Substrate-Dependent Dihydroxylation of Substituted Cyclopentenes: Towards the Syntheses of Carbocyclic Sinefungin and Noraristeromycin

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Materials and Methods:

All chromatography was performed with silica gel unless otherwise noted; flash chromatography was conducted on silica gel 60 (mesh size 230-400). Solvents were distilled prior to use. ^{1}H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, in $CDCl_3$ unless specified otherwisethe; residual $CHCl_3$ was defined as 7.24 ppm and 77.00 ppm, respectively. Melting points are uncorrected. FT-IR spectra were recorded neat on NaCl plates.

(*S*)-7-Benzyl 1-*tert*-butyl 2-(*tert*-butoxycarbonyl)-5-oxoheptanedioate (15). To a solution of benzyl acetate (3.82 mL, 26.5 mmol) in THF (50 mL) at -78 °C was added LDA (13.2 mL, 26.5 mmol). The resulting solution was stirred at -78 °C for 35 min before **14**[16] (6.88 g, 24 mmol) in THF (40 mL) was added via cannula. The yellowish brown solution was stirred at -78 °C for 50 min then at 0 °C for 2.5 h. H_2O (20 mL) was added and THF was removed. 1N citric acid was added to adjust the pH to 6. The mixture was extracted with EtOAc and the organic layer was dried over Na_2SO_4. Solvent was removed. *in vacuo*. Flash chromatography of the residue (hexanes-ethyl acetate: 3:1) gave 10.7 g (100%) of **15** as an off-white oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.47 (s, 9H), 1.92-2.01 (m, 1H), 2.08-2.22 (m, 3H), 2.88-3.01(m,1H), 3.38-3.48 (m, 1H), 4.47 (dd, J = 4.7, 2.4Hz, 1H), 5.10 (s, 2H), 6.61 (bs, 1H), 7.25-7.35 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.5, 27.9, 28.0, 30.1, 62.8, 65.1, 81.9, 82.6, 96.2, 127.7, 127.8, 128.4, 136.9, 151.2, 157.5, 168.6, 170.7; IR (neat) ν 3334, 2980, 1724, 1500, 1251, 1152 cm^{-1}; HRMS calcd. for $C_{23}H_{32}NO_7$ $(M-H)^+$: 434.2179, found 436.2188.

(1*S*, 4*R*)-4-(5-Amino-6-chloropyrimidin-4-ylamino)cyclopent-2-enyl acetate (16). To a solution of **11** (400 mg, 1.66 mmol) in CH_2Cl_2 (8 mL) at 0^oC was added TFA (1.28 mL, 16.6 mmol) dropwise. The reaction was stirred at 0^oC for 15 min, then warmed up to room

temperature for 30 min. The reaction was monitored by TLC. When the reaction was complete, it was diluted with toluene and the solvents were removed under reduced pressure. The residue was dissolved in toluene again and the solvents were removed. After that, the residue was dried under vacuum for 1 h. Then it was dissolved in *n*-BuOH (2 mL). To the *n*-BuOH solution was added 5-amino-4,6-dichloropyrimidine (0.38 g, 3.32 mmol) and Et_3N (2.3 mL, 16.6 mmol). The mixture was heated to 110°C and stirred at 110°C for 3d. After it was cooled down, column purification with hexanes to EtOAc from 4:1 to 1:1 gave 0.26 g (59%) of the desired product as a white solid. Mp=130-131°C. $[\alpha]_D$ = + 58.4° (c=1.67, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62, 1.67 (dt, J = 14.7, 3.9 Hz, 1H), 2.02 (s, 3H), 2.92, 2.97 (dt, J = 14.4, 7.8 Hz, 1H), 4.00 (bs, 2H), 5.15-5.16 (m, 1H), 5.47 (d, J = 6.9 Hz, 1H), 5.55-5.59 (m, 1H), 5.99-6.02 (m, 1H), 6.07-6.10 (m, 1H), 8.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 38.5, 55.0, 77.6, 122.1, 132.8, 136.3, 141.7, 148.8, 153.7, 170.7. IR (neat) 3355, 1731, 1578, 1246 cm^{-1}; HRMS calcd. for $C_{11}H_{14}{}^{35}ClN_4O_2$ $(M+H)^+$: 269.0805, found 269.0788.

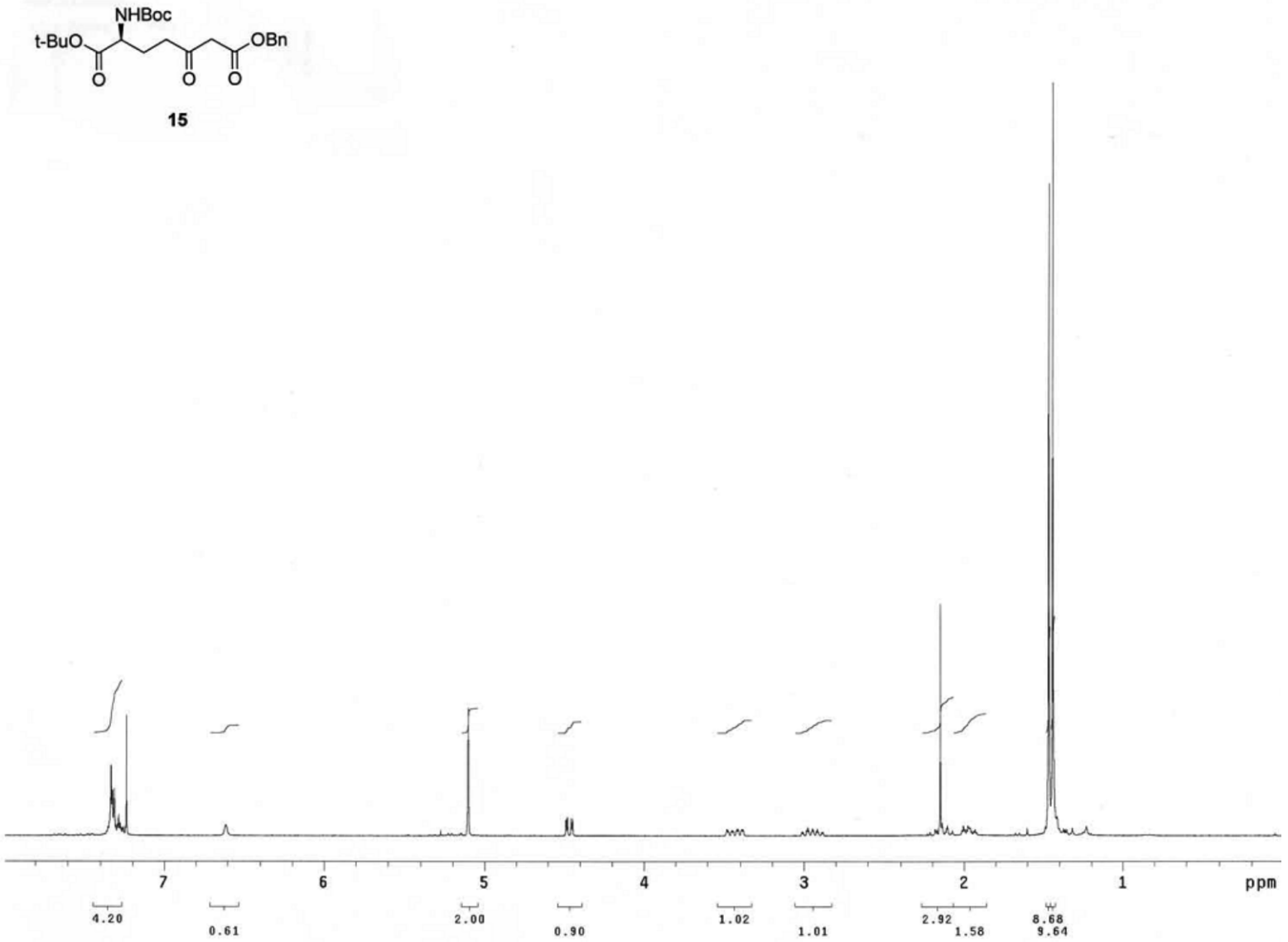
(1*S*, 4*R*)-4-(6-Chloro-9*H*-purin-9-yl)cyclopent-2-enyl acetate (17). To a flask containing **16** (0.5g, 1.86 mmol) was added $CH(OEt)_3$ (9 mL) and CSA(130 mg, 0.3 equiv.). The reaction was stirred at room temperature for 6h and was monitored by TLC. The reaction was quenched with saturated $NaHCO_3$ solution, extracted with EtOAc, washed with H_2O and brine. After the solvent was removed, the residue was purified on silica gel with 2:2:1 of hexanes:EtOAc:CH_2Cl_2 to give 0.47g (91%) of the desired product as a white solid. Mp= 145-147°C. $[\alpha]_D$ = + 8.6° (c=4.2, CH_2Cl_2). ^{1}H NMR (300 MHz, CDCl3) δ 1.95 (dt, J = 15.3, 3 Hz, 1H), 2.06 (s, 3H), 3.05-3.15 (m, 1H), 5.74-5.78 (m, 2H), 6.18-6.21 (m, 1H), 6.38-6.41 (m, 1H), 8.17 (s, 1H), 8.75 (s, 1H); ^{13}C NMR (75 MHz, CDCl3) δ 21.0, 38.6, 57.4, 76.7, 131.7, 133.4,

136.5, 143.4, 151.0, 151.3, 152.0, 170.3; IR (neat) 1731, 1590, 1560, 1242 cm^{-1}; HRMS calcd. for $C_{12}H_{11}{}^{35}ClN_4O_2$ $(M+H)^+$: 279.0649, found 279.0634.

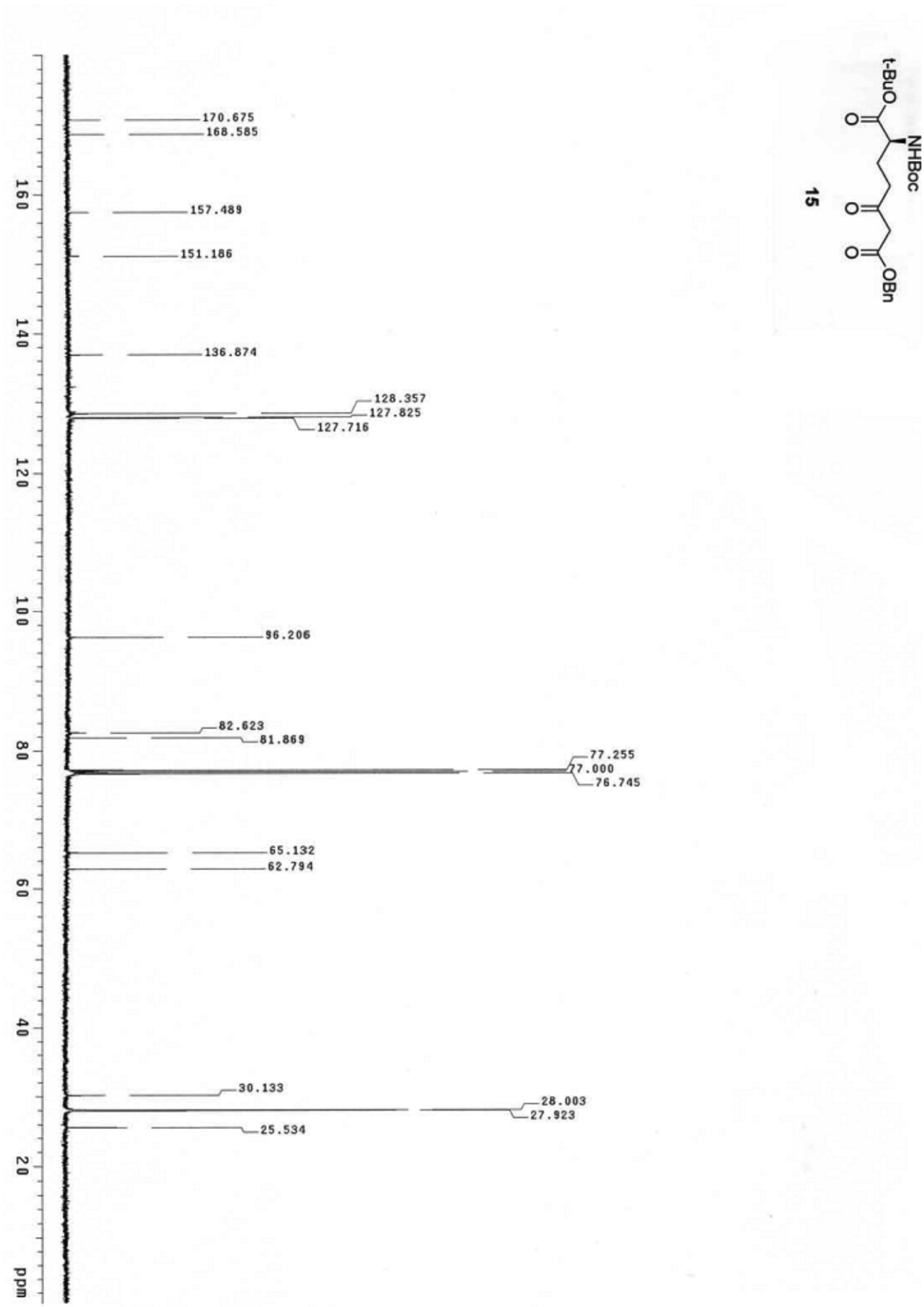
(*S*) -*tert*-Butyl 2-(*tert*-butoxycarbonyl)-6-((1*R*, 4*R*)-4-(tert-butoxycarbonyl)cyclopent-2-enyl)-5-oxohexanoate (28) The compound was prepared using the same procedure for the synthesis of compound **21**. $[\alpha]_D$ = +3° (c = 1.5, $CHCl_3$). Mp = 118-120°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.07 (dt, J = 13.2, 6.6 Hz, 1H), 1.41 (s, 9H), 1.42 (s, 9H), 1.44 (s, 9H), 1.74-1.86 (m, 1H), 2.05-2.14 (m, 1H), 2.35-2.54 (m, 4H), 2.62 (dt, J = 13.2, 8.1 Hz, 1H), 2.95- 3.04 (m, 1H), 4.08-4.14 (m, 1H), 4.55-4.64 (m, 2H), 5.02 (d, *J* = 7.5 Hz, 1H), 5.64-5.69 (m, 1H), 5.72-5.75 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.8, 28.0, 28.3, 28.4, 38.6, 38.8, 39.6, 49.2, 53.4, 56.4, 79.3, 79.7, 82.1, 132.3, 136.5, 155.2, 155.5, 171.5, 208.5; IR (neat, CH_2Cl_2) ν 2978, 1711, 1514, 1367, 1158 cm^{-1}; HRMS (FAB) calcd. for $C_{25}H_{43}N_2O_7$ $(M+H)^+$: 483.3070, found 483.3093.

(*S*)-*tert*-Butyl 2-(*tert*-butoxycarbonyl)-4-(3a*R*,5*R*,6*R*,6a*S*)-5-(*tert*-butoxycarbonyl)-2,6-dihydroxy-hexahydro-2*H*-cyclopenta[*b*]furan-2-yl)butanoate (29) The compound was prepared using the same procedure for the synthesis of compound **20**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34, 1.35, 1.37, 1.38, 1.39, 1.41 (s, 54H), 1.52-1.63 (m, 2H), 1.75-2.24 (m, 12H), 2.33-2.40 (m, 2H), 2.53-2.65 (m, 1H), 2.92-2.99 (m, 1H), 3.85-3.90 (m, 4H), 4.07- 4.10 (m, 1H), 4.18 (d, J = 8.7 Hz, 1H), 4.25 (dd, *J* = 9.9, 4.2 Hz, 1H), 4.71 (dd, *J* = 7.8, 5.4 Hz, 1H), 5.06-5.08 (m, 1H), 5.34-5.37 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 26.8, 28.0(2C), 28.2, 28.3, 28.4(2C), 35.7, 37.2, 38.0, 38.1, 39.4, 40.6, 40.8, 43.3, 55.1, 55.5, 60.9, 61.5, 71.1, 72.0, 77.2, 78.9, 80.3, 81.1, 81.2, 81.3, 81.5, 86.5, 104.6, 104.7, 152.8, 153.0, 155.4, 155.6, 171.3, 171.9; IR

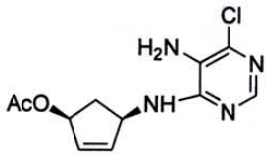
(neat, CH_2Cl_2) ν 3441, 3384, 2977, 2931, 1741, 1702, 1502, 1367, 1167 cm^{-1}; HRMS (FAB) calcd. for $C_{25}H_{43}N_2O_8$ $(M-H_2O)^+$ 499.3019, found 499.3023.



^{1}H NMR Spectrum of 15



^{13}C NMR Spectrum 15



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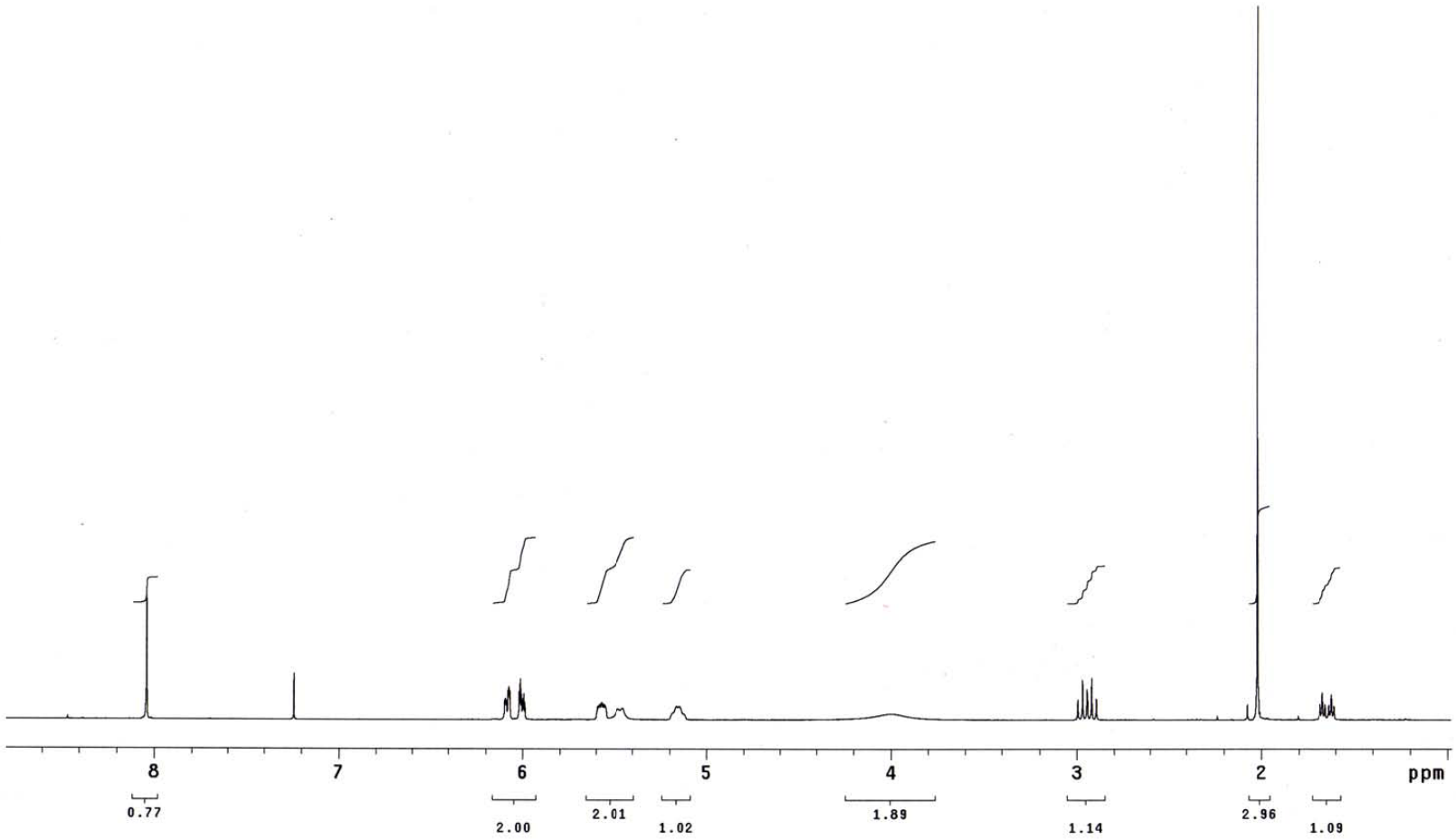
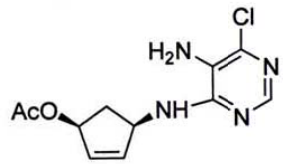


^{1}H NMR Spectrum of 16



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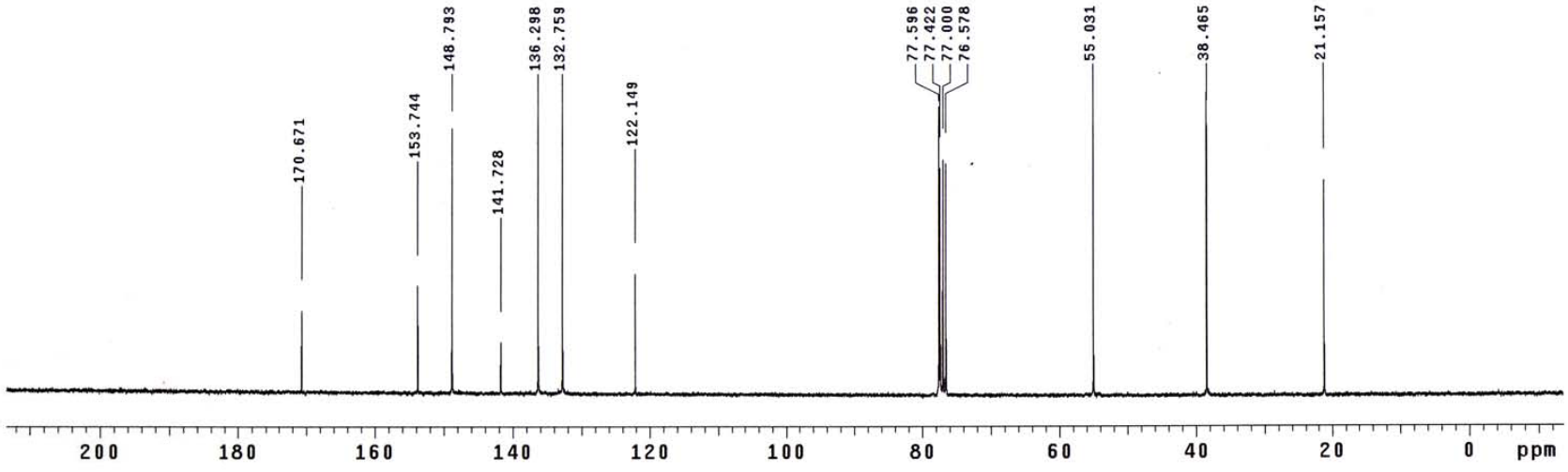
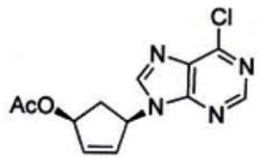


^{13}C NMR Spectrum of 16



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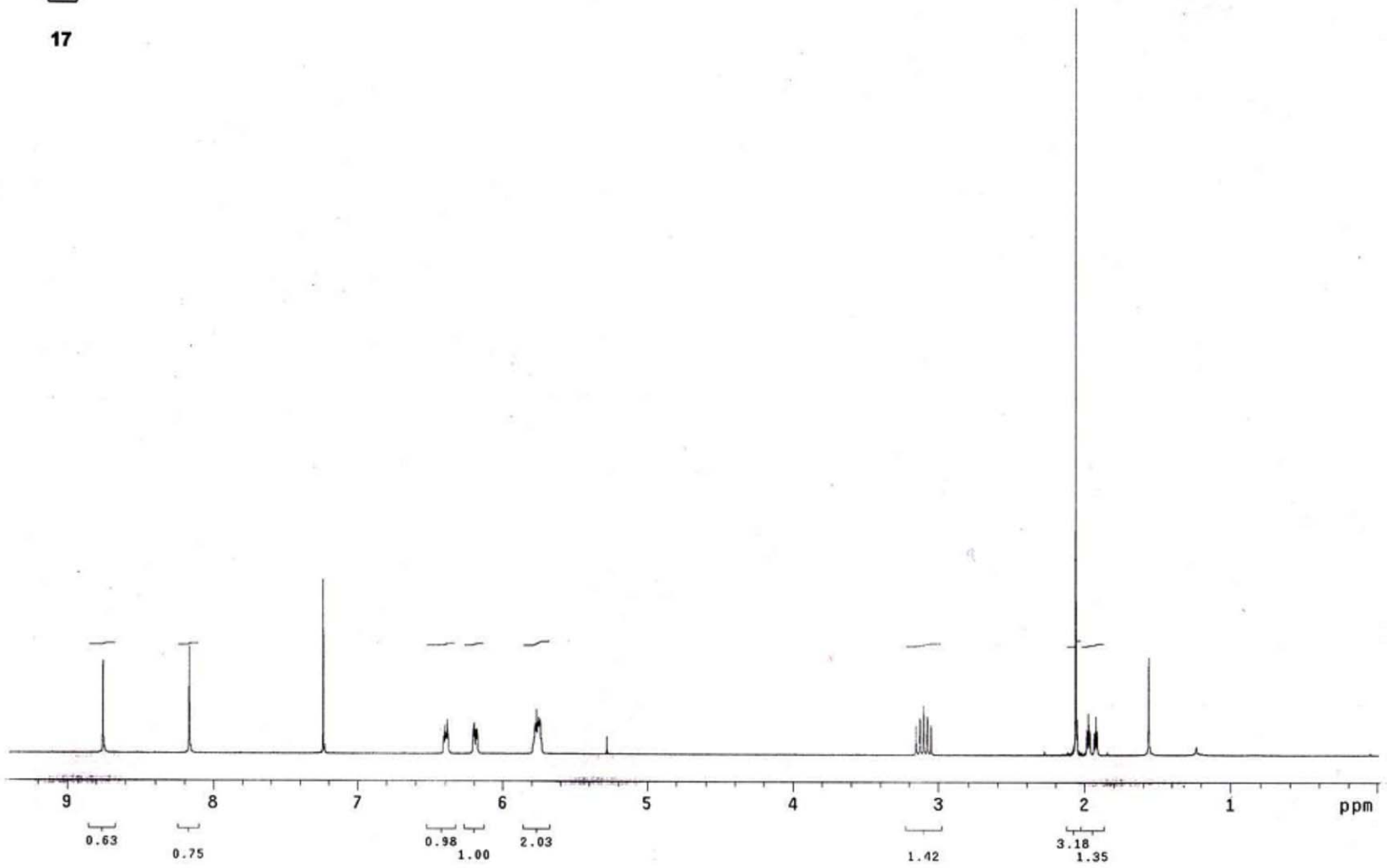
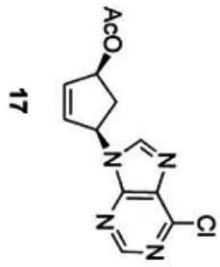


^{1}H NMR Spectrum of 17



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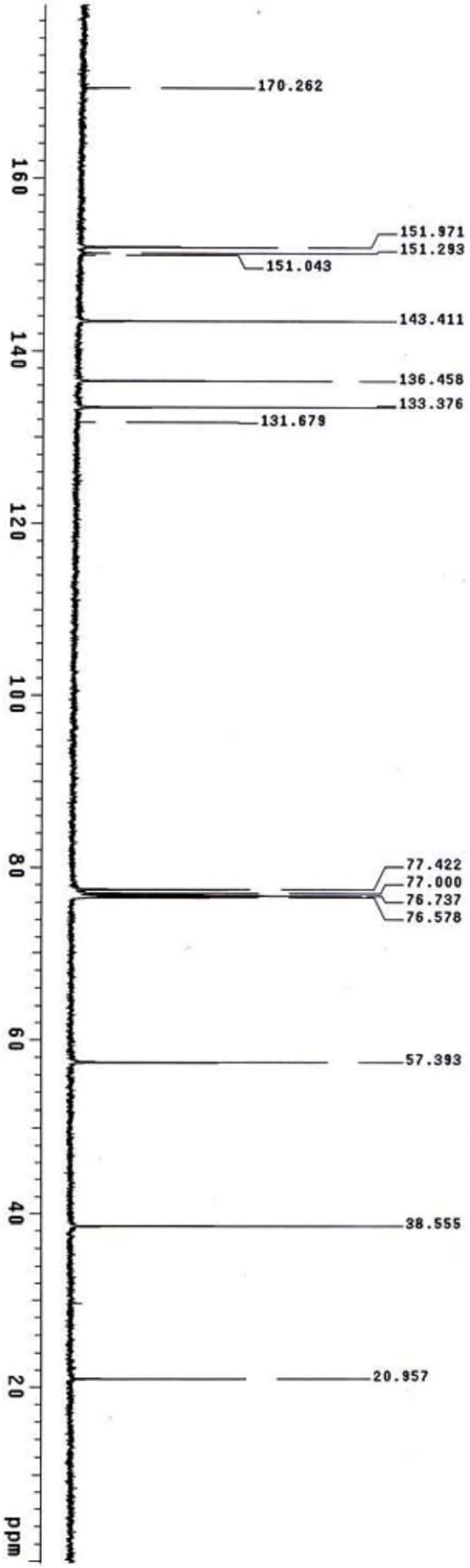
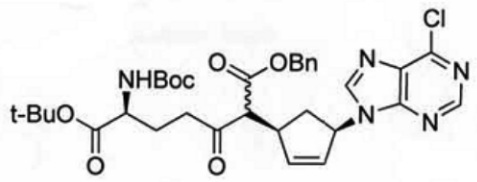


13C NMR Spectrum 17



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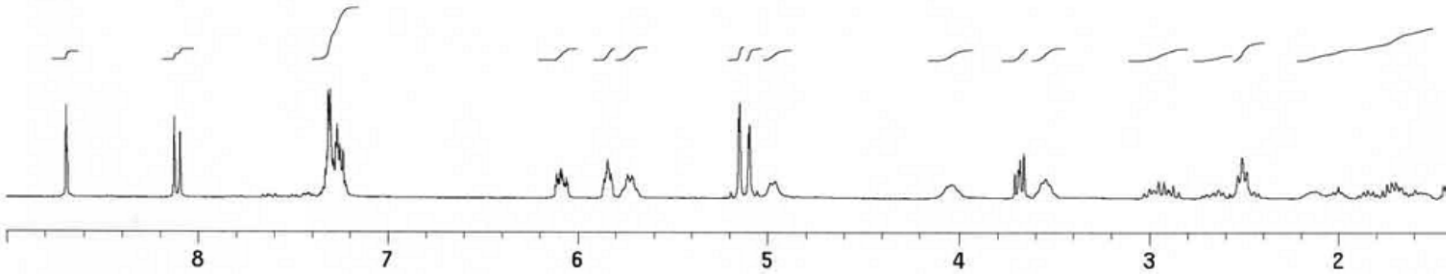

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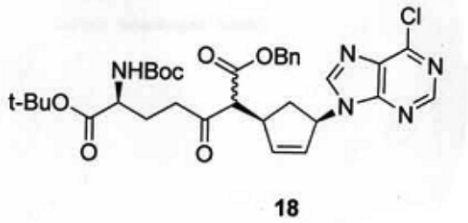

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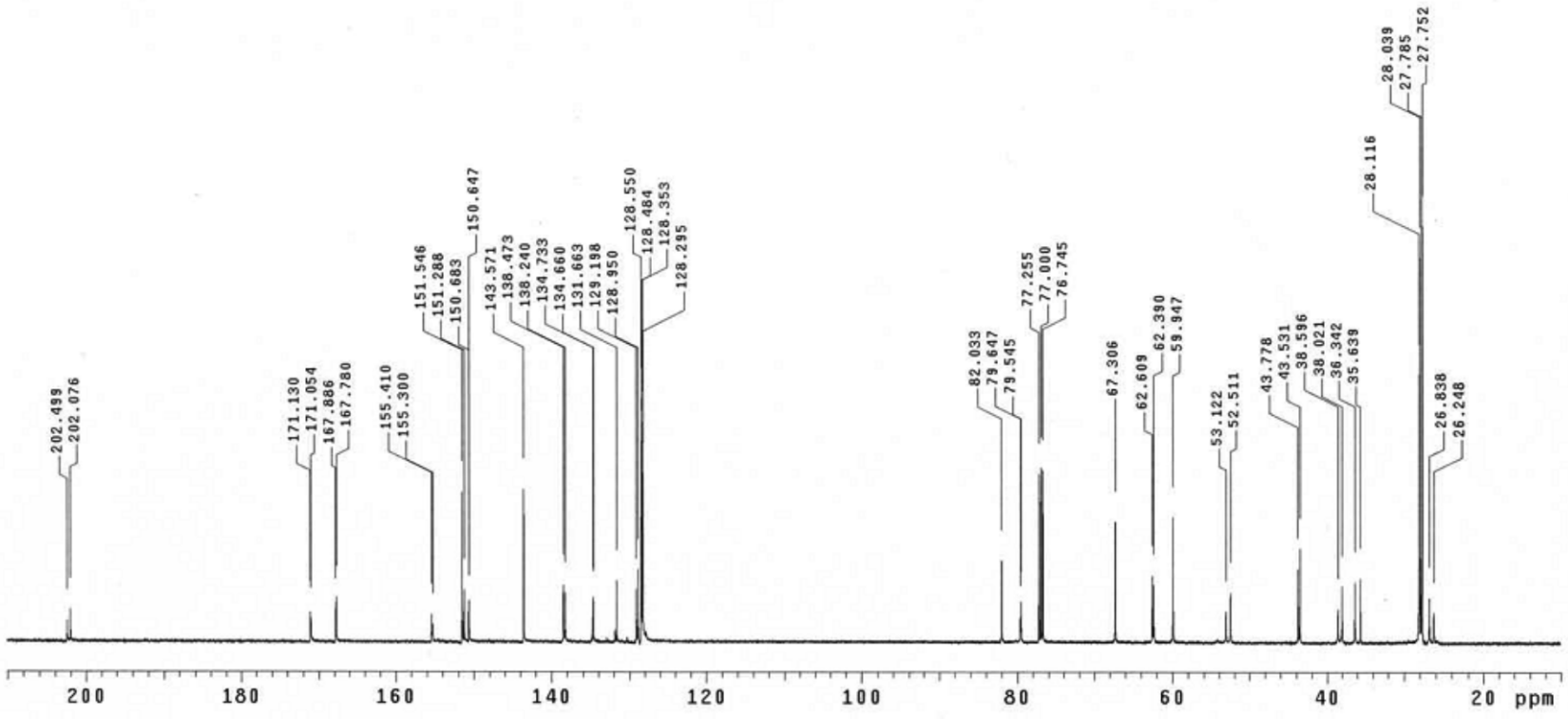
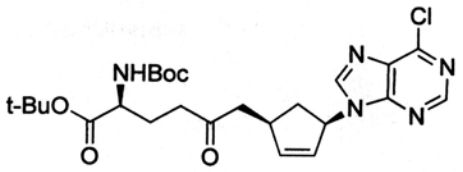


^{13}C NMR Spectrum of 18



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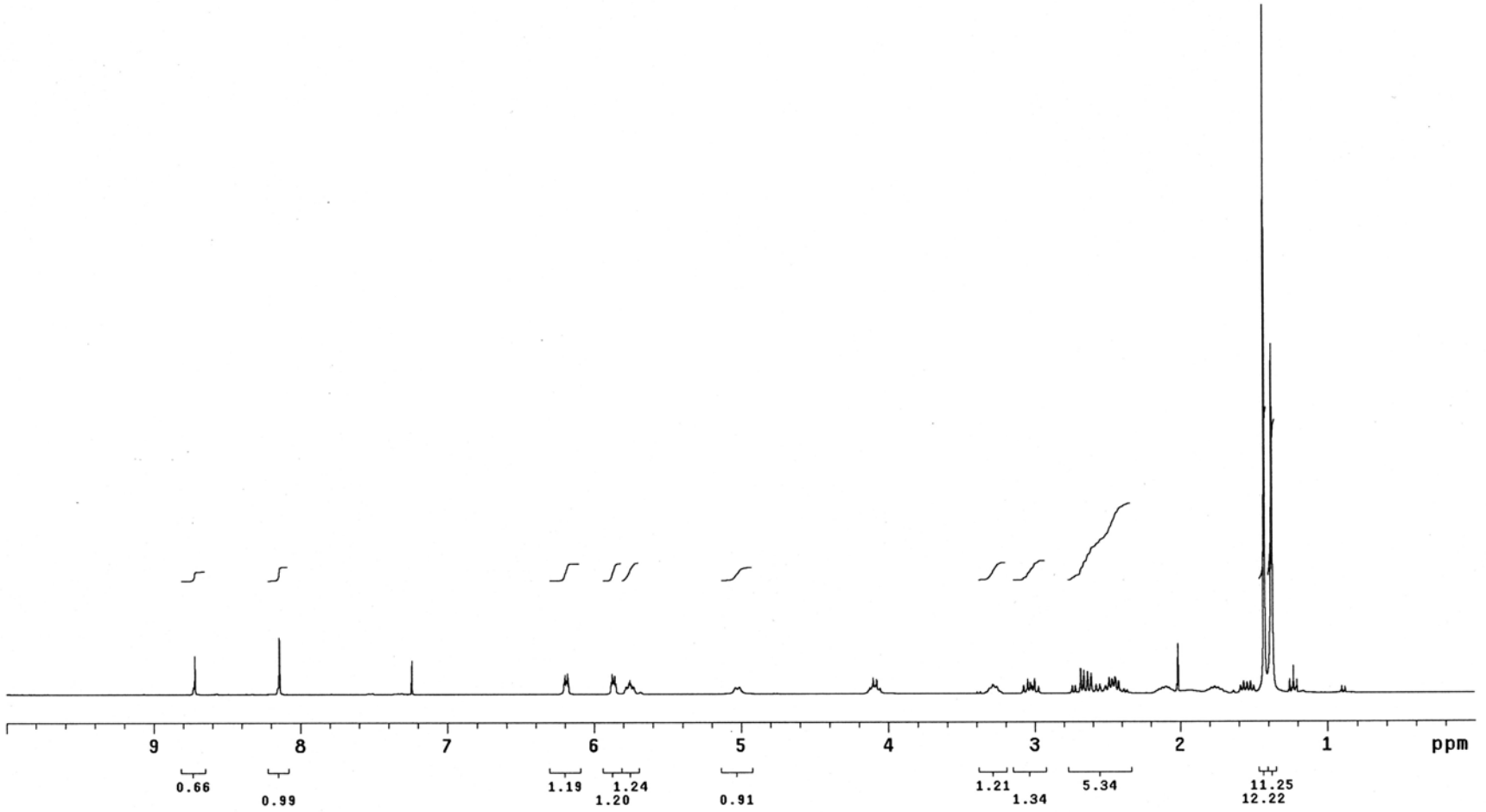
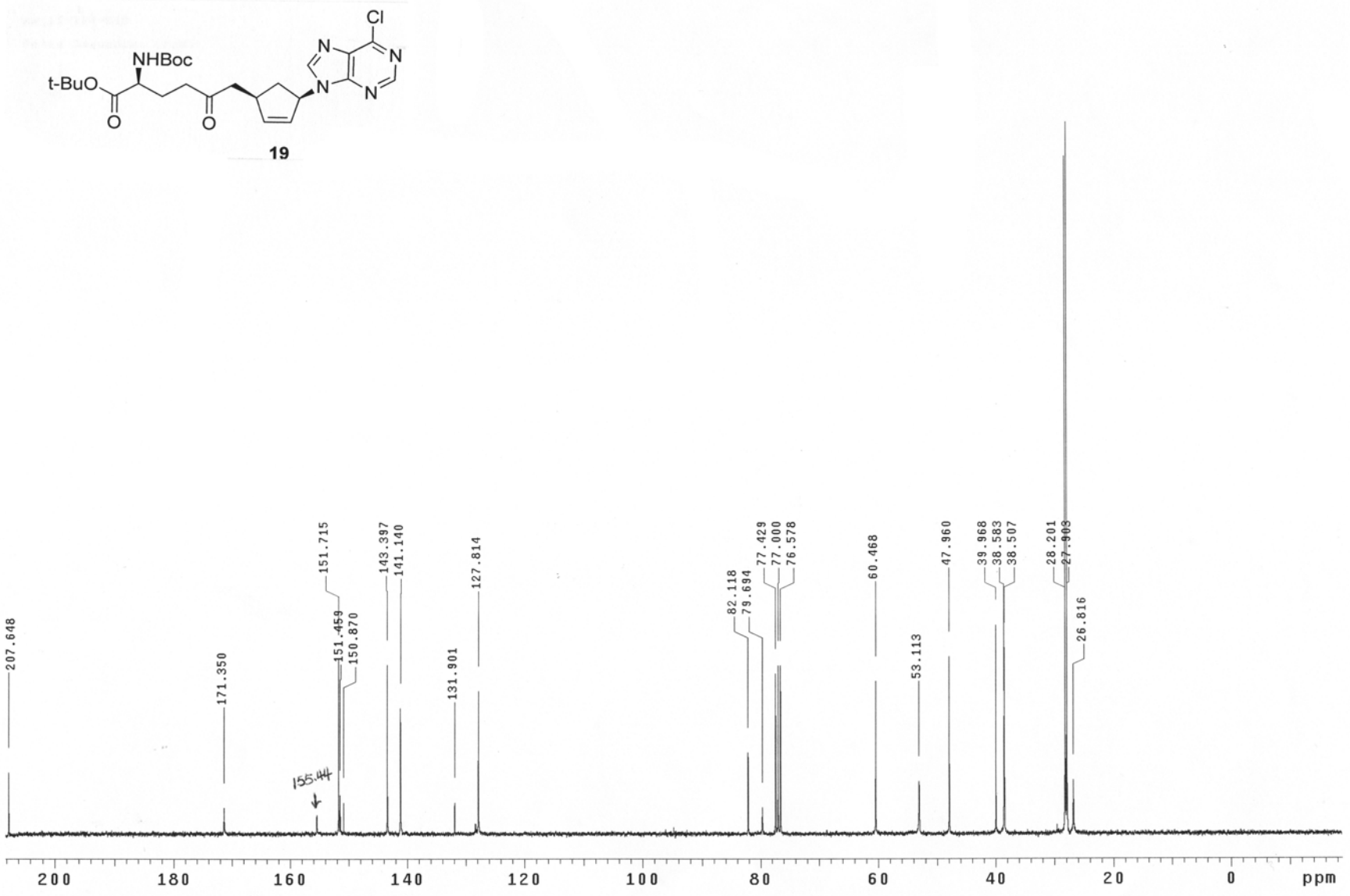
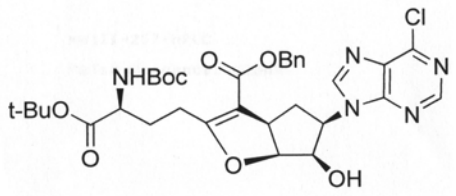


^{1}H NMR Spectrum of **19**



^{13}C NMR Spectrum of **19**



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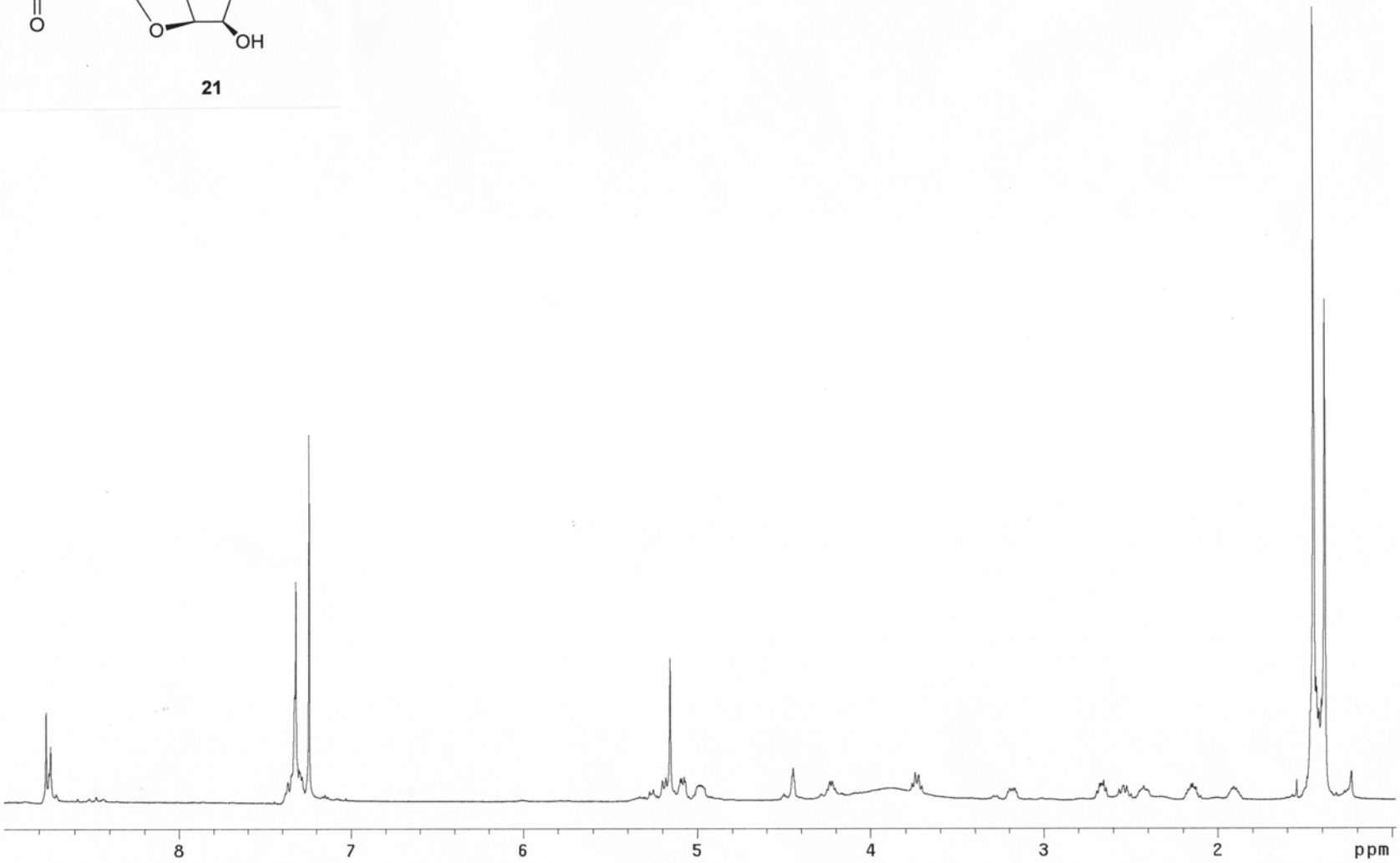
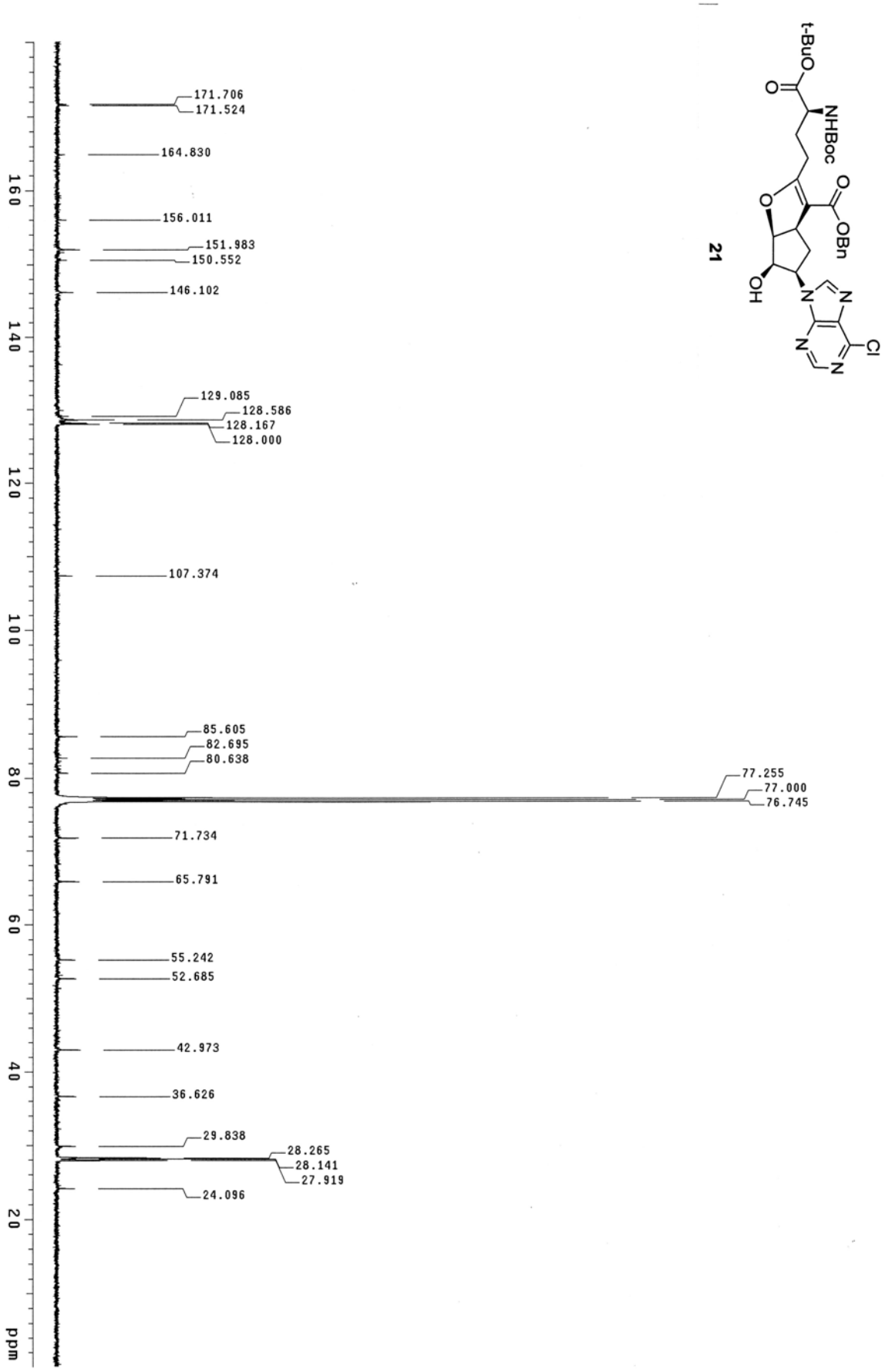
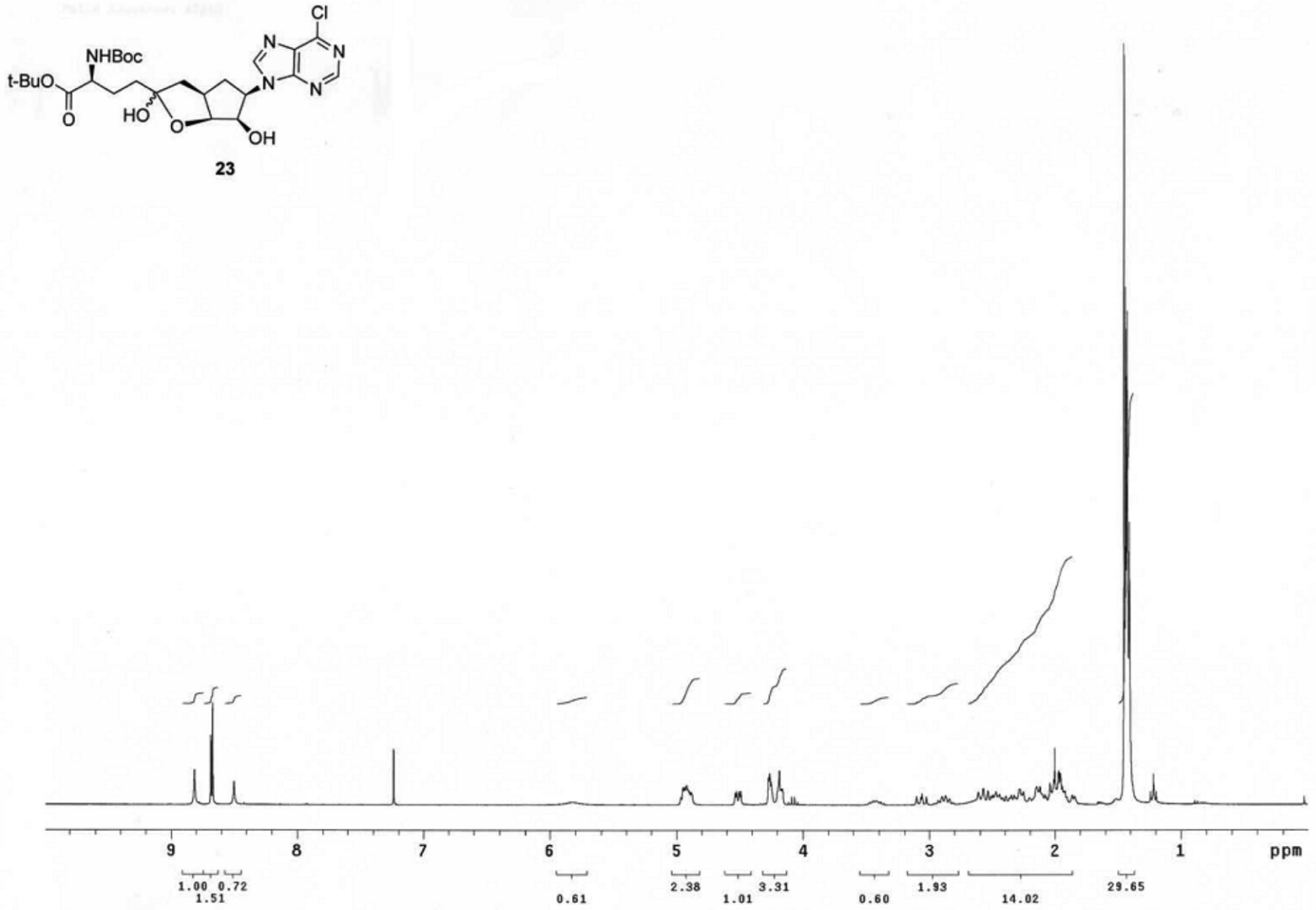


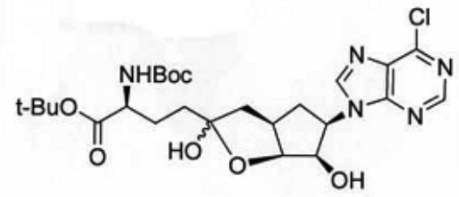
^{1}H NMR Spectrum of **21**

^{13}C NMR Spectrum of **21**





[1]HNMR Spectrum of 23



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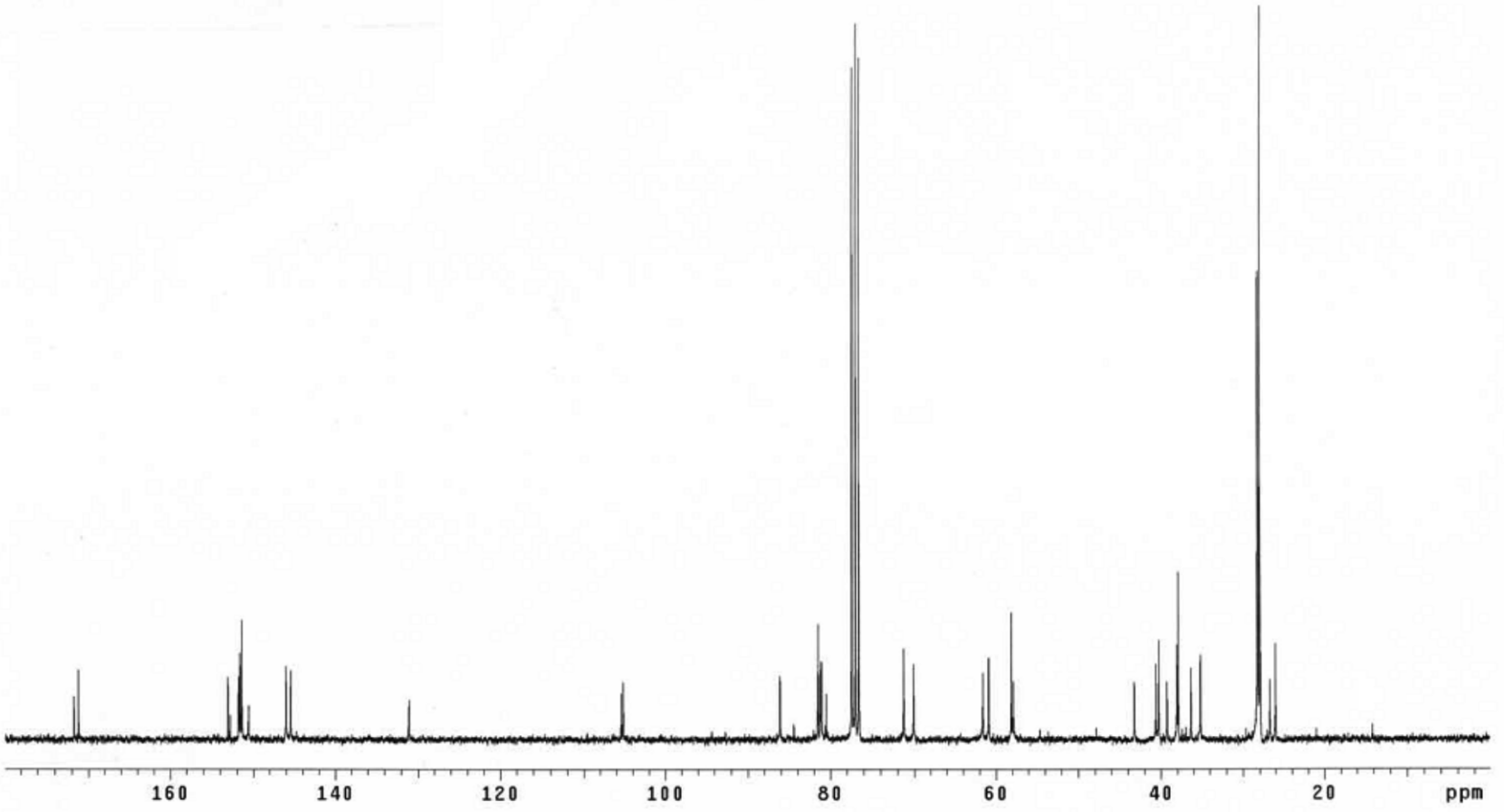
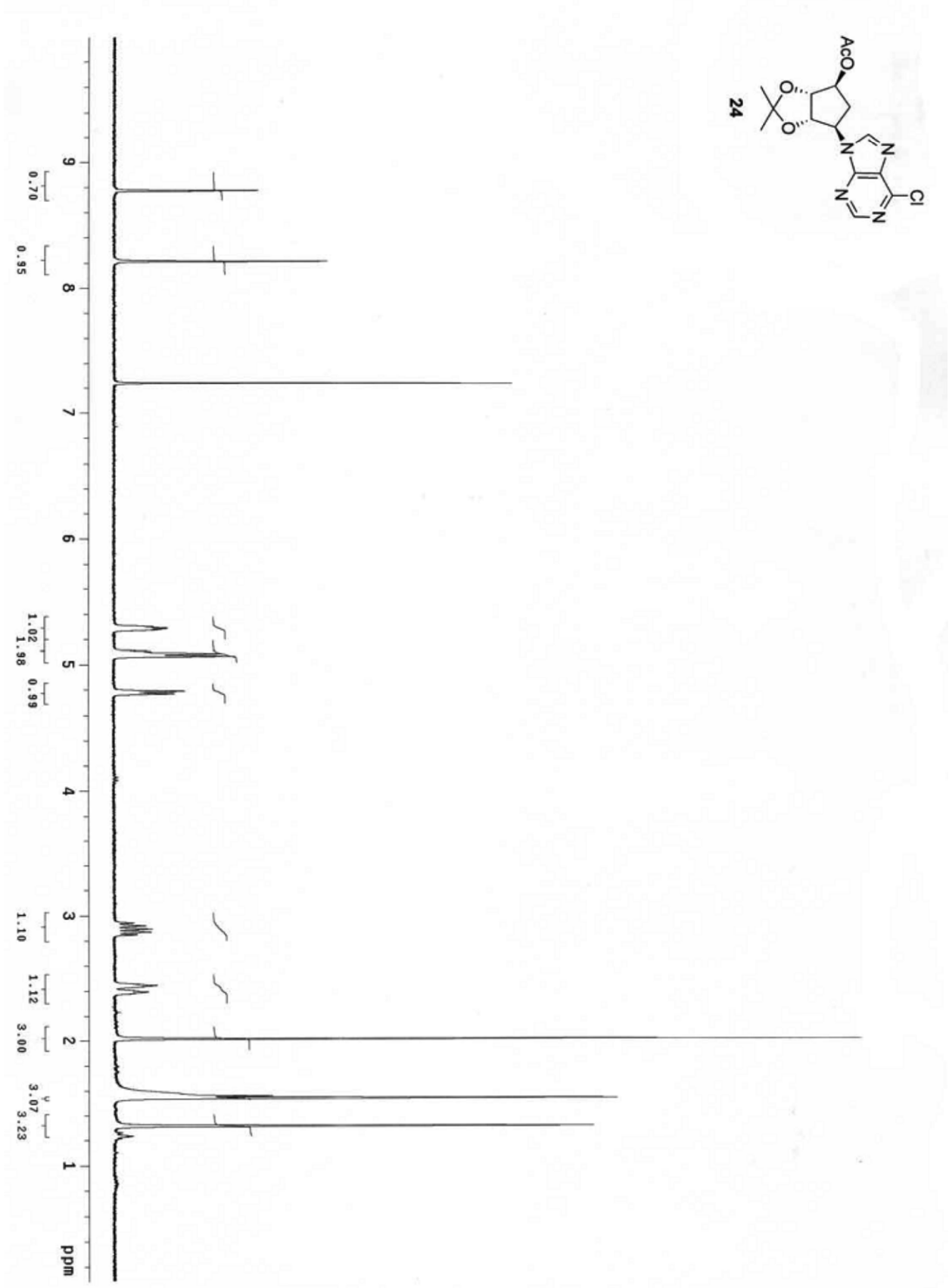


^{13}C NMR Spectrum of 23



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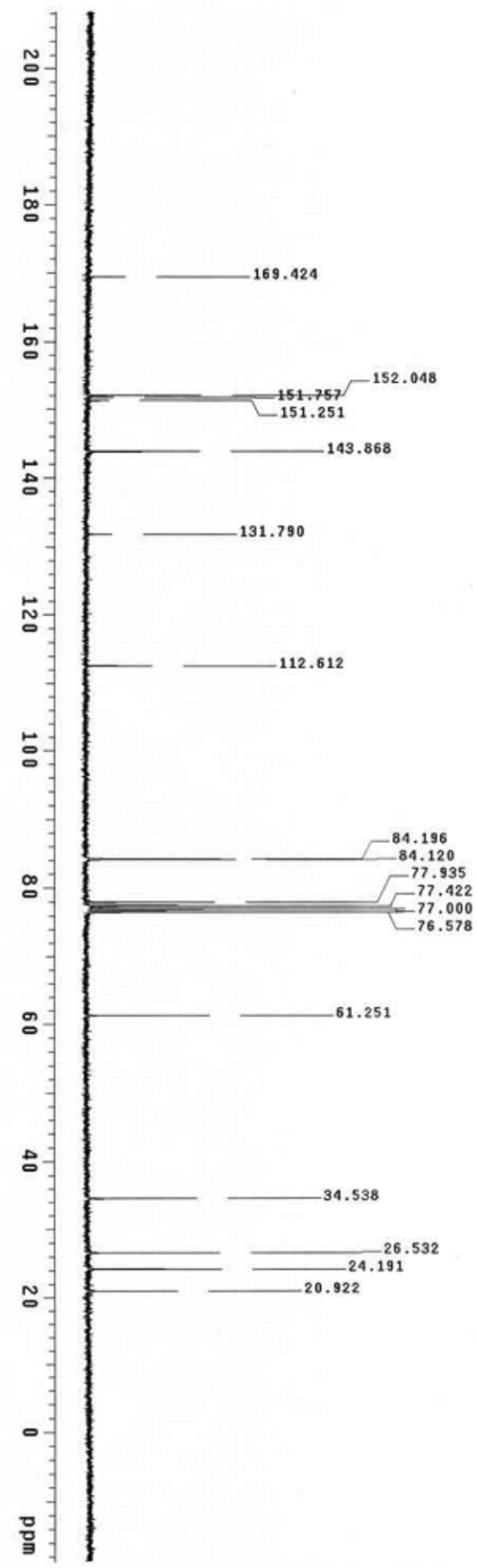

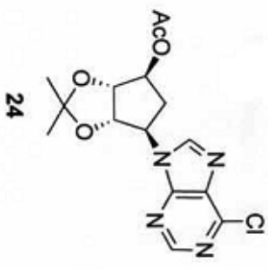

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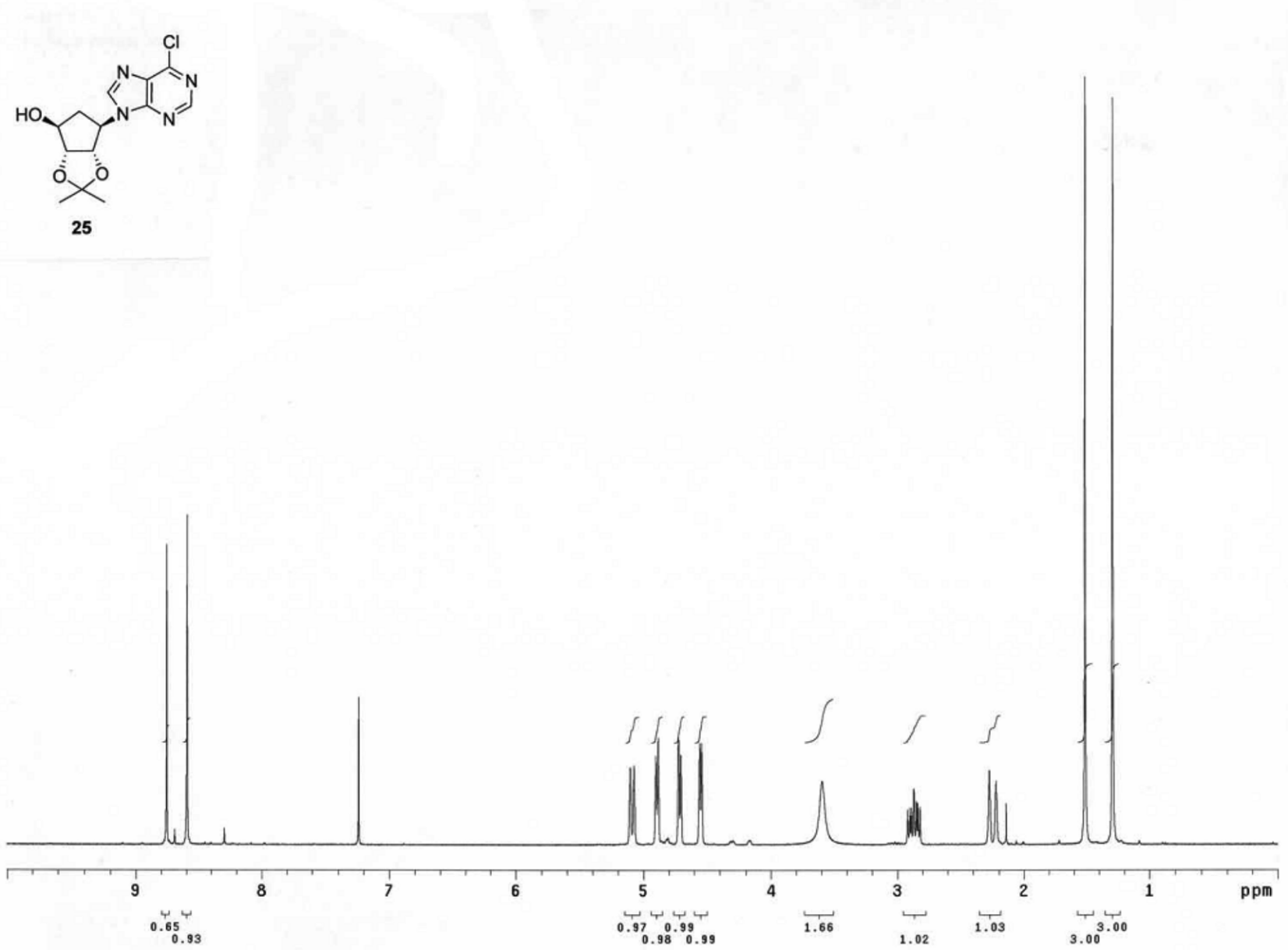
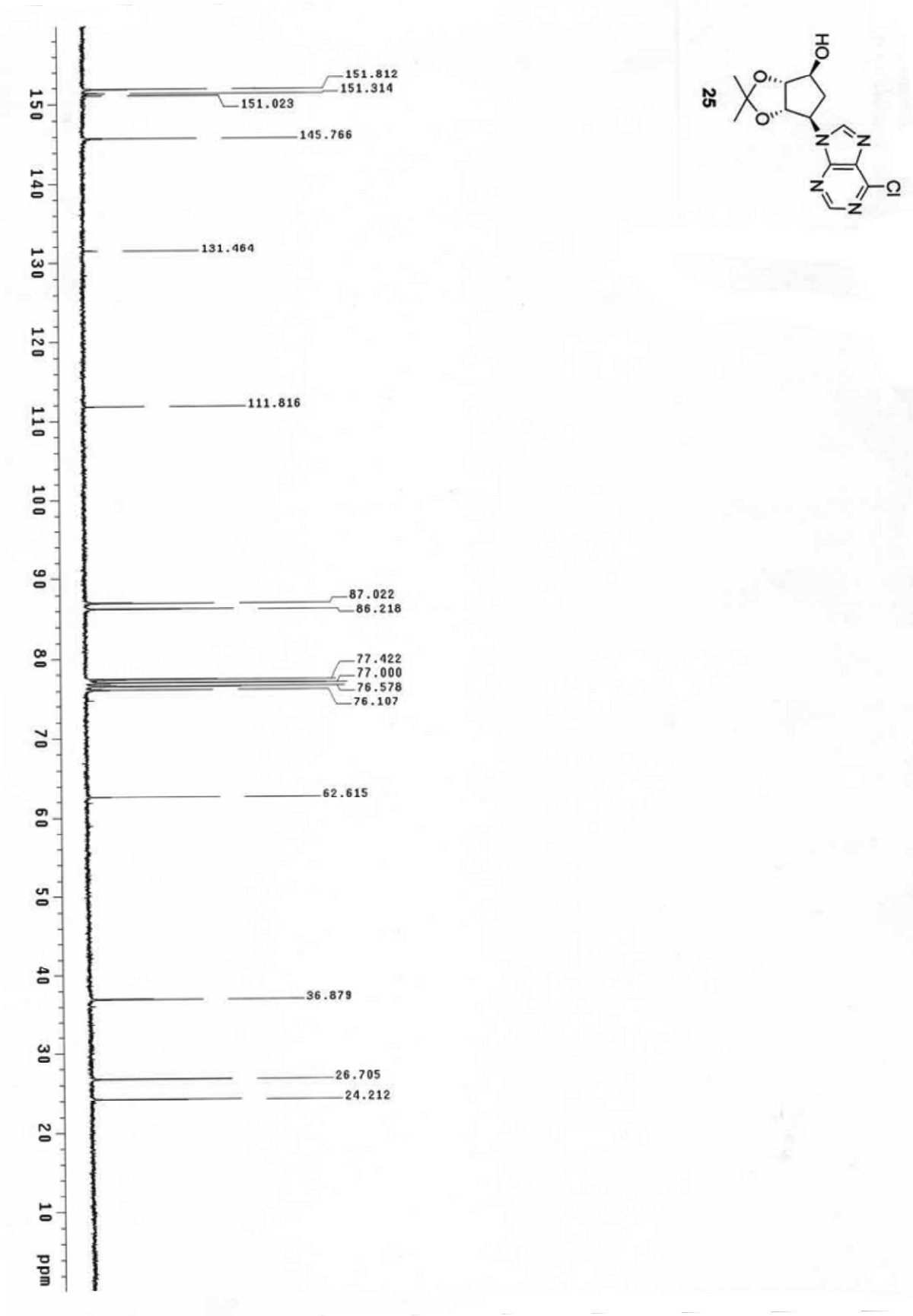
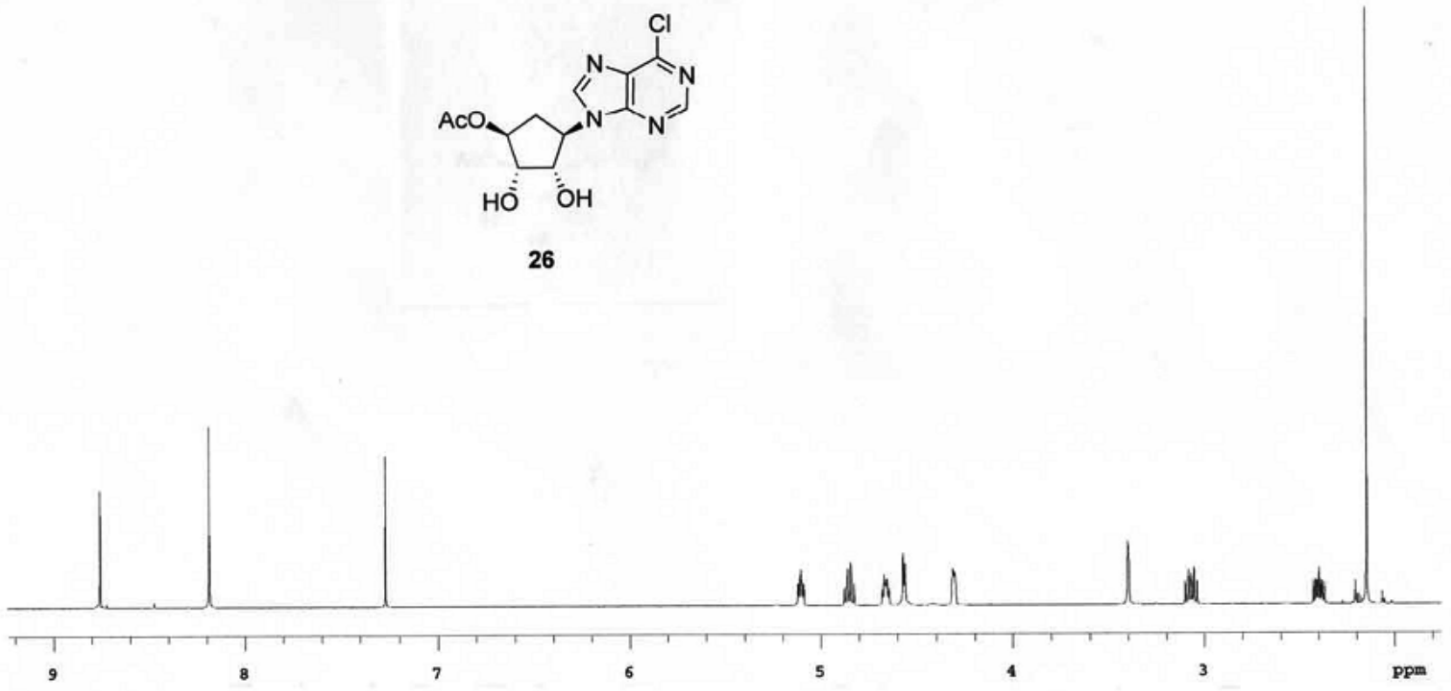
^{13}C NMR Spectrum of 24



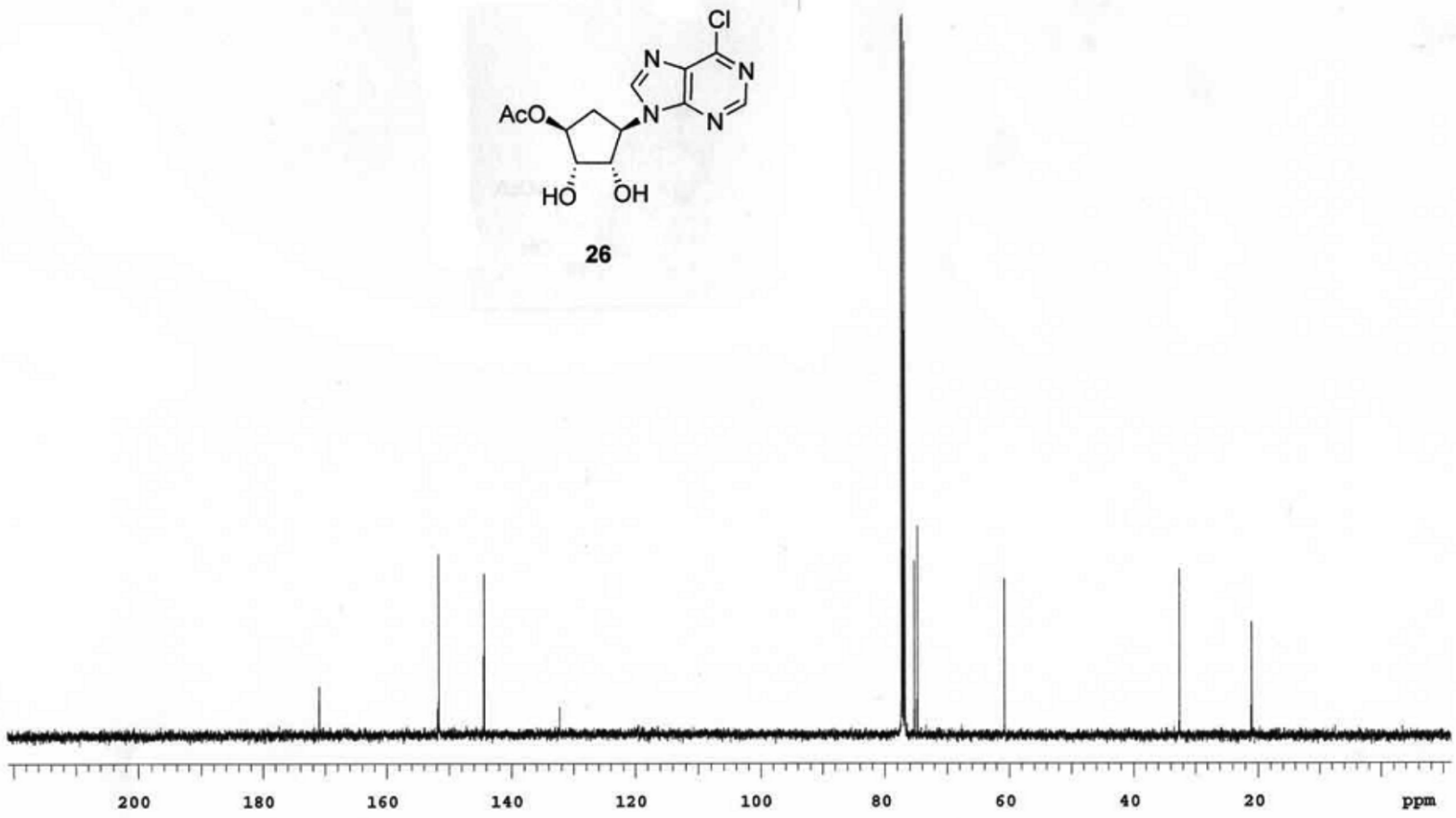
1H NMR Spectrum 25



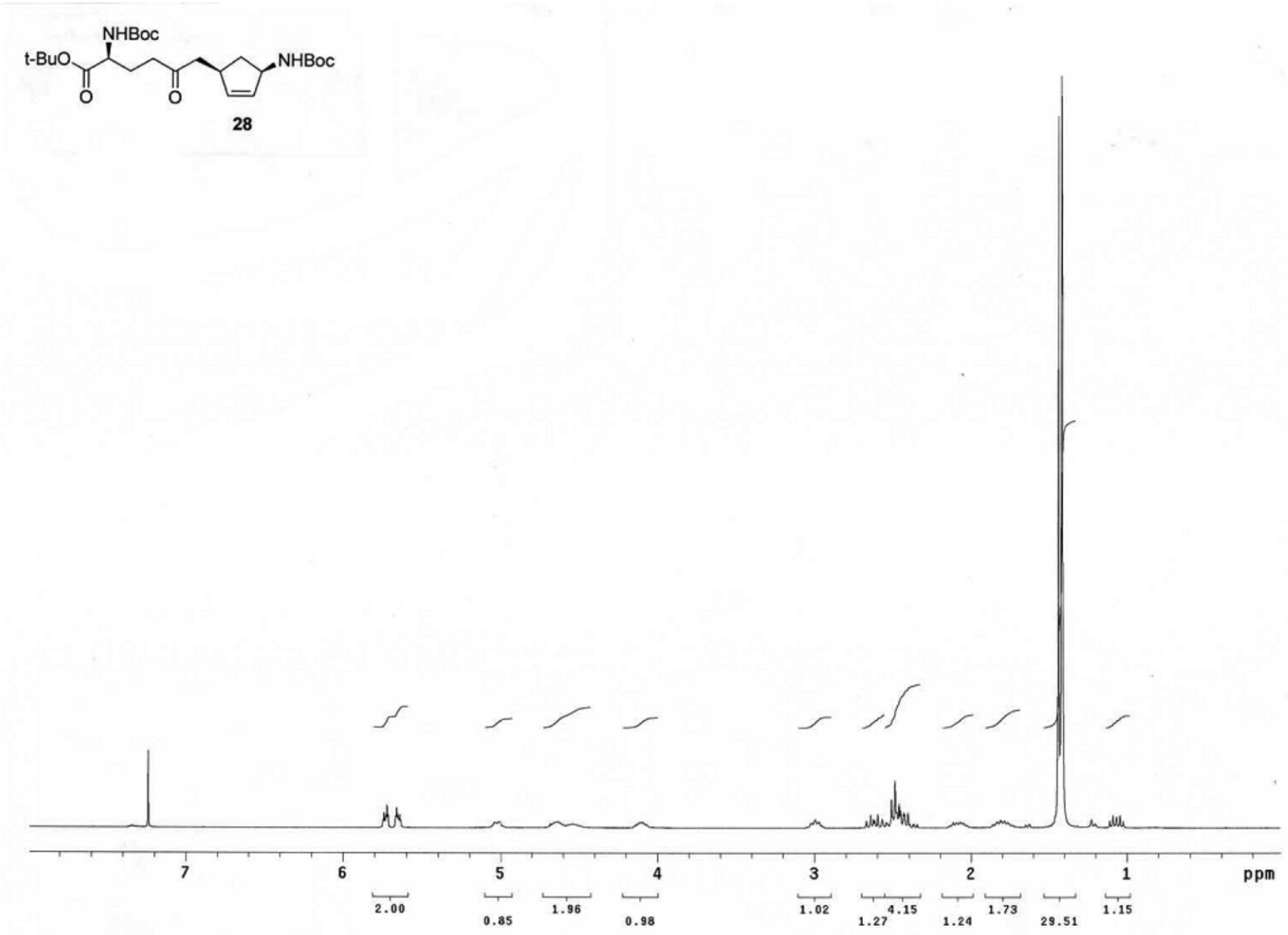
^{13}C NMR Spectrum of 25



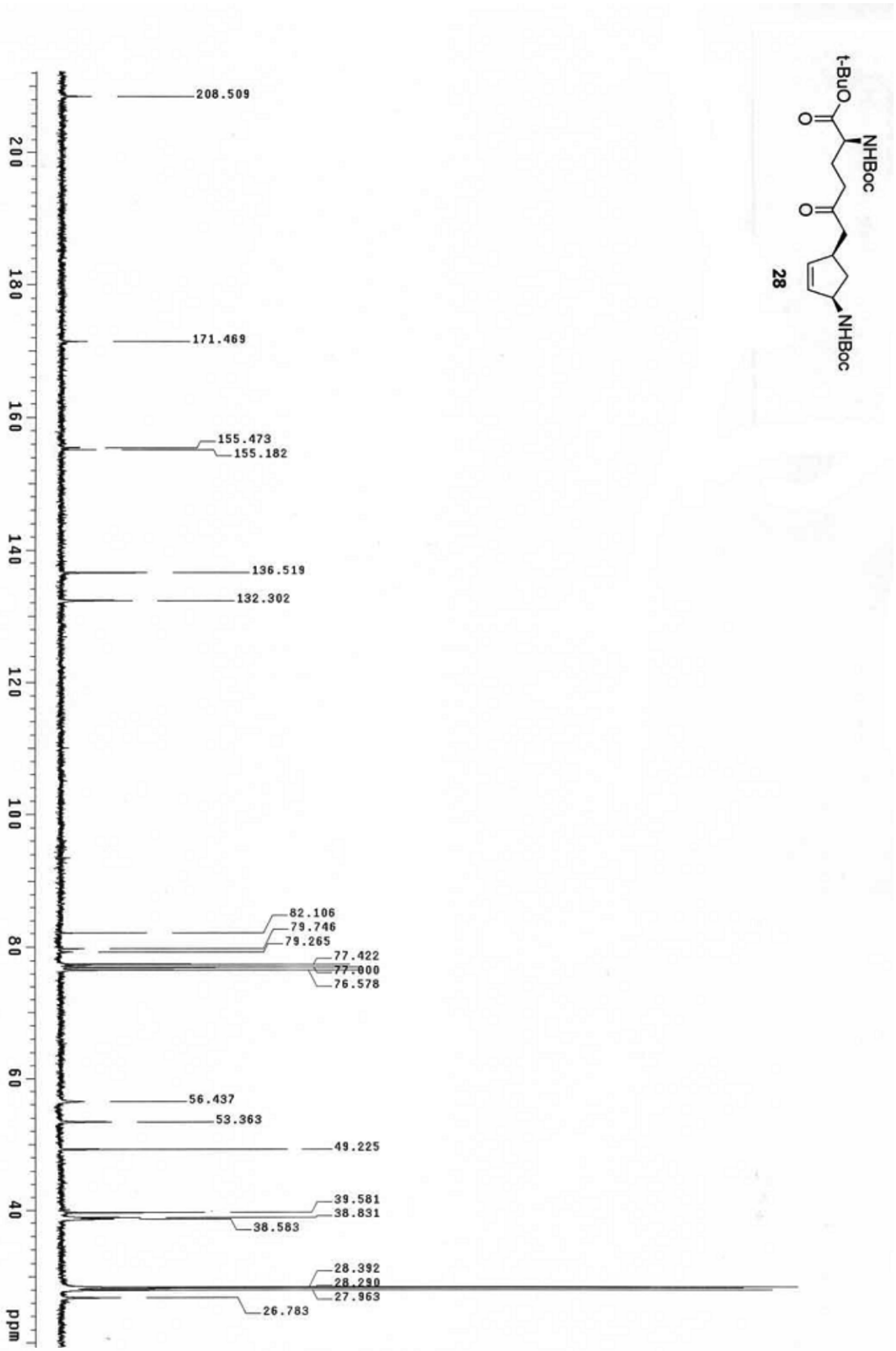
^{1}H NMR Spectrum of 26



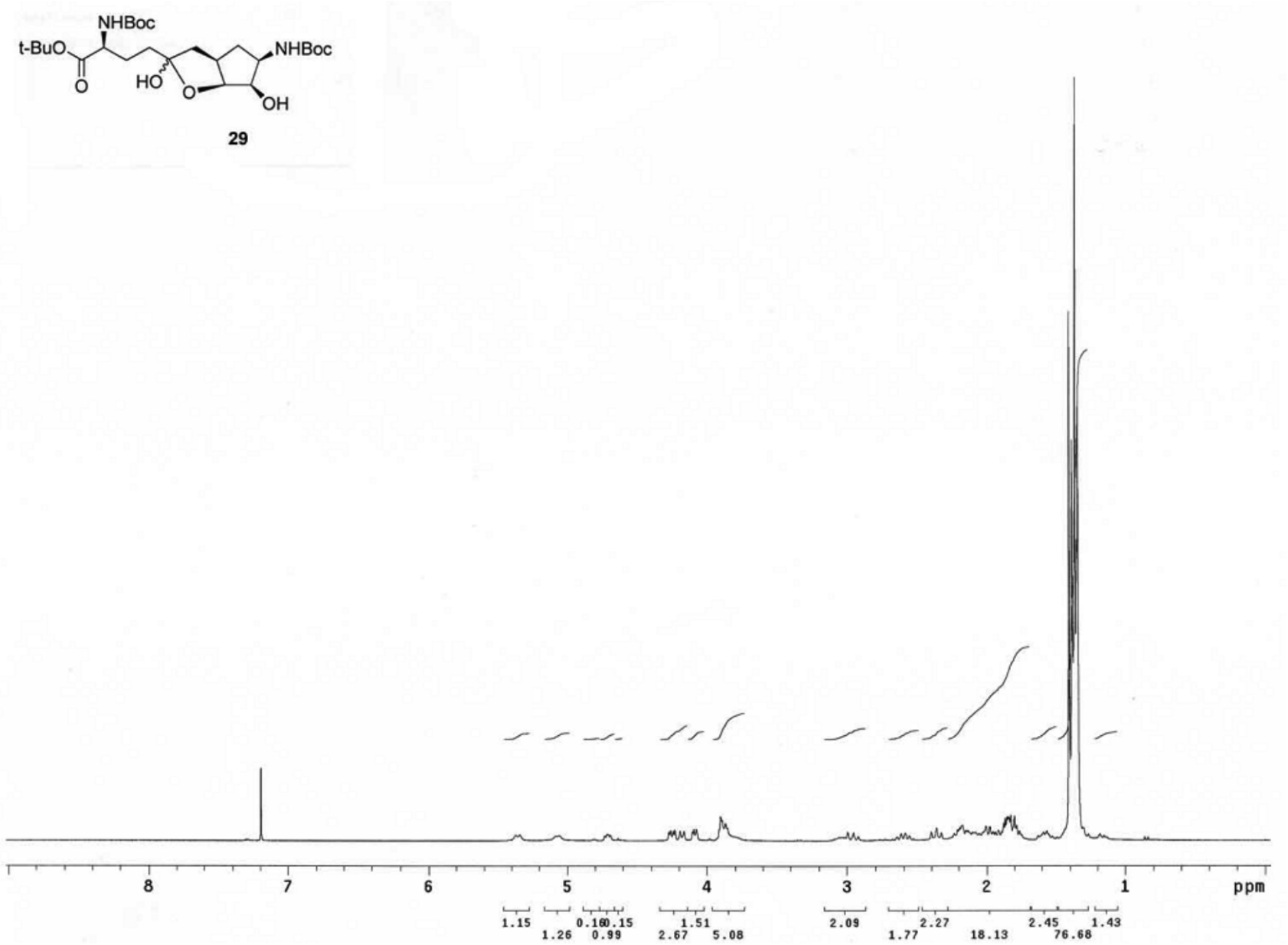
^{13}C NMR Spectrum of 26



^{1}H NMR Spectrum of 28

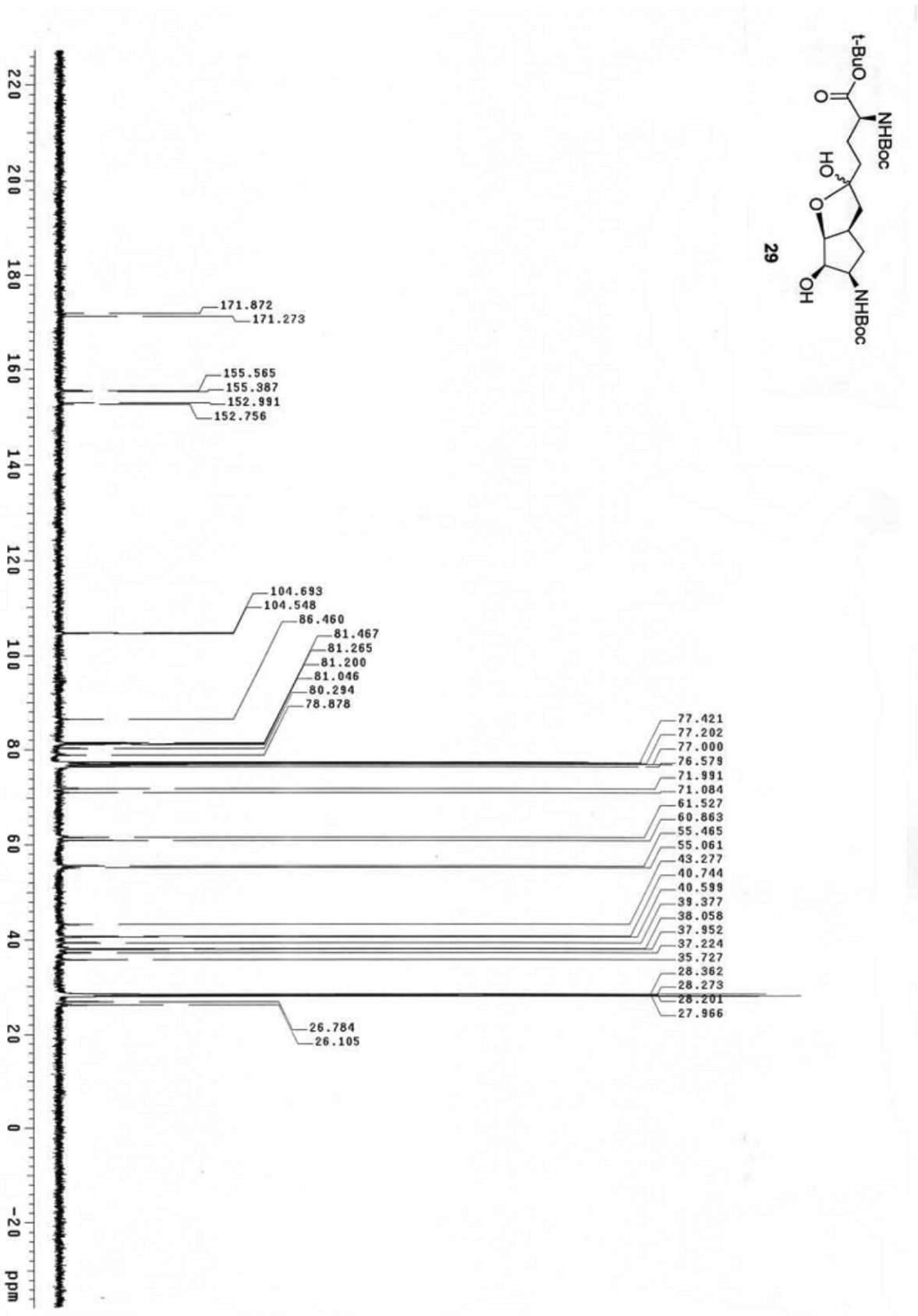


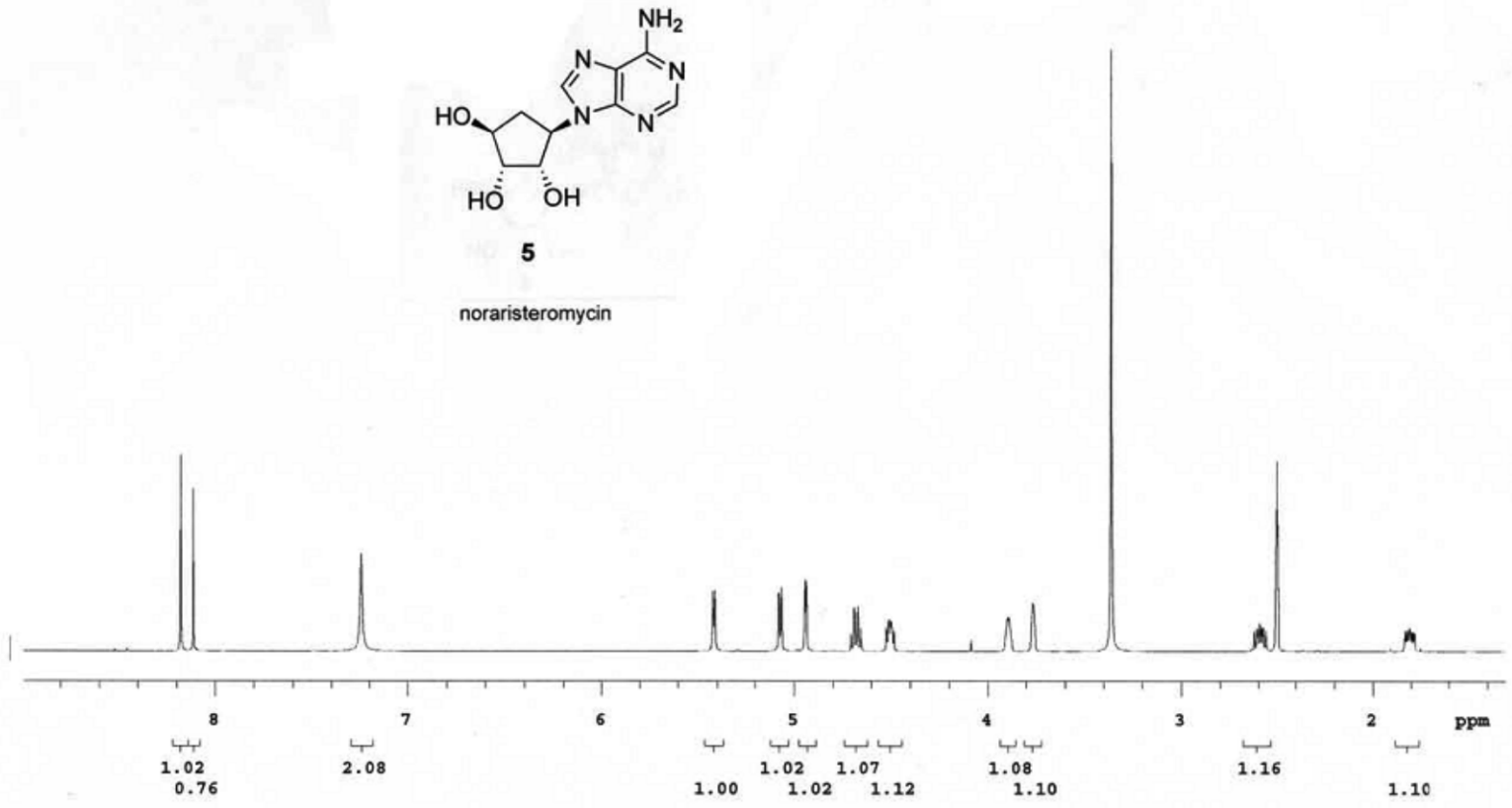
^{13}C NMR Spectrum of 28



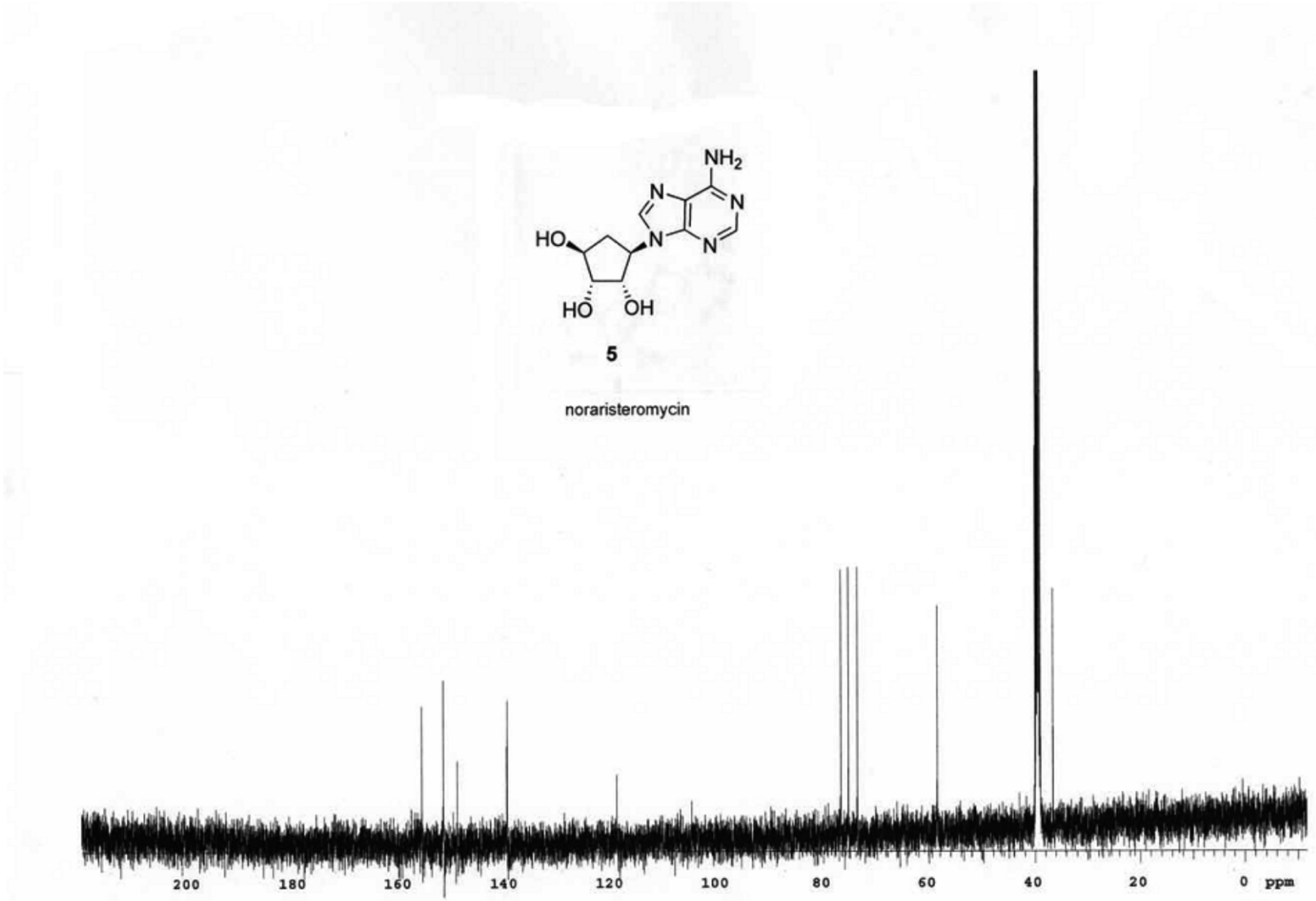
^{1}H NMR Spectrum 29

^{13}C NMR Spectrum of 29





1H NMR Spectrum of 5



^{13}C NMR Spectrum of 5