Electronic Supplementary Material (ESI) for Chemical Communications

Synthesis of inosine 6-phosphate diesters *via* phosphitylation of the carbonyl oxygen

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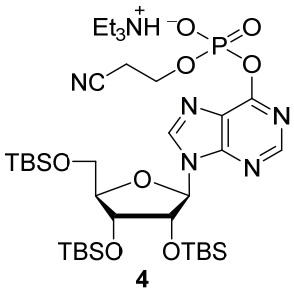
Supplementary information

General Information

Commercially available reagents were used without purification. Dry organic solvents were prepared by appropriate procedures prior to use. The other organic solvents were reagent grade and used as received. All reactions in dry solvents were carried out under argon. Analytical thin-layer chromatography (TLC) was performed on Merck TLC plates (No. 5715) precoated with silica gel 60 F_{254}. Silica gel column chromatography was carried out using Kanto silica gel 60N (spherical, neutral, 63–210 μm). RP-HPLC was carried out using Inertsil ODS-3 columns (C_{18}) (analytical: 4.6 × 150 mm; preparative: 10 × 150 mm, 5 μm particle size) (GL Sciences). ^{1}H, ^{13}C and ^{31}P NMR spectra (400, 100, 161.7 MHz) were recorded on a JNM-AL-400 or a JNM-ECS-400 spectrometer (JEOL). Tetramethylsilane (TMS) and $CDCl_3$ were used as internal standards for ^{1}H and ^{13}C NMR in $CDCl_3$, respectively (0.0, 77.0 ppm). 85% H_3PO_4 was used as an external standard for ^{31}P NMR in D_2O (0.0 ppm). CHD_2OD was used as an internal standard for ^{1}H NMR in CD_3OD (3.31 ppm). Sodium 3-trimethylsilyl-1-propanesulfonate was used as an external standard for ^{1}H and ^{13}C NMR in D_2O (0.0 ppm). ^{1}H NMR data are reported as follows: chemical shift (multiplicity, coupling constants, integration). Multiplicity is indicated as follows: s (singlet); d (doublet); dd (doublet of doublets); t (triplet); q (quartet); brs (broad singlet); m (multiplet); dt (doublet of triplets); dsept (doublet of septets). IR spectra were recorded on a PerkinElmer Spectrum 400 FT-IR spectrometer in attenuated total reflectance (ATR) mode. High-resolution mass spectra were recorded on a Waters Xevo Q-Tof mass spectrometer (ESI) or a JEOL AccuTof DART mass spectrometer (DART).

2′,3′,5′-Tri-*O*-TBS-inosine 6-(triethylammonium 2-cyanoethyl phosphate) 4.

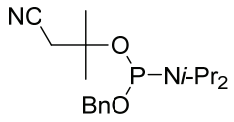


4

2′,3′,5′-Tri-*O*-TBS-inosine **1** (0.214 g, 0.350 mmol) and bis(2-cyanoethyl) *N*,*N*-diisopropylphosphoramidite (0.219 mL, 0.835 mmol) were dried by repeated coevaporation with dry MeCN and dissolved in dry THF (2.8 mL) under Ar. A 0.5 M solution of CMPT in dry MeCN (2.8 mL, 1.4 mmol), which was dried over MS 3A prior to use, was added dropwise to the solution with stirring, and the solution was further stirred for 1 h at rt. (2*R*,8a*S*)-(+)-(camphorylsulfonyl)oxaziridine (0.321 g, 1.40 mmol) was then added and the solution was continuously stirred for another 1 h at rt. $MeNO_2$ (93.7 μL, 1.75 mmol) and DBU (0.261 mL, 1.75 mmol) were then successively added dropwise and the solution was kept stirring for 1 h again at rt. The solution was then diluted with CH_2Cl_2 (300 mL) and washed with 0.1 M TEAB buffer (pH 7) (200 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 50 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure.

The residue was then purified by silica gel column chromatography [CH_2Cl_2–MeOH–Et_3N (99:1:0.5 to 95.5:3.5:0.5, v/v/v)]. The fractions containing the desired product **4** were combined and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (100 mL) and washed with 0.1 M TEAB buffer (pH 7) (100 mL). The aqueous layer was separated and extracted with $CHCl_3$ (3 × 50 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure to afford **4** (0.248 g, 0.293 mmol, 84%) as a pale yellow foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.31 (s, 1H), 6.07 (d, J = 4.4 Hz, 1H), 4.63 (t, J = 4.4 Hz, 1H), 4.48 (dt, J = 8.8, 6.6 Hz, 2H), 4.31 (t, J = 4.4 Hz, 1H), 4.14 (m, 1H), 4.03 (dd, J = 11.3, 4.0 Hz, 1H), 3.79 (dd, J = 11.3, 2.6 Hz, 1H), 3.03 (m, 6H), 2.86 (t, J = 6.6 Hz, 2H), 1.29 (t, J = 7.4 Hz, 9H), 0.96 (s, 9H), 0.93 (s, 9H), 0.81 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), –0.03 (s, 3H), –0.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2 (d, $^2J_{PC}$ = 6.6 Hz), 153.0, 152.0, 141.8, 123.5 (d, $^3J_{PC}$ = 8.1 Hz), 117.9, 88.5, 85.2, 75.9, 71.7, 62.4, 61.2 (d, $^2J_{PC}$ = 5.7 Hz), 45.9, 26.1, 25.8, 25.7, 19.8 (d, $^3J_{PC}$ = 7.2 Hz), 18.5, 18.1, 17.8, 9.3, –4.4, –4.7, –4.8, –4.9, –5.4. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ –6.7. HRMS (ESI): *m*/*z* calcd for $C_{31}H_{57}N_5O_8PSi_3^-$ [(M – H)$^-$] 742.3258, found 742.3242.

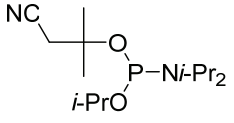
Benzyl 2-cyano-1,1-dimethylethyl *N*,*N*-diisopropylphosphoramidite 5b.



5b

A solution of 2-cyano-1,1-dimethylethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite[1] (1.46 g, 4.43 mmol) in dry CH_2Cl_2 (3.0 mL) was added dropwise to a stirred solution of diisopropylammonium tetrazolide (0.380 g, 2.22 mmol), which was dried by repeated coevaporation with dry MeCN prior to use, and benzyl alcohol (0.462 mL, 4.46 mmol) in dry CH_2Cl_2 (5.0 mL) at 0 °C under Ar. After being stirred for 2 h at 0 °C, the mixture was diluted with CH_2Cl_2 (30 mL) and washed with a saturated $NaHCO_3$ aqueous solution (30 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (10 mL). The organic layers were combined, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography [hexane–AcOEt (92.5:7.5, v/v)] to afford **5b** (1.24 g, 3.69 mmol, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.23 (m, 5H), 4.70 (dd, J = 12.5, 8.0 Hz, 1H), 4.57 (dd, J = 12.5, 8.6 Hz, 1H), 3.66 (dsept, J = 10.6, 6.8 Hz, 2H), 2.61 (d, J = 16.4 Hz, 1H), 2.53 (d, J = 16.4 Hz, 1H), 1.50 (s, 3H), 1.49 (s, 3H), 1.22 (d, J = 6.8 Hz, 6H), 1.18 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.3, 128.2, 127.2, 127.0, 117.6, 73.7 (d, $^2J_{PC}$ = 9.6 Hz), 64.7 (d, $^2J_{PC}$ = 16.2 Hz), 43.2, 43.0, 32.7 (d, $^3J_{PC}$ = 5.8 Hz), 28.3 (d, $^3J_{PC}$ = 9.5 Hz), 28.2 (d, $^3J_{PC}$ = 10.5 Hz), 24.5, 24.4, 24.3, 24.2. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ 139.5. HRMS (DART): *m*/*z* calcd for $C_{18}H_{30}N_2O_2P^+$ [(M + H)$^+$] 337.2039, found 337.2033.

2-Cyano-1,1-dimethylethyl isopropyl *N*,*N*-diisopropylphosphoramidite 5c.

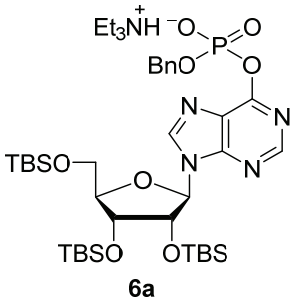


5c

Compound **5c** (colorless oil, 0.404 g, 1.40 mmol, 70% yield) was synthesized from 2-cyano-1,1-dimethylethyl *N*,*N*,*N*′,*N*′-tetraisopropylphosphorodiamidite (0.659 g, 2.00 mmol) by the same procedure used for the synthesis of compound **5b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (dsept, J = 11.2, 6.0 Hz, 1H), 3.61 (dsept, J = 10.6, 6.8 Hz, 2H), 2.65 (d, J = 16.2 Hz, 1H), 2.56 (d, J = 16.2 Hz, 1H), 1.51 (s, 3H), 1.50 (s, 3H), 1.24 (d, J = 6.0 Hz, 3H), 1.20 (d, J = 6.0 Hz, 3H), 1.20 (d, J = 6.8 Hz, 6H), 1.16 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.5, 73.4 (d, $^2J_{PC}$ = 9.5 Hz), 65.9 (d, $^2J_{PC}$ = 18.1 Hz), 42.9, 42.8, 32.6 (d, $^3J_{PC}$ = 4.8 Hz), 28.2 (d, $^3J_{PC}$ = 10.5 Hz), 28.0 (d, $^3J_{PC}$ = 9.6 Hz), 24.3, 24.3, 24.2, 24.2, 24.2, 24.1. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ 137.4. HRMS (DART): *m*/*z* calcd for

$C_{14}H_{30}N_2O_2P^+$ [$(M + H)^+$] 289.2039, found 289.2041.

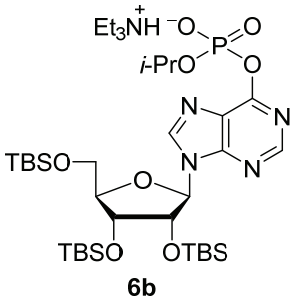
2′,3′,5′-Tri-*O*-TBS-inosine 6-(triethylammonium benzyl phosphate) 6a.



6a

Compound **6a** (pale yellow foam, 19.3 mg, 21.9 μmol, 88% yield) was synthesized from 2′,3′,5′-tri-*O*-TBS-inosine **1** (15.3 mg, 25.0 μmol) by the same procedure used for the synthesis of compound **4** except that CMPT and bis(2-cyanoethyl) *N*,*N*-diisopropylphosphoramidite were replaced by CMMT and compound **5b** (17.8 mg, 60 μmol), respectively, and that the reaction time for step (i) (condensation of compounds **1** and **5b**) was shortened from 1 h to 15 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.4 (brs, 1H), 8.58 (s, 1H), 8.28 (s, 1H), 7.47 (d, J = 7.2 Hz, 2H), 7.30–7.20 (m, 3H), 6.07 (d, J = 4.3 Hz, 1H), 5.31 (d, J = 6.8 Hz, 2H), 4.65 (t, J = 4.3 Hz, 1H), 4.32 (t, J = 4.3 Hz, 1H), 4.13 (m, 1H), 4.03 (dd, J = 11.3, 4.0 Hz, 1H), 3.79 (dd, J = 11.3, 3.0 Hz, 1H), 3.11 (q, J = 7.2 Hz, 6H), 1.32 (t, J = 7.2 Hz, 9H), 0.96 (s, 9H), 0.93 (s, 9H), 0.81 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), –0.04 (s, 3H), –0.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3 (d, $^2J_{PC}$ = 6.6 Hz), 152.8, 151.9, 141.3, 138.5 (d, $^3J_{PC}$ = 8.6 Hz), 127.8, 127.6, 127.1, 123.3 (d, $^3J_{PC}$ = 7.6 Hz), 88.3, 85.1, 75.7, 71.6, 68.2 (d, $^2J_{PC}$ = 5.7 Hz), 62.3, 45.6, 25.9, 25.7, 25.5, 18.4, 17.9, 17.7, 9.2, –4.5, –4.9, –4.9, –5.1, –5.5. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ –5.7. HRMS (ESI): *m*/*z* calcd for $C_{35}H_{60}N_4O_8PSi_3^-$ [$(M - H)^-$] 779.3462, found 779.3476.

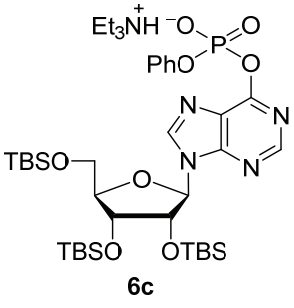
2′,3′,5′-Tri-*O*-TBS-inosine 6-(triethylammonium isopropyl phosphate) 6b.



6b

Compound **6b** (pale yellow foam, 0.171 g, 0.205 mmol, 82% yield) was synthesized from 2′,3′,5′-tri-*O*-TBS-inosine **1** (0.153 g, 0.250 mmol) by the same procedure used for the synthesis of compound **4** except that CMPT and bis(2-cyanoethyl) *N*,*N*-diisopropylphosphoramidite were replaced by CMMT and compound **5c** (0.173 g, 0.600 mmol), respectively, and that the reaction time for step (i) (condensation of compounds **1** and **5c**) was shortened from 1 h to 15 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.6 (brs, 1H), 8.56 (s, 1H), 8.25 (s, 1H), 6.06 (d, J = 4.4 Hz, 1H), 4.88 (dsept, J = 8.0, 6.4 Hz, 1H), 4.67 (t, J = 4.4 Hz, 1H), 4.31 (t, J = 4.4 Hz, 1H), 4.13 (m, 1H), 4.01 (dd, J = 11.4, 4.2 Hz, 1H), 3.78 (dd, J = 11.4, 3.0 Hz, 1H), 3.16 (q, J = 7.2 Hz, 6H), 1.35 (t, J = 7.2 Hz, 9H), 1.35 (d, J = 6.4 Hz, 6H), 0.95 (s, 9H), 0.93 (s, 9H), 0.80 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), –0.04 (s, 3H), –0.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4 (d, $^2J_{PC}$ = 6.7 Hz), 152.6, 151.8, 141.2, 123.2 (d, $^3J_{PC}$ = 7.6 Hz), 88.1, 85.1, 75.5, 71.6, 70.0 (d, $^2J_{PC}$ = 5.8 Hz), 62.3, 45.5, 25.8, 25.6, 25.4, 23.7 (d, $^3J_{PC}$ = 4.8 Hz), 18.2, 17.8, 17.6, 8.9, –4.7, –5.0, –5.0, –5.3, –5.7. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ –6.4. HRMS (ESI): *m*/*z* calcd for $C_{31}H_{60}N_4O_8PSi_3^-$ [$(M - H)^-$] 731.3462, found 731.3445.

2′,3′,5′-Tri-*O*-TBS-inosine 6-(triethylammonium phenyl phosphate) 6c.

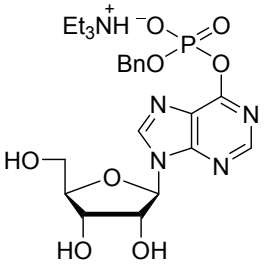


6c

Compound **6c** (pale yellow foam, 0.189 g, 0.218 mmol, 87% yield) was synthesized from 2′,3′,5′-tri-*O*-TBS-inosine **1** (0.153 g, 0.250 mmol) by the same procedure used for the synthesis of compound **4** except that CMPT and bis(2-cyanoethyl) *N*,*N*-diisopropylphosphoramidite were replaced by CMMT and compound **5d** (0.177 g, 0.601 mmol), respectively, and that the reaction time for step (i) (condensation of compounds **1** and **5d**) was shortened from 1 h to 15 min. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 12.0 (brs, 1H), 8.60 (s, 1H), 8.28 (s, 6H), 7.38 (d, J = 7.8 Hz, 2H), 7.23 (t, J = 7.8 Hz, 2H), 7.01 (t, J = 7.8 Hz, 1H), 6.06 (d, J = 4.5 Hz, 1H), 4.65 (t, J = 4.5 Hz, 1H), 4.31 (t, J = 4.5 Hz, 1H), 4.13 (m, 1H), 4.02 (dd, J = 11.5, 3.8 Hz, 1H), 3.79 (dd, J = 11.5, 2.8 Hz, 1H), 3.11 (q, J = 7.4 Hz, 6H), 1.31 (t, J = 7.4 Hz, 9H), 0.95 (s, 9H), 0.93 (s, 9H), 0.80 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.10 (s, 3H), –0.04 (s, 3H), –0.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2 (d, $^2J_{PC}$ = 6.7 Hz), 153.1 (d, $^2J_{PC}$ = 7.6 Hz), 153.0, 152.1, 141.7, 129.0, 123.5 (d, $^3J_{PC}$ = 8.1 Hz), 123.1, 120.7 (d, $^3J_{PC}$ = 4.7 Hz), 88.5, 85.2, 75.8, 71.7, 62.4, 45.7, 26.1, 25.8, 25.7, 18.5, 18.0, 17.8, 8.6, –4.4, –4.7, –4.8, –5.0, –5.4. ^{31}P NMR (161.7 MHz, $CDCl_3$) δ –11.8. HRMS (ESI): m/z calcd for $C_{34}H_{58}N_4O_8PSi_3^-$ [(M – H)$^-$] 765.3306, found 765.3289.

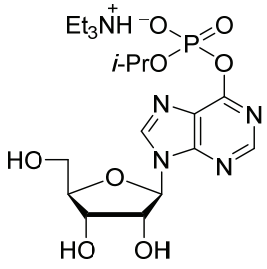
Inosine 6-(triethylammonium benzyl phosphate) 7a.



7a

A 1.0 M solution of TBAF in THF (0.560 mL, 0.560 mmol) was added dropwise to a stirred solution of compound **6a** (43.3 mg, 49.1 μmol) in dry THF (0.40 mL) at rt under Ar and the solution was further stirred for 2 h at rt. The solution was then diluted with AcOEt (20 mL) and extracted with TEAB buffer (pH 7) (3 × 20 mL). The aqueous layers were combined and lyophilized. The residue was then purified by RP-HPLC with a linear gradient of 0–40% acetonitrile for 40 min in 0.1 M triethylammonium bicarbonate buffer (pH 7) at 40 °C at a flow rate of 2 mL/min using an Inertsil ODS-3 column (C_{18}, 10 × 150 mm, 5 μm particle size). The fractions containing **7a** were collected and repeatedly lyophilized from distilled H_2O to remove the excess salt to give **7a** (12.5 mg, 23.2 μmol, 47%) as a white amorphous solid. ^{1}H NMR (400 MHz, CD_3OD) δ 8.57 (s, 1H), 8.56 (s, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.31–7.21 (m, 3H), 6.09 (d, J = 5.6 Hz, 1H), 5.20 (d, J = 6.8 Hz, 2H), 4.74 (t, J = 5.6 Hz, 1H), 4.36 (m, 1H), 4.17 (m, 1H), 3.90 (dd, J = 12.2, 2.4 Hz, 1H), 3.77 (dd, J = 12.2, 2.4 Hz, 1H), 3.17 (q, J = 7.1 Hz, 6H), 1.28 (t, J = 7.1 Hz, 9H). ^{13}C NMR (100 MHz, D_2O) δ 155.8 (d, $^2J_{PC}$ = 6.7 Hz), 152.1, 151.6, 143.2, 135.8, 128.3, 128.0, 127.8, 122.2 (d, $^3J_{PC}$ = 7.6 Hz), 88.5, 85.7, 73.9, 70.5, 69.4 (d, $^2J_{PC}$ = 5.7 Hz), 61.4, 46.7, 8.3. ^{31}P NMR (161.7 MHz, D_2O) δ –6.3. HRMS (ESI): m/z calcd for $C_{17}H_{18}N_4O_8P^-$ [(M – H)$^-$] 437.0868, found 437.0877.

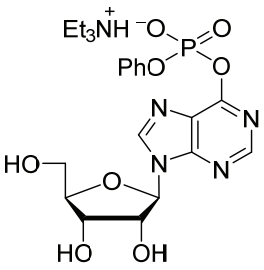
Inosine 6-(triethylammonium isopropyl phosphate) 7b.



7b

Compound **7b** (white amorphous solid, 6.7 mg, 13.6 μmol, 67% yield) was synthesized from compound **6b** (16.9 mg, 20.3 μmol) by the same procedure used for the synthesis of compound **7a**. ^{1}H NMR (400 MHz, D_2O) δ 8.50 (s, 1H), 8.47 (s, 1H), 6.07 (d, J = 5.6 Hz, 1H), 4.73 (t, J = 5.6 Hz, 1H), 4.58 (dsept, J = 7.6, 6.3 Hz, 1H), 4.35 (dd, J = 5.6, 4.0 Hz, 1H), 4.19 (m, 1H), 3.82 (dd, J = 12.8, 2.8 Hz, 1H), 3.74 (dd, J = 12.8, 4.0 Hz, 1H), 3.09 (q, J = 7.4 Hz, 6H), 1.18 (d, J = 7.6 Hz, 6H), 1.17 (t, J = 7.4 Hz, 9H). ^{13}C NMR (100 MHz, D_2O) δ 156.4 (d, $^2J_{PC}$ = 7.7 Hz), 152.5, 152.0, 143.7, 122.6 (d, $^3J_{PC}$ = 7.6 Hz), 88.7, 85.7, 73.8, 72.5 (d, $^2J_{PC}$ = 7.6 Hz), 70.5, 61.4, 46.7, 23.0 (d, $^3J_{PC}$ = 5.8 Hz), 8.3. ^{31}P NMR (161.7 MHz, D_2O) δ –6.3. HRMS (ESI): m/z calcd for $C_{13}H_{18}N_4O_8P^-$ [(M – H)$^-$] 389.0868, found 389.0873.

Inosine 6-(triethylammonium phenyl phosphate) 7c.



7c

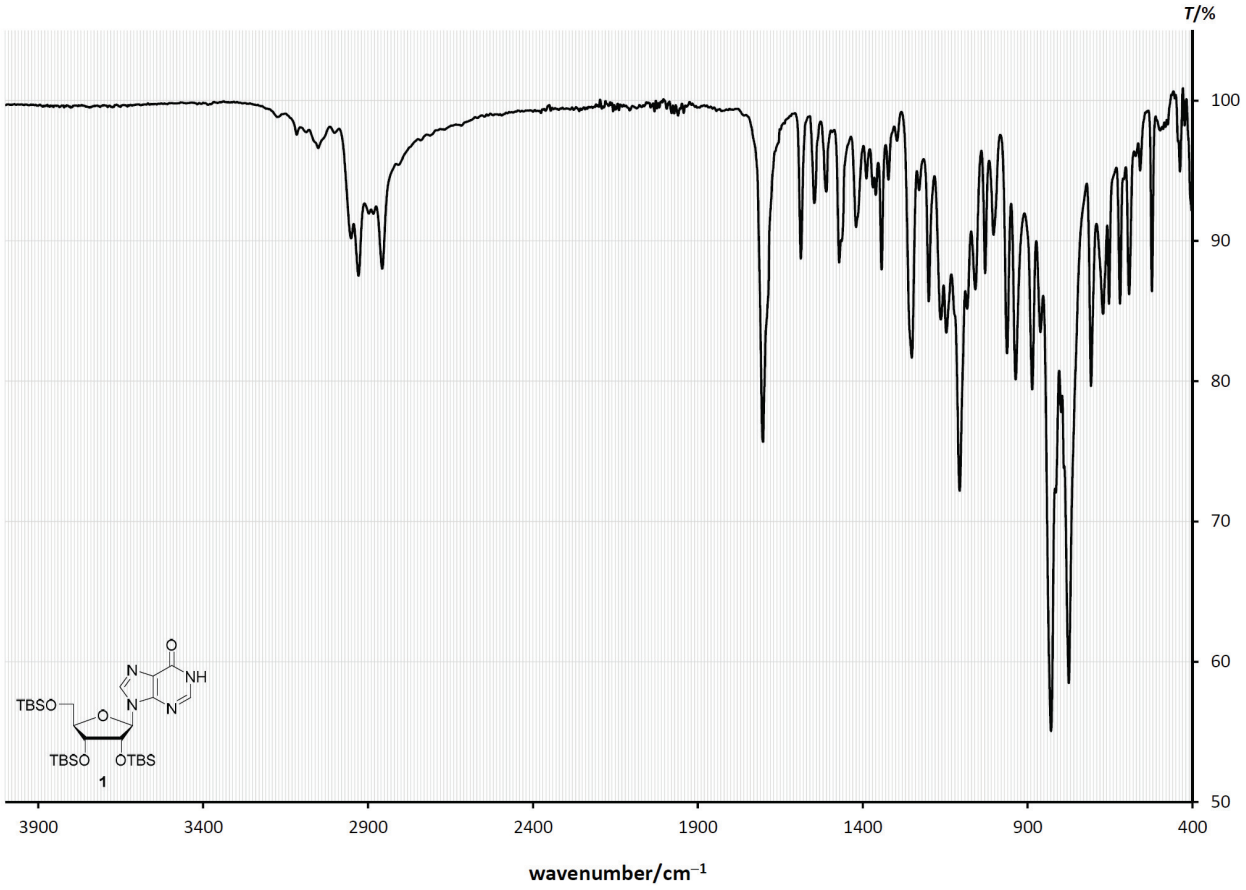
Compound **7c** (white amorphous solid, 7.3 mg, 14 μmol, 68% yield) was synthesized from compound **6c** (17.8 mg, 20.5 μmol) by the same procedure used for the synthesis of compound **7a**. ^{1}H NMR (400 MHz, CD_3OD) δ 8.58 (s, 1H), 8.58 (s, 1H), 7.35–7.26 (m, 4H), 7.08 (t, J = 7.2 Hz, 1H), 6.09 (d, J = 5.3 Hz, 1H), 4.74 (t, J = 5.3 Hz, 1H), 4.36 (dd, J = 5.3, 3.4 Hz, 1H), 4.16 (m, 1H), 3.90 (dd, J = 12.3, 2.8 Hz, 1H), 3.77 (dd, J = 12.3, 3.4 Hz, 1H), 3.19 (q, J = 7.4 Hz, 6H), 1.29 (t, J = 7.4 Hz, 9H). ^{13}C NMR (100 MHz, D_2O) δ 156.0 (d, $^{2}J_{PC}$ = 6.7 Hz), 152.8, 152.0, 151.4 (d, $^{2}J_{PC}$ = 7.6 Hz), 144.0, 129.9, 124.9, 122.6 (d, $^{3}J_{PC}$ = 8.6 Hz), 120.5 (d, $^{3}J_{PC}$ = 3.8 Hz), 88.7, 85.6, 73.8, 70.4, 61.3, 46.7, 8.3. ^{31}P NMR (161.7 MHz, D_2O) δ −10.8. HRMS (ESI): m/z calcd for $C_{16}H_{16}N_4O_8P^-$ [$(M - H)^-$] 423.0711, found 423.0717.

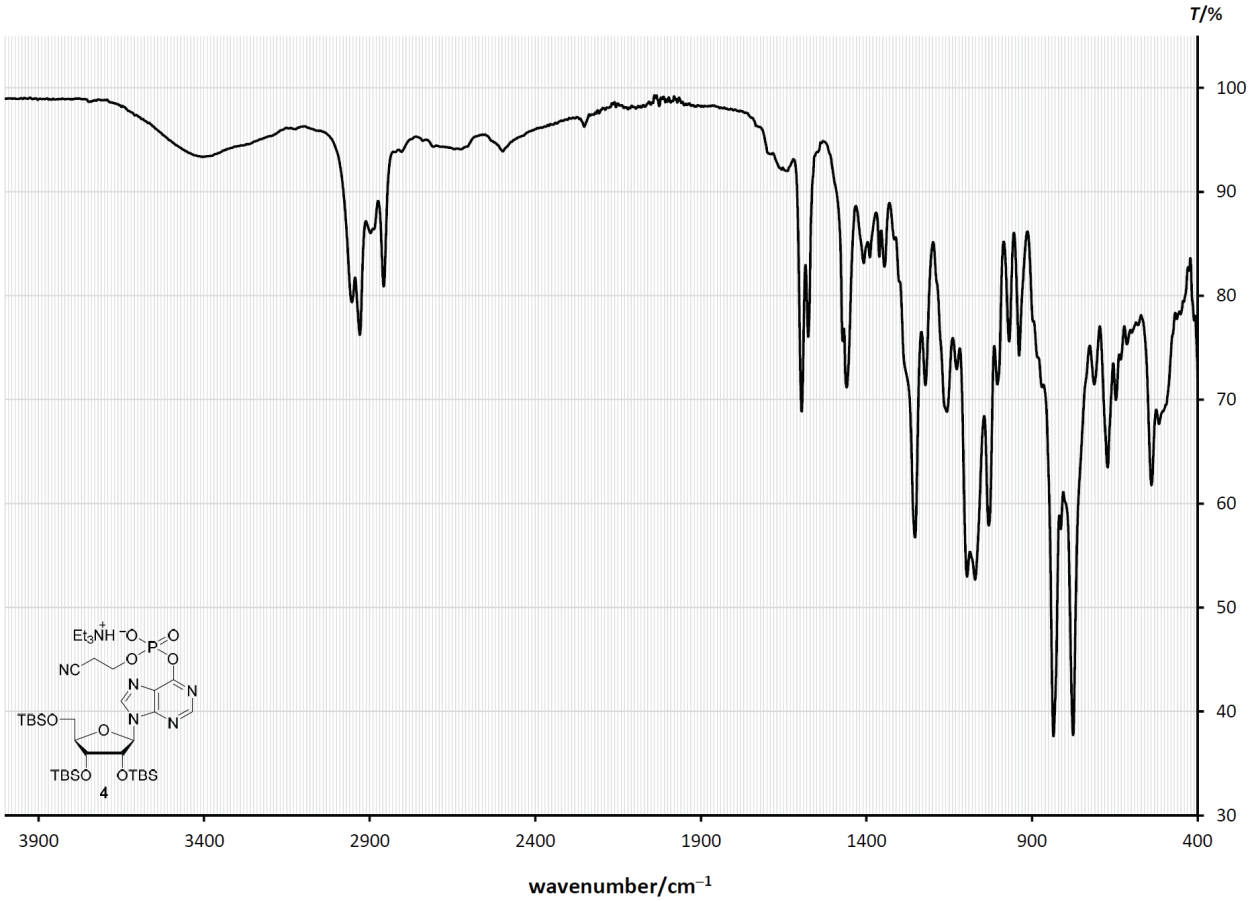
Stability test of compound 7c.

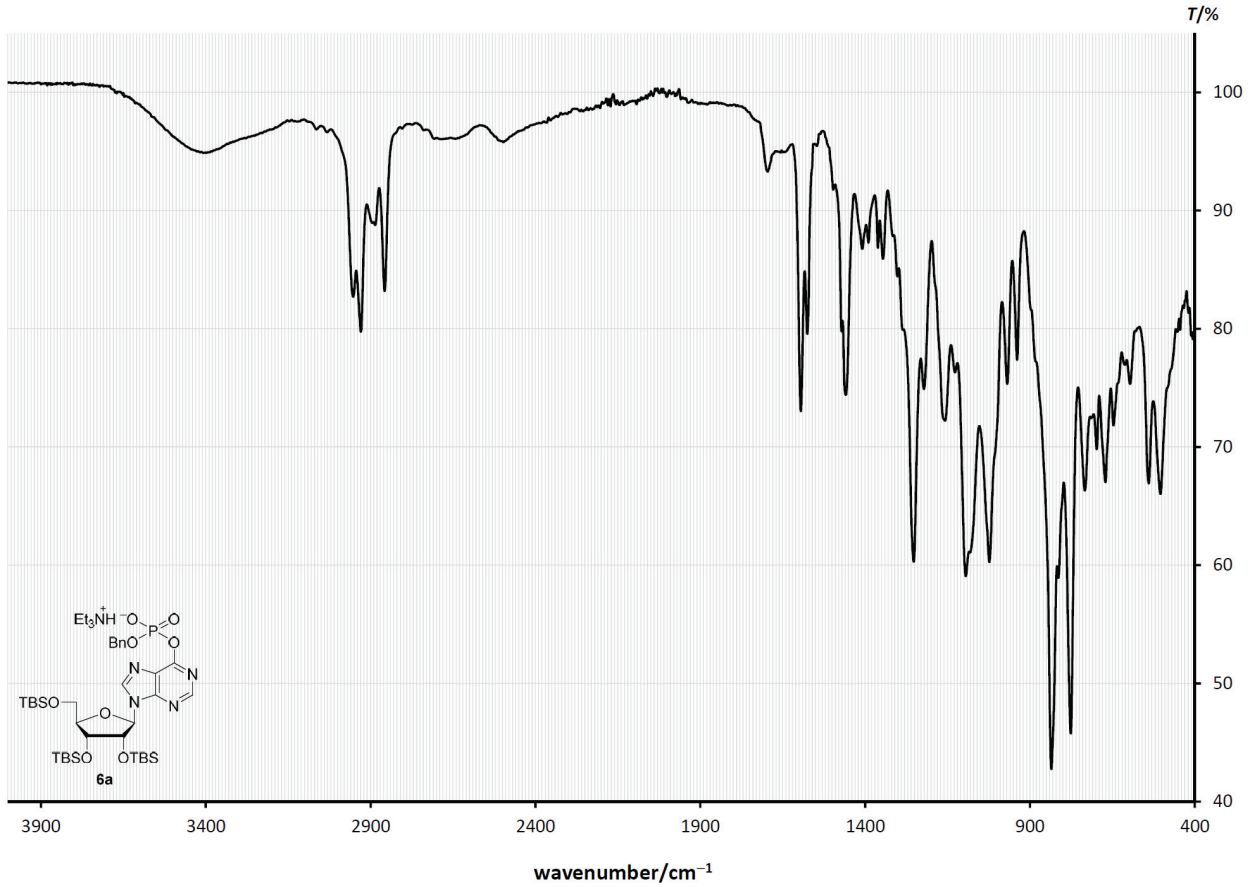
1 mM solutions of compound **7c** (50 μL) at pH 4.4 (0.2 M NaH_2PO_4 aq.), 6.8 (0.2 M NaH_2PO_4–Na_2HPO_4 aq.), and 8.7 (0.2 M Na_2HPO_4 aq.) were incubated at 37 °C. Aliquots (5 μL) were taken after 0, 1, and 3 h, and analyzed by RP-HPLC using uridine (1 mM) as an internal standard. Conditions for RP-HPLC: Inertsil ODS-3 column (C_{18}, 4.6 × 150 mm, 5 μm particle size), linear gradient of 0–40% acetonitrile for 40 min in 0.1 M triethylammonium bicarbonate buffer (pH 7), 25 °C, 0.5 mL/min.

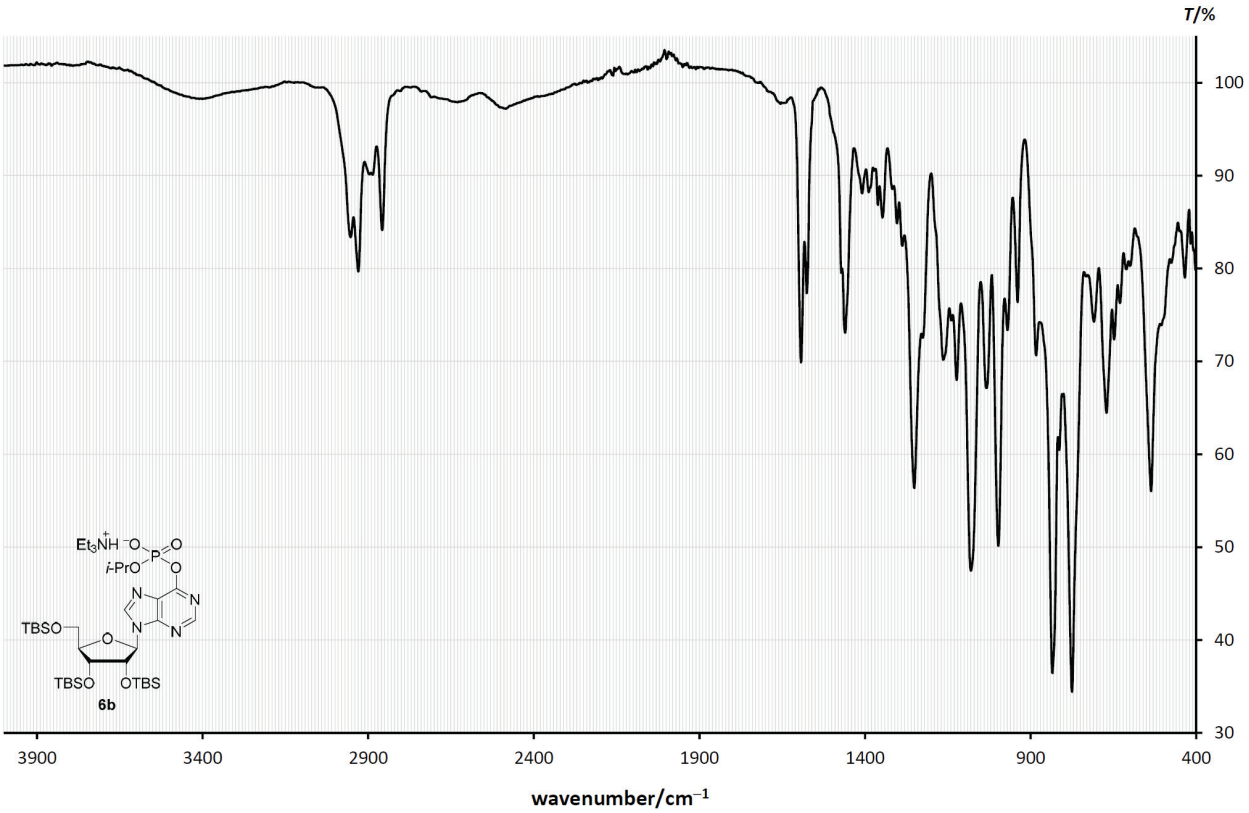
Reference for Supplementary Information

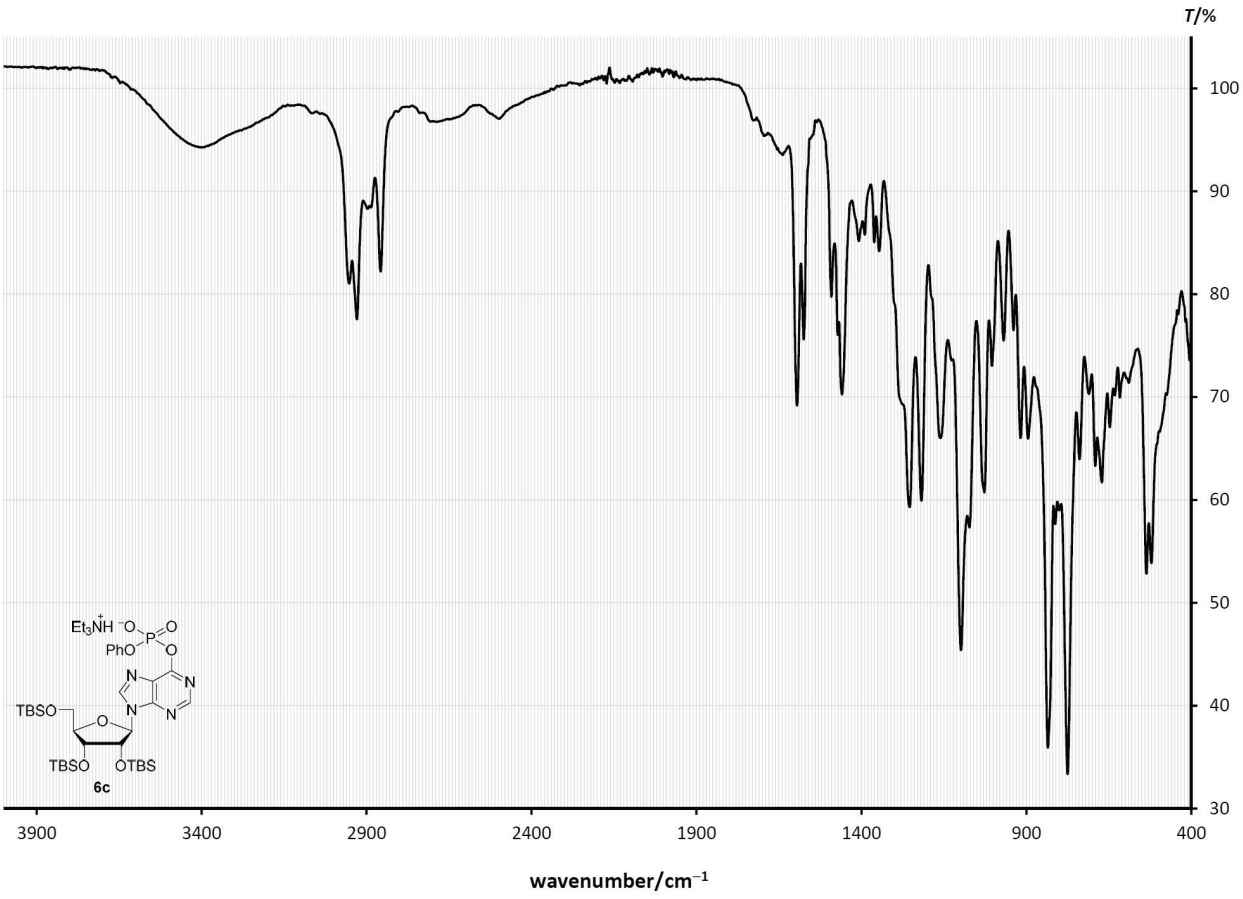
1. Nielsen, J.; Marugg, J. E.; van Boom, J. H.; Honnens, J.; Taagaard, M.; Dahl, O. *J. Chem. Res. (S)* **1986**, 26–27.

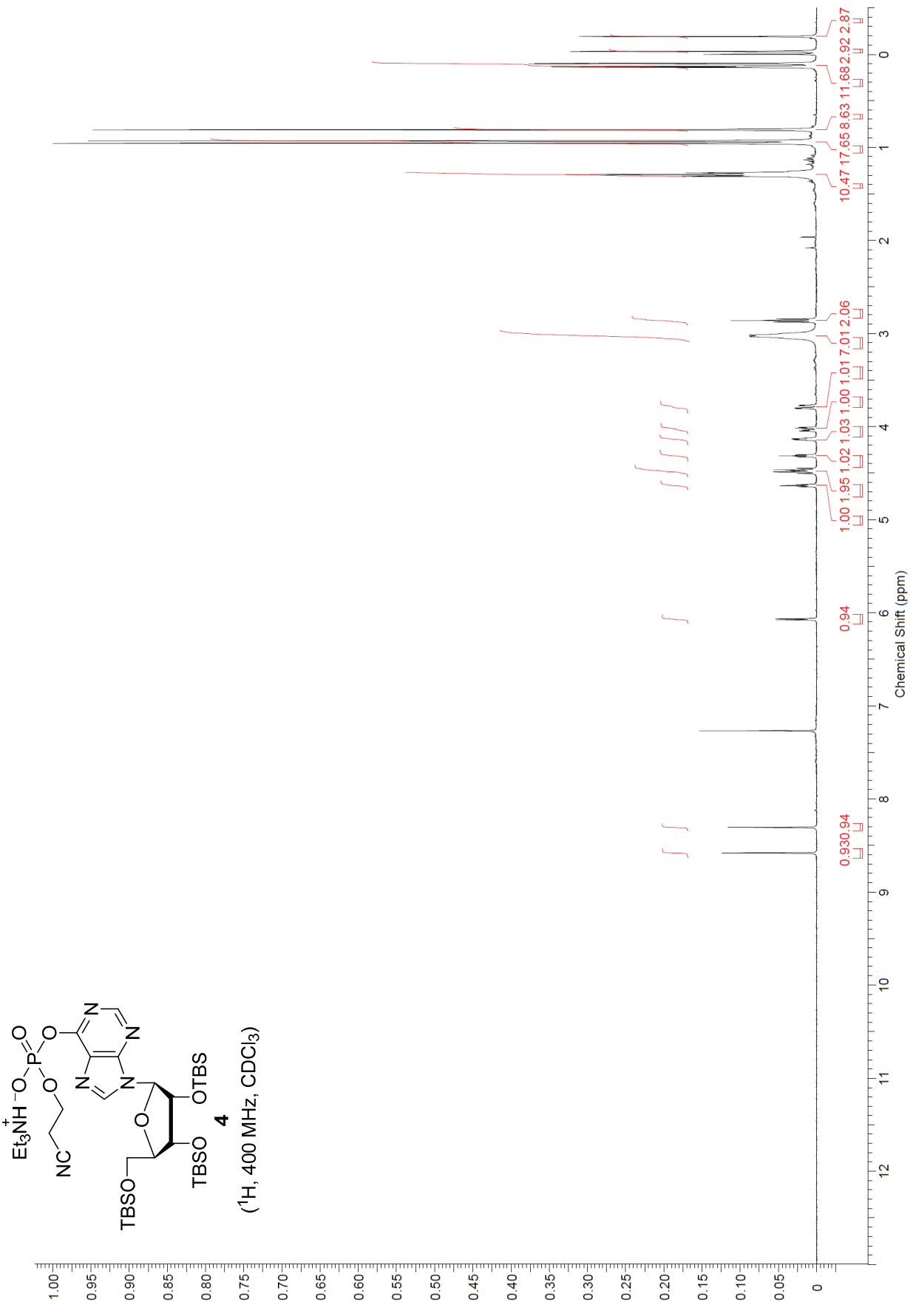

T/%
100
90
80
70
60
50
3900
3400
2900
2400
1900
1400
900
400
wavenumber/cm⁻¹
TBSO
TBSO
OTBS
1

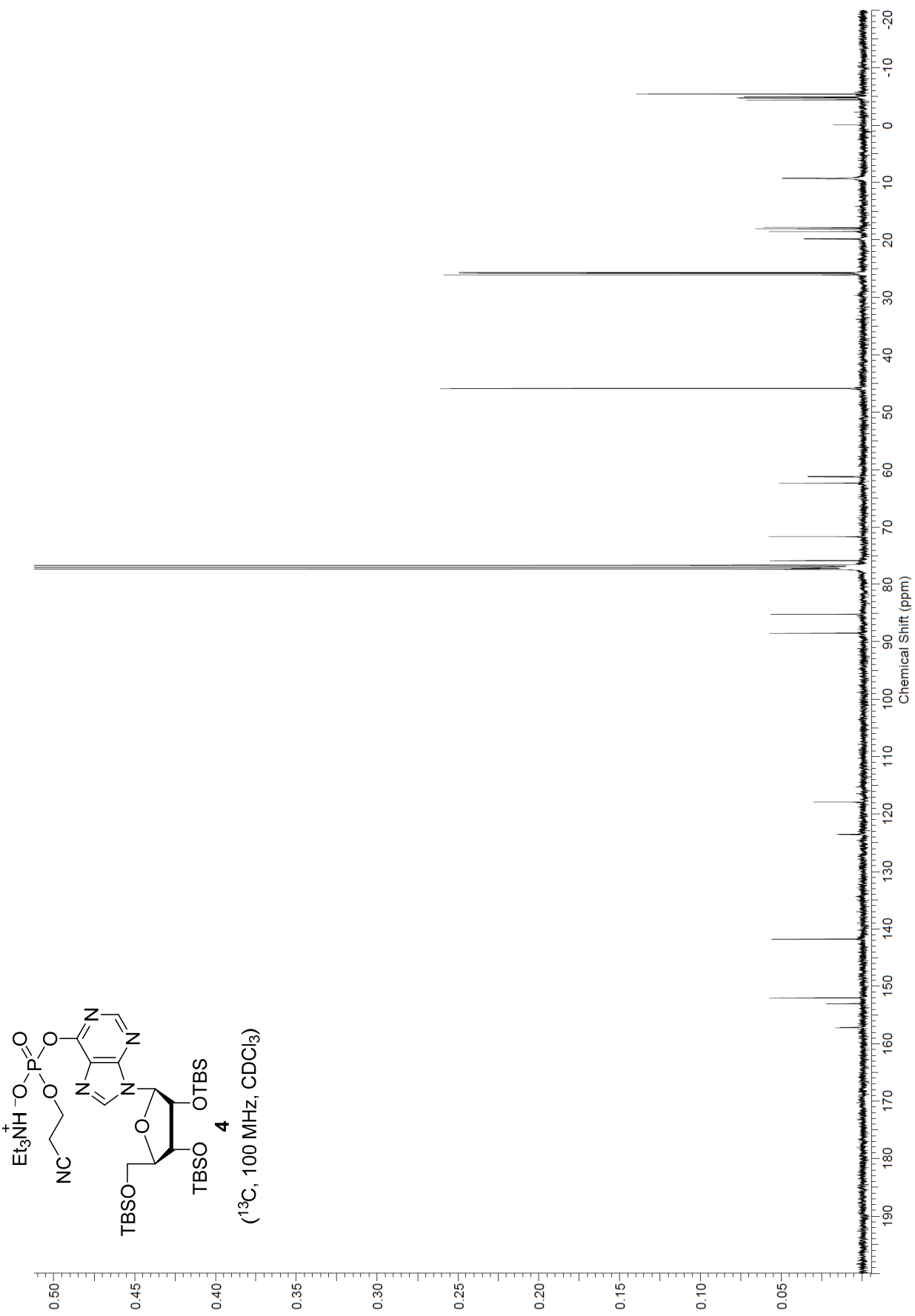

T/%
100
90
80
70
60
50
40
30
3900
3400
2900
2400
1900
1400
900
400
wavenumber/cm⁻¹
Et3NH
NC
TBSO
TBSO
OTBS
4

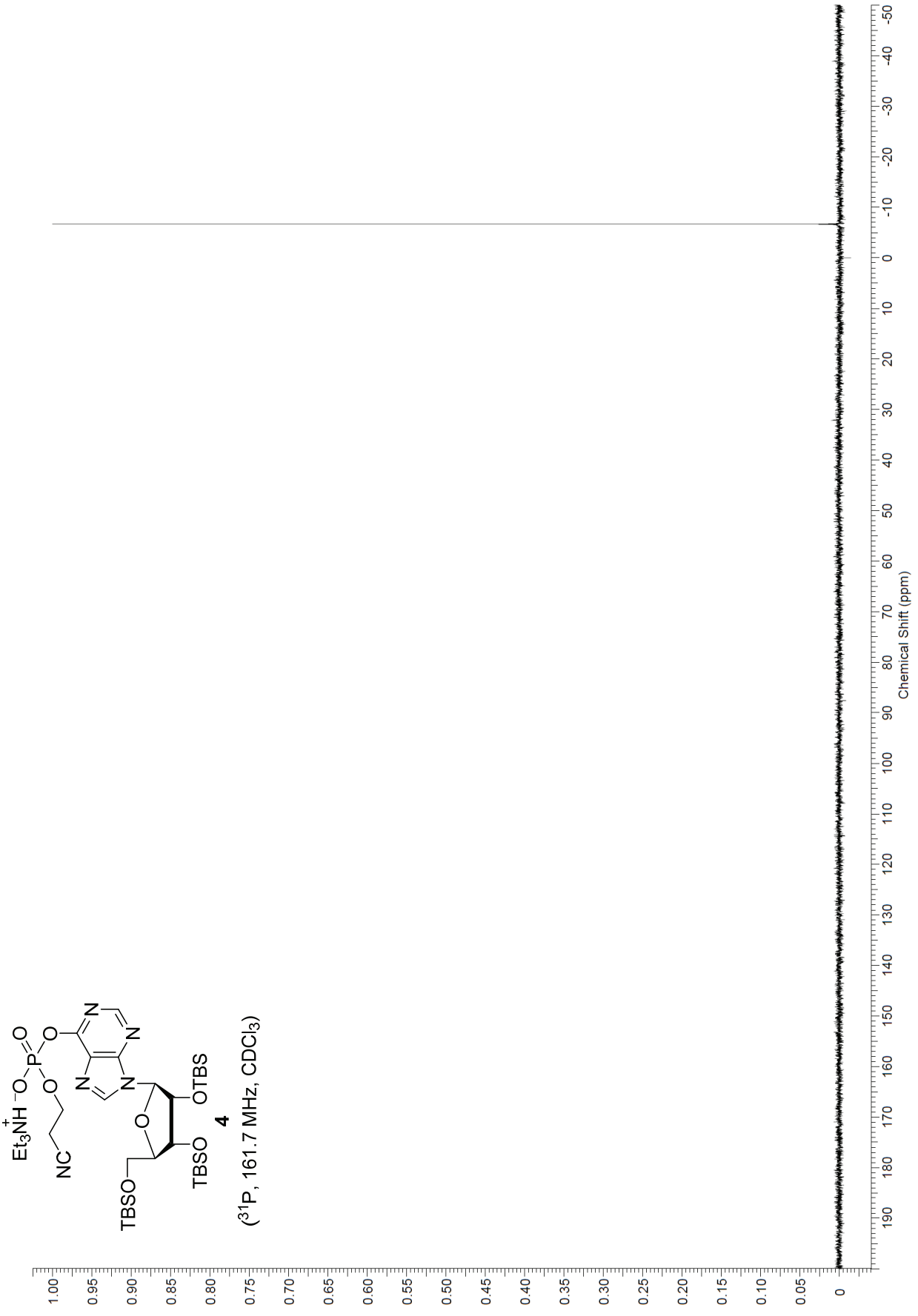

T/%
100
90
80
70
60
50
40
3900
3400
2900
2400
1900
1400
900
400
wavenumber/cm⁻¹
Et3NH
BnO
TBSO
TBSO
OTBS
6a

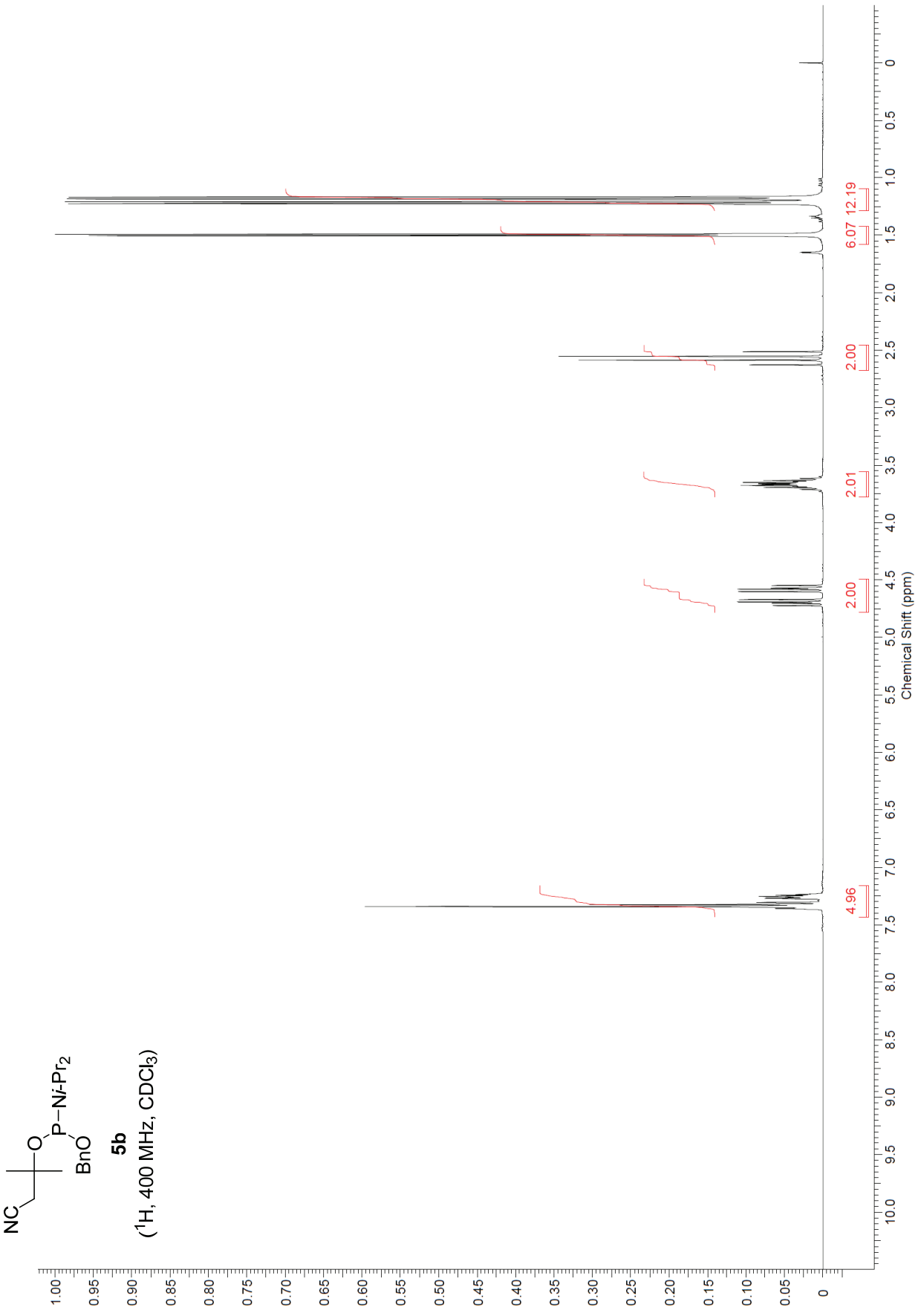

T/%
100
90
80
70
60
50
40
30
3900
3400
2900
2400
1900
1400
900
400
wavenumber/cm⁻¹
Et3NH
i-PrO
TBSO
TBSO
OTBS
6b

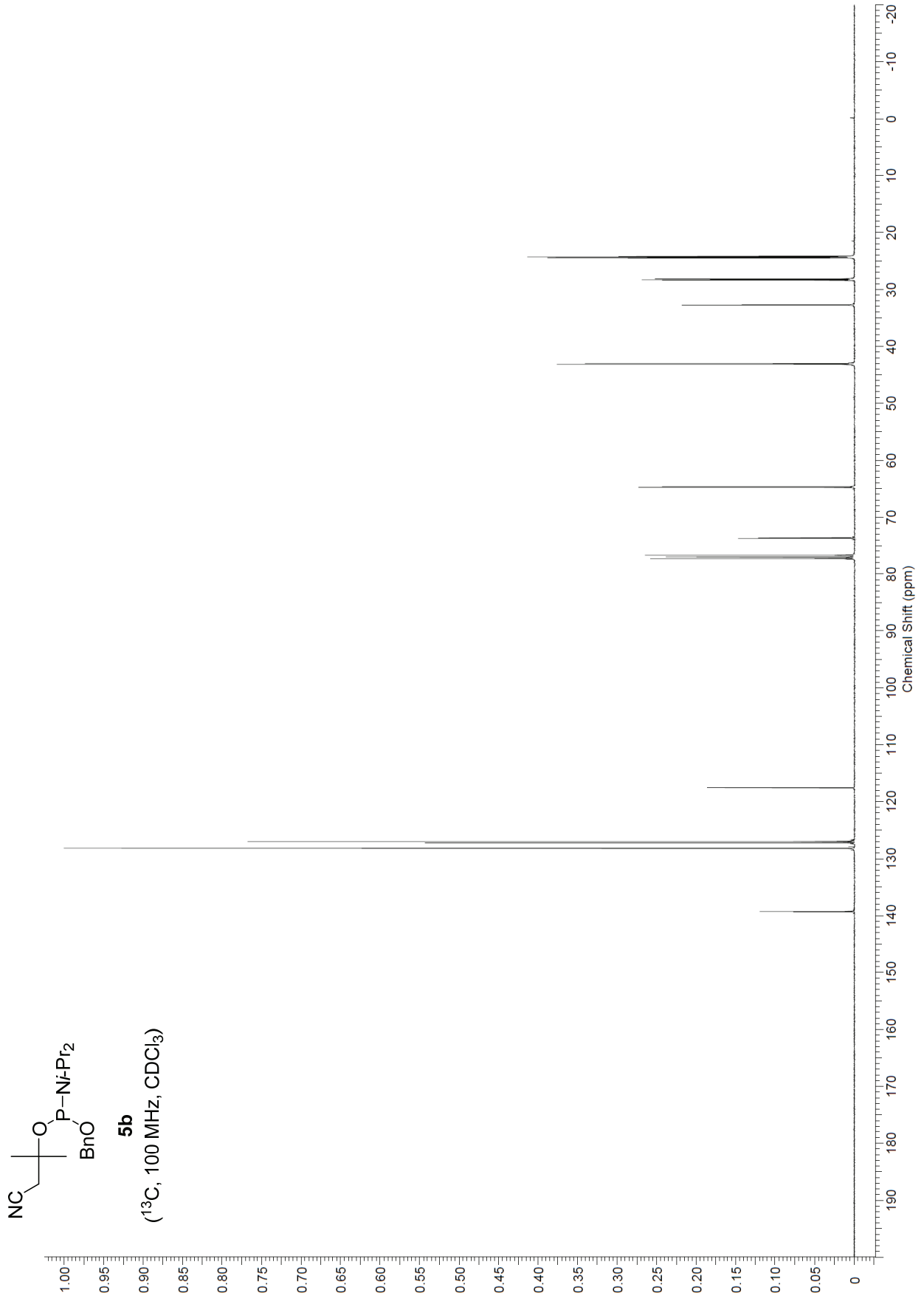

T/%
100
90
80
70
60
50
40
30
3900
3400
2900
2400
1900
1400
900
400
wavenumber/cm⁻¹
Et3NH
PhO
TBSO
TBSO
OTBS
6c

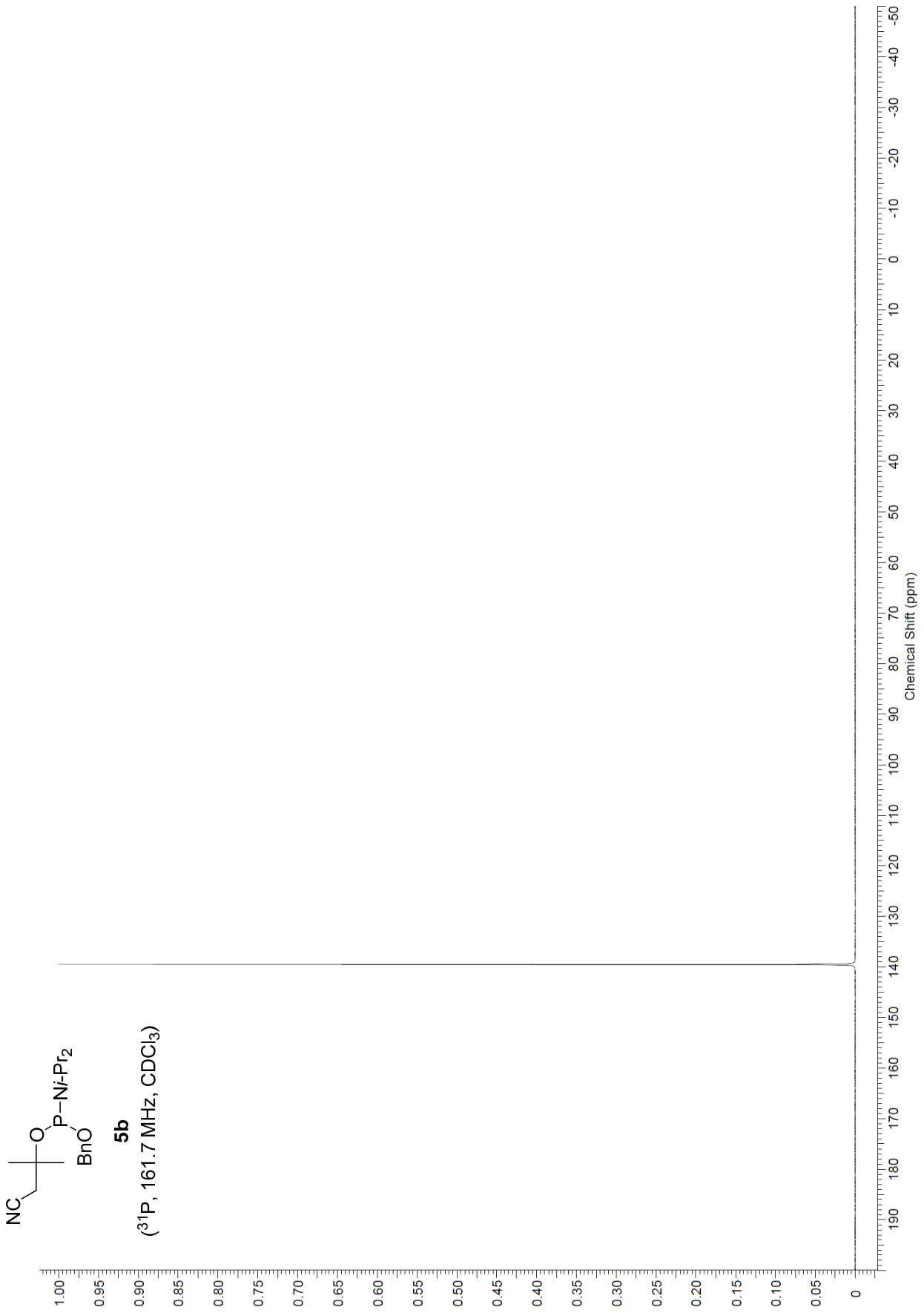


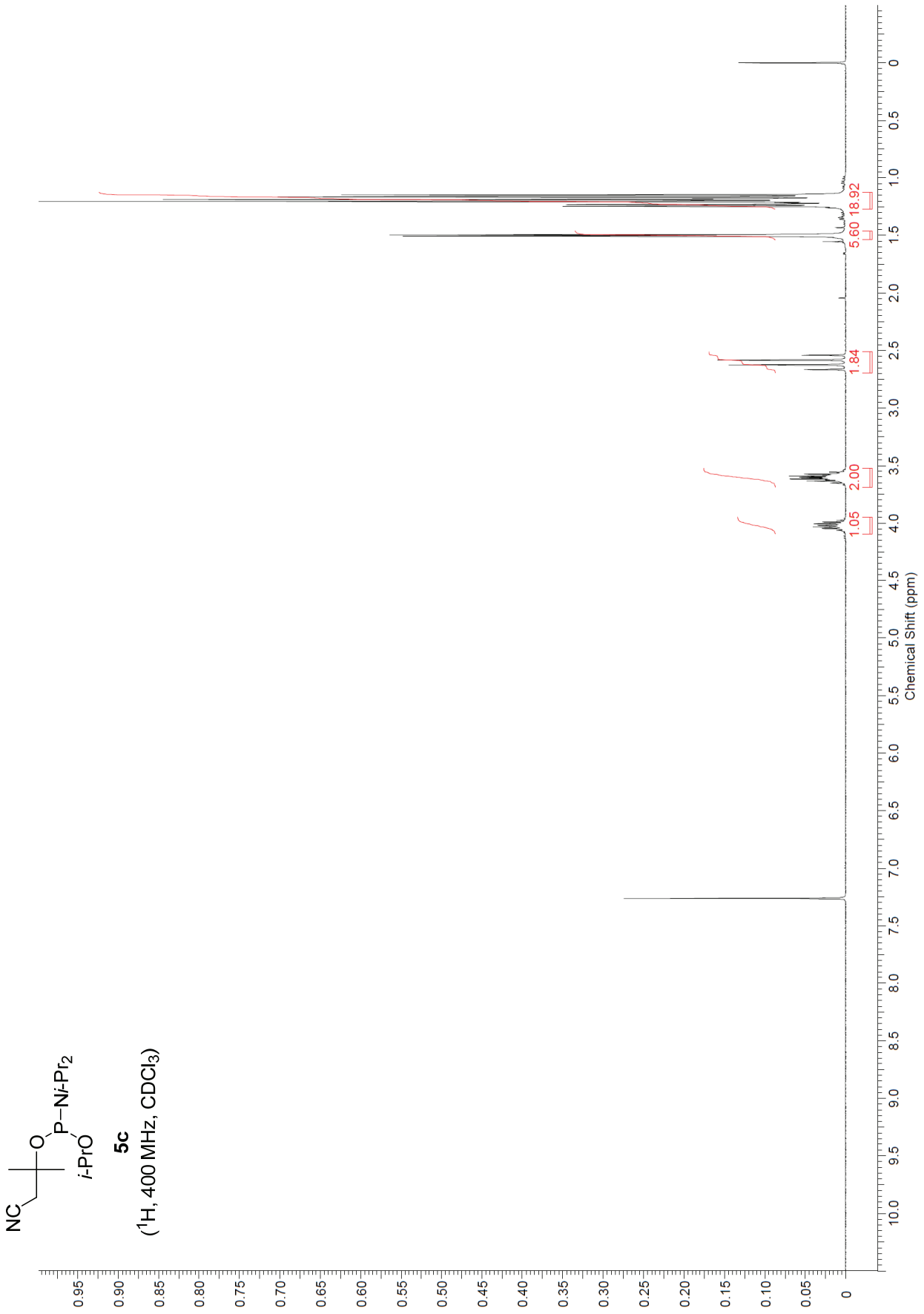


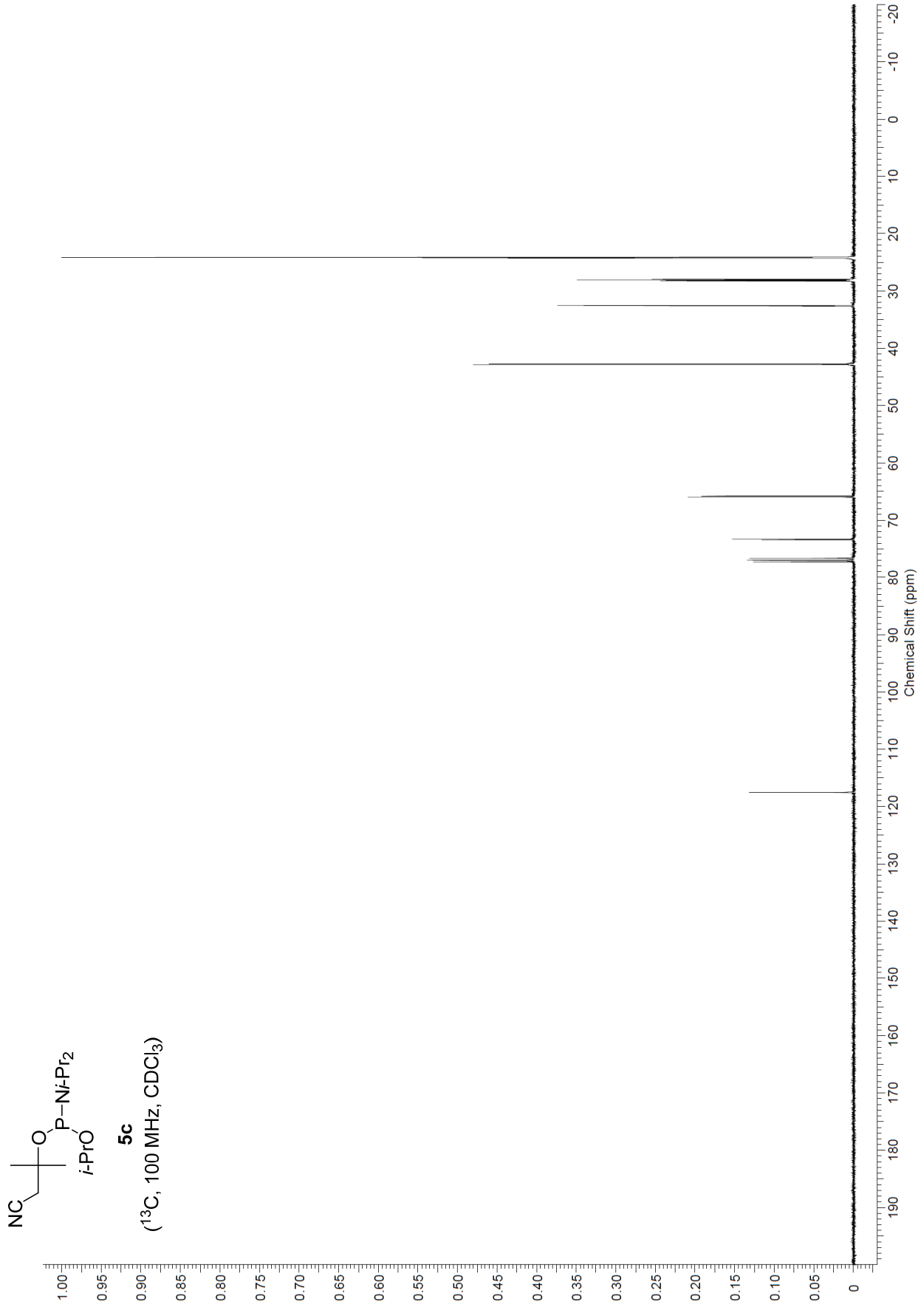

Et3NH
NC
TBSO
TBSO
OTBS
4
(31P, 161.7 MHz, CDCl3)
Chemical Shift (ppm)

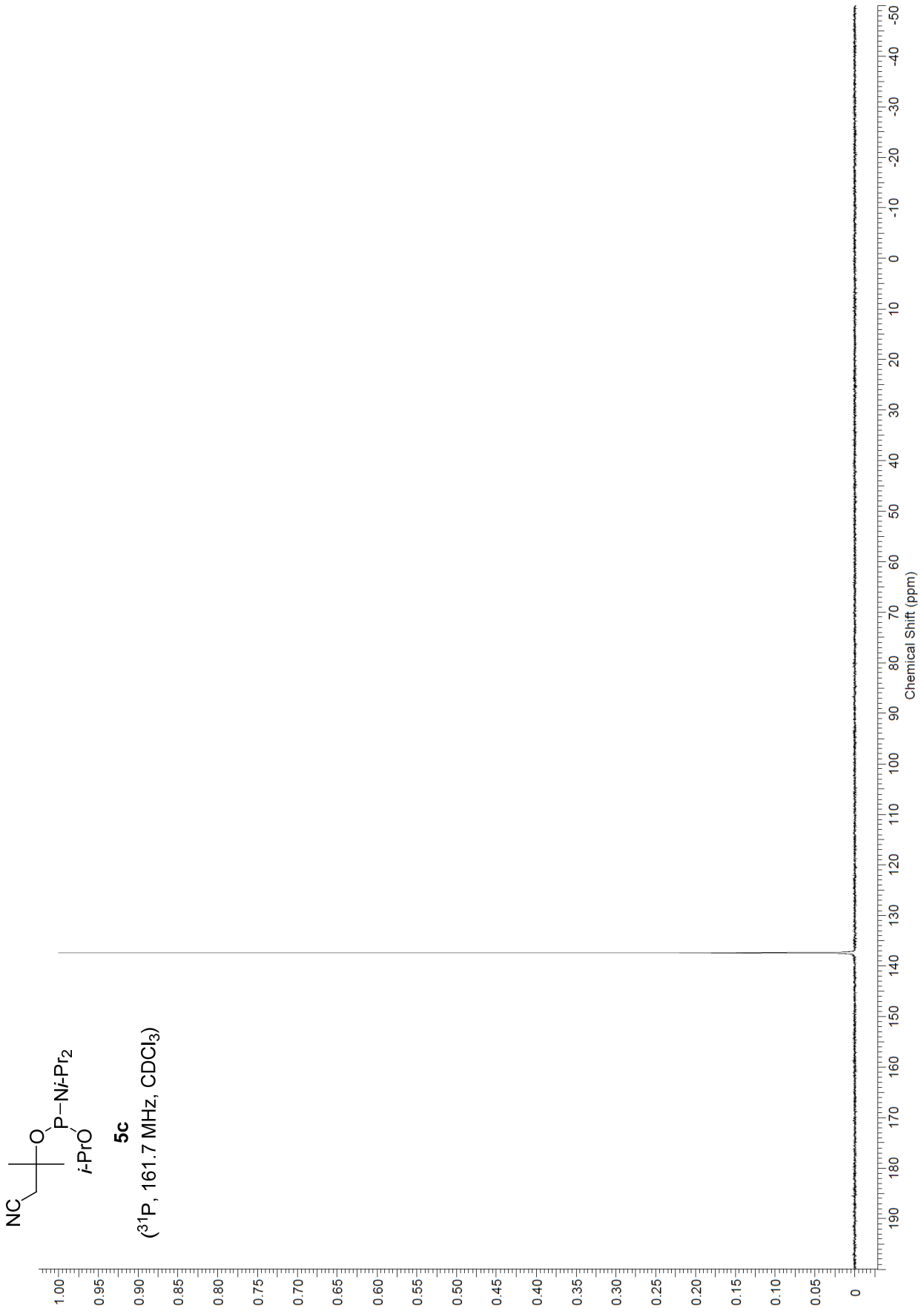

NC
O
P–N*i*-Pr$_2$
BnO
5b
(^{1}H, 400 MHz, CDCl$_3$)
4.96
2.00
2.01
2.00
6.07
12.19
Chemical Shift (ppm)

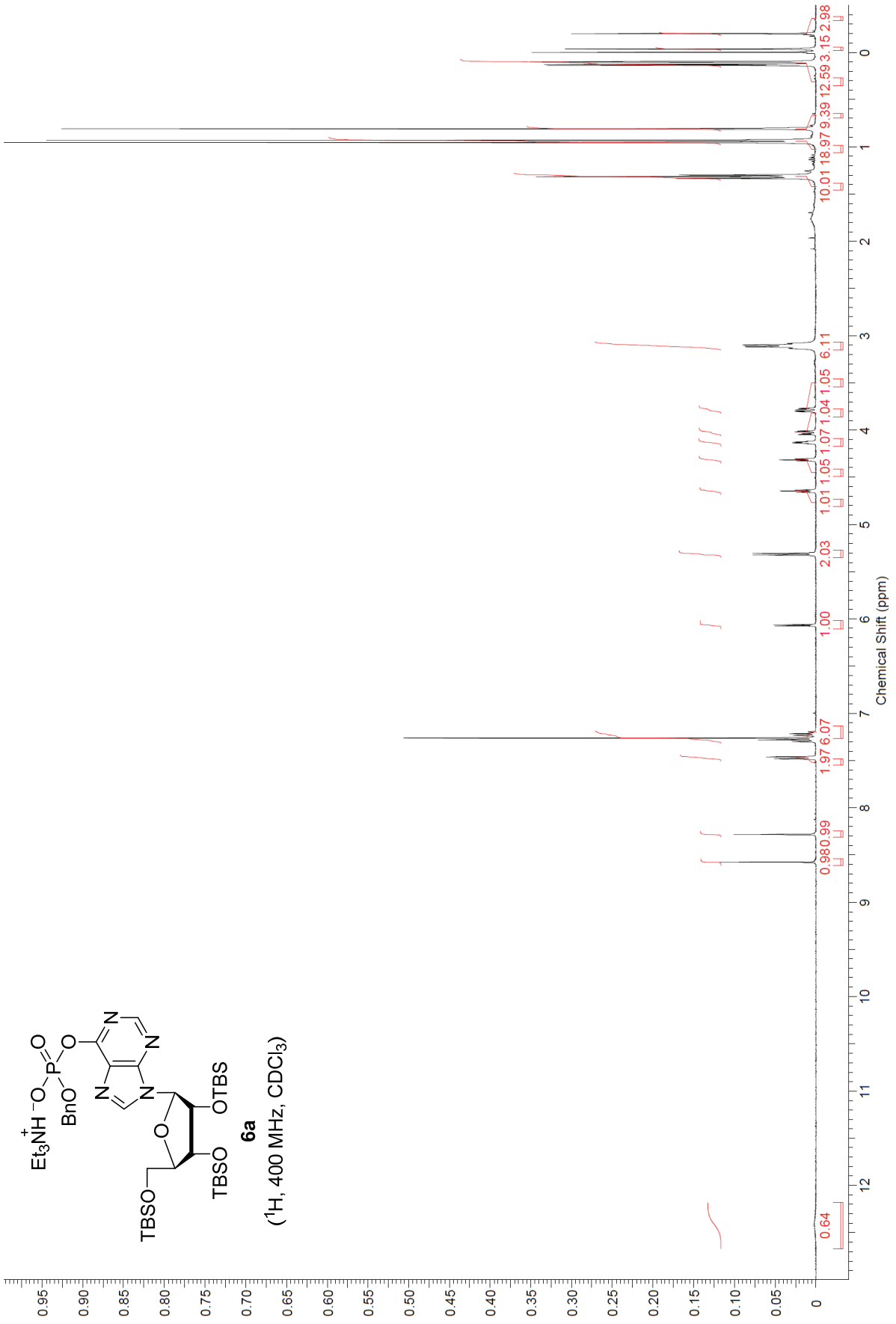

NC
O
P–N-Pr2
BnO
5b
(13C, 100 MHz, CDCl3)
Chemical Shift (ppm)

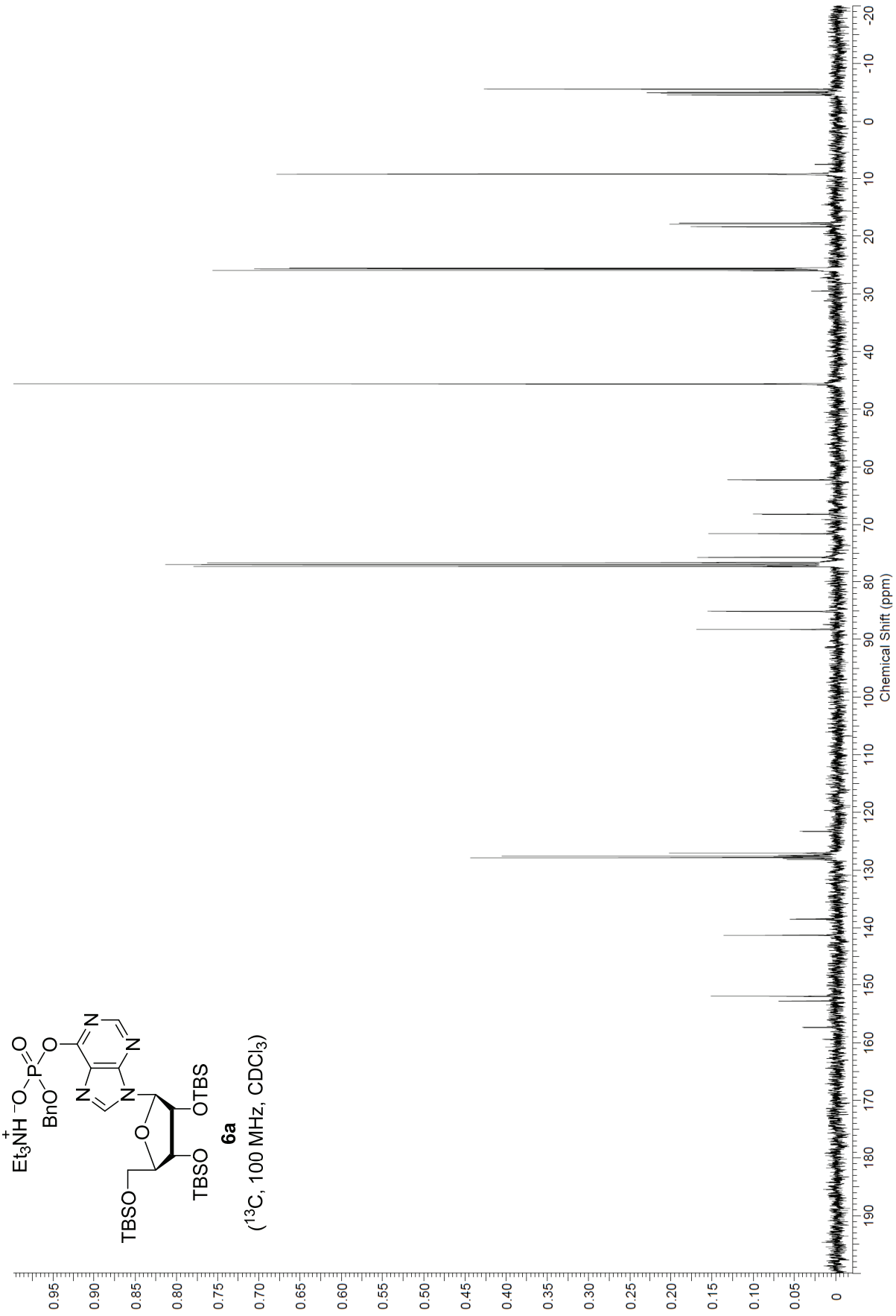

NC
O
P–N*i*-Pr$_2$
BnO
5b
(^{31}P, 161.7 MHz, CDCl$_3$)
Chemical Shift (ppm)

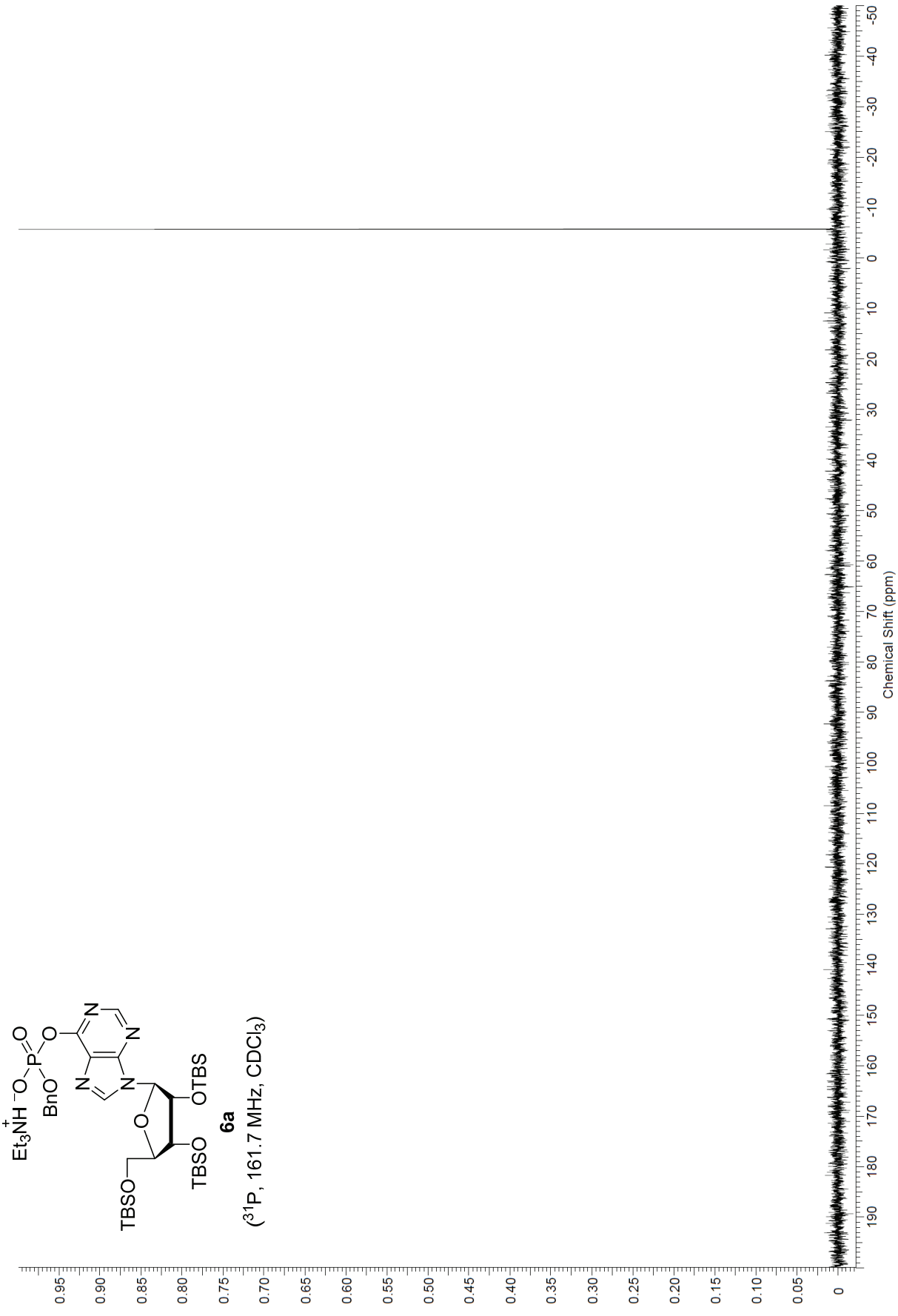

NC
O
P–N*i*-Pr$_2$
i-PrO
5c
(^{1}H, 400 MHz, CDCl$_3$)
1.05
2.00
1.84
5.60
18.92
Chemical Shift (ppm)

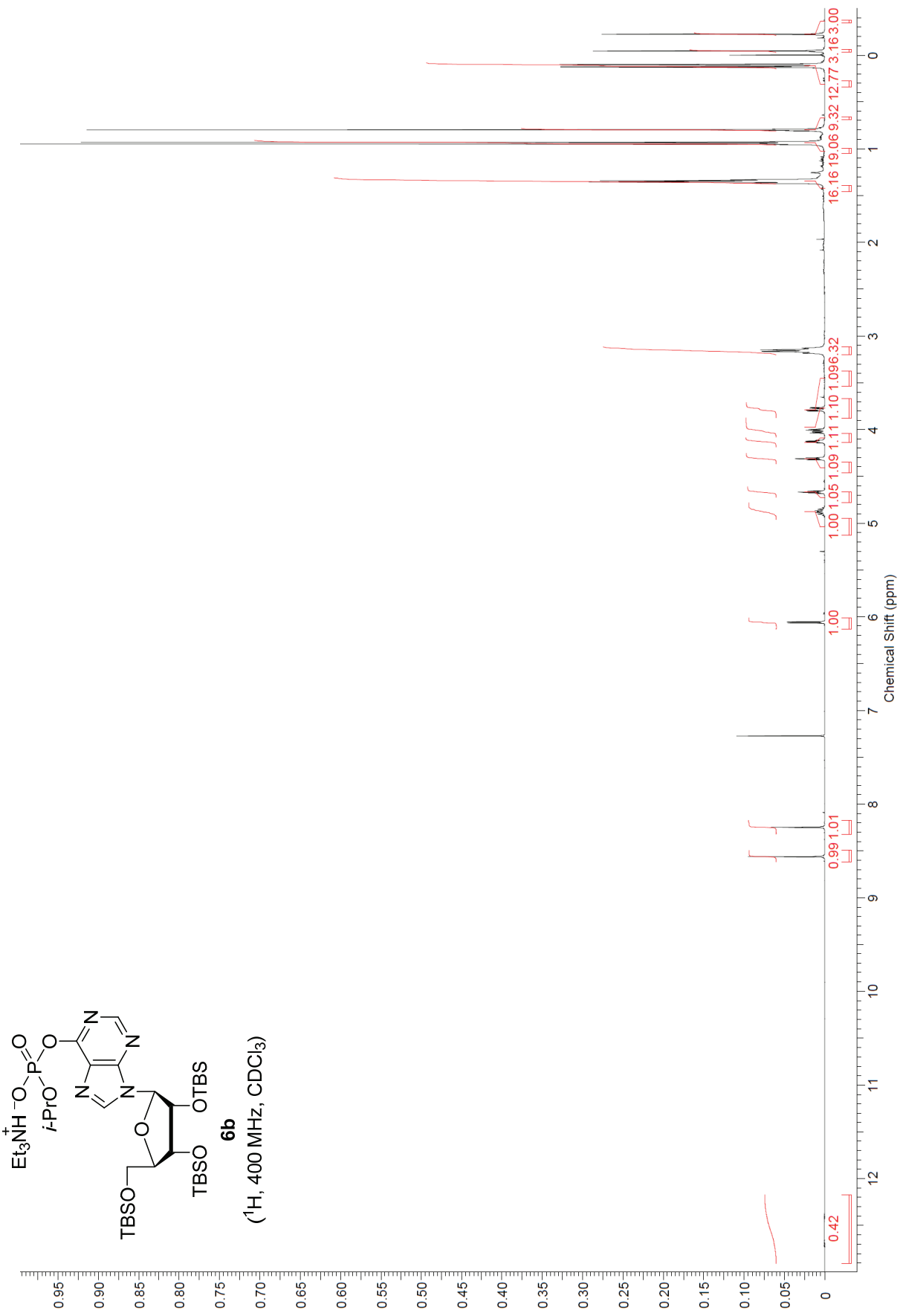


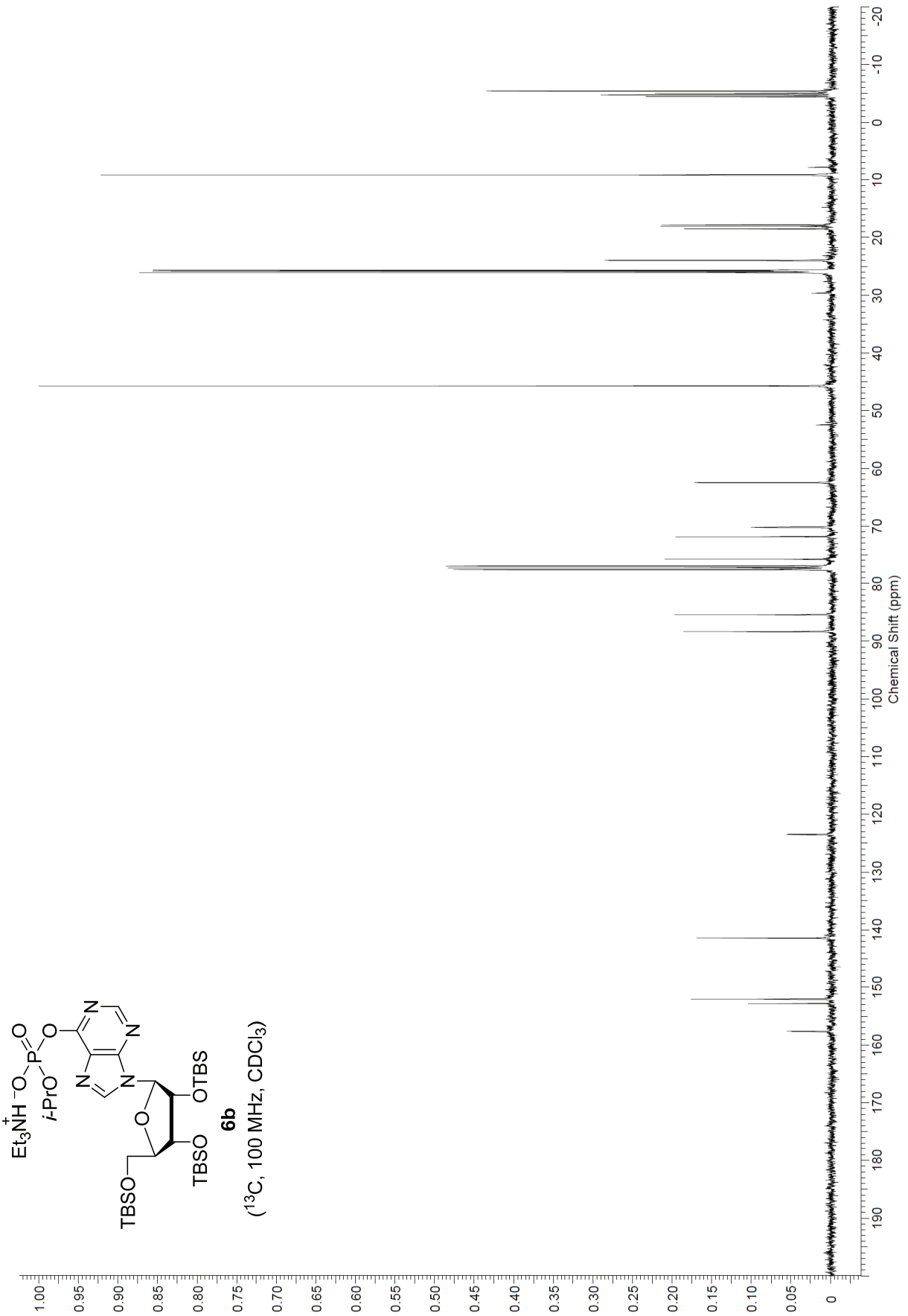

NC
O
P–N*i*-Pr$_2$
i-PrO
5c
(^{31}P, 161.7 MHz, $CDCl_3$)
Chemical Shift (ppm)

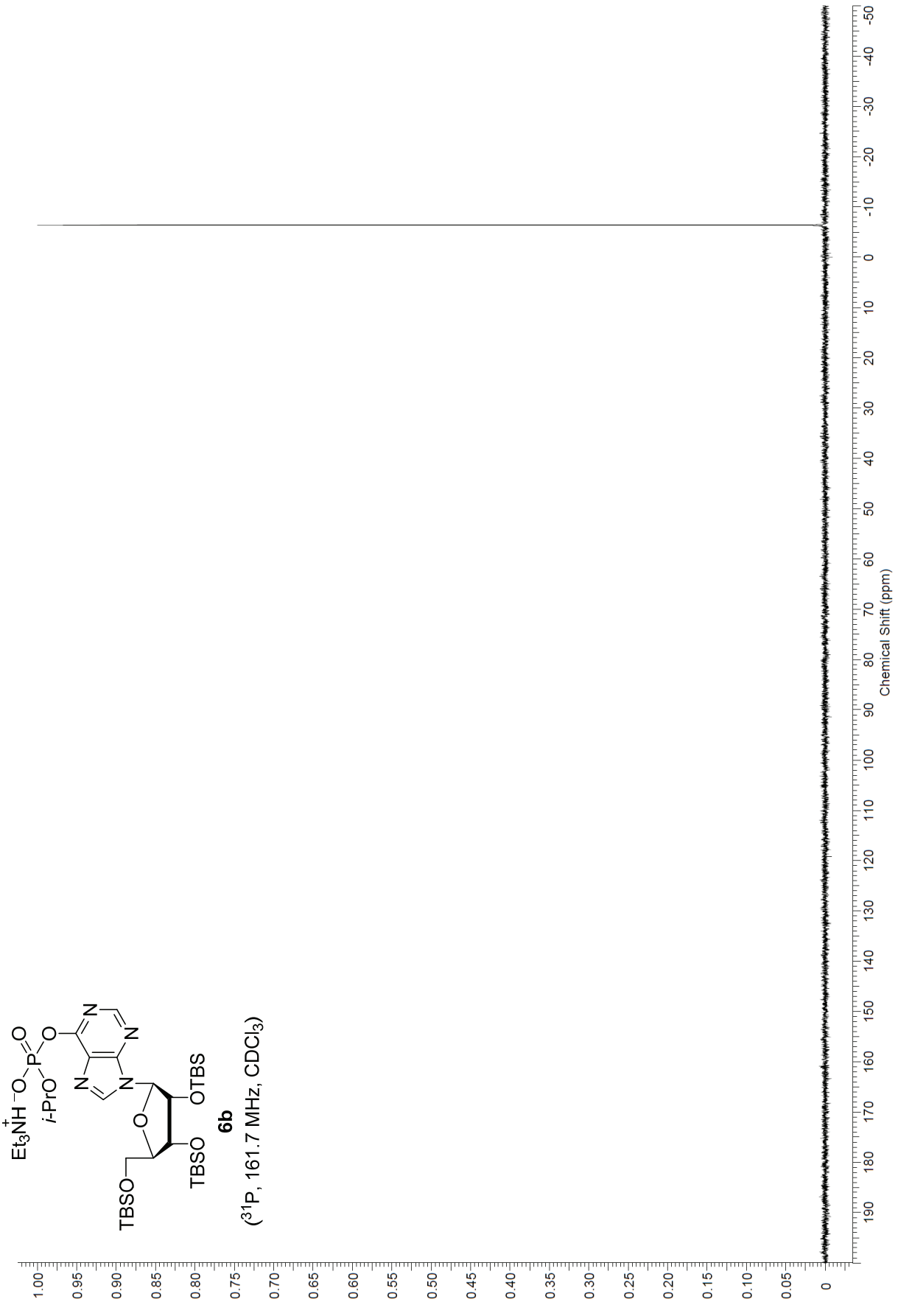

Et3NH+ −O
BnO
TBSO
TBSO
OTBS
6a
(1H, 400 MHz, CDCl3)
Chemical Shift (ppm)

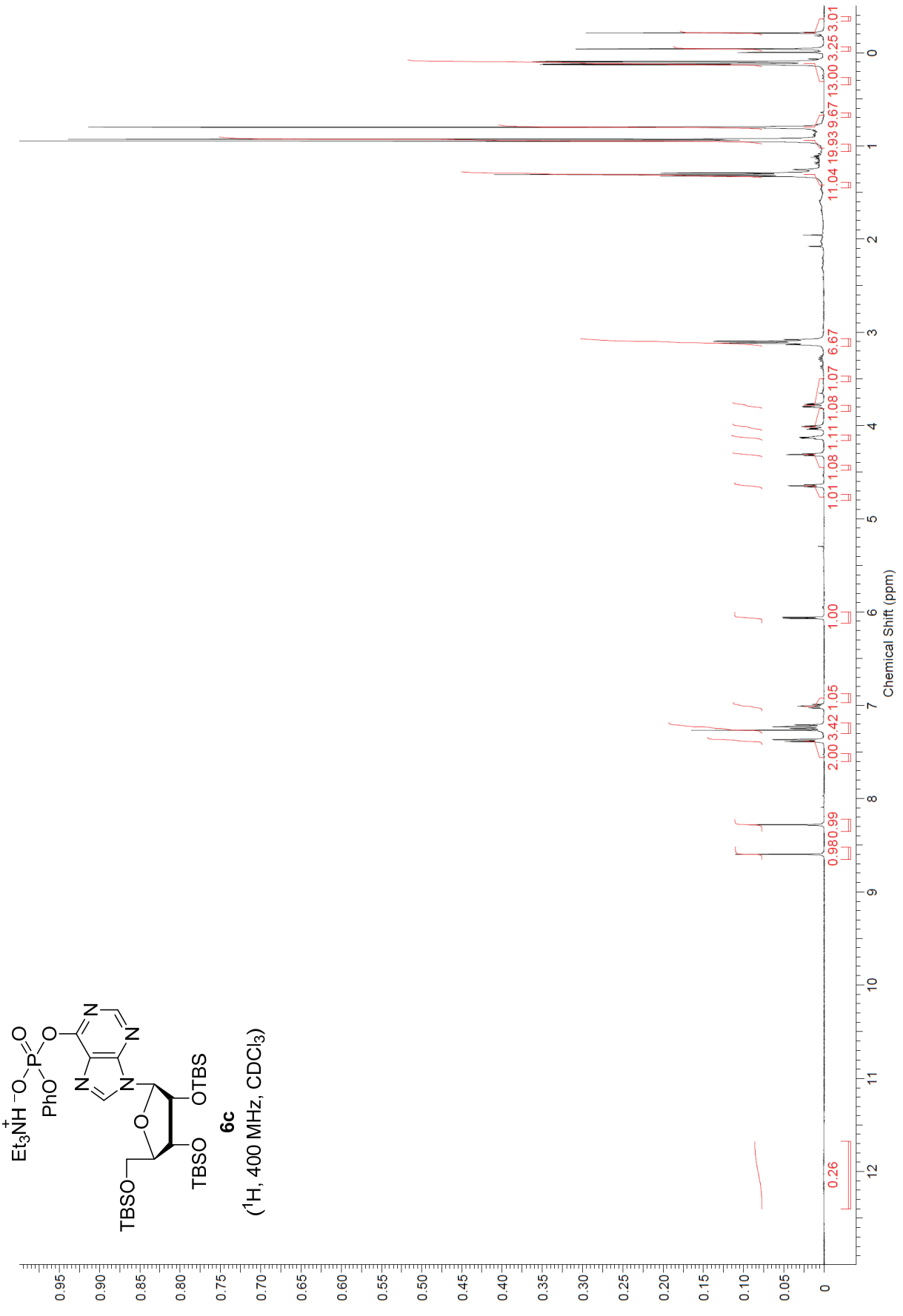

Et3NH+ −O
BnO
P
O
O
N
N
N
N
O
TBSO
TBSO
OTBS
6a
(13C, 100 MHz, CDCl3)
Chemical Shift (ppm)

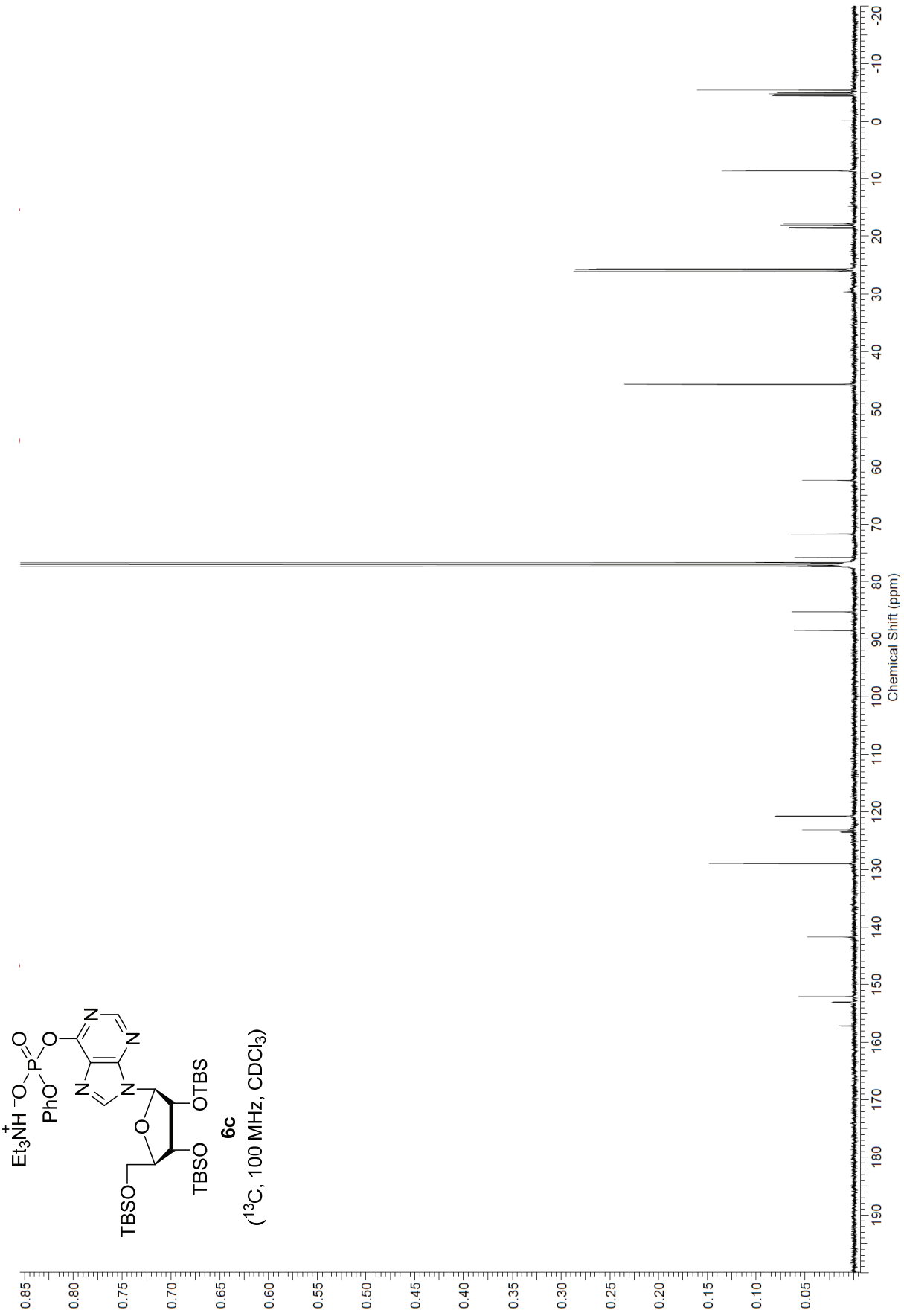

Et3NH+ −O
BnO
TBSO
TBSO
OTBS
6a
(31P, 161.7 MHz, CDCl3)
Chemical Shift (ppm)

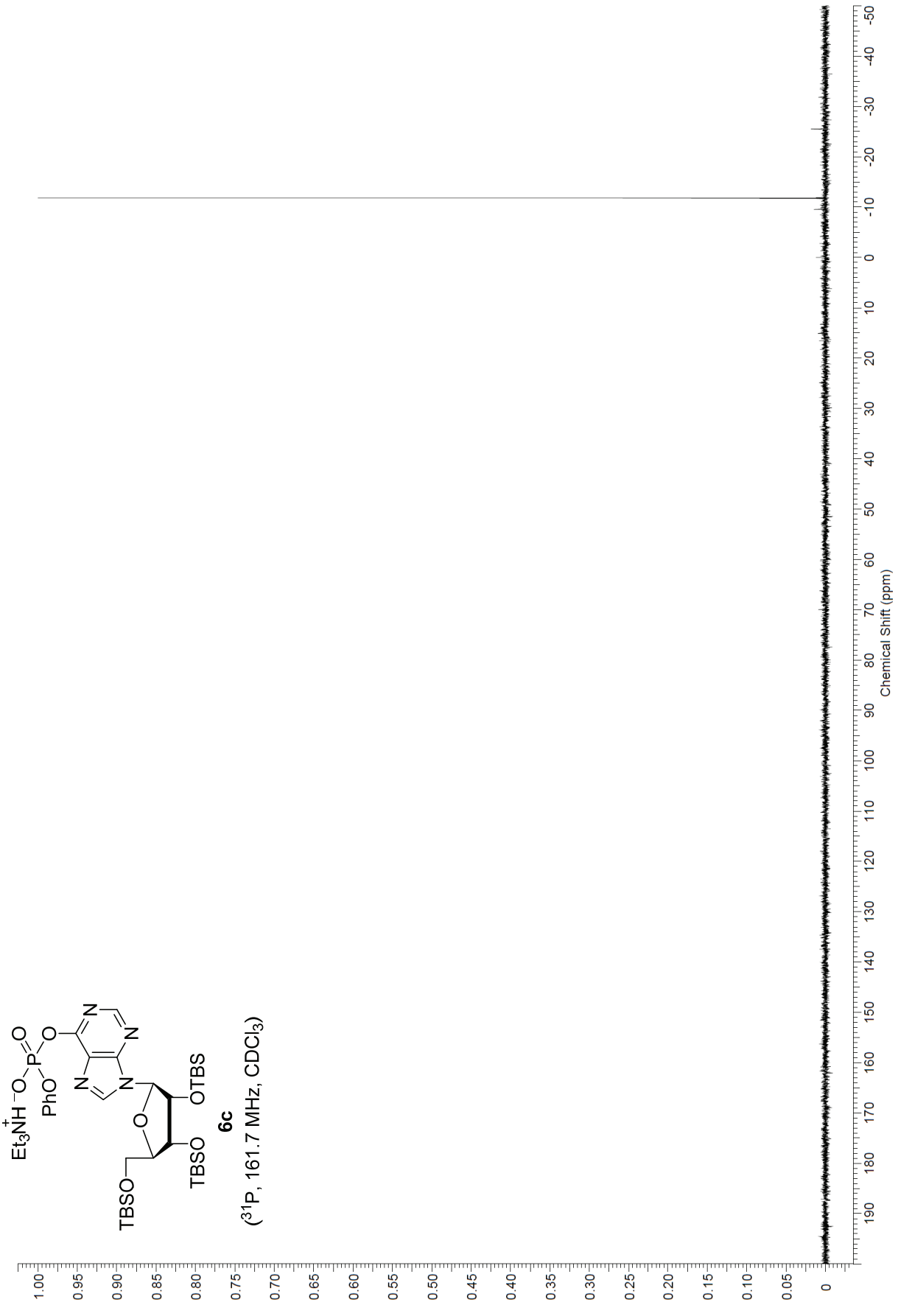

Et3NH+ −O
i-PrO
TBSO
TBSO
OTBS
6b
(1H, 400 MHz, CDCl3)
Chemical Shift (ppm)
0.42
0.99 1.01
1.00
1.00 1.05 1.09 1.11 1.10 1.09 6.32
16.16 19.06 9.32 12.77 3.16 3.00


Et3NH+ −O
i-PrO
TBSO
TBSO
OTBS
6b
(13C, 100 MHz, CDCl3)
Chemical Shift (ppm)


Et3NH+ −O
i-PrO
TBSO
TBSO
OTBS
6b
(31P, 161.7 MHz, CDCl3)
Chemical Shift (ppm)

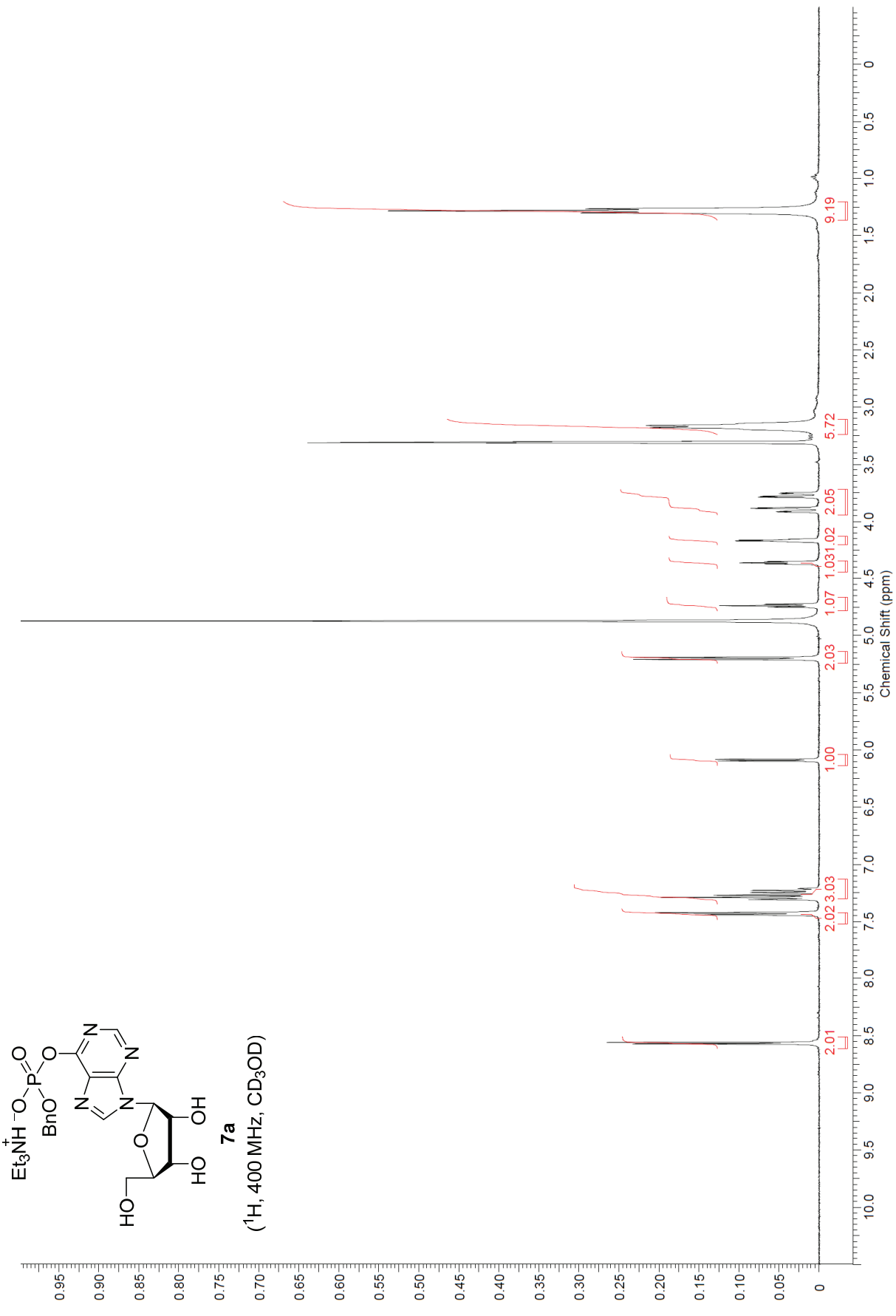

Et3NH+ −O
PhO
O
P
O
N
N
N
N
O
TBSO
OTBS
TBSO
6c
(1H, 400 MHz, CDCl3)
0.26
0.98 0.99
2.00 3.42 1.05
1.00
1.01 1.08 1.11 1.08 1.07 6.67
11.04 19.93 9.67 13.00 3.25 3.01
Chemical Shift (ppm)

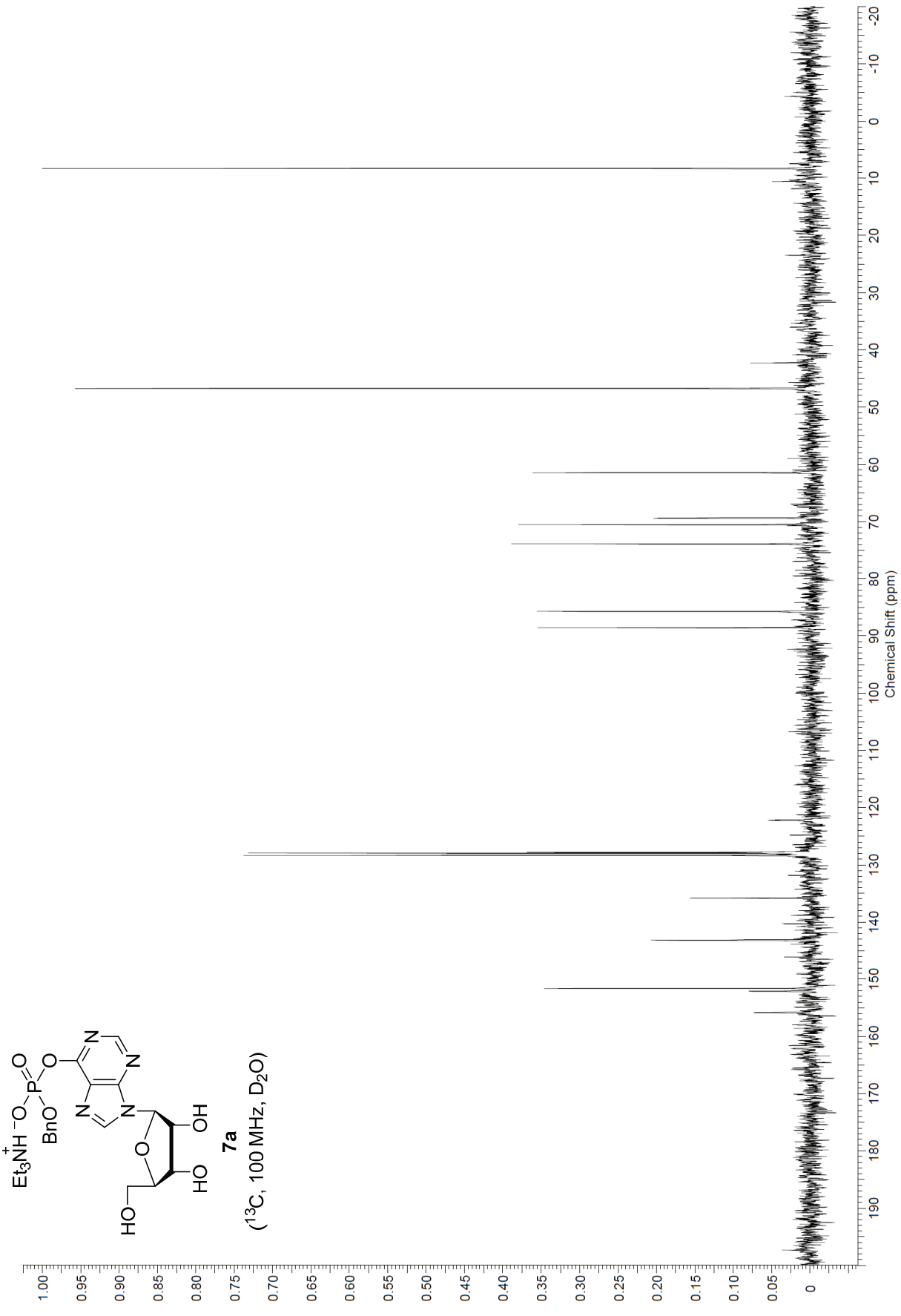

Et3NH+ −O
PhO
O
P
O
O
N
N
N
N
O
TBSO
TBSO
OTBS
6c
(13C, 100 MHz, CDCl3)
Chemical Shift (ppm)

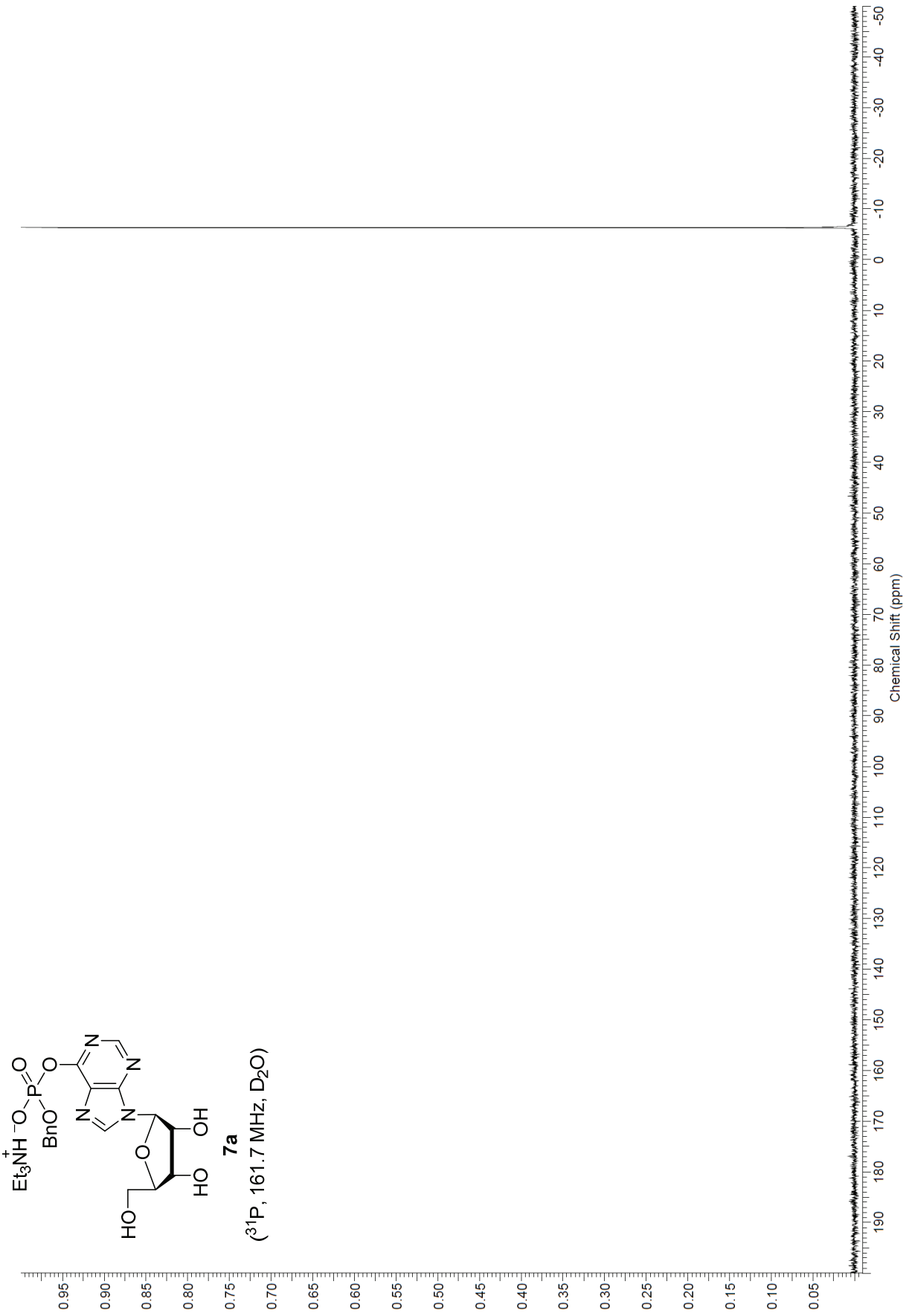


6c

(^{31}P, 161.7 MHz, $CDCl_3$)

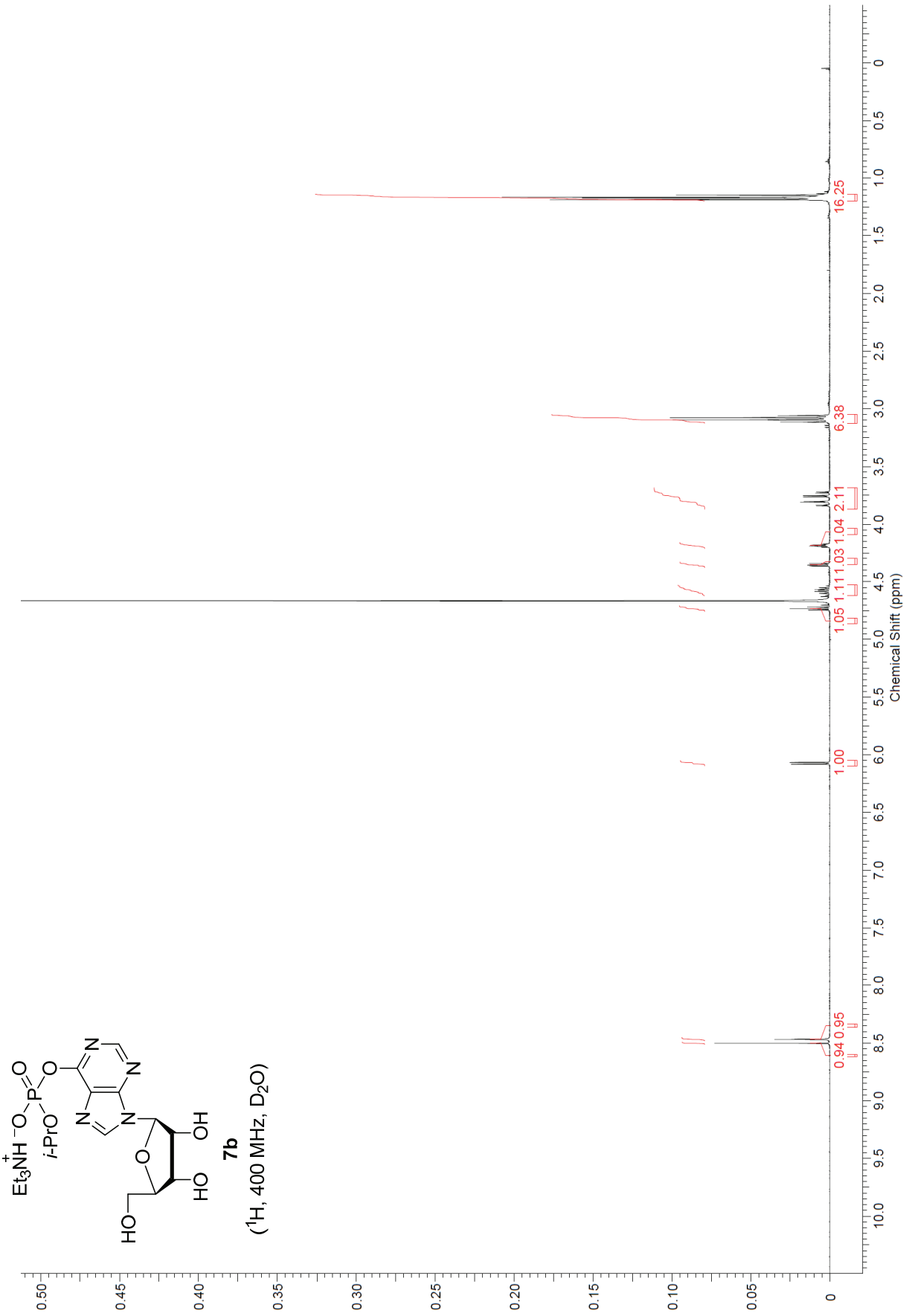

Et3NH+ −O
BnO
O
P
O
N
N
N
N
O
HO
HO
OH
7a
(1H, 400 MHz, CD3OD)
2.01
2.02
3.03
1.00
2.03
1.07
1.03
1.02
2.05
5.72
9.19
Chemical Shift (ppm)

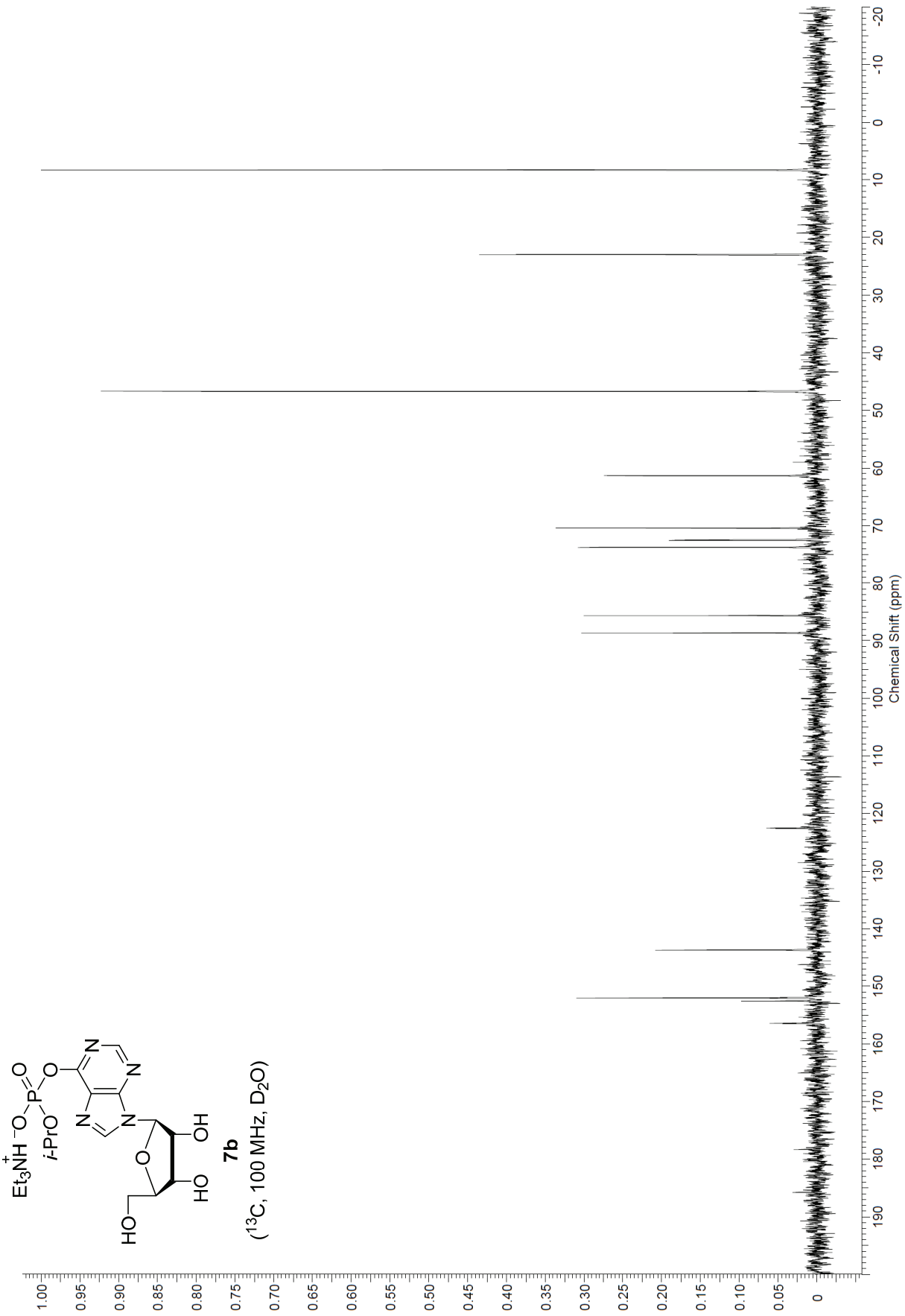


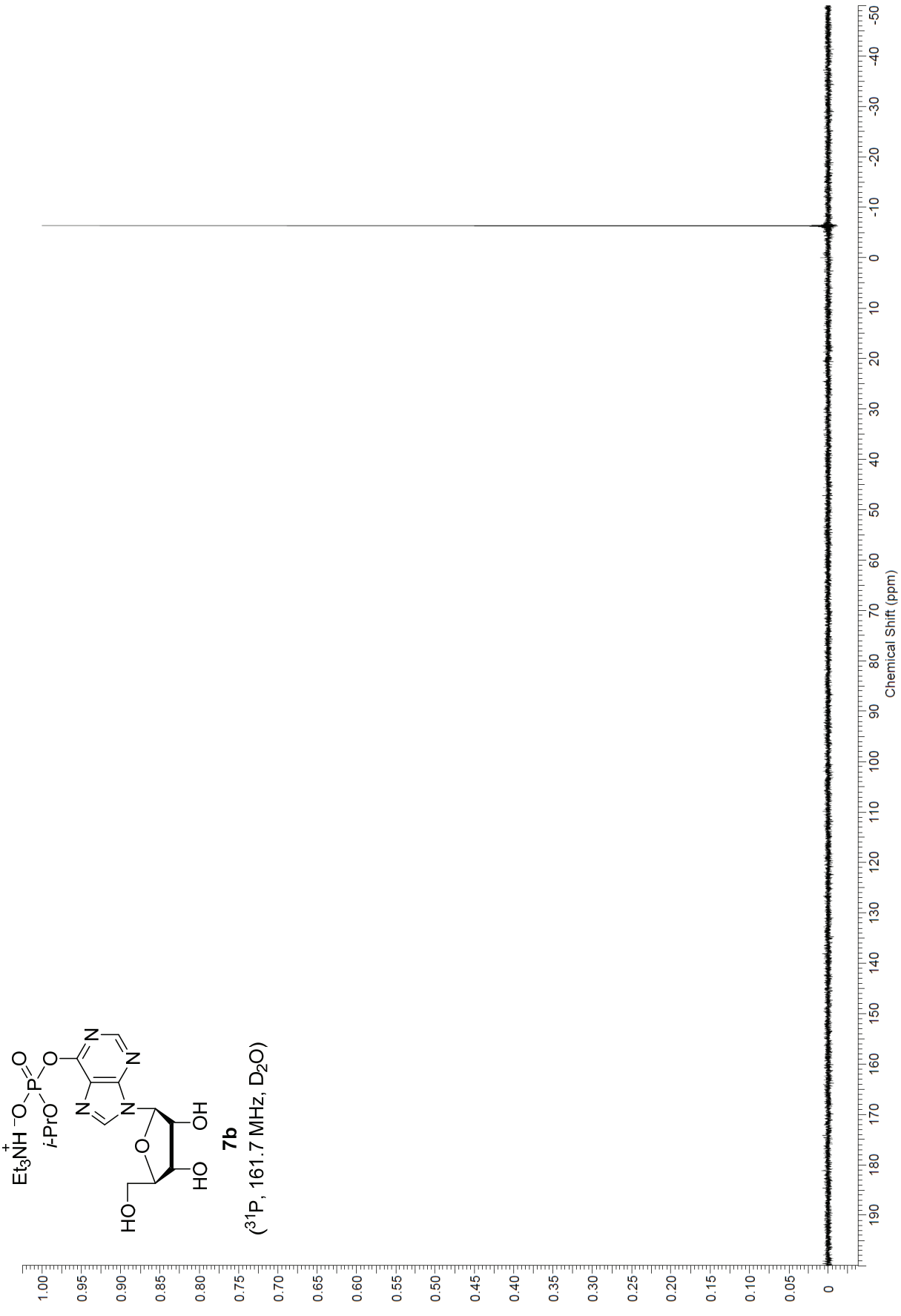


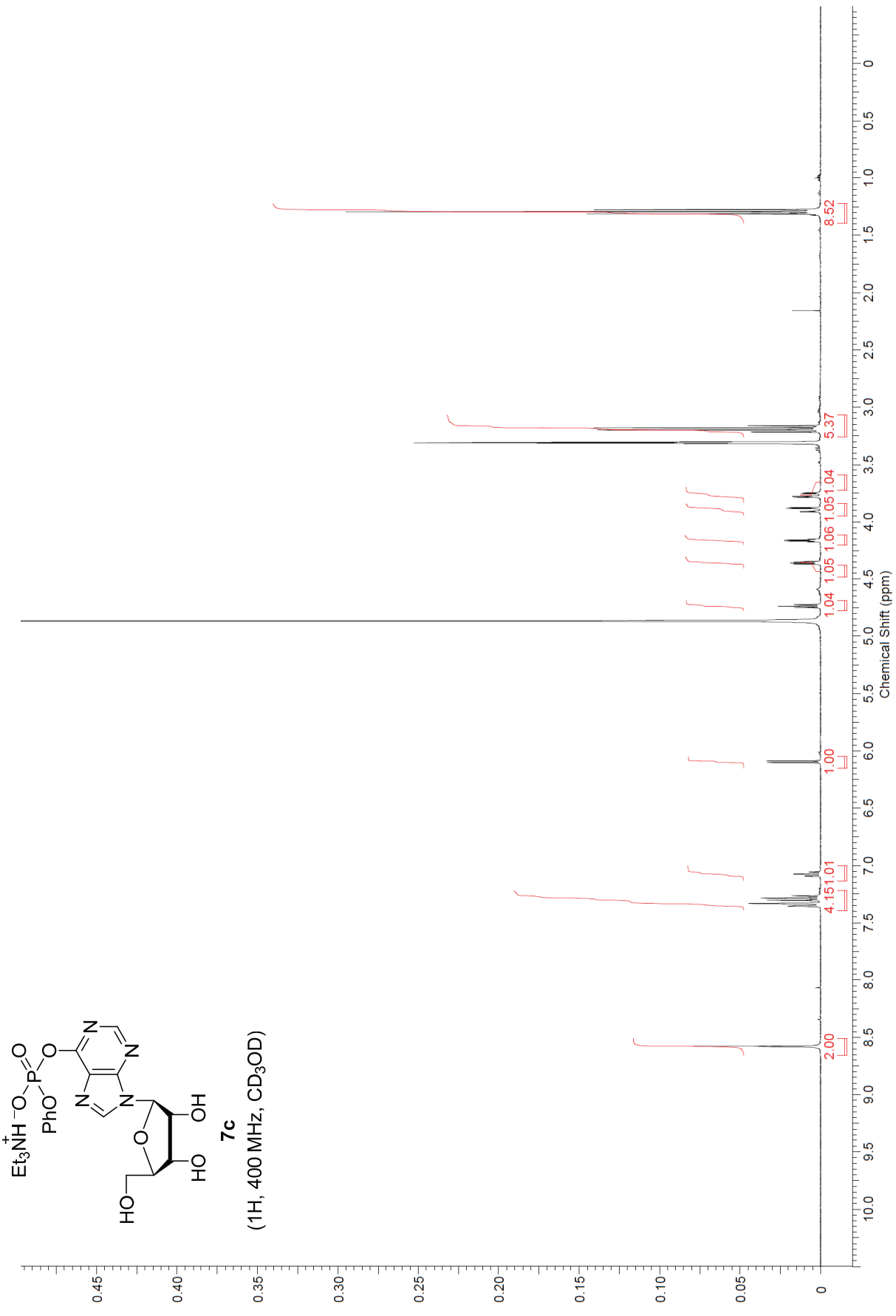
7a

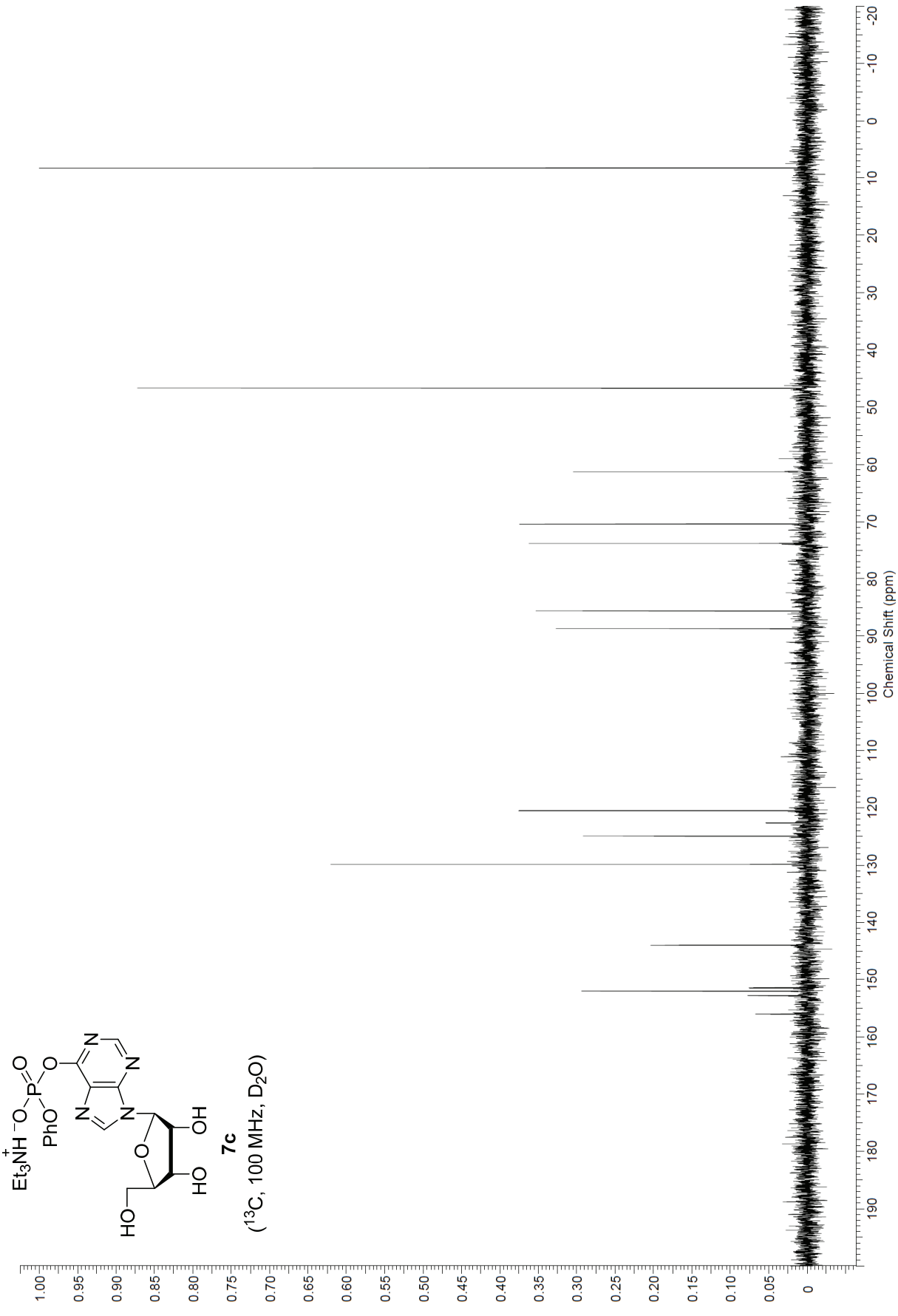
(^{31}P, 161.7 MHz, D_2O)

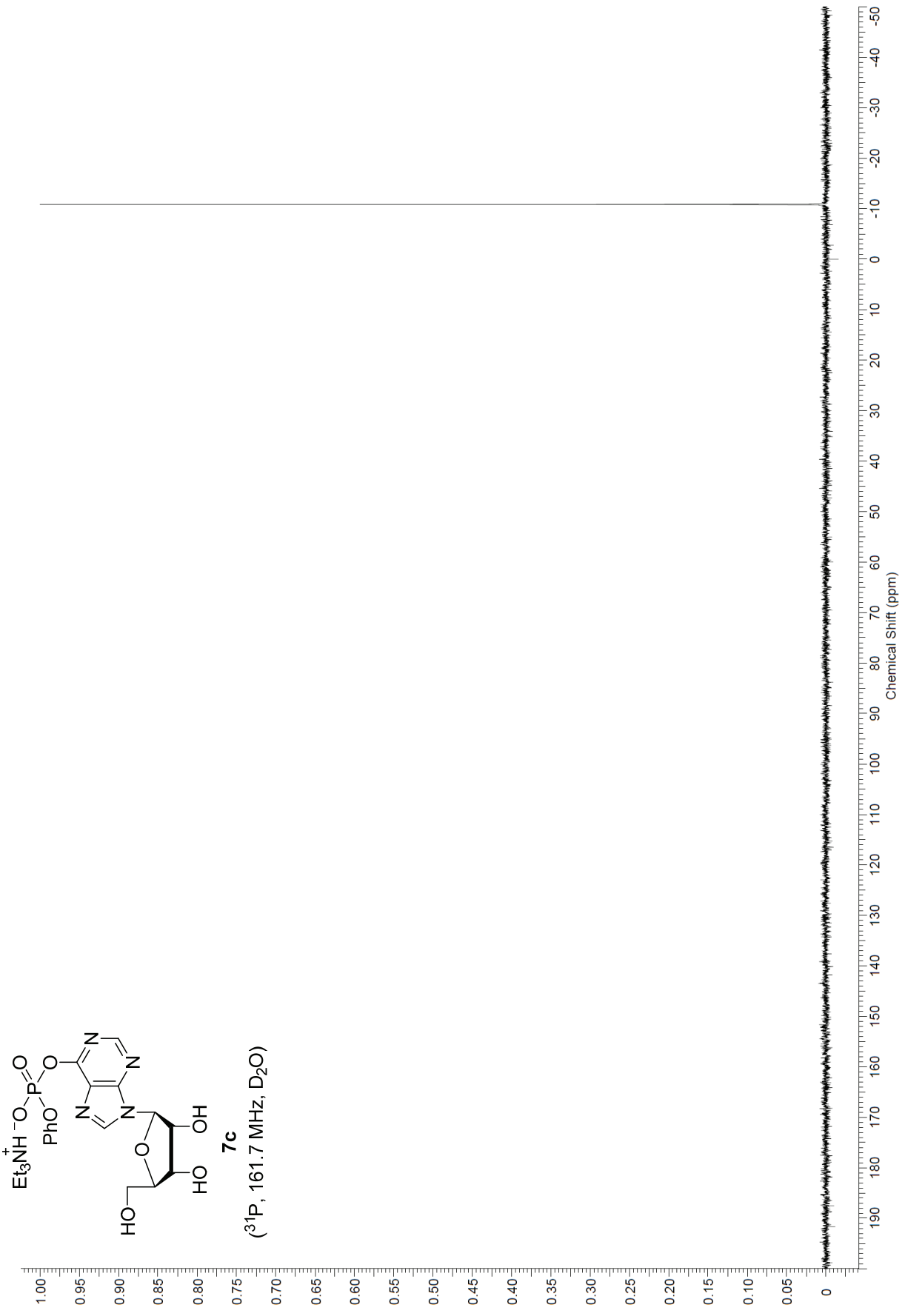

Et3NH+ −O
i-PrO
O
P
O
N
N
N
N
O
OH
HO
HO
7b
(1H, 400 MHz, D2O)
0.94 0.95
1.00
1.05 1.11 1.03 1.04 2.11
6.38
16.25
Chemical Shift (ppm)


Et3NH+ −O
i-PrO
O
P
O
N
N
N
N
O
OH
HO
HO
7b
(13C, 100 MHz, D2O)
Chemical Shift (ppm)


Et3NH+ −O
i-PrO
HO
HO
OH
7b
(31P, 161.7 MHz, D2O)
Chemical Shift (ppm)


Et3NH+ −O
PhO
O
P
O
O
N
N
N
N
O
HO
OH
HO
7c
(1H, 400 MHz, CD3OD)
2.00
4.15
1.01
1.00
1.04
1.05
1.06
1.05
1.04
5.37
8.52
Chemical Shift (ppm)


Et3NH+ −O
PhO
HO
HO
OH
7c
(13C, 100 MHz, D2O)
Chemical Shift (ppm)



7c

(^{31}P, 161.7 MHz, D_2O)