Supporting Information

Bismethylene Triphosphate Nucleotides of Uridine-4-Phosphate Analogues – A New Class of Anionic-Pyrimidine Nucleotide Analogues

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General. All starting materials and reagents were obtained commercially and used without further purification with the exception of TMSBr and trimethylphosphite which were distilled under Ar and stored under Ar in a Schlenk tube. Tetrahydrofuran (THF) was distilled from sodium metal in the presence of benzophenone under argon. CH_2Cl_2 was distilled from calcium hydride under nitrogen. DMF was distilled under aspirator pressure from CaH and stored under Ar. Methanol was dried by refluxing over magnesium metal and distilled under Ar and stored over 4 Å molecular sieves. Silica gel flash chromatography (flash chromatography) was performed using silica gel 60 Å (230-400 mesh). $CDCl_3$ was used as the solvent for all NMR experiments unless stated otherwise. For ^1H NMR in $CDCl_3$, chemical shifts (δ) are reported in ppm relative to tetramethylsilane (δ 0.0, internal standard). For ^1H NMR in CD_3OD, chemical shifts are reported in ppm relative to the solvent residual peak (δ 3.31, central peak). For ^1H NMR in D_2O, chemical shifts are reported in ppm relative to the solvent residual peak (δ 4.79). For ^1H NMR in DMSO-d_6, chemical shifts are reported in ppm relative to the solvent residual peak (δ 2.49). For ^{13}C NMR in $CDCl_3$, chemical shifts are reported in ppm relative to $CDCl_3$ (δ 77.0 for the central peak). For ^{13}C NMR spectra run in CD_3OD, chemical shifts are reported in ppm relative to the solvent residual peak (δ 49.00, central peak). For ^{13}C NMR in DMSO-d_6, chemical shifts are reported in ppm relative to DMSO-d_6, (δ 39.5 for the central peak). For ^{13}C NMR spectra run in D_2O, chemical shifts are reported in ppm relative to CH_3OH in D_2O (δ 49.5, external standard). All ^{31}P NMR spectra chemicals shifts are reported in ppm relative to 85% H_3PO_4 (δ 0.0, external standard). All ^{19}F spectra chemical shifts are reported in ppm relative to an external trichlorofluoromethane standard (δ 0.0, Cflash chromatographyl$_3$). Melting points are uncorrected. Semi-preparative and analytical HPLC were performed using C-18 columns.

2′,3′,5′-Tri-*O*-acetyl-3-deazacytidine 4-*N*-[*O*,*O*-Bis(2-cyanoethyl)phosphoramidate] (13). The same procedure as for compound **12** was employed except the following quantities were used: 2′,3′,5′-tri-*O*-acetyl-3-deazacytidine (**10**[1], 0.775 g, 2.1 mmol) in dry THF (10 mL), tetrazole (0.297 g, 4.2 mmol), phosphoramidate **15** (1.14 g, 4.2 mmol) in dry THF (5 mL), *tert*-butyl hydroperoxide (1.25 mL, 12.6 mmol). Purification was achieved using flash chromatography (4% MeOH-96% EtOAc then 10% MeOH-90% EtOAc) to give **13** as a white foam (0.785 g, 68%). ^{1}H NMR (300 MHz): δ 7.83 (d, *J* = 9.9 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 6.20 (dd, *J* = 8.0, 1.9, 1H), 6.16 (d, *J* = 3.3 Hz, 1H), 6.04 (d, *J* = 2.0 Hz, 1H), 5.39 (overlapping dd, *J* = 5.3 Hz, 1H), 5.28 (overlapping dd, *J* = 5.9 Hz, 1H), 4.20-4.39 (m, 7H), 2.75-2.81 (m, 4H), 2.08-2.12 (three overlapping singlets, 9H); ^{13}C NMR (75 MHz): δ 170.4, 169.6, 169.5, 162.7, 150.7, 133.6, 116.7, 102.26 (d, *J* = 7.6 Hz), 101.06 (d, *J* = 8.5 Hz), 88.5, 79.2, 73.8, 69.6, 62.8, 62.01, 61.99 (d, *J* = 4.2 Hz), 20.8, 20.5, 20.4, 19.6 (d, *J* = 6.7 Hz);^{31}P NMR (121 MHz): δ 1.7; LR^{+}ESIMS *m/z* (relative intensity) 555.1 (M + 1, 100), 297.1 (41), 259.1 (35); HR^{+}ESIMS *m/z* calculated for $C_{22}H_{28}N_4O_{11}P$ (M + 1): 555.1481, found 555.1492.

2′,3′,5′-Tri-*O*-benzoyl-3-deazacytidine 4-*N*-[*O*,*O*-Bis(2-cyanoethyl)phosphoramidate] (14). Same procedure as for compound **12** except the following quantities were used: 2′,3′,5′-tri-*O*-benzoyl-3-deazacytidine (**11**,[1] 1.70 g, 3.07 mmol) in dry THF (20 mL), tetrazole (0.430 g, 6.14 mmol), phosphoramidate **15** (1.67 g, 6.14 mmol) in dry THF (10 mL), *tert*-butyl hydroperoxide (3.1 mL, 30.7 mmol). Purification was achieved using flash chromatography (EtOAc then 2% MeOH-98% EtOAc) to give **14** as a white foam (1.82 g, 80%). ^{1}H NMR (300 MHz): δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.87-7.95 (m, 4H), 7.10-7.60 (m, 10 H), 7.12, (d, *J* = 9.0 Hz, 1H), 6.42 (d, *J* = 3.3 Hz, 1H), 6.05 (s overlapping with d, 2H), 5.79-5.87 (m, 2H), 4.65-4.82 (m, 3H), 4.20-4.369 (m, 4H), 2.71-2.81 (m, 4H); ^{13}C NMR (75 MHz): δ 166.1, 165.24, 165. 17, 162.7, 150.9, 134.1, 133.66, 133.60, 133.4, 129.8, 129.75, 129.71, 129.4, 128.73, 128.70, 128.57, 128.;53, 128.44, 116.80, 102.36 (d, *J* = 7.2 Hz), 101.28 (d, *J* = 8.4 Hz), 89.8, 79.7, 74.8, 70.1, 63.7, 62.0

(d, J = 3.6 Hz), 19.6, (d, J = 7.8 Hz); ^{31}P NMR (121 MHz): δ 1.72; LR^{+}ESIMS *m/z* (relative intensity) 741.2 (M + 1, 97), 445.2 (100); HR^{+}ESIMS *m/z* calculated for $C_{37}H_{34}N_4O_{11}P$ (M + 1): 741.1962, found 741.1945.

{1-[3,4-bis-(acetoyloxy)-5-acetoyloxymethyltetrahydro-furan-2-yl]-2-oxo-1,2-dihydro-pyridin-4-ylmethyl}phosphonic acid dimethyl ester (22). (2-Hydroxypyridin-4-ylmethyl)phosphonic acid dimethyl ester[2] (0.330 g, 1.52 mmol) and acetyl 2,3,5-tri-*O*-acetyl-β-D-ribofuranose (0.484 g, 1.52 mmol) were suspended in dry CH_3CN (6 mL) under Ar at 0 ^{o}C (ice bath). After addition of bis(trimethylsilyl)trifluoroacetamide (0.606 mL, 2.25 mmol) to the suspension, the ice bath was removed and the solution stirred for 1 h. Trimethylsilyltriflate (0.412 mL, 2.25 mmol) was added and the solution stirred for 2 h. The reaction was diluted with EtOAc (200 mL) and ether (100 mL) and washed with sat. $NaHCO_3$ and sat. brine. The organic layer was dried and concentrated and the residue purified by flash chromatography (5% MeOH-95% EtOAc then 10% MeOH-90% EtOAc) which gave pure compound **22** as a white foam (0.450 g, 62%). ^{1}H NMR (300 MHz): δ 7.44 (d, J = 7.2 Hz, 1H), 6.37 (s, 1H), 6.24 (s overlapping with d, 2H), 5.35 (overlapping dd, J = 4.6 Hz, 1H), 5.30 (overlapping dd, J = 5.1 Hz, 1H), 4.30-4.40 (m, 3 H), δ 3.72 (d, J = 10.7 Hz, 3H), 3.72 (d, J = 10.9 Hz, 3H), 2.51 (d, J = 36.7 Hz, 2H), 2.08, (three overlapping singlets, 9H); ^{13}C NMR (75 MHz): δ 170.1, 169.4, 169.3, 161.49 (d, J = 2.4 Hz), 145.37 (d, J = 8.6 Hz), 132.0, 120.83 (d, J = 8.5 Hz), 108.34 (d, J = 4.5 Hz), 88.1, 79.3, 73.8, 69.6, 62.7, 52.98 (d, J = 6.5 Hz), 32.21 (d, J = 136.2 Hz), 20.6, 20.3; ^{31}P NMR (121 MHz): δ 27.6; LR^{+}ESIMS *m/z* (relative intensity) 476.1 (M + 1, 100); HR^{+}ESIMS *m/z* calculated for $C_{19}H_{27}NO_{11}P$ (M + 1): 476.1322, found 476.1321.

1-(2′,3′-Di-*O*-acetyl-β-D-ribofuranosyl)-2-oxo-1,2-dihydropyridine (24). Prepared from compound **21** as a white foam in 75 % yield (90% EtOAc-10% hexane) using the general deacetylation procedure described in the experimental section. ^{1}H NMR (300 MHz): δ 7.76 (d, J = 7.4 Hz, 1H), 7.15-7.21 (m,

1H), 6.32 (d, *J* = 9.6 Hz, 1H), 6.07-6.16 (m, 2H), 5.30-5.39 (m, 2H), 4.54 (bs, 1H), 4.10 (s, 1H), 3.80 (d, *J* = 11.6 Hz, 1H), 3.65 (d, *J* = 12.4 Hz, 1H); ^{13}C NMR (75 MHz): δ 169.7, 169.3, 162.5, 140.3, 133.8, 120.1, 106.8, 87.8, 83.1, 73.9, 70.4, 60.8, 20.4, 20.2; LREIMS *m/z* (relative intensity) 311.1 (M+, 14), 217.1 (100), 162.1 (17), 127.1 (40), 85 (37); HREIMS *m/z* calculated for $C_{14}H_{17}NO_7$: 311.1005, found 311.1004

{1-[3,4-bis-(acetoyloxy)-5-hydroxymethyltetrahydro-furan-2-yl]-2-oxo-1,2-dihydro-pyridin-4-ylmethyl}phosphonic acid dimethyl ester (25). Prepared from compound **22** as a white foam in 87% yield (5% MeOH-90% $CHCl_3$) using the general deacetylation procedure described in the experimental section. ^{1}H NMR (300 MHz): δ 7.73 (d, *J* = 5.9 Hz, 1H), 6.26 (s, 1H), 6.17 (d, *J* = 4.8 Hz, 1H), 6.13 (d, *J* = 7.4 Hz, 1H), 5.34-5.40 (m, 2H), 4.23 (bs, 1H), 4.11 (s, 1H), 3.80 (d, *J* = 13.8 Hz, 1H), 3.67 (d, *J* = 13.9 Hz, 1H), 3.61 (d, *J* = 11.0 Hz, 3H), 3.60 (d, *J* = 11.4 3 Hz, 3H), 2.87 (d, *J* = 22.4 Hz, 2H), 1.97 (s, 3H), 1.93 (s, 3H); ^{13}C NMR (75 MHz): δ 170.0, 169.6, 162.13 (d, *J* = 2.3 Hz), 145.49 (d, *J* = 8.8 Hz), 133.63 (d, *J* = 2.0 Hz), 120.53 (d, *J* = 9.0 Hz), 108.73 (d, *J* = 3.7 Hz), 87.7, 83.5, 74.1, 70.8, 61.2, 53.20 (d, *J* = 6.9 Hz), 53.17 (d, *J* = 6.1 Hz), 32.2 (d, *J* = 136.9 Hz), 20.7, 20.5. ^{31}P NMR (121 MHz): δ 28.0; LR^{+}ESIMS *m/z* (relative intensity) 434.1 (M + 1, 100), 217 (25); HR^{+}ESIMS *m/z* calculated for $C_{17}H_{25}NO_{10}P$ (M + 1): 434.1216, found 434.1216.

2′,3′,5′-Di-*O*-acetyl-3-deazacytidine 4-*N*-[*O*,*O*-Bis(2-cyanoethyl)phosphoramidate] (28). Prepared from compound **13** as a white foam in 84% yield (10% MeOH-95% EtOAc) using the general deacetylation procedure described in the experimental section. ^{1}H NMR (300 MHz): δ 7.54 (d, *J* = 7.5 Hz, 1H), 6.94 (s, 1H), 6.17 (d, *J* = 9.4 Hz, 1H), 6.03 (s, 1H), 5.94 (d, *J* = 4.4 Hz, 1H), 5.67 (d, *J* = 5.3 Hz, 1H), 5.58 (d, *J* = 3.6 Hz, 1H), 5.49 (d, *J* = 5.3 Hz, 1H), 4.30 (m, 5H), 3.96 (d, *J* = 12.1 Hz, 1H), 3.78 (d, *J* = 13.8 Hz, 1H), 3.64 (s, 1H), 2.80 (t, *J* = 5.9 Hz, 4H), 2.07, 2.09 (two overlapping singlets, 6H);

^{13}C NMR (75 MHz): δ 170.1, 169.8, 163.2, 151.1, 135.4, 117.0, 102.2 (d, *J* = 6.5 Hz), 101.4 (d, *J* = 9.6 Hz), 89.2, 83.2, 73.6, 70.4, 62.2 (d, *J* = 4.3 Hz), 61.1, 20.6, 20.5, 19.6 (d, *J* = 7.8 Hz); ^{31}P NMR (121 MHz): δ 1.6; LR^{+}ESIMS *m/z* (relative intensity) 513.1 (M +1, 100), HR^{+}ESIMS *m/z* calculated for $C_{20}H_{26}N_4O_{10}P$: 513.1387, found 513.1406.

2′,3′-Di-*O*-benzoyluridine (34). Prepared from compound **29** as a white solid in 81% yield (70% EtOAc-30% hexane) using the general debenzoylation procedure described in the experimental section. Mp (EtOAc) 195-197 ^{o}C (lit.[3] mp 194-196 ^{o}C); ^{1}H NMR (300 MHz, CD_3OD): δ 8.15 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 6.9 Hz, 2H), 7.88 (d, *J* = 8.3, 2H), 7.37-7.67 (m, 6H), 6.42 (d, *J* = 6.0 Hz, 1H), 5.79-5.88 (m, 3H), 4.52 (d, *J* = 2.4 Hz, 1H), 3.91-4.01 (m, 2H).

1-(2′,3′-Di-*O*-benzoyl-β-D-ribofuranosyl)-2-oxo-1,2-dihydropyridine (35). Prepared from compound **30** using the general debenzoylation procedure described in the experimental section. Purification was achieved by re-crystallation from MeOH which gave **35** as a white solid in 84% yield. Mp 203-204 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6-$CDCl_3$): δ 8.04 (d, *J* = 6.1 Hz, 1H), 7.79-7.88 (m, 4H), 7.44-7.50 (m, 2H), 7.28-7.36 (m, 4H), 6.57 (d, *J* = 5.3 Hz, 1H), 6.33 (d, *J* = 8.9 Hz, 1H), 6.21 (overlapping dd, *J* = 6.2 Hz, 1H), 5.66-5.73 (m, 2H), 5.33 (bt, *J* = 4.5 Hz, 1H), 4.42 (s, 1H), 3.70-3.90 (m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6-$CDCl_3$): δ 165.0, 164.7, 161.9, 140.2, 134.1, 133.6, 129.6, 129.5, 129.1, 128.8, 128.6, 128.5, 120.2, 106.2, 86.7, 83.7, 75.0, 71.7, 60.9; LR^{+}ESIMS *m/z* (relative intensity) 436.1 (M + 1, 100), 341.1 (75), 183.0 (30); HR^{+}ESIMS *m/z* calculated for $C_{24}H_{22}NO_7$: 436.1396 (M + 1), found 436.1396.

2′,3′,5′-Di-*O*-acetyl-3-deazacytidine 4-*N*-[*O,O*-Bis(2-cyanoethyl)phosphoramidate] (38). Catalyst **20** (30 mol %) was added to a solution of the nucleoside **14** (200 mg, 0.27 mmol) in dry MeOH-dry THF (8 mL, 1:1) and the resulting solution was stirred at 48 ^{o}C (oil bath). After 48 h, an additional 16 mol% catalyst was added and the reaction stirred for an additional 24 h at 48 ^{o}C. The solution was concentrated and the resulting residue purified using flash chromatography (4% MeOH-96% EtOAc) to give nucleoside **38**

as a white foam (95.8 mg, 56%). ^{1}H NMR (300 MHz): δ 7.91 (d, *J* = 7.5 Hz, 4H), 7.64 (d, *J* = 8.0 Hz 1H), 7.48.7.55 (m, 2H), 7.29-7.42 (m, 5H), 6.25 (d, *J* = 7.3 Hz, 1H), 6.20 (d, *J* = 4.4 Hz, 1H), 6.10 (s, 1H), 5.98 (overlapping dd, *J* = 5.3 Hz, 1H), 5.88 (overlapping dd, *J* = 5.5 Hz, 1H), 4.47 (d, *J* = 4.4 Hz, 1H), 4.31 (t, *J* = 8.1 Hz, 4H), 4.06 (d, *J* = 12.2 Hz, 1H), 3.91 (d, *J* = 12.7 Hz, 1H), 2.78 (t, *J* = 5.9 Hz, 4H), 1.63 (bs, 1H); ^{13}C NMR (75 MHz): δ 165.7, 165.4, 163.3, 151.0, 135.9, 133.7 (d, *J* = 4.6 Hz), 129.92, 129.86, 129.0, 128.9, 128.6, 102.6 (d, *J* = 7.2 Hz), 101.4 (d, *J* = 8.1 Hz), 90.7, 83.7, 74.6, 71.2, 62.1 (d, *J* = 4.8 Hz), 61.5, 19.7 (d, *J* = 7.2 Hz); ^{31}P NMR (121 MHz): δ 1.67; LR^{+}ESIMS *m/z* (relative intensity): 637.1 (M + 1, 100), 341.1 (23); HR^{+}ESIMS *m/z* calculated for $C_{30}H_{30}N_4O_{10}P$ (M + 1): 637.1700, found 637.1687.

1-(2′,3′-Di-*O*-acetyl-5′-(bis-[(benzyloxyphosphorylmethyl)benzyloxyphosphorylmethyl]-methyloxyphosphoryl)-β-D-ribofuranosyl)-2-oxo-1,2-dihydropyridine (45). Prepared from compound **35** as a white foam in 64% yield (100% EtOAc then 5% MeOH-95% EtOAc) using the general procedure described in the experimental section. ^{1}H NMR (300 MHz): δ 7.94-7.85 (m, 4H), 7.67-7.76 (m, 1H), 7.48-7.53 (m, 2H), 7.20-7.35 (m, 20H), 6.60-6.70 (m, 1H), 6.49 (d, *J* = 8.8 Hz, 1H), 6.17-6.25 (m, 1H), 5.91 (overlapping dd, *J* = 5.3 Hz, 0.4 H), 5.79 (overlapping dd, *J* = 5.3 Hz, 0.6 H), 5.63-5.73 (m, 1H), 4.90-5.20 (m, 6H), 4.37-4.69 (m, 3H), 3.81 (d, *J* = 11.9 Hz, 1H), 3.73 (d, *J* = 11.7 Hz, 2H), 2.68-3.12 (m, 4H); ^{13}C NMR (75 MHz): δ 165.1, 165.04, 165.00, 164.9, 162.1, 162.03, 162.00, 139.8, 139.72, 139.68, 135.68, 135.66, 135.58, 135.55, 135.49, 133.40, 133.37, 13.31, 133.15, 133.07, 132.95, 132.92, 129.7, 129.6, 128.6, 128.52, 128.48, 128.4, 128.3, 128.2, 128.00, 127.91, 127.87, 127.82, 127.80, 120.86, 120.82, 120.75, 106.5, 106.30, 106.27, 87.5, 87.3, 87.2, 86.9, 81.01, 80.95, 80.91, 80.86, 74.51, 74.47, 74.44, 70.55, 70.49, 70.44, 70.40, 68.04, 67.98,l 67.92, 67.86, 67.81, 67.76, 67.08, 67.03, 67.00, 66.93, 66.88, 65.45, 65.41, 65.17, 65.12, 65.07, 65.00, 53.47, 53.43, 53.21, 53.18, 53.16, 53.14, 52.84, 52.80, 26.78-29.49 (m); ^{31}P NMR (121 MHz): δ 39.73-39.80 (m), 39.37-39.50 (m), 23.74-23.84 (m), 23.29-23.43 (m), 21.74-21.85 (m); LR^{+}ESIMS *m/z* (relative intensity): 956 (M + 1); HR^{+}ESIMS *m/z* calculated for $C_{48}H_{49}NO_{14}P_3$: 956.2350, found 956.2366.

{1-[3,4-Bis-(hydroxy)-5-{[(dihydroxyphosphorylmethyl)hydroxyphosphorylmethyl]-hydroxyphosphoryl}tetrahydro-furan-2-yl]- 2-oxo-1,2-dihydropyridine tetrasodium salt (49). Prepared from compound **45** (0.100 g, 0.105 mmol) using the general procedure described in the experimental section. The following solvent system was used for preparative HPLC: solvent A: 100 mM TEAA, pH 7.0, solvent B: CH_3CN. The following elution profile was used: 0-13 min: 99% A-1% B; 13-50 min: linear gradient of 99% A-1% B to 93% A-7% B. Flow rate = 8 mL/min. t_r = 23.36 min. The tetrasodium salt of nucleotide **49**, generated using a Dowex 50Wx8 Na^+ ion exchange column, was a white powder (27.8 mg, 48%). ^{1}H NMR (300 MHz, D_2O): δ 7.92 (d, *J* = 5.8 Hz, 1H), 7.49 (overlapping dd, *J* = 7.2 Hz, 1H), 6.51 (overlapping dd, *J* = 6.8 Hz, 1H), 6.46 (d, *J* = 8.8 Hz, 1H), 6.60, (d, *J* = 2.7 Hz, 1H), 3.97-4.28 (m, 5H), 1.93-2.35 (m, 4H); ^{13}C NMR (75 MHz, D_2O): δ 164.0, 142.4, 133.3, 118.8, 109.4, 89.3, 82.8 (d, *J* = 7.1 Hz), 75.0, 68.9, 62.7, 30.5-32.6 (m); ^{31}P NMR (121 MHz, D_2O): δ 28.4 (P_β), 18.2 (P_α), 15.5 (P_γ); LR$^-$ESIMS *m/z* (relative intensity) 462 (M - 4Na + 3H^+, 100). HR$^-$ESIMS *m/z* calculated for $C_{12}H_{19}NO_{12}P_3$ (M - 4Na + 3H^+): 462.0120, found 462.0123. The analytical HPLC chromatogram of **49** (elution profile: linear gradient of 99% A-1% B to 93% A-7% B over 50 minutes) indicated **49** to be greater than 99.8% pure (flow rate 1 mL/min, t_r = 13.46 min).

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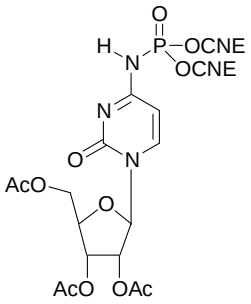
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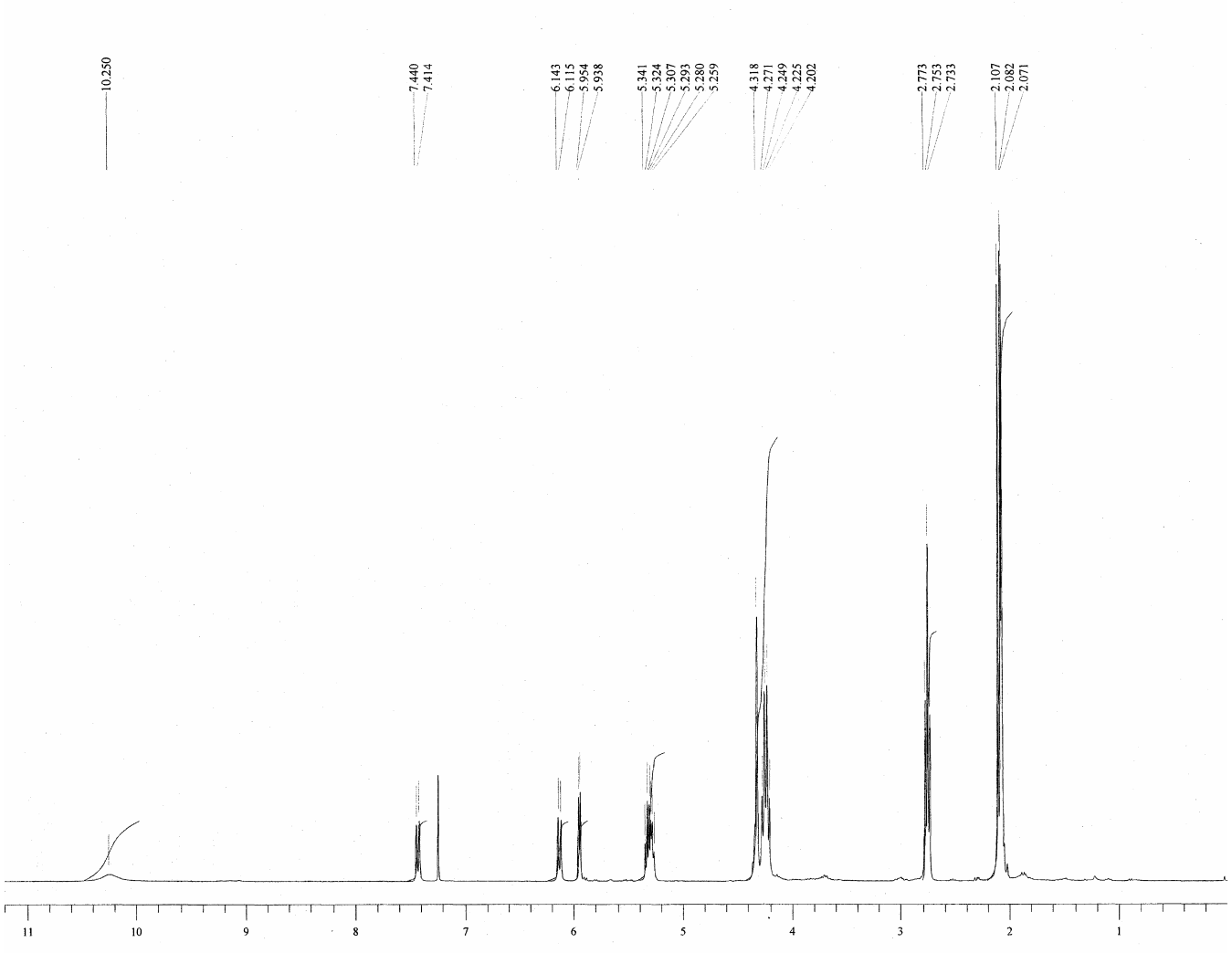
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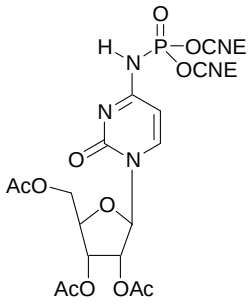
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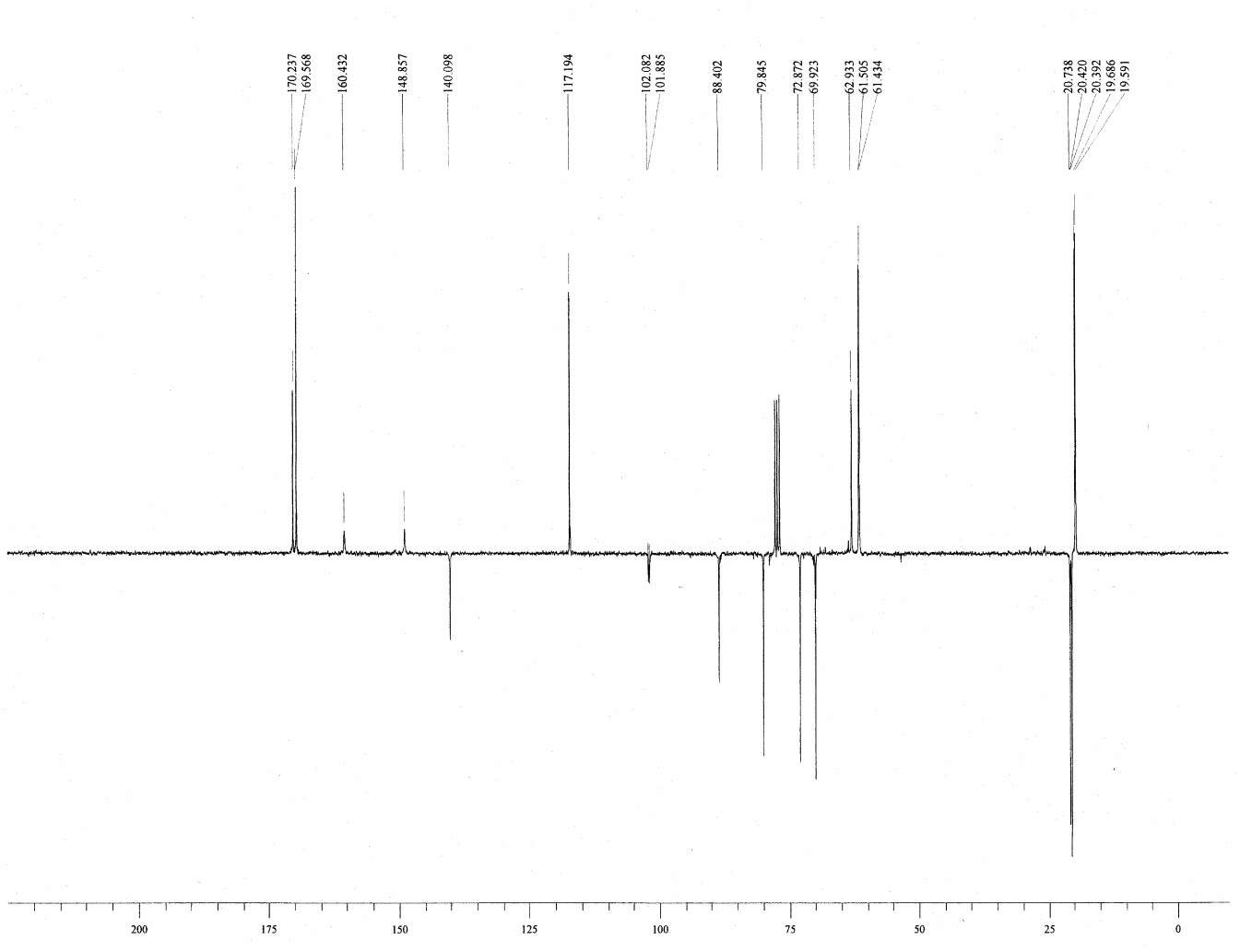
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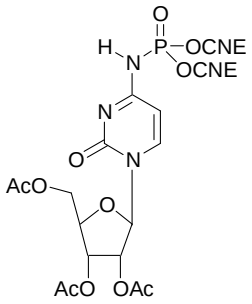
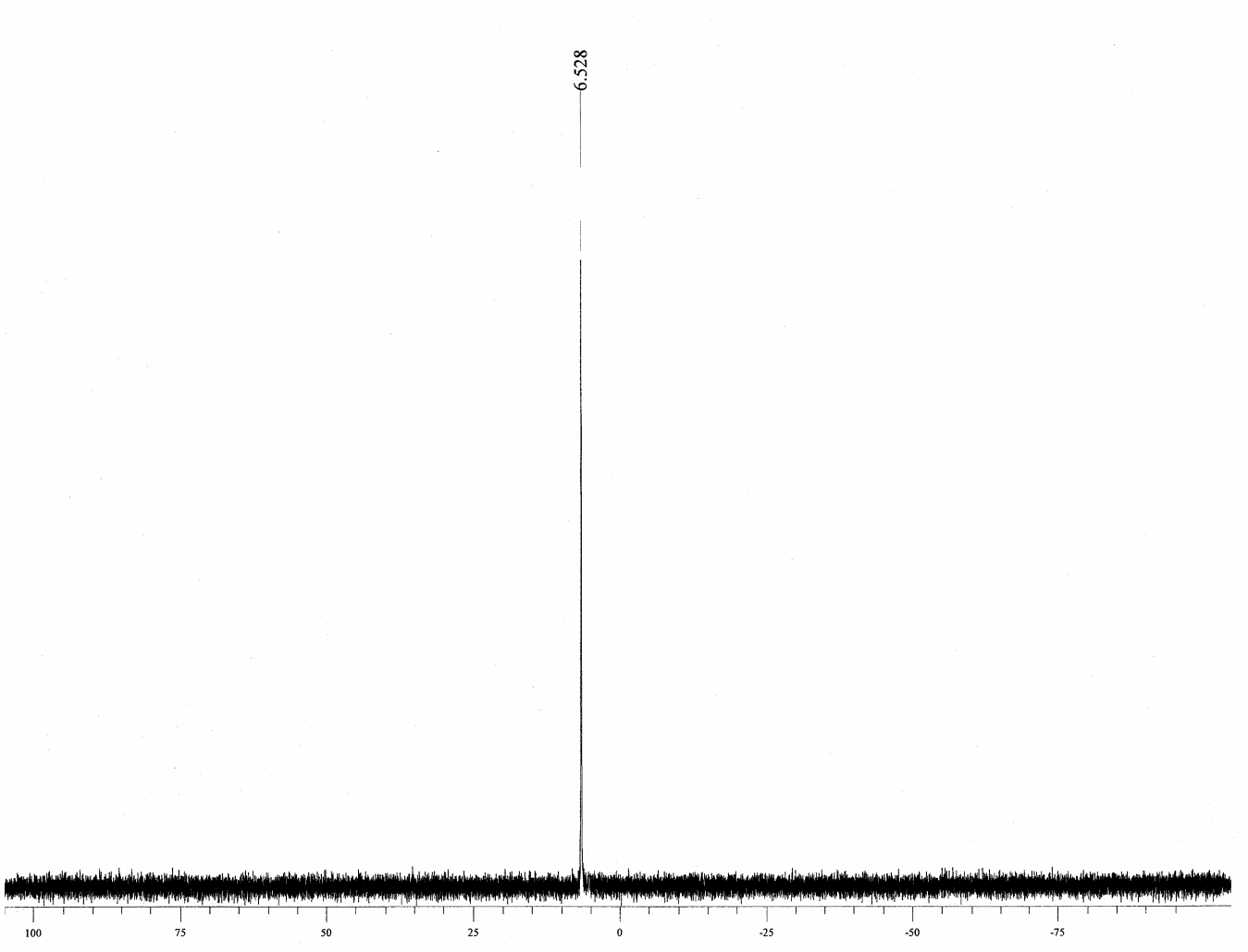
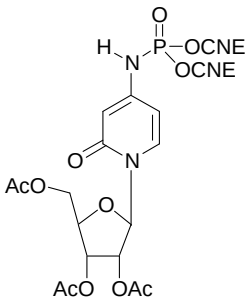


12 ($CDCl_3$)

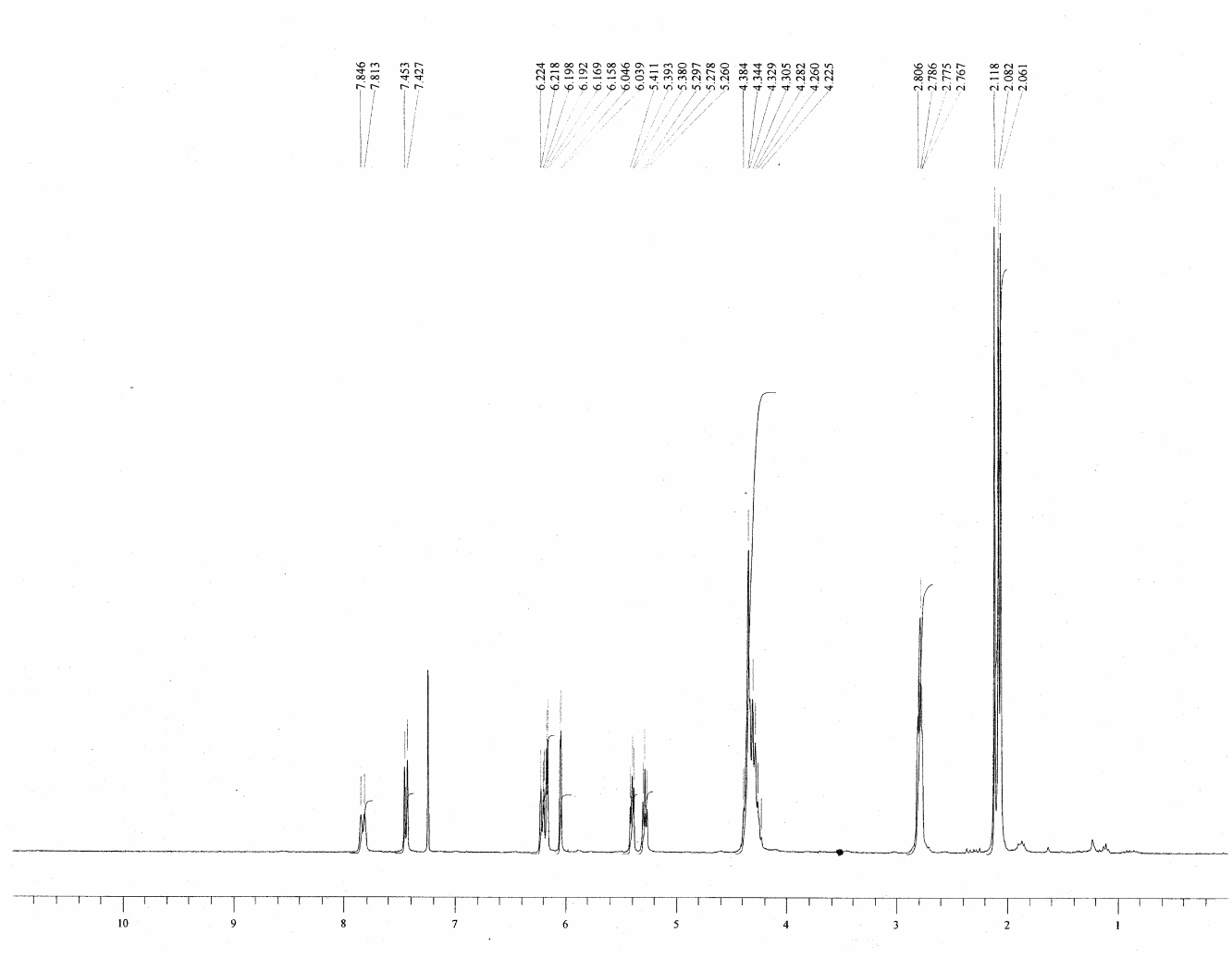
^{31}P

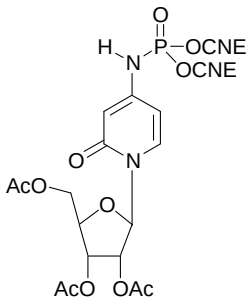



O
H
N
P
OCNE
OCNE
O
N
AcO
O
AcO
OAc

13 ($CDCl_3$)

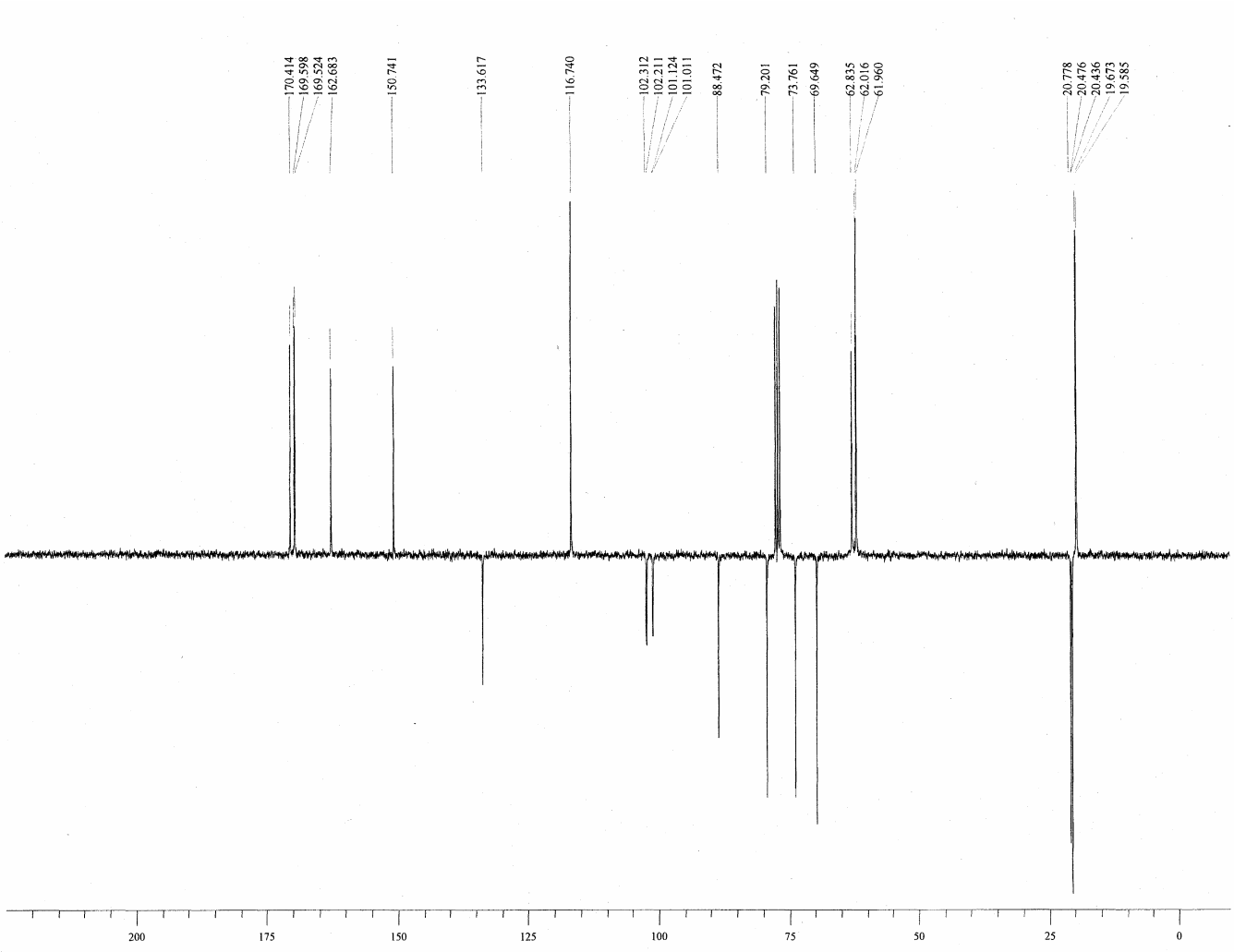
^1H

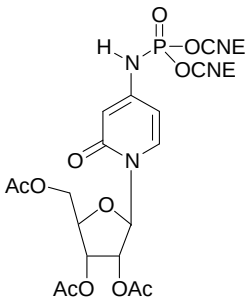

7.846
7.813
7.453
7.427
6.224
6.218
6.198
6.192
6.169
6.158
6.046
6.039
5.411
5.393
5.380
5.297
5.278
5.260
4.384
4.344
4.329
4.305
4.282
4.260
4.225
2.806
2.786
2.775
2.767
2.118
2.082
2.061
10
9
8
7
6
5
4
3
2
1


O
H
N
P
OCNE
OCNE
O
N
AcO
O
AcO
OAc

13 ($CDCl_3$)

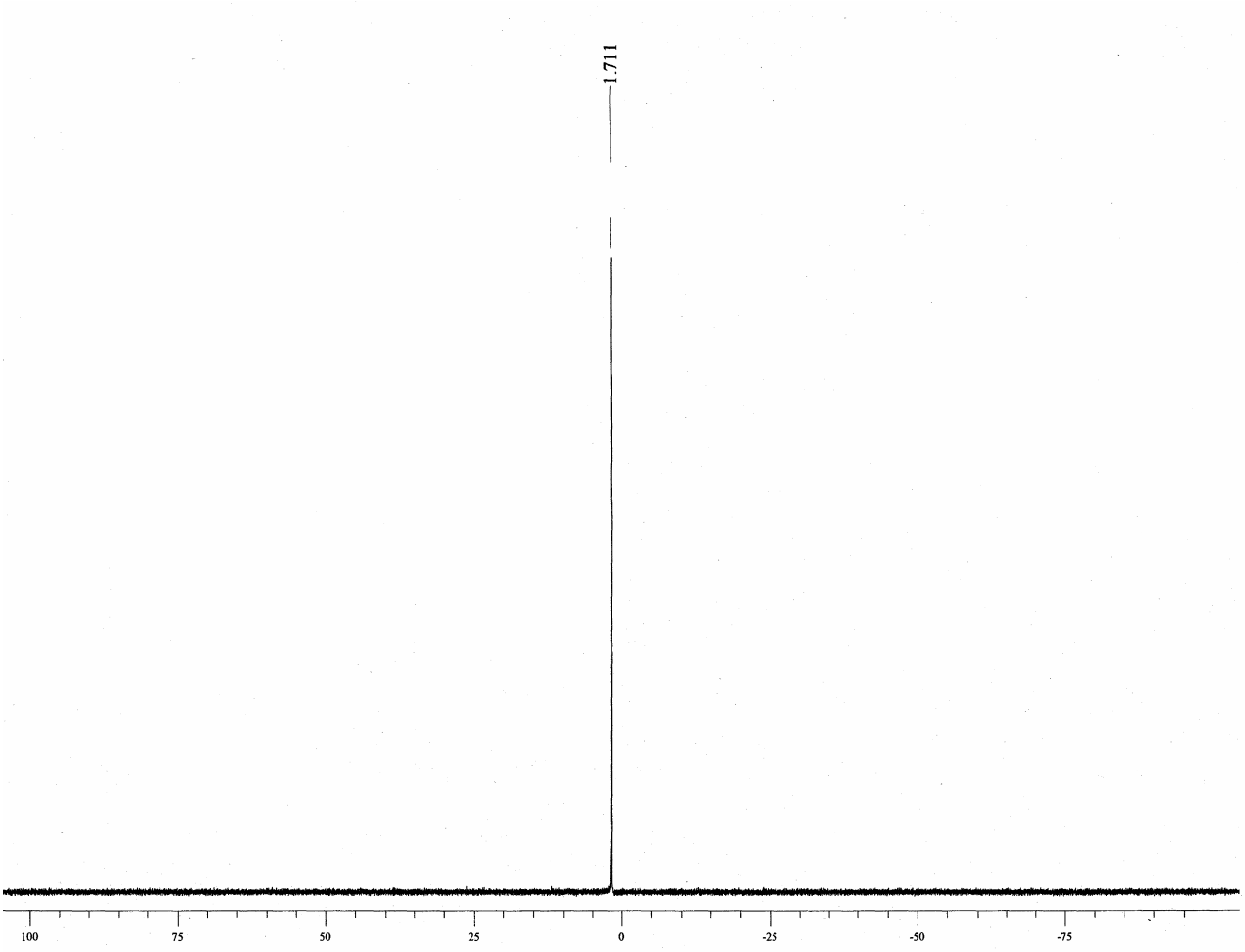
^{13}C

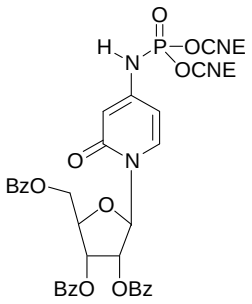

170.414
169.598
169.524
162.683
150.741
133.617
116.740
102.312
102.211
101.124
101.011
88.472
79.201
73.761
69.649
62.835
62.016
61.960
20.778
20.476
20.436
19.673
19.585
200
175
150
125
100
75
50
25
0



13 ($CDCl_3$)

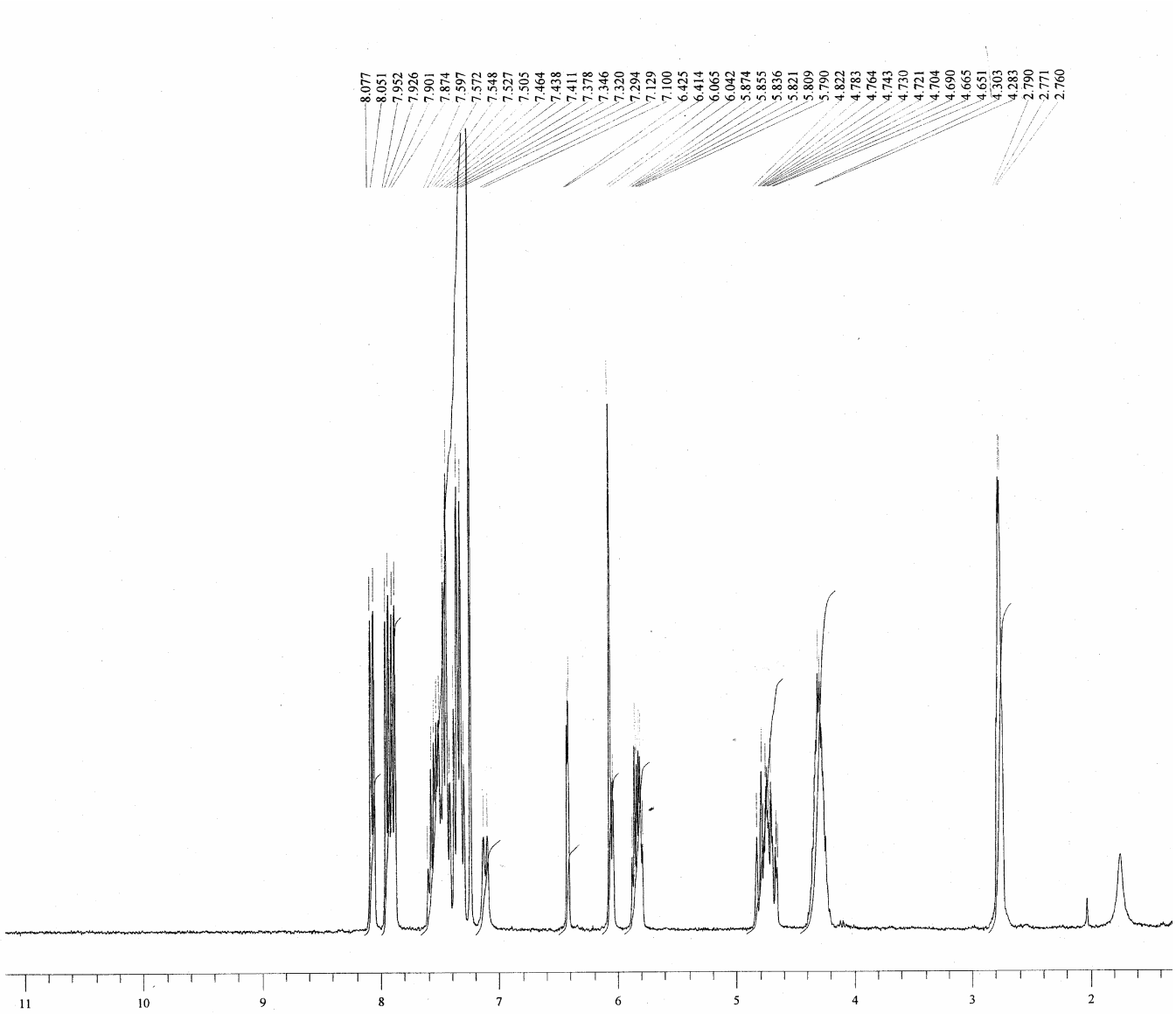
^{31}P

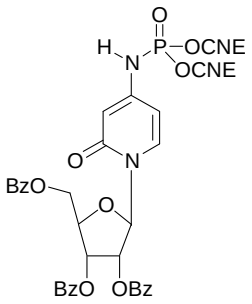



O
H
N
P
OCNE
OCNE
O
N
BzO
O
BzO
OBz

14 ($CDCl_3$)

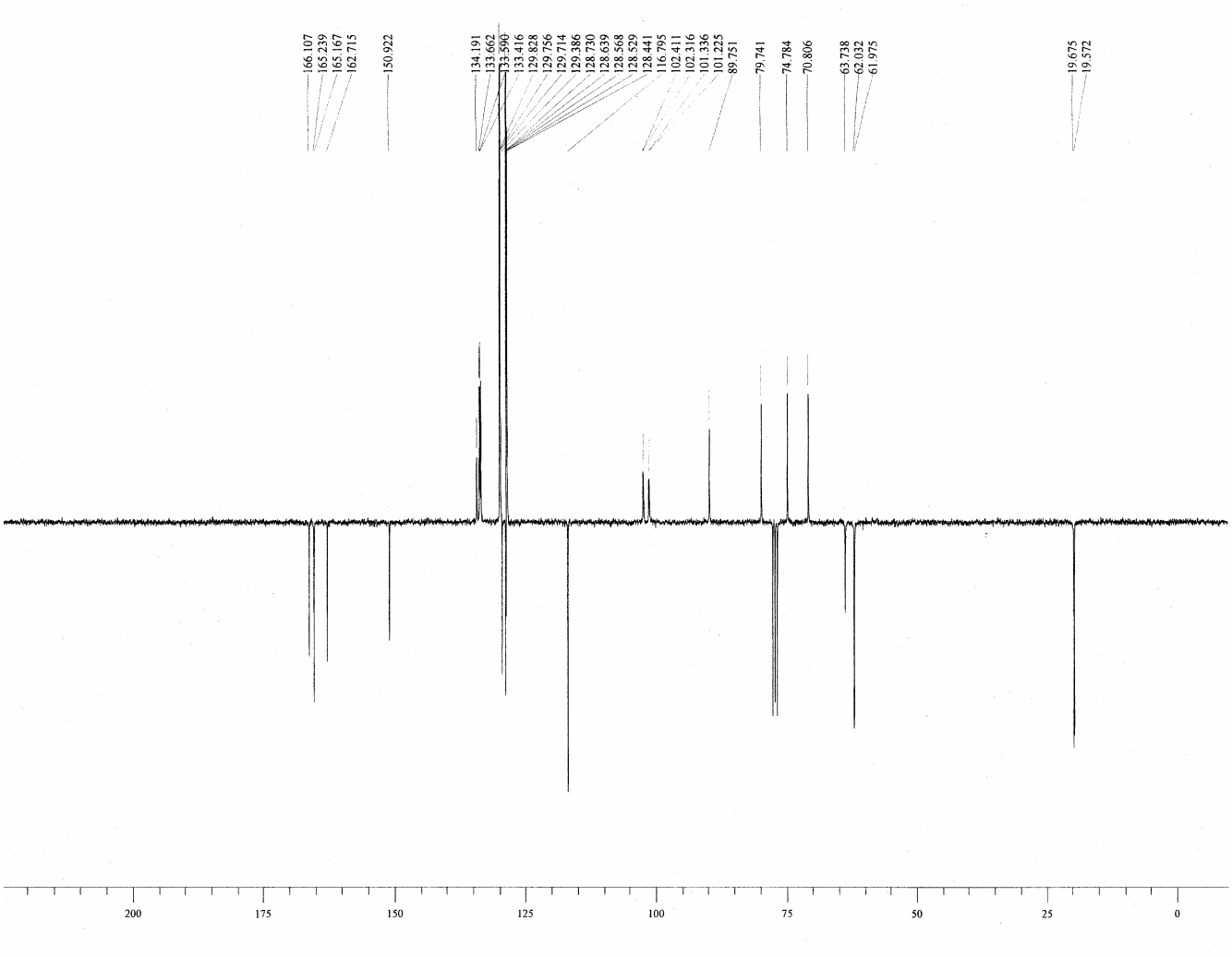
^1H

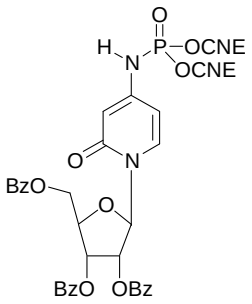

8.077
8.051
7.952
7.926
7.901
7.874
7.597
7.572
7.548
7.527
7.505
7.464
7.438
7.411
7.378
7.346
7.320
7.294
7.129
7.100
6.425
6.414
6.065
6.042
5.874
5.855
5.836
5.821
5.809
5.790
4.822
4.783
4.764
4.743
4.730
4.721
4.704
4.690
4.665
4.651
4.303
4.283
2.790
2.771
2.760
11
10
9
8
7
6
5
4
3
2


O
H
N
P
OCNE
OCNE
O
N
BzO
O
BzO
OBz

14 ($CDCl_3$)

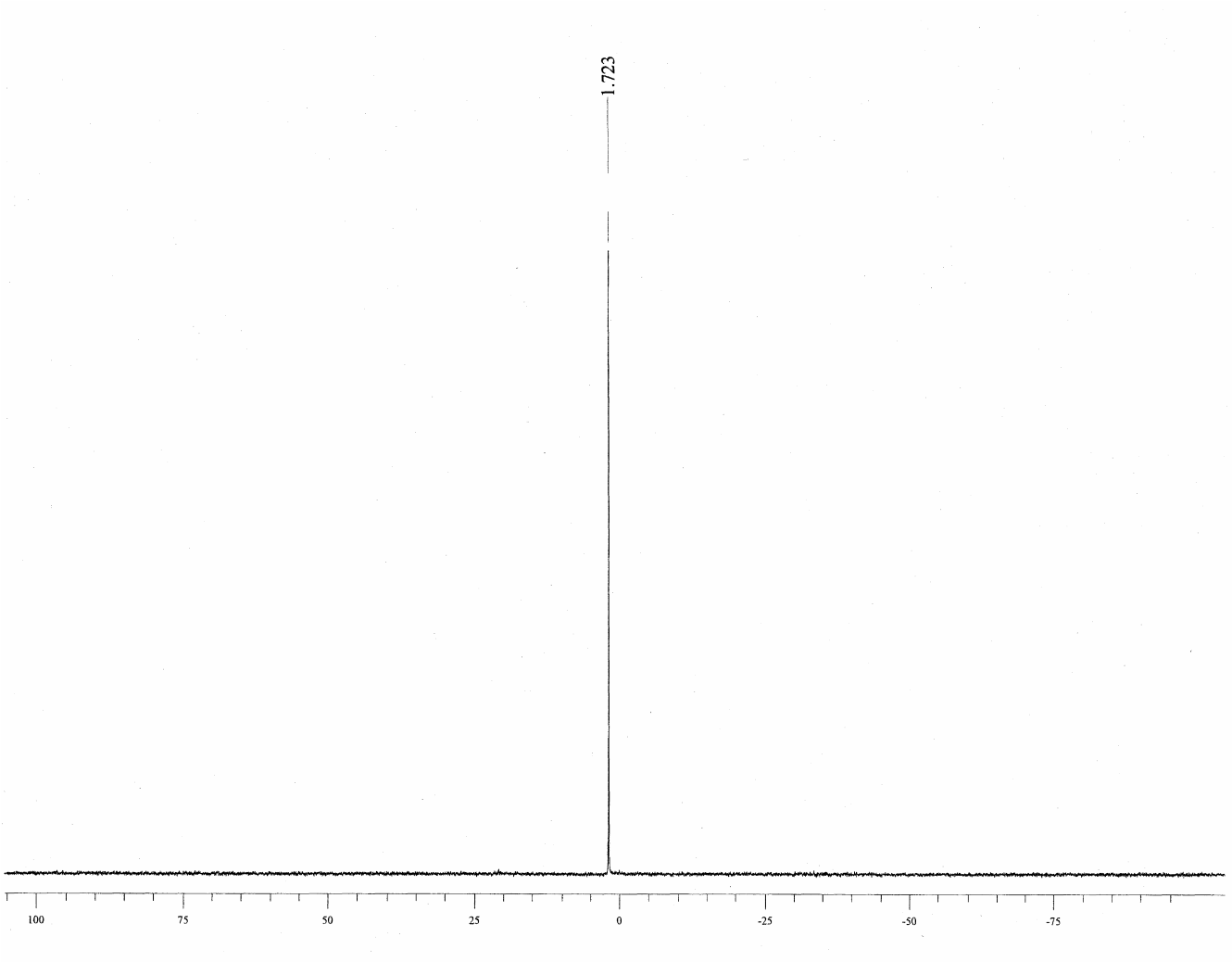
^{13}C

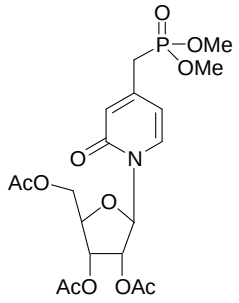

166.107
165.239
165.167
162.715
150.922
134.191
133.662
133.590
133.416
129.828
129.756
129.714
129.386
128.730
128.639
128.568
128.529
128.441
116.795
102.411
102.316
101.336
101.225
89.751
79.741
74.784
70.806
63.738
62.032
61.975
19.675
19.572
200
175
150
125
100
75
50
25
0



14 ($CDCl_3$)

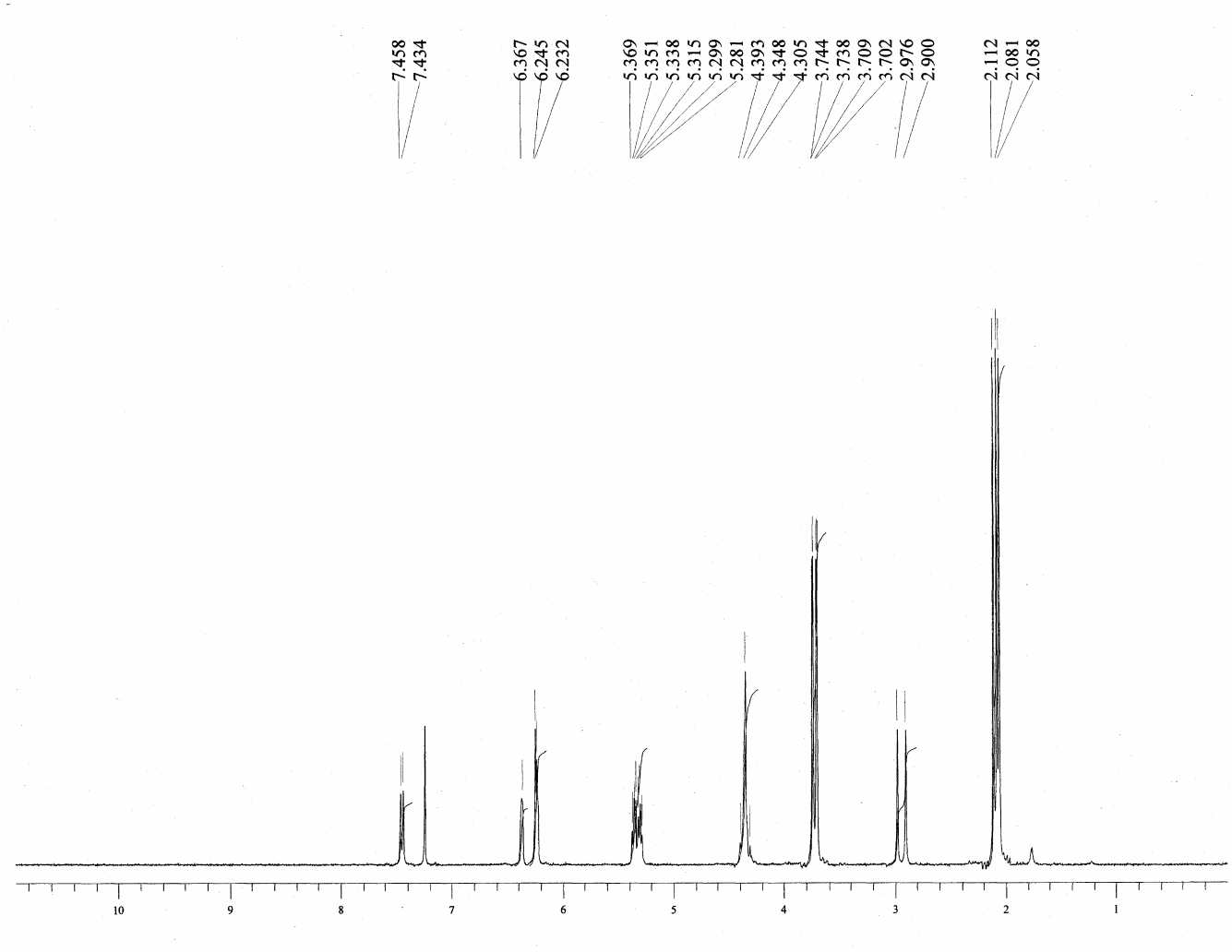
^{31}P

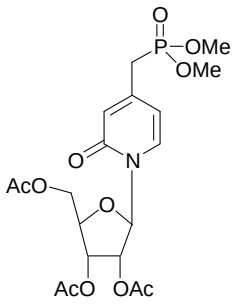



O
P
OMe
OMe
O
N
AcO
O
AcO
OAc

22 ($CDCl_3$)

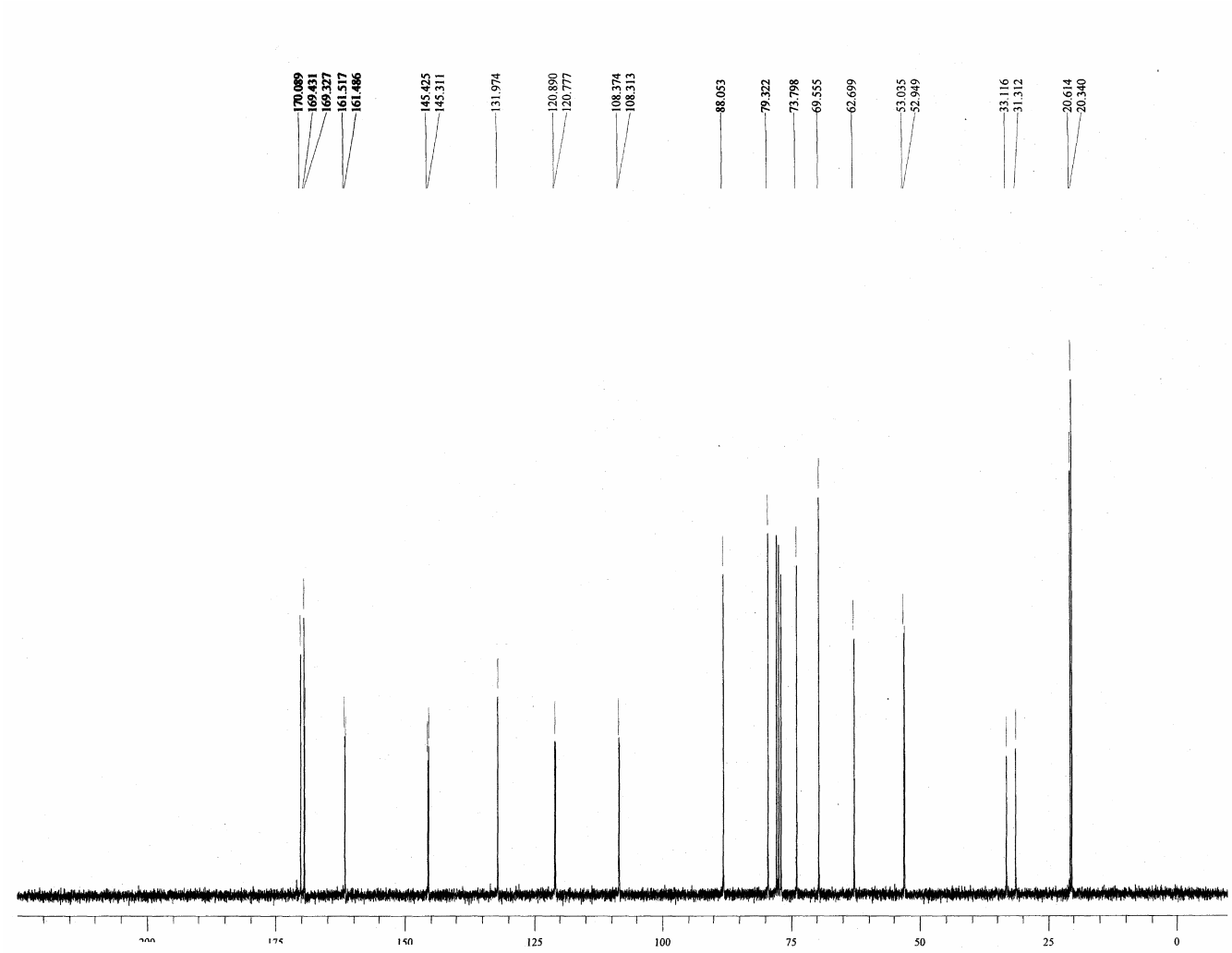
^1H

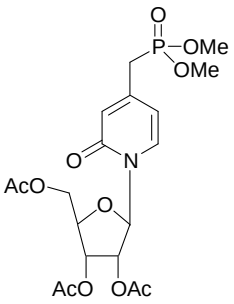

7.458
7.434
6.367
6.245
6.232
5.369
5.351
5.338
5.315
5.299
5.281
4.393
4.348
4.305
3.744
3.738
3.709
3.702
2.976
2.900
2.112
2.081
2.058
10
9
8
7
6
5
4
3
2
1


O
P
OMe
OMe
O
N
AcO
O
AcO
OAc

22 ($CDCl_3$)

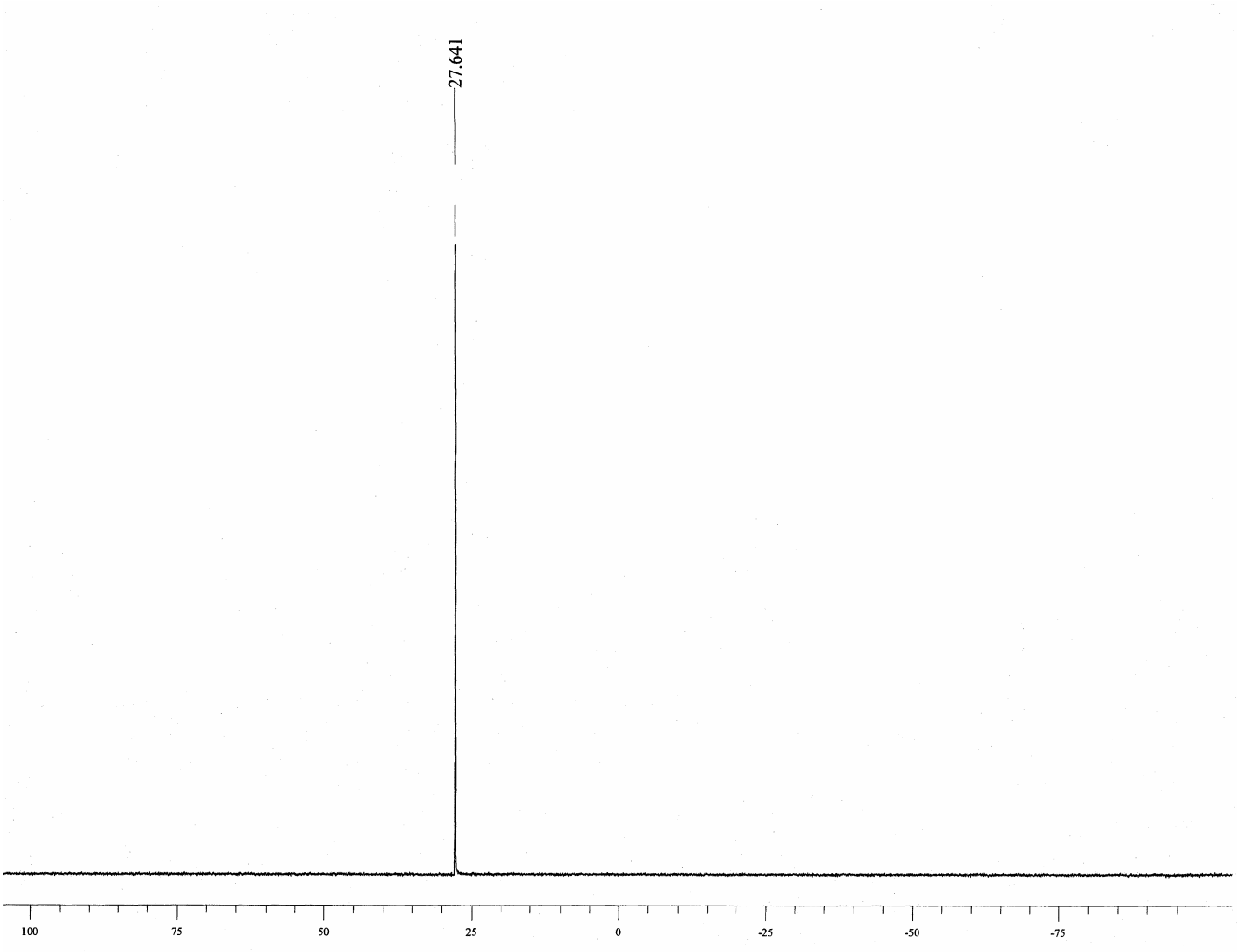
^{13}C

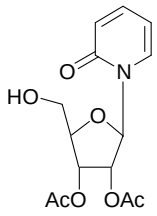

170.089
169.431
169.327
161.517
161.486
145.425
145.311
131.974
120.890
120.777
108.374
108.313
88.053
79.322
73.798
69.555
62.699
53.035
52.949
33.116
31.312
20.614
20.340
200
175
150
125
100
75
50
25
0



22 ($CDCl_3$)

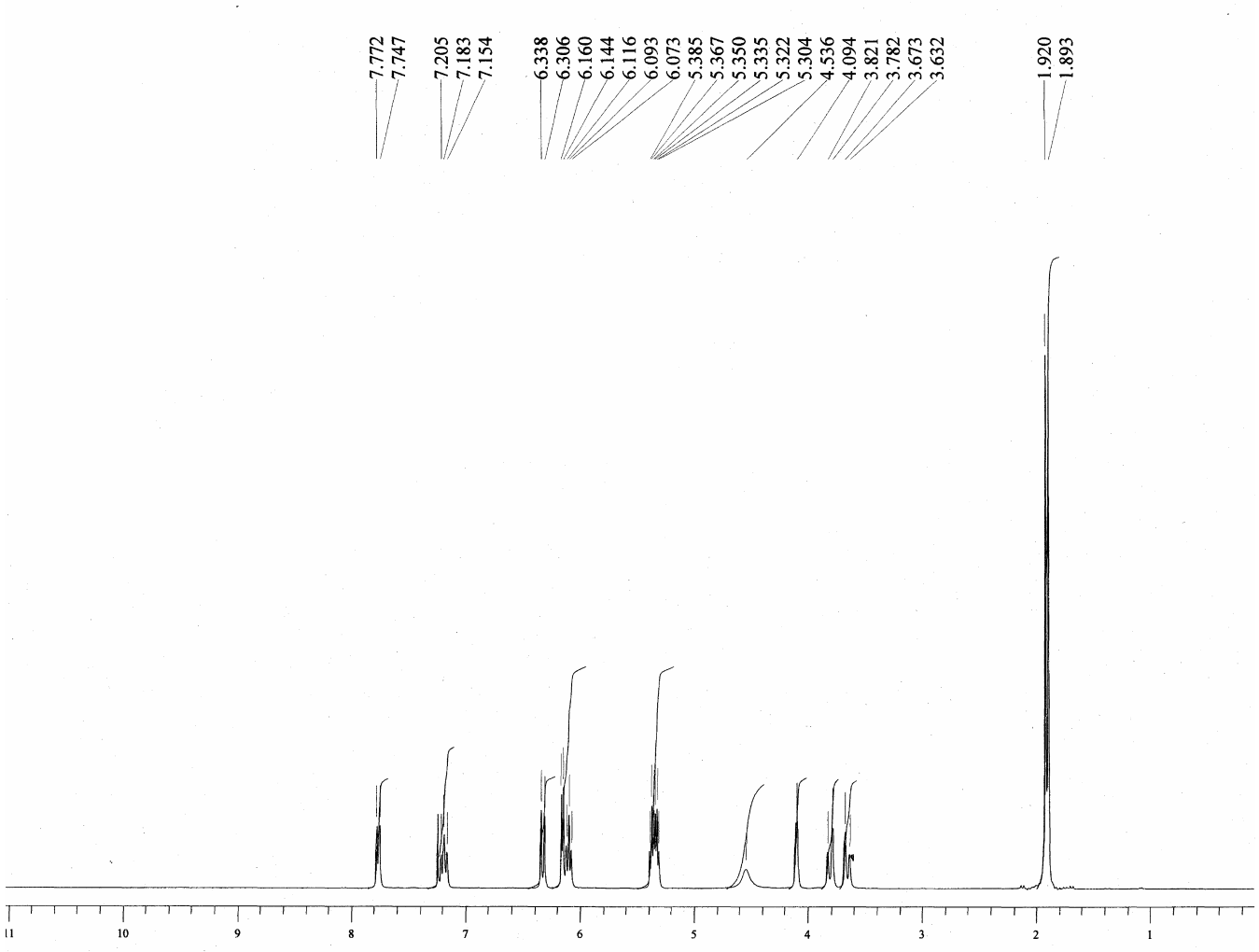
^{31}P

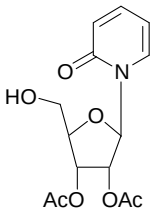



O
N
HO
O
AcO
OAc

24 ($CDCl_3$)

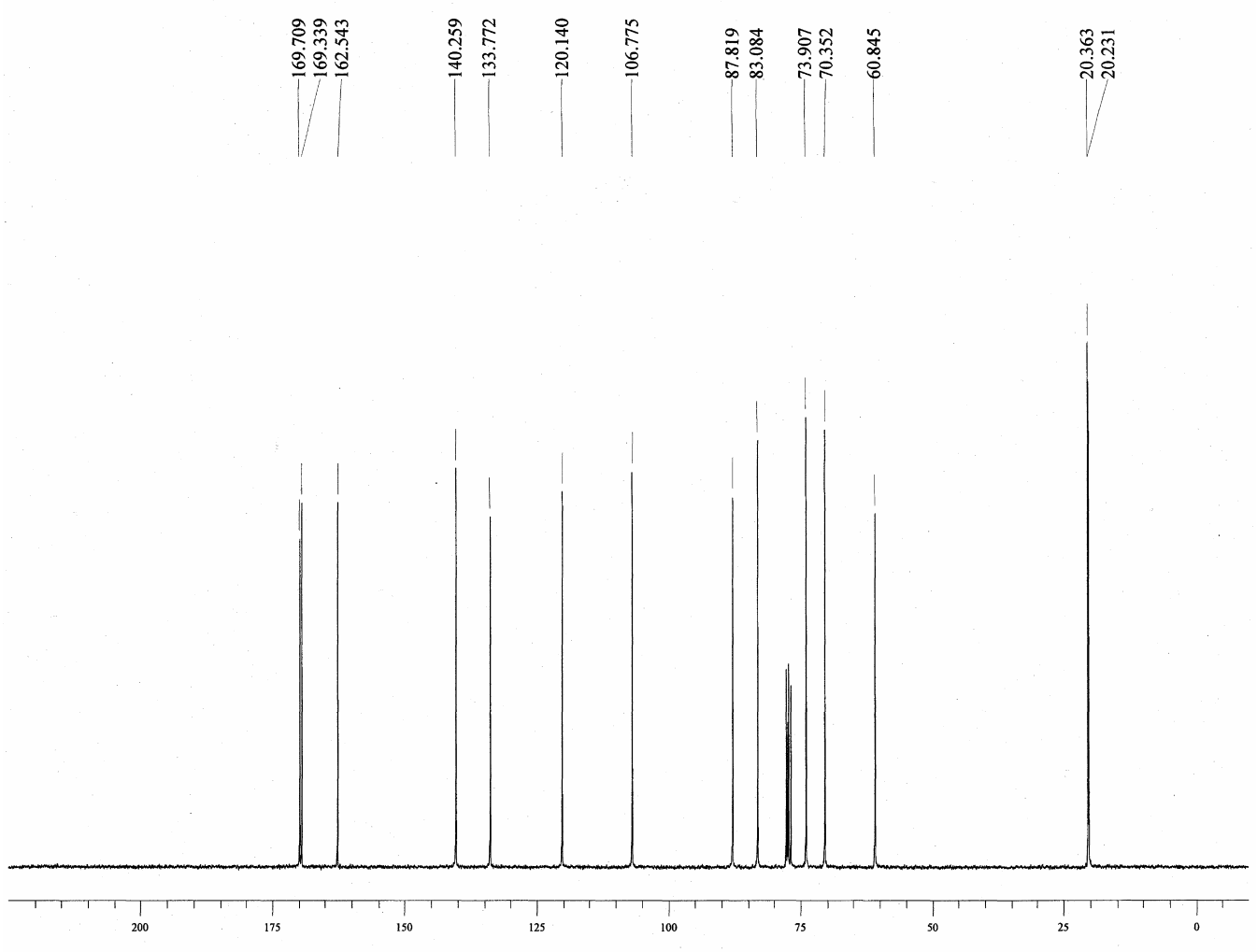
^1H

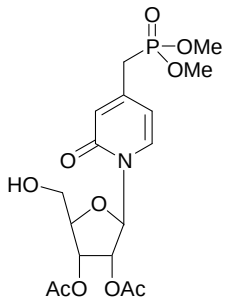

7.772
7.747
7.205
7.183
7.154
6.338
6.306
6.160
6.144
6.116
6.093
6.073
5.385
5.367
5.350
5.335
5.322
5.304
4.536
4.094
3.821
3.782
3.673
3.632
1.920
1.893
11
10
9
8
7
6
5
4
3
2
1


O
N
HO
O
AcO
OAc

24 ($CDCl_3$)

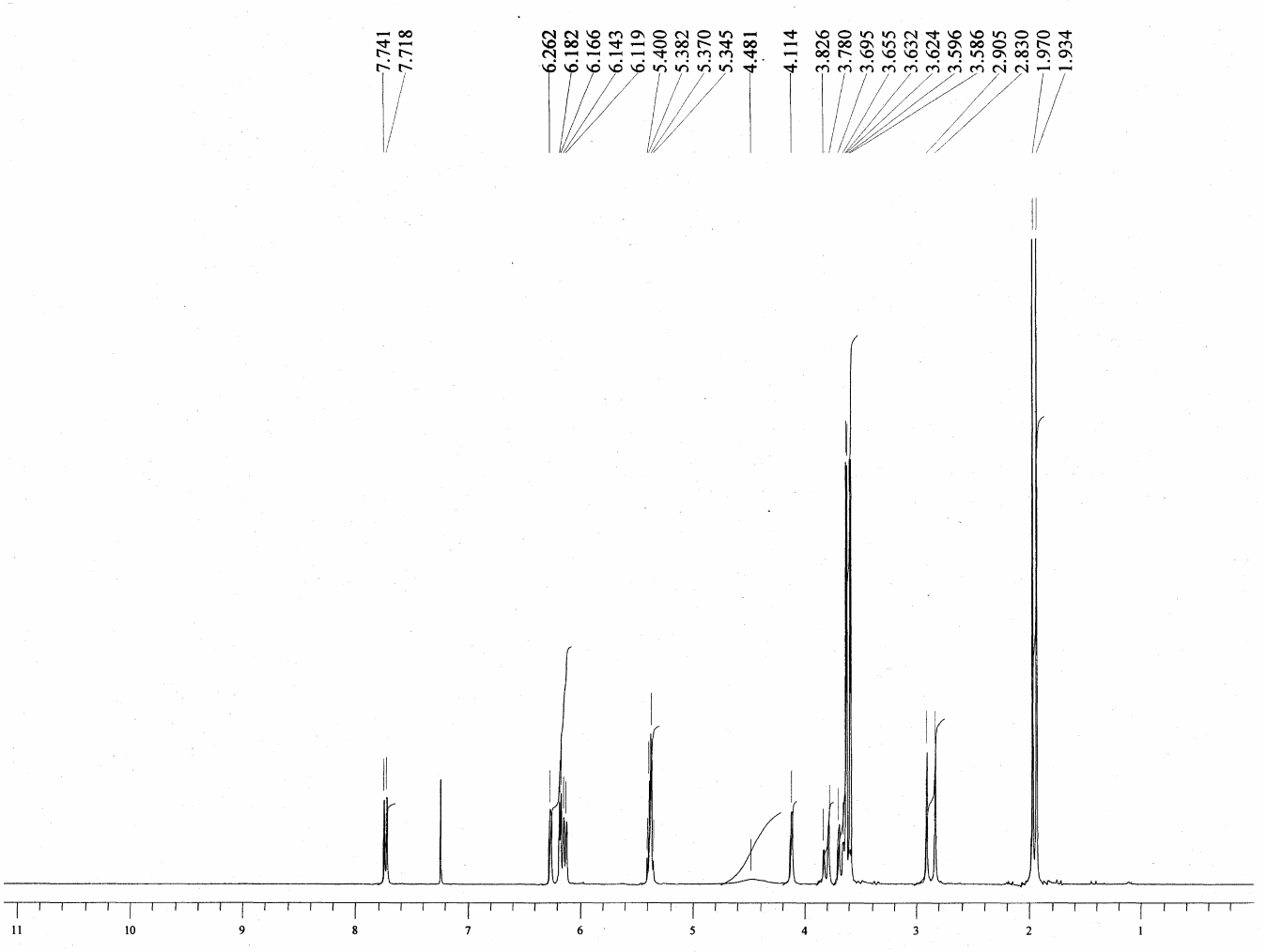
^{13}C

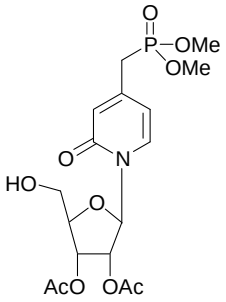

169.709
169.339
162.543
140.259
133.772
120.140
106.775
87.819
83.084
73.907
70.352
60.845
20.363
20.231
200
175
150
125
100
75
50
25
0


O
P
OMe
OMe
O
N
HO
O
AcO
OAc

25 ($CDCl_3$)

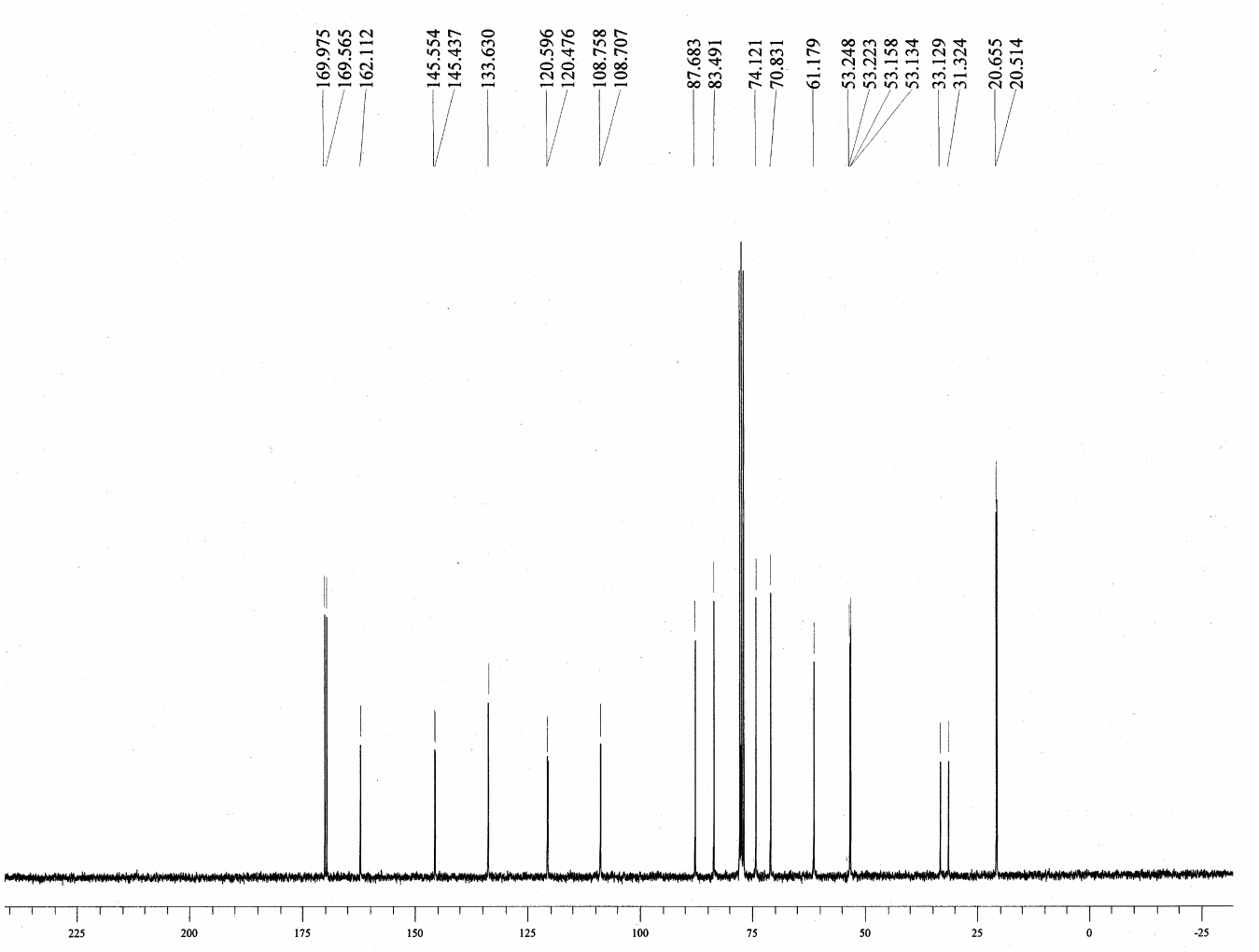
^1H

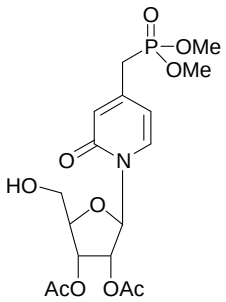

7.741
7.718
6.262
6.182
6.166
6.143
6.119
5.400
5.382
5.370
5.345
4.481
4.114
3.826
3.780
3.695
3.655
3.632
3.624
3.596
3.586
2.905
2.830
1.970
1.934
11
10
9
8
7
6
5
4
3
2
1


O
P
OMe
OMe
O
N
HO
O
AcO
OAc

25 ($CDCl_3$)

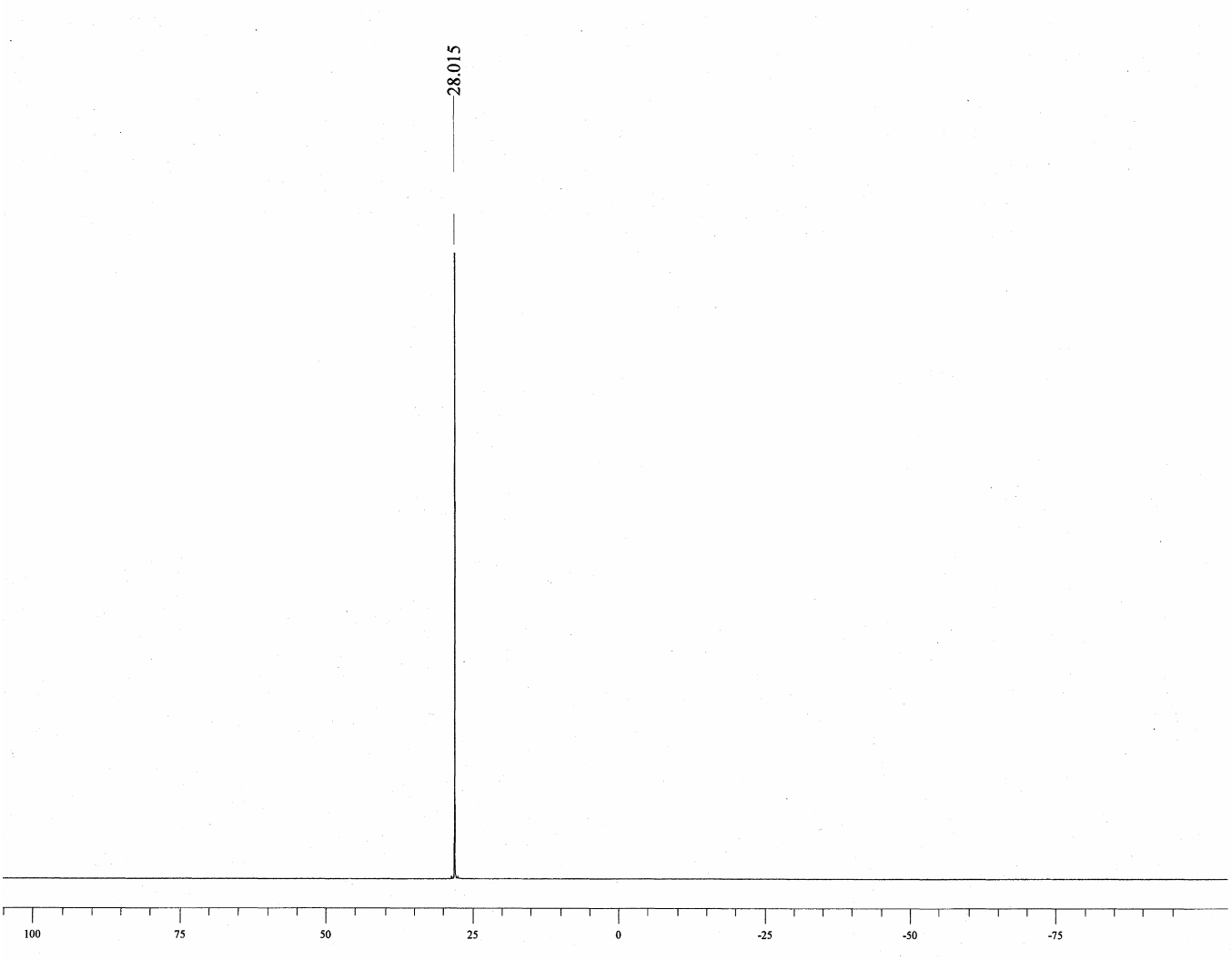
^{13}C

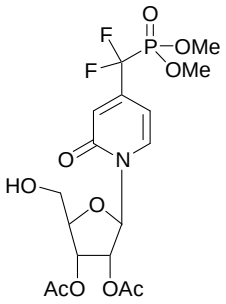

169.975
169.565
162.112
145.554
145.437
133.630
120.596
120.476
108.758
108.707
87.683
83.491
74.121
70.831
61.179
53.248
53.223
53.158
53.134
33.129
31.324
20.655
20.514
225
200
175
150
125
100
75
50
25
0
-25



25 ($CDCl_3$)

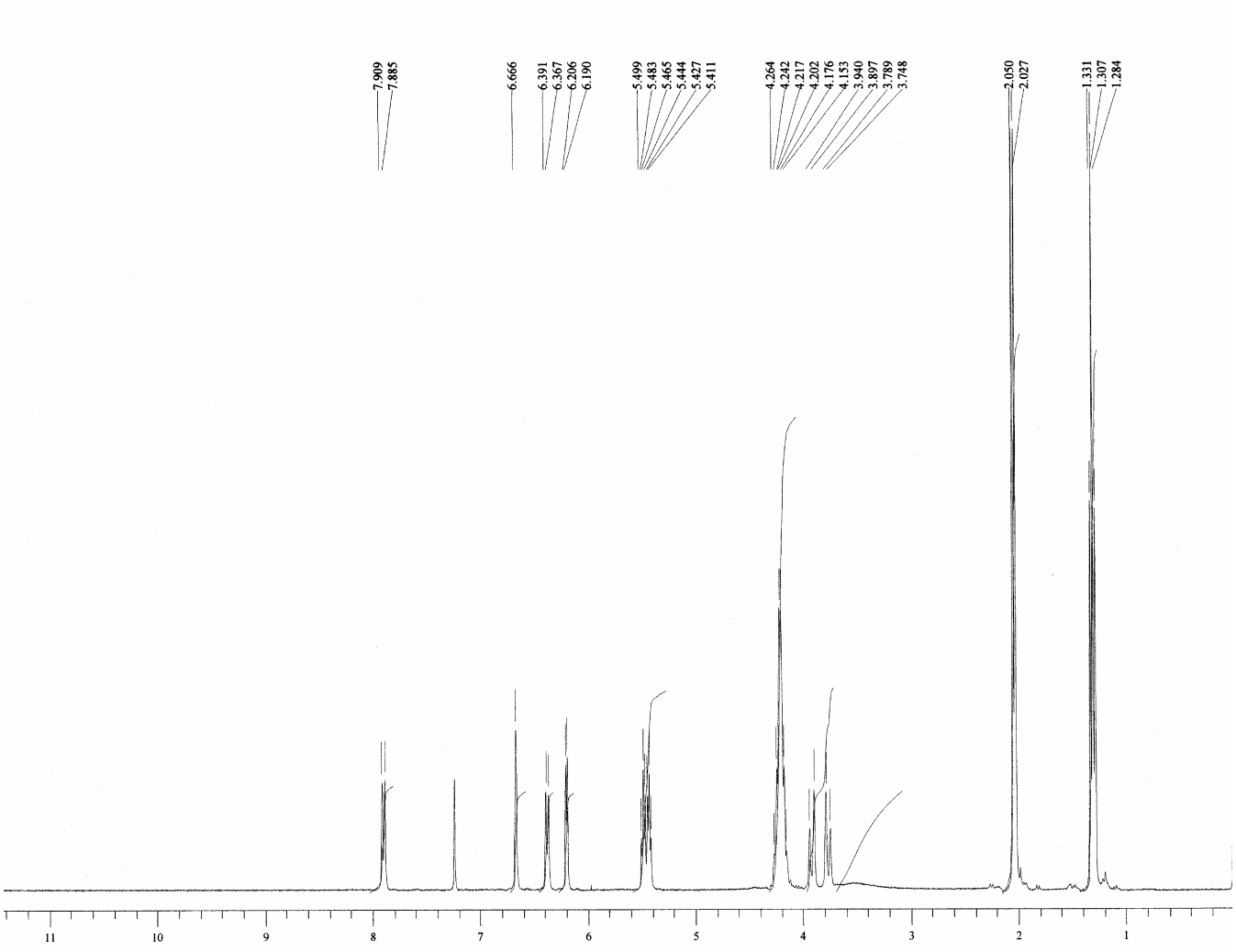
^{31}P

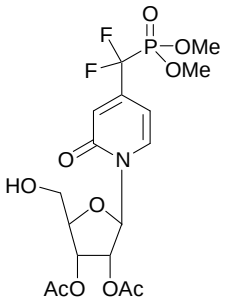



O
F
P
OMe
F
OMe
O
N
HO
O
AcO
OAc

26 ($CDCl_3$)

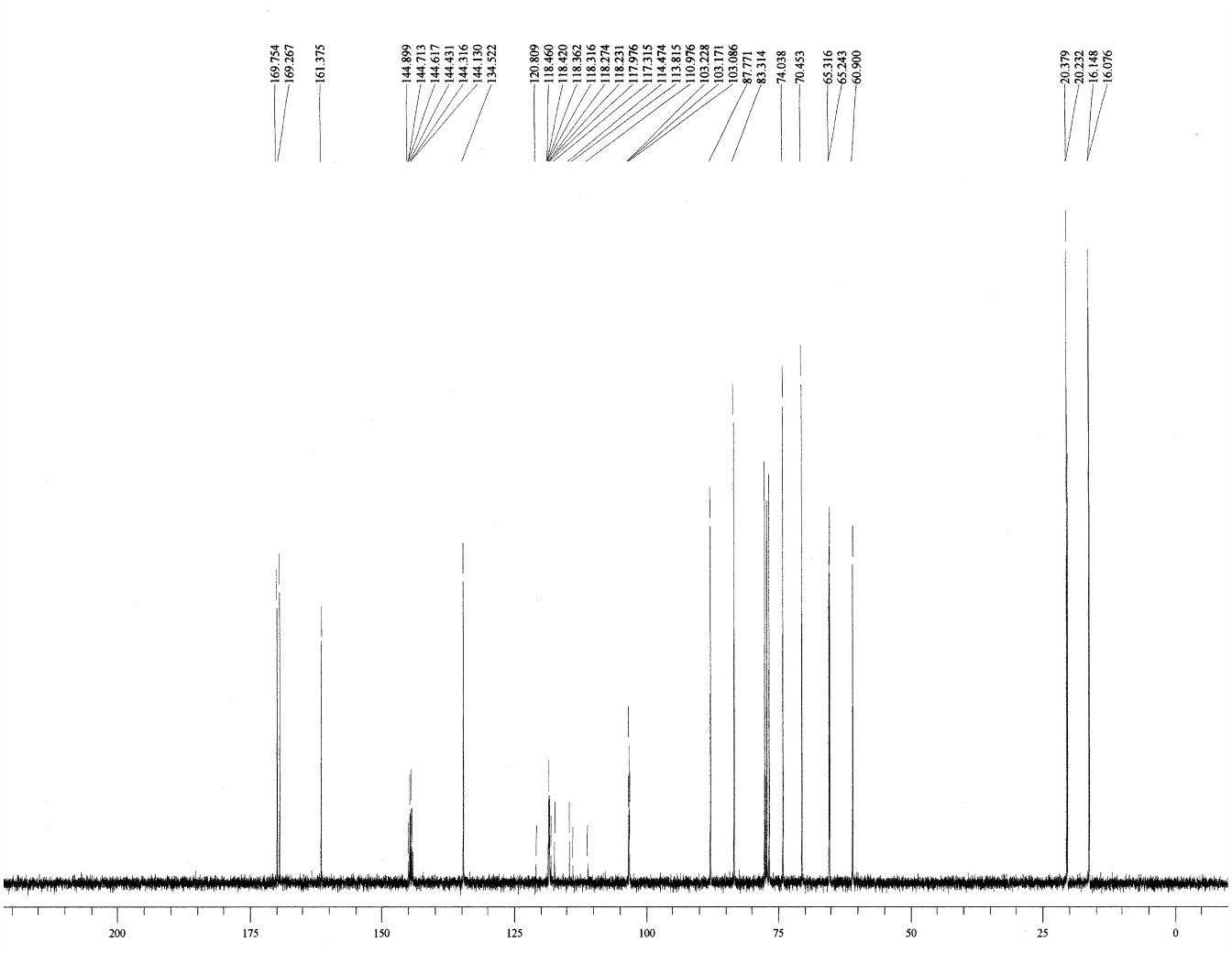
^1H

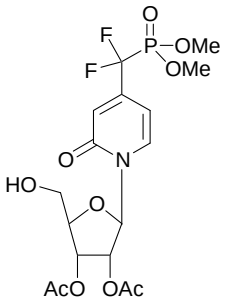

7.909
7.885
6.666
6.391
6.367
6.206
6.190
5.499
5.483
5.465
5.444
5.427
5.411
4.264
4.242
4.217
4.202
4.176
4.153
3.940
3.897
3.789
3.748
2.050
2.027
1.331
1.307
1.284
11
10
9
8
7
6
5
4
3
2
1


O
F
P
OMe
F
OMe
O
N
HO
O
AcO
OAc

26 ($CDCl_3$)

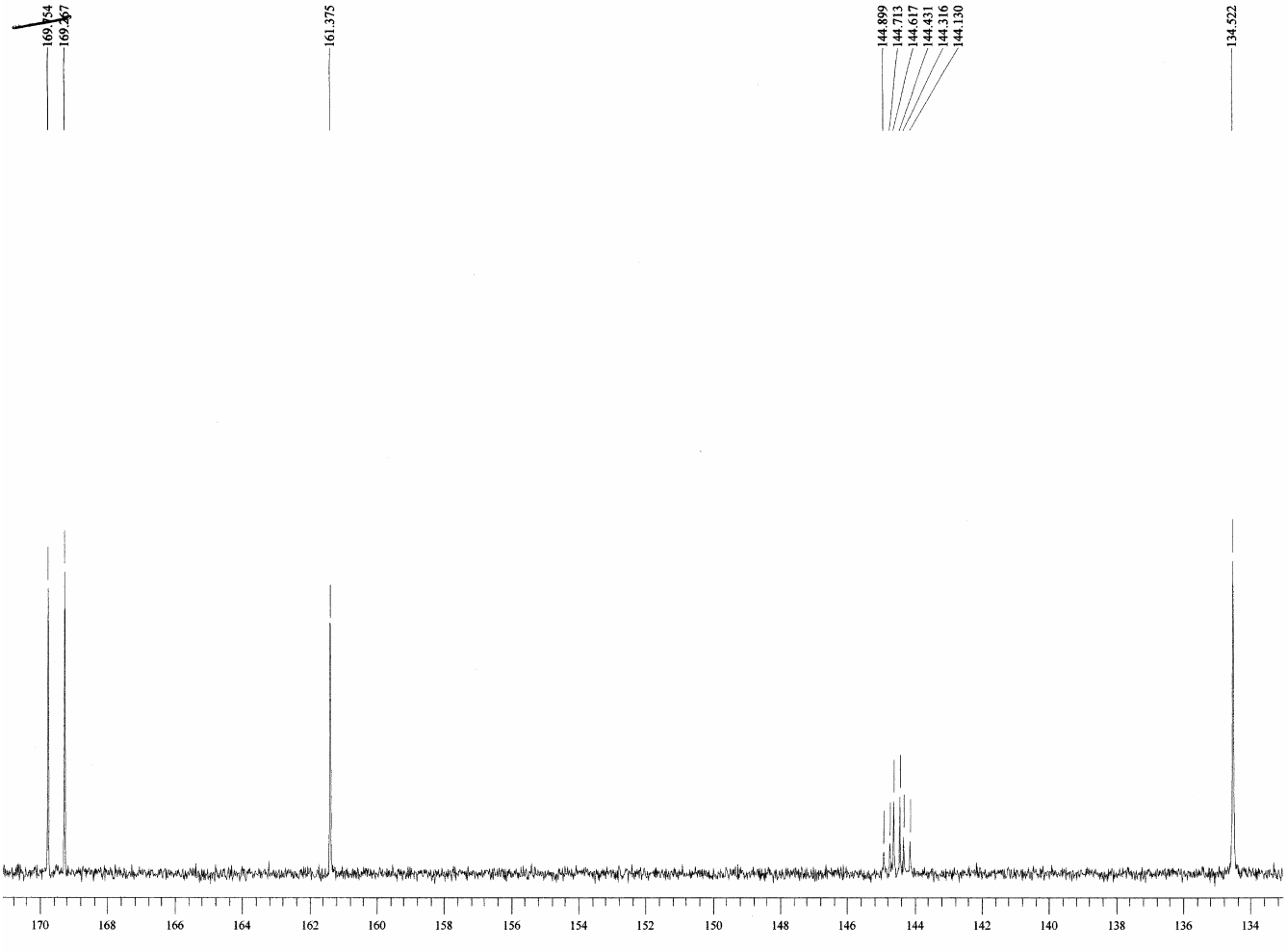
^{13}C

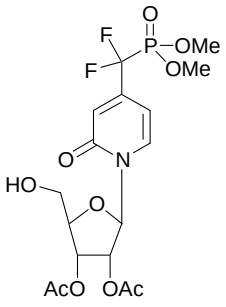

169.754
169.267
161.375
144.899
144.713
144.617
144.431
144.316
144.130
134.522
120.809
118.460
118.420
118.362
118.316
118.274
118.231
117.976
117.315
114.474
113.815
110.976
103.228
103.171
103.086
87.771
83.314
74.038
70.453
65.316
65.243
60.900
20.379
20.232
16.148
16.076
200
175
150
125
100
75
50
25
0



26 ($CDCl_3$)

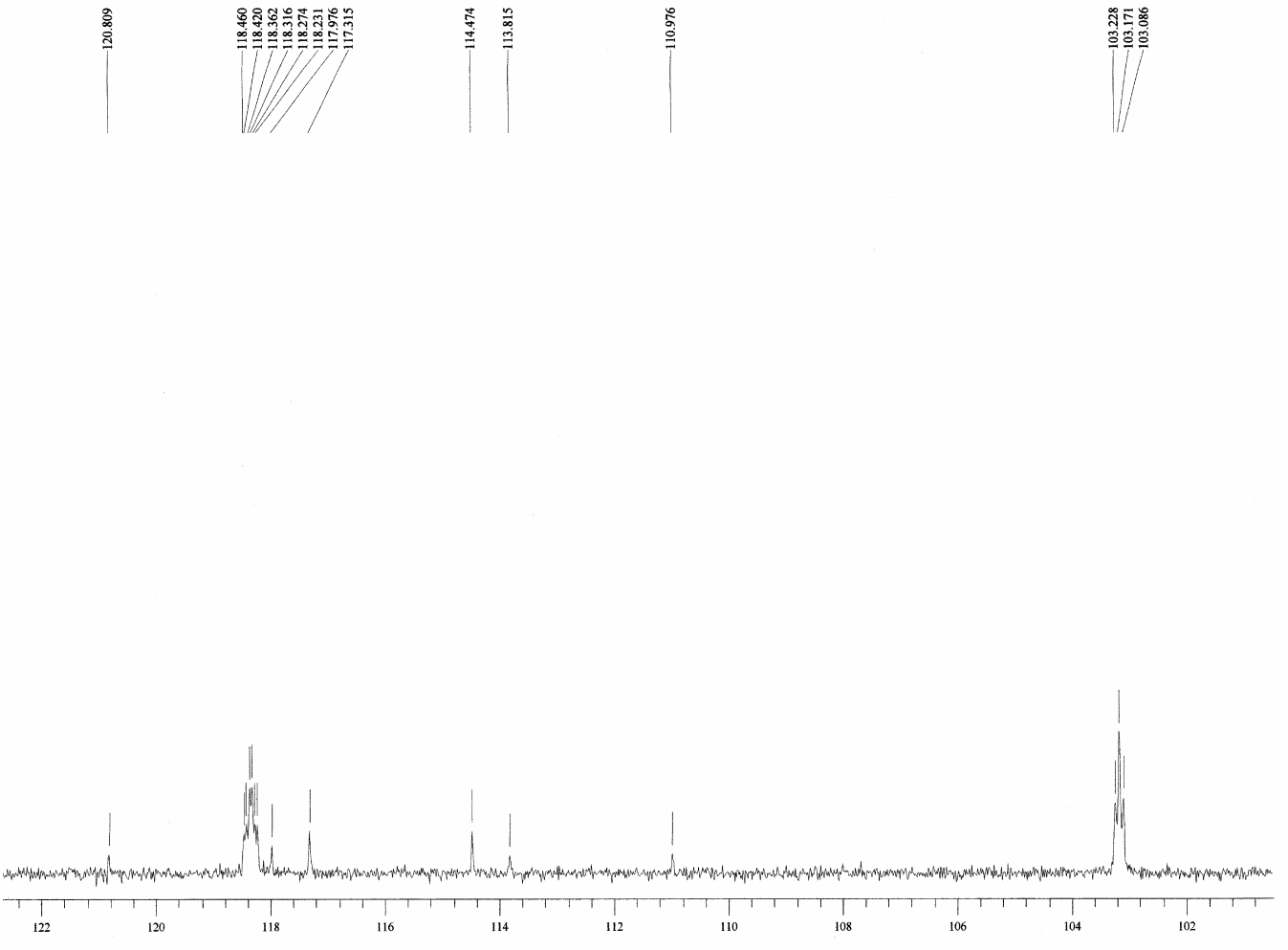
^{13}C (expanded)

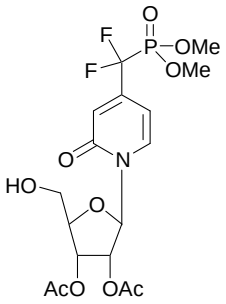




26 ($CDCl_3$)

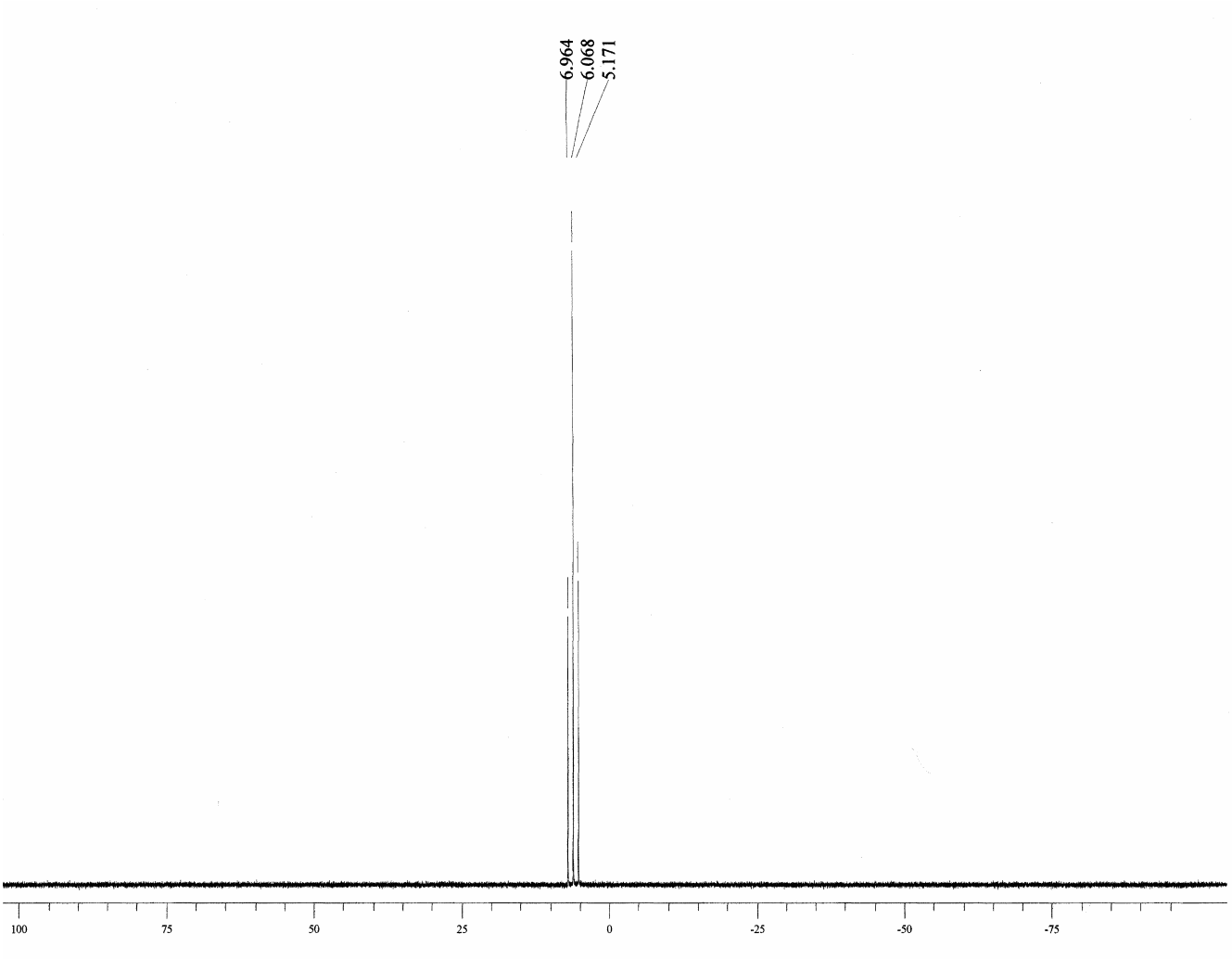
^{13}C (expanded)

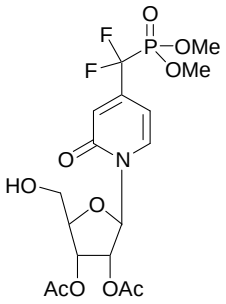




26 ($CDCl_3$)

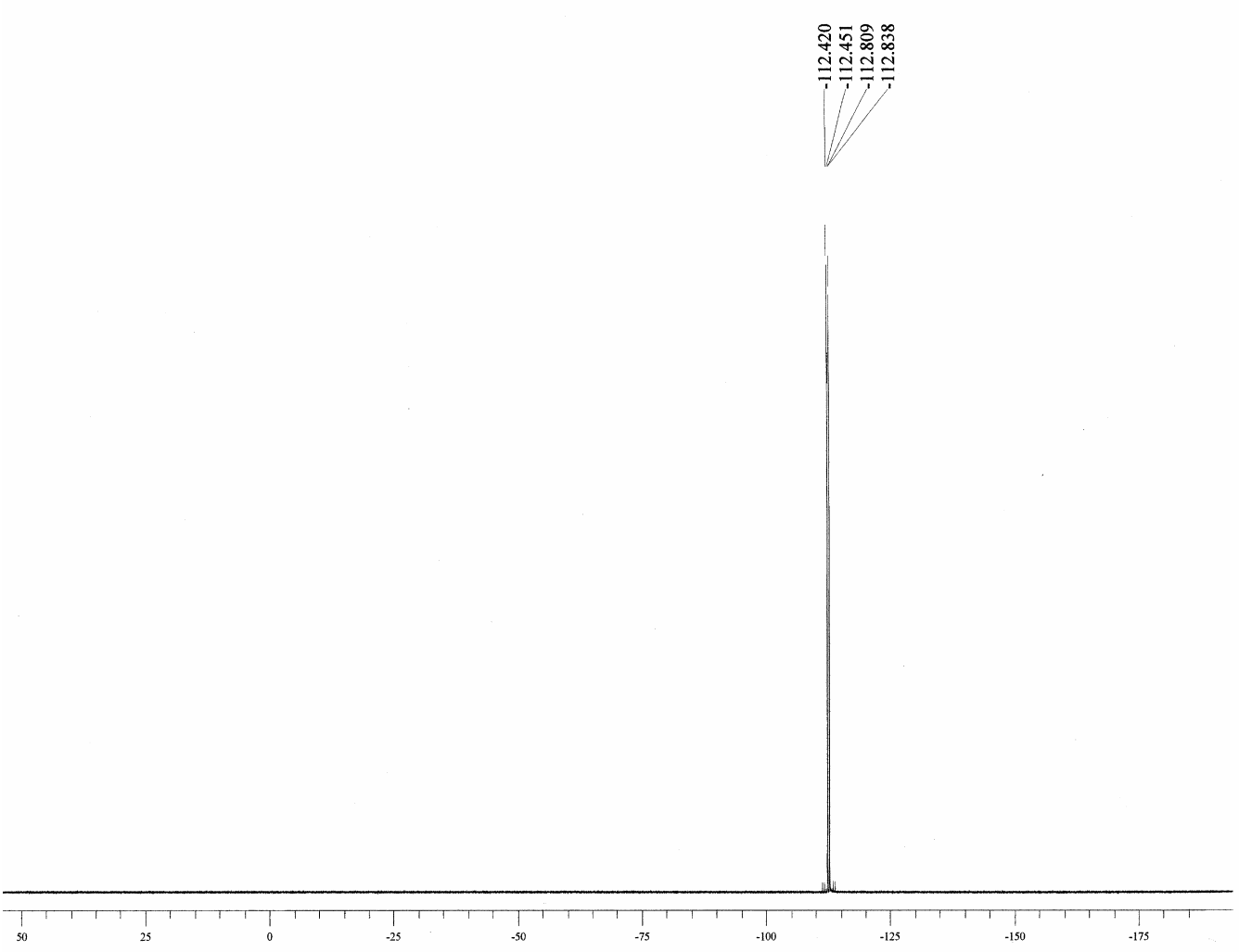
^{31}P

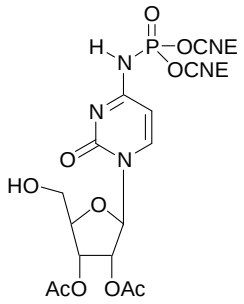



O
F
P
OMe
F
OMe
O
N
HO
O
AcO
OAc

26 ($CDCl_3$)

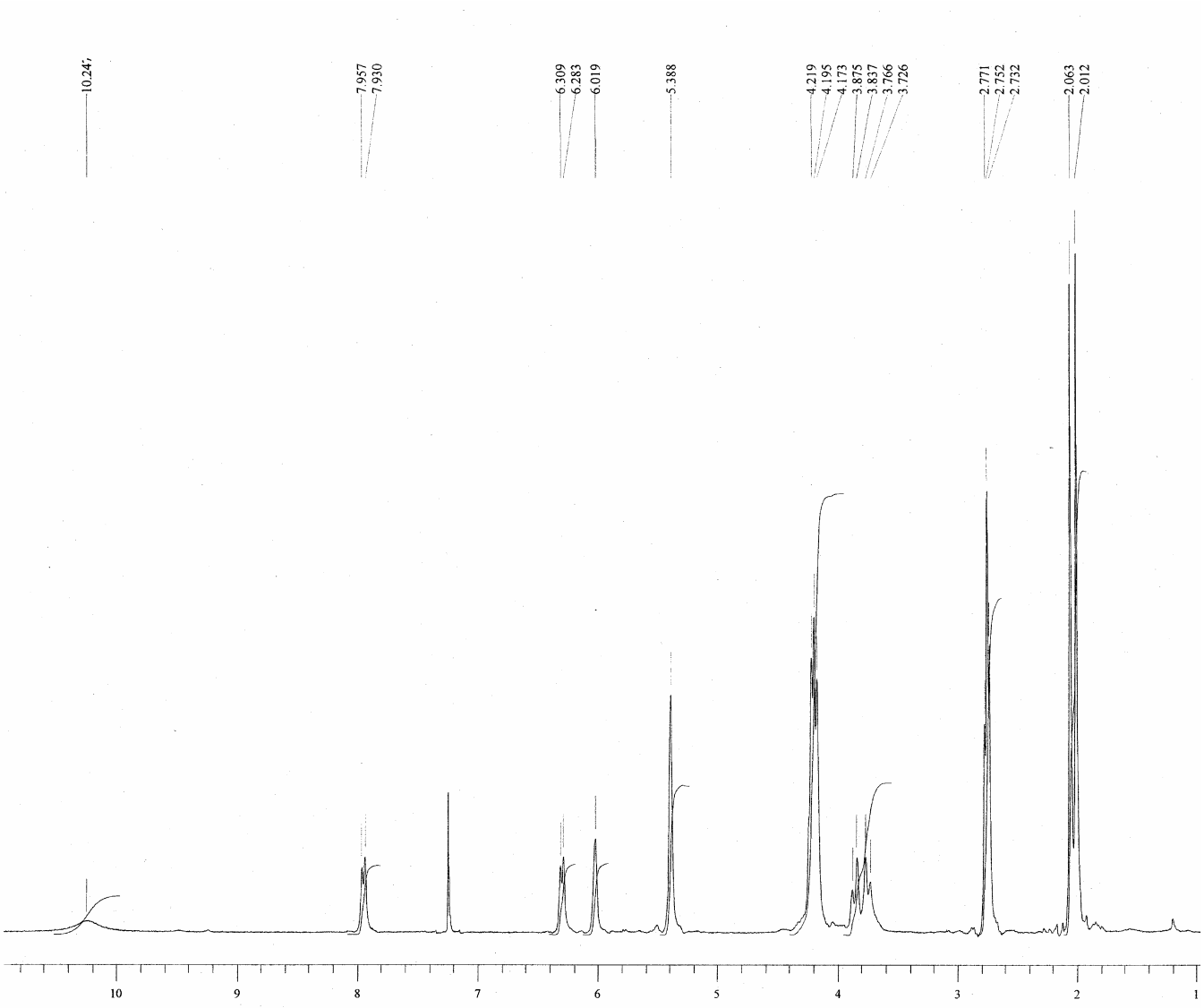
^{19}F

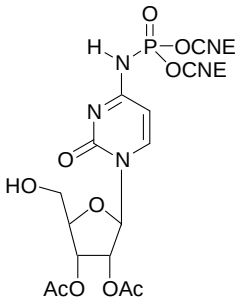

-112.420
-112.451
-112.809
-112.838
50
25
0
-25
-50
-75
-100
-125
-150
-175


O
H
N
P
OCNE
OCNE
N
O
N
HO
O
AcO
OAc

27 ($CDCl_3$)

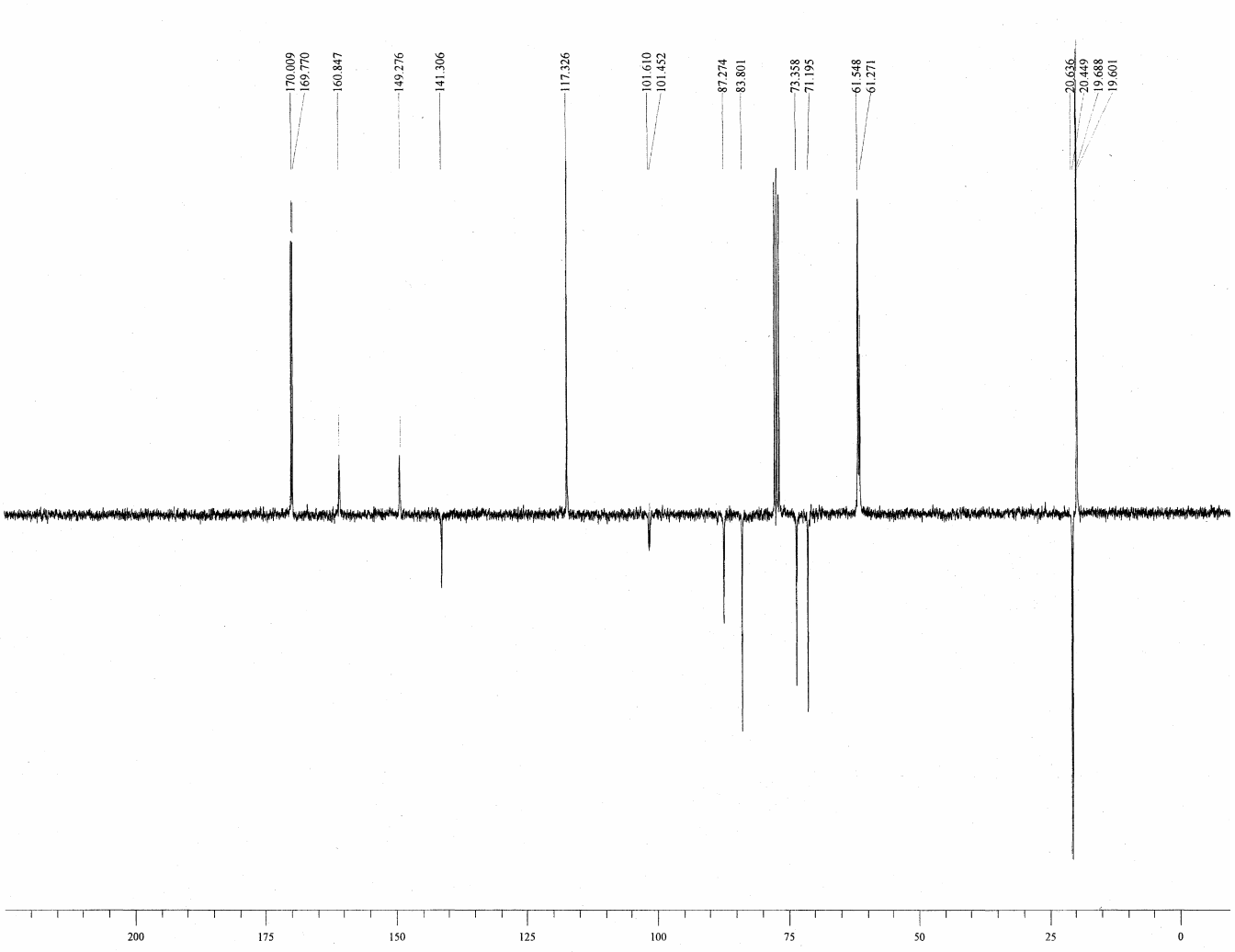
^1H

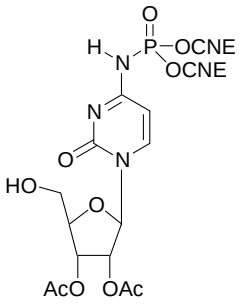

10.247
7.957
7.930
6.309
6.283
6.019
5.388
4.219
4.195
4.173
3.875
3.837
3.766
3.726
2.771
2.752
2.732
2.063
2.012
10
9
8
7
6
5
4
3
2
1


O
H
N
P
OCNE
OCNE
N
O
N
HO
O
AcO
OAc

27 ($CDCl_3$)

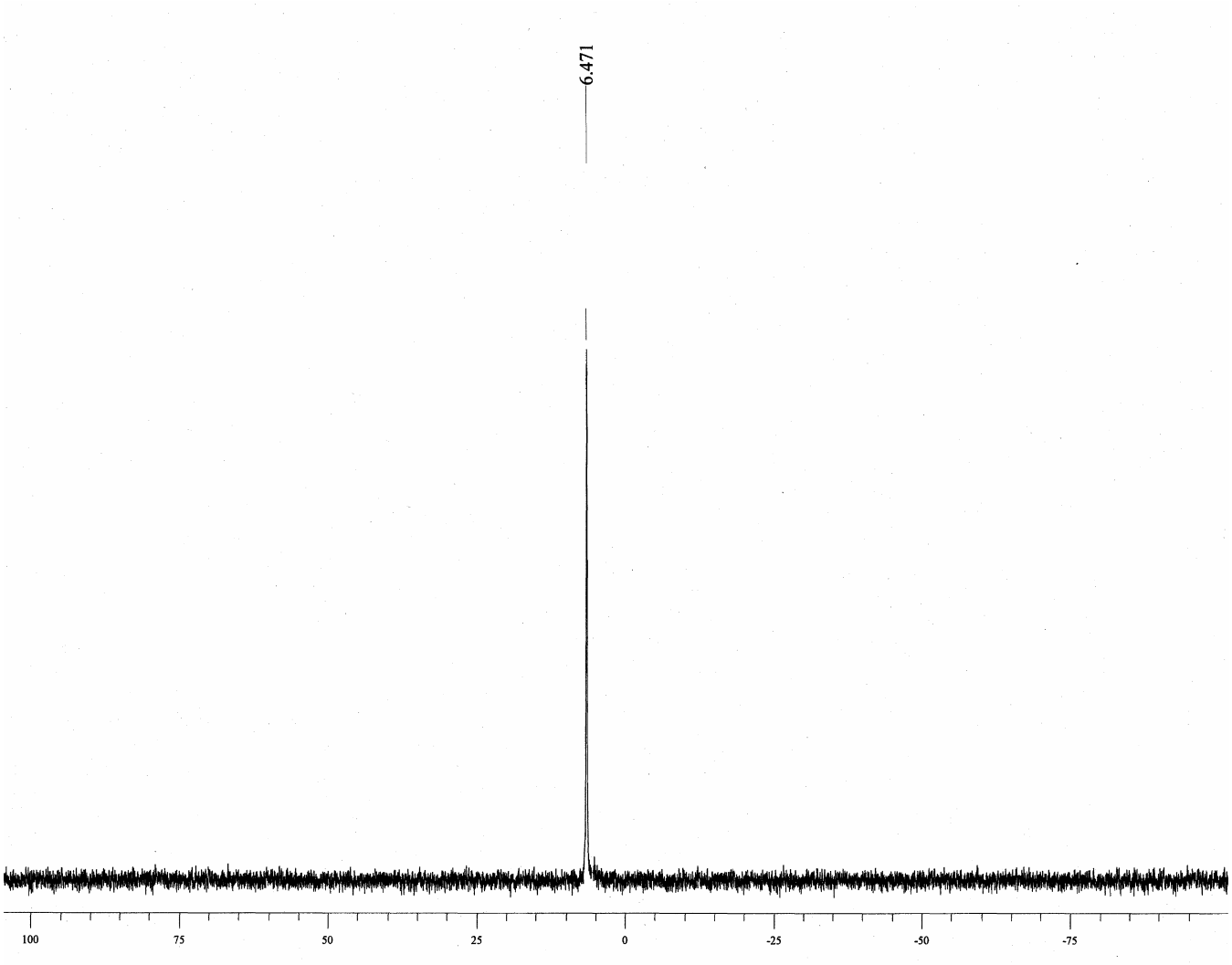
^{13}C

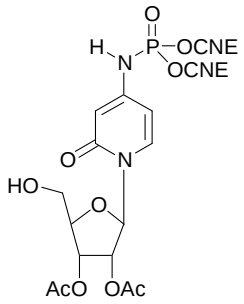

170.009
169.770
160.847
149.276
141.306
117.326
101.610
101.452
87.274
83.801
73.358
71.195
61.548
61.271
20.636
20.449
19.688
19.601
200
175
150
125
100
75
50
25
0



27 ($CDCl_3$)

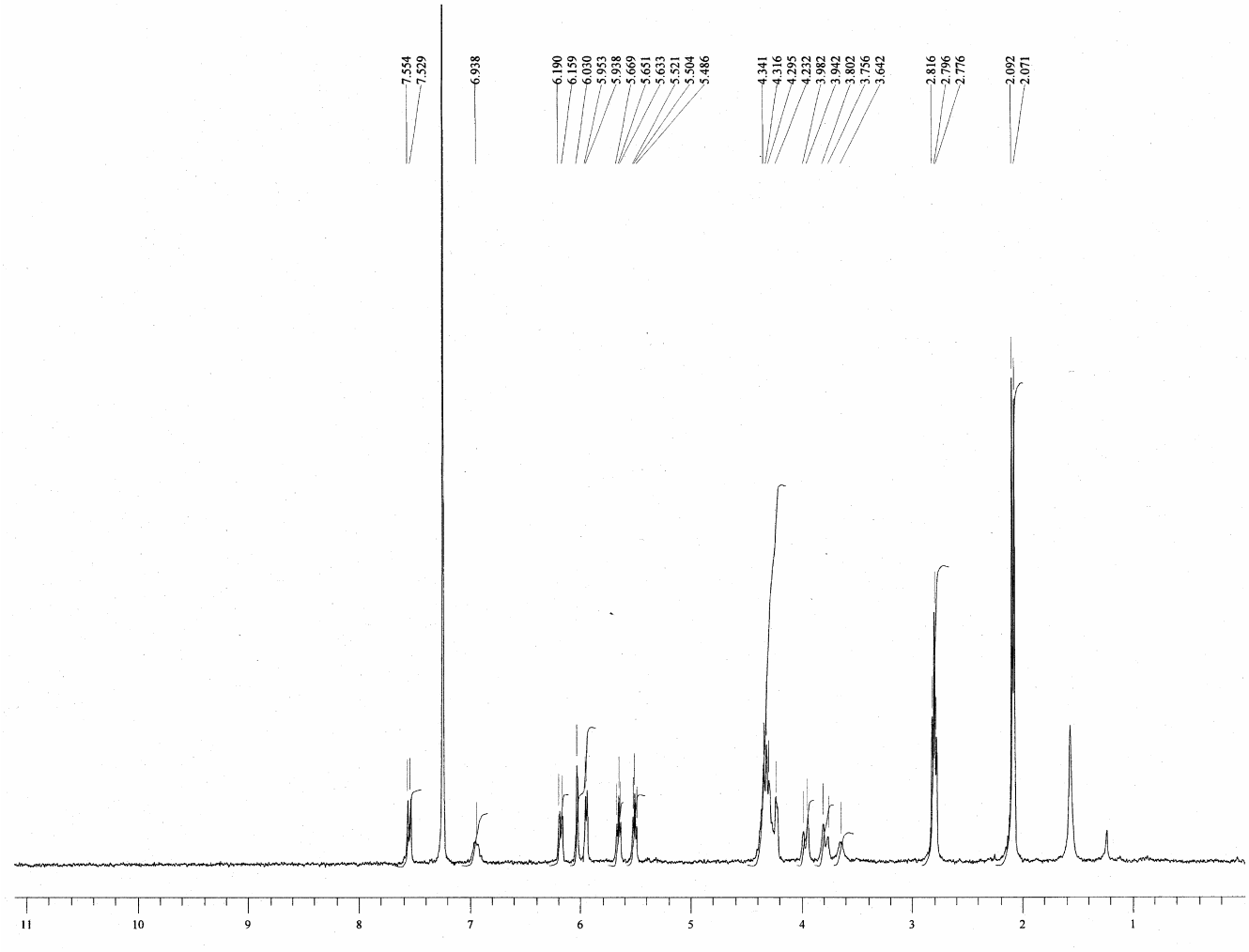
^{31}P

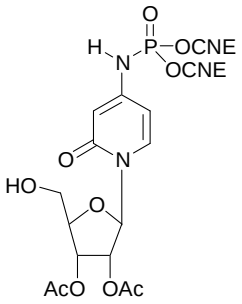



O
H
N
P
OCNE
OCNE
O
N
HO
O
AcO
OAc

28 ($CDCl_3$)

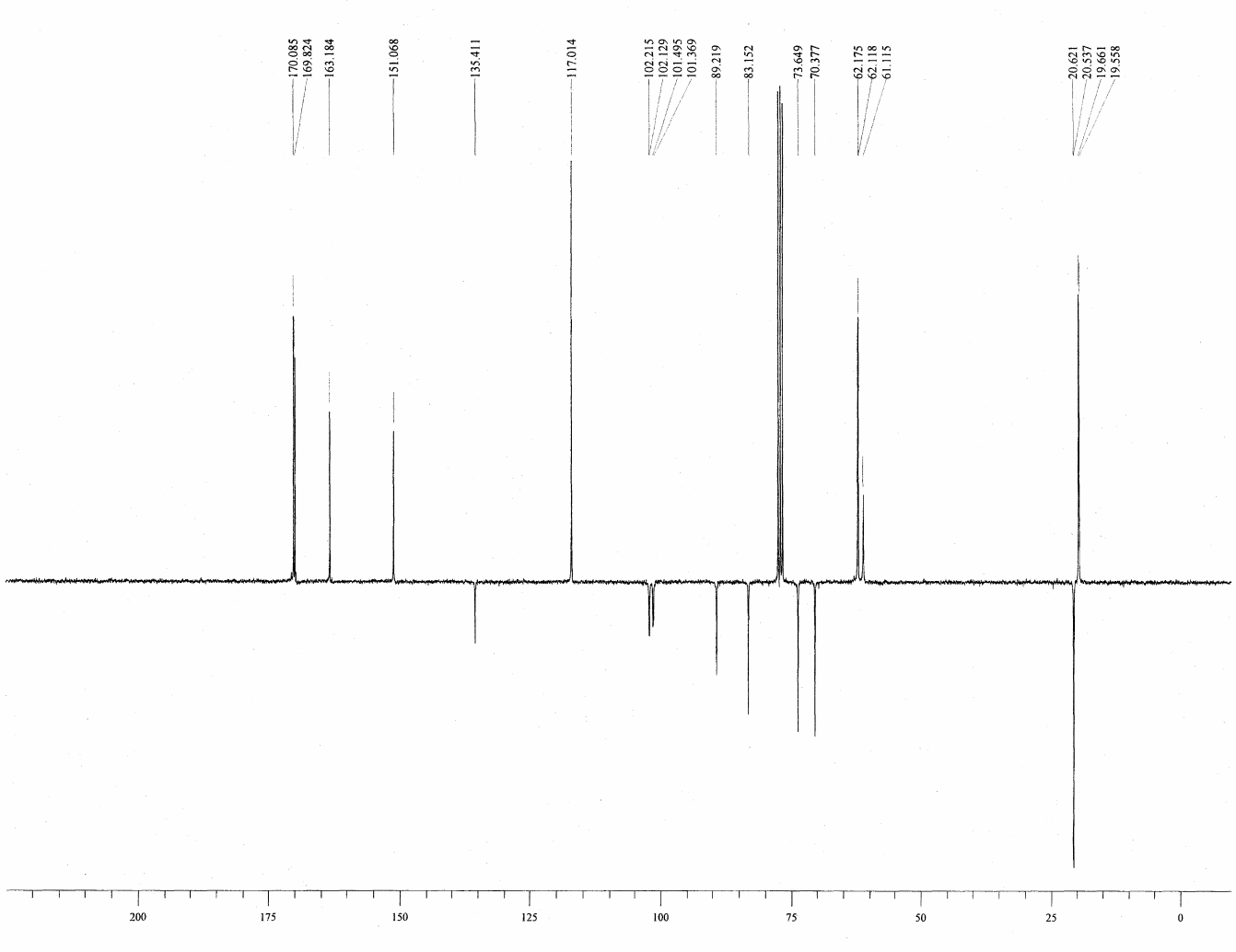
^1H

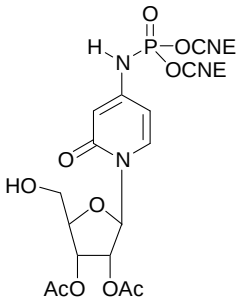

7.554
7.529
6.938
6.190
6.159
6.030
5.953
5.938
5.669
5.651
5.633
5.521
5.504
5.486
4.341
4.316
4.295
4.232
3.982
3.942
3.802
3.756
3.642
2.816
2.796
2.776
2.092
2.071
11
10
9
8
7
6
5
4
3
2
1


O
H
N
P
OCNE
OCNE
O
N
HO
O
AcO
OAc

28 ($CDCl_3$)

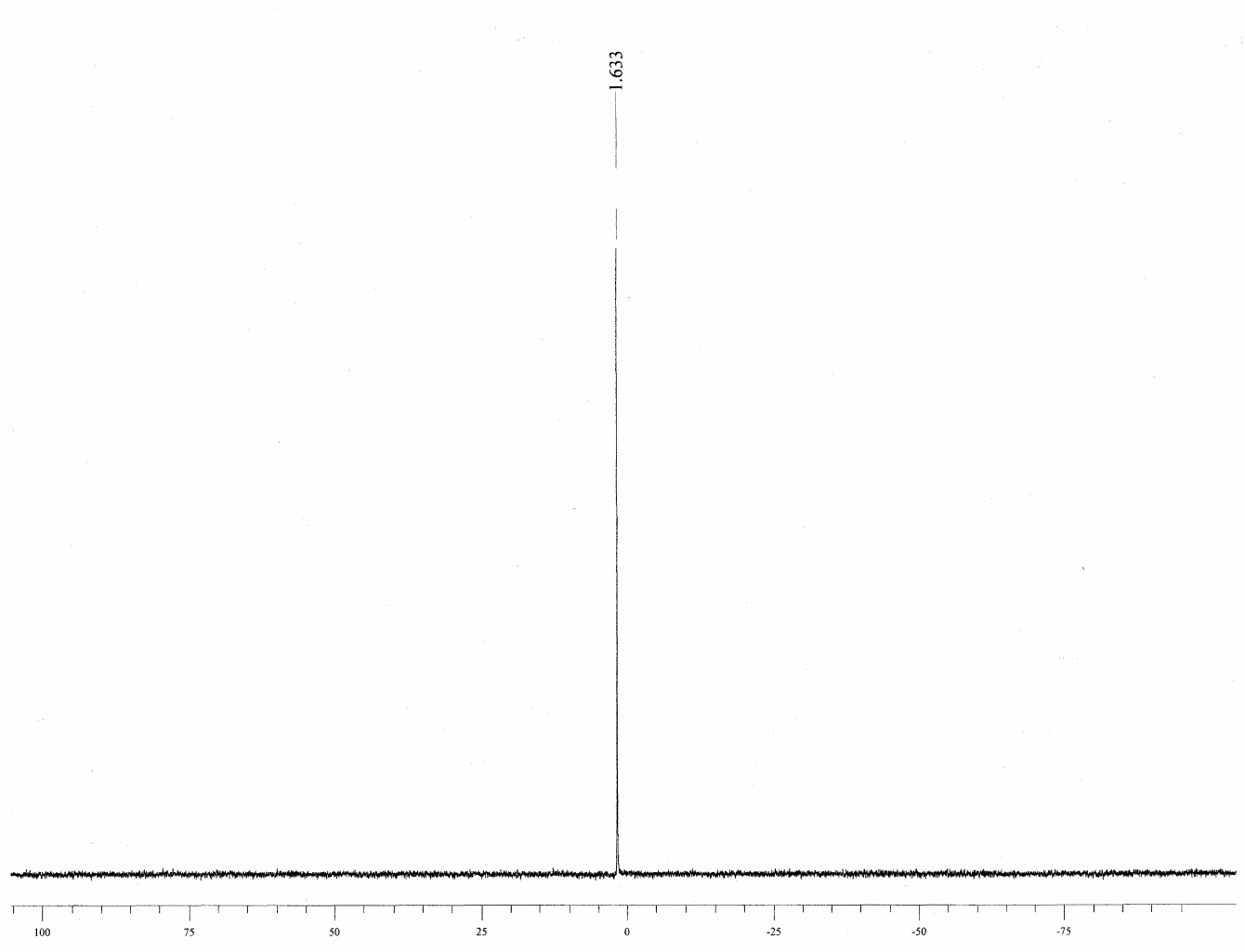
^{13}C

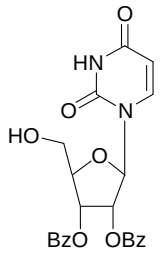

170.085
169.824
163.184
151.068
135.411
117.014
102.215
102.129
101.495
101.369
89.219
83.152
73.649
70.377
62.175
62.118
61.115
20.621
20.537
19.661
19.558
200
175
150
125
100
75
50
25
0



28 ($CDCl_3$)

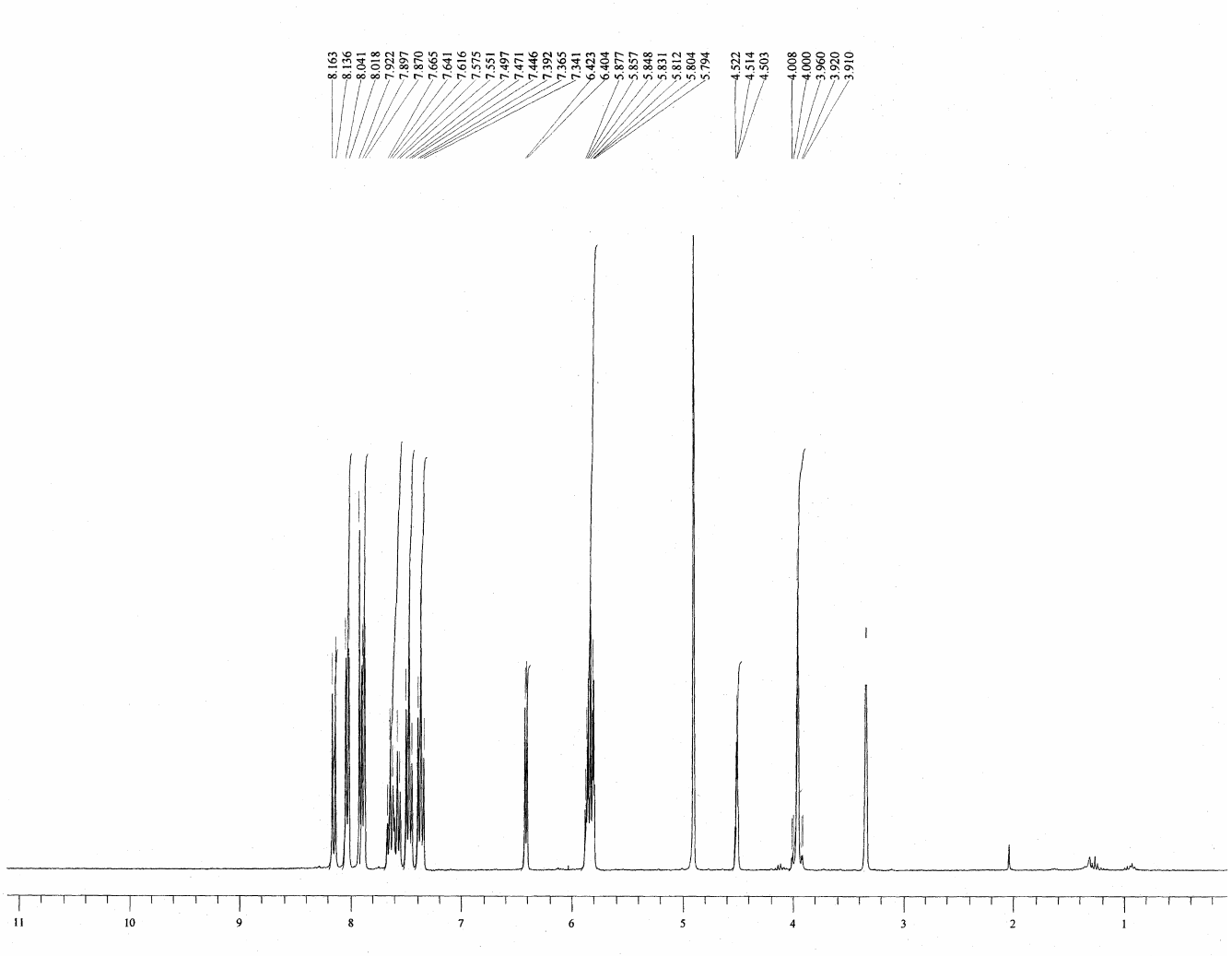
^{31}P

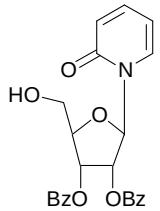



O
HN
O
N
HO
O
BzO
OBz

34 (CD_3OD)

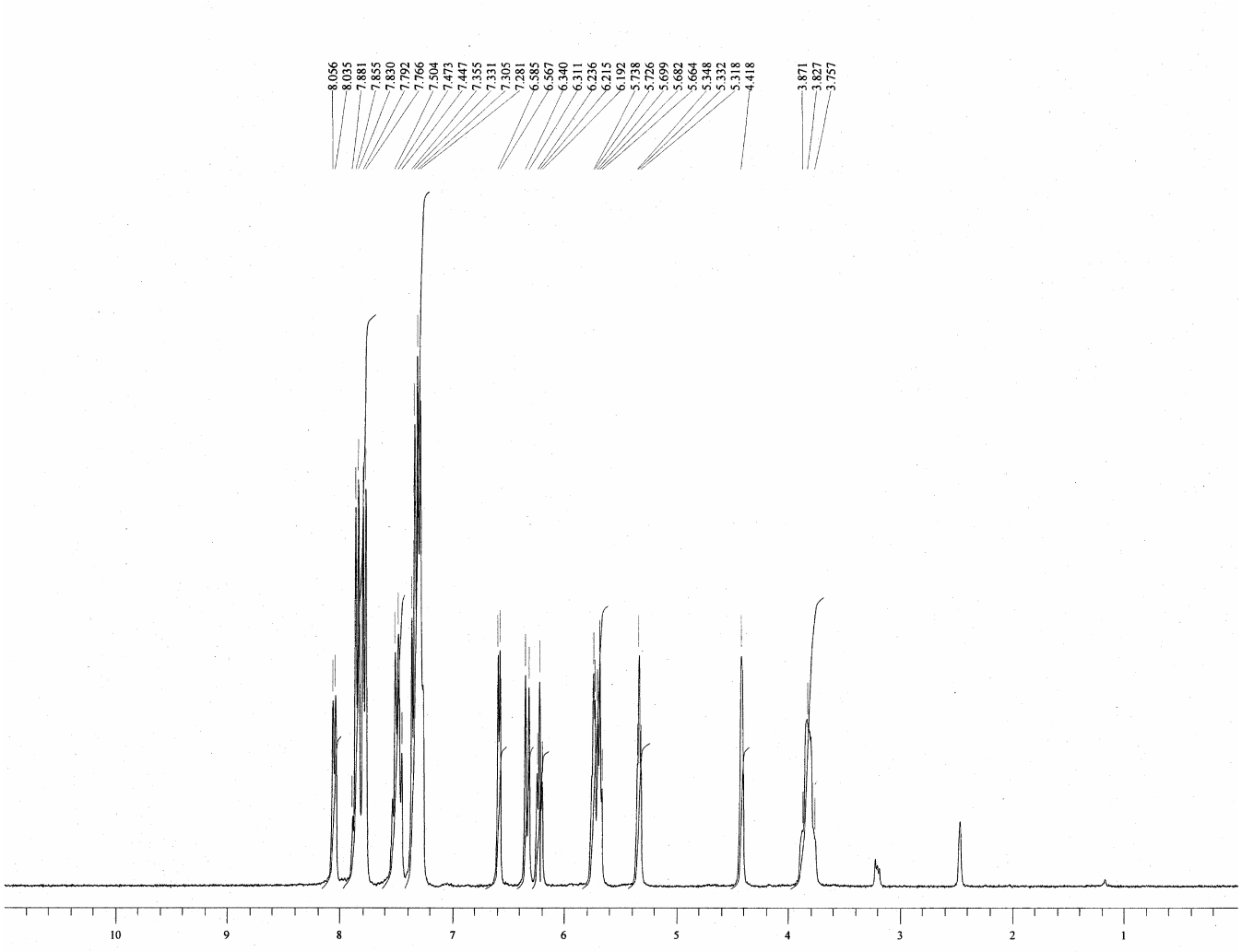
^1H

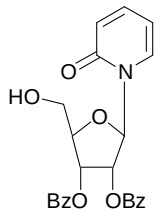

8.163
8.136
8.041
8.018
7.922
7.897
7.870
7.665
7.641
7.616
7.575
7.551
7.497
7.471
7.446
7.392
7.365
7.341
6.423
6.404
5.877
5.857
5.848
5.831
5.812
5.804
5.794
4.522
4.514
4.503
4.008
4.000
3.960
3.920
3.910
11
10
9
8
7
6
5
4
3
2
1



35 (DMSO-d_6-$CDCl_3$)

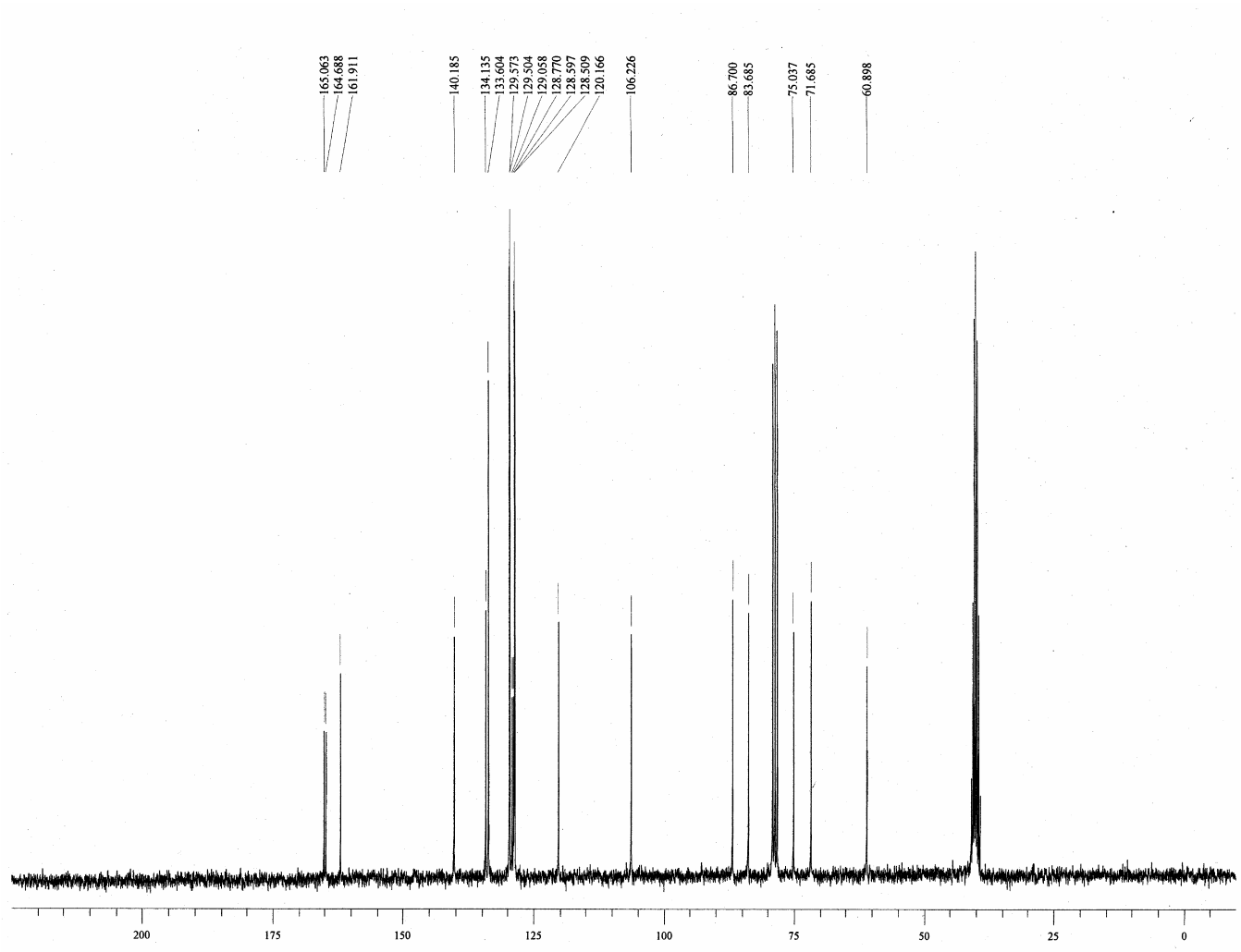
^1H

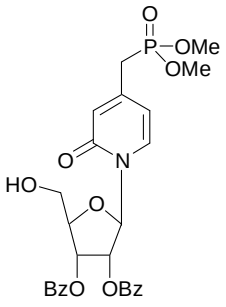




35 (DMSO-d_6-$CDCl_3$)

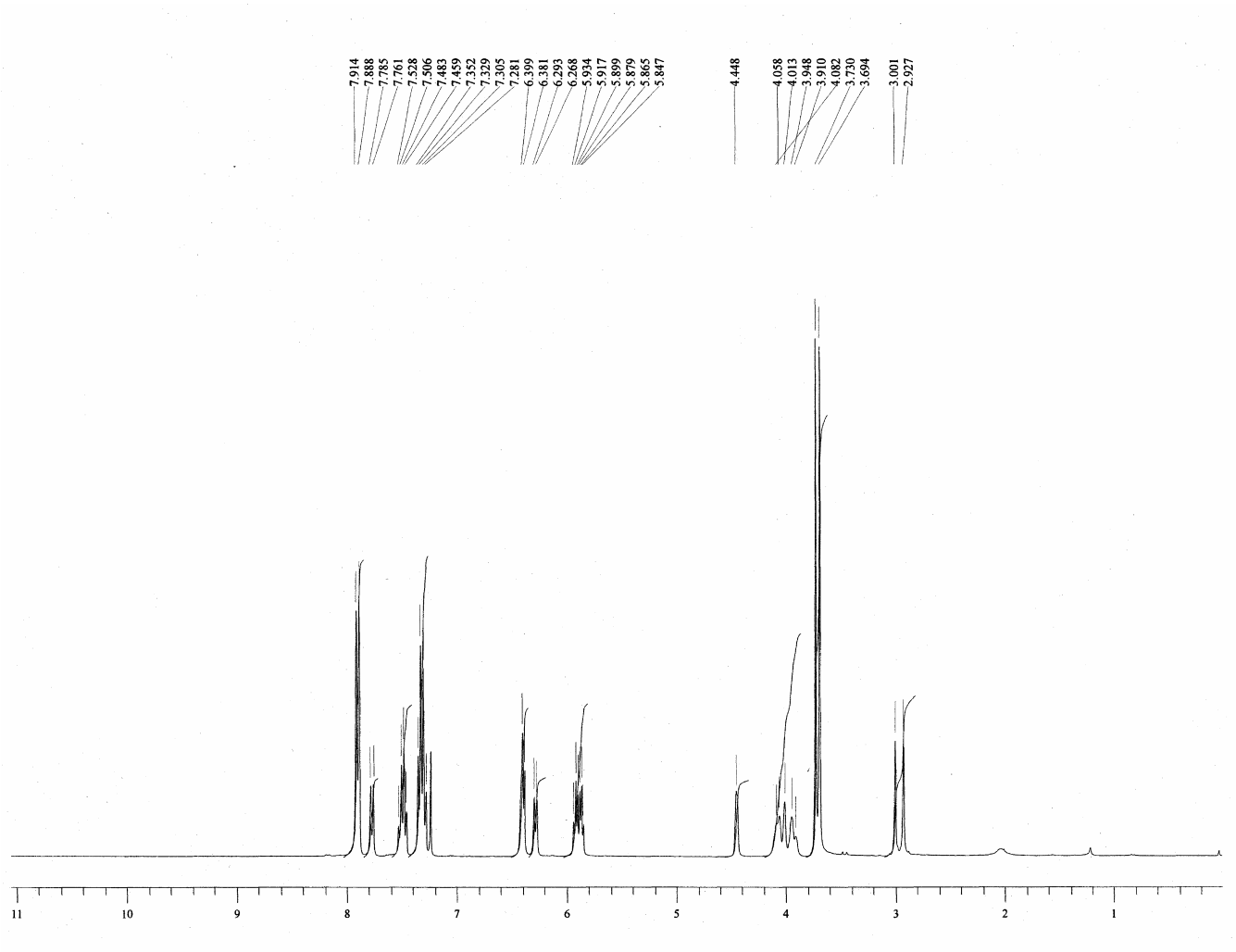
^{13}C

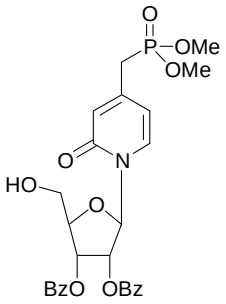



O
P
OMe
OMe
O
N
HO
O
BzO
OBz

36 ($CDCl_3$)

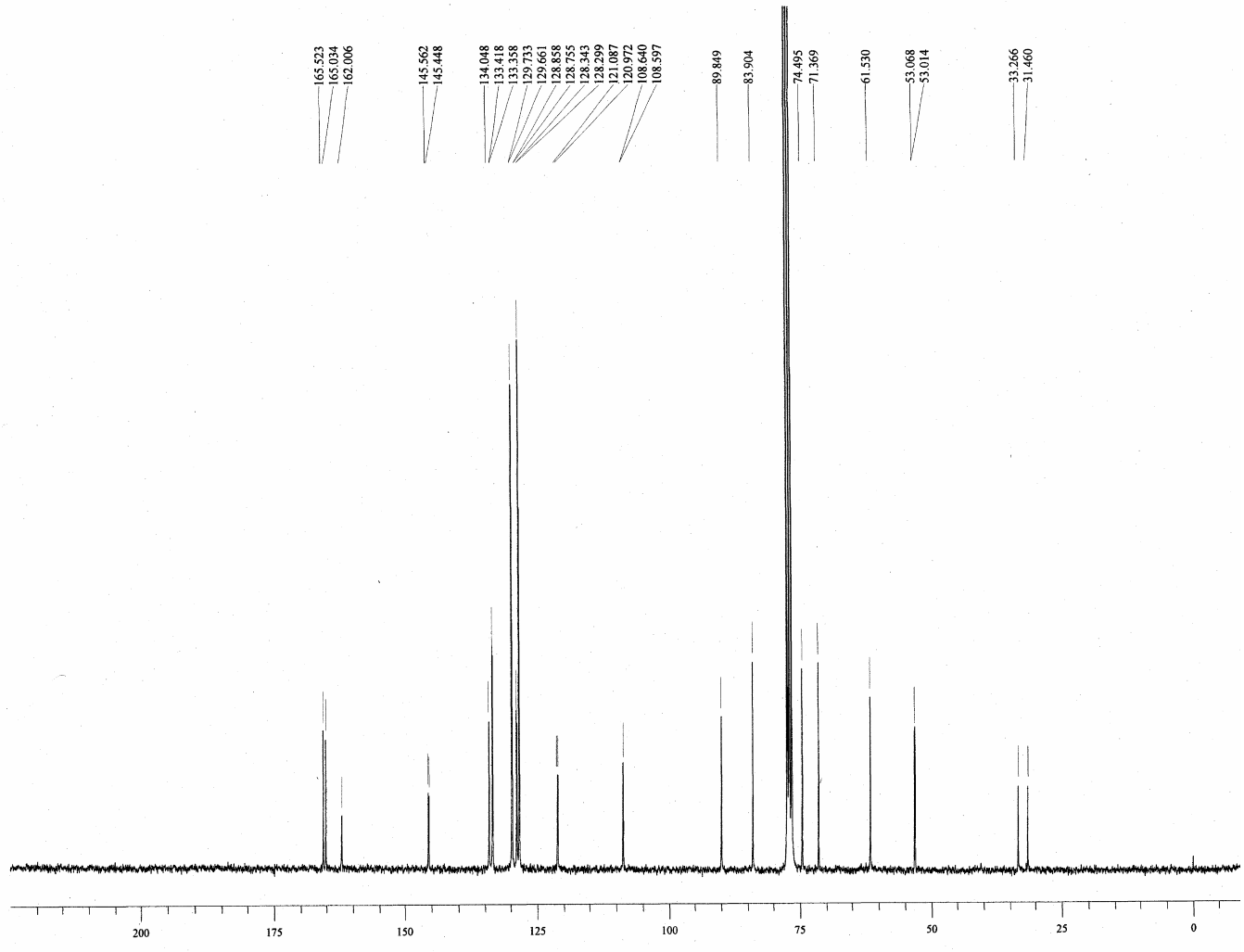
^1H

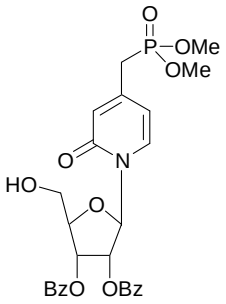

7.914
7.888
7.785
7.761
7.528
7.506
7.483
7.459
7.352
7.329
7.305
7.281
6.399
6.381
6.293
6.268
5.934
5.917
5.899
5.879
5.865
5.847
4.448
4.058
4.013
3.948
3.910
4.082
3.730
3.694
3.001
2.927
11
10
9
8
7
6
5
4
3
2
1


O
P
OMe
OMe
O
N
HO
O
BzO
OBz

36 ($CDCl_3$)

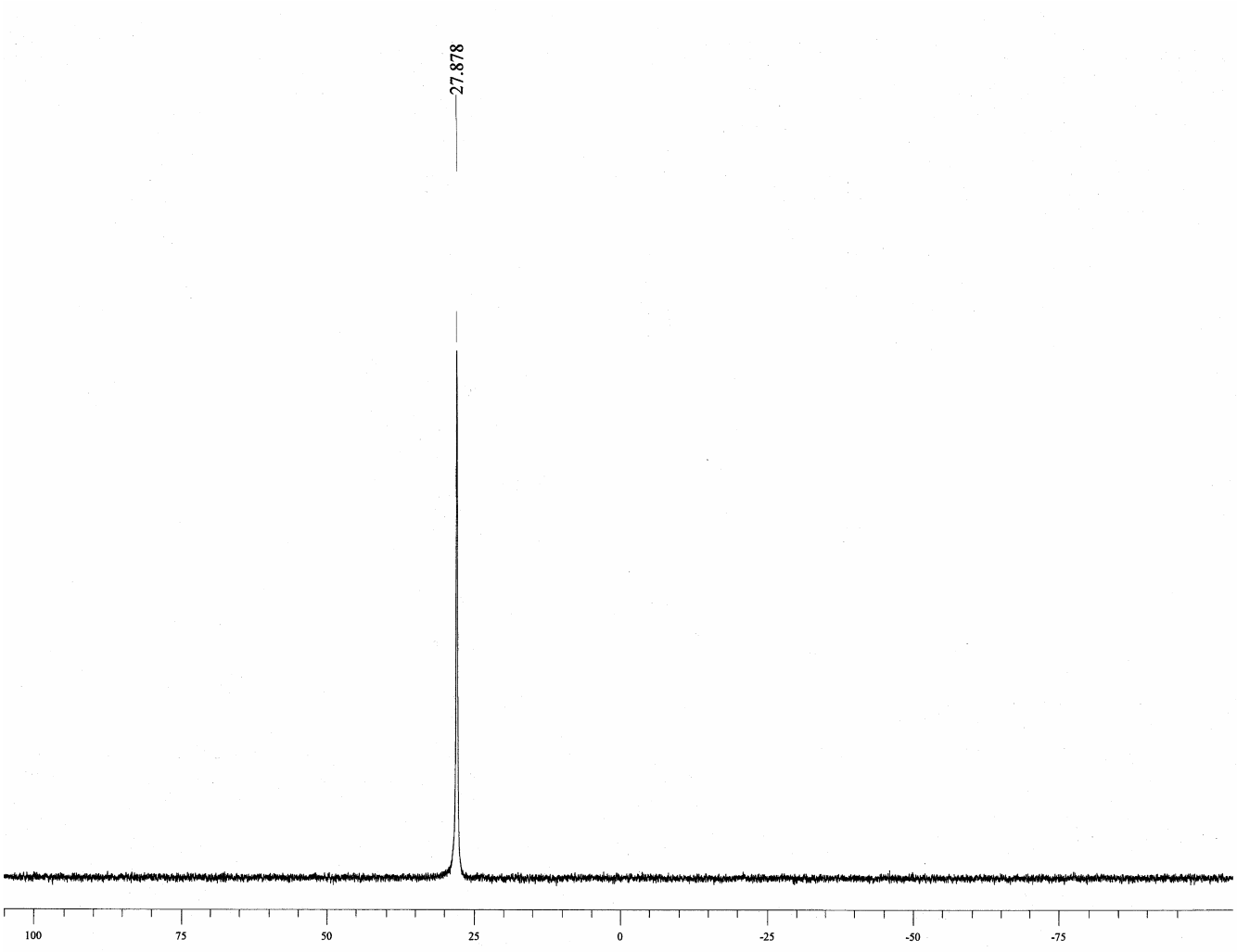
^{13}C

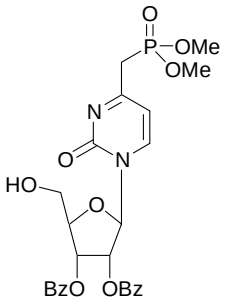

165.523
165.034
162.006
145.562
145.448
134.048
133.418
133.358
129.733
129.661
128.858
128.755
128.343
128.299
121.087
120.972
108.640
108.597
89.849
83.904
74.495
71.369
61.530
53.068
53.014
33.266
31.460
200
175
150
125
100
75
50
25
0



36 ($CDCl_3$)

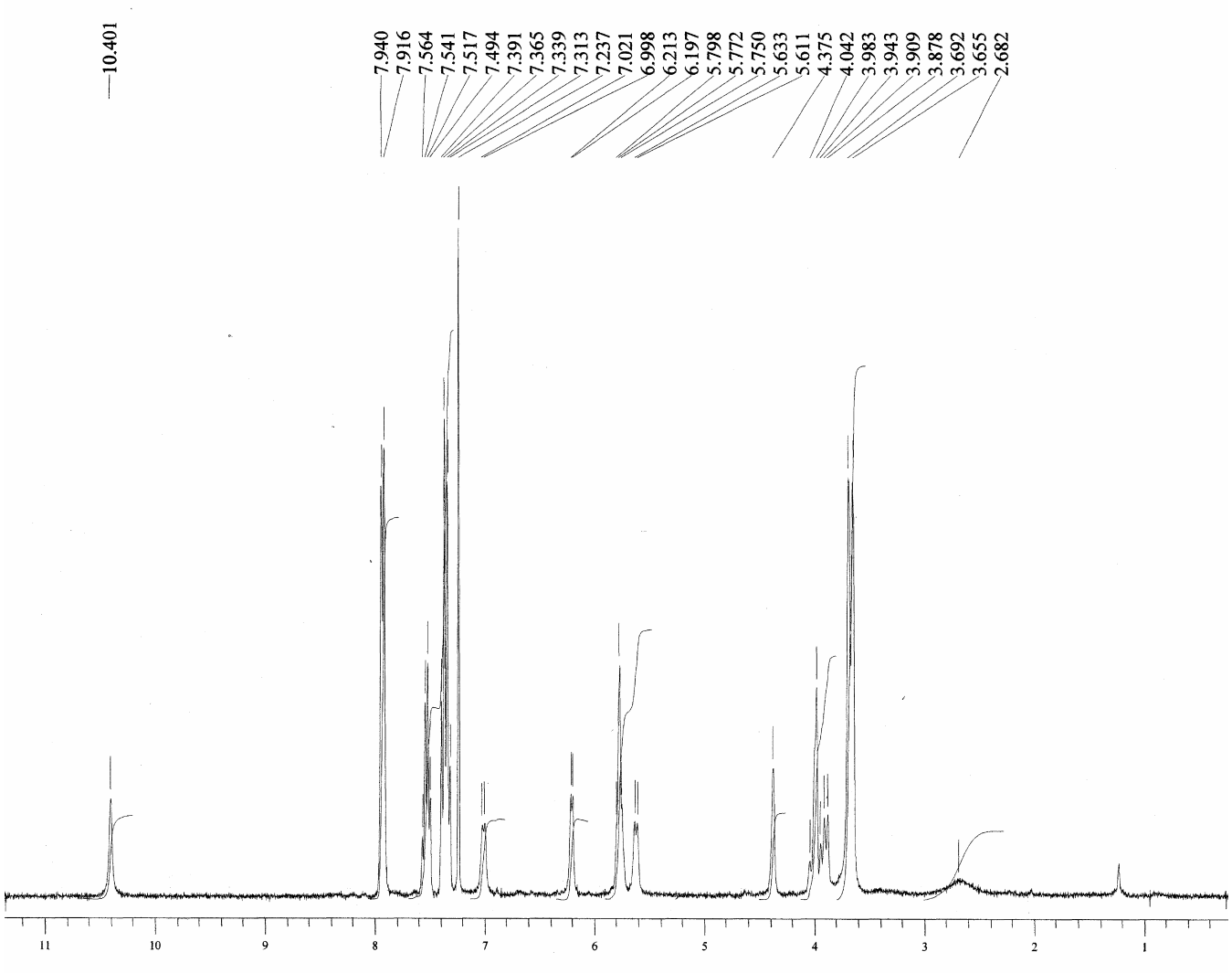
^{31}P

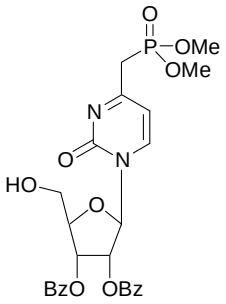



O
P
OMe
OMe
N
O
N
HO
O
BzO
OBz

37 ($CDCl_3$)

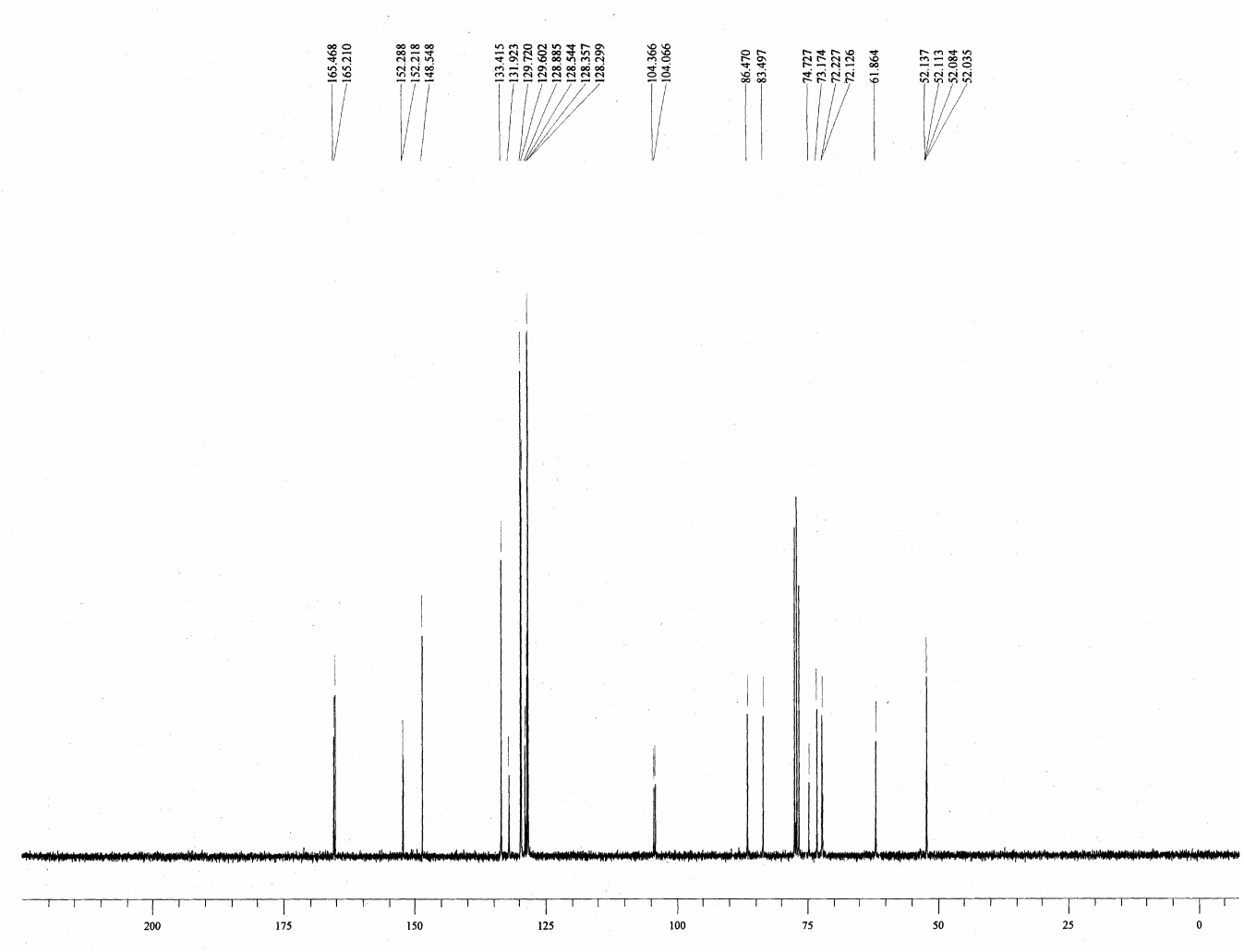
^1H

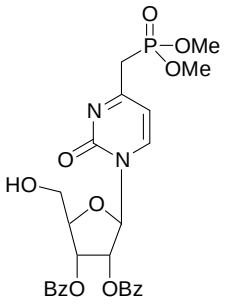

10.401
7.940
7.916
7.564
7.541
7.517
7.494
7.391
7.365
7.339
7.313
7.237
7.021
6.998
6.213
6.197
5.798
5.772
5.750
5.633
5.611
4.375
4.042
3.983
3.943
3.909
3.878
3.692
3.655
2.682
11
10
9
8
7
6
5
4
3
2
1


O
P
OMe
OMe
N
O
N
HO
O
BzO
OBz

37 ($CDCl_3$)

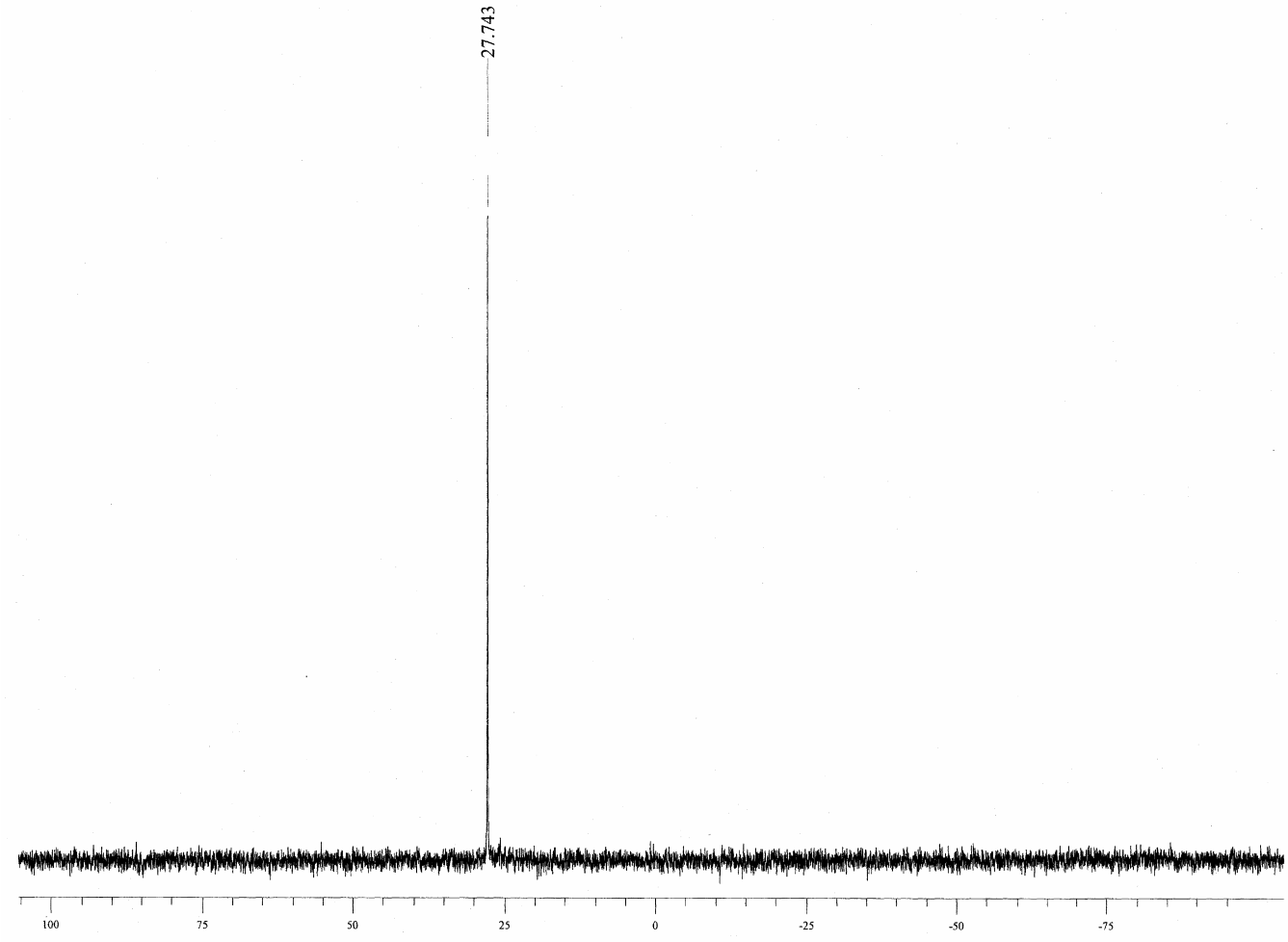
^{13}C

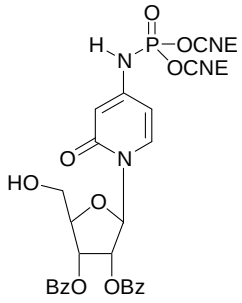

165.468
165.210
152.288
152.218
148.548
133.415
131.923
129.720
129.602
128.885
128.544
128.357
128.299
104.366
104.066
86.470
83.497
74.727
73.174
72.227
72.126
61.864
52.137
52.113
52.084
52.035
200
175
150
125
100
75
50
25
0



37 ($CDCl_3$)

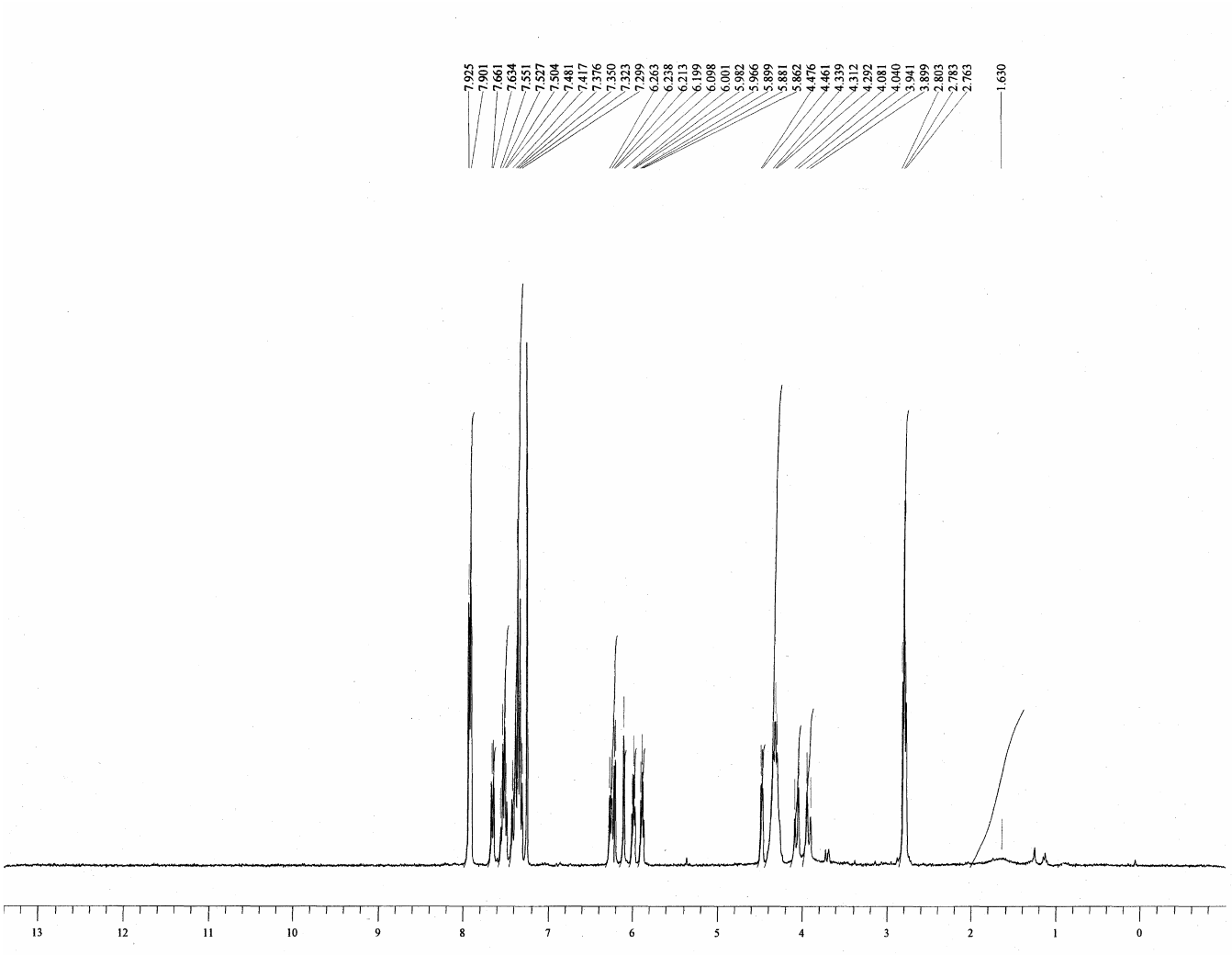
^{31}P

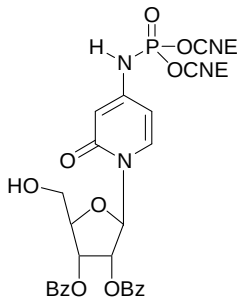



O
H
N
P
OCNE
OCNE
O
N
HO
O
BzO
OBz

38 ($CDCl_3$)

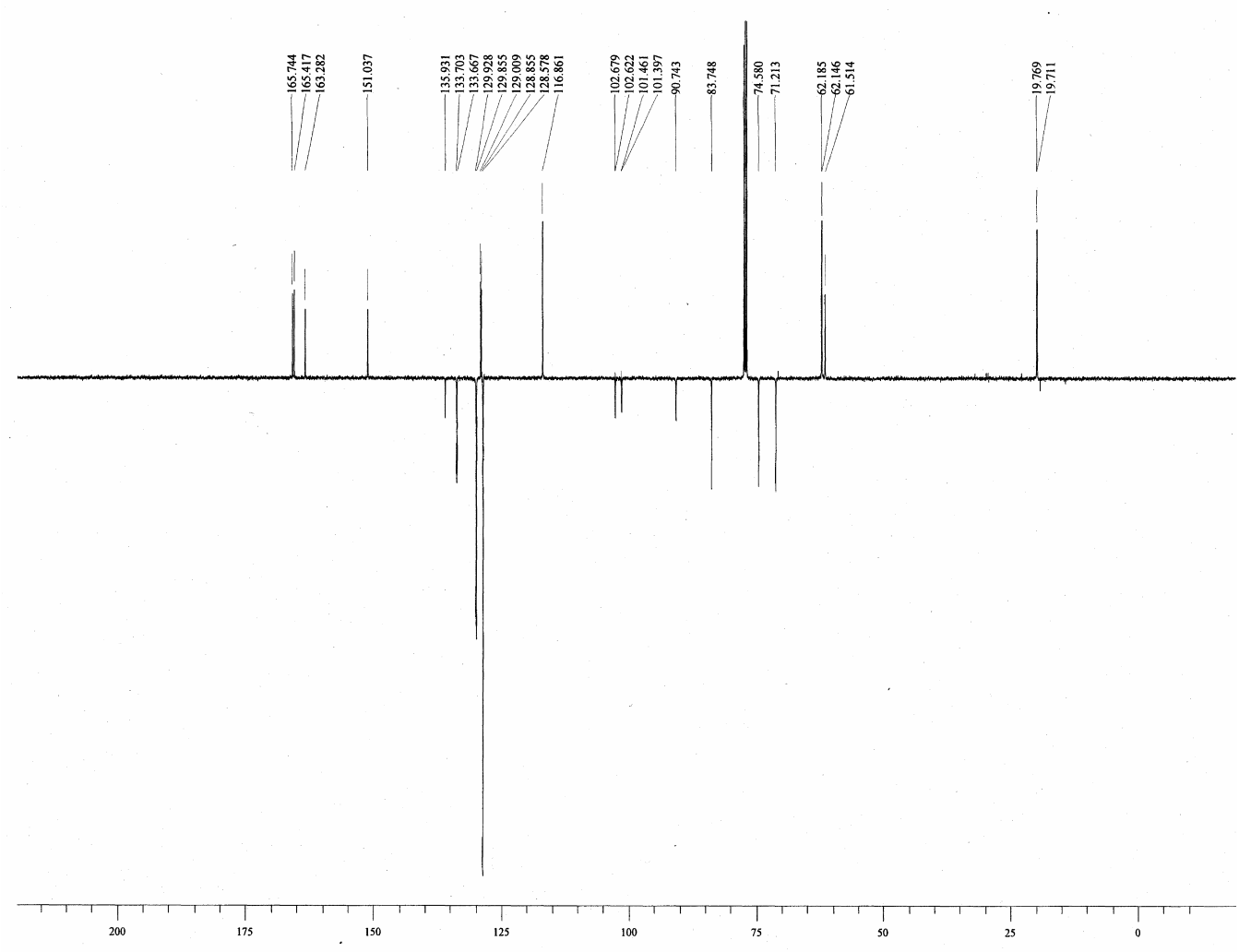
^1H

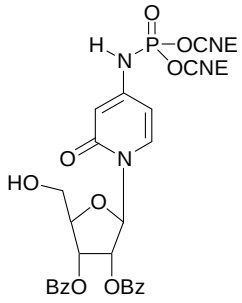

7.925
7.901
7.661
7.634
7.551
7.527
7.504
7.481
7.417
7.376
7.350
7.323
7.299
6.263
6.238
6.213
6.199
6.098
6.001
5.982
5.966
5.899
5.881
5.862
4.476
4.461
4.339
4.312
4.292
4.081
4.040
3.941
3.899
2.803
2.783
2.763
1.630
13
12
11
10
9
8
7
6
5
4
3
2
1
0


O
H
N
P
OCNE
OCNE
O
N
HO
O
BzO
OBz

38 ($CDCl_3$)

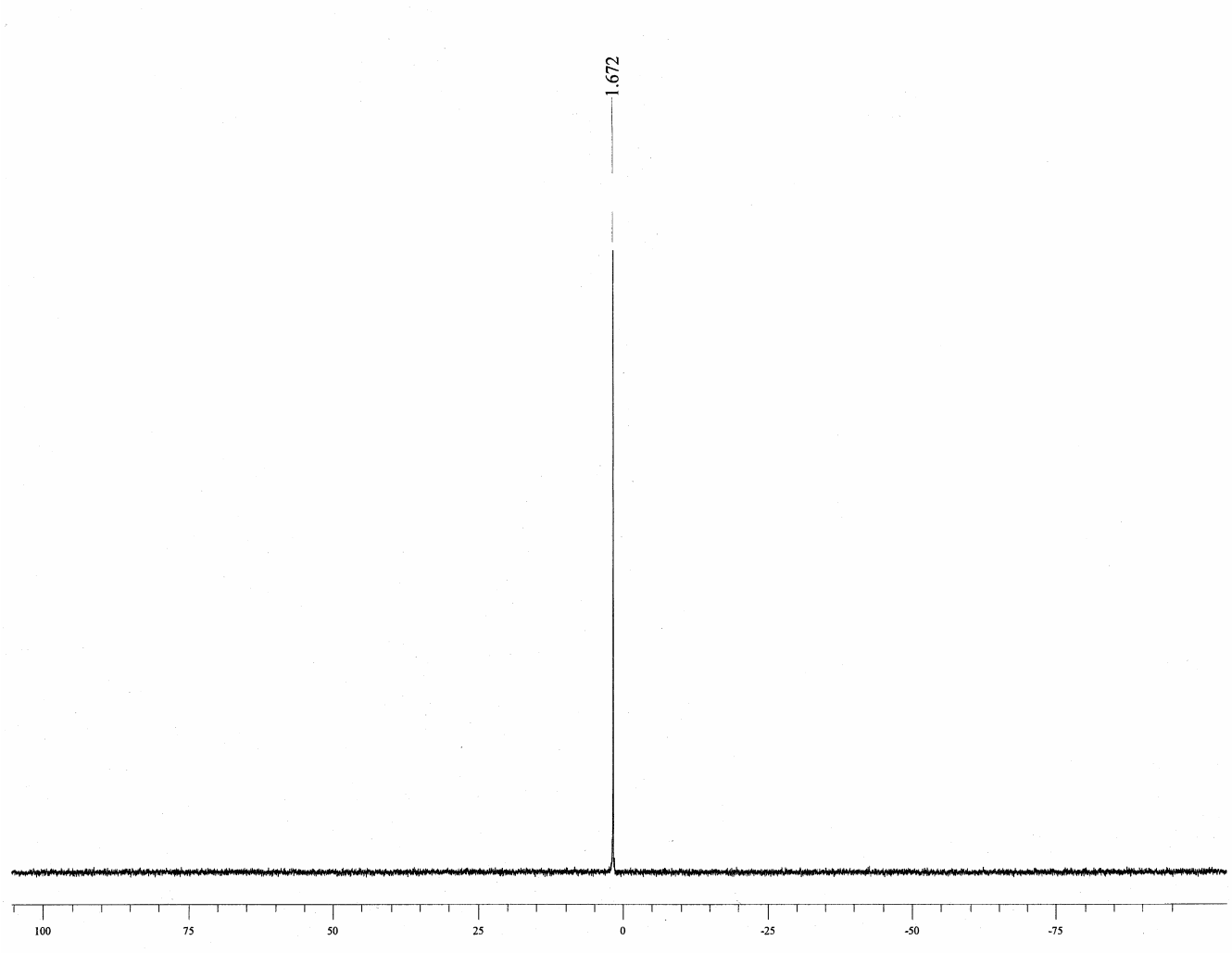
^{13}C

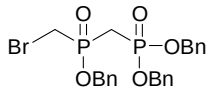

165.744
165.417
163.282
151.037
135.931
133.703
133.667
129.928
129.855
129.009
128.855
128.578
116.861
102.679
102.622
101.461
101.397
90.743
83.748
74.580
71.213
62.185
62.146
61.514
19.769
19.711
200
175
150
125
100
75
50
25
0



38 ($CDCl_3$)

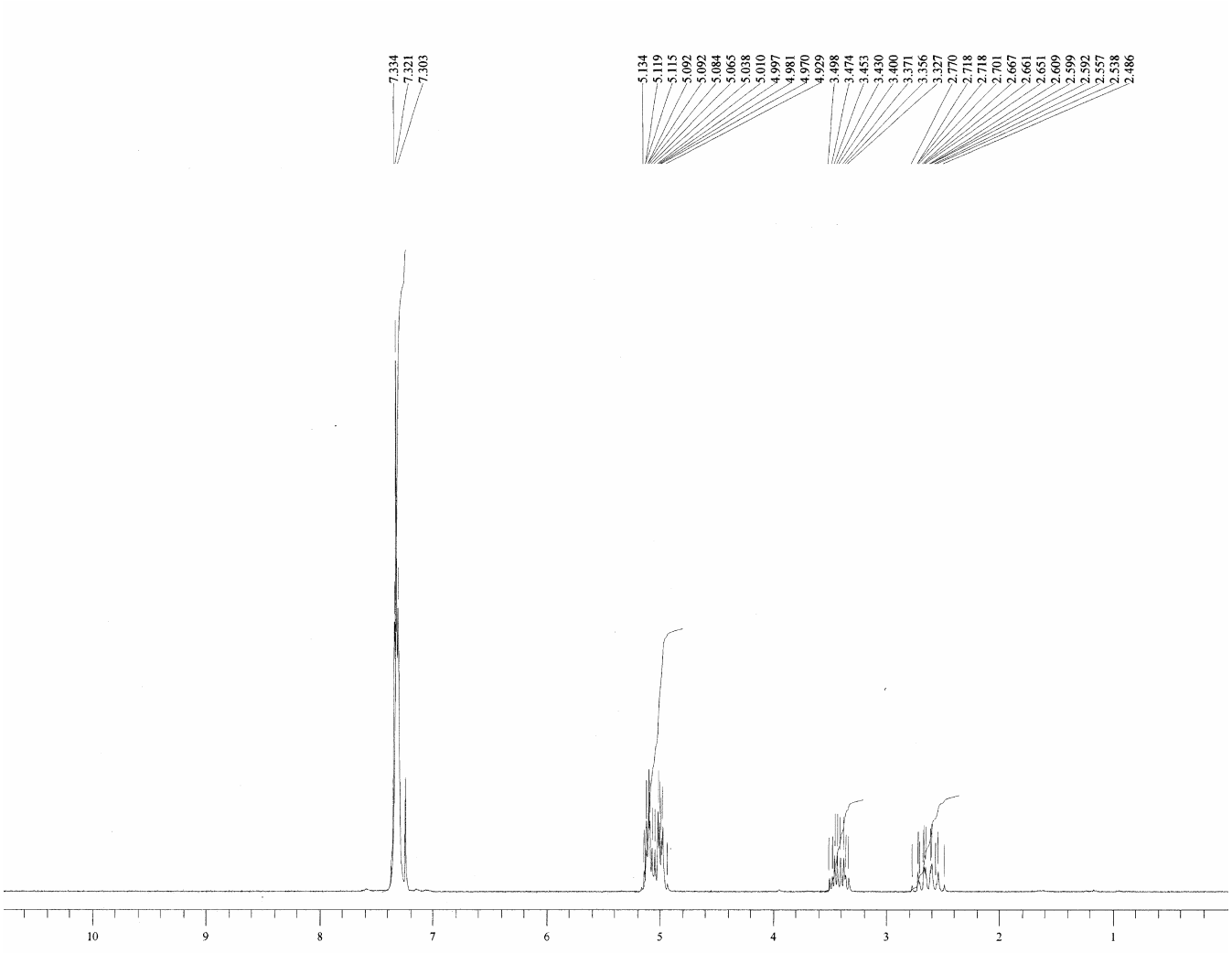
^{31}P

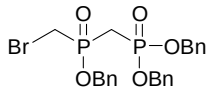



O
O
Br
P
P
OBn
OBn
OBn

42 ($CDCl_3$)

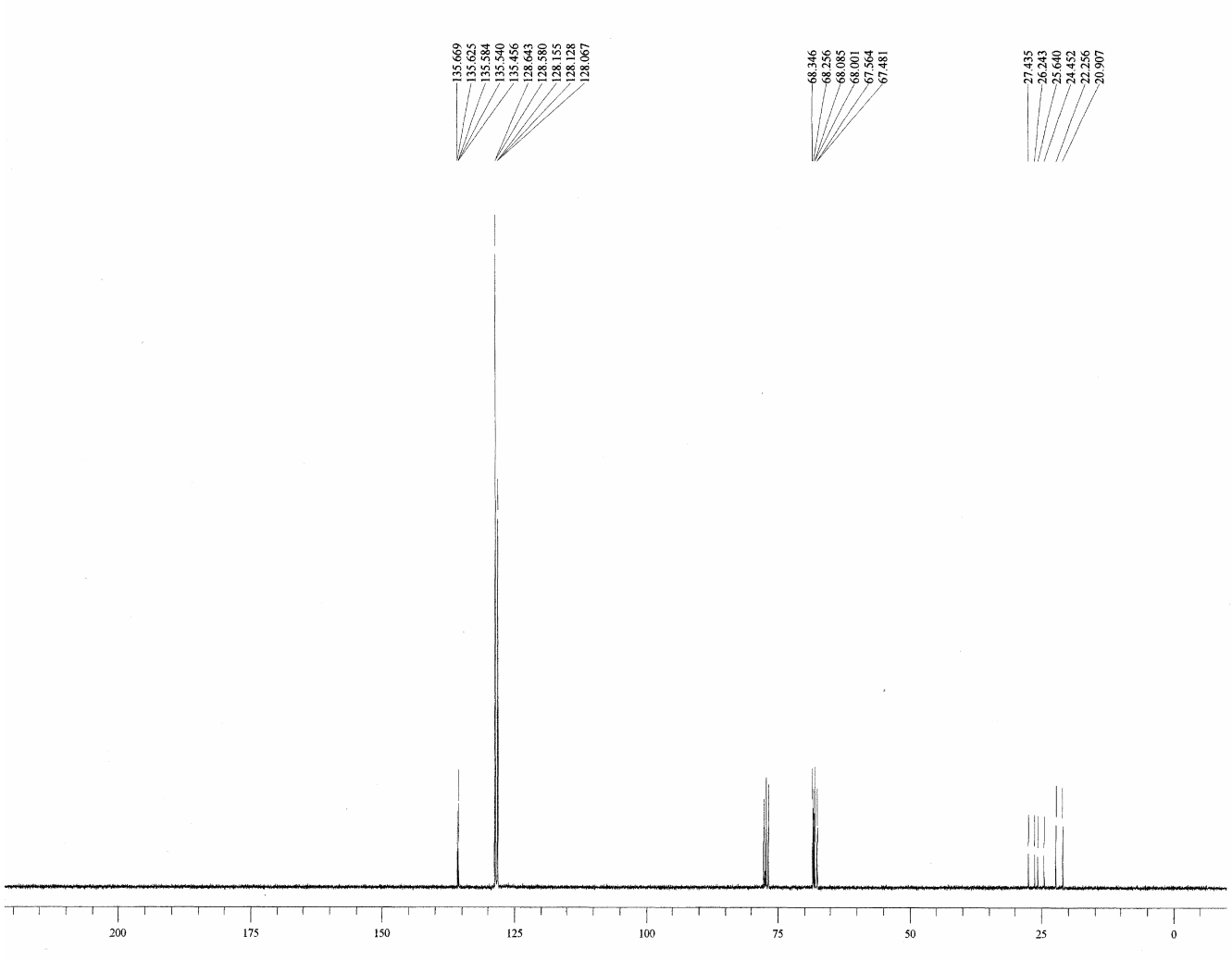
^1H

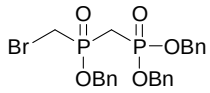

7.334
7.321
7.303
5.134
5.119
5.115
5.092
5.092
5.084
5.065
5.038
5.010
4.997
4.981
4.970
4.929
3.498
3.474
3.453
3.430
3.400
3.371
3.356
3.327
2.770
2.718
2.718
2.701
2.667
2.661
2.651
2.609
2.599
2.592
2.557
2.538
2.486
10
9
8
7
6
5
4
3
2
1


O
O
Br
P
P
OBn
OBn
OBn

42 ($CDCl_3$)

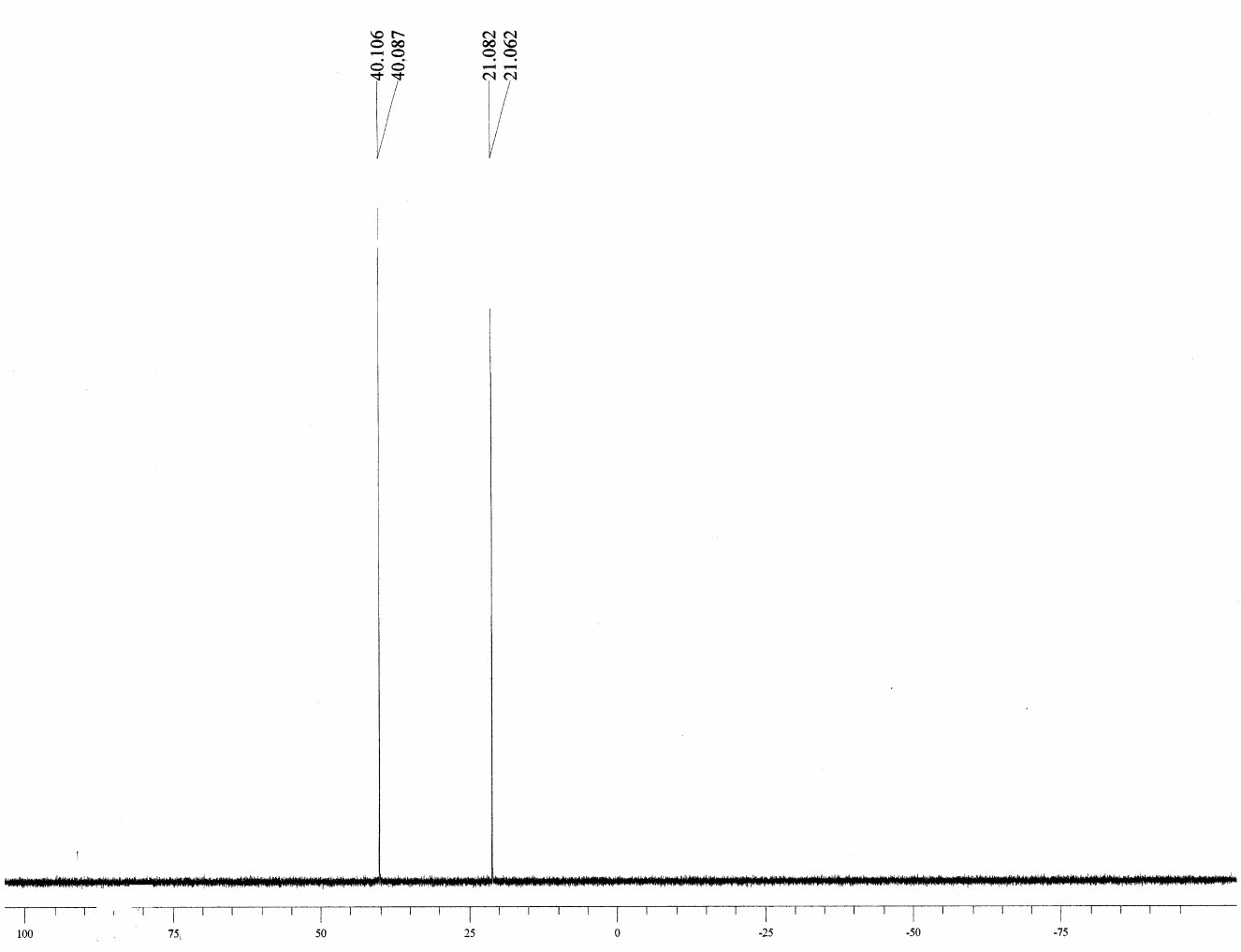
^{13}C

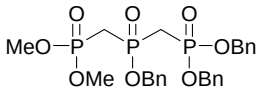

135.669
135.625
135.584
135.540
135.456
128.643
128.580
128.155
128.128
128.067
68.346
68.256
68.085
68.001
67.564
67.481
27.435
26.243
25.640
24.452
22.256
20.907
200
175
150
125
100
75
50
25
0


O
O
Br
P
P
OBn
OBn
OBn

42 ($CDCl_3$)

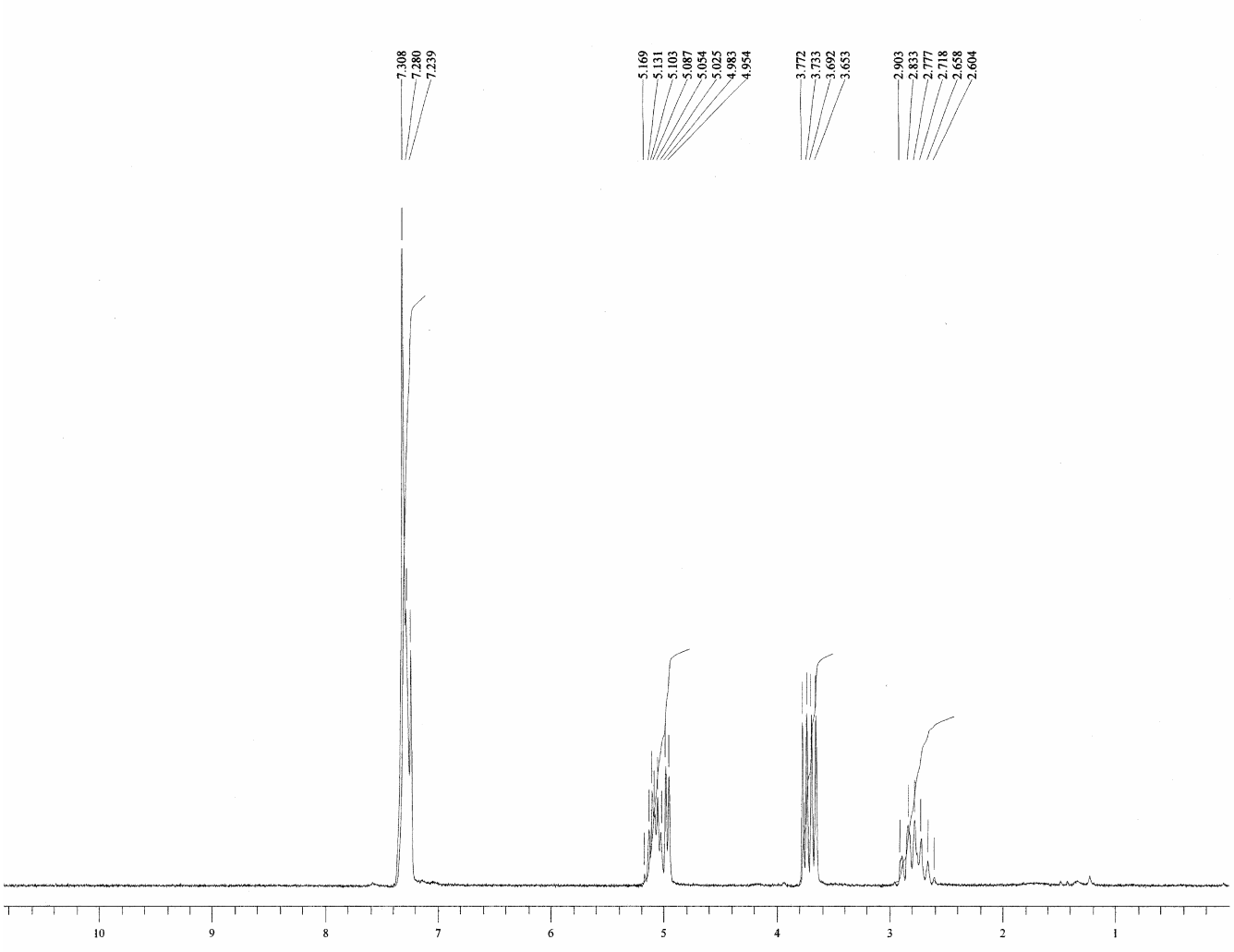
^{31}P

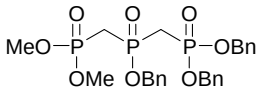

40.106
40.087
21.082
21.062
100
75
50
25
0
-25
-50
-75


MeO
OMe
OBn
OBn
OBn

43 ($CDCl_3$)

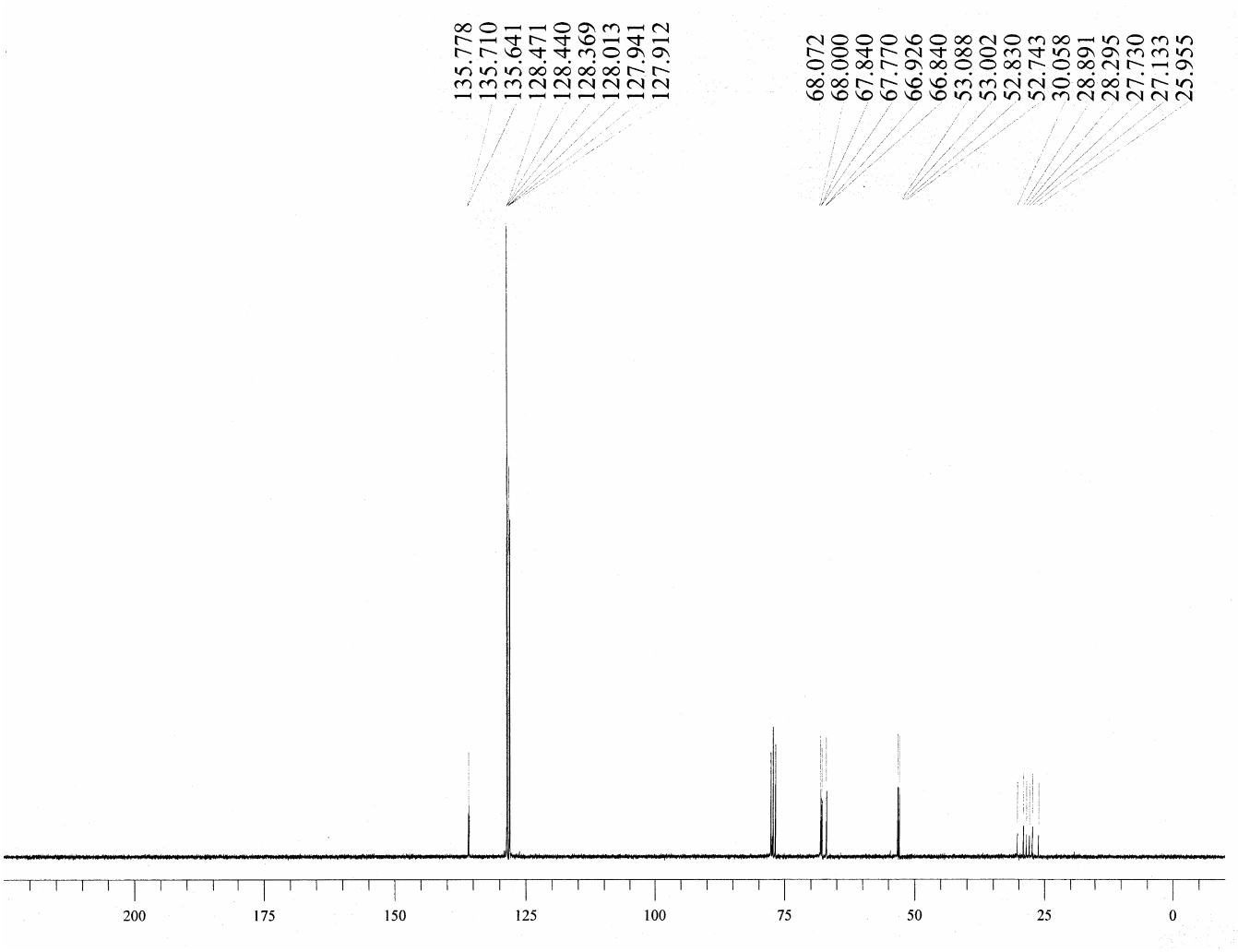
^1H

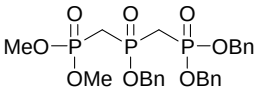

7.308
7.280
7.239
5.169
5.131
5.103
5.087
5.054
5.025
4.983
4.954
3.772
3.733
3.692
3.653
2.903
2.833
2.777
2.718
2.658
2.604
10
9
8
7
6
5
4
3
2
1


MeO
OBn
OMe
OBn
OBn

43 ($CDCl_3$)

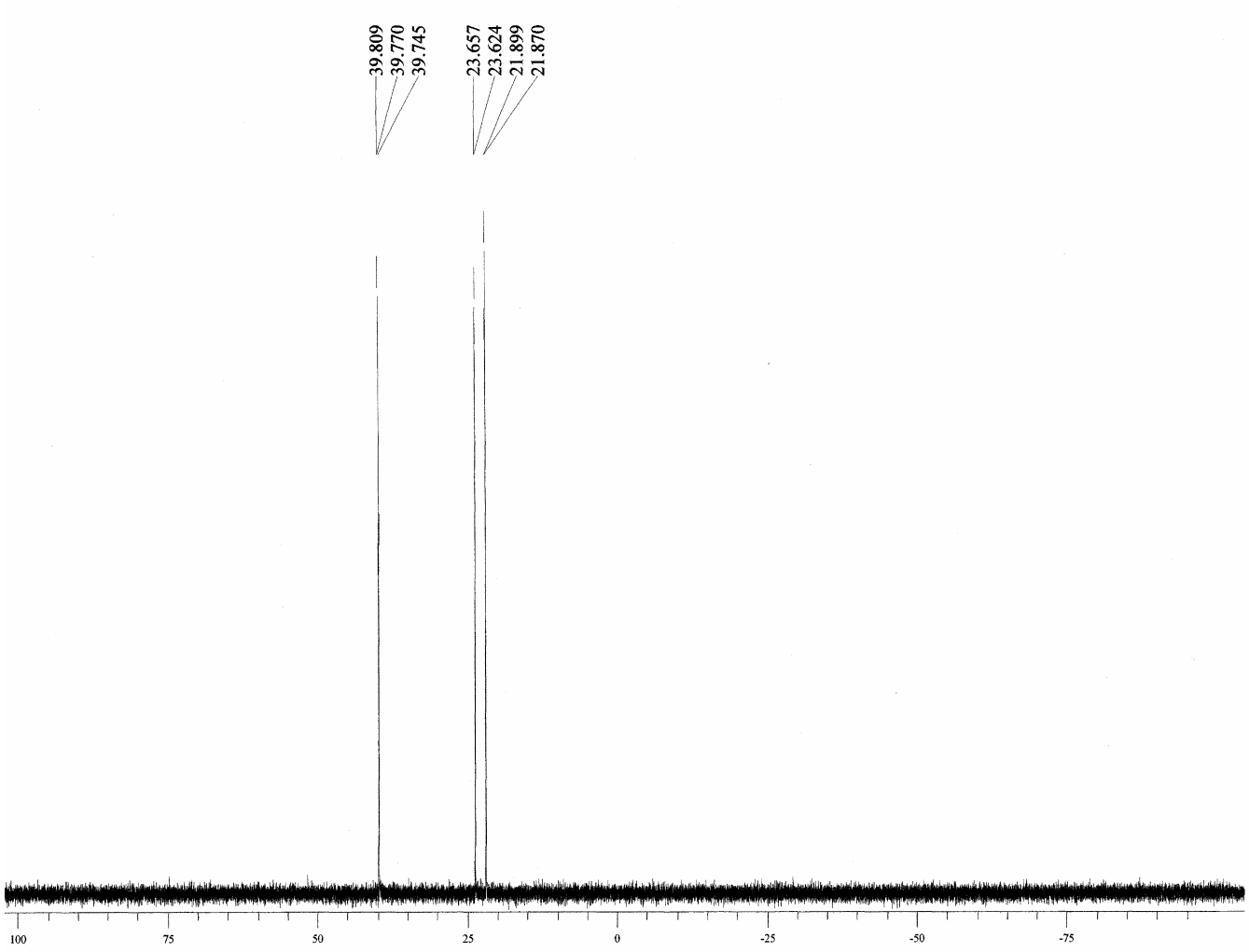
^{13}C

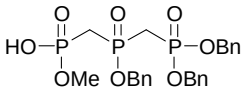

135.778
135.710
135.641
128.471
128.440
128.369
128.013
127.941
127.912
68.072
68.000
67.840
67.770
66.926
66.840
53.088
53.002
52.830
52.743
30.058
28.891
28.295
27.730
27.133
25.955
200
175
150
125
100
75
50
25
0


O
O
O
MeO—P
P
P—OBn
OMe OBn OBn

43 ($CDCl_3$)

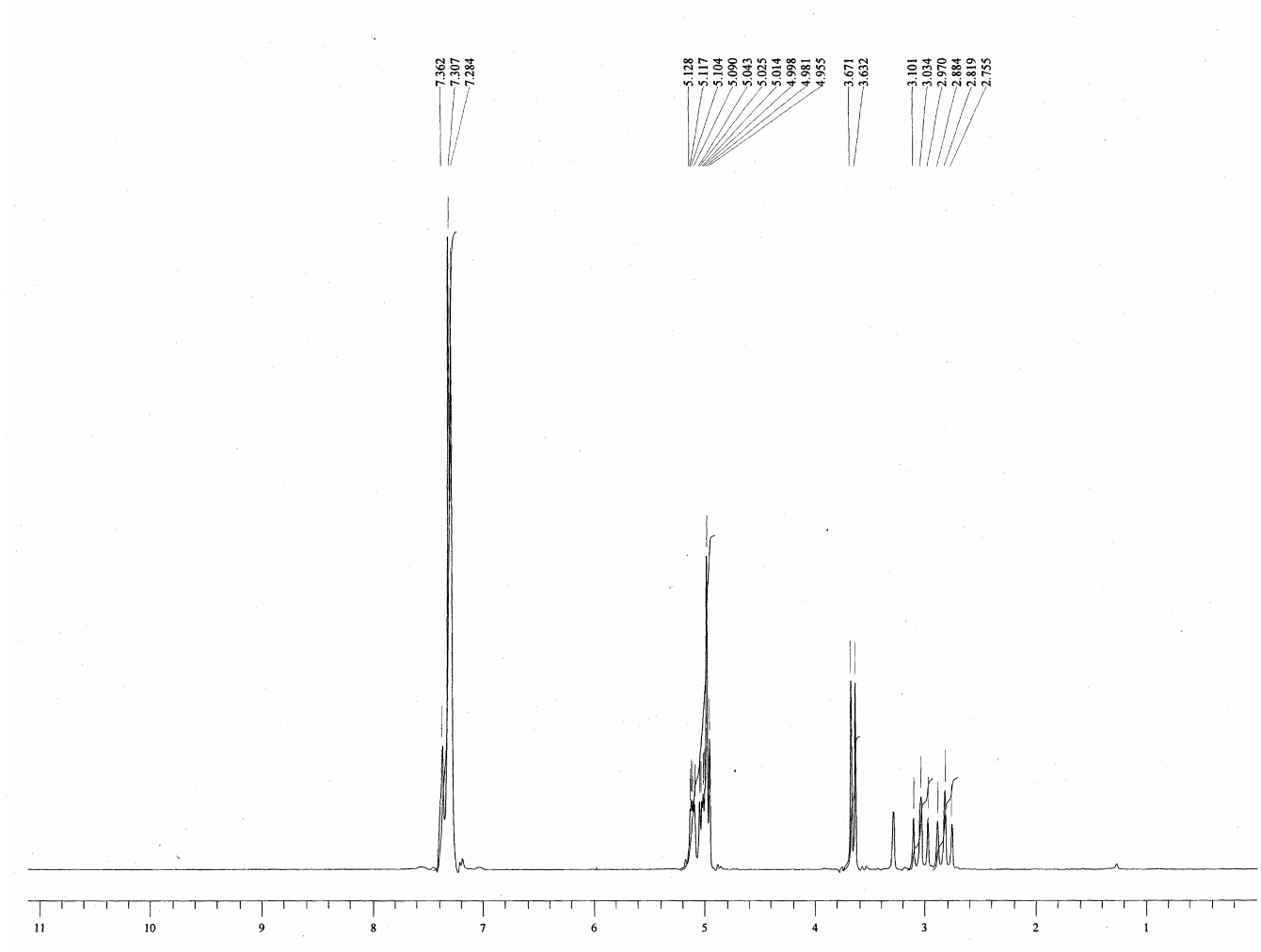
^{31}P

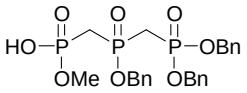

39.809
39.770
39.745
23.657
23.624
21.899
21.870
100
75
50
25
0
-25
-50
-75


HO
P
OMe
P
OBn
P
OBn
OBn

44 (CD_3OD)

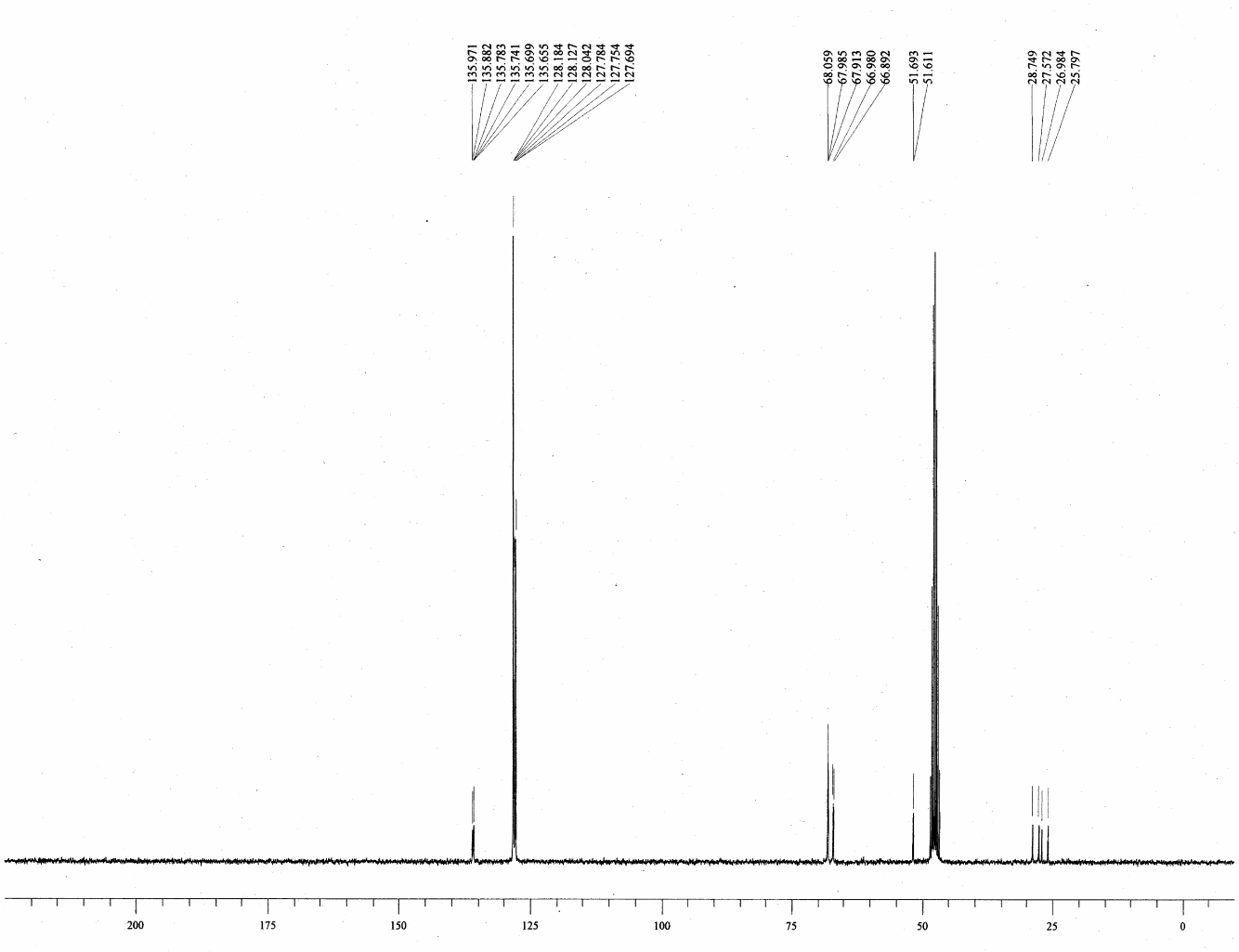
^1H

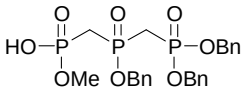

7.362
7.307
7.284
5.128
5.117
5.104
5.090
5.043
5.025
5.014
4.998
4.981
4.955
3.671
3.632
3.101
3.034
2.970
2.884
2.819
2.755
11
10
9
8
7
6
5
4
3
2
1



44 (CD_3OD)

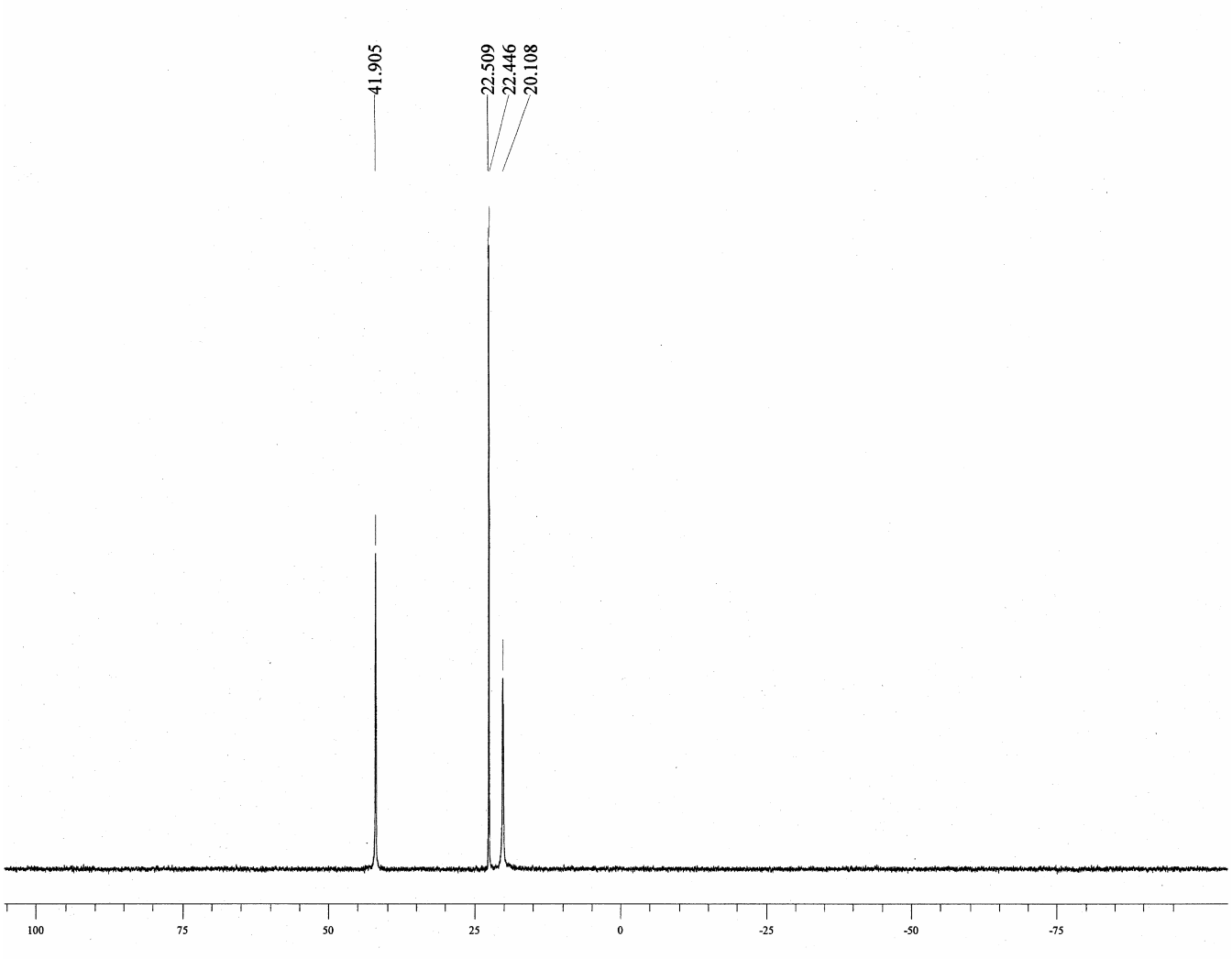
^{13}C

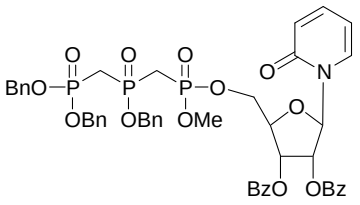

135.971
135.882
135.783
135.741
135.699
135.655
128.184
128.127
128.042
127.784
127.754
127.694
68.059
67.985
67.913
66.980
66.892
51.693
51.611
28.749
27.572
26.984
25.797
200
175
150
125
100
75
50
25
0



44 (CD_3OD)

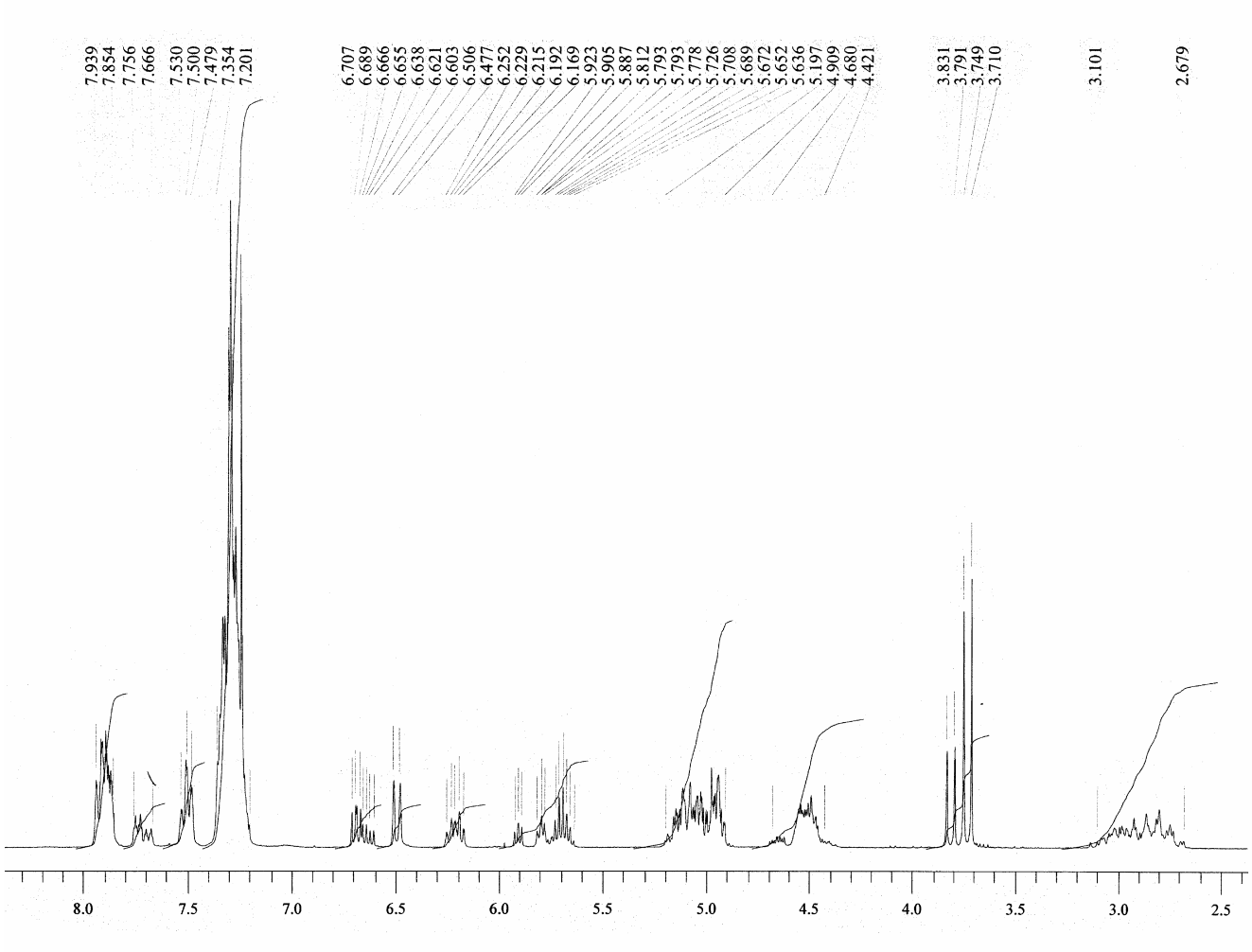
^{31}P

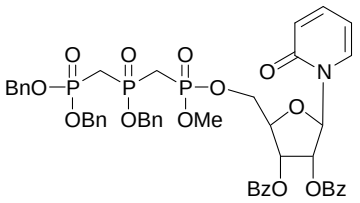



BnO
OBn
OBn
OMe
BzO
OBz

45 ($CDCl_3$)

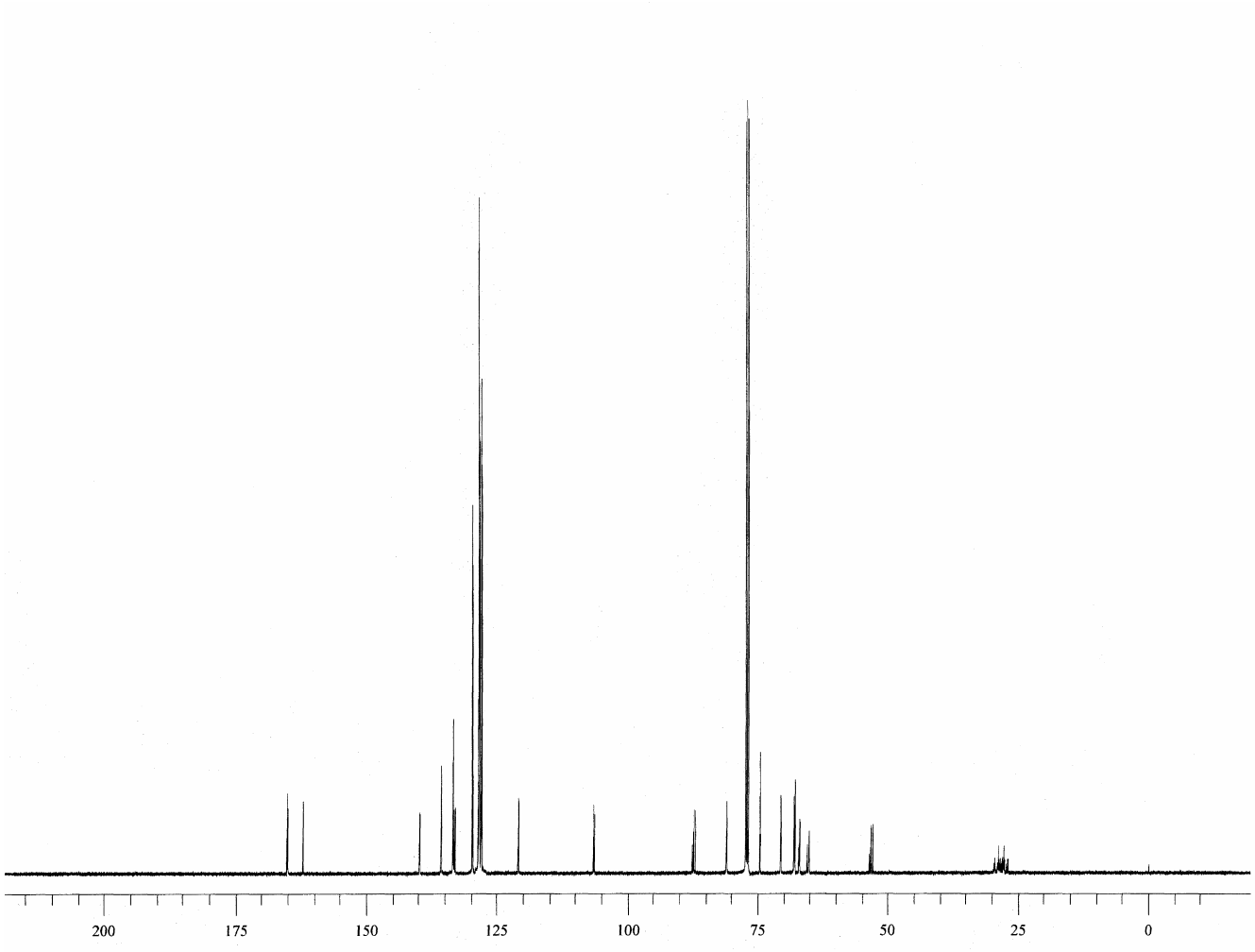
^1H

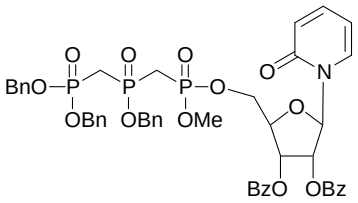

7.939
7.854
7.756
7.666
7.530
7.500
7.479
7.354
7.201
6.707
6.689
6.666
6.655
6.638
6.621
6.603
6.506
6.477
6.252
6.229
6.215
6.192
6.169
5.923
5.905
5.887
5.812
5.793
5.793
5.778
5.726
5.708
5.689
5.672
5.652
5.636
5.197
4.909
4.680
4.421
3.831
3.791
3.749
3.710
3.101
2.679
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5



45 ($CDCl_3$)

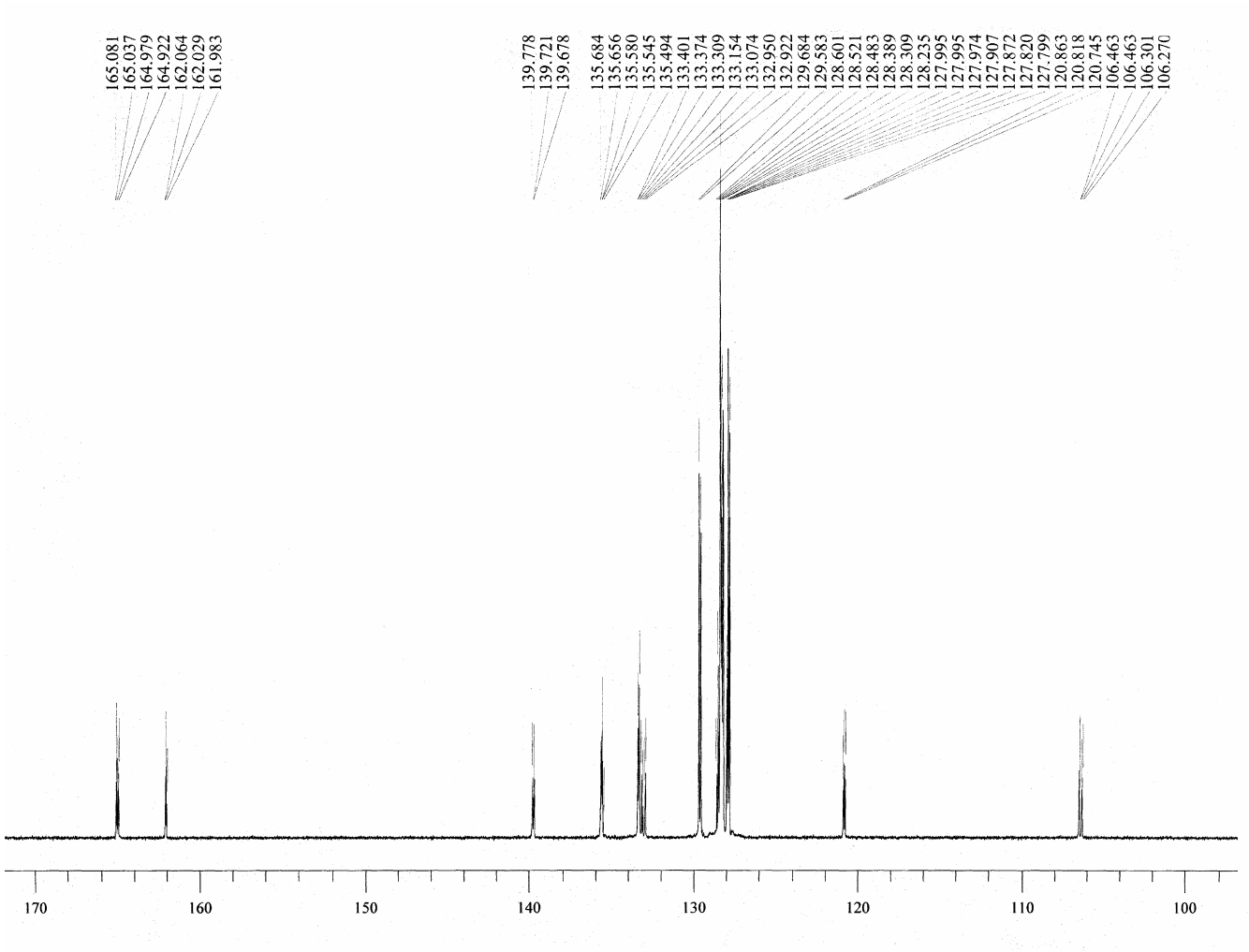
^{13}C

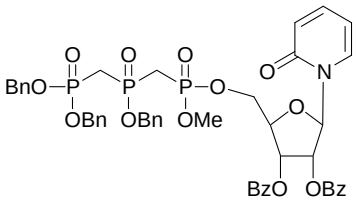




45 ($CDCl_3$)

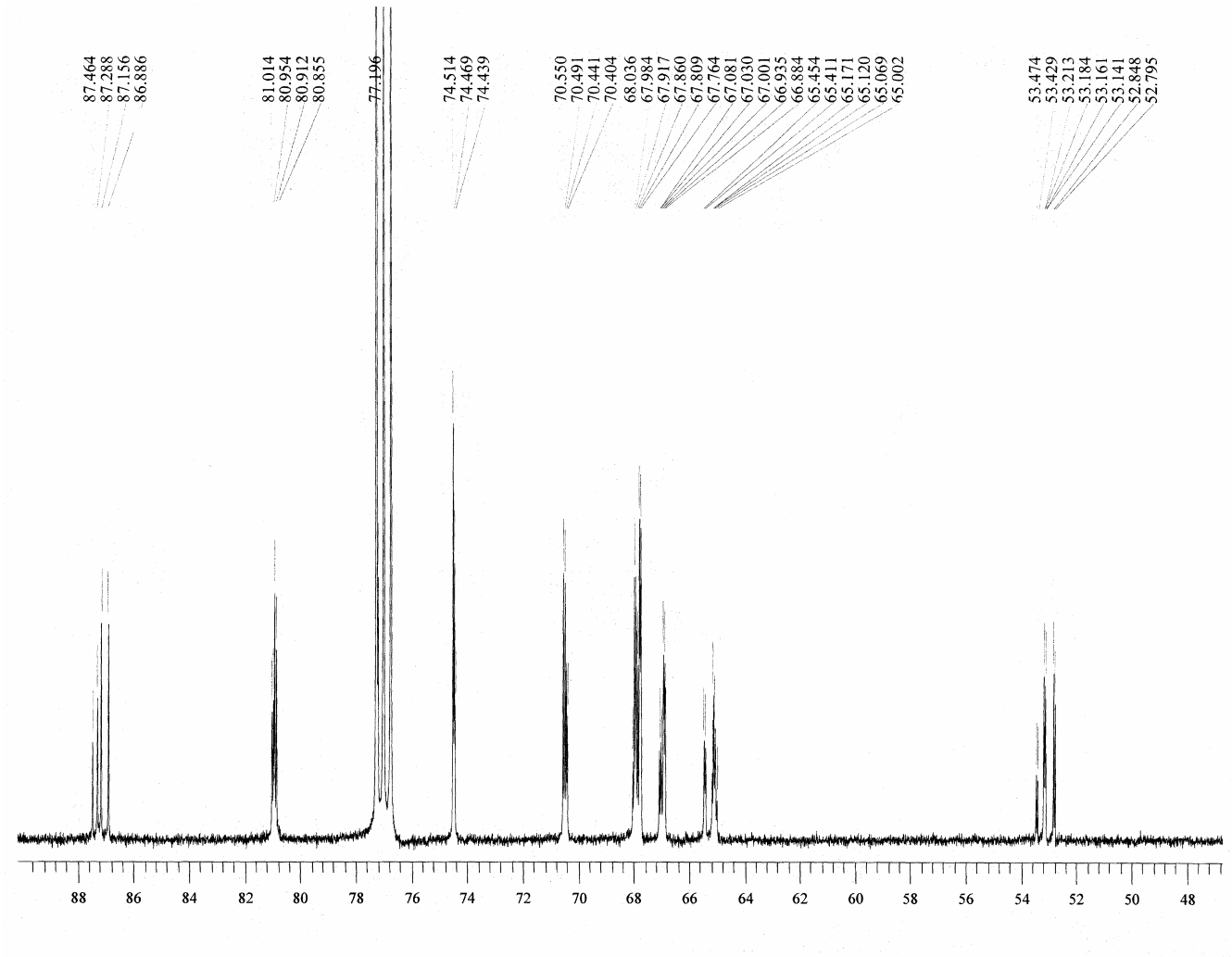
^{13}C (expanded)

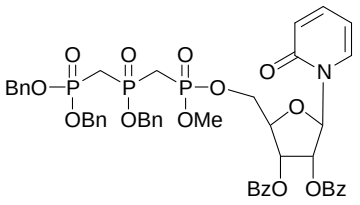




45 ($CDCl_3$)

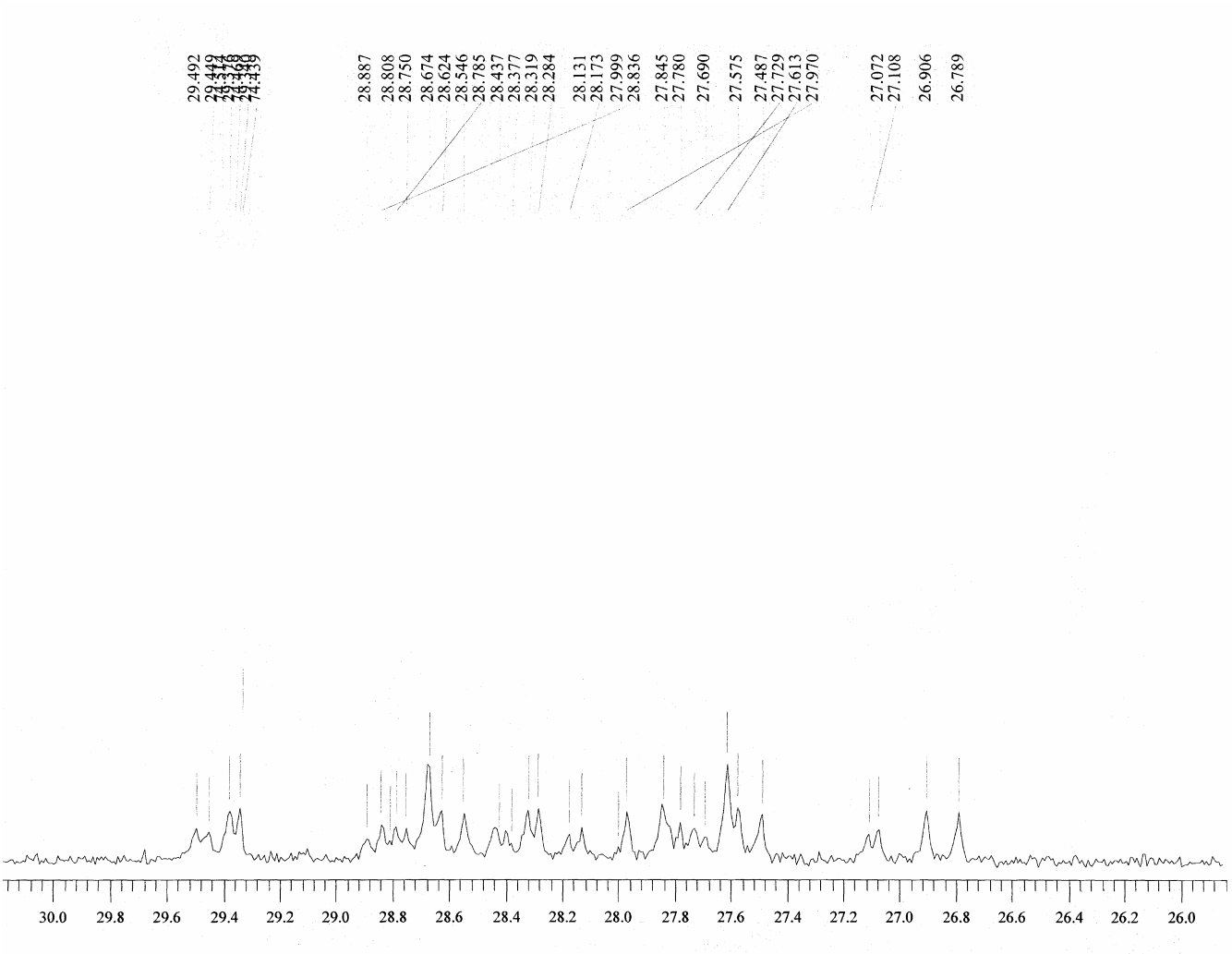
^{13}C (expanded)

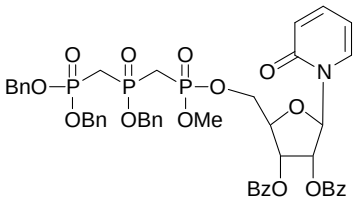




45 ($CDCl_3$)

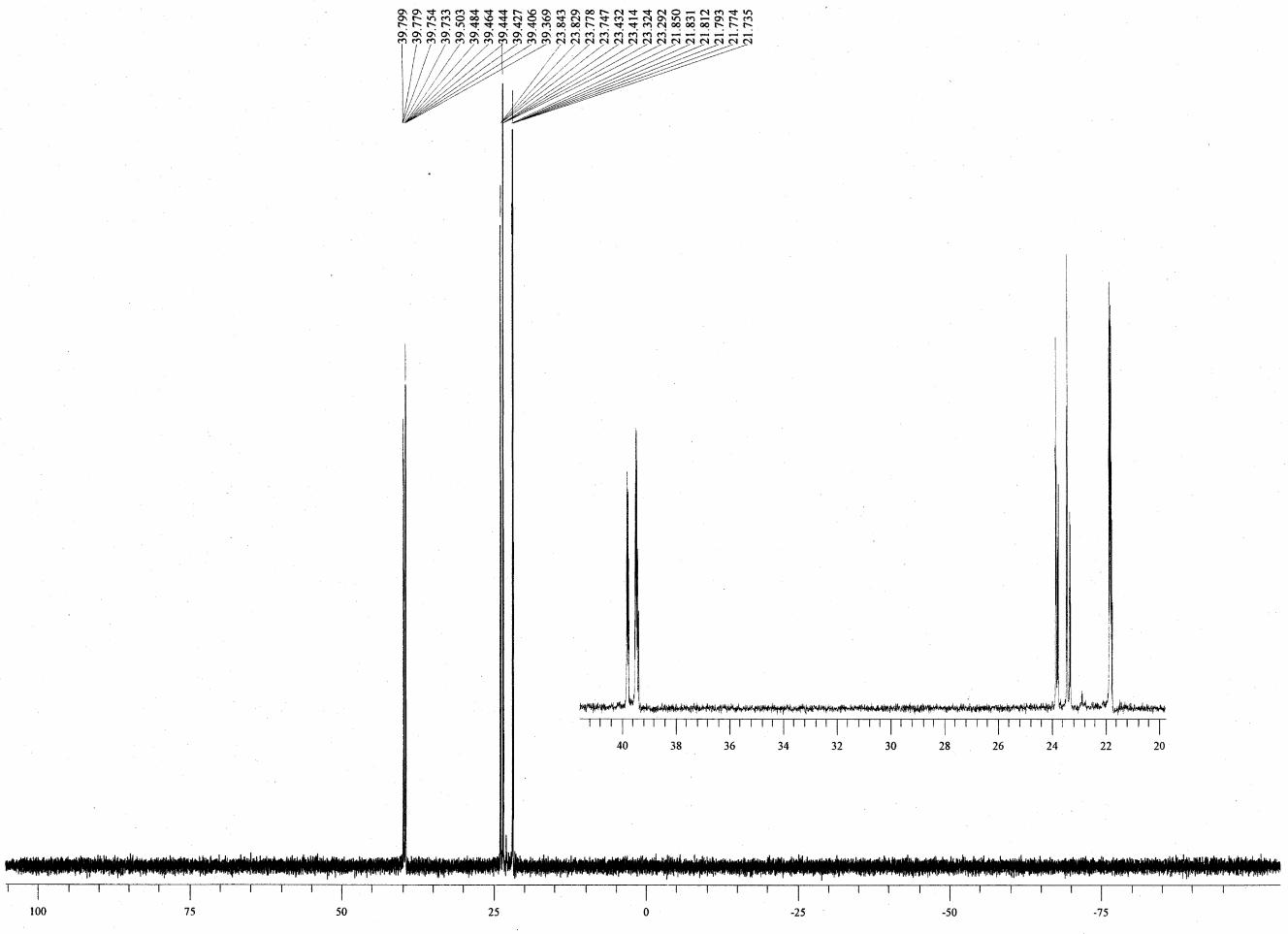
^{13}C (expanded)

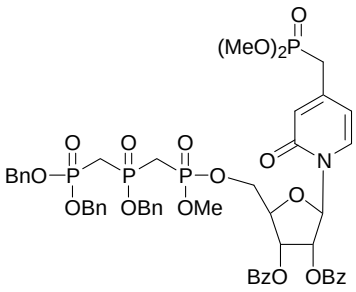



BnO
OBn
OBn
OMe
BzO
OBz

45 ($CDCl_3$)

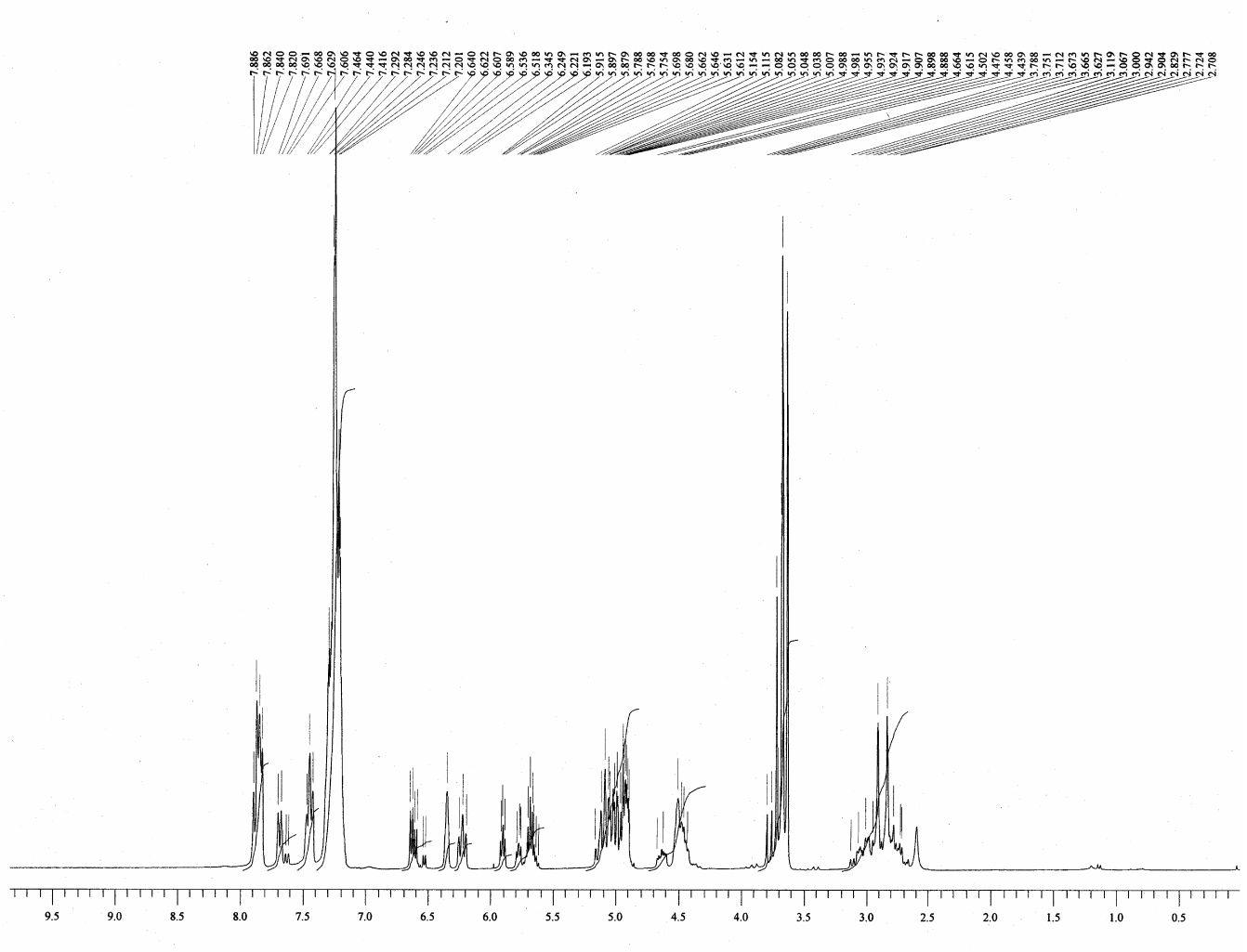
^{31}P

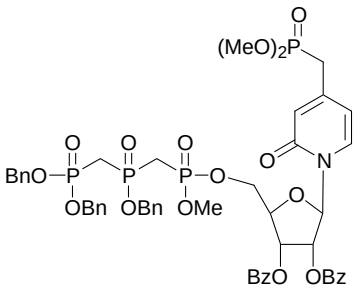

39.799
39.779
39.754
39.733
39.503
39.484
39.464
39.444
39.427
39.406
39.369
23.843
23.829
23.778
23.747
23.432
23.414
23.324
23.292
21.850
21.831
21.812
21.793
21.774
21.735
100
75
50
25
0
-25
-50
-75
40
38
36
34
32
30
28
26
24
22
20


(MeO)2P
O
O
N
BnO
OBn
OBn
OMe
BzO
OBz

46 ($CDCl_3$)

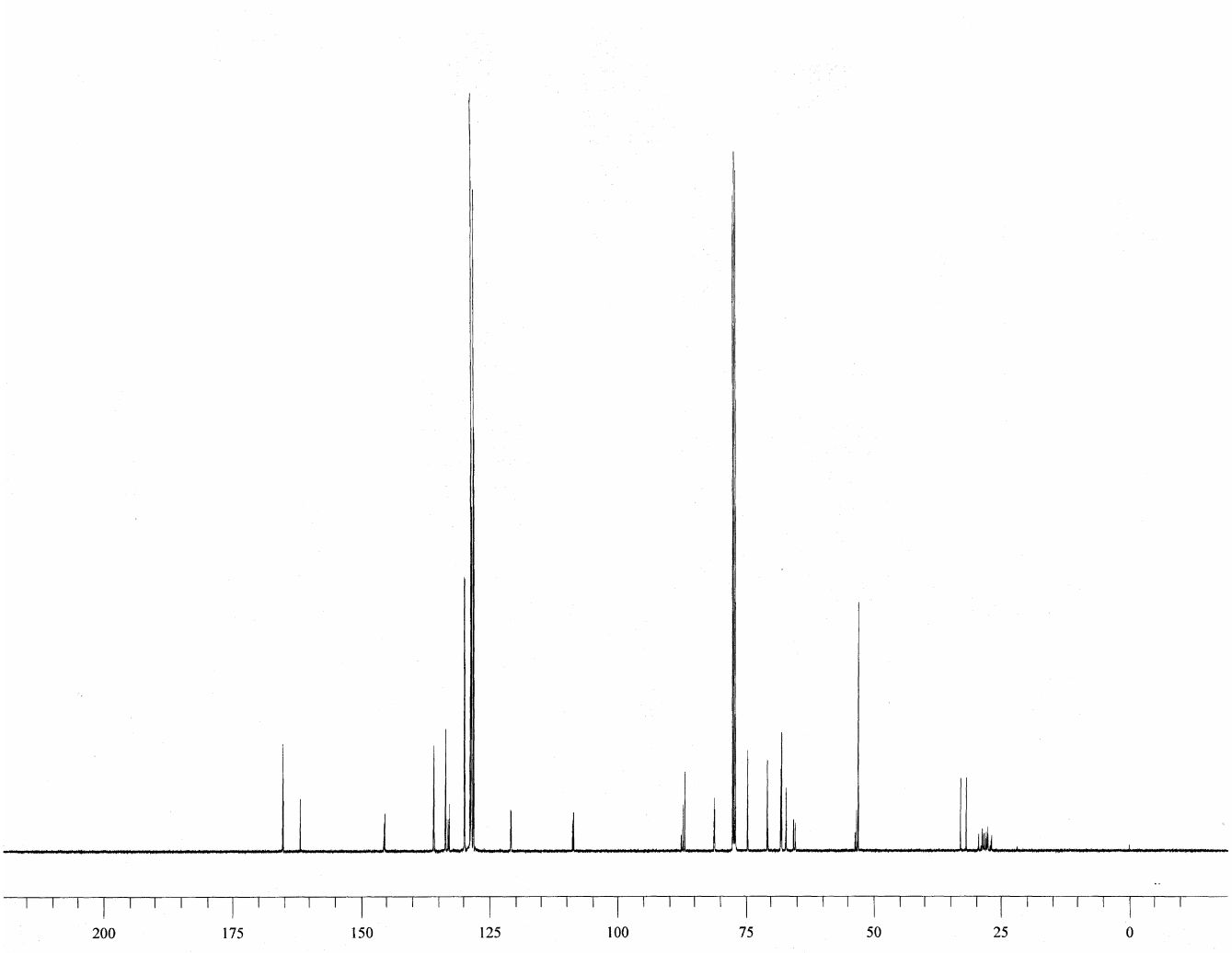
^1H

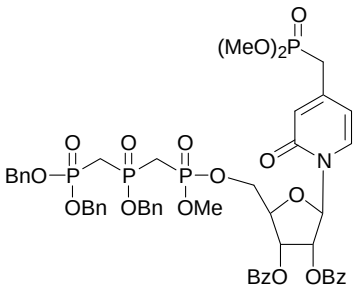

7.886
7.862
7.840
7.820
7.691
7.668
7.629
7.606
7.464
7.440
7.416
7.292
7.284
7.246
7.236
7.212
7.201
6.640
6.622
6.607
6.589
6.536
6.518
6.345
6.249
6.221
6.193
5.915
5.897
5.879
5.788
5.768
5.754
5.698
5.680
5.662
5.646
5.631
5.612
5.154
5.115
5.082
5.055
5.048
5.038
5.007
4.988
4.981
4.955
4.937
4.924
4.917
4.907
4.898
4.888
4.664
4.615
4.502
4.476
4.458
4.439
3.788
3.751
3.712
3.673
3.665
3.627
3.119
3.067
3.000
2.942
2.904
2.829
2.777
2.724
2.708
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5



46 ($CDCl_3$)

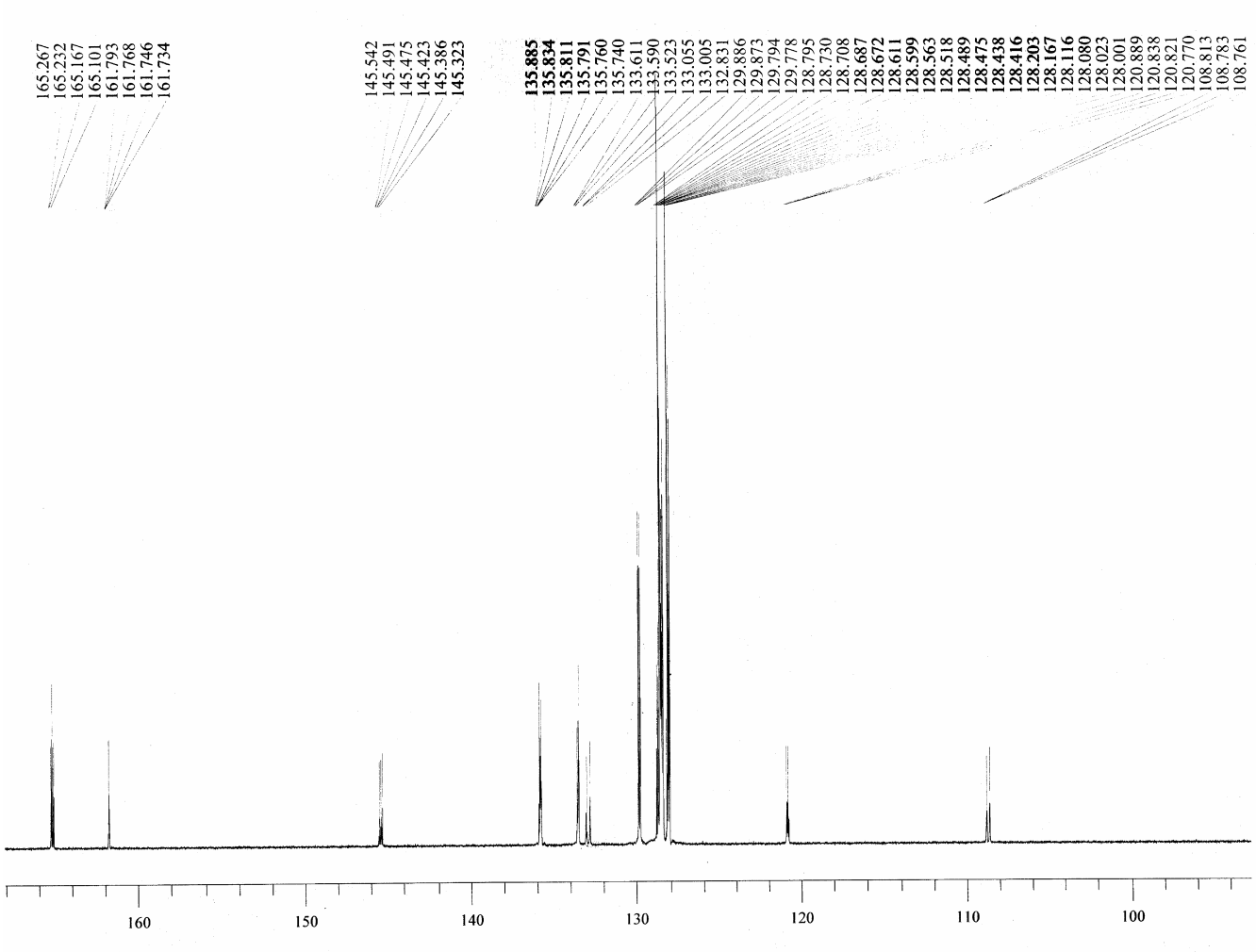
^{13}C

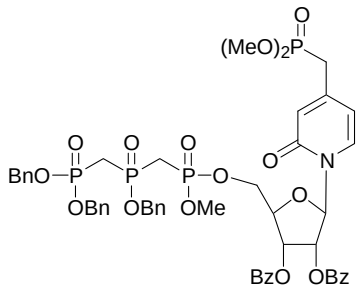




46 ($CDCl_3$)

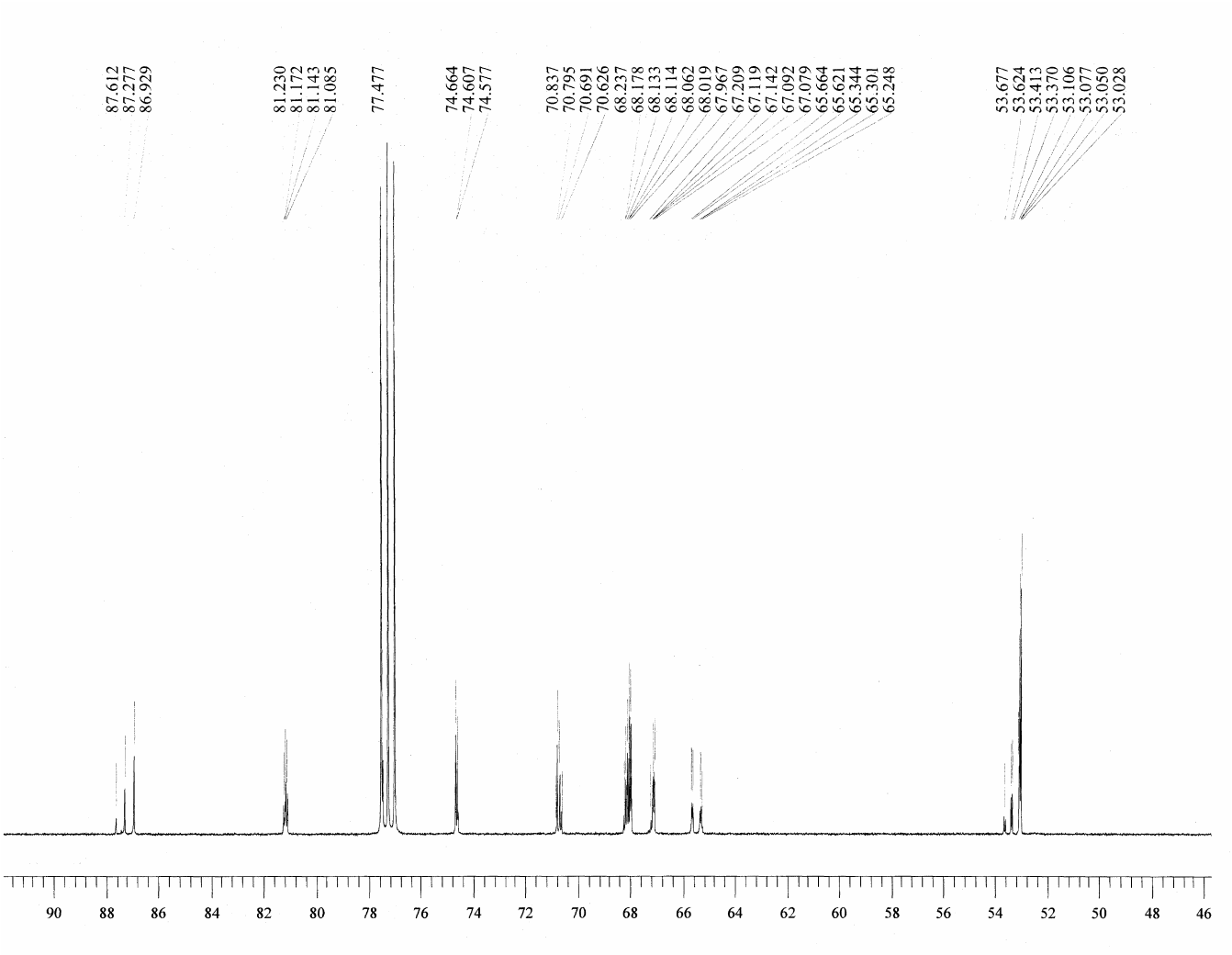
^{13}C (expanded)

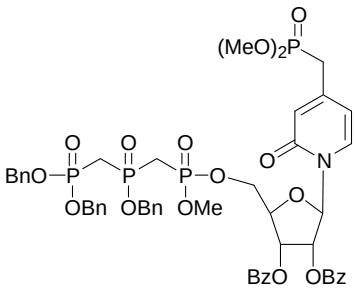




46 ($CDCl_3$)

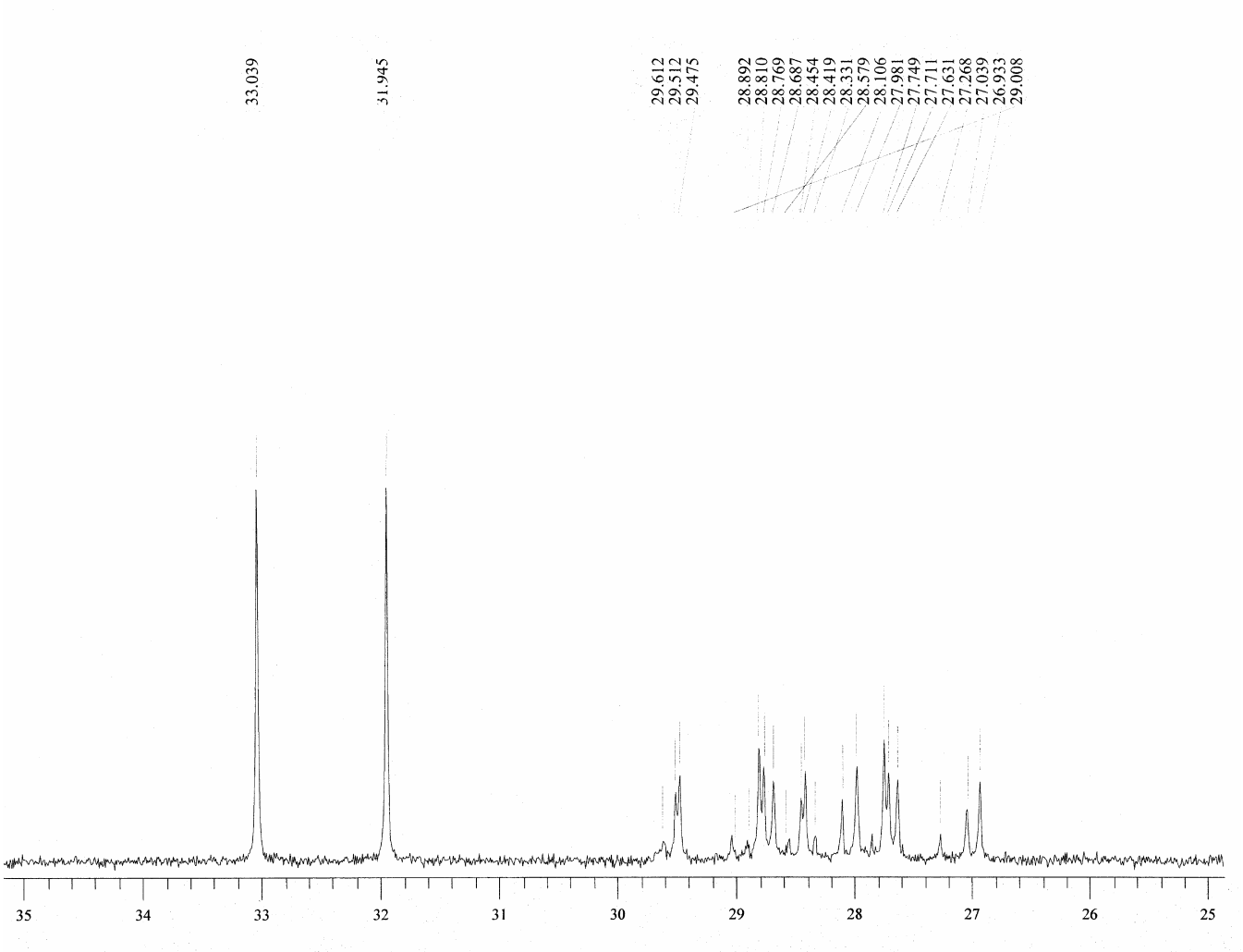
^{13}C (expanded)

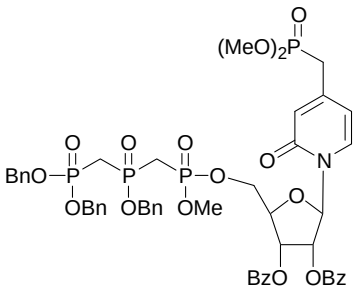




46 ($CDCl_3$)

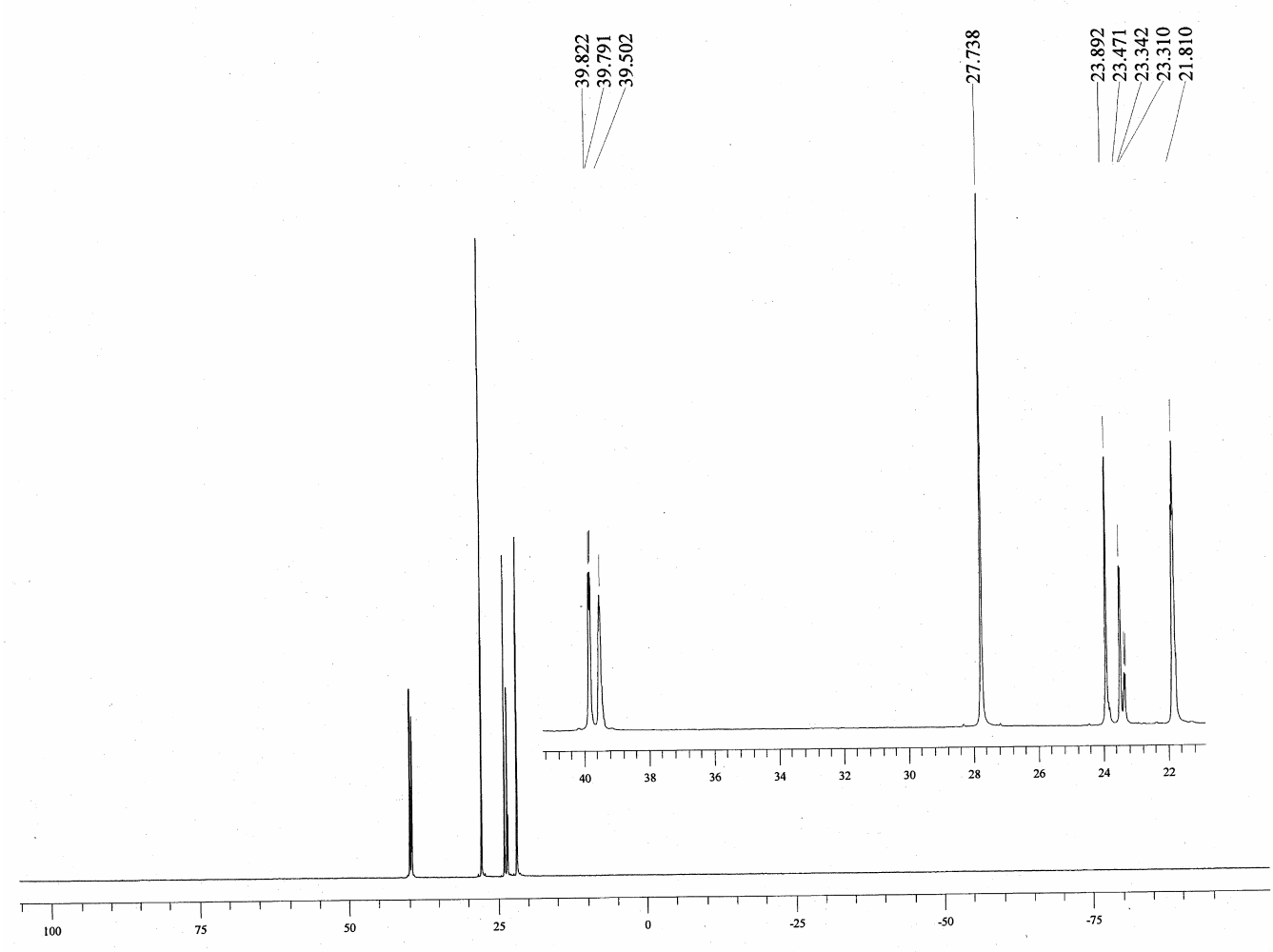
^{13}C (expanded)

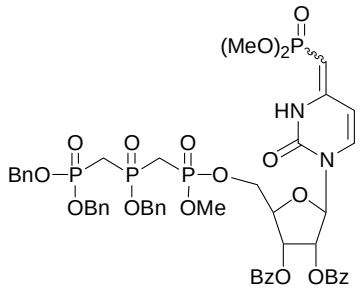




46 ($CDCl_3$)

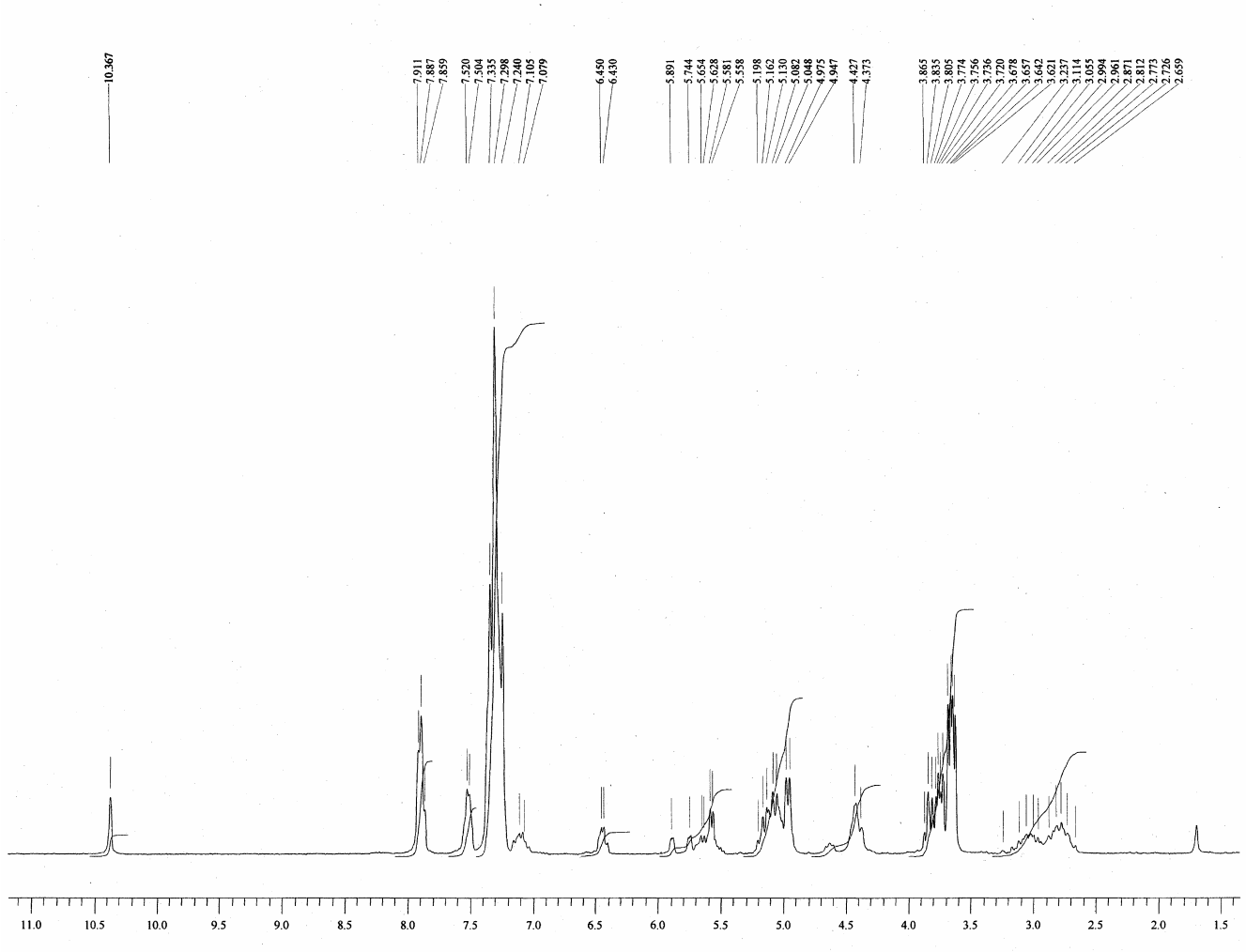
^{31}P

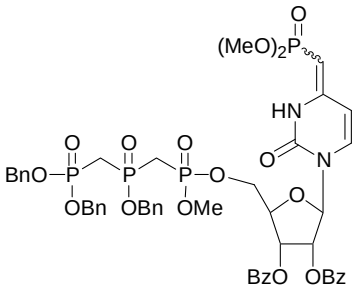

39.822
39.791
39.502
27.738
23.892
23.471
23.342
23.310
21.810
40
38
36
34
32
30
28
26
24
22
100
75
50
25
0
-25
-50
-75


O
(MeO)2P
HN
O
N
O
O
O
O
BnO—P—P—P—O
OBn OBn OMe
O
BzO OBz

47 ($CDCl_3$)

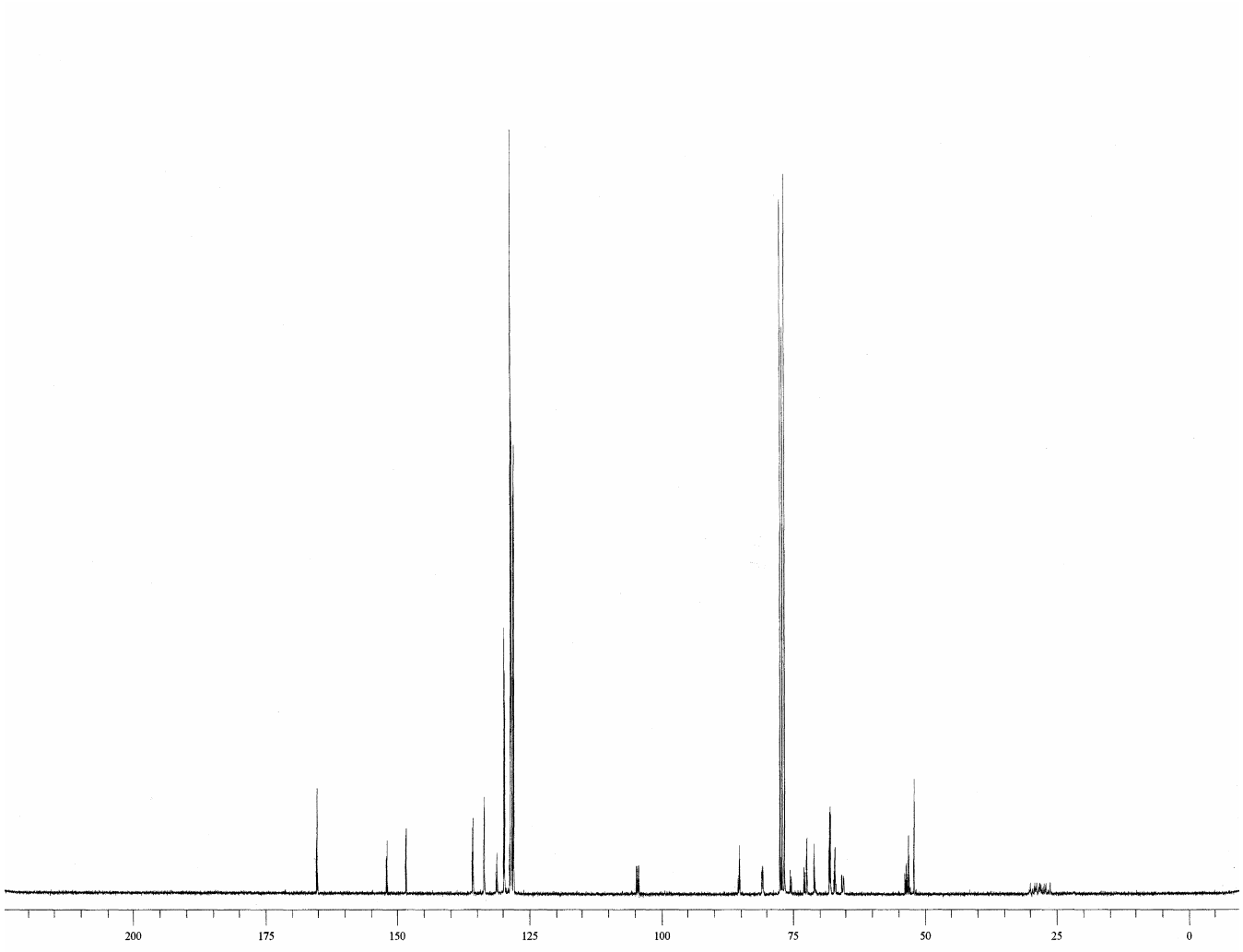
^1H

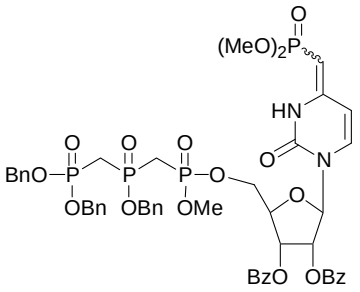

10.367
7.911
7.887
7.859
7.520
7.504
7.335
7.298
7.240
7.105
7.079
6.450
6.430
5.891
5.744
5.654
5.628
5.581
5.558
5.198
5.160
5.130
5.082
5.048
4.975
4.947
4.427
4.373
3.865
3.835
3.805
3.774
3.756
3.736
3.720
3.678
3.657
3.642
3.621
3.237
3.114
3.055
2.994
2.961
2.871
2.812
2.773
2.726
2.659
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


O
(MeO)2P
HN
O
N
O
BnO—P—O—P—O—P—O
OBn OBn OMe
O
BzO OBz

47 ($CDCl_3$)

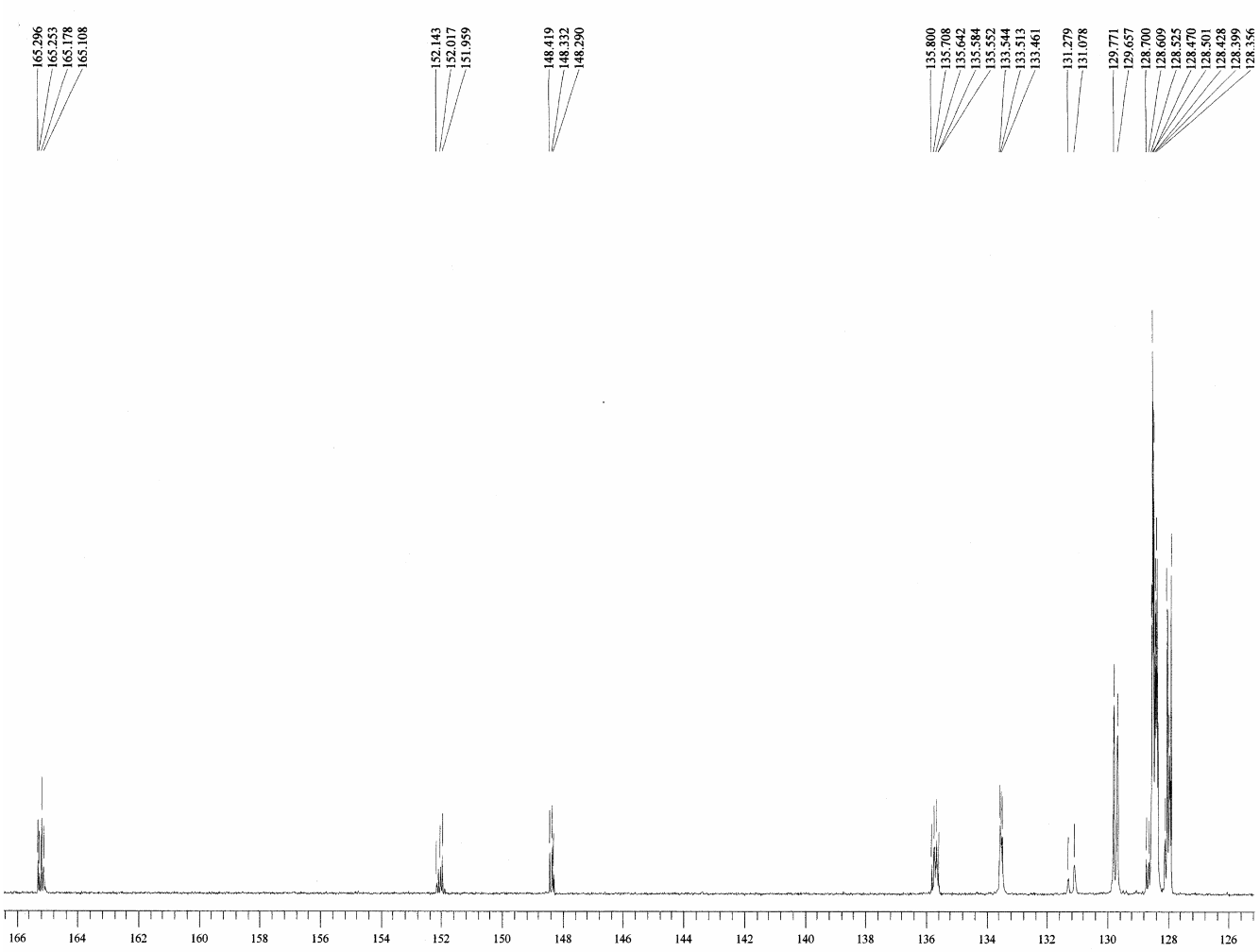
^{13}C

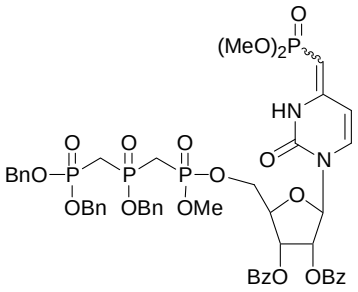

200
175
150
125
100
75
50
25
0



47 ($CDCl_3$)

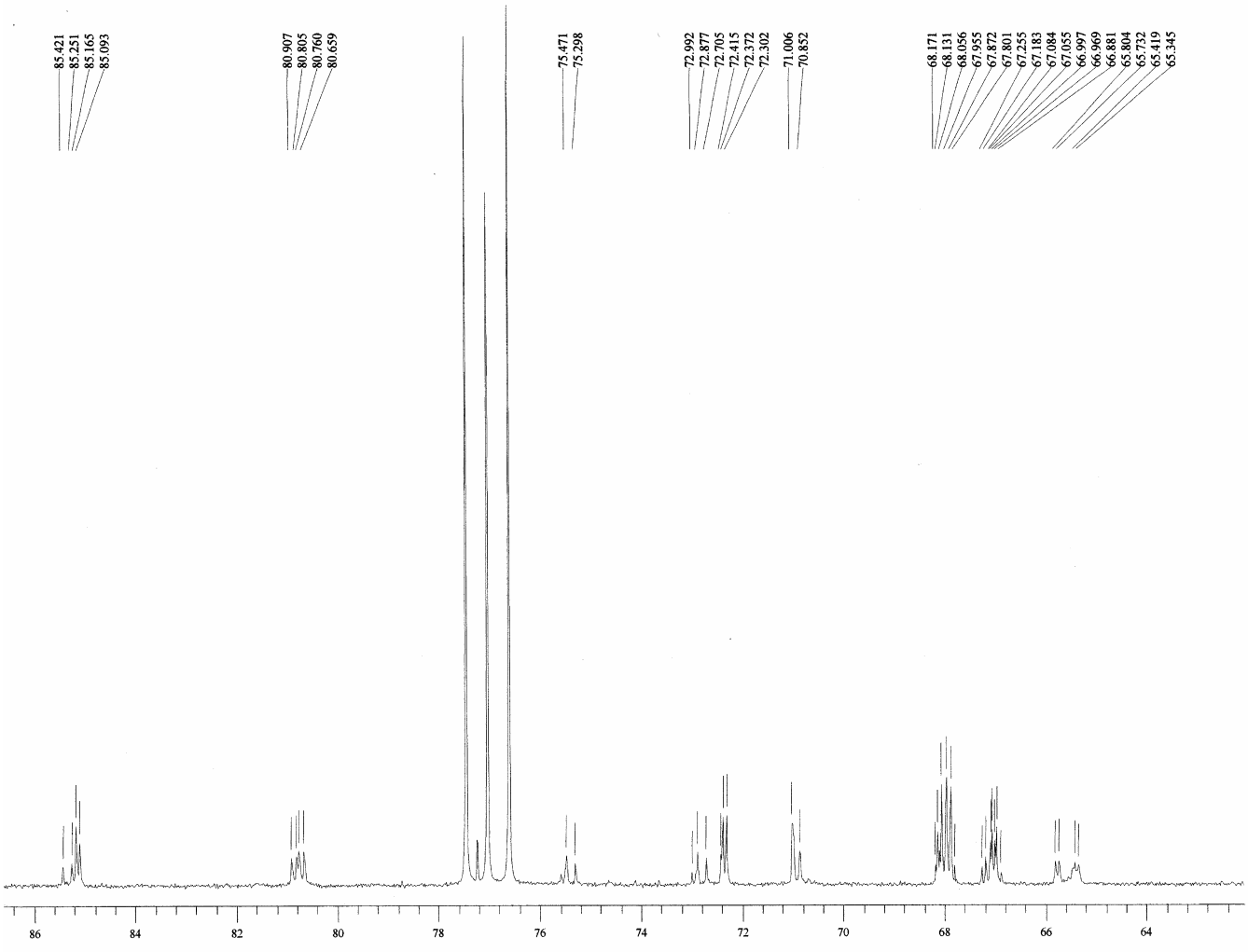
^{13}C (expanded)

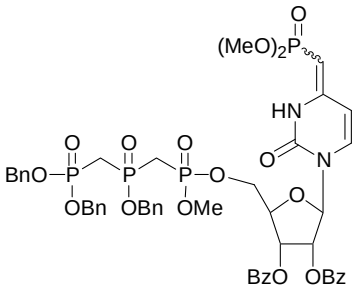




47 ($CDCl_3$)

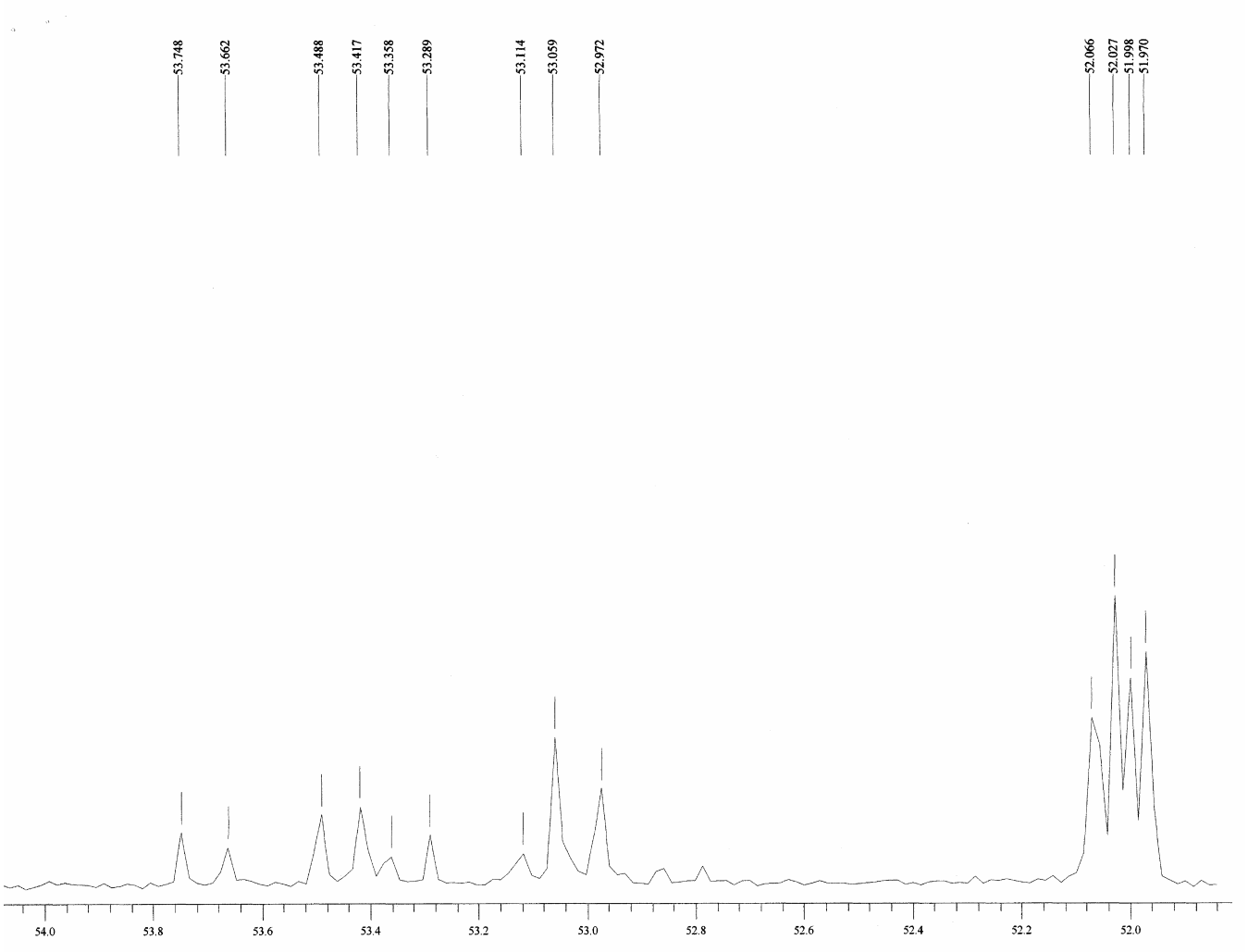
^{13}C (expanded)

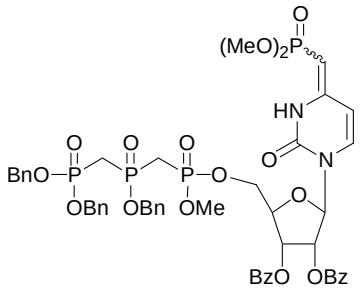




47 ($CDCl_3$)

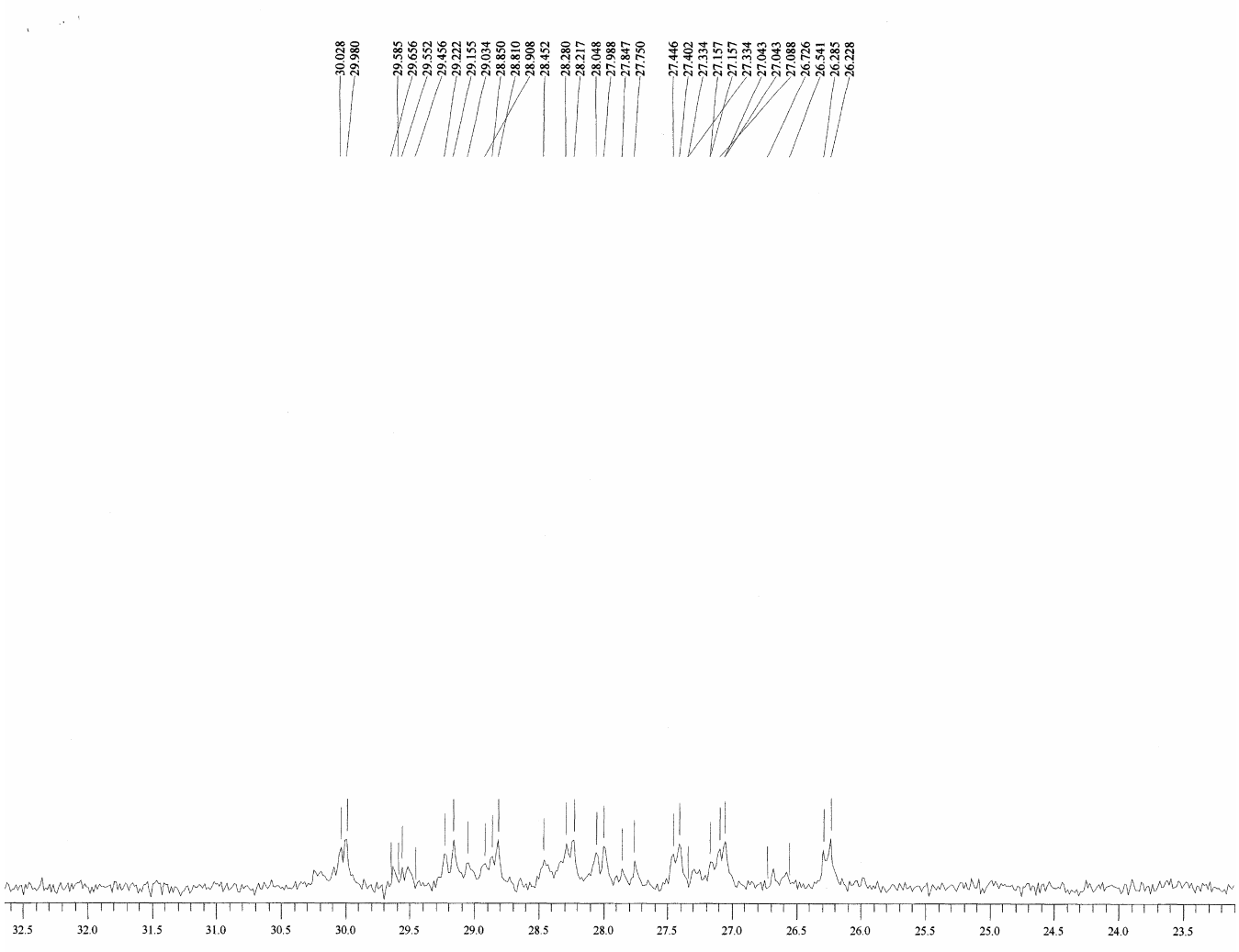
^{13}C (expanded)

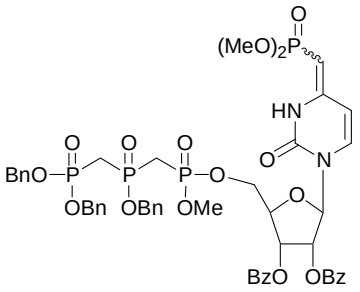




47 ($CDCl_3$)

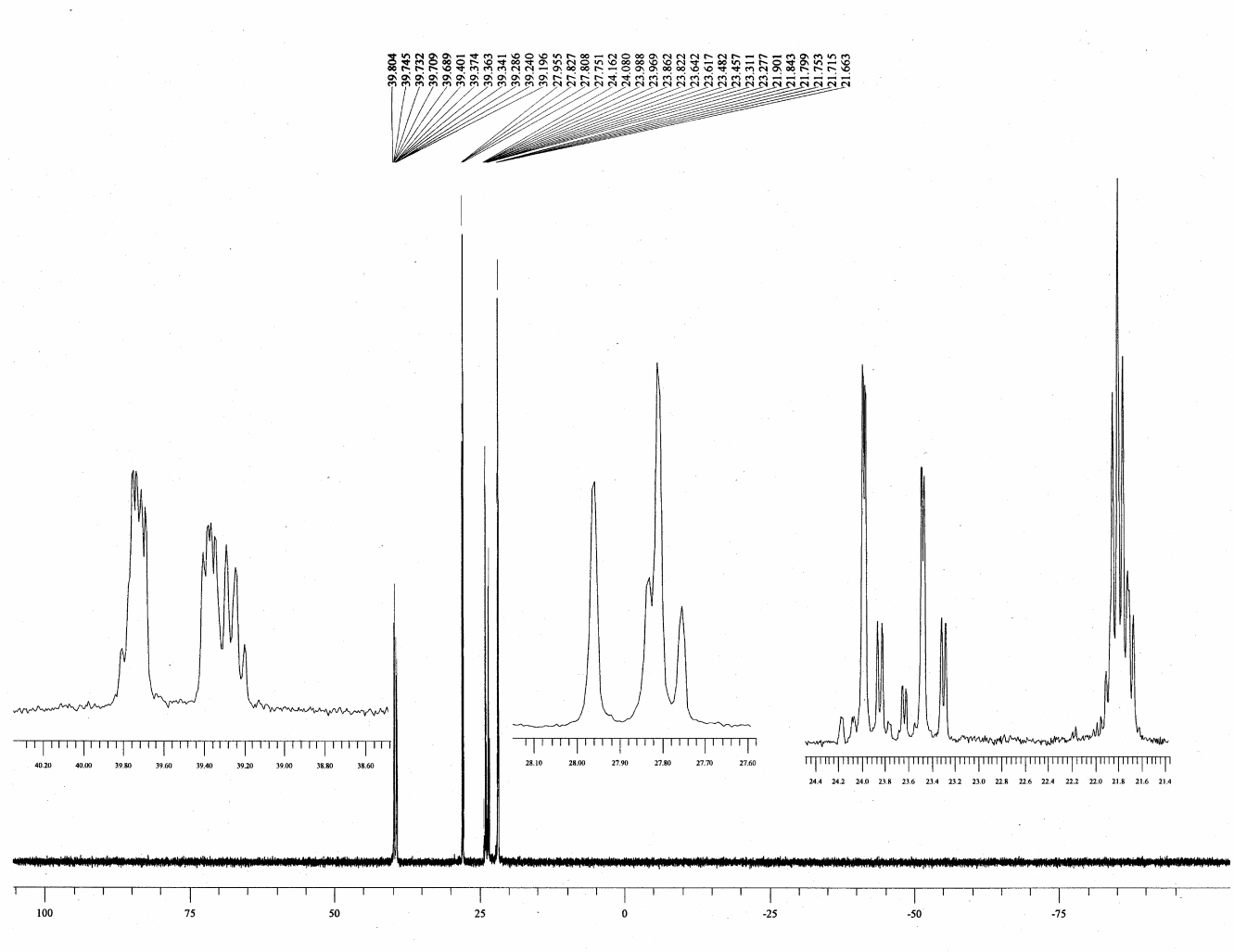
^{13}C (expanded)

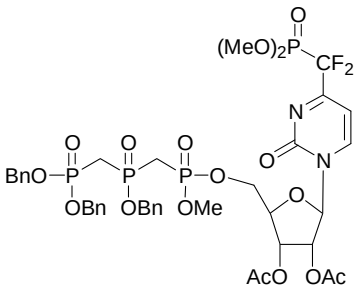




47 ($CDCl_3$)

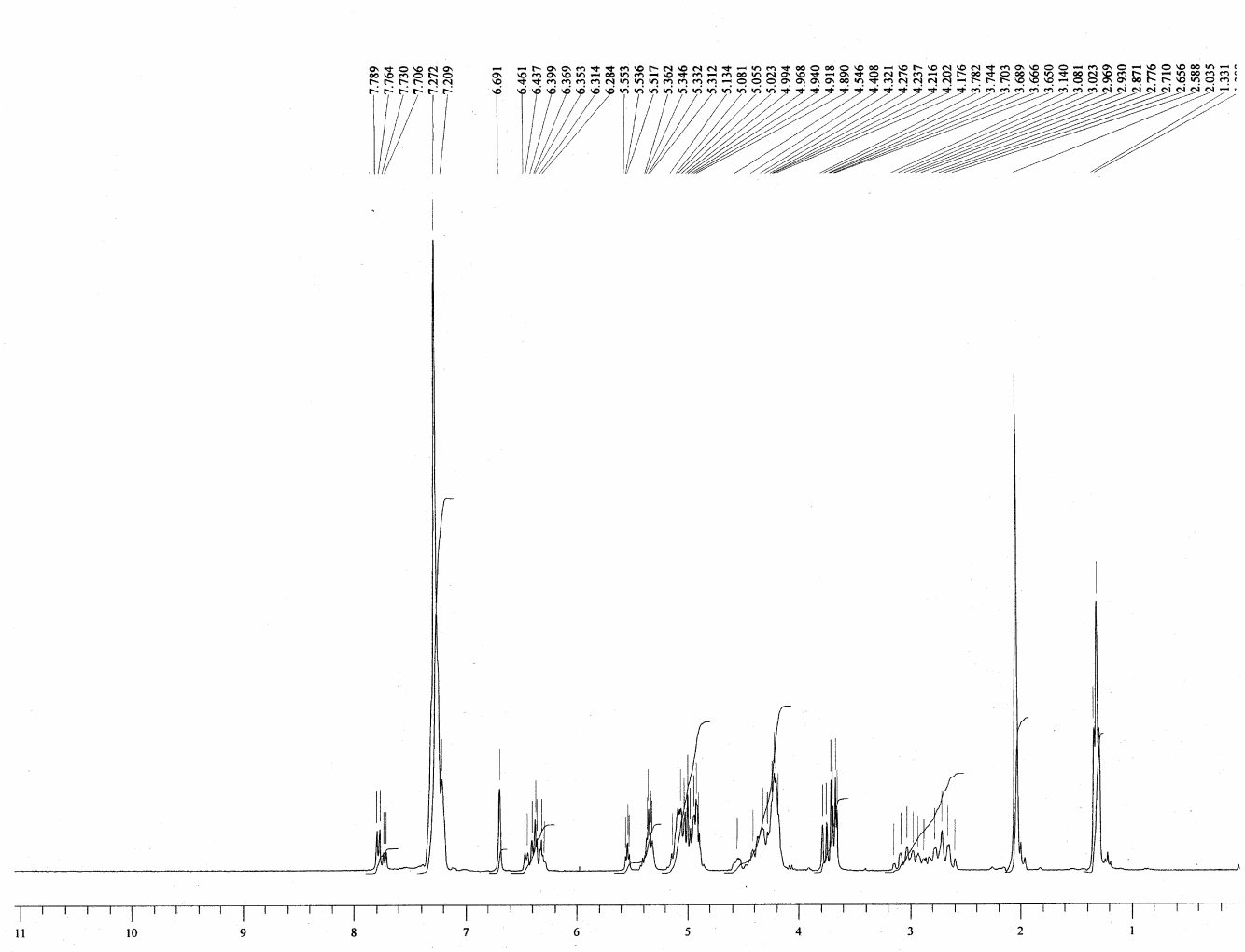
^{31}P

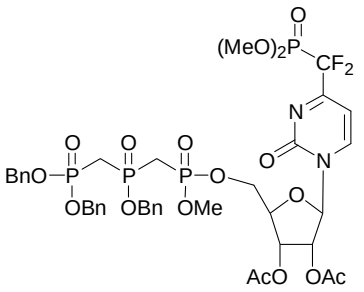

39.804
39.745
39.732
39.709
39.689
39.401
39.374
39.363
39.341
39.286
39.240
39.196
27.955
27.827
27.808
27.751
24.162
24.080
23.988
23.969
23.862
23.822
23.642
23.617
23.482
23.457
23.311
23.277
21.901
21.843
21.799
21.753
21.715
21.663
100
75
50
25
0
-25
-50
-75


(MeO)2P
CF2
BnO
OBn
OBn
OMe
AcO
OAc

48 ($CDCl_3$)

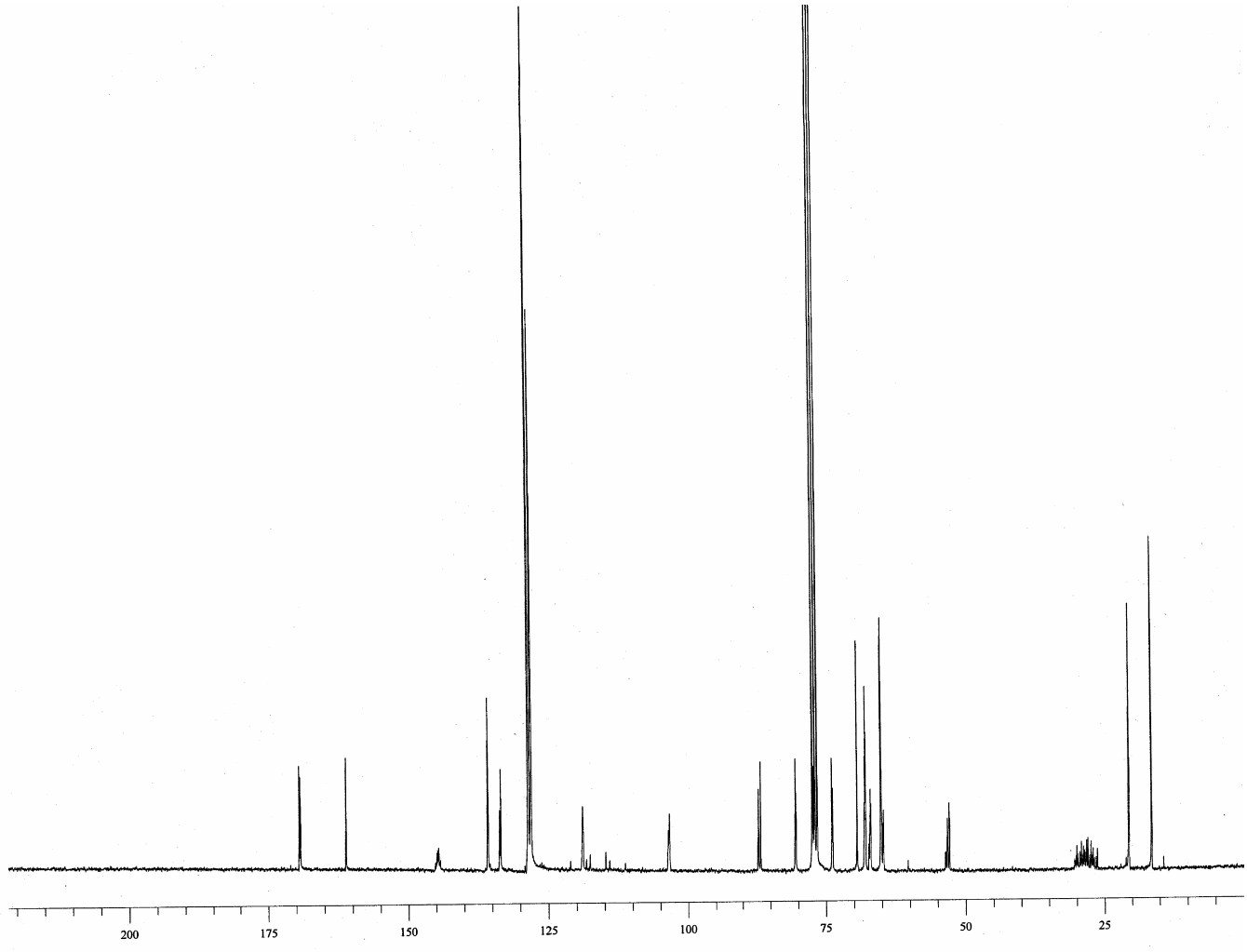
^1H

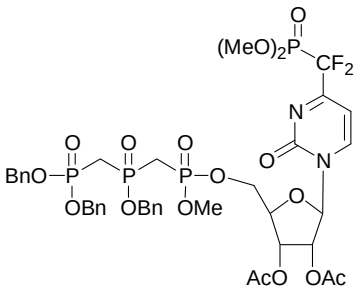

7.789
7.764
7.730
7.706
7.272
7.209
6.691
6.461
6.437
6.399
6.369
6.353
6.314
6.284
5.553
5.536
5.517
5.362
5.346
5.332
5.312
5.134
5.081
5.055
5.023
4.994
4.968
4.940
4.918
4.890
4.546
4.408
4.321
4.276
4.237
4.216
4.202
4.176
3.782
3.744
3.703
3.689
3.666
3.650
3.140
3.081
3.023
2.969
2.930
2.871
2.776
2.710
2.656
2.588
2.035
11
10
9
8
7
6
5
4
3
2
1


O
(MeO)2P
CF2
N
N
O
O
N
O
O
O
BnO—P—P—P—O
OBn OBn OMe
O
AcO OAc

48 ($CDCl_3$)

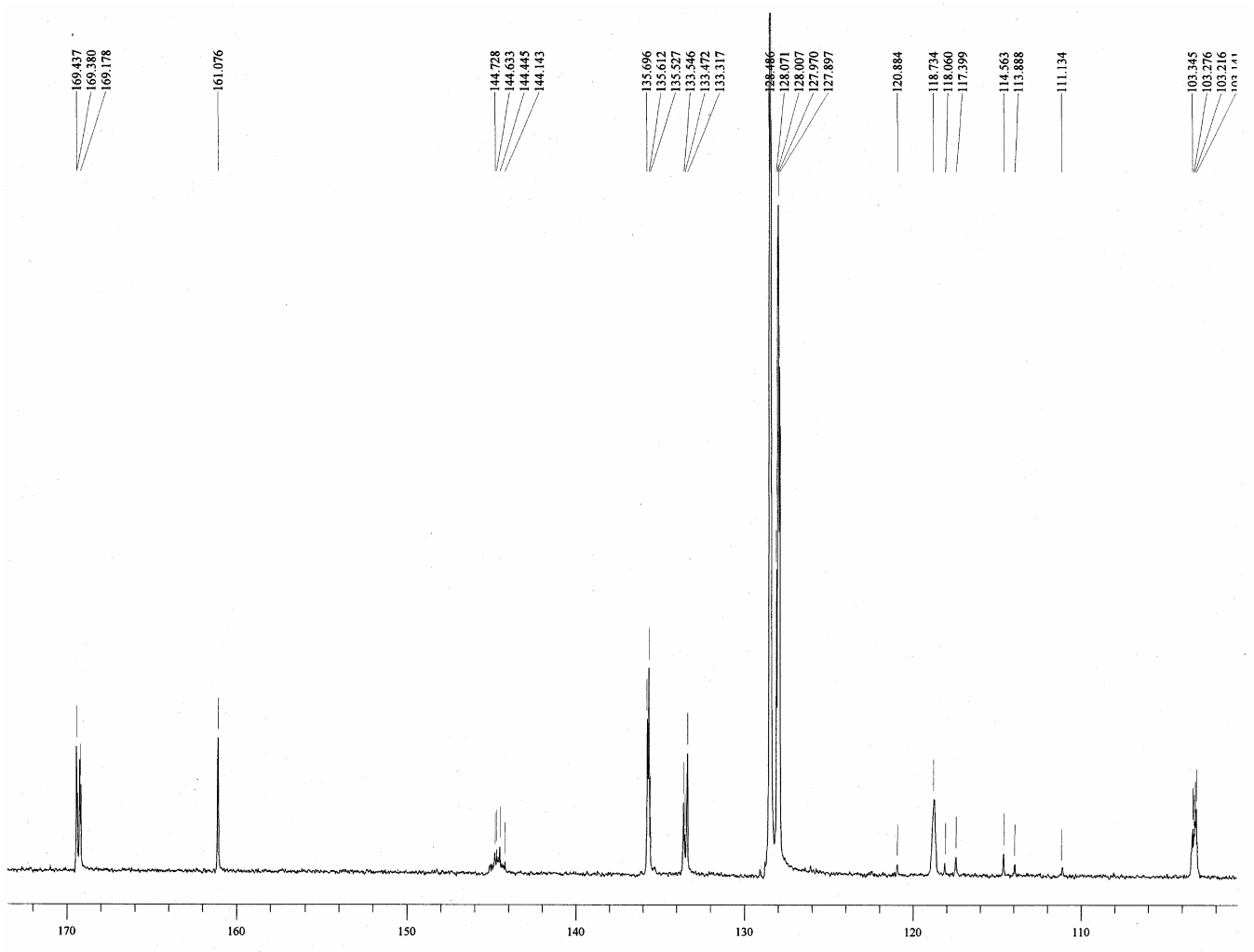
^{13}C

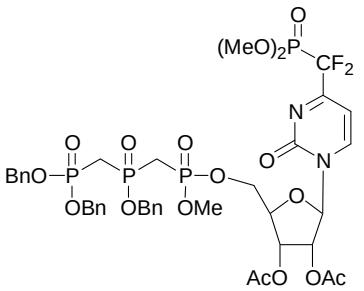

200
175
150
125
100
75
50
25



48 ($CDCl_3$)

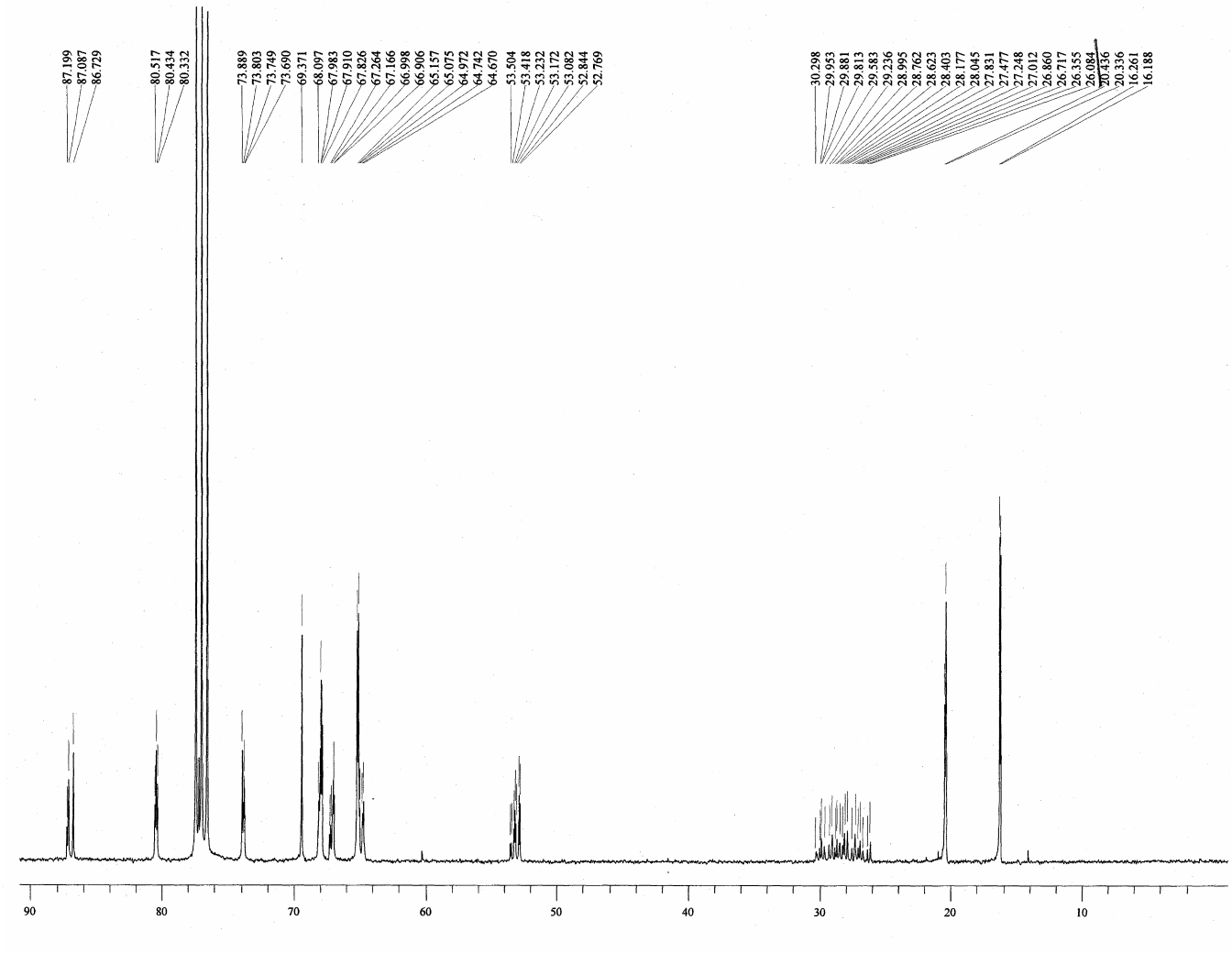
^{13}C (expanded)

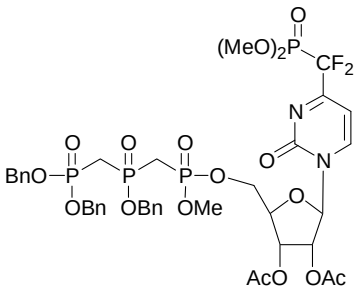




48 ($CDCl_3$)

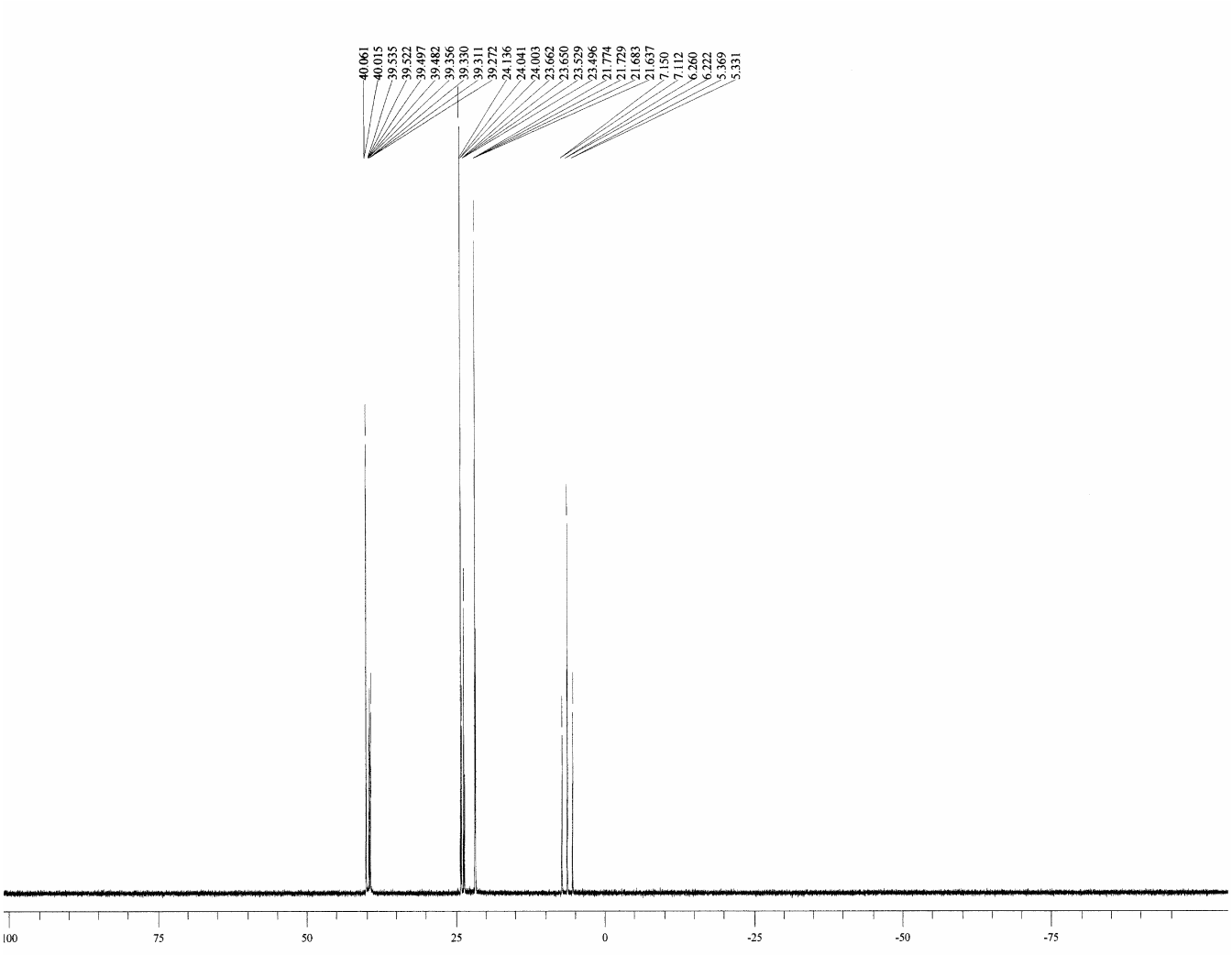
^{13}C (expanded)

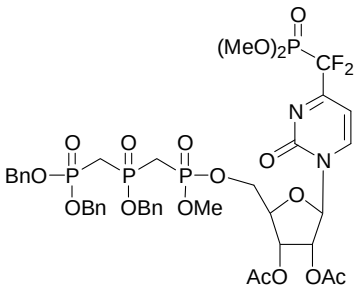




48 ($CDCl_3$)

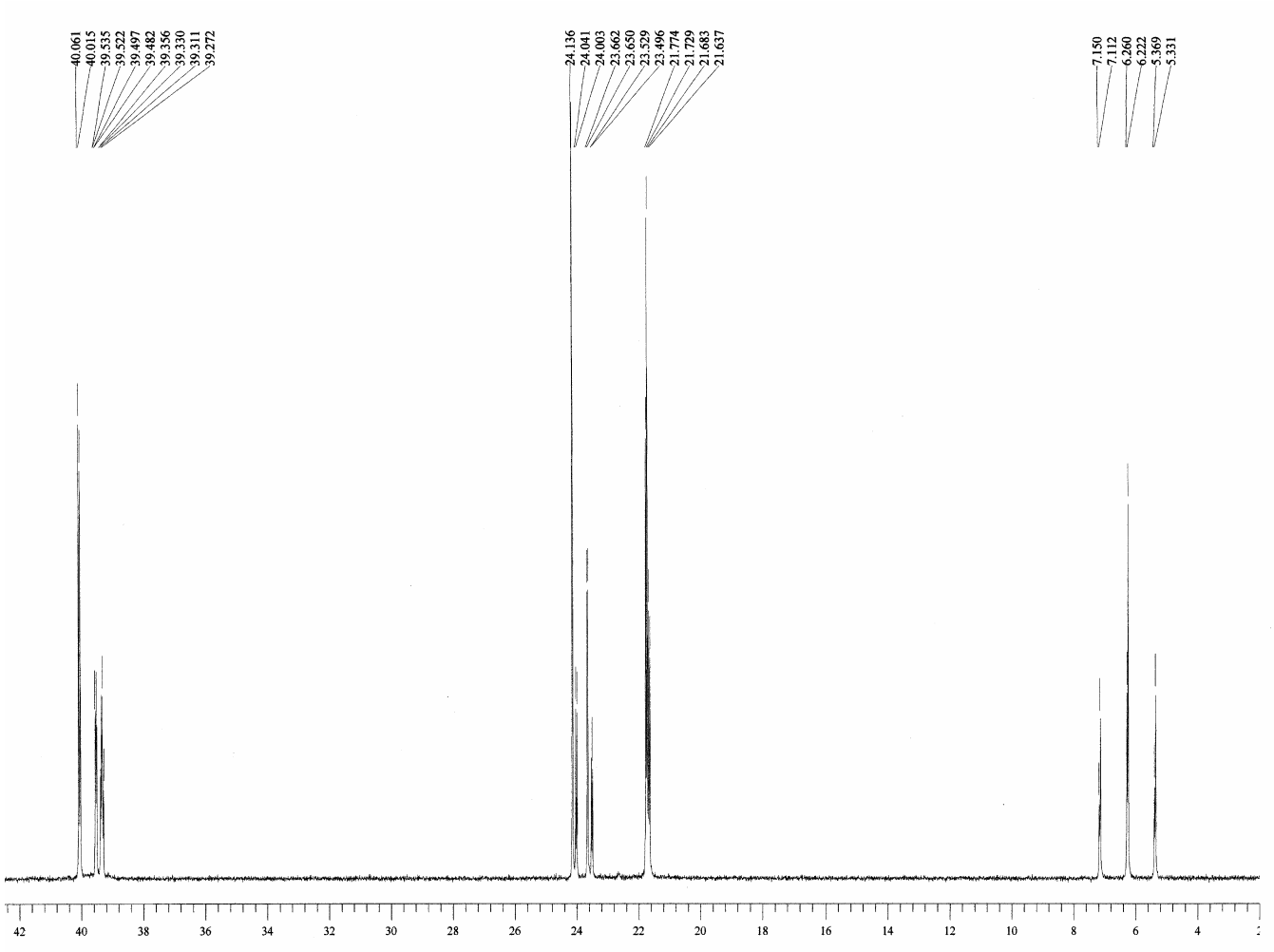
^{31}P

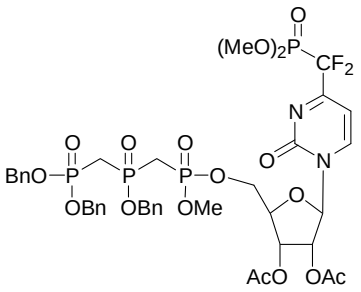

40.061
40.015
39.535
39.522
39.497
39.482
39.356
39.330
39.311
39.272
24.136
24.041
24.003
23.662
23.650
23.529
23.496
21.774
21.729
21.683
21.637
7.150
7.112
6.260
6.222
5.369
5.331
100
75
50
25
0
-25
-50
-75



48 ($CDCl_3$)

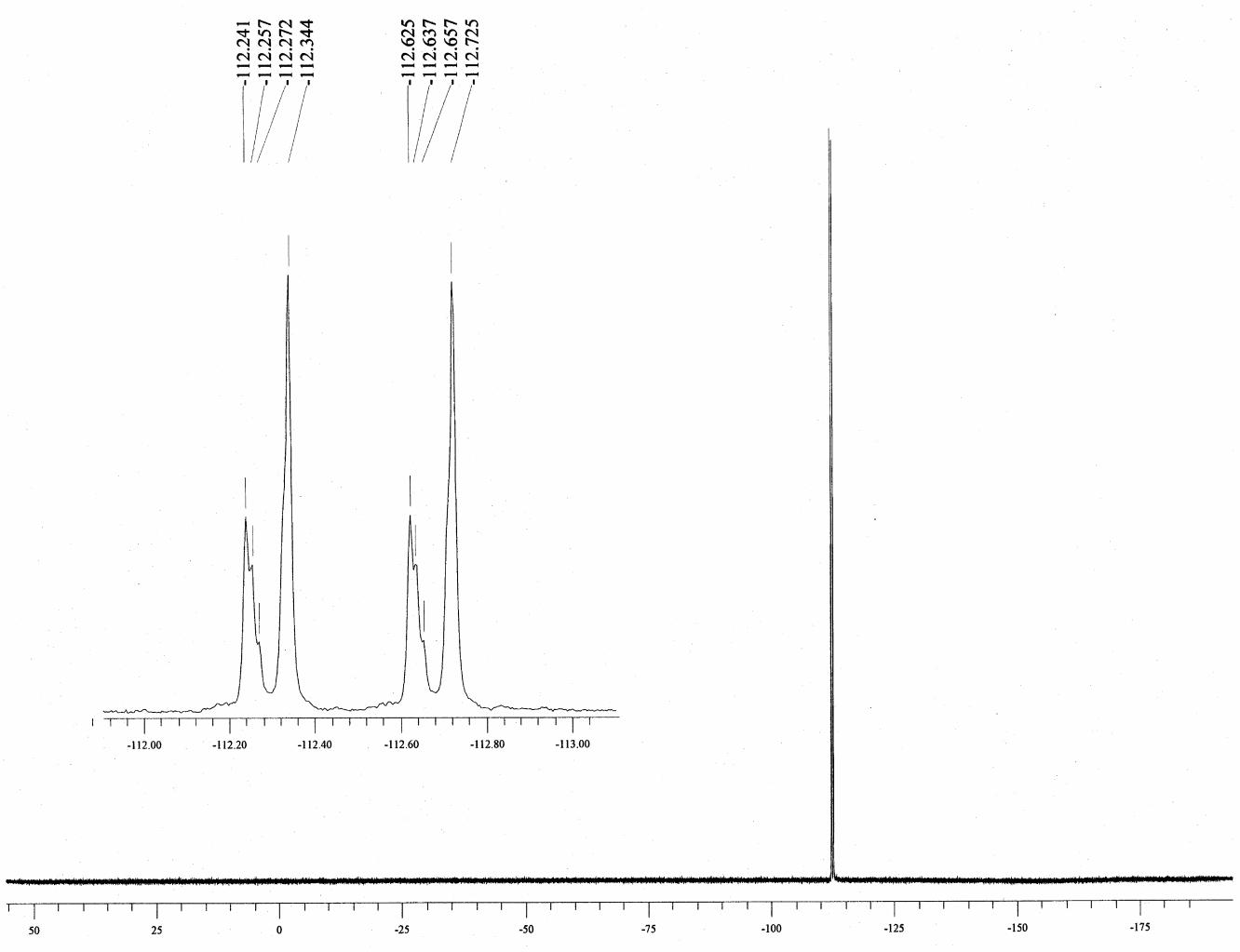
^{31}P (expanded)

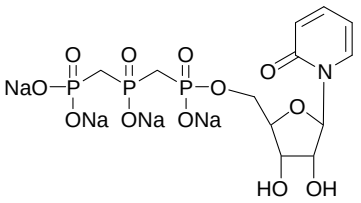



(MeO)2P
CF2
BnO
OBn
OBn
OMe
AcO
OAc

48 ($CDCl_3$)

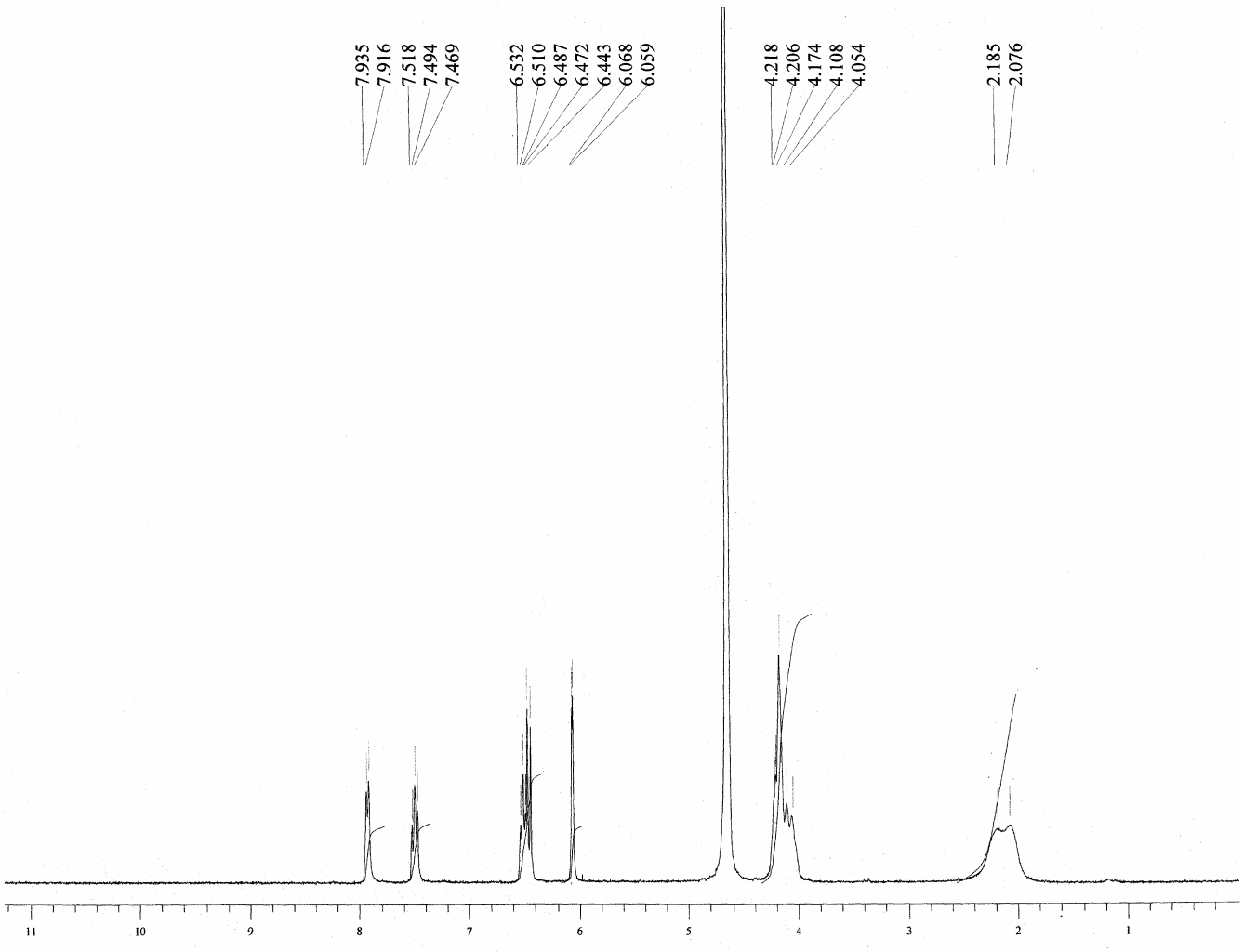
^{19}F

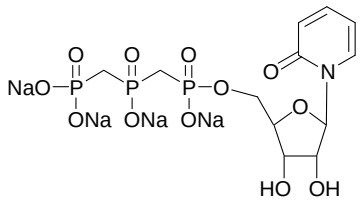

-112.241
-112.257
-112.272
-112.344
-112.625
-112.637
-112.657
-112.725
-112.00
-112.20
-112.40
-112.60
-112.80
-113.00
50
25
0
-25
-50
-75
-100
-125
-150
-175



49 (D_2O)

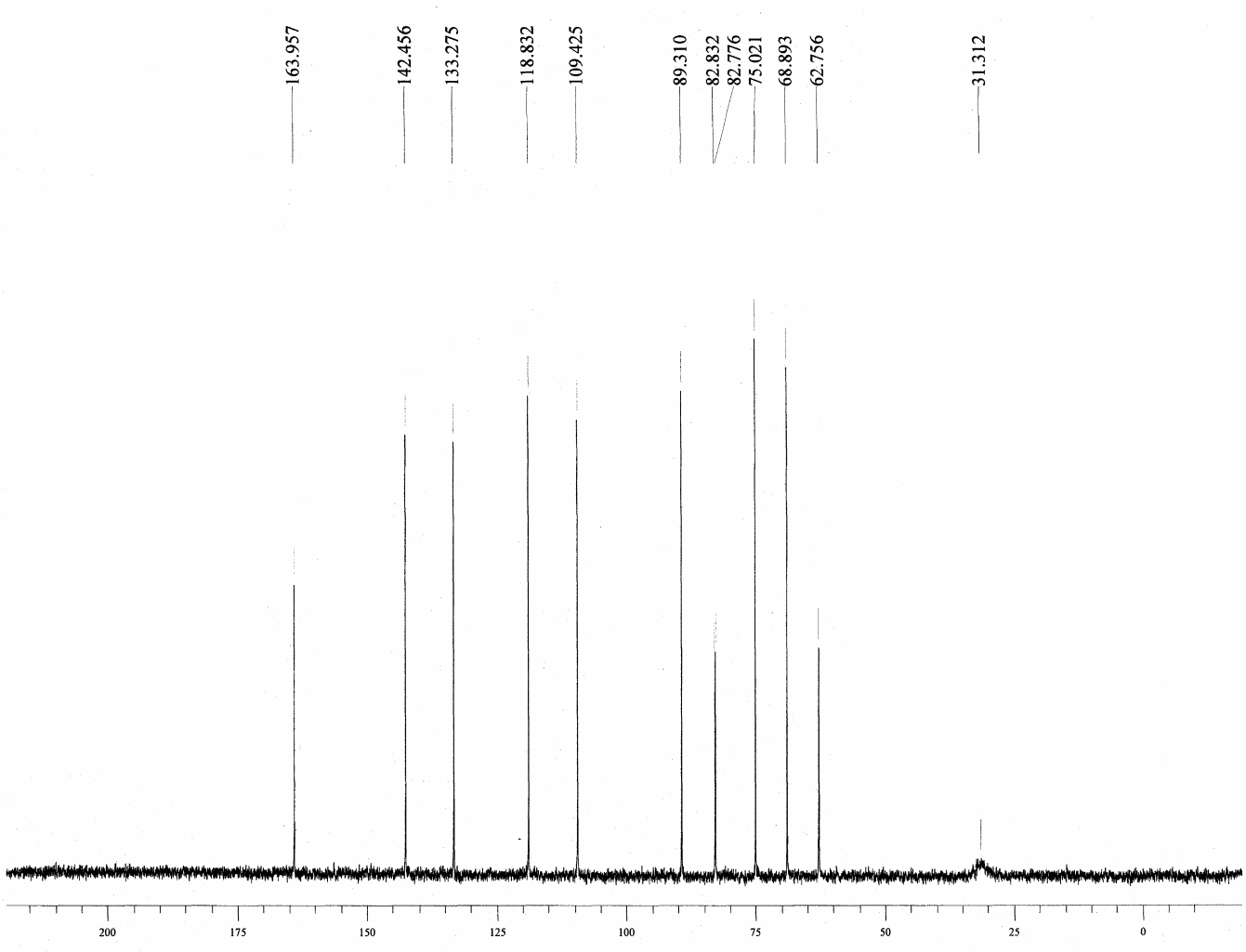
^1H

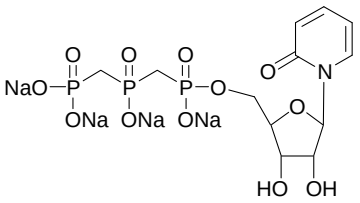

7.935
7.916
7.518
7.494
7.469
6.532
6.510
6.487
6.472
6.443
6.068
6.059
4.218
4.206
4.174
4.108
4.054
2.185
2.076
11
10
9
8
7
6
5
4
3
2
1


NaO
ONa ONa ONa
HO OH

49 (D_2O)

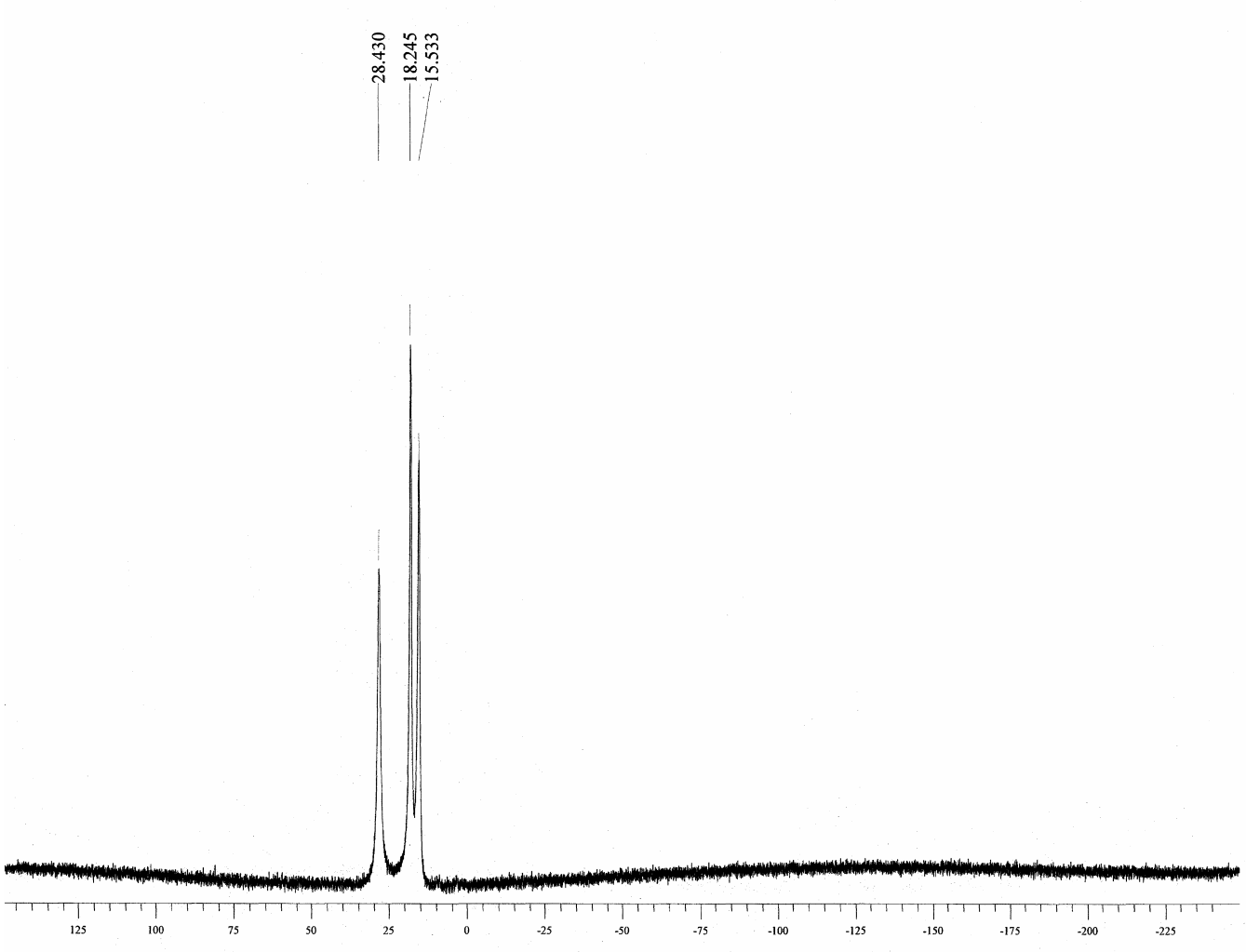
^{13}C

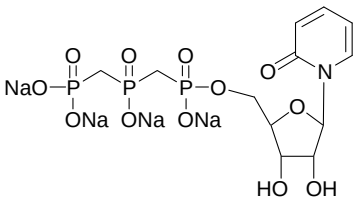

163.957
142.456
133.275
118.832
109.425
89.310
82.832
82.776
75.021
68.893
62.756
31.312
200
175
150
125
100
75
50
25
0



49 (D_2O)

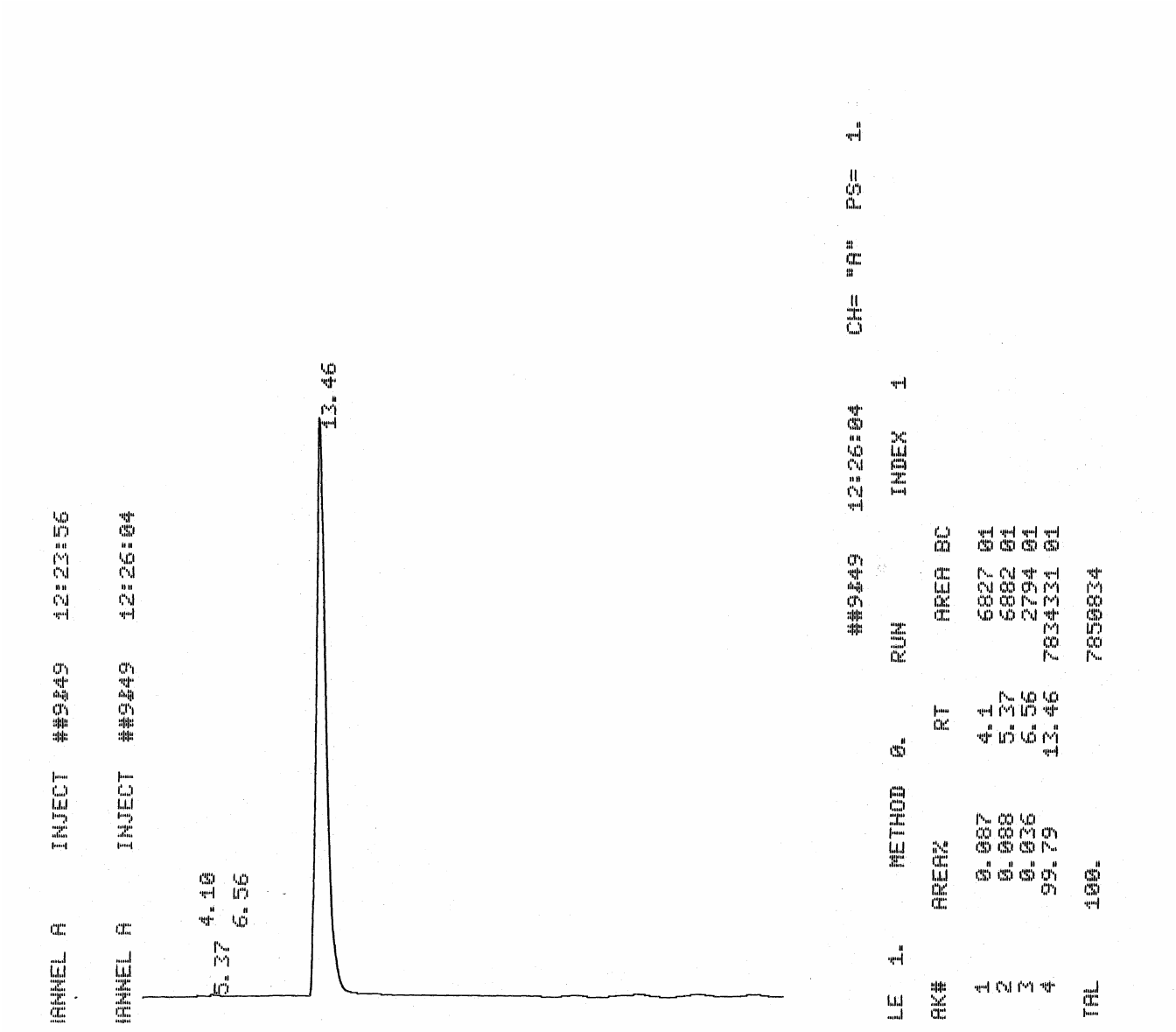
^{31}P


28.430
18.245
15.533
125
100
75
50
25
0
-25
-50
-75
-100
-125
-150
-175
-200
-225

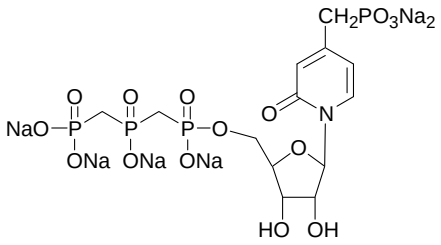


49

Analytical HPLC

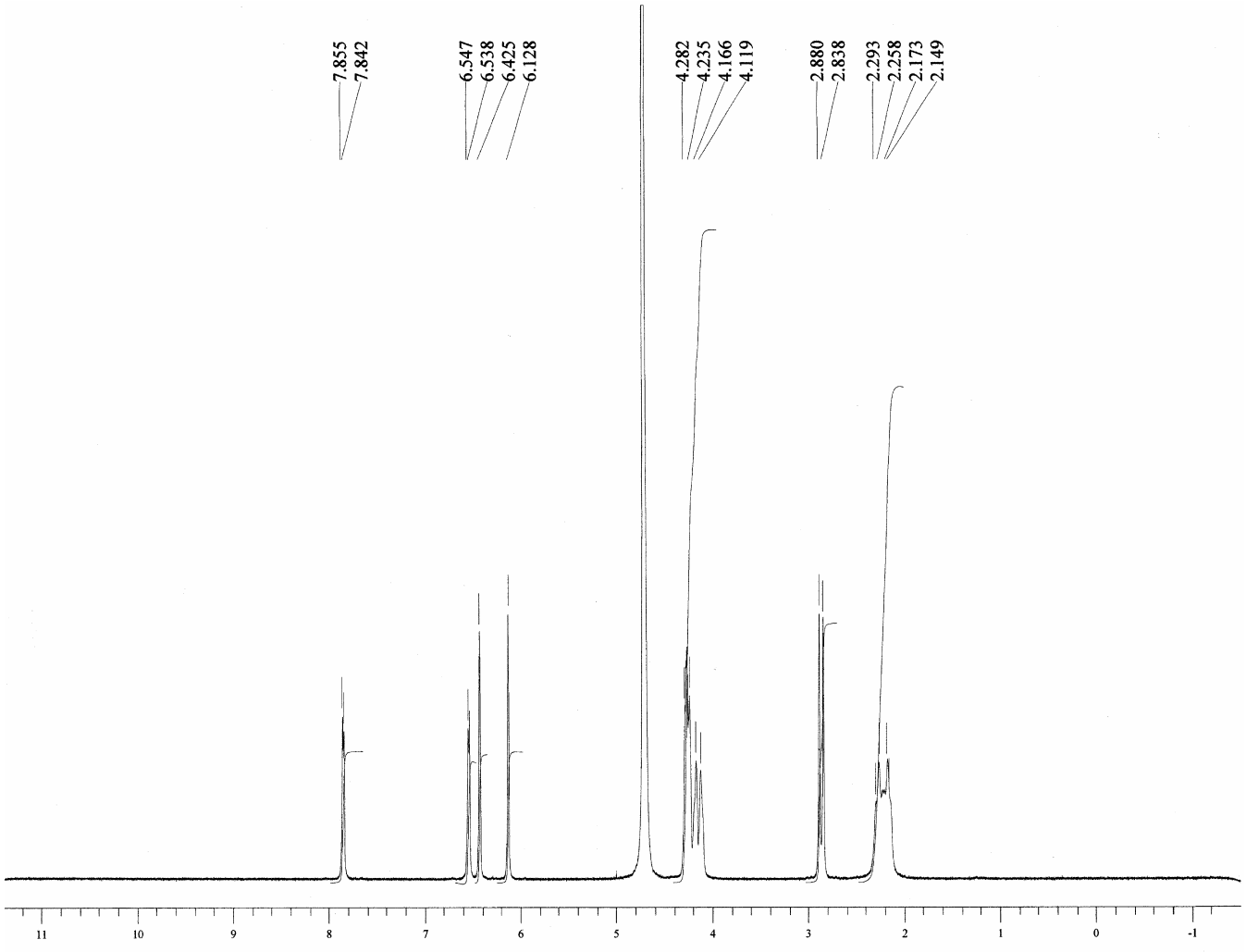


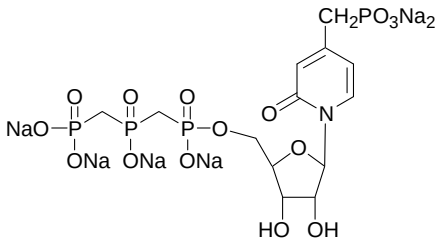
The analytical HPLC chromatogram of **49**. . The following solvents were used: solvent A: 100 mM TEAA, pH 7.0, solvent B: CH_3CN. The following elution profile was used: linear gradient of 99% A-1% B to 93% A-7% B over 50 minutes. Flow rate 1 mL/min, $\lambda_{detector}$ = 260 nM.


CH2PO3Na2
NaO
ONa ONa ONa
HO OH

50 (D_2O)

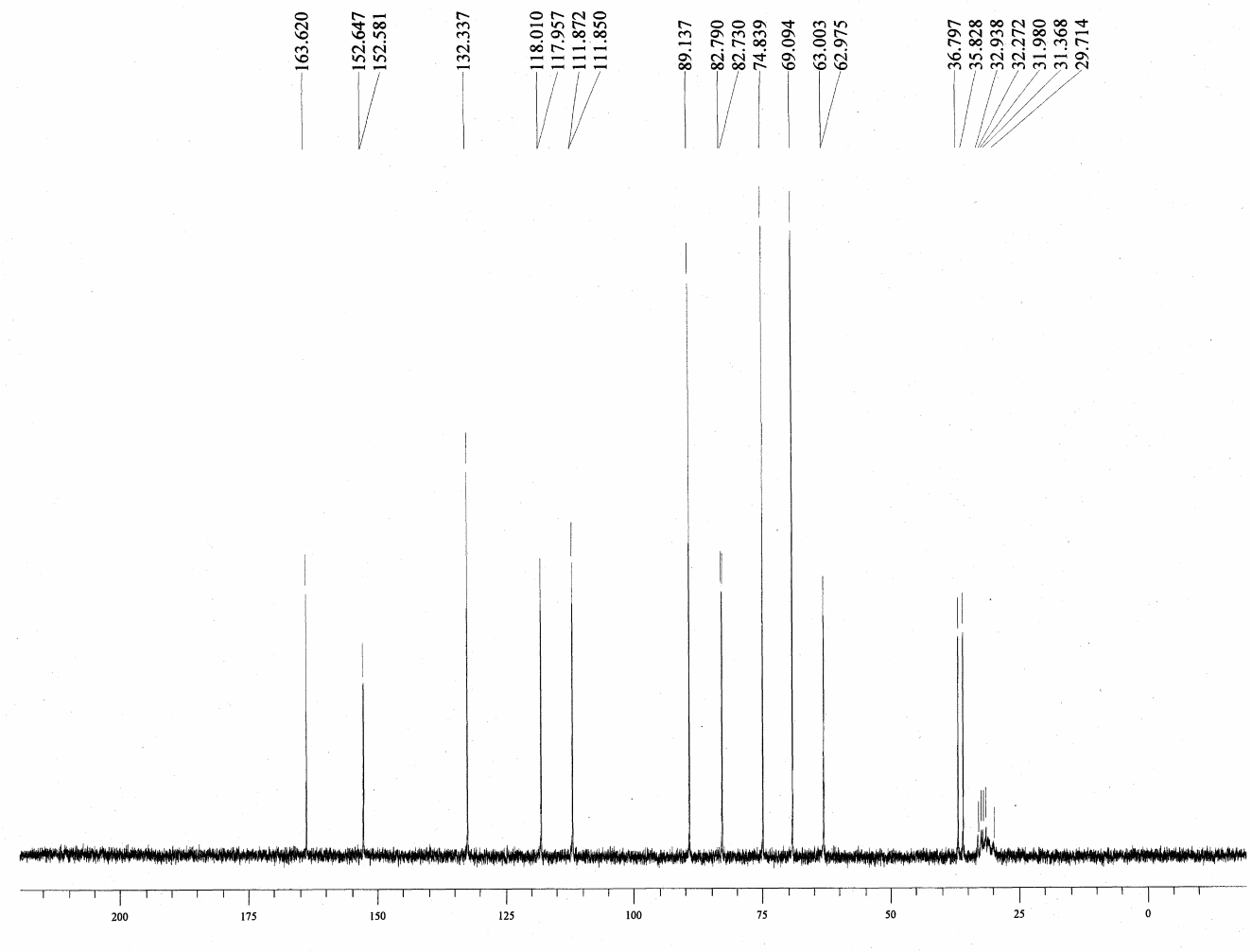
^1H

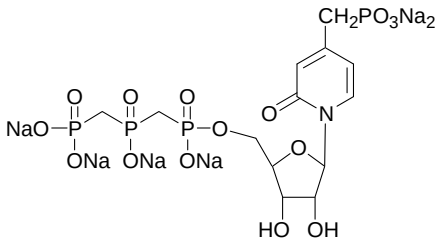

7.855
7.842
6.547
6.538
6.425
6.128
4.282
4.235
4.166
4.119
2.880
2.838
2.293
2.258
2.173
2.149
11
10
9
8
7
6
5
4
3
2
1
0
-1


CH2PO3Na2
NaO
ONa ONa ONa
HO OH

50 (D_2O)

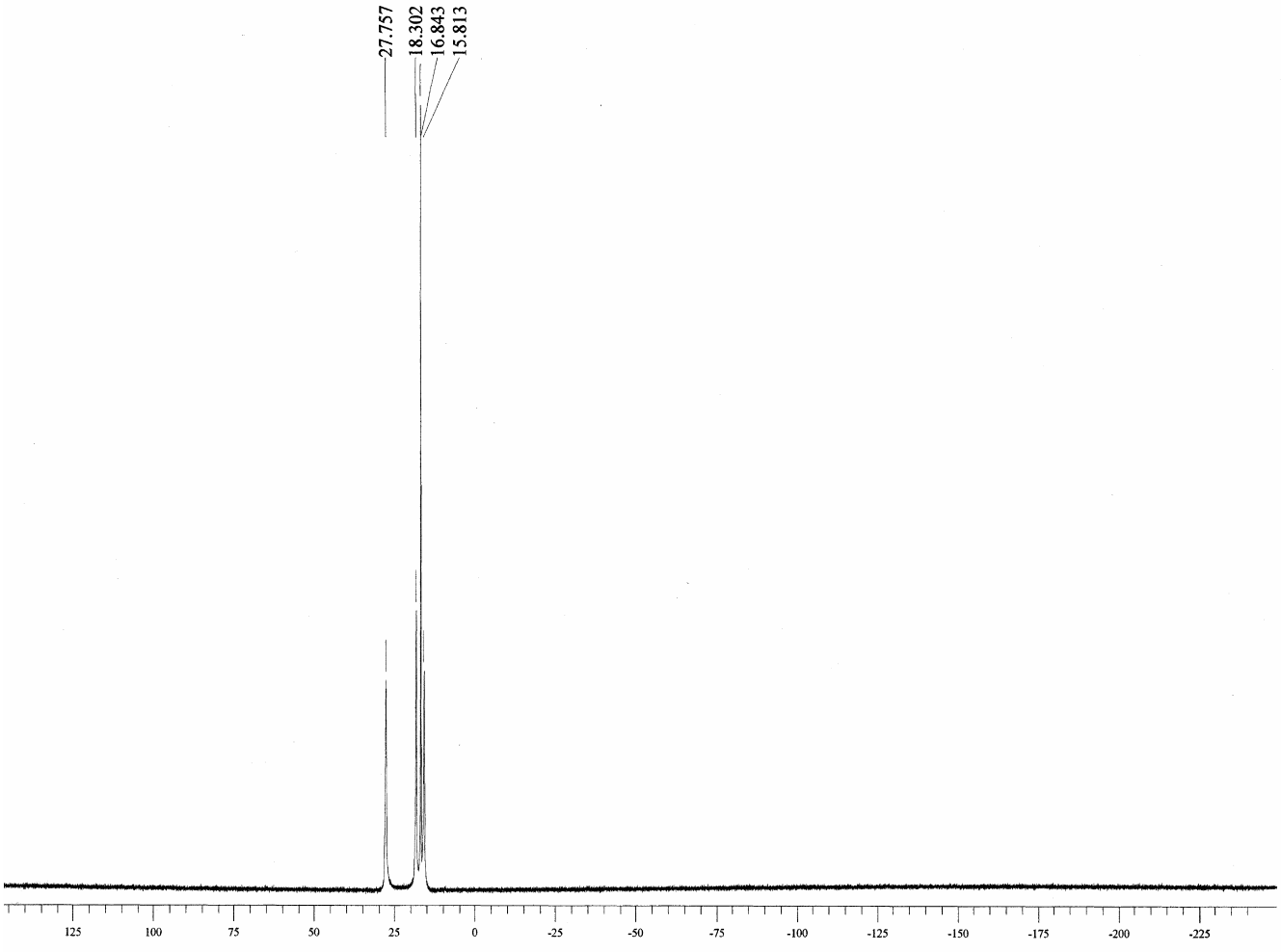
^{13}C

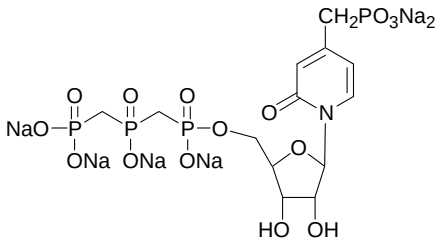

163.620
152.647
152.581
132.337
118.010
117.957
111.872
111.850
89.137
82.790
82.730
74.839
69.094
63.003
62.975
36.797
35.828
32.938
32.272
31.980
31.368
29.714
200
175
150
125
100
75
50
25
0


CH2PO3Na2
NaO
ONa ONa ONa
O
N
HO OH

50 (D_2O)

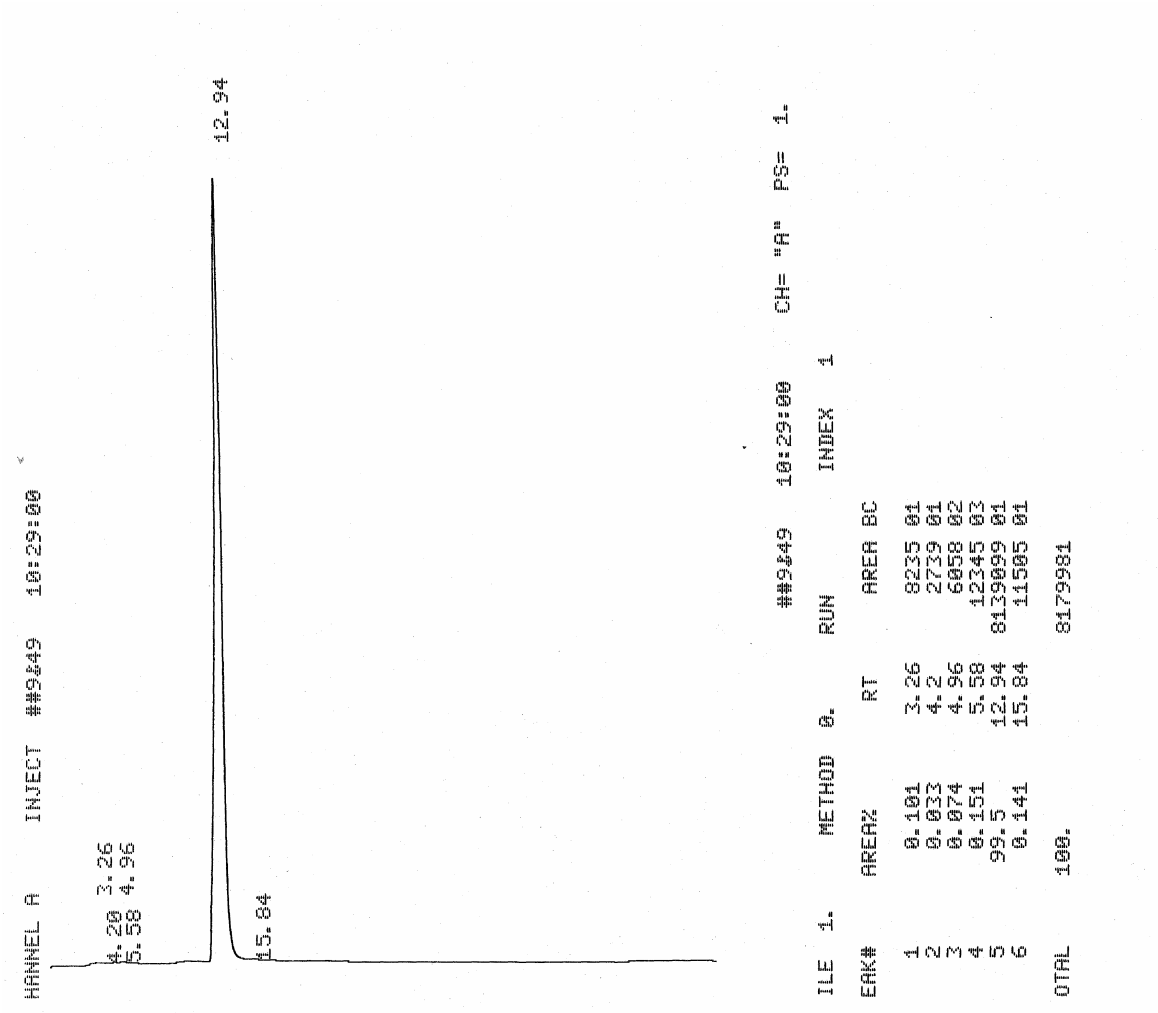
^{31}P


27.757
18.302
16.843
15.813
125
100
75
50
25
0
-25
-50
-75
-100
-125
-150
-175
-200
-225

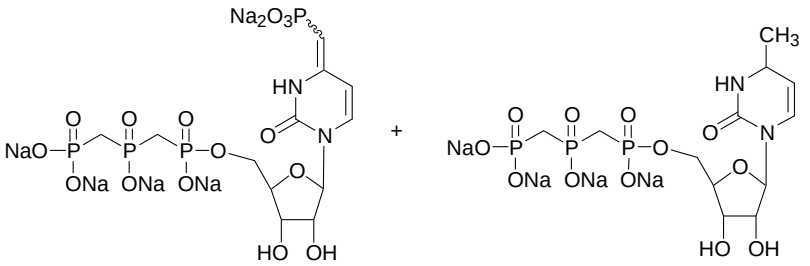


50

Analytical HPLC

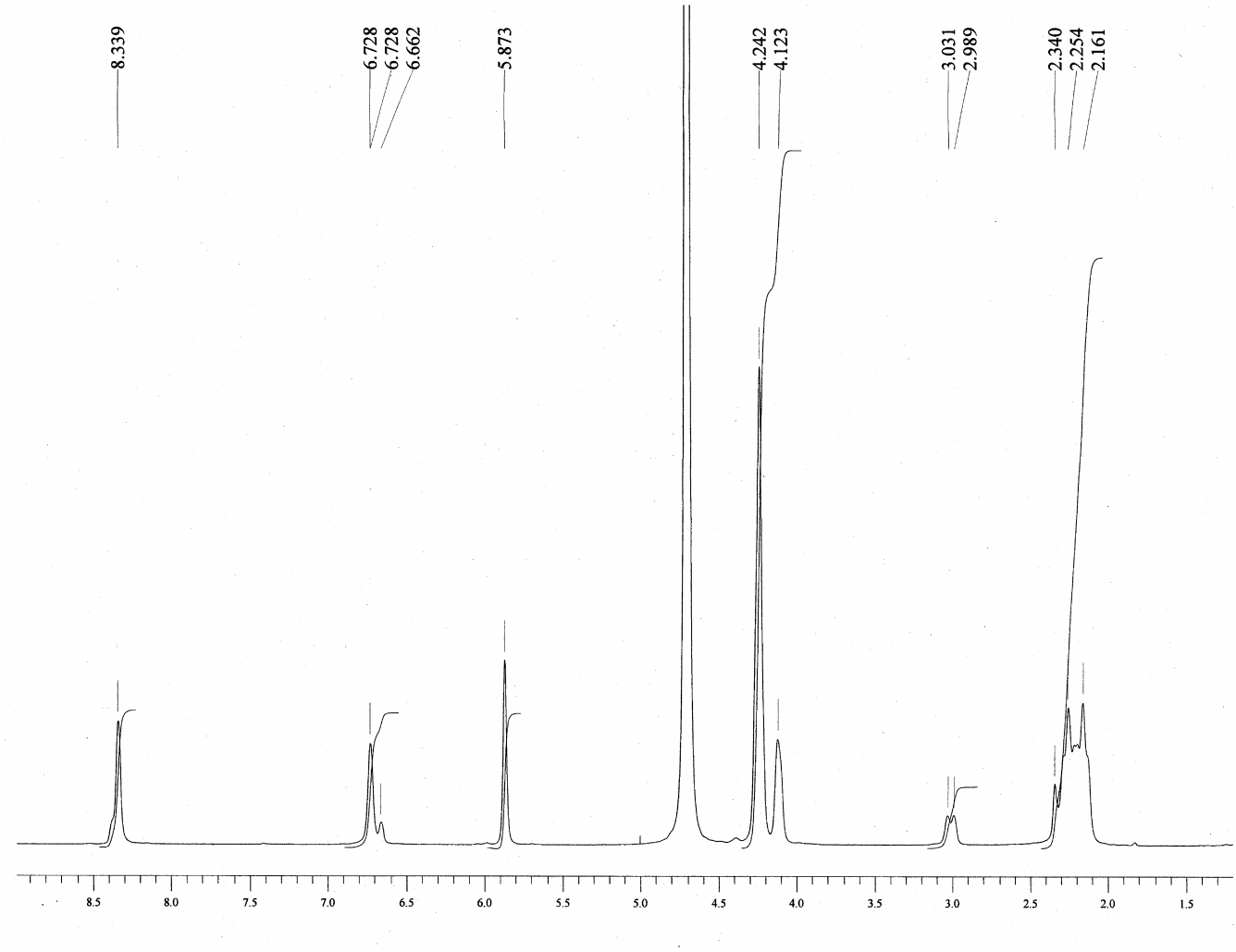


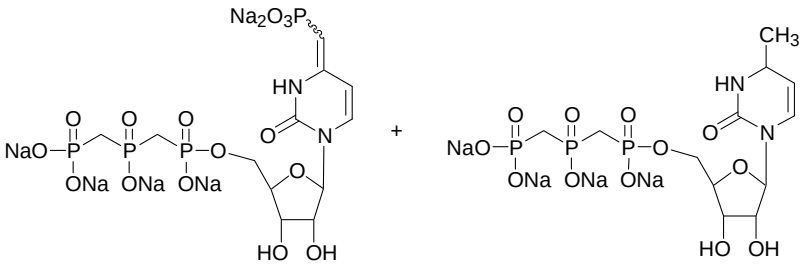
Analytical HPLC chromatogram of compound **50**. The following solvent system were used: solvent A: 100 mM TEAA, pH 7.0, solvent B: CH_3CN. The following elution profile was used: 0-15 min: 99% A-1% B; 15-50 min: linear gradient of 99% A-1% B to 94% A-6% B. Flow rate = 1 mL/min. $\lambda_{detector}$ = 260 nM.



51 (D_2O) **52** (app. 15 %)

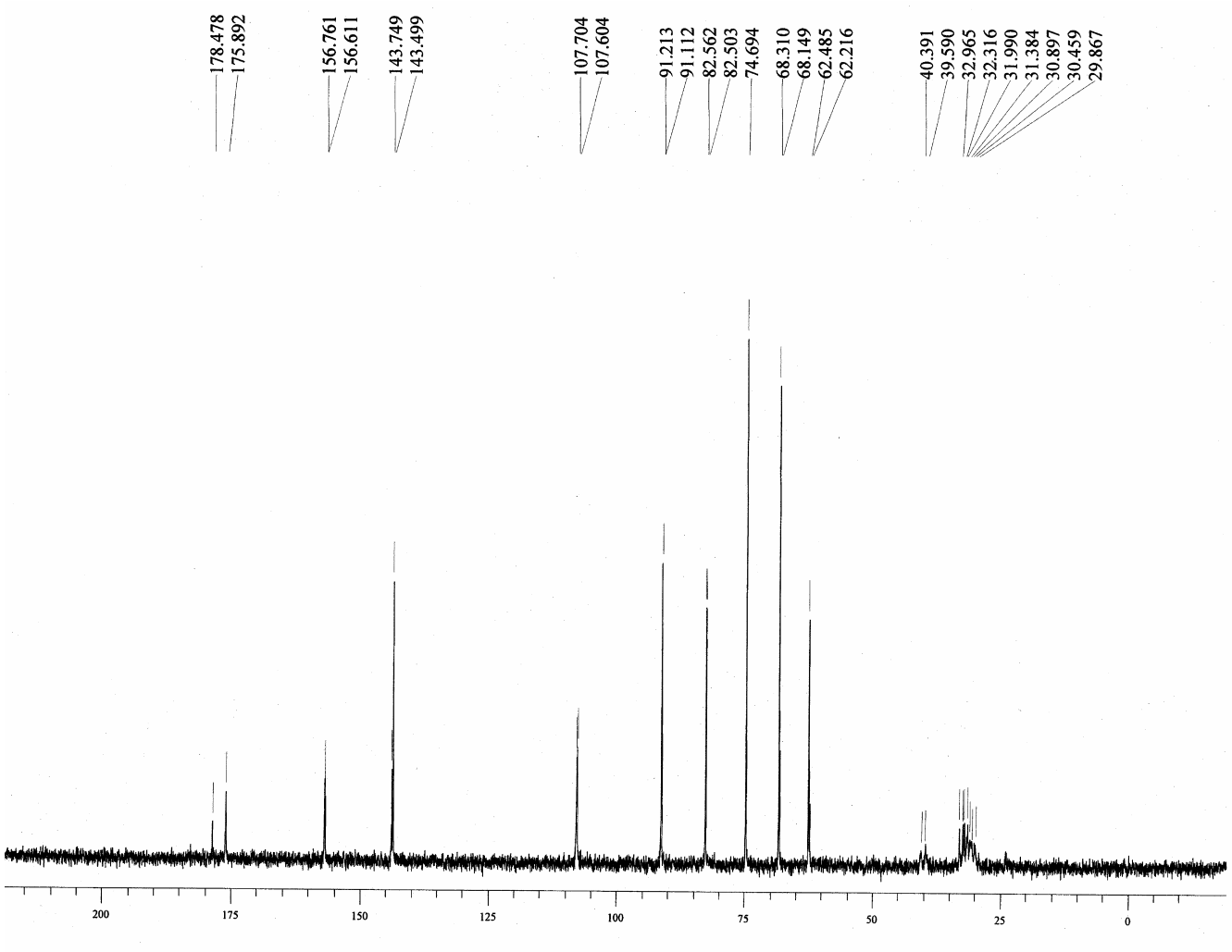
^1H

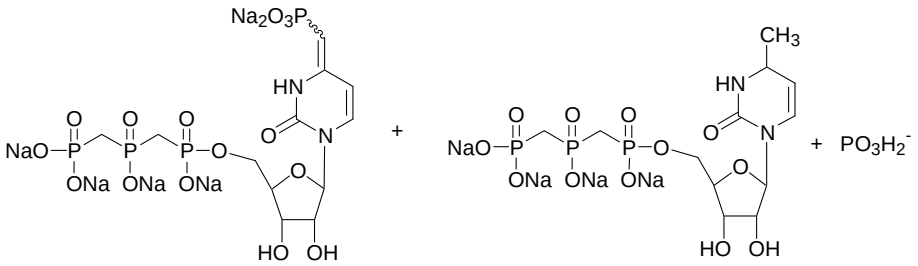




51 (D_2O) **52** (app. 15 %)

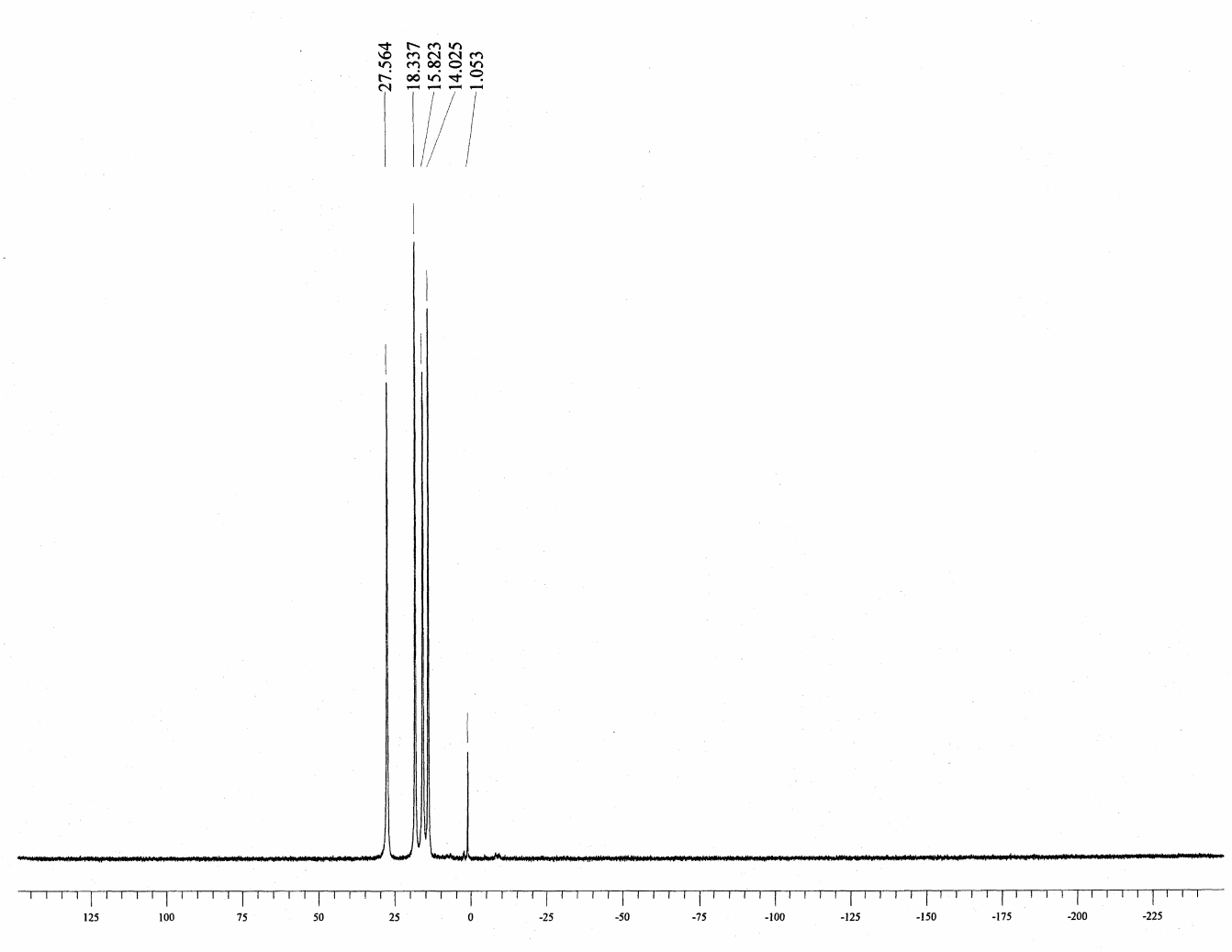
^{13}C

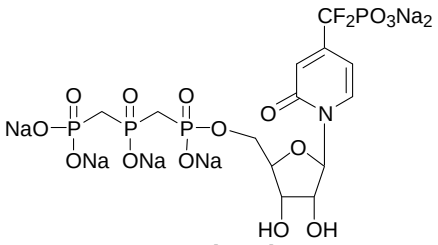



Na2O3P
HN
O
N
O
NaO
P
ONa
O
HO
OH
+
CH3
+ PO3H2-

51 (D_2O) **52**

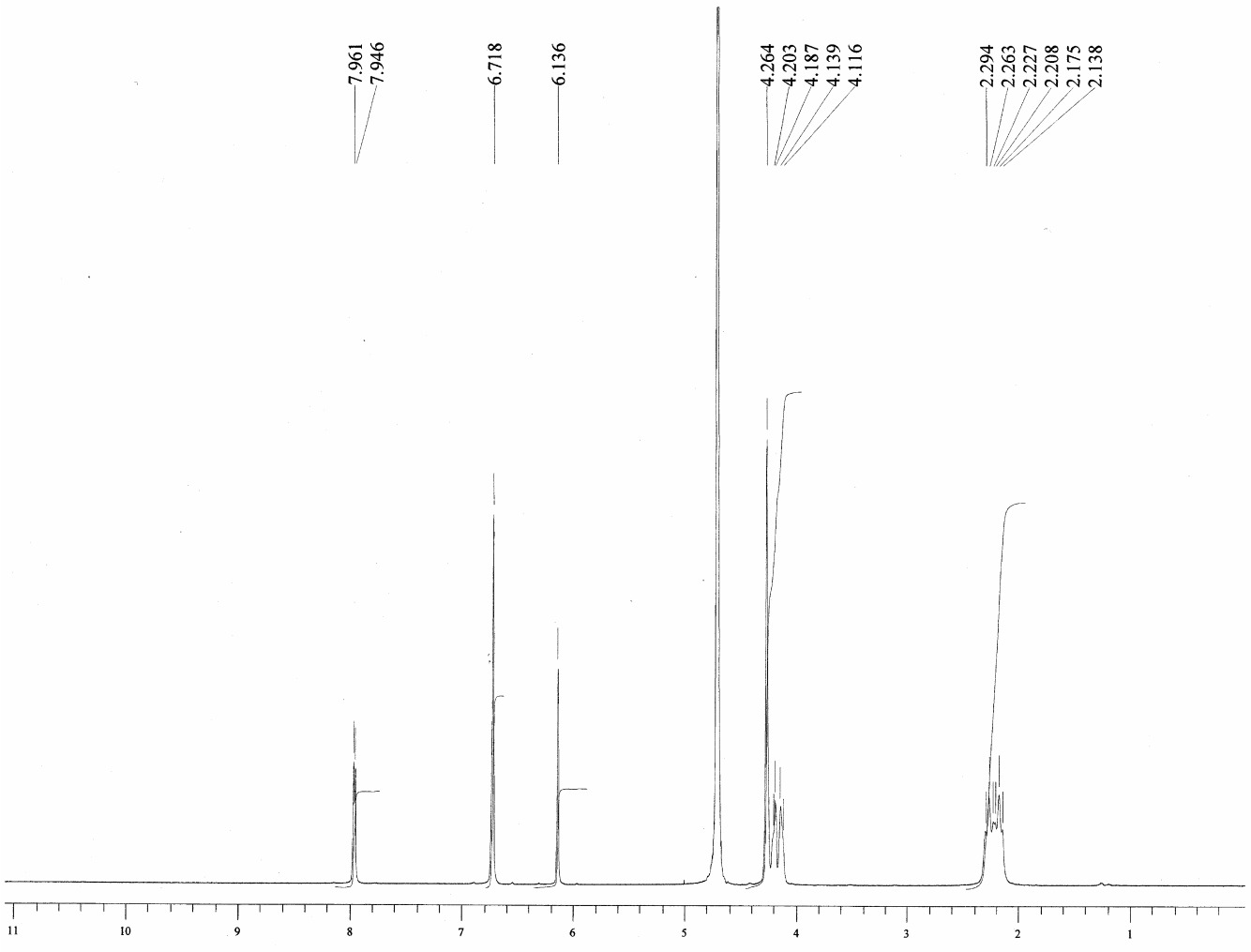
^{31}P

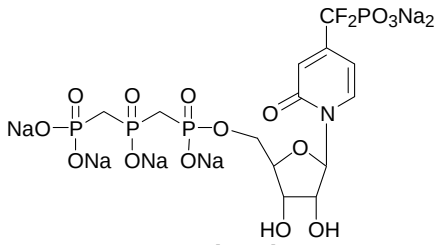

27.564
18.337
15.823
14.025
1.053
125
100
75
50
25
0
-25
-50
-75
-100
-125
-150
-175
-200
-225


CF2PO3Na2
NaO
ONa ONa ONa
HO OH

53 (D_2O)

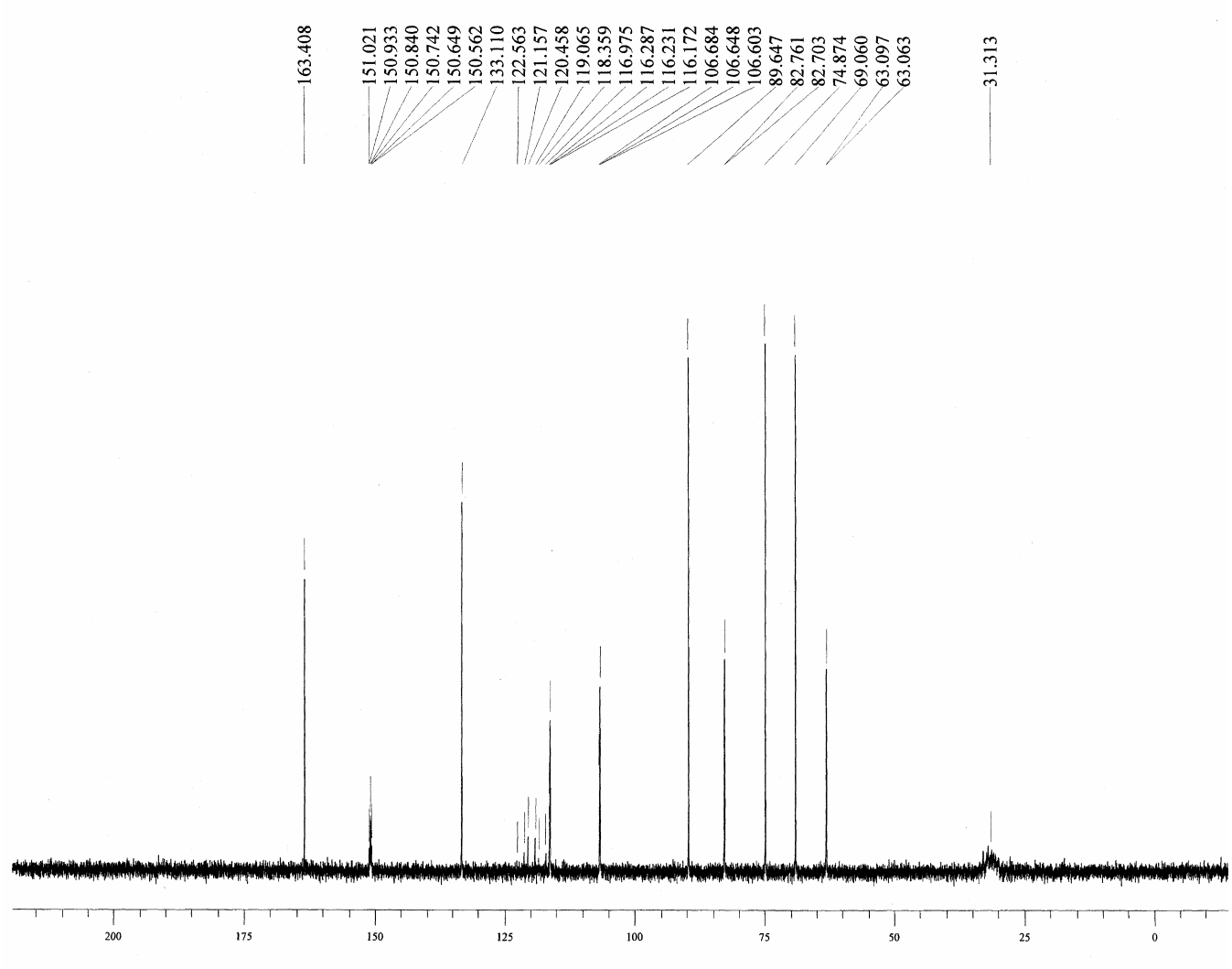
^1H

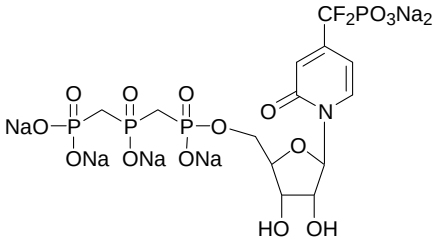

7.961
7.946
6.718
6.136
4.264
4.203
4.187
4.139
4.116
2.294
2.263
2.227
2.208
2.175
2.138
11
10
9
8
7
6
5
4
3
2
1


CF2PO3Na2
NaO
ONa ONa ONa
HO OH

53 (D_2O)

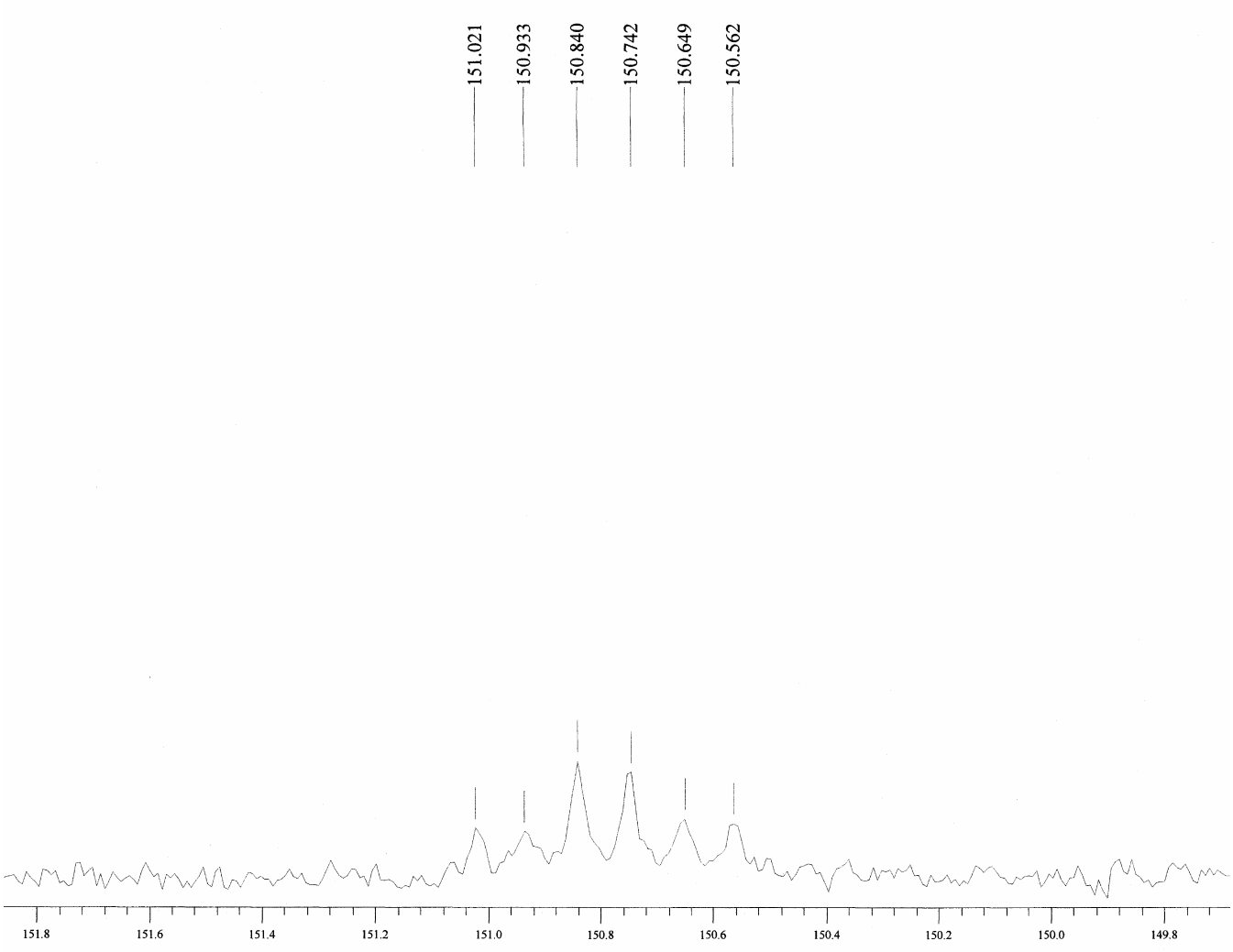
^{13}C

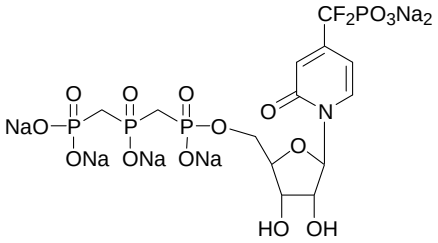

163.408
151.021
150.933
150.840
150.742
150.649
150.562
133.110
122.563
121.157
120.458
119.065
118.359
116.975
116.287
116.231
116.172
106.684
106.648
106.603
89.647
82.761
82.703
74.874
69.060
63.097
63.063
31.313
200
175
150
125
100
75
50
25
0



53 (D_2O)

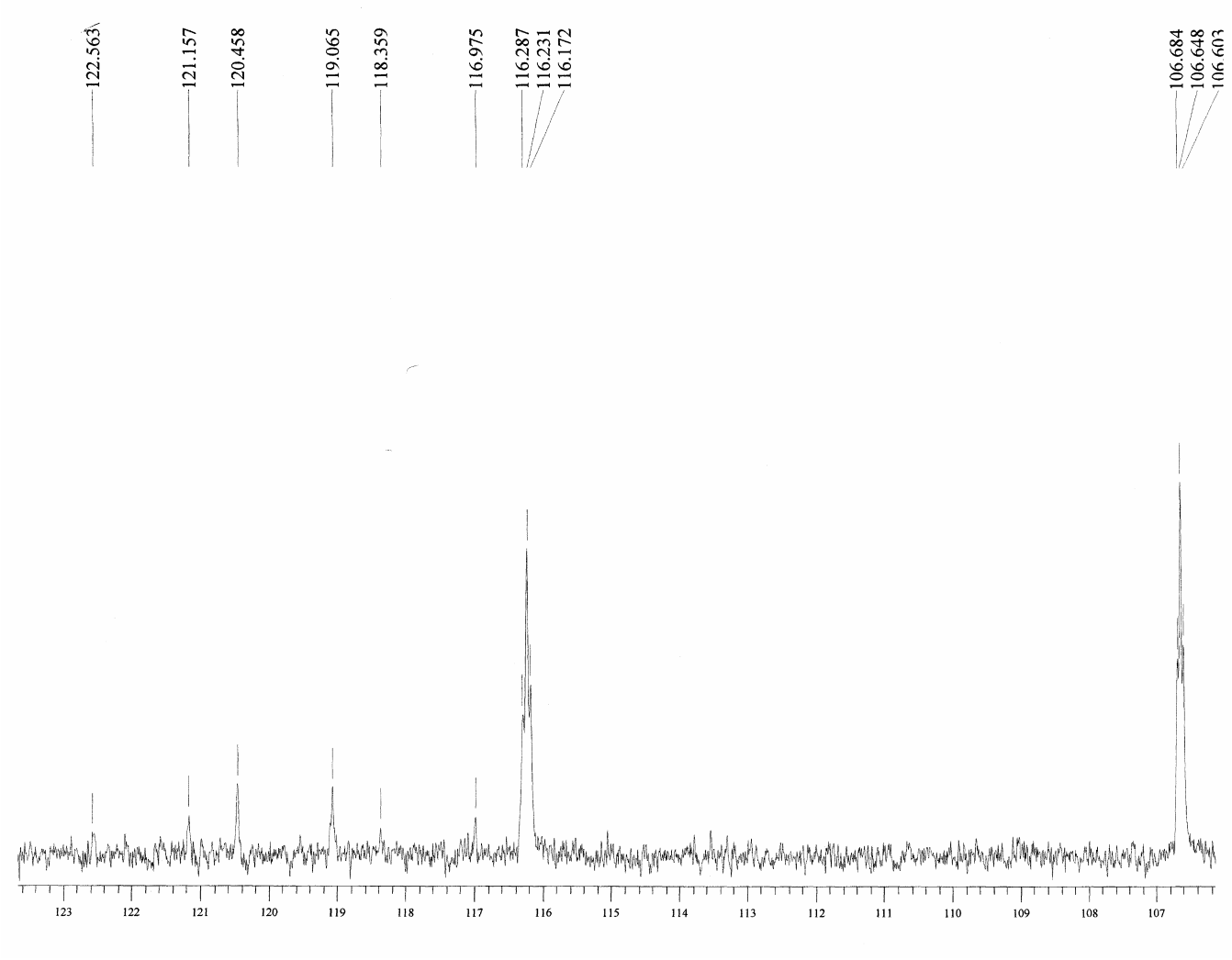
^{13}C (expanded)

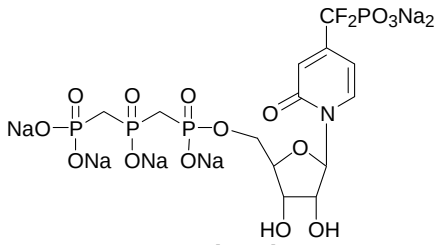




53 (D_2O)

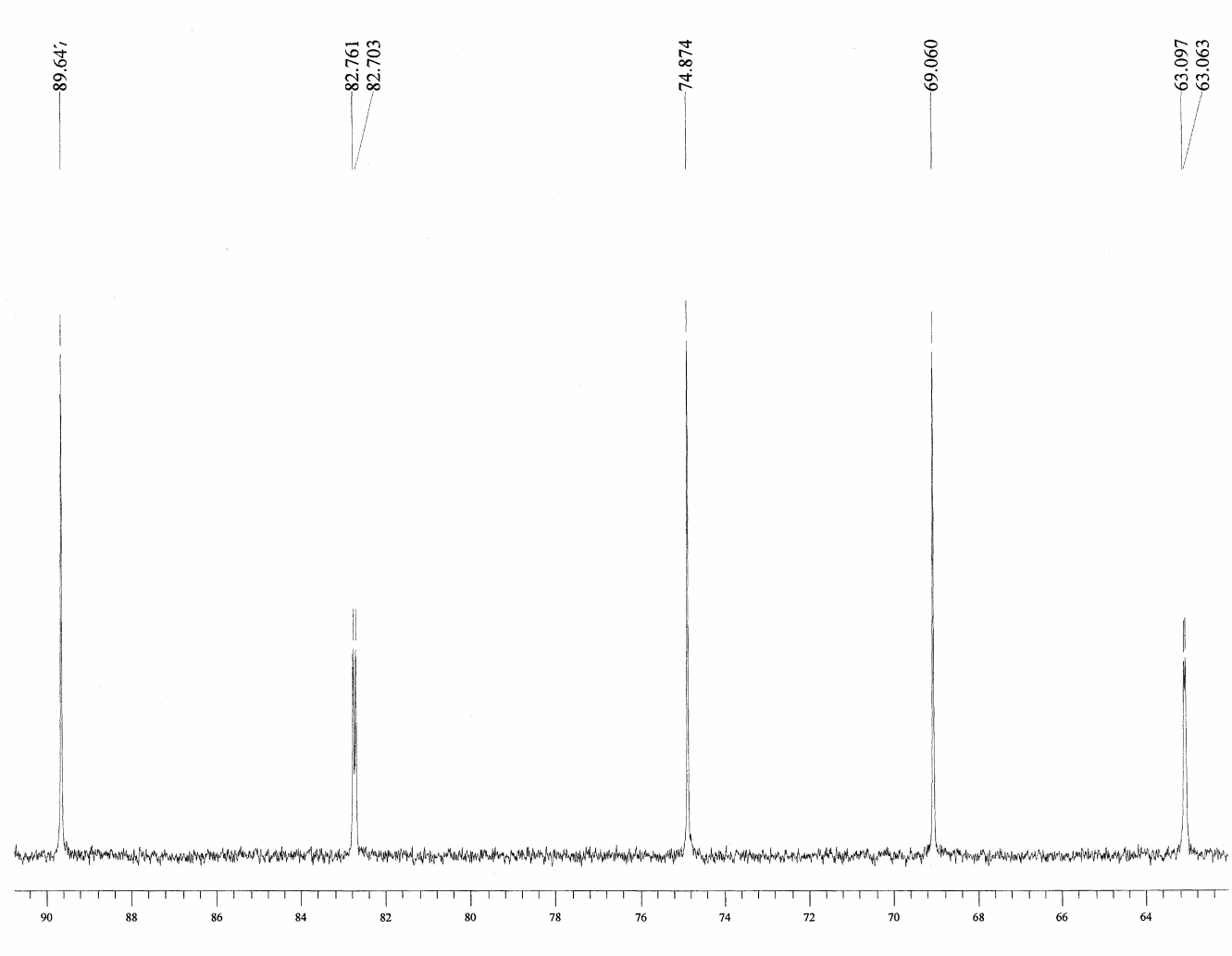
^{13}C (expanded)

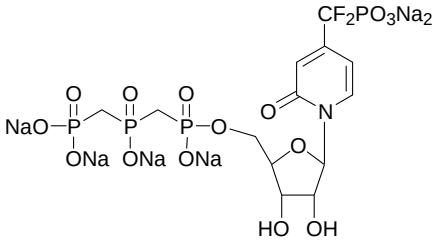




53 (D_2O)

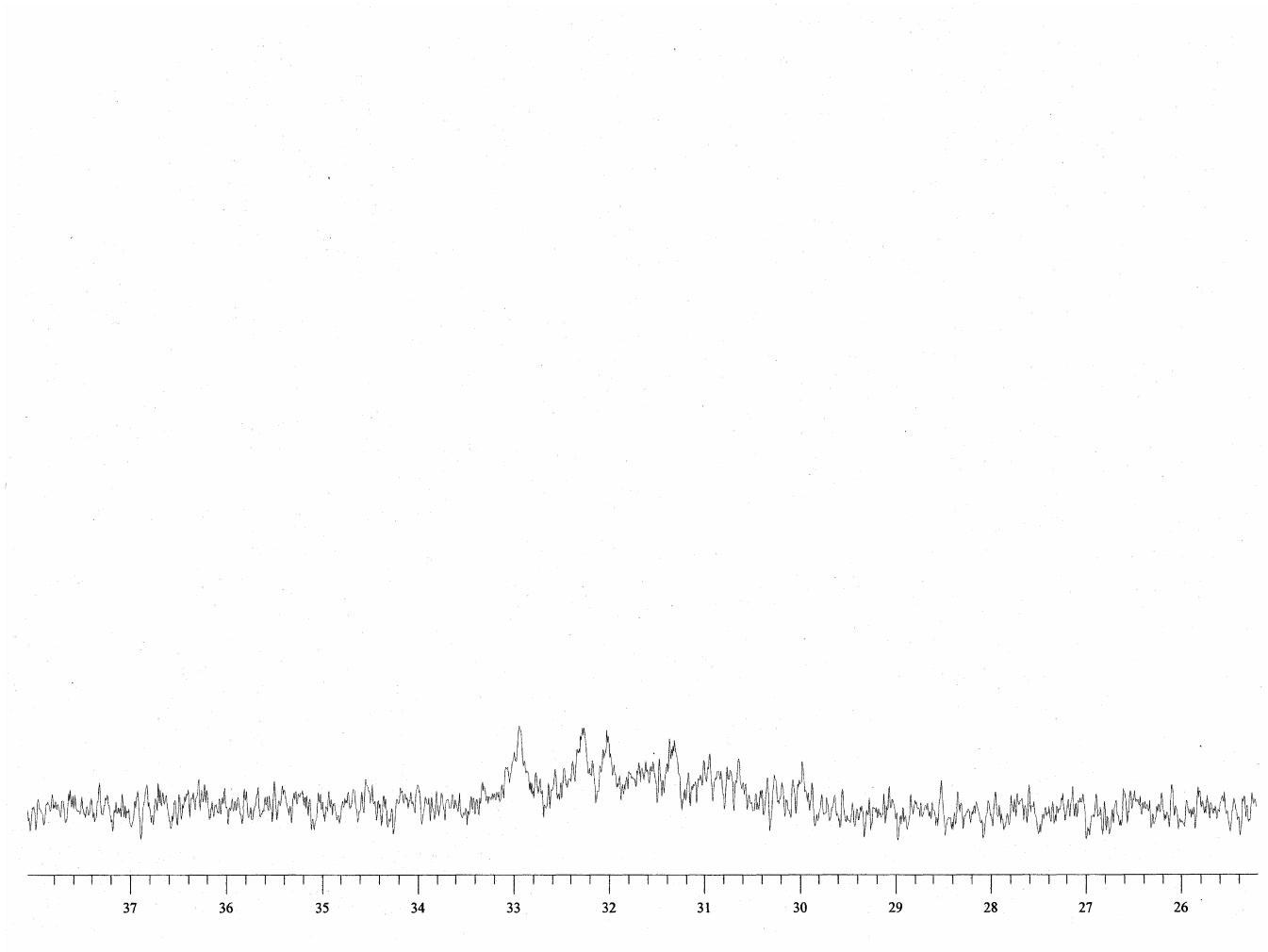
^{13}C (expanded)

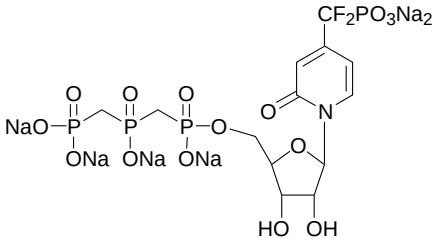




53 (D_2O)

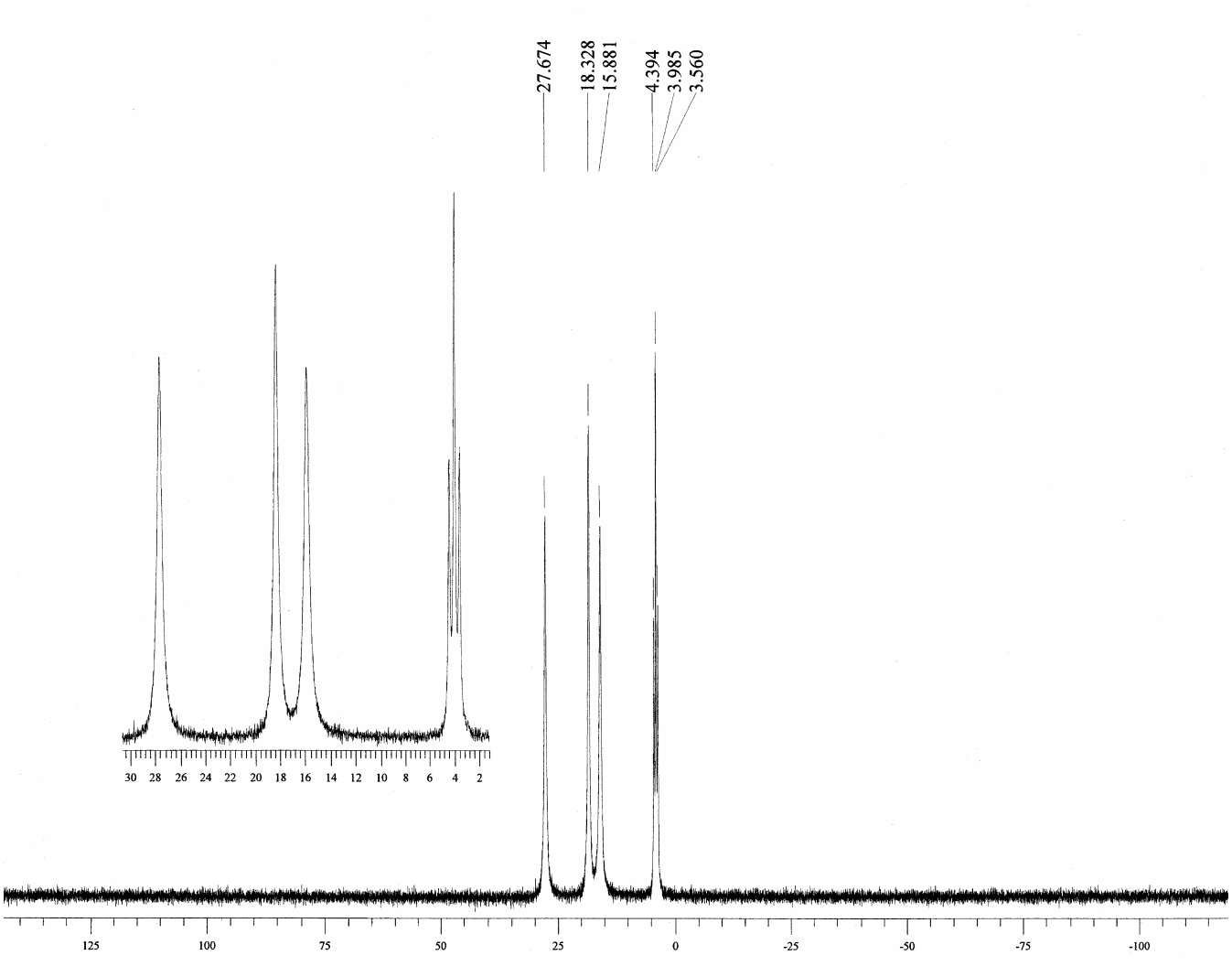
^{13}C (expanded)

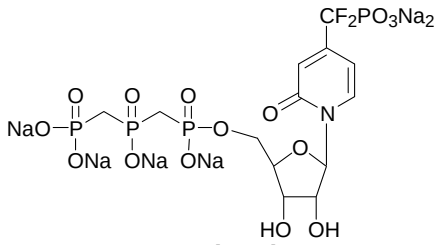



CF2PO3Na2
NaO
ONa ONa ONa
HO OH

53 (D_2O)

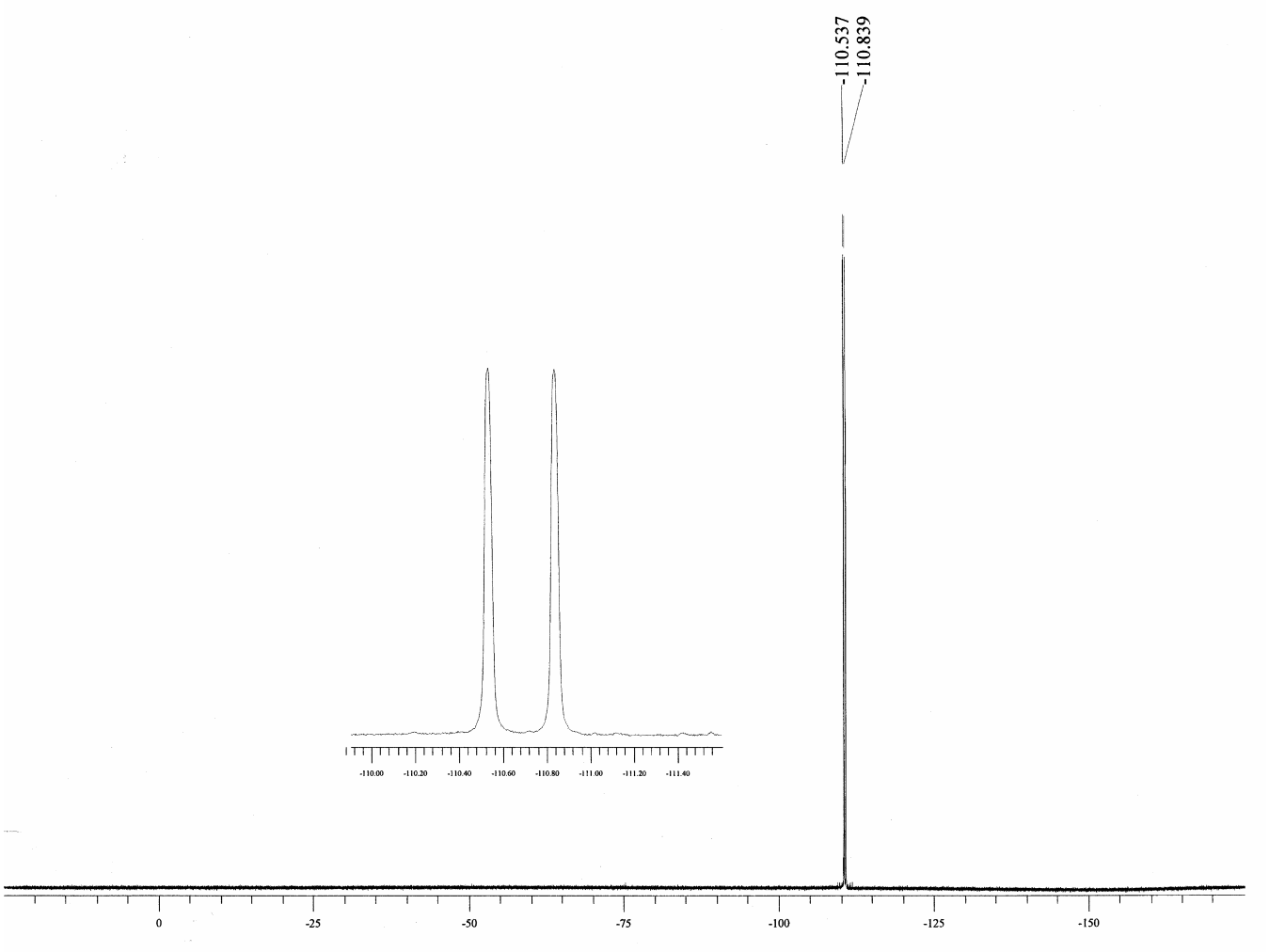
^{31}P

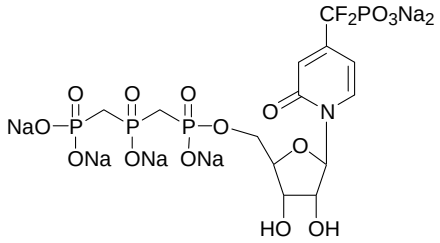

27.674
18.328
15.881
4.394
3.985
3.560
30 28 26 24 22 20 18 16 14 12 10 8 6 4 2
125 100 75 50 25 0 -25 -50 -75 -100


CF2PO3Na2
NaO
ONa
ONa
ONa
O
N
HO
OH

53 (D_2O)

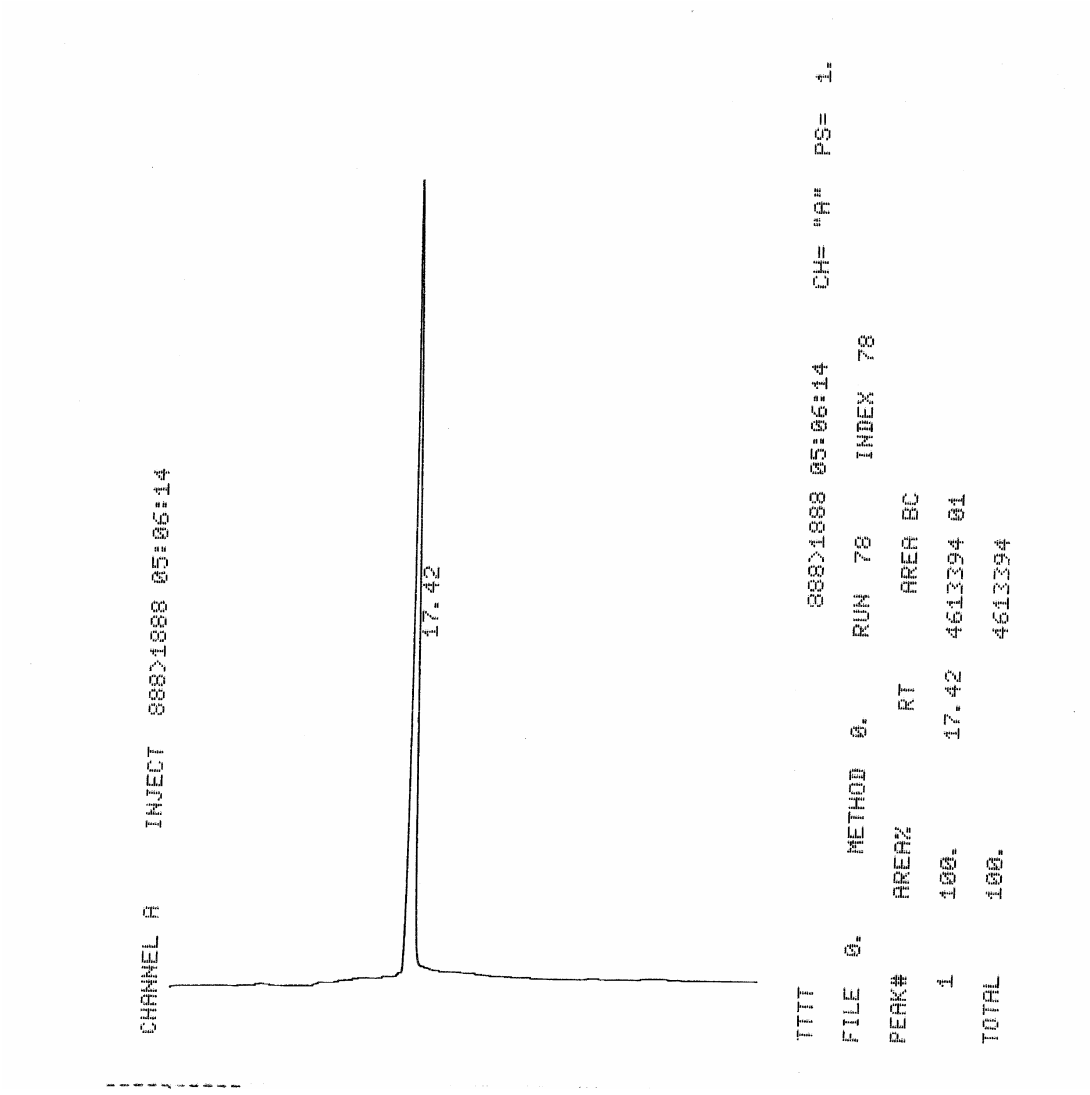
^{19}F


-110.537
-110.839
-110.00
-110.20
-110.40
-110.60
-110.80
-111.00
-111.20
-111.40
0
-25
-50
-75
-100
-125
-150

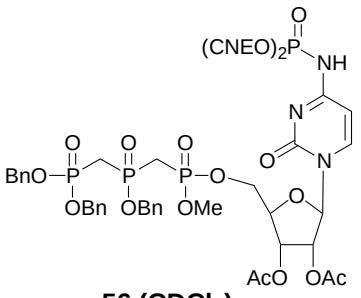


53

Analytical HPLC

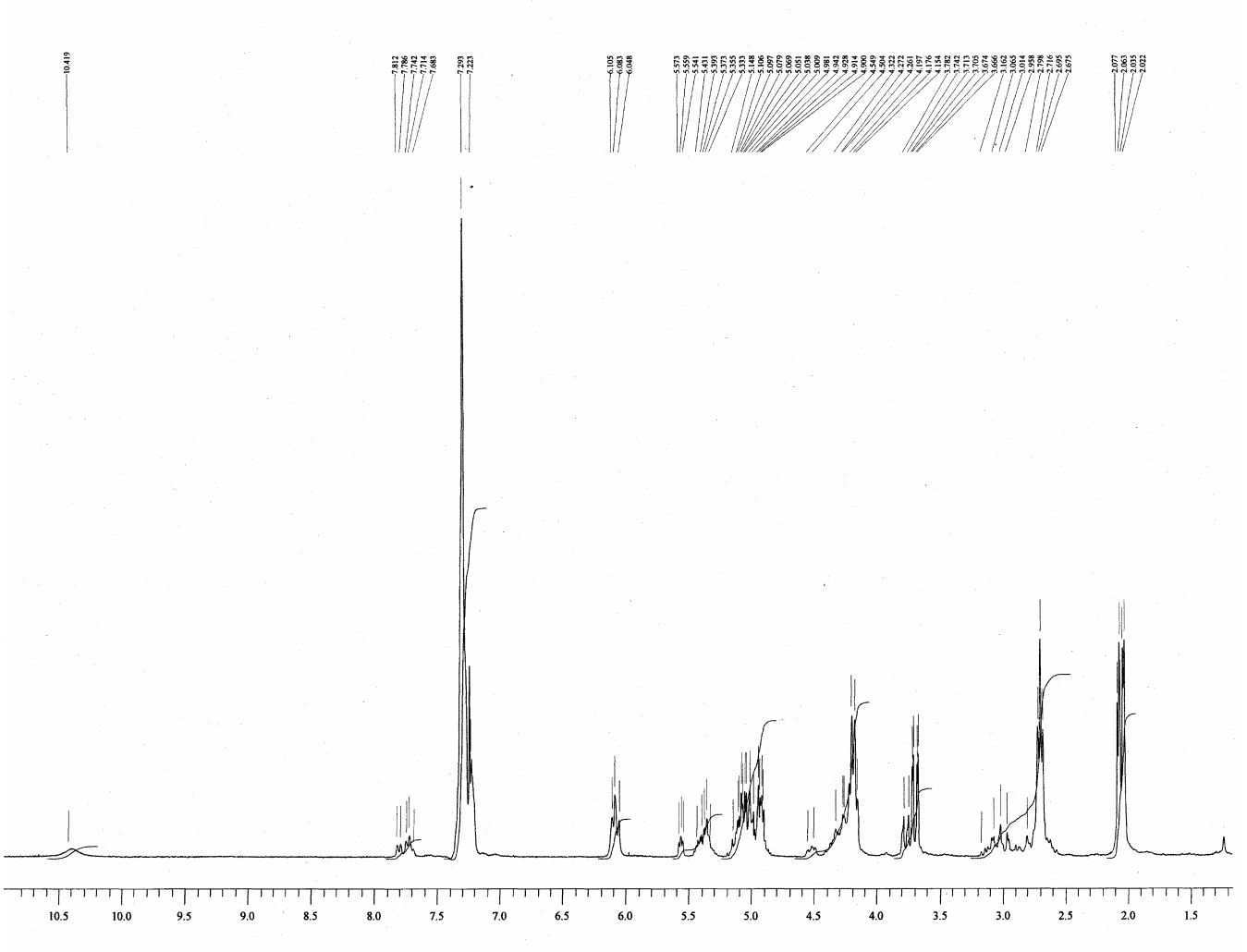


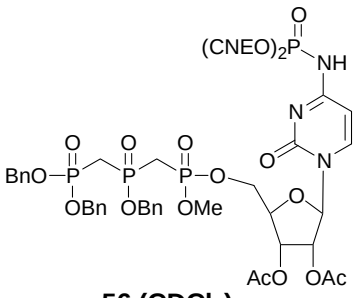
Analytical HPLC chromatogram of compound **53**. The following solvents were used: solvent A: 100 mM TEAA, pH 7.0, solvent B: CH_3CN. The following elution profile was used: linear gradient of 99% A-1% B to 93% A-7% B over 40 minutes. Flow rate = 1 mL/min. $\lambda_{detector}$ = 260 nM.


(CNEO)2P
NH
N
O
N
BnO
OBn
OBn
OMe
O
AcO
OAc

56 ($CDCl_3$)

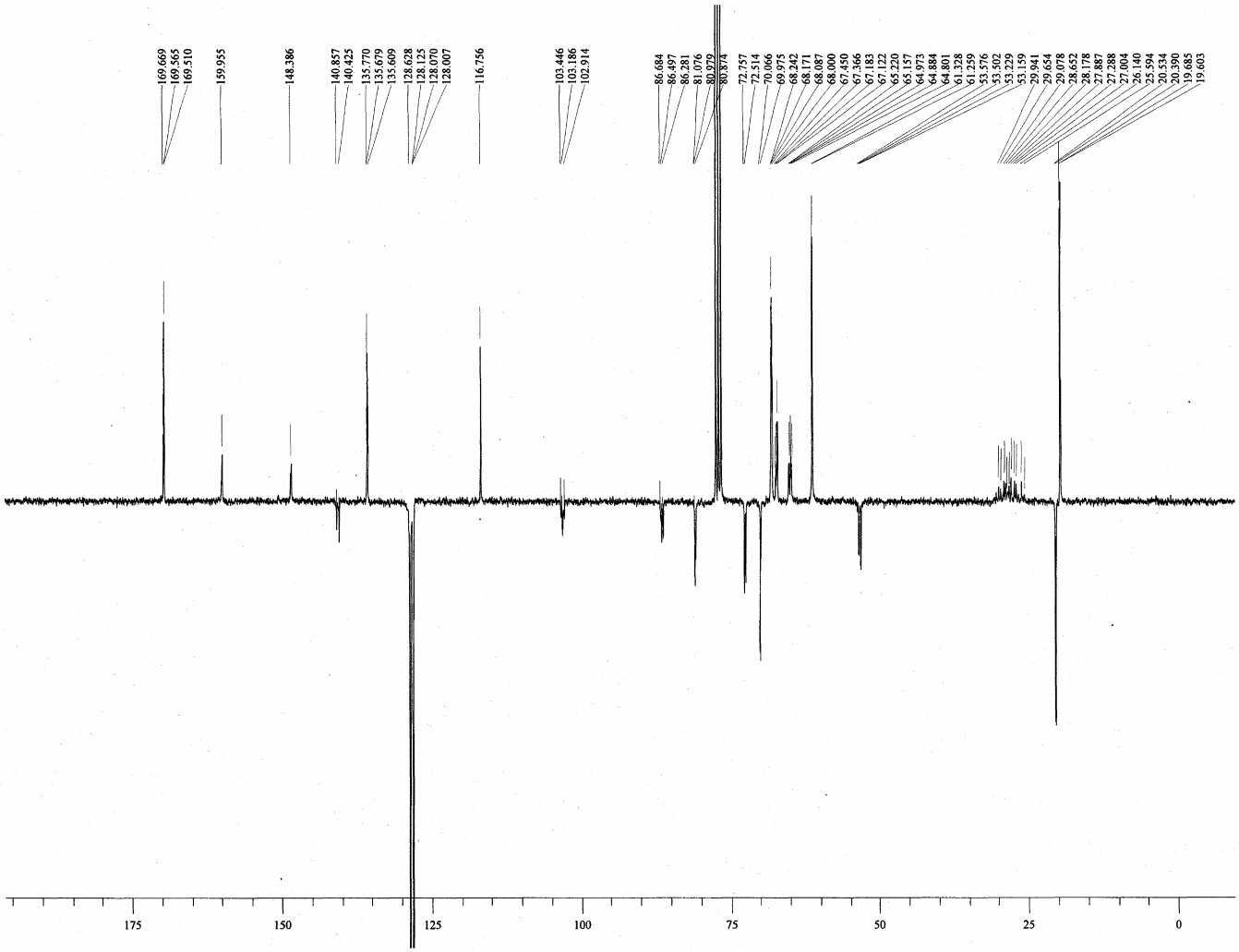
^1H

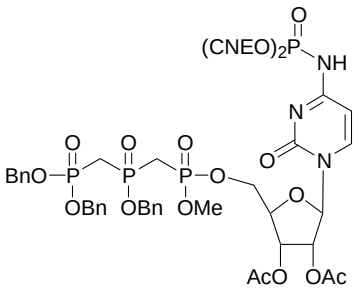

10.419
7.812
7.786
7.742
7.714
7.683
7.293
7.223
6.105
6.068
6.048
5.573
5.559
5.541
5.431
5.393
5.373
5.353
5.333
5.148
5.106
5.097
5.079
5.069
5.051
5.038
5.009
4.981
4.941
4.928
4.914
4.900
4.549
4.304
4.293
4.272
4.261
4.197
4.156
4.154
3.782
3.743
3.713
3.705
3.674
3.666
3.162
3.065
3.014
2.958
2.798
2.716
2.696
2.675
2.077
2.055
2.035
2.022
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5


(CNEO)2P
NH
N
O
N
BnO
P
OBn
P
OBn
P
OMe
O
AcO
OAc

56 ($CDCl_3$)

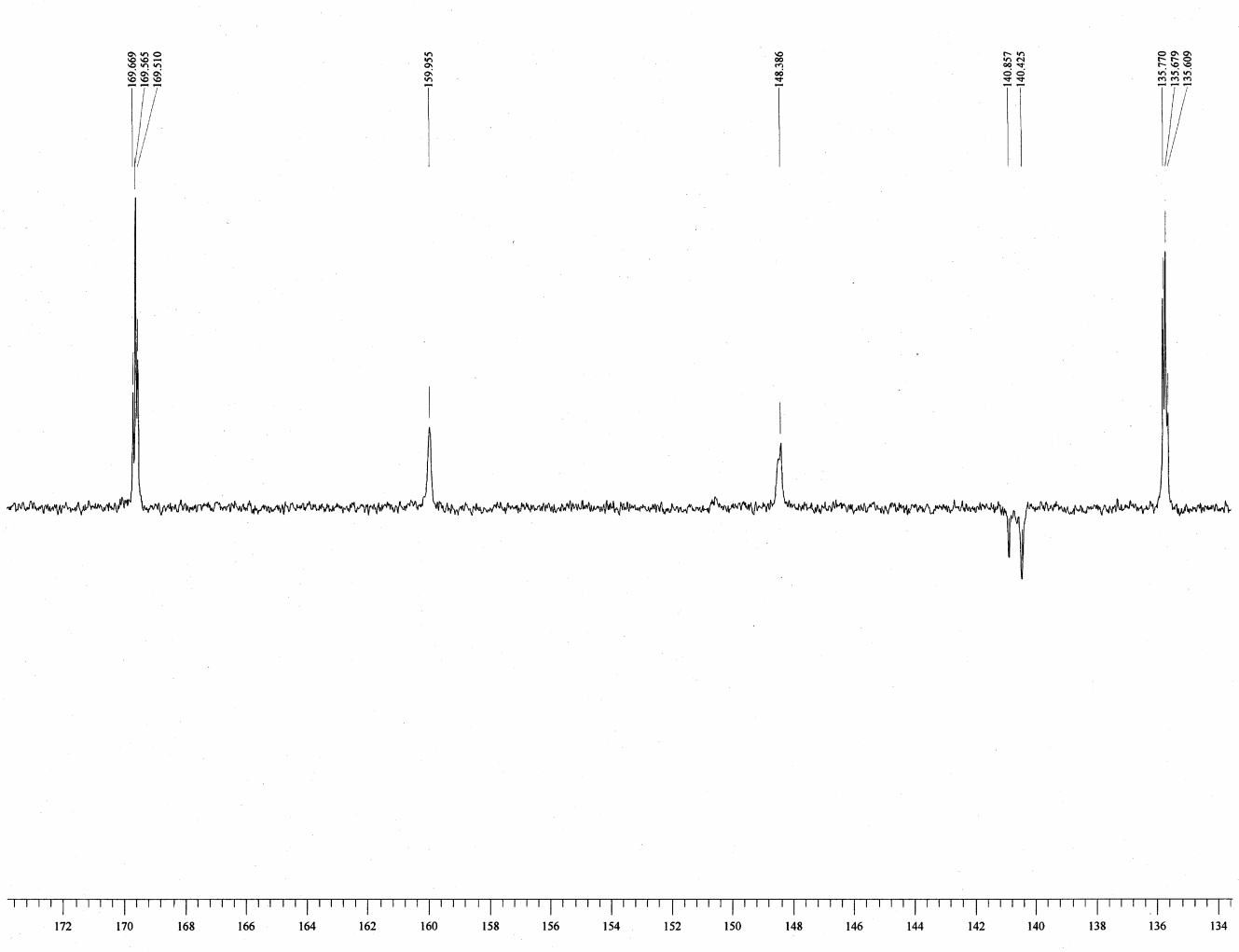
^{13}C

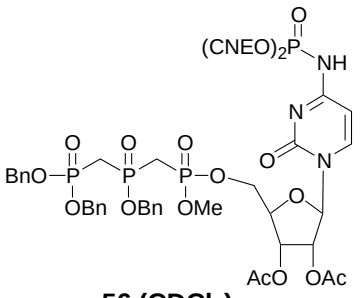

169.669
169.565
169.510
159.955
148.386
140.857
140.425
135.770
135.679
135.609
128.628
128.125
128.070
128.007
116.756
103.446
103.186
102.914
86.684
86.497
86.281
81.076
80.979
80.874
72.757
72.514
70.066
69.975
68.242
68.171
68.087
68.000
67.450
67.366
67.183
67.122
65.220
65.157
64.973
64.884
64.801
61.328
61.259
53.576
53.502
53.229
53.159
29.941
29.654
29.078
28.652
28.178
27.887
27.288
27.004
26.140
25.594
20.534
20.390
19.685
19.603
175
150
125
100
75
50
25
0



56 ($CDCl_3$)

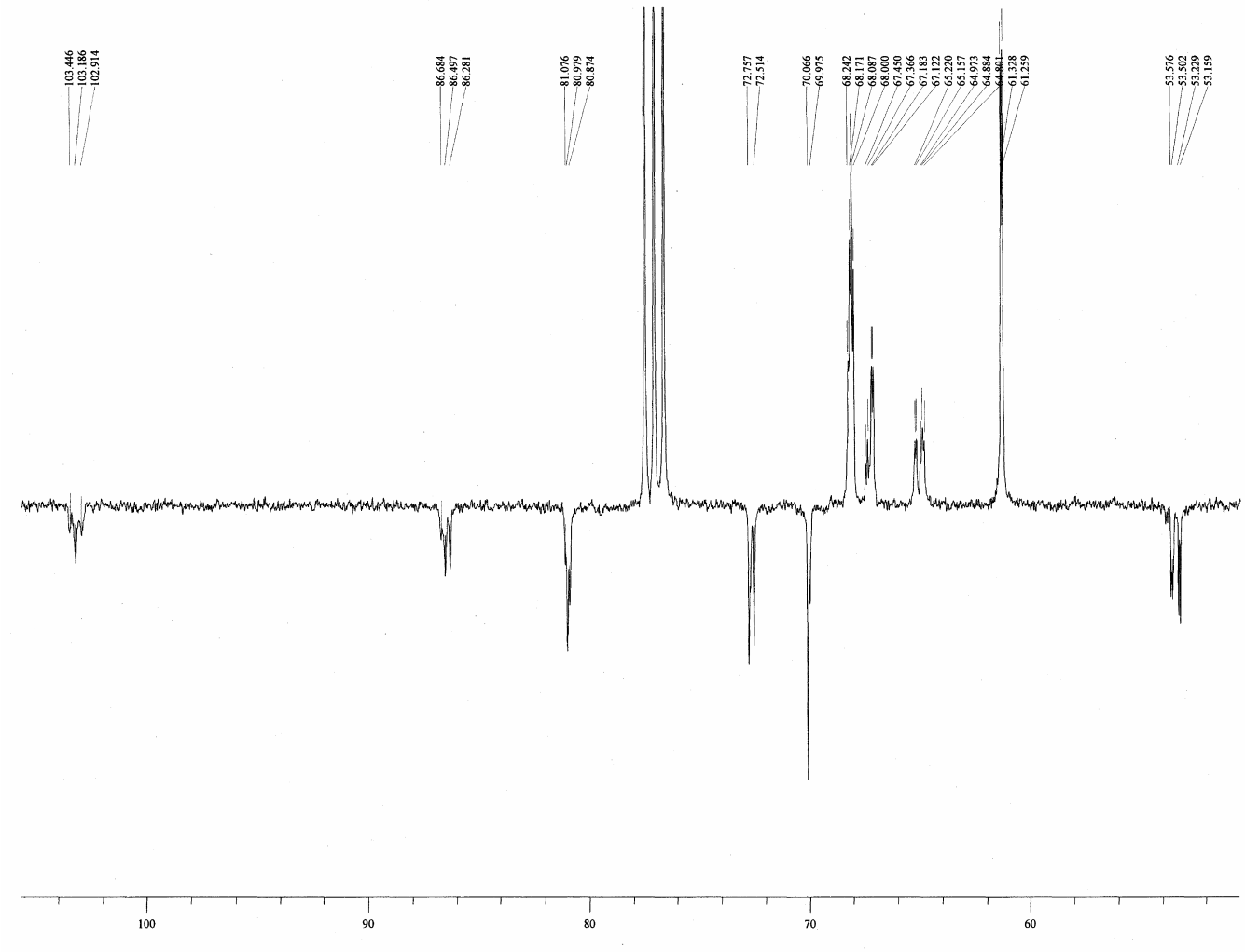
^{13}C (expanded)

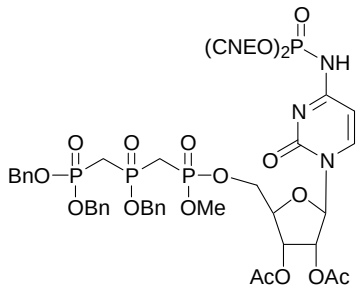




56 ($CDCl_3$)

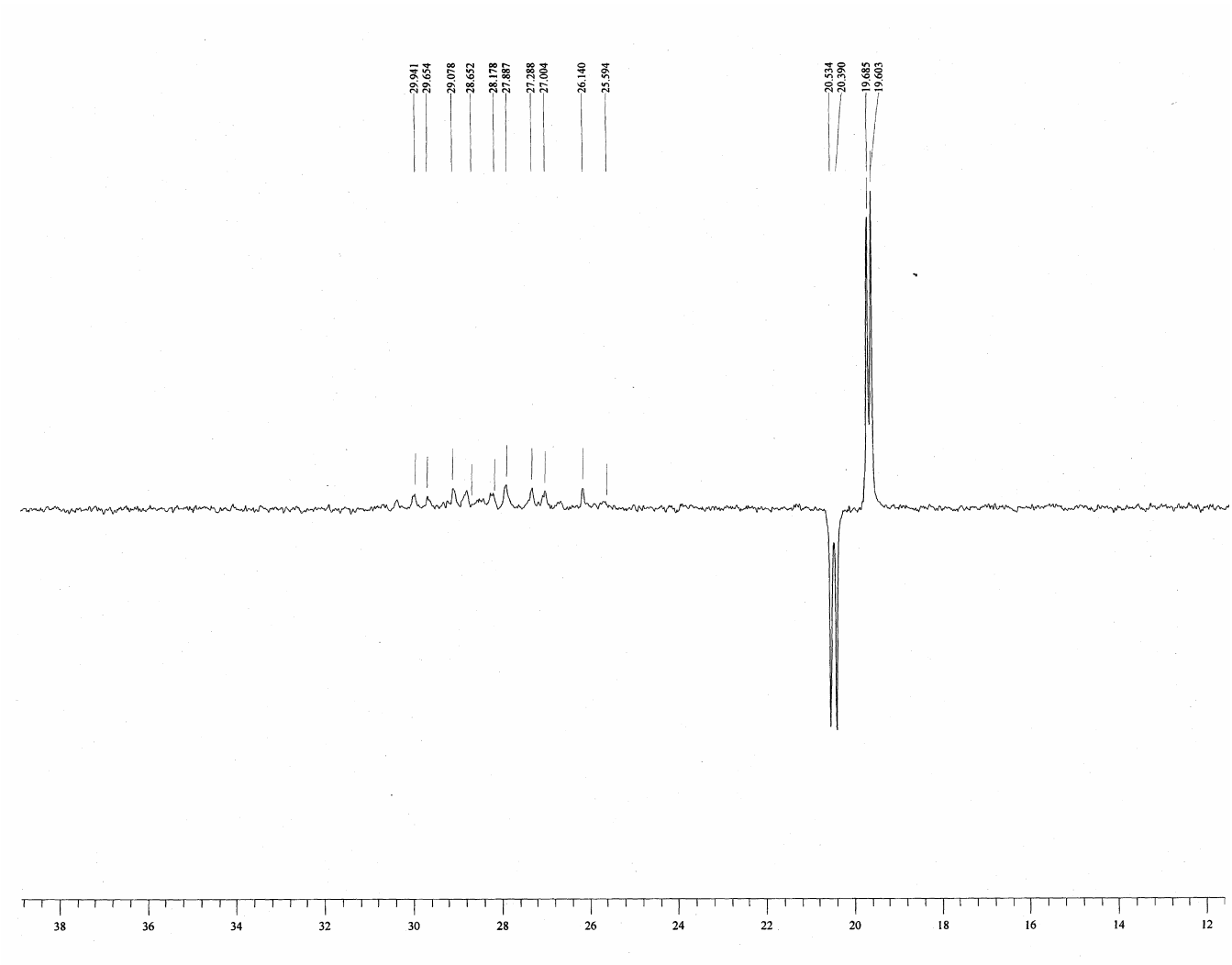
^{13}C (expanded)

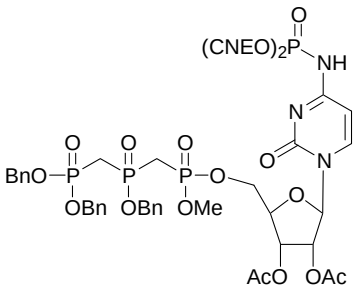




56 ($CDCl_3$)

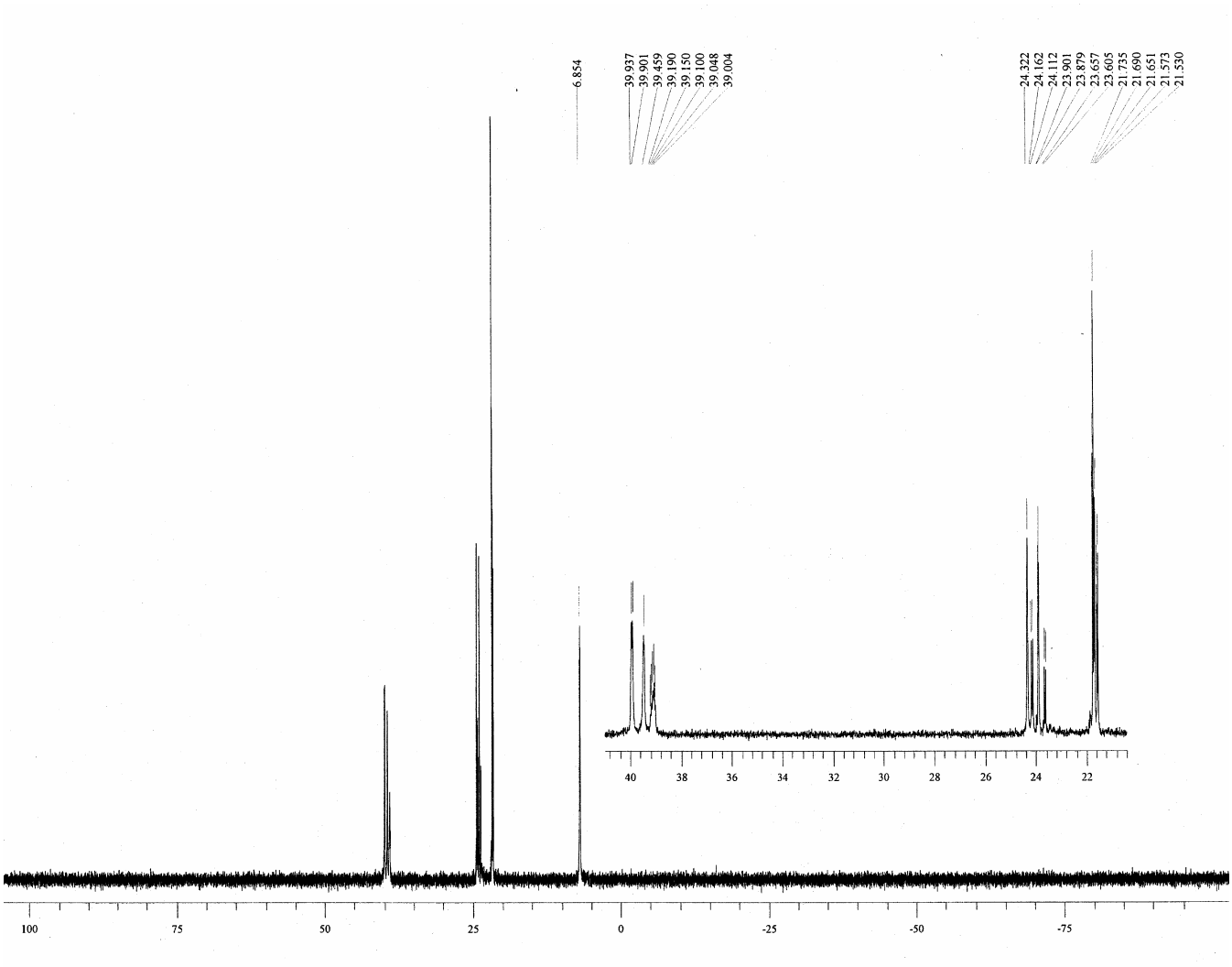
^{13}C (expanded)

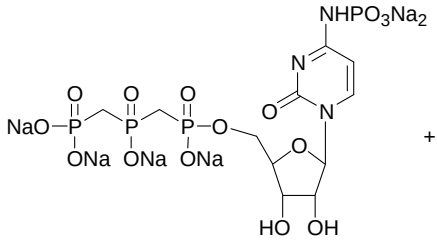



(CNEO)2P
O
NH
N
N
O
O
N
O
BnO—P—O—P—O—P—O
OBn OBn OMe
AcO OAc

56 ($CDCl_3$)

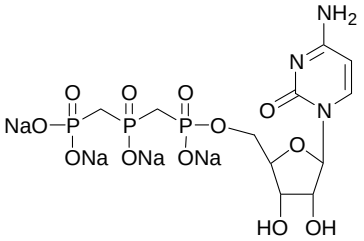
^{31}P


6.854
39.937
39.901
39.459
39.190
39.150
39.100
39.048
39.004
24.322
24.162
24.112
23.901
23.879
23.657
23.605
21.735
21.690
21.651
21.573
21.530
100
75
50
25
0
-25
-50
-75
40
38
36
34
32
30
28
26
24
22



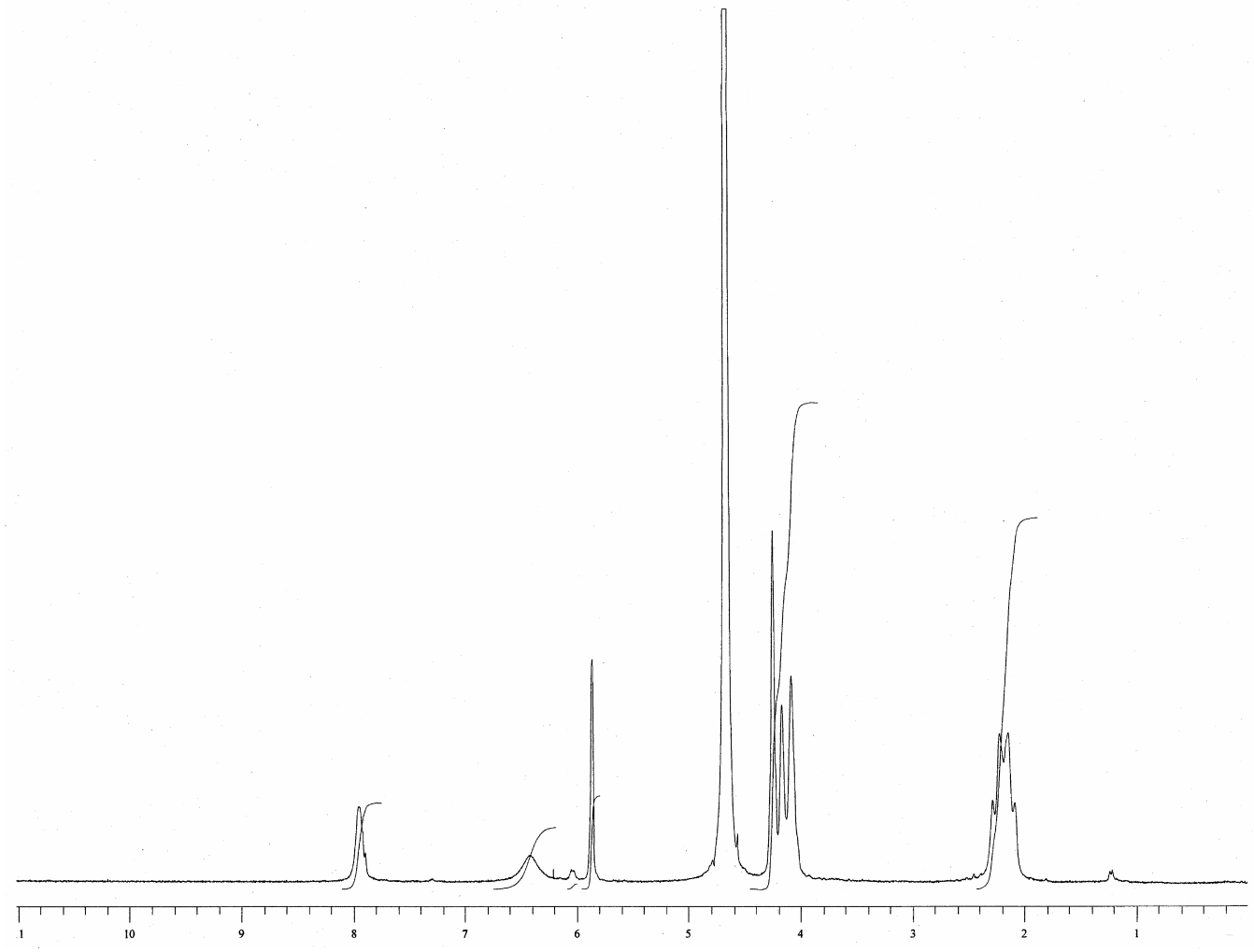
57 (D_2O)

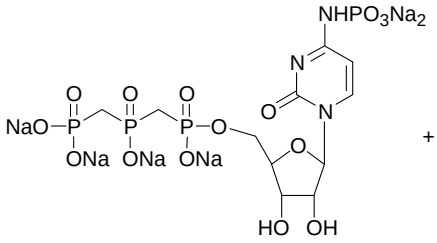
+



58 (app. 3-4% by ^{1}H NMR)

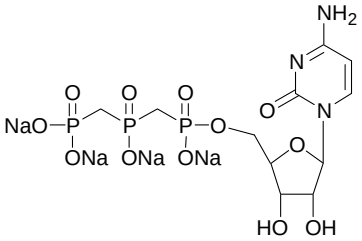
^{1}H





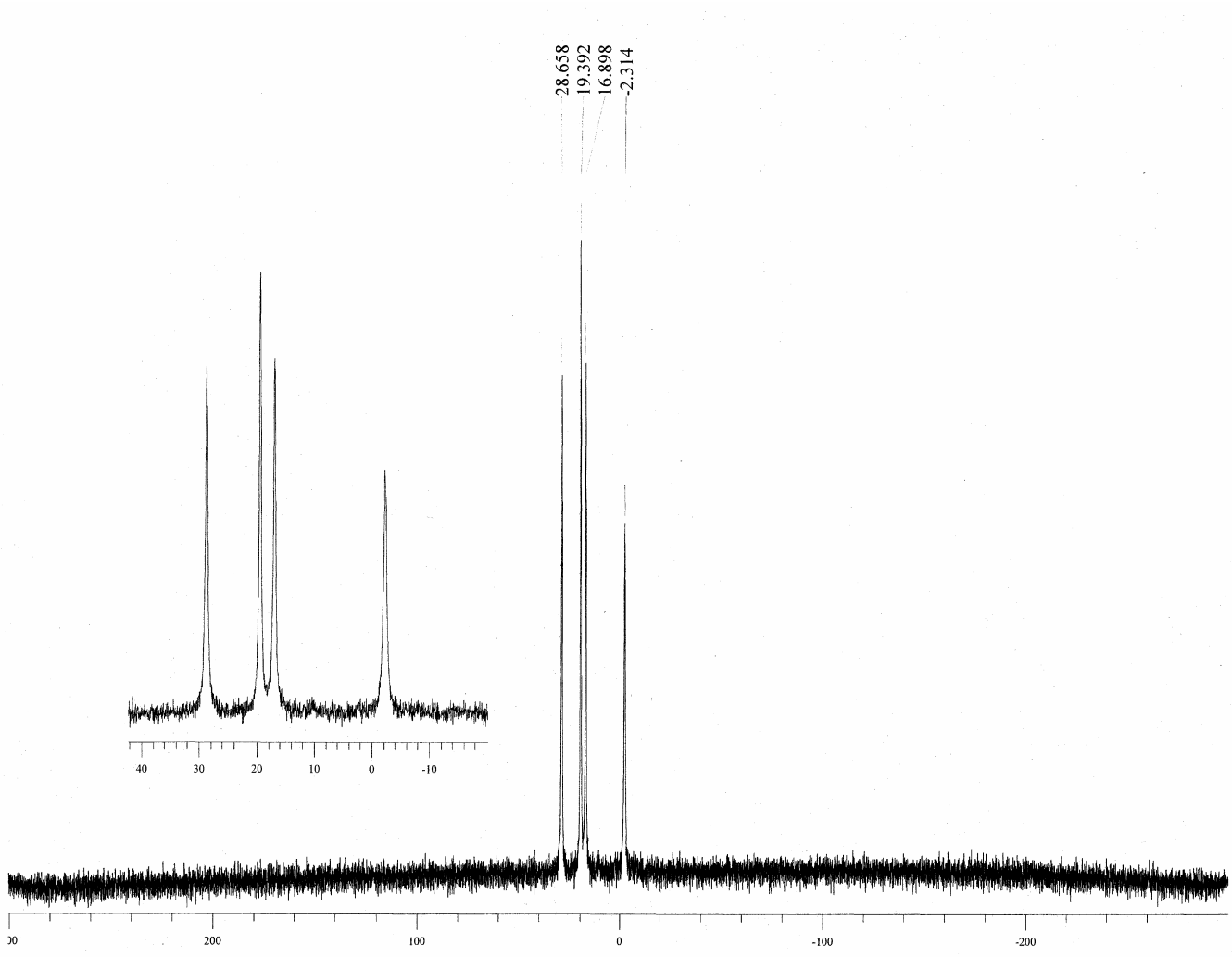
57 (D_2O)

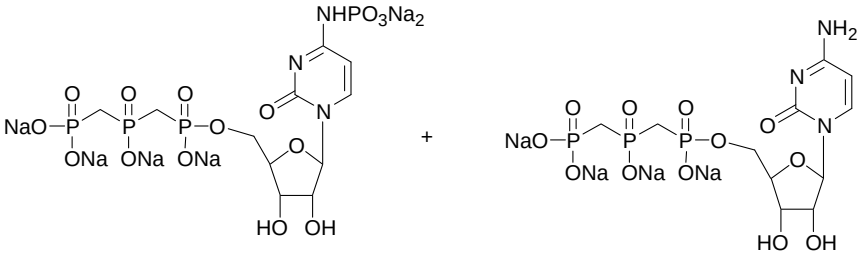
+



58 (app. 3-4% by ^{1}H NMR)

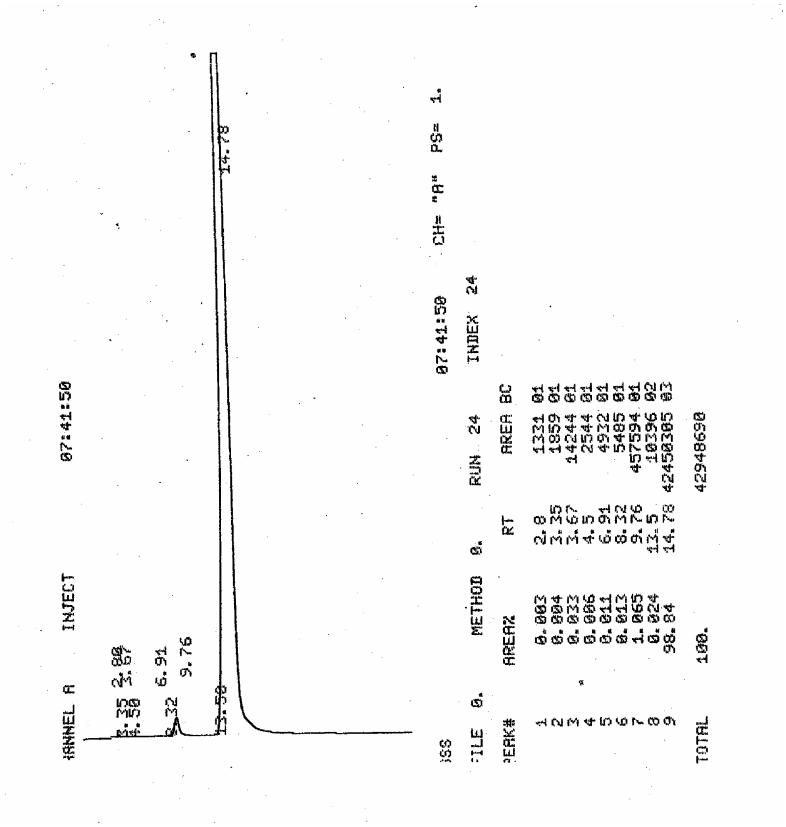
^{31}P





57 **58** (app. 1% by HPLC)

Analytical HPLC



Analytical HPLC chromatogram of compound **57**. The following elution profile was used: 100 mM TEAA, pH 9.0 for 30 min. Flow rate = 1 mL/min. $\lambda_{detector}$ = 260 nM.