}O_8SiNa$ $[M + Na]^+$ 451.1764, found 451.1766.

(-)-**11**: $[\alpha]^{25}_{D}$ –48.4 (*c* 2.54, $CHCl_3$); IR (cm^{-1}): 1748, 1684; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.09 (s, 1H), 6.14 (s, 2H), 5.37 (d, *J* = 13.5 Hz, 1H), 4.88 (d, *J* = 13.2 Hz, 1H), 3.56 (s, 1H), 3.52 (s, 1H), 2.18 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 188.2, 170.5, 170.3, 170.0, 147.0, 133.5, 67.7, 62.6, 56.8, 51.5, 50.8, 21.0, 20.9, 20.8; HRMS (ES) m/z calcd for $C_{14}H_{16}NaO_8$ $[M + Na]^+$ 335.0743, found 335.0737.

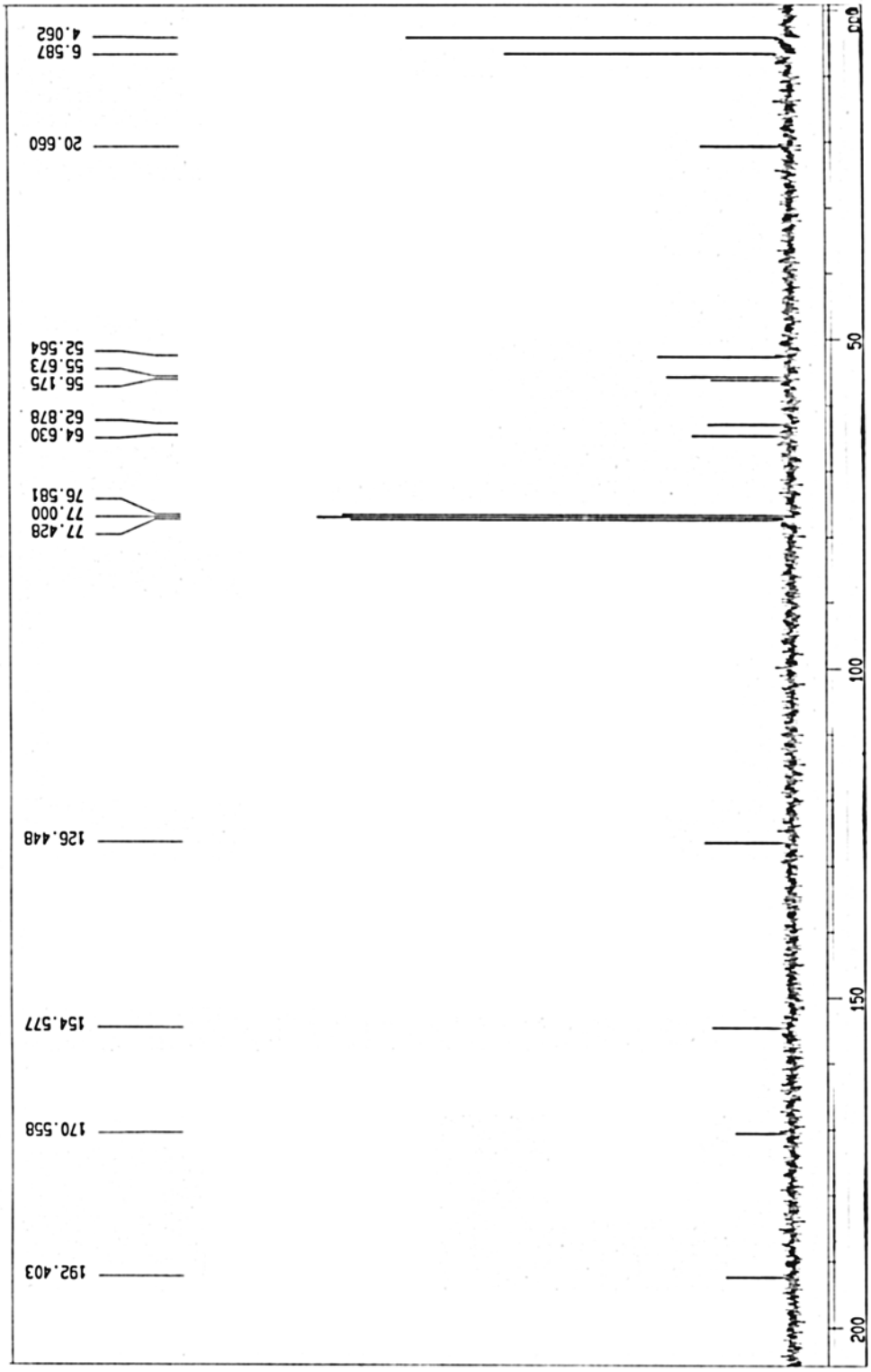
(-)-**12**: $[\alpha]^{26}_{D}$ –3.5 (*c* 0.86, $CHCl_3$); IR (cm^{-1}): 3454, 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 5.93 (s, 1H), 5.64 (dd, *J* = 8.5, 5.7 Hz, 1H), 4.80 (d, *J* = 12.6 Hz, 1H), 4.71 (d, *J* = 12.3 Hz, 1H), 4.69 (s, 1H), 3.54 (t, *J* = 4.2, 2.4 Hz, 1H), 3.49 (dd, *J* = 4.2, 2.1 Hz, 1H), 2.13 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.78 (m, 1H, H-10), 1.51 (m, 1H, H-10), 1.27 (br s, 9H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 170.5, 170.4, 137.1, 127.3, 73.0, 67.6, 63.2, 58.8, 52.8, 50.9, 33.6, 31.5, 28.9, 25.2, 22.5, 21.1, 20.8, 20.7, 14.0; HRMS (ES) m/z calcd for $C_{20}H_{30}NaO_8$ $[M + Na]^+$ 421.1838, found 421.1835.

15: IR (cm^{-1}): 3384; ^1H NMR (300 MHz, CD_3OD) δ 4.68 (m, 1H), 4.67 (s, 1H), 4.57 (s, 1H), 4.30 (d, *J* = 12.3 Hz, 1H), 4.22 (d, *J* = 12 Hz, 1H), 3.46 (t, *J* = 3.6 Hz, 1H), 3.36 (dd, *J* = 4.1, 2.4 Hz, 1H), 1.60 (m, 1H, H-10), 1.44 (m, 1H, H-10), 1.29 (br s, 9H), 0.89 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 137.0, 133.8, 71.9., 66.6, 64.5, 58.1, 55.1, 54.8, 37.5, 32.9, 30.4, 26.6, 23.7, 14.4; HRMS (ES) m/z calcd for $C_{14}H_{24}NaO_5$ $[M + Na]^+$ 295.1521, found 295.1520.

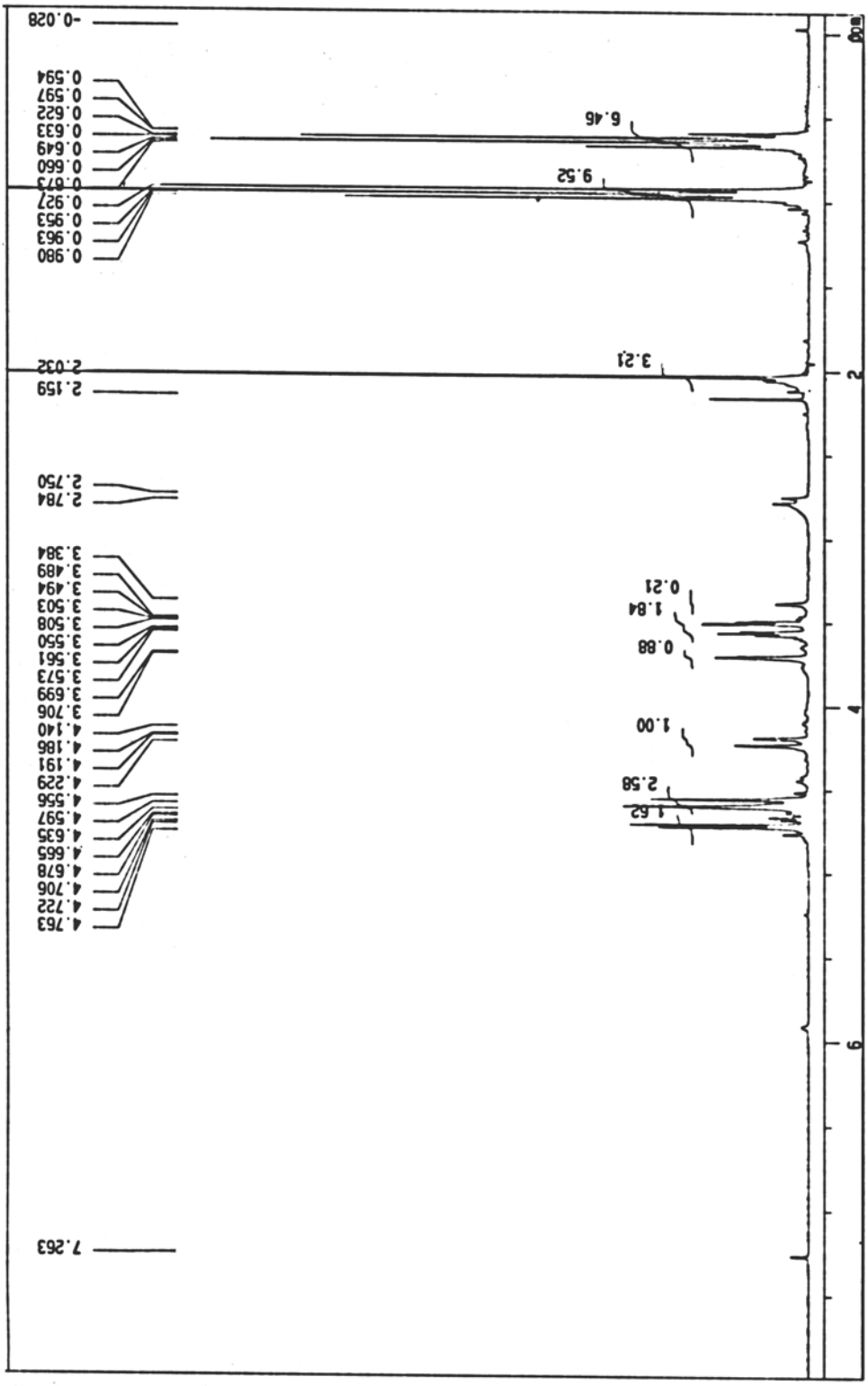
(+)-3. (Synthetic) ^1H NMR (500 MHz, CD_3OD) δ 4.98 – 4.97 (m, 1H), 4.78 (brs, 1H), 4.67 (brs, 1H), 3.54 (t, *J* = 3.1 Hz, 1H), 3.47 (dd, *J* = 3.6, 0.9 Hz, 1H), 2.14 – 2.09 (m, 1H), 1.61 – 1.56 (m, 1H), 1.49 – 1.27 (series of multiplets, 8H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, CD_3OD) δ 173.3, 162.0, 126.0, 84.5, 62.2, 62.1, 57.1, 55.8, 34.2, 32.8, 30.2, 25.9, 23.6, 14.4. *cf.* **(+)- 3** (Natural) ^{13}C NMR (125 MHz, CD_3OD) δ 173.3, 162.0, 126.0, 84.4, 62.2, 62.1, 57.1, 55.7, 34.2, 32.8, 30.1, 25.9, 23.6, 14.4.



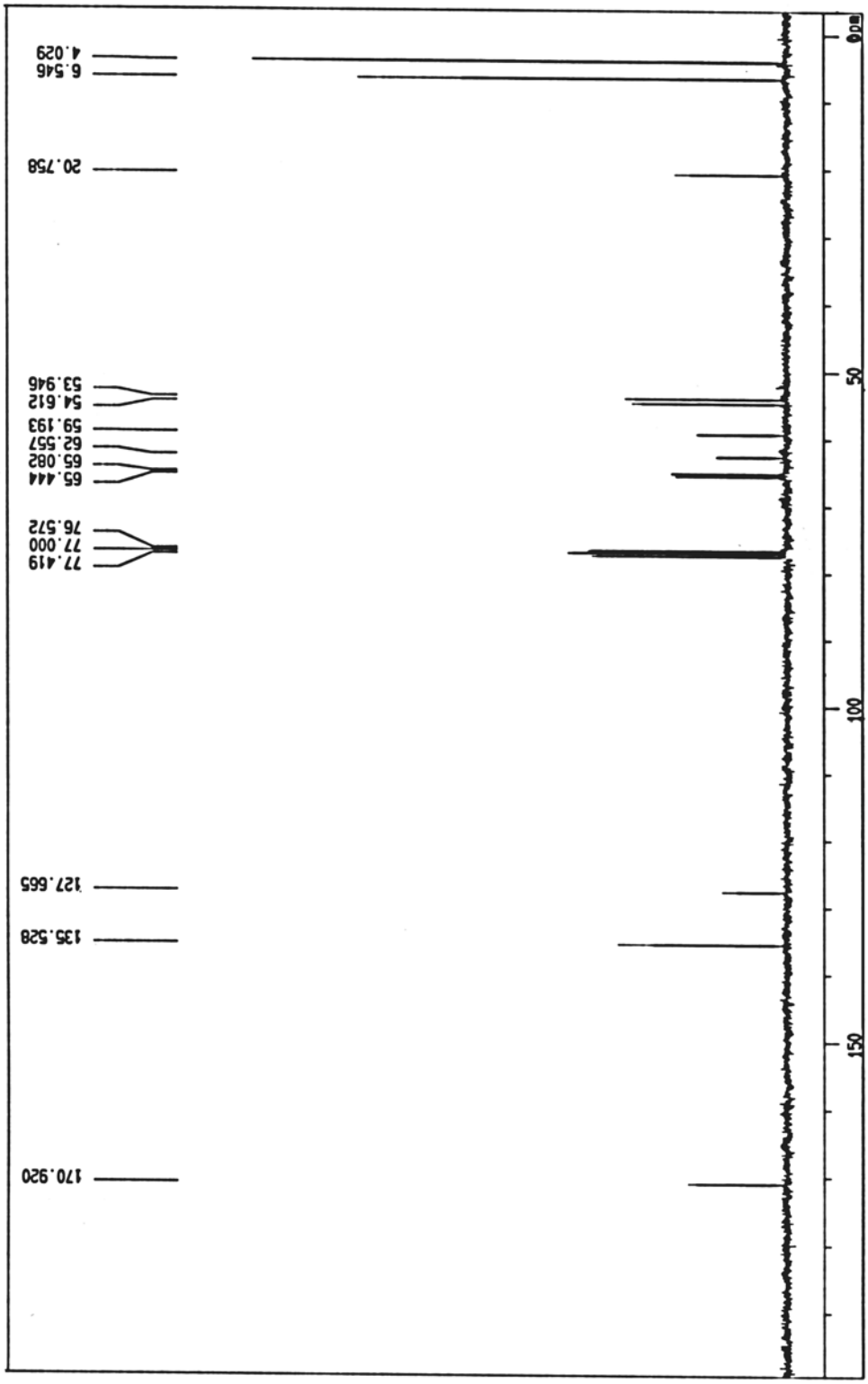
^{1}HNMR spectrum of compound **8**



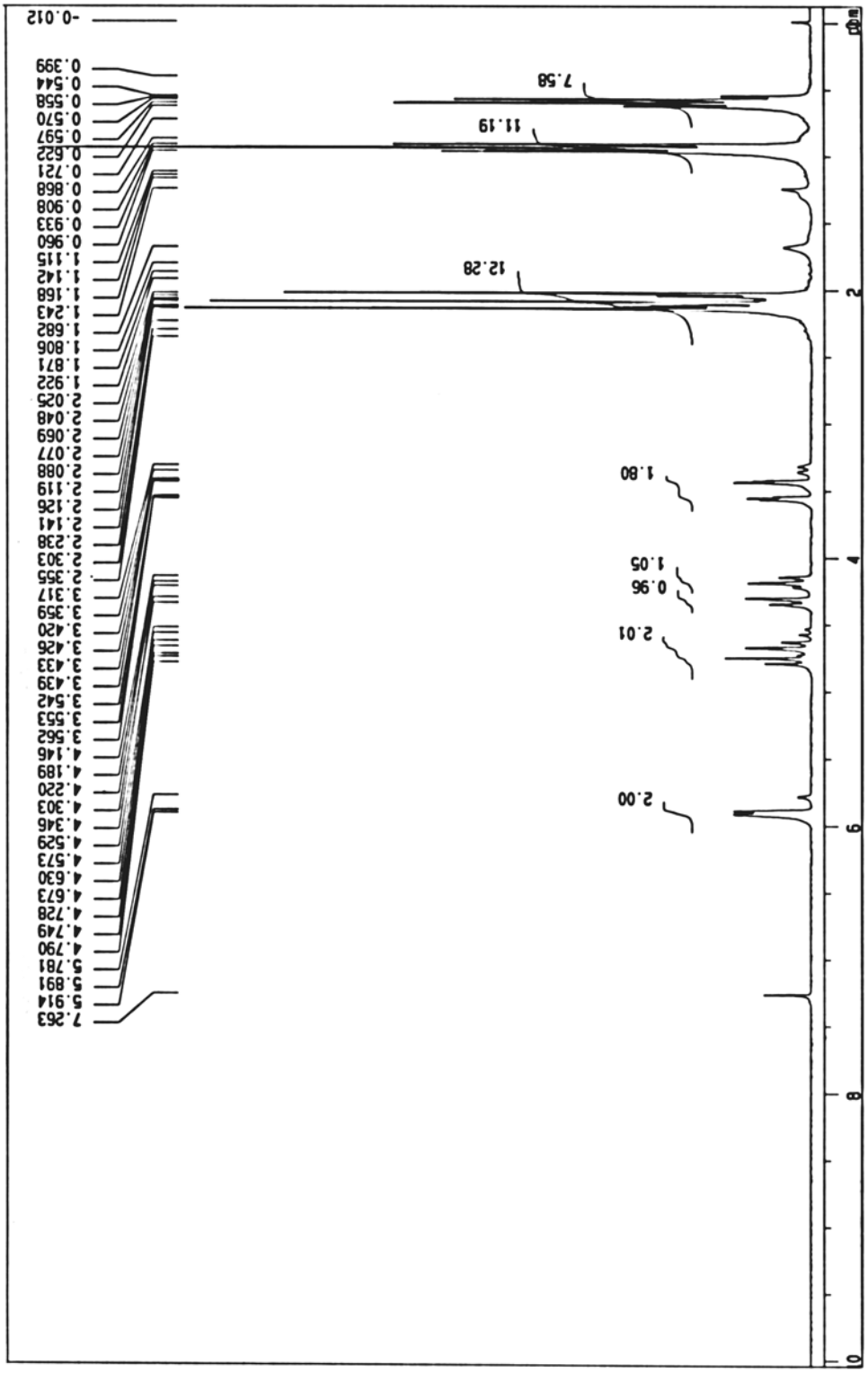
^{13}CNMR spectrum of compound **8**



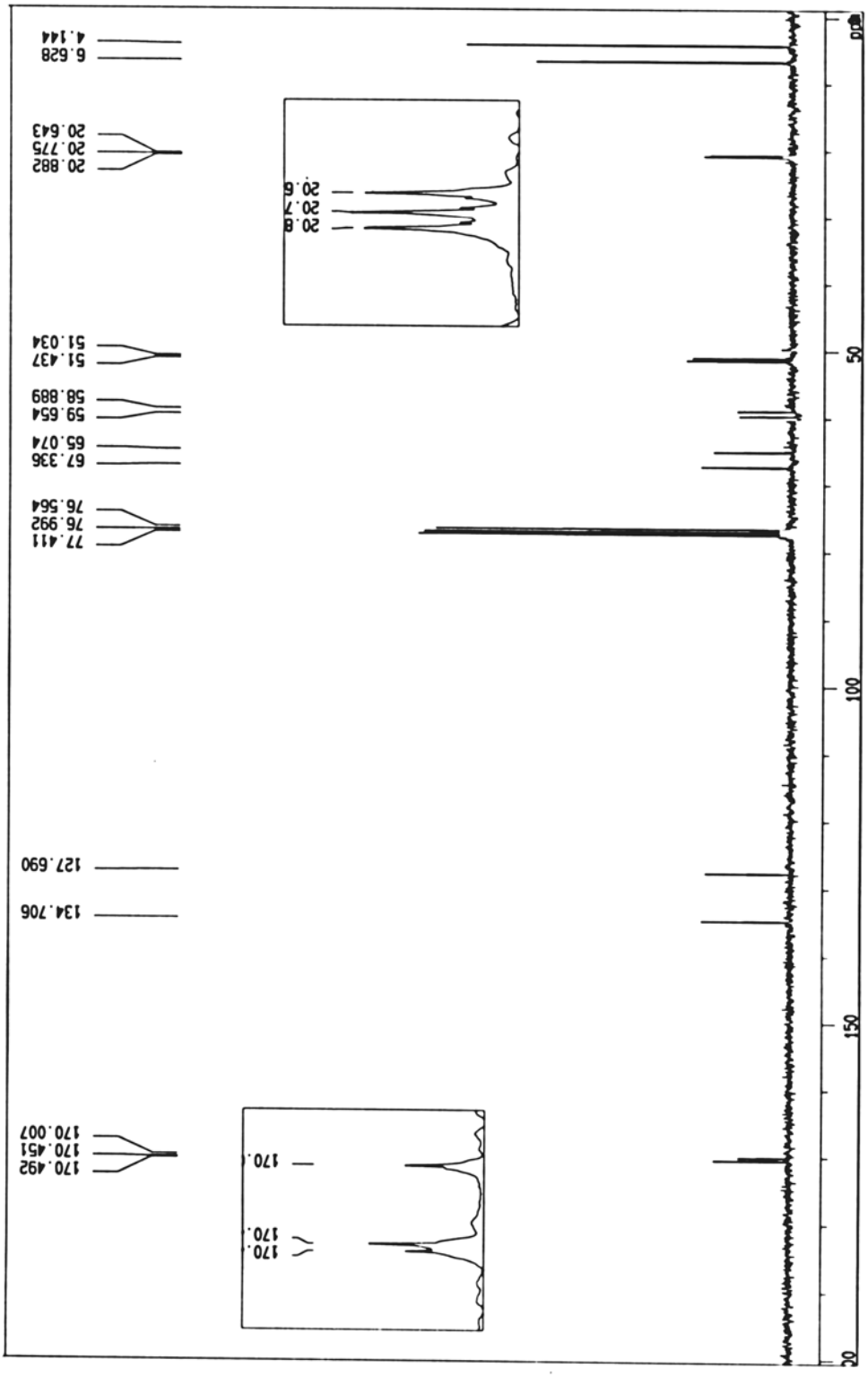
[1]HNMR spectrum of compound **9**



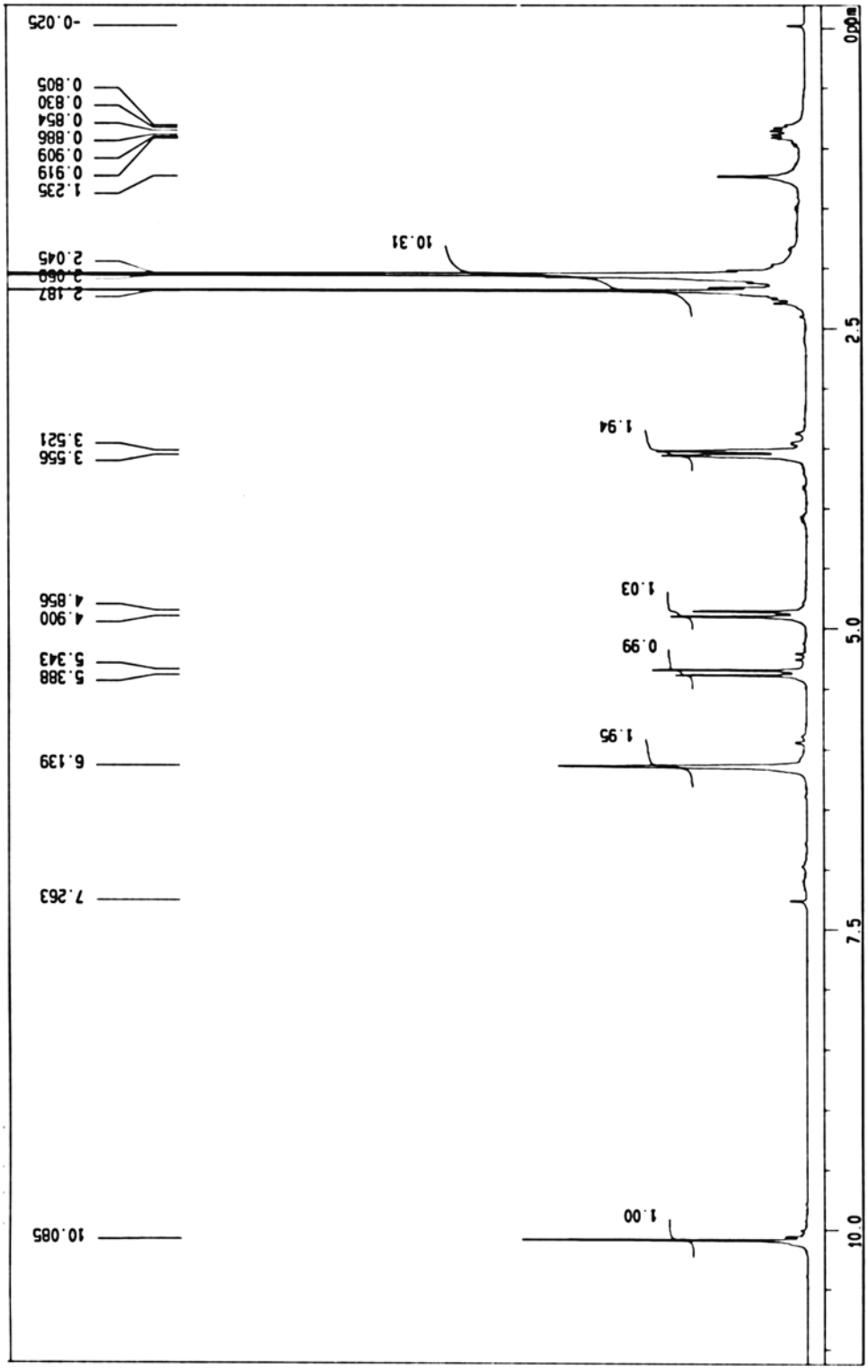
^{13}CNMR spectrum of compound **9**



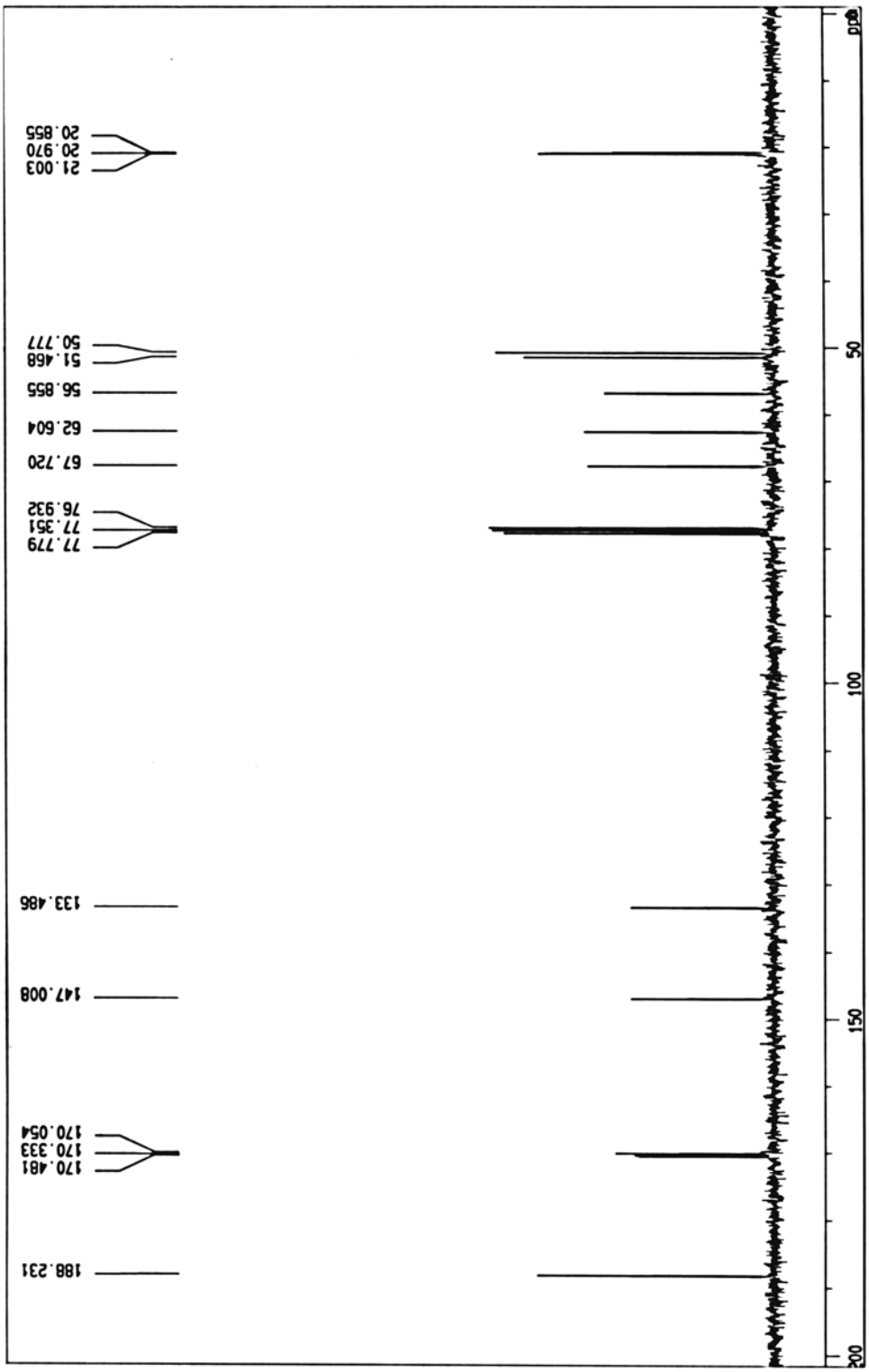
^{1}HNMR spectrum of compound **10**



^{13}CNMR spectrum of compound **10**



[1]HNMR spectrum of compound **11**



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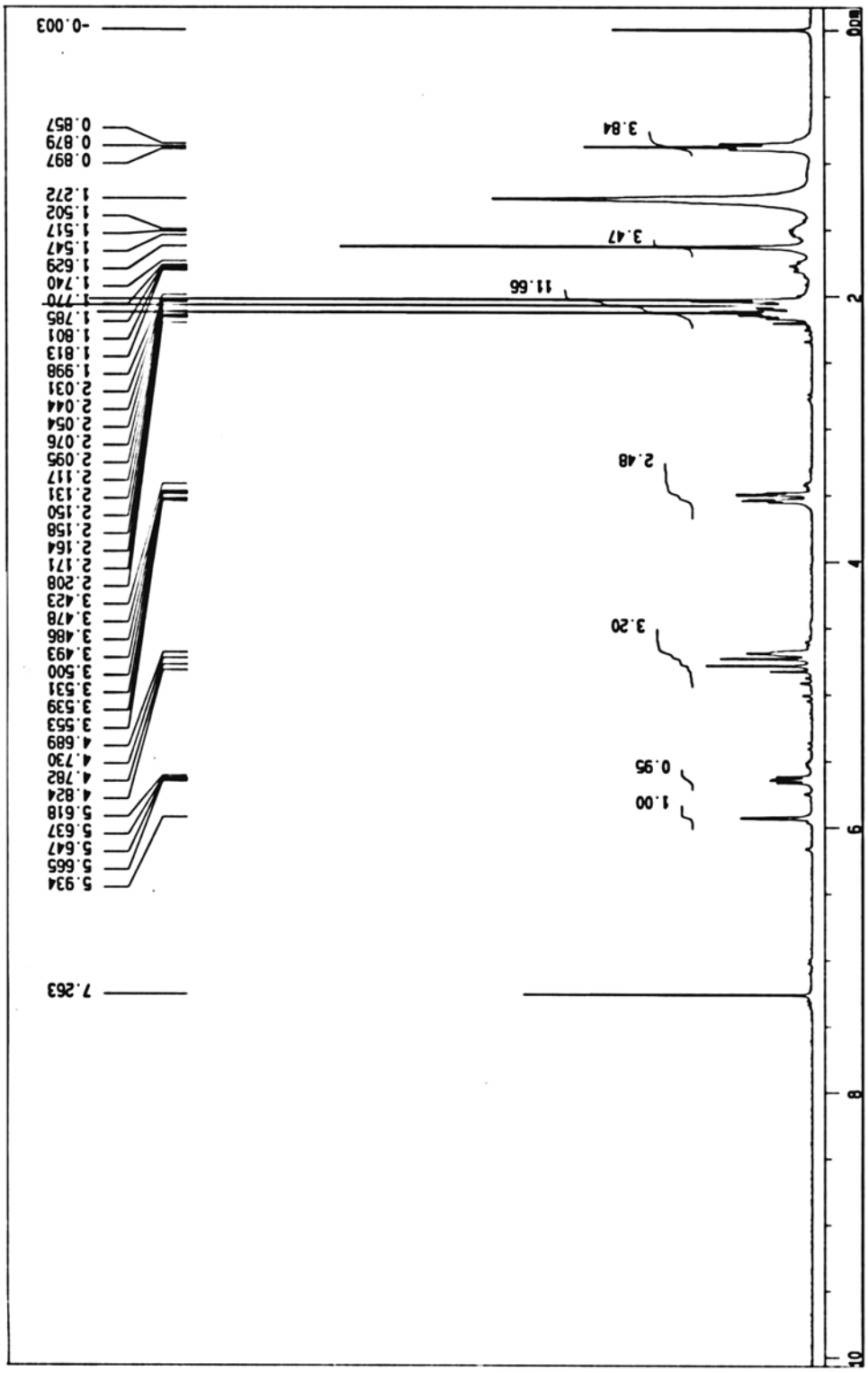

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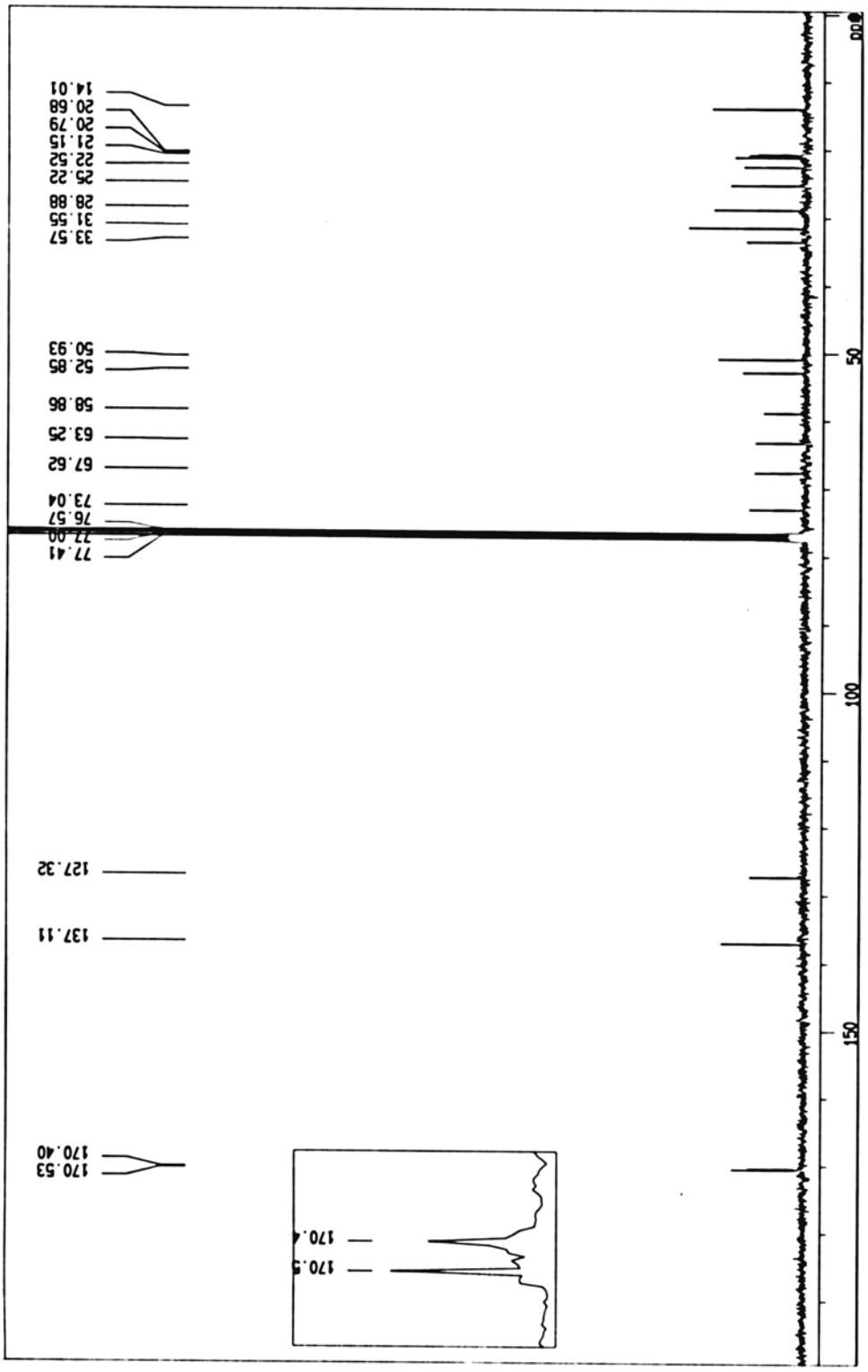
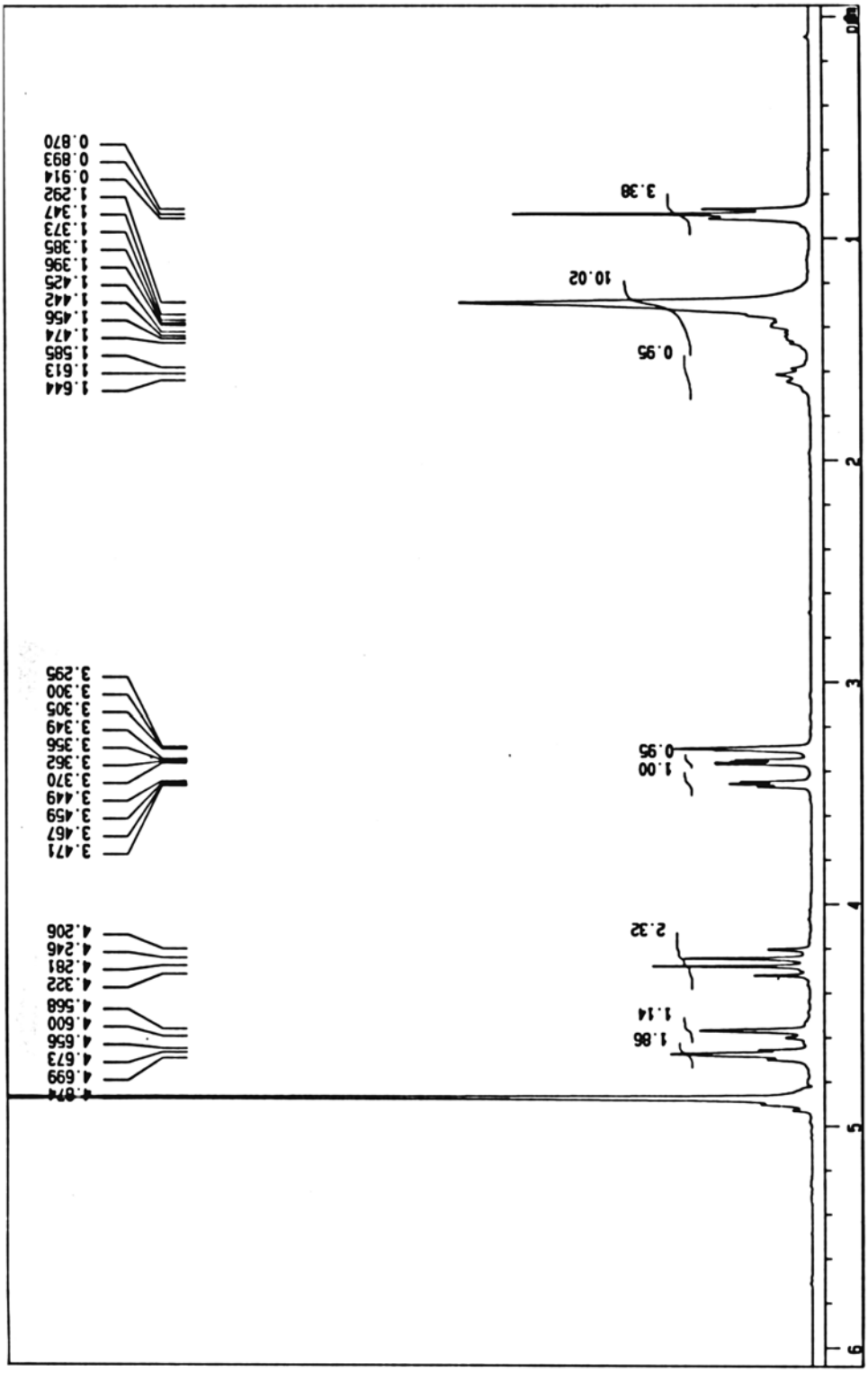
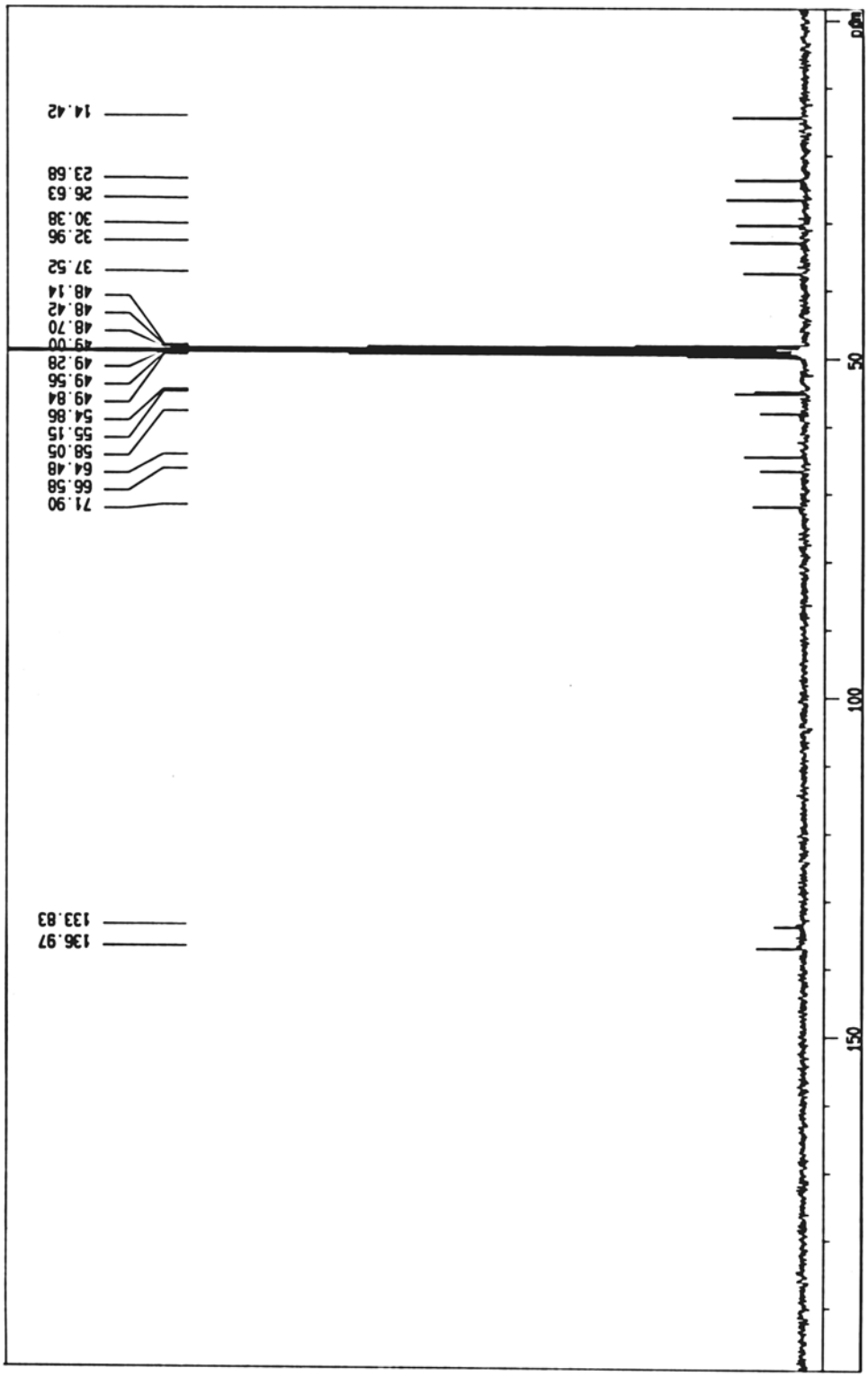


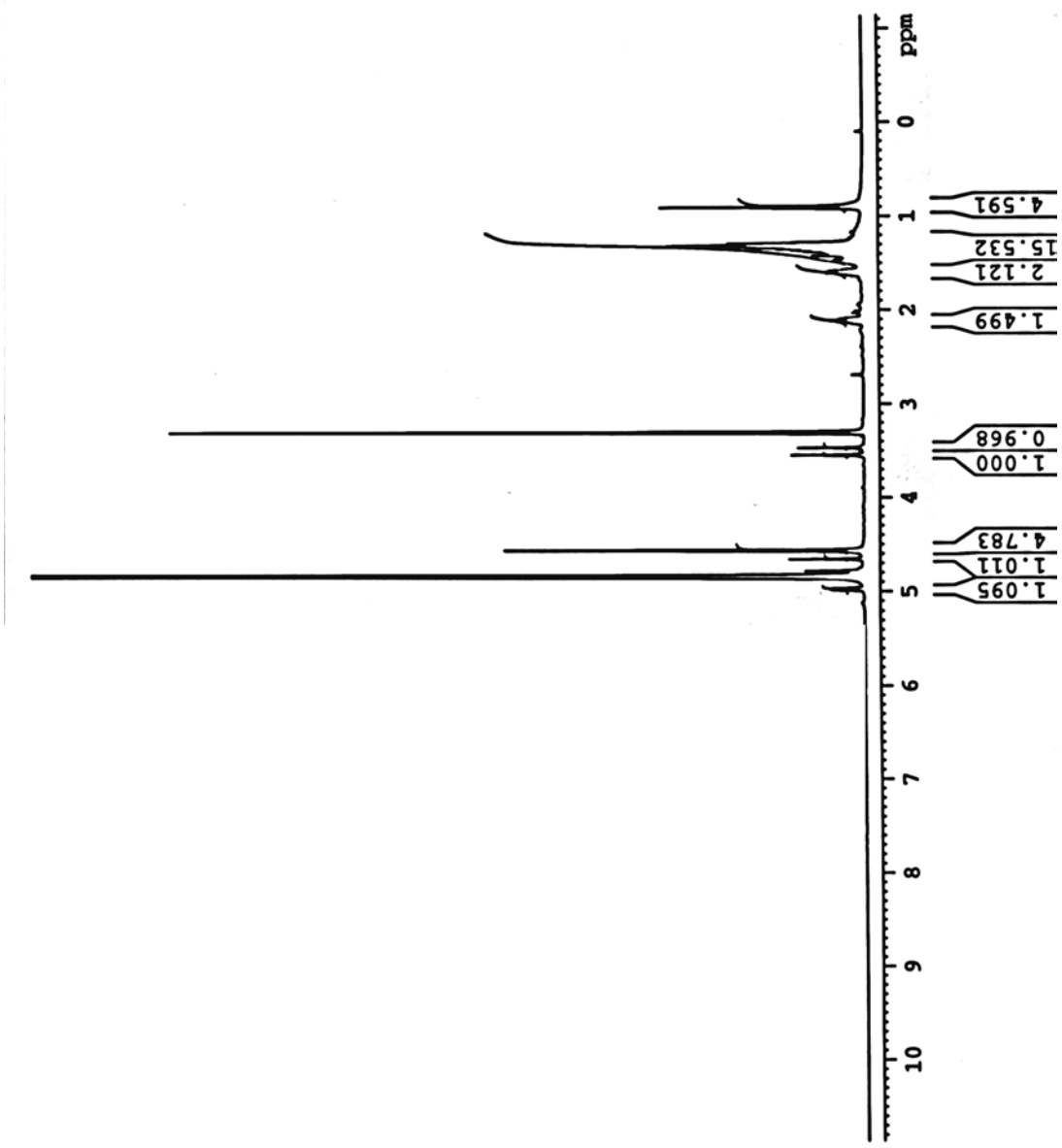
^{13}CNMR spectrum of compound **12**



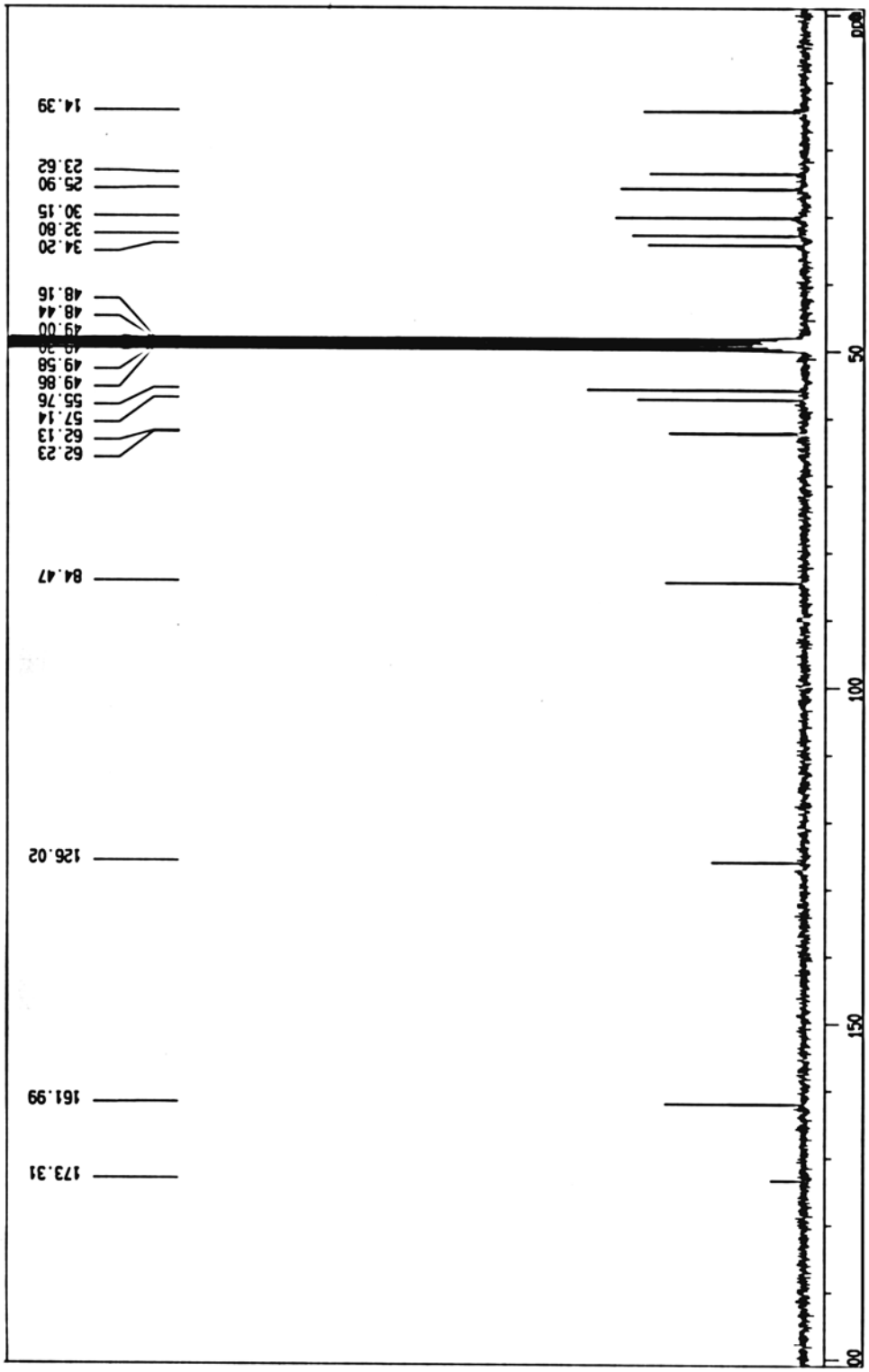
[1]HNMR spectrum of compound **15**



^{13}CNMR spectrum of compound **15**



[1]HNMR spectrum of compound **3** (synthetic integrasone)



^{13}CNMR spectrum of compound **3** (synthetic integrasone)