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Supporting Information

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2–Benzamidoethyl Group – a Novel Type of Phosphate Protecting Group for Oligonucleotide Synthesis

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Materials and methods. Anhydrous MeCN (water content <0.001%) was from Burdick and Jackson (Muskegon, MI). 2–(*N*–isopropylamino)ethanol was purchased from TCI America (Portland, OR). Compound **19** was purchased from Maybridge Chemical Company Ltd. (Cornwall, UK). Protected nucleosides **8** and **61–64** were from Chem-Impex International (Wood Dale, IL). Standard phosphoramidites **77–80** and ancillary reagents for oligonucleotide synthesis were purchased from PE Biosystems (Foster City, CA). DMT–T derivatized Tentagel N was purchased from Rapp Polymere (Tübingen, Germany). All other reagents and dry solvents were obtained from Aldrich and used without further purification. Compounds **18** and **20**[1] were synthesized as previously reported.

Melting points were uncorrected. ^{1}H NMR spectra were recorded at 199.975 or 400 MHz, ^{13}C NMR spectra were recorded at 50.289 MHz. Unless otherwise specified, the solvent was $CDCl_3$. Dioxane was used as an internal standard for recording ^{1}H and ^{13}C NMR in D_2O (δ 3.75 and 67.19 ppm, respectively). ^{31}P NMR spectra were recorded at 80.950 MHz. ^{31}P NMR spectra in gel phase were recorded using 10 to 15 mg of solid supports **36–39** and **51** loaded at 208 μmol g^{-1} using liquid phases specified in Table 2 with the spinning switched off. With the phosphate-unprotected oligonucleotide **51**, the best resolution was obtained when the liquid phase contained 10% of pyridine. FAB high resolution MS were acquired for samples dissolved in 4-nitrobenzyl alcohol in the presence of NaI.

HPLC Techniques. Crude oligonucleotides were analyzed and isolated on a DeltaPak C18 column (15 μm; 300Å; 3.8 × 300 mm) at a flow rate 1.5 mL min^{-1} eluting with a linear gradient from 0 to 60% B in 40 min (**33** and **69–74**) or from 0 to 75% B in 40 min (**75** and **76**) and using 0.1 M aq NH_4OAc as buffer A, 80% aq MeCN as buffer B. Authentic DMTr–T_{12}, T_{12}, and **69–76** synthesized

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1 Sicher, J.; Pánková, M.; Jonáš, J.; Svoboda, M. *Coll. Czech. Chem. Commun.* **1959**, *24*, 2727–2740.

from **77–80** by the standard method were used as reference samples. Reverse phase HPLC profiles for **69–76** (crude deprotection mixtures) are presented in Fig. S13–S20. Desalting was performed on the same column eluting with a step gradient of 0.1 M aqueous NH_4OAc (10 min), water (10 min), and 60% aqueous MeCN (20 min) at a flow rate 1.5 mL min^{-1}. The oligonucleotide **75** was isolated on a DeltaPak C18 column (15 μm; 300Å; 25 × 100 mm) eluting with a linear gradient from 0 to 60% B in 60 min (0.1 M aq NH_4OAc as buffer A, 80% aq MeCN as buffer B) at a flow rate 15 mL min^{-1}.

Compounds **47**, **54**, and **58** were isolated by HPLC on a DeltaPak C18 column (15 μm; 300Å; 7.8 × 300 mm) using 0.1% aq TFA as buffer A, 0.1% TFA in 80% aq MeCN as buffer B and a linear gradient from 0 to 75% B in 30 min at a flow rate 4 mL min^{-1}. Collected fractions were evaporated, co-evaporated twice with MeCN and dried.

***N*–(2–hydroxyethyl)–3–nitrobenzamide (12)** was synthesized according to the general method from 2–aminoethanol (6.1 g, 100 mmol), 3–nitrobenzoyl chloride (3.7 g, 20 mmol) to give, after re-crystallization from water, **12** (3.6 g, 86%), mp 133–134 °C. ^1H NMR ($CDCl_3$): δ 8.63–8.61 (1H, m); 8.42–8.34 (1H, m); 8.21–8.15 (1H, m); 7.72–7.62 (1H, m); 6.80–6.64 (1H, br. s); 3.93–3.85 (2H, m); 3.75–3.64 (2H, m); 2.18–2.09 (1H, br. s). ^{13}C NMR ($CDCl_3$): δ 164.3, 147.8, 136.0, 133.7, 130.0, 125.7, 122.0, 59.6, 42.4. FAB–HRMS: calcd for $C_9H_{10}N_2O_4$ ($M + H^+$) 211.0719, found 211.0720.

***N*–(2–hydroxyethyl)–4–(dimethylamino)benzamide (16)**: *O*–(7–azabenzotriazol–1–yl) –*N*,*N*,*N*',*N*'–tetramethyluronium hexafluorophosphate (HATU; 9.5 g, 25 mmol) was added in portions to a solution of 4–dimethylaminobenzoic acid (4.1 g, 25 mmol) in DMF (25 mL), and the mixture was magnetically stirred for 15 min. The obtained solution was added dropwise to 2–(methylamino)ethanol (7.2 g, 100 mmol) in CH_2Cl_2 (30 mL) at 4 °C. The mixture was additionally stirred for 30 min, evaporated in vacuo, and worked-up as described in the general method. Re-crystallization from a toluene–hexane mixture gave **16** (5.0 g, 89%), mp 74-74.5 °C (toluene–hexane). ^1H NMR ($CDCl_3$): δ 7.42 (2H, m); 6.66 (2H, m); 3.84 (2H, t, J = 4.9 Hz); 3.64 (2H, t, J = 4.9 Hz); 3.11 (3H, s); 3.00 (6H, s). ^{13}C NMR ($CDCl_3$): δ 173.9, 151.6, 129.6, 122.2, 111.16, 60.9, 52.0, 40.2. FAB–HRMS: calcd for $C_{12}H_{18}N_2O_2$ ($M + H^+$) 223.1447, found 223.1448.

General Procedure for the Preparation of 21 – 31. Phosphoramidite 28: A solution of chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (3.07 g, 11.5 mmol) in dry CH_2Cl_2 (25 mL) was added dropwise to a mixture of **8** (5.45 g, 10.0 mmol) and *N*–ethyl–*N*,*N*–diisopropylamine (1.55 g, 12.0

mmol) in dry CH_2Cl_2 (25 mL) under magnetic stirring at –20°C. The reaction mixture was allowed to warm up to room temperature, and the stirring was continued for 1 h. Dry **17**, (2.78 g, 12 mmol) was added followed by 1*H*-tetrazole (0.45 M in MeCN; 13.3 mL, 6.0 mmol), and the resulting mixture was kept at room temperature for 2 h. Aqueous $NaHCO_3$ (5%; 20 mL) was added, the emulsion was diluted with brine (50 mL), and the product was extracted with ethyl acetate (3 × 100 mL). Extracts were washed with brine (3 × 50 mL), dried over Na_2SO_4, and evaporated to dryness. The residue was dissolved in toluene (50 mL), applied on a silica gel column, and separated eluting with a gradient from 30:65:5 to 90:5:5 ethyl acetate / hexane / triethylamine. Collected fractions were evaporated, co-evaporated with dry MeCN (2 × 50 mL), and dried on an oil pump to give **28**, fast diastereomer (0.48 g), **28**, slow diastereomer (0.58 g), and their mixture (6.96 g) totaled in 8.02 g (88%) of **28**, both diastereomers of which were identical to those obtained from **8** and **60**, as described in the experimental section.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–O–(*N*,*N*–diisopropylamino)[2–(benzamido)ethoxy]phosphinyl–2'–deoxythymidine (21) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (640 mg, 2.4 mmol), and **10** (413 mg, 2.5 mmol). Column separation gave **21**, fast diastereomer (317 mg), **21**, slow diastereomer (435 mg), and their mixture (516 mg) to total in 1268 mg (75.6%) of **21**.

21, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.05 (1H, br. s); 7.69 (2H, m); 7.65 (1H, d, J = 0.9 Hz); 7.50-7.20 (12H, m); 6.9-6.8 (4H, m); 6.50 (1H, br. t); 6.40 (1H, dd, J = 7.5, 5.8 Hz); 4.67 (1H, m); 4.16 (1H, m); 3.77 (6H, s); 3.70-3.42 (7H, m); 3.31 (1H, dd, J = 10.4, 2.4 Hz); 2.47 (1H, ddd, J = 13.2, 5.8, 2.5 Hz); 2.31 (1H, ddd, J = 13.2, 7.5, 7.5 Hz); 1.42 (3H, s); 1.15 (12H, d, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 167.4, 163.8, 158.8, 150.4, 144.4, 135.6, 135.4, 134.5, 131.5, 130.2, 128.6, 128.2, 128.0, 127.8, 127.2, 126.8, 113.3, 111.3, 87.0, 85.8, 84.8, 73.4, 73.1, 63.0, 62.5, 62.2, 55.3, 43.33, 43.1, 41.0, 40.9, 40.1, 24.6 br, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.9. FAB–HRMS: calcd for $C_{46}H_{55}N_4O_9P$ ($M + Na^+$) 861.3604, found 861.3620.

21, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.06 (1H, br. s.); 7.79 (1H, br.s); 7.77 (1H, br. s); 7.60 (1H, br. s); 7.50-7.20 (13H, m); 6.9-6.8 (4H, m); 6.50 (1H, br. t); 6.42 (1H, dd, J = 8.2, 5.9 Hz); 4.65 (1H, m); 4.15 (1H, m); 3.78 (6H, s); 3.70-3.41 (7H, m); 3.38-3.20 (1H, m); 2.66-2.50 (1H, m); 2.40-2.18 (1H, m); 1.44 (3H, s); 1.13 (6H, d, J = 6.8 Hz); 1.04 (6H, d, J = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 167.6, 163.8, 158.8, 150.5, 144.4, 135.6, 135.4, 134.6, 131.4, 130.1, 128.6, 128.2, 128.0, 127.8, 127.2, 126.8, 113.3, 111.3, 87.0, 85.7, 84.9, 74.4, 74.0, 63.5, 62.4, 62.1, 55.3, 43.3, 43.2, 41.2, 41.0,

40.1, 24.6 br, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.2. FAB–HRMS: calcd for $C_{46}H_{55}N_4O_9P$ (M + Na^+) 861.3604, found 861.3621.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–(4–methoxybenzamido)ethoxy]phosphinyl–2'–deoxythymidine (22) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (587 mg, 2.2 mmol), and **11** (449 mg, 2.3 mmol). Column separation gave **22**, fast diastereomer (295 mg), **22**, slow diastereomer (420 mg) and their mixture (481 mg) to total in 1196 mg (68.8%) of **22**.

22, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.35 (1H, br. s); 7.70-7.60 (3H, m); 7.44-7.16 (10H, m); 6.90-6.76 (6H, m); 6.46-6.35 (2H, m); 4.67 (1H, m); 4.16 (1H, m); 3.81 (3H, s); 3.80 (6H, s); 3.70-3.42 (7H, m); 3.31 (1H, dd, *J* = 10.6, 2.7 Hz); 2.50 (1H, ddd, *J* = 13.7, 5.8, 2.9); 2.33 (1H, ddd, *J* = 13.7, 6.8, 6.8); 1.42 (3H, s); 1.14(12H, d, *J* = 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 166.9, 163.9, 162.2, 158.8, 150.4, 144.3, 135.6, 135.3, 130.1, 128.6, 128.2, 128.0, 127.2, 126.7, 113.7, 113.3, 111.2, 86.9, 85.8, 85.7, 84.8, 73.4, 73.1, 63.0, 62. 6, 62.2, 55.4, 55.3, 43.3, 43.0, 41.0, 40.8, 40.2, 24.7, 24.6, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.8. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_{10}P$ (M + Na^+) 891.3710, found 891.3689.

22, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.20 (1H, br. s); 7.74 (2H, d, *J* = 8.7 Hz); 7.59 (1H, s); 7.43-7.20 (10H, m); 6.91-6.78 (6H, m); 6.71 (1H, br. t); 6.41 (1H, dd, *J* = 7.6, 5.5 Hz); 4.63 (1H, m); 4.14 (1H, m); 3.80 (3H, s); 3.78 (6H, s); 3.92-3.20 (8H, m); 2.56 (1H, dd, *J* = 13.2, 5.5 Hz); 2.24 (1H, ddd, *J* = 13.2, 7.6, 6.2 Hz); 1.42 (3H, s); 1.12 (6H, d, *J* = 6.3 Hz); 1.04 (6H, d, *J* = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 167.1, 163.9, 162.1, 158.8, 150.5, 144.3, 135.6, 135.4, 135.3, 130.1, 128.8, 128.2, 128.0, 127.7, 127.2, 126.9, 113.7, 113.3, 111.3, 87.0, 85.7, 85.6, 84.8, 74.4, 74.0, 63.5, 62.4, 62.1, 55.3, 43.2, 42.9, 41.1, 41.0, 40.0, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.1. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_{10}P$ (M + Na^+) 891.3710, found 891.3688.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–(3–nitrobenzamido)ethoxy]phosphinyl–2'–deoxythymidine (23) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (587 mg, 2.2 mmol), and **12** (483 mg, 2.3 mmol). Column separation gave **23**, fast diastereomer (404 mg), **23**, slow diastereomer (379 mg) and their mixture (294 mg) to total in 1077 mg (61.0%) of **23**.

23, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.17 (1H, br. s); 8.56 (1H, t, *J* = 1.9 Hz); 8.33-8.27 (1H, m); 8.08-7.99 (1H, m); 7.65-7.50 (2H, m); 7.42-7.20 (10H, m); 6.90-6.75 (4H, m); 6.36 (1H, dd, *J* = 7.3, 6.0 Hz); 4.67 (1H, m); 4.18 (1H, m); 3.77 (6H, s); 3.85-3.26 (8H, m); 2.46 (1H, ddd, 13.6, 6.0, 2.8 Hz); 2.33 (1H, ddd, *J* = 13.6, 7.3, 7.3 Hz); 1.41 (3H, s); 1.16 (6H, d, *J* = 6.6 Hz); 1.15 (6H, d, *J* =

6.4 Hz). ^{13}C NMR ($CDCl_3$): δ 165.0, 163.9, 158.8, 150.5, 148.2, 144.3, 136.1, 135.6, 135.3, 133.1, 130.1, 129.8, 128.1, 128.0, 127.2, 126.0, 121.9, 113.3, 111.3, 86.9, 85.6, 85.5, 84.9, 73.5, 73.2, 63.1, 62.2, 61.8, 55.3, 43.3, 43.1, 41.4, 41.2, 40.0, 24.8, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.3. FAB–HRMS: calcd for $C_{46}H_{54}N_5O_{11}P$ ($M + Na^+$) 906.3455, found 906.3435.

23, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.25 (1H, br. s); 8.65 (1H, t, J = 1.8 Hz); 8.33-8.18 (2H, m); 7.68-7.55 (2H, m); 7.45-7.20 (10H, m); 6.90-6.75 (4H, m); 6.37 (1H, dd, J = 8.6, 5.1 Hz); 4.63 (1H, m); 4.16 (1H, m); 3.78 (6H, s); 3.90-3.20 (8H, m); 2.64 (1H, dd, 13.6, 5.1 Hz); 2.27 (1H, ddd, J = 13.6, 8.6, 5.7 Hz); 1.45 (3H, s); 1.14 (6H, d, J = 6.6 Hz); 1.06 (6H, d, J = 5.5 Hz). ^{13}C NMR ($CDCl_3$): δ 165.3, 163.8, 158.8, 150.7, 148.1, 144.2, 136.2, 135.6, 135.4, 135.3, 133.5, 130.1, 129.8, 128.1, 128.0,127.2, 125.9, 122.0, 113.3, 111.5, 87.1, 85.9, 85.8, 85.1, 74.8, 74.5, 63.6, 62.0, 61.7, 55.3, 43.2, 43.0, 41.5, 41.3, 40.0, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 147.7. FAB–HRMS: calcd for $C_{46}H_{54}N_5O_{11}P$ ($M + Na^+$) 906.3455, found 906.3437.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–(benzamido)–2–methylpropoxy]phosphinyl–2'–deoxythymidine (24) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (640 mg, 2.4 mmol), and **13** (483 mg, 2.5 mmol). Column separation gave **24** as a mixture of R_P and S_P diastereomers (1396 mg, 80.5%).

24, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.79 (1H, br. s); 7.77-7.61 (2H, m); 7.53 (1H, s); 7.45-7.22 (12H, m); 6.88-6.76 (4H, m); 6.39 (1H, br. t); 6.36 (1H, dd, J = 7.5, 6.5 Hz); 4.71 (1H, m); 4.13 (1H, m); 3.79 (6H, s); 3.90-3.38 (5H, m); 3.36-3.22 (1H, m); 2.6-2.1 (2H, m); 1.47 (3H, s); 1.43 (3H, s); 1.39 (3H, s); 1.14(6H, d, J = 6.5 Hz); 1.04 (6H, d, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 167.0, 163.7, 158.8, 150.3, 144.3, 135.9, 135.6, 135.3, 131.2, 131.0, 130.5, 128.4, 128.2, 128.0, 127.7, 127.2, 126.7, 113.3, 111.3, 87.0, 85.6, 84.7, 73.4, 73.0, 70.4, 70.2, 63.2, 55.3, 54.4, 54.3, 43.4, 43.2, 40.0, 25.5, 24.9, 23.8, 23.6, 11.7. ^{31}P NMR ($CDCl_3$): δ 149.2. FAB–HRMS: calcd for $C_{48}H_{59}N_4O_9P$ ($M + Na^+$) 889.3917, found 889.3944.

24, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.79 (1H, br. s); 7.77-7.61 (2H, m); 7.53 (1H, s); 7.45-7.22 (12H, m); 6.88-6.76 (4H, m); 6.39 (1H, br. t); 6.36 (1H, dd, J = 7.2, 5.5 Hz); 4.63 (1H, m); 4.11 (1H, m); 3.78 (6H, s); 3.92-3.40 (5H, m); 3.36-3.22 (1H, m); 2.6-2.1 (2H, m); 1.49 (3H, s); 1.40 (6H, s); 1.17 (6H, d, J = 6.7 Hz); 1.14 (6H, d, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 167.2, 163.7, 158.8, 150.3, 144.3, 135.9, 135.6, 135.3, 131.2, 131.0, 130.5, 128.4, 128.2, 128.0, 127.7, 127.2, 126.8, 113.3, 111.3, 87.0, 85.6, 84.7, 74.4, 74.0, 69.5, 69.2, 63.5, 55.3, 54.6, 54.4, 43.3, 43.0, 40.0, 24.6, 24.4, 24.2,

23.8, 11.7. ^{31}P NMR ($CDCl_3$): δ 148.8. FAB–HRMS: calcd for $C_{48}H_{59}N_4O_9P$ (M + Na^+) 889.3917, found 889.3944.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–(*N*–methylbenzamido)ethoxy]phosphinyl–2'–deoxythymidine (25) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (640 mg, 2.3 mmol), and **14** (412 mg, 2.3 mmol). Column separation gave **25**, fast diastereomer (282 mg), **25**, slow diastereomer (518 mg) and their mixture (546 mg) to total in 1346 mg (78.9%) of **25**.

25, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.94 (1H, br. s); 7.64 (1H, m); 7.45-7.20 (14H, m); 6.85-6.75 (4H, m); 6.41 (1H, dd, *J* = 7.3, 7.3 Hz); 4.65 (1H, m); 4.16 (1H, m); 3.81 (6H, s); 3.90-3.20 (8H, m); 3.04 and 2.97 (total 3H, br. s); 2.56-2.39 (1H, m); 2.39-2.21 (1H, m); 1.41 (3H, s); 1.15 (12H, m). ^{13}C NMR ($CDCl_3$): δ 163.9, 158.8, 150.4, 144.3, 136.5, 135.7, 135.5, 135.3, 130.2,129.5, 128.4, 128.2, 128.0, 127.2, 127.0, 113.3, 111.2, 87.0, 85.8, 84.8, 73.64, 73.3, 63.3, 61.7, 61.4, 55.3, 50.0, 48.9, 43.3, 43.0, 40.1, 39.4, 24.7, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.6, 148.3. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_9P$ (M + Na^+) 875.3761, found 875.3753.

25, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.92 (1H, br. s); 7.59 (1H, m); 7.45-7.20 (14H, m); 6.87-6.77 (4H, m); 6.41 (1H, dd, *J* = 7.4, 7.4 Hz); 4.62 (1H, m); 4.14 (1H, m); 3.78 (6H, s); 3.90-3.20 (8H, m); 3.12 and 3.06 (total 3H, br. s); 2.60-2.38 (1H, m); 2.38-2.18 (1H, m); 1.41 (3H, s); 1.18-1.0 (12H, m). ^{13}C NMR ($CDCl_3$): δ 171.5, 163.8, 158.8, 150.4, 144.3, 136.5, 135.7, 135.4, 135.3, 130.1, 129.5, 128.4, 128.2, 128.0,127.2, 127.0, 113.3, 111.3, 87.0, 85.6, 85.5, 84.7, 74.0, 73.7, 63.4, 61.5, 61.3, 55.3, 49.1, 49.0, 43.2, 43.0, 40.2, 39.3, 24.7, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.4. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_9P$ (M + Na^+) 875.3761, found 875.3754.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–(*N*–methyl–4–methoxybenzamido)ethoxy]phosphinyl–2'–deoxythymidine (26) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (640 mg, 2.4 mmol) and **15**, (523 mg, 2.5 mmol). Column separation gave **26**, fast diastereomer (529 mg), **26**, slow diastereomer (398 mg), and their mixture (523 mg) totaled in 1450 mg (82.1%) of **26**.

26, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.01 (1H, br. s.); 7.64 (1H, s); 7.45-7.18 (11H, m); 6.9-6.7 (6H, m); 6.40 (1H, dd, *J* = 7.5, 5.9 Hz); 4.65 (1H, m); 4.16 (1H, m); 3.79 (3H, s); 3.77 (6H, s); 3.90-3.24 (8H, m); 3.01 (3H, s); 2.55-2.38 (1H, m); 2.38-2.20 (1H, m); 1.41 (3H, s); 1.15 (12H, d, *J* = 6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 163.9, 160.6, 158.8, 150.4, 144.3, 135.7, 135.4, 135.3, 130.2, 129.0, 128.2, 128.0, 127.2, 113.6, 113.3, 111.2, 87.0, 85.9, 85.8, 84.8, 73.6, 73.3, 63.3, 61.2, 55.3, 45.3, 43.2,

43.0, 40.1, 24.7, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.4. FAB–HRMS: calcd for $C_{48}H_{59}N_4O_{10}P$ (M + Na^+) 905.3867, found 905.3845.

26, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.13 (1H, br. s.); 7.58 (1H, s); 7.45-7.18 (11H, m); 6.9-6.7 (6H, m); 6.41 (1H, dd, *J* = 7.9, 6.0 Hz); 4.62 (1H, m); 4.12 (1H, m); 3.79 (3H, s); 3.77 (6H, s); 3.90-3.20 (8H, m); 3.01 (3H, s); 2.60-2.41 (1H, m); 2.38-2.18 (1H, m); 1.41 (3H, s); 1.12 (6H, d, *J* = 7.1 Hz); 1.02 (6H, d, *J* = 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 163.9, 160.6, 158.8, 150.4, 144.3, 135.7, 135.4, 135.3, 130.1, 129.1, 128.6, 128.2, 128.0, 127.2, 113.6, 113.3, 111.3, 86.9, 85.6, 85.5, 84.7, 74.0, 73.6, 63.4, 61.3, 61.1, 55.3, 45.3, 43.2, 42.9, 40.2, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.4. FAB–HRMS: calcd for $C_{48}H_{59}N_4O_{10}P$ (M + Na^+) 905.3867, found 905.3844.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–[*N*–methyl–4–(dimethylamino)benzamido]ethoxy]phosphinyl–2'–deoxythymidine (27) was synthesized as described in the general method from **8** (2178 mg, 4.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (1280 mg, 4.8 mmol) and **16**, (1111 mg, 5.0 mmol). Column separation gave **27**, fast diastereomer (1068 mg), **27**, slow diastereomer (987 mg), and their mixture (1038 mg) totaled in 3093 mg (86.3%) of **27**.

27, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.90 (1H, br. s.); 7.64 (1H, s); 7.45-7.18 (11H, m); 6.90-6.78 (4H, m); 6.68-6.58 (2H, m); 6.40 (1H, br. t); 4.65 (1H, m); 4.16 (1H, m); 3.77 (6H, s); 3.80-3.40 (8H, m); 3.03 (3H, s); 2.95 (6H, s); 2.53-2.38 (1H, m); 2.38-2.20 (1H, m); 1.41 (3H, s); 1.15 (12H, d, *J* = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 172.2, 163.9, 158.7, 151.3, 150.4, 144.3, 135.7, 135.4, 135.3, 130.2, 129.1, 128.2, 128.0, 127.7, 127.4, 127.2, 123.2, 113.3, 111.2, 86.9, 85.9, 84.8, 73.6, 73.2, 63.3, 61.6, 61.3, 55.3, 43.3, 43.0, 40.3, 40.1, 24.7, 24.6, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.5. FAB–HRMS: calcd for $C_{49}H_{62}N_5O_9P$ (M + Na^+) 918.4183, found 918.4164.

27, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.75 (1H, br. s.); 7.57 (1H, s); 7.44-7.16 (11H, m); 6.88-6.75 (4H, m); 6.67-6.58 (2H, m); 6.41 (1H, dd, *J* = 7.9, 6.1 Hz); 4.62 (1H, m); 4.11 (1H, m); 3.78 (6H, s); 3.84-3.20 (8H, m); 3.12 (3H, s); 2.96 (6H, s); 2.50 (1H, ddd, *J* = 13.3, 5.4, ≈1 Hz); 2.38-2.18 (1H, m); 1.42 (3H, s); 1.14 (6H, d, *J* = 6.7 Hz); 1.04 (6H, d, *J* = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 172.3, 163.8, 158.8, 151.3, 150.3, 144.3, 135.8, 135.4, 135.3, 130.1, 129.1, 128.2, 128.0, 127.7, 127.2, 123.2, 113.3, 111.3, 86.9, 85.6, 85.5, 84.7, 84.5, 74.0, 73.6, 63.4, 61.4, 61.1, 55.3, 43.2, 42.9, 40.3, 40.1, 24.6, 24.5, 11.7. ^{31}P NMR ($CDCl_3$): δ 148.4. FAB–HRMS: calcd for $C_{49}H_{62}N_5O_9P$ (M + Na^+) 918.4183, found 918.4165.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–[[thioxo(phenyl)methyl]amino]ethoxy]phosphinyl–2'–deoxythymidine (29) was synthesized as described in the general method

from **8** (5446 mg, 10.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (3068 mg, 11.5 mmol), and **18** (2139 mg, 11.8 mmol). Column separation gave **29**, fast diastereomer (460 mg), **29**, slow diastereomer (420 mg) and their mixture (4550 mg) to total in 5430 mg (63.5%) of **29**.

29, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.3 (1H, br.s); 8.01 (1H, br.t); 7.76-7.54 (2H, m); 7.46-7.20 (13H, m); 6.86-6.76 (4H, m); 6.32 (1H, dd, *J* = 6.5, 6.5 Hz); 4.65 (1H, m); 4.04 (1H, m); 4.0-3.85 (2H, m); 3.76 (6H, s); 3.71-3.36 (5H, m); 3.28 (1H, dd, *J*= 2, 10.5 Hz); 2.39 (1H, m); 2.31 (1H, m); 1.41 (3H, s); 1.14 (12H, d, *J* = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 199.3, 164.0, 158.8, 150.5, 144.3, 141.8, 135.6, 135.3, 131.1, 130.2, 128.5, 128.2, 128.0, 127.2, 126.6, 113.3, 111.3, 87.0, 85.5, 84.8, 73.3, 72.9, 62.9, 61.1, 60.8, 55.3, 47.5, 47.4, 43.4, 43.2, 40.0, 24.8, 24.7, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 149.3. FAB–HRMS: calcd for $C_{46}H_{55}N_4O_8PS$ ($M + Na^+$) 877.3376, found 877.3351.

29, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 9.4 (1H, br.s); 8.32 (1H, br.t); 7.76-7.68 (2H, m); 7.56 (1H, s); 7.44-7.20 (12H, m); 6.86-6.76 (4H, m); 6.36 (1H, dd, *J* = 8.3, 5.5 Hz); 4.60 (1H, m); 4.14-4.0 (3H, m); 4.0-3.85 (1H, m); 3.77 (6H, s); 3.66-3.38 (3H, m); 3.28 (1H, dd, *J*= 10.6, 2.4 Hz); 2.54 (1H, m); 2.21 (1H, m); 1.42 (3H, s); 1.13 (6H, d, *J* = 6.6 Hz); 1.03 (6H, d, *J* = 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 199.5, 164.0, 158.8, 150.6, 144.3, 135.6, 135.3, 131.0, 130.1, 128.4, 128.2, 128.0, 127.7, 127.2, 126.7, 113.3, 111. 5, 87.0, 85.7, 85.6, 84.9, 74.5, 74.1, 63.5, 60.8, 60.5, 55.3, 47.6, 47.5, 43.3, 43.0, 40.1, 24.6, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.2. FAB–HRMS: calcd for $C_{46}H_{55}N_4O_8PS$ ($M + Na^+$) 877.3376, found 877.3351.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–[[(phenylamino)thioxomethyl]amino]ethoxy]phosphinyl–2'–deoxythymidine (30) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (587 mg, 2.2 mmol), and **19** (451 mg, 2.3 mmol). Column separation gave **30**, fast diastereomer (134 mg), **30**, slow diastereomer (395 mg) and their mixture (697 mg) to total in 1226 mg (70.5%) of **30**.

30, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.10 (1H, br. s); 7.64 (1H, s); 7.42-7.14 (15H, m); 6.88-6.78 (4H, m); 6.42-6.32 (2H, m); 4.55 (1H, m); 4.02 (1H, m); 3.79 (6H, s); 3.90-3.64 (2H, m); 3.63-3.53 (2H, m); 3.50-3.30 (3H, m); 3.22 (1H, dd, *J* = 10.6, 2.4 Hz); 2.40 (1H, ddd, *J* = 13.7, 6.1, 2.5 Hz); 2.25 (1H, ddd, *J* = 13.7, 7.3, 6.4 Hz); 1.40 (3H, s); 1.09 (6H, d, *J* = 6.8 Hz); 1.03 (6H, d, *J* = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 180.6, 163.9, 158.8, 150.4, 144.2, 136.2, 135.6, 135.3, 130.1, 128.2, 128.0, 127.3, 125.1, 113.3, 111.3, 87.0, 85.8, 85.7, 84.8, 73.6, 73.2, 63.2, 61.9, 61.6, 55.3, 46.4, 46.2, 43.3, 43.0, 40.0, 24.7, 24.6, 24.4, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.7. FAB–HRMS: calcd for $C_{46}H_{56}N_5O_8PS$ ($M + Na^+$) 892.3485, found 892.3469.

30, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.51 (1H, br. s); 7.60 (1H, d, J = 1 Hz); 7.42-7.16 (15H, m); 6.88-6.78 (4H, m); 6.60 (1H, br. t); 6.37 (1H, dd, J = 8.3, 5.6 Hz); 4.57 (1H, m); 4.05 (1H, m); 3.78 (6H, s); 3.90-3.20 (8H, m); 2.48 (1H, dd, J = 13.3, 5.6 Hz); 2.22 (1H, ddd, J = 13.3, 8.3, 5.9 Hz); 1.42 (3H, s); 1.03 (6H, d, J = 6.7 Hz); 0.98 (6H, d, J = 6.7 Hz). ^{13}C NMR ($CDCl_3$): δ 180.9, 163.9, 158.8 150.6, 144.2, 136.7, 135.6, 135.4, 130.1, 129.9, 128.2, 128.0, 127.2, 126.9, 125.1, 113.3, 111.5, 87.0, 85.7, 85.6, 84.9, 74.4, 74.0, 63.5, 61.9, 61.6, 55.3, 46.4, 46.2, 43.2, 43.0, 40.0, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.3. FAB–HRMS: calcd for $C_{46}H_{56}N_5O_8PS$ ($M + Na^+$) 892.3485, found 892.3469.

5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–(*N*,*N*–diisopropylamino)[2–[[thioxo(phenyl)methyl]amino]propoxy]phosphinyl–2'–deoxythymidine (31) was synthesized as described in the general method from **8** (1089 mg, 2.0 mmol), chloro bis[(*N*,*N*,-diisopropyl)amino]phosphite (587 mg, 2.2 mmol), and **20** (449 mg, 2.3 mmol). Column separation gave **31**, fast diastereomer (276 mg), **31**, slow diastereomer (296 mg) and their mixture (653 mg) to total in 1225 mg (70.5%) of **31**.

31, fast diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.36 (1H, br. t); 7.71-7.65 (2H, m); 7.61 (1H, d, J = 1 Hz); 7.45-7.20 (13H, m); 6.86-6.78 (4H, m); 6.34 (1H, dd, J = 7.3; 5.7 Hz); 4.62 (1H, m); 4.01 (1H, m); 3.78 (6H, s); 3.94-3.37 (7H, m); 3.23 (1H, dd, J = 10.5, 2.6 Hz); 2.39 (1H, ddd, J = 13.8, 5.7, 2.9 Hz); 2.26 (1H, ddd, J = 13.8, 7.3, 6.9 Hz); 1.93 (2H, p, J = 5.9); 1.41 (3H, s); 1.11 (6H, d, J = 6.6 Hz); 1.08 (6H, d, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 198.9, 163.8, 158.8, 150.3, 144.3, 142.0, 135.6, 135.3, 131.0, 130.2, 128.4, 128.2, 128.0, 127.7, 127.2, 126.7, 113.3, 111.3, 86.9, 85.6, 85.5, 84.8, 73.6, 73.2, 63.2, 63.0, 62.8, 55.3, 45.9, 43.3, 43.1, 40.1, 28.9, 28.8, 24.7, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 148.7. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_8PS$ ($M + Na^+$) 891.3532, found 891.3511.

31, slow diastereomer: ^{1}H NMR ($CDCl_3$): δ 8.61 (1H, br. t); 7.8-7.7 (2H, m); 7.59 (1H, s); 7.45-7.20 (13H, m); 6.88-6.78 (4H, m); 6.37 (1H, dd, J = 7.9; 5.5 Hz); 4.57 (1H, m); 4.06 (1H, m); 4.02-3.65 (4H, m); 3.56-3.34 (3H, m); 3.27 (1H, dd, J = 10.3, 2.3 Hz); 2.48 (1H, dd, J = 13.4, 5.5 Hz); 2.23 (1H, ddd, J = 13.4, 7.9, 5.6 Hz); 2.08 (2H, m); 1.42 (3H, s); 1.09 (6H, d, J = 6.8 Hz); 0.99 (6H, d, J = 6.5 Hz). ^{13}C NMR ($CDCl_3$): δ 198.9, 163.8, 158.8, 150.5, 144.3, 142.0, 135.6, 135.4, 130.8, 130.1, 128.3, 128.2, 128.0, 127.2, 126.8, 113.3, 111.4, 87.0, 85.6, 84.8, 74.2, 73.8, 63.5, 63.1, 62.7, 55.3, 45.7, 43.2, 43.0, 40.1, 29.1, 29.0, 24.6, 24.5, 11.8. ^{31}P NMR ($CDCl_3$): δ 147.7. FAB–HRMS: calcd for $C_{47}H_{57}N_4O_8PS$ ($M + Na^+$) 891.3532, found 891.3511.

Ethyl 2–(4–Methoxybenzamido)–*N*–(isopropyl)ethyl 5'–*O*–(4,4'–Dimethoxytrityl)–3'–*O*–thymidylate (49). 1*H*–tetrazole (28 mg, 0.4 mmol) was added to a solution of **28** (274 mg, 0.3 mmol)

and ethanol (28 mg, 0.6 mmol) in anhydrous CH_2Cl_2 (3 mL), and the mixture was stirred for 30 min. Pyridine (56 mg, 0.7 mmol) and 3–chloroperbenzoic acid (86 mg, 0.5 mmol) were added, and the stirring was continued for 15 min. The reaction mixture was diluted with toluene (45 mL) and applied on a silica gel column. The column was eluted with CH_2Cl_2 / ethanol / pyridine 96.9:3:0.1. Collected fractions were diluted with toluene, evaporated, and dried on an oil pump to give 255 mg (97.5%) of **49** as a white solid foam. ^{1}H NMR ($CDCl_3$): δ 7.57 (0.5H, d, J = 1.2 Hz); 7.55 (0.5H, d, J = 1.6 Hz); 7.39–7.22 (7H, m); 7.20–7.12 (4H, m); 6.93–6.88 (2H, m); 6.86–6.81 (4H, m); 6.48–6.41 (1H, m); 5.15 (1H, m); 4.34–4.02 (6H, m); 3.82 (3H, s); 3.78 (6H, s); 3.59 (1H, t, J = 6.2 Hz); 3.54 (1H, t, J = 6.4 Hz); 3.52–3.48 (1H, m); 3.39 (1H, dd, J = 10.8, 2.4 Hz); 2.66–2.59 (1H, m); 2.47–2.37 (1H, m); 1.37 (3H, s); 1.32 (1.5 H, dt, J = 6.8, 0.8 Hz); 1.26 (1.5H, dt, J = 7.2, 0.8 Hz); 1.16 (3H, d, J = 6.4 Hz); 1.13 and 1.12 (3H, d, J = 6.8 Hz and d, J = 6.4 Hz). ^{13}C NMR ($CDCl_3$): δ 172.4, 164.1, 160.8, 159.0, 144.3, 138.0, 135.6, 135.4, 135.3, 130.3, 129.2, 129.0, 128.5, 128.4, 128.3, 128.2, 127.5, 125.5, 114.1, 113.5, 111.8, 87.4, 84.9, 84.8, 84.5, 78.9, 78.5, 65.3, 65.1, 64.7, 64.6, 64.5, 63.6, 63.5, 55.5, 55.4, 50.4, 46.3, 41.1, 39.4, 21.7, 21.4, 16.4, 16.3, 11.9. ^{31}P NMR ($CDCl_3$): δ –0.8 (0.5P, s), –0.9 (0.5P, s). FAB–HRMS: calcd for $C_{46}H_{54}N_3O_{12}P$ ($M + Na^+$) 894.3343, found 894.3332.

2–(4–Methoxybenzamido)–*N*–(isopropyl)ethanaminium trifluoroacetate (58): A solution of anisoyl chloride (171 mg, 1 mmol) in THF (10 mL) was added dropwise to magnetically stirred *N*–isopropylethanediamine (511 mg, 5 mmol) in THF (10 mL). The resulting solution was stirred for 2 days, evaporated, and dissolved in water (10 mL). The mixture was brought to pH 2 by adding 25% aqueous TFA and filtered. The filtrate was separated by preparative HPLC. The fractions were evaporated, and the solid residue was re-crystallized from toluene to give **58** (291 mg, 83%), m.p. 80–81 °C. ^{1}H NMR (DMSO–d_6): δ 8.53 (1H, t, J = 5.4 Hz); 8.44 (2H, br. s); 7.85–7.82 (2H, m); 7.05–6.98 (2H, m); 3.52 (2H, dt, J = 5.4 Hz); 3.34 (1H, sept., J = 6.4 Hz); 3.11–3.03 (2H, m); 1.21 (6H, d, J = 6.4 Hz). ^{13}C NMR (DMSO–d_6): δ 166.4, 161.8, 129.1, 126.2, 113.5, 55.3, 49.6, 43.6, 36.0, 18.5. Anal. Calcd for $C_{15}H_{21}F_3N_2O_4$: C, 51.43; H, 6.04; N, 8.00. Found: C, 51.27; H, 5.82; N, 7.85.

Table S1. ESMS Data for oligonucleotides **69–76**.

Compound	Sequence (5' → 3')	Backbone	Observed Mass	Expected Mass
DMT–**69**	DMT–T_{20}	P=O	6323.9	6324.3
DMT–**70**	DMT–$GC_3A_2GCTG_2CATC_2GTCA$	P=O	6364.9	6365.2
70	$GC_3A_2GCTG_2CATC_2GTCA$	P=O	6063.1	6062.8
DMT–**71**	DMT–$TC_3GC_2(TG)_2ACATGCAT_2$	P=O	6345.5	6346.2
71	$TC_3GC_2(TG)_2ACATGCAT_2$	P=O	6042.5	6043.8
DMT–**72**	DMT–$GC_3A_2GCTG_2CATC_2GTCA$	P=S	6669.9	6670.5
72	$GC_3A_2GCTG_2CATC_2GTCA$	P=S	6367.6	6368.1
DMT–**73**	DMT–$TC_3GC_2(TG)_2ACATGCAT_2$	P=S	6650.8	6651.5
73	$TC_3GC_2(TG)_2ACATGCAT_2$	P=S	6348.5	6349.1
DMT–**74**	DMT–$ATGCAT_2CTGC_5A_2G_2A$	P=S	6668.6	6669.5
74	$ATGATGCAT_2CTGC_5A_2G_2A$	P=S	6366.9	6367.1
DMT–**75**	DMT–$AGCT_2CT_3G(CA)_2TGTA_3$	P=S	6698.2	6698.6
75	$AGCT_2CT_3G(CA)_2TGTA_3$	P=S	6395.6	6396.2
DMTr–**76**	DMT–T^*_{20}[a]	P=S	8110.0	8111.1
76	T^*_{20}[a]	P=S	7808.4	7808.7

a. T* stands for 2'–*O*–(2–methoxyethyl)–5–methyluridine residue.

Figure S1. ^{31}P NMR Spectrum of Compound **37** (CD_3CN as a liquid phase).

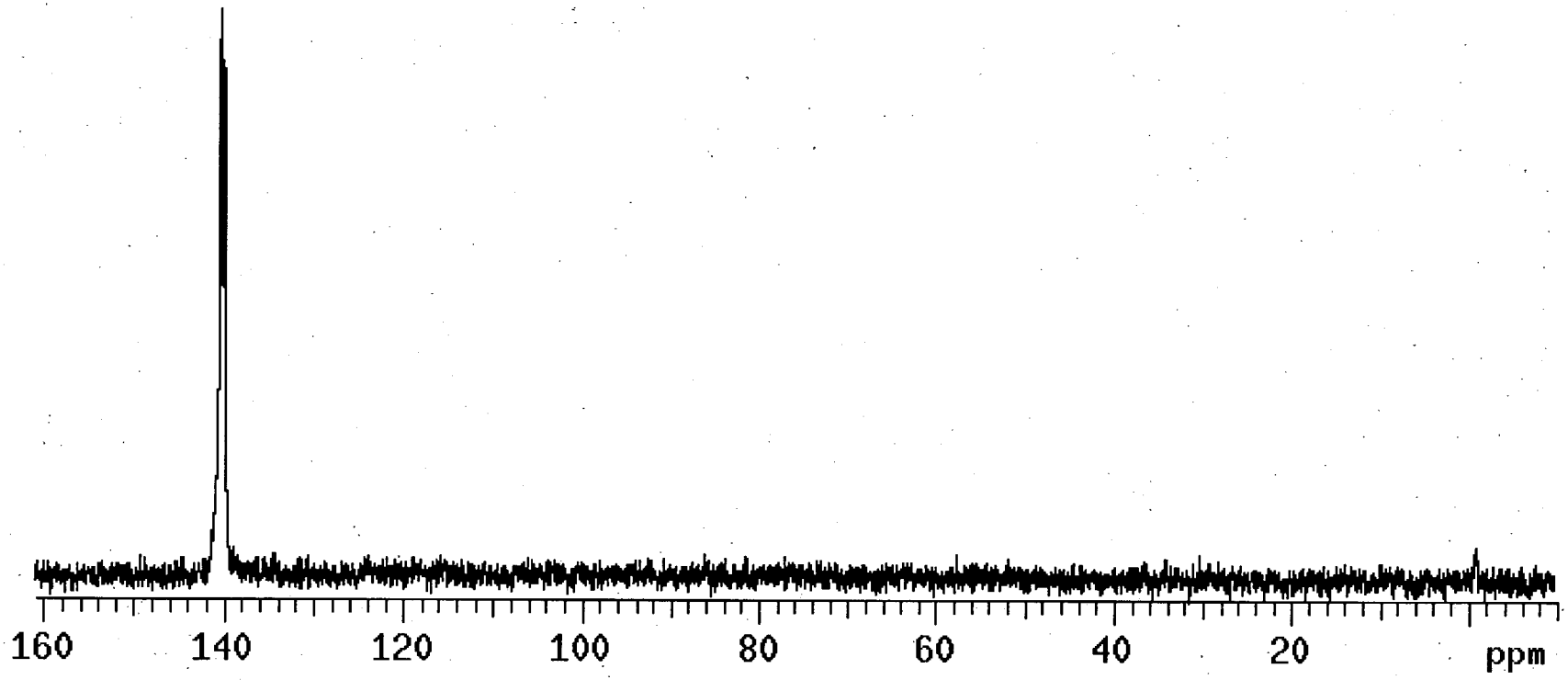


Figure S2. ^{31}P NMR Spectrum of Compound **41** at *ca.* One Half Life (CD_3CN as a liquid phase).

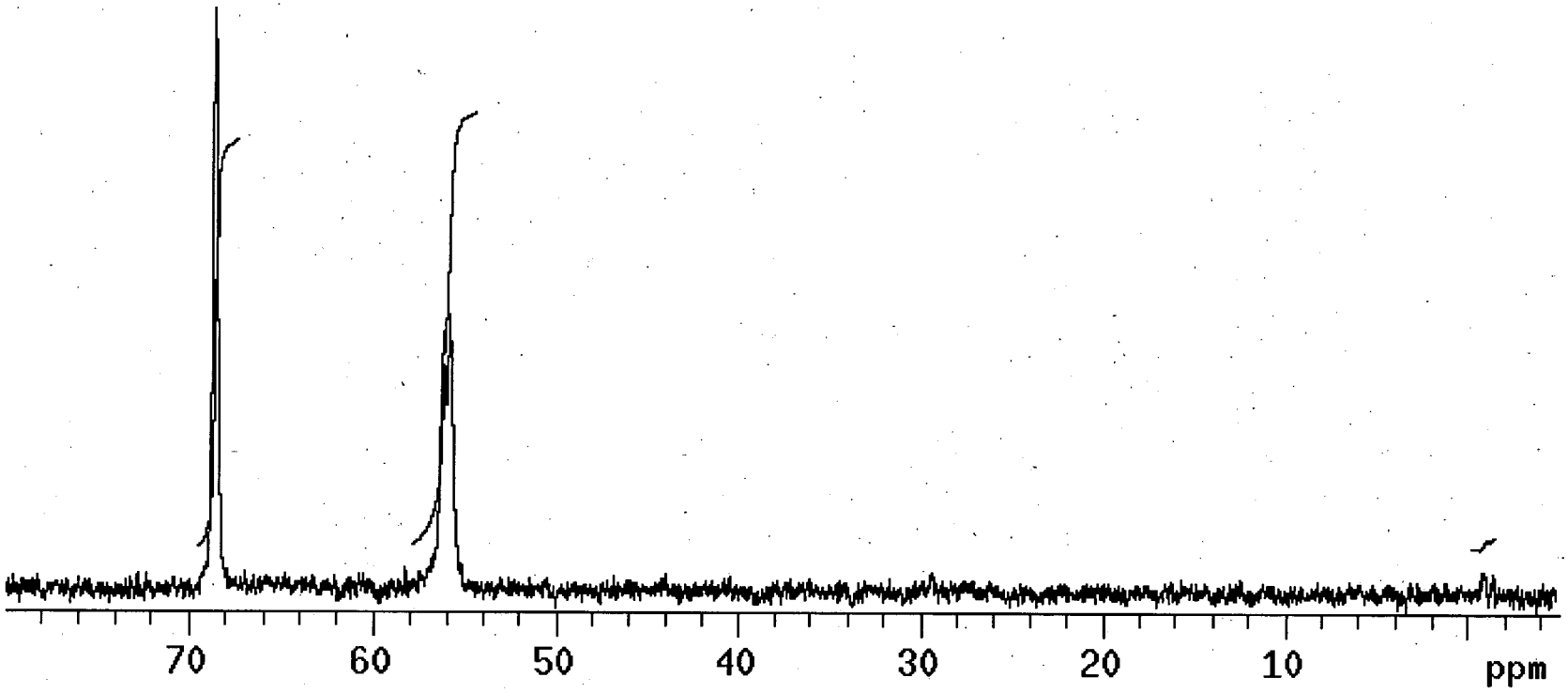


Figure S3. ^{31}P NMR Spectrum of Compound **44** (CD_3CN as a liquid phase).

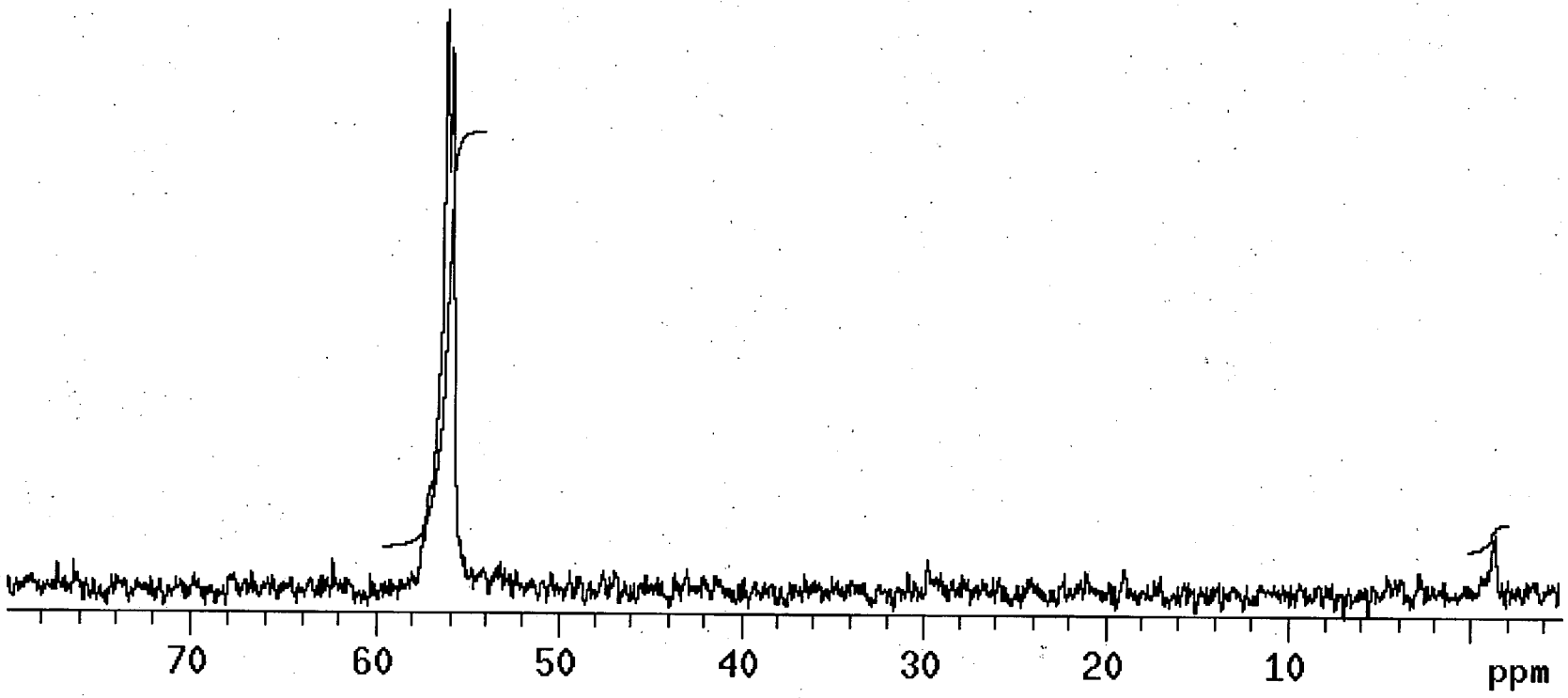


Figure S4. ^{31}P NMR Spectrum of Compound **39** (5% pyridine in CD_3CN as a liquid phase).

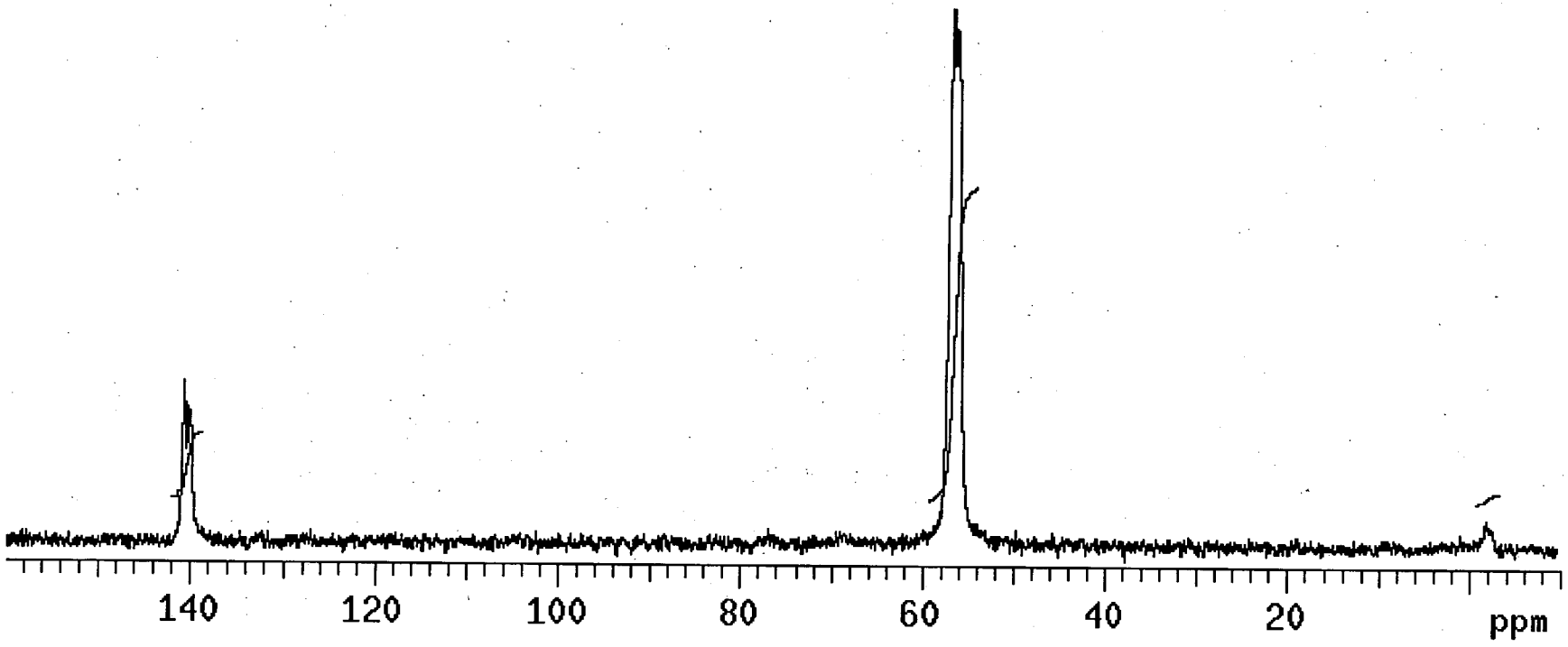


Figure S5. ^{31}P NMR Spectrum of Compound **43** (5% pyridine in CD_3CN as a liquid phase).

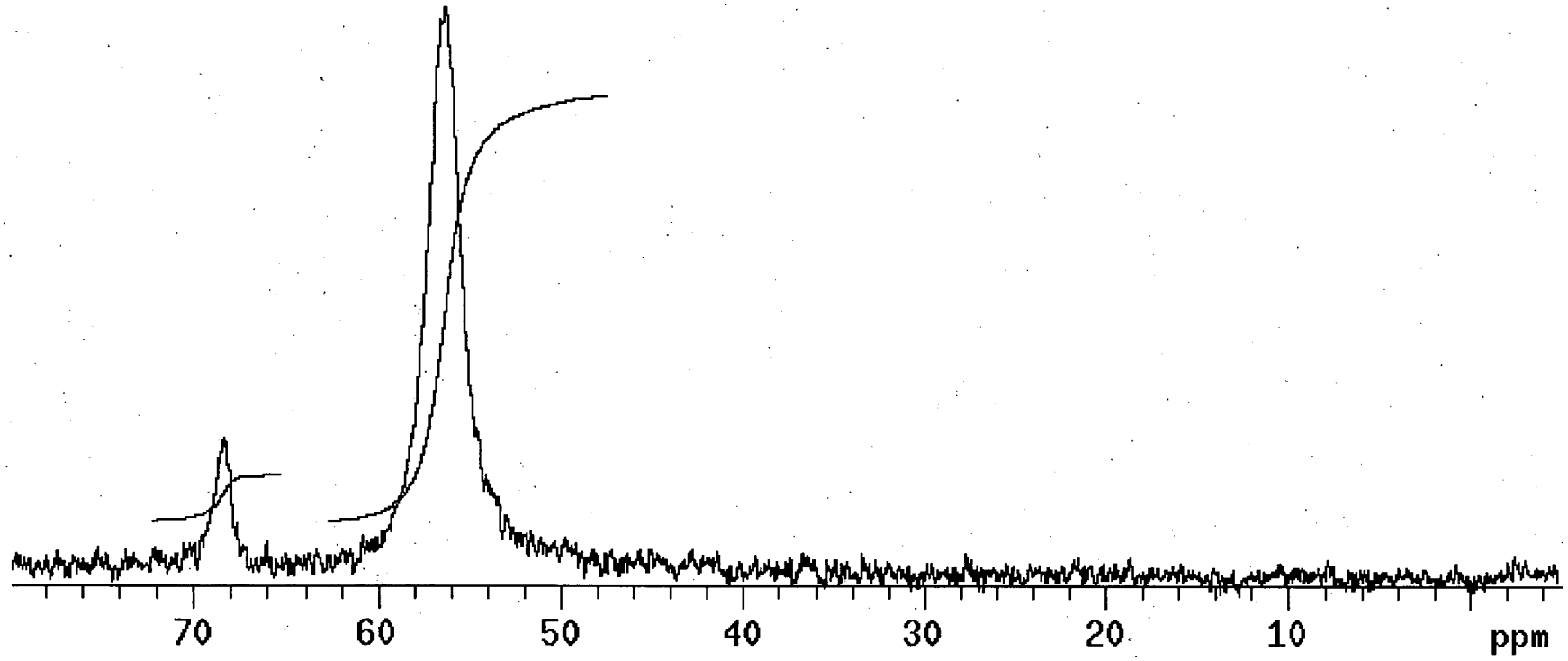


Figure S6. ^{31}P NMR Spectrum of Compound **45** (5% pyridine in CD_3CN as a liquid phase).

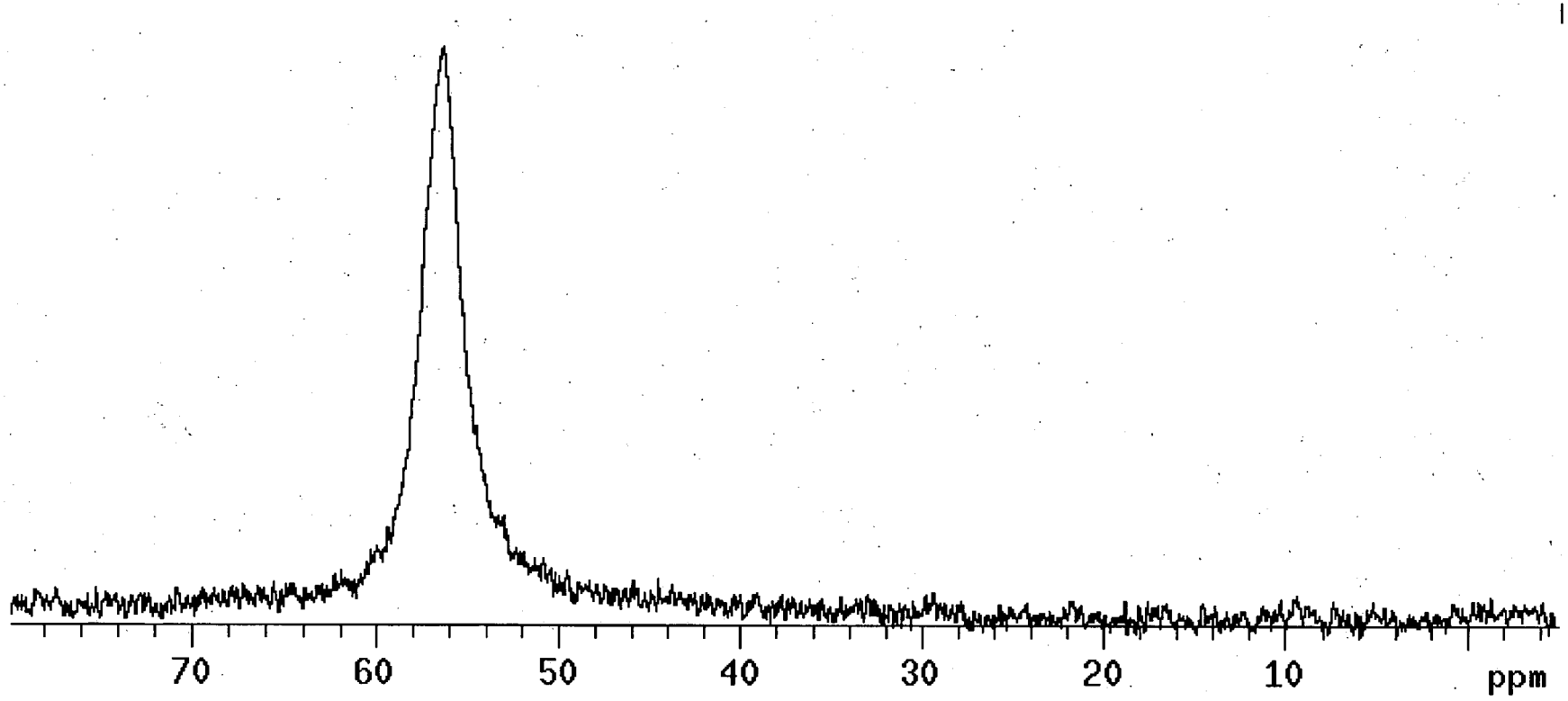


Figure S7. ^{31}P NMR Spectrum of Compound **51** recorded in pyridine/CD_3CN (1:9) immediately after the synthesis was complete.

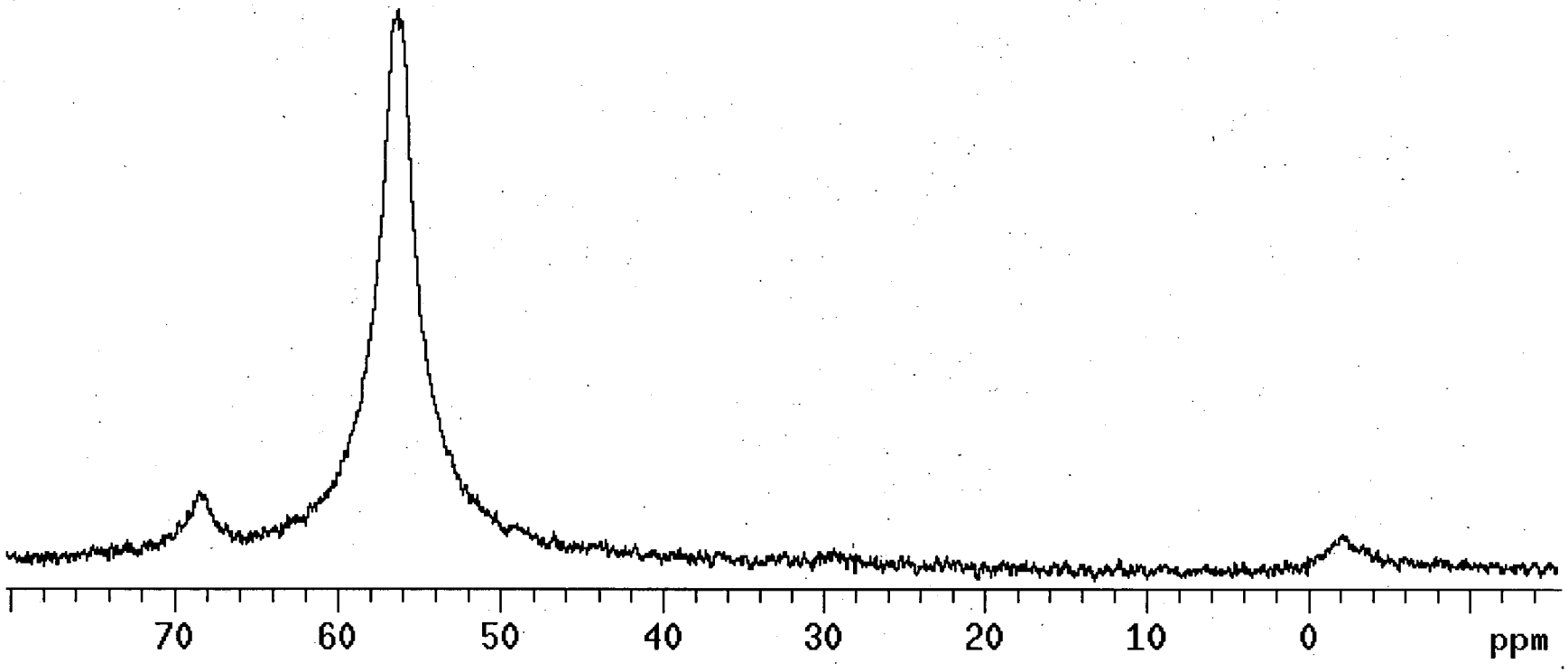
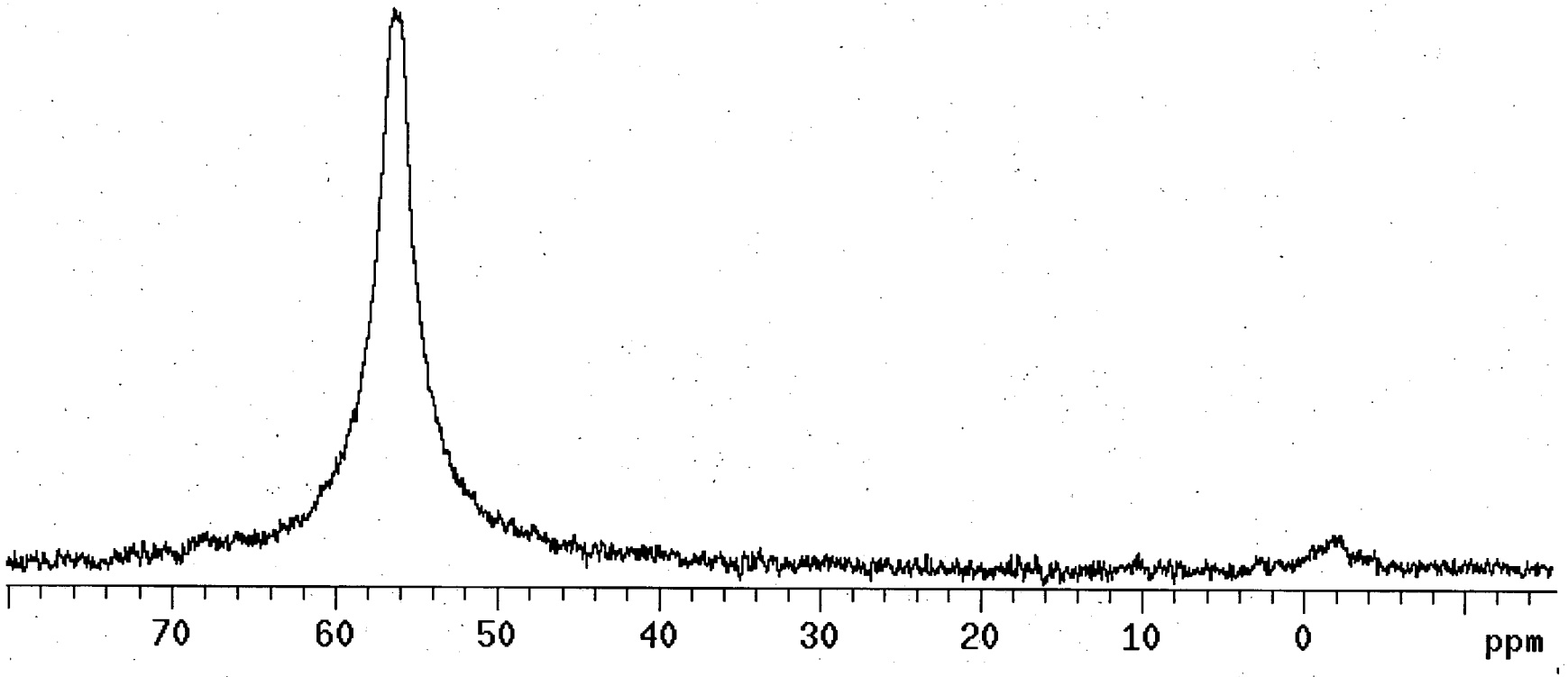


Figure S8. ^{31}P NMR Spectrum of Compound **51** after 1 h in pyridine/CD_3CN (1:9).



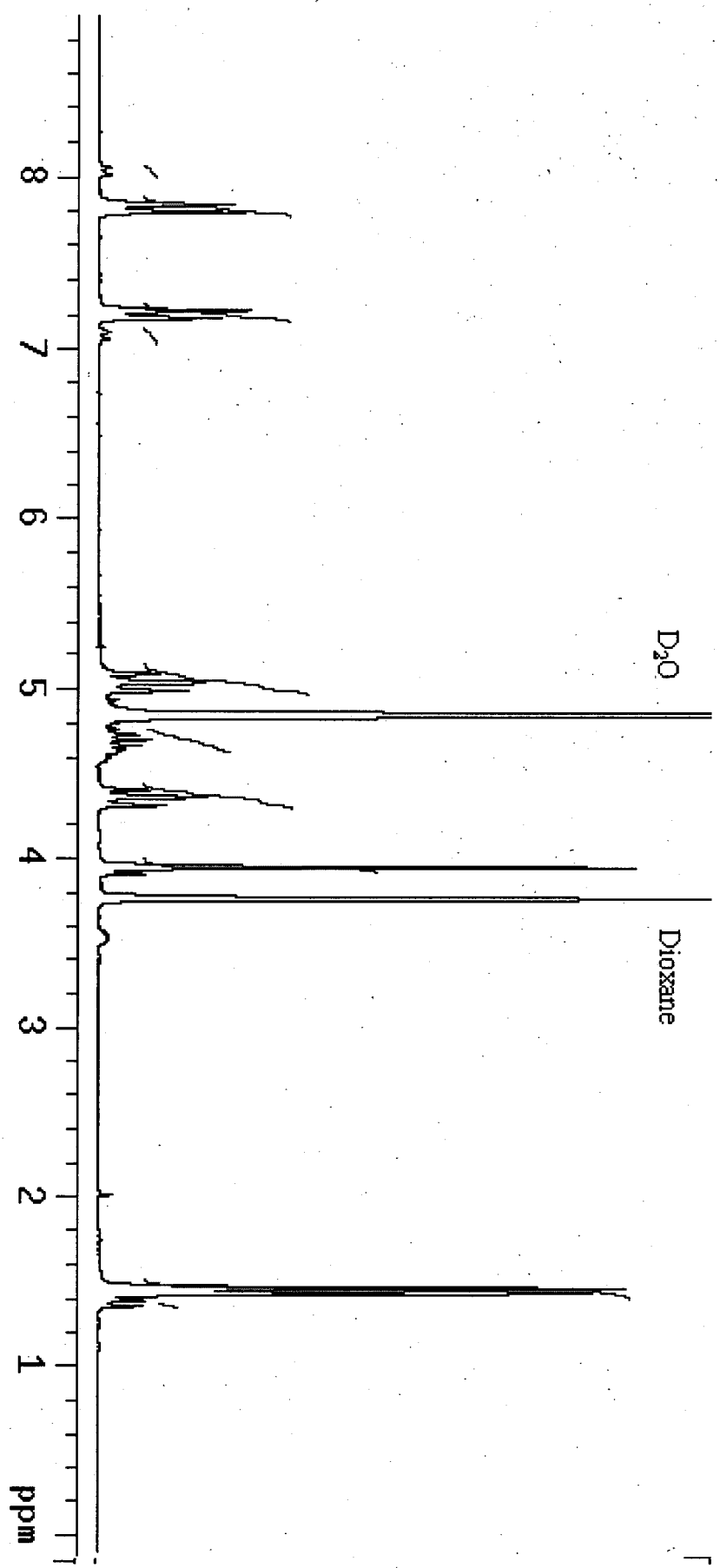
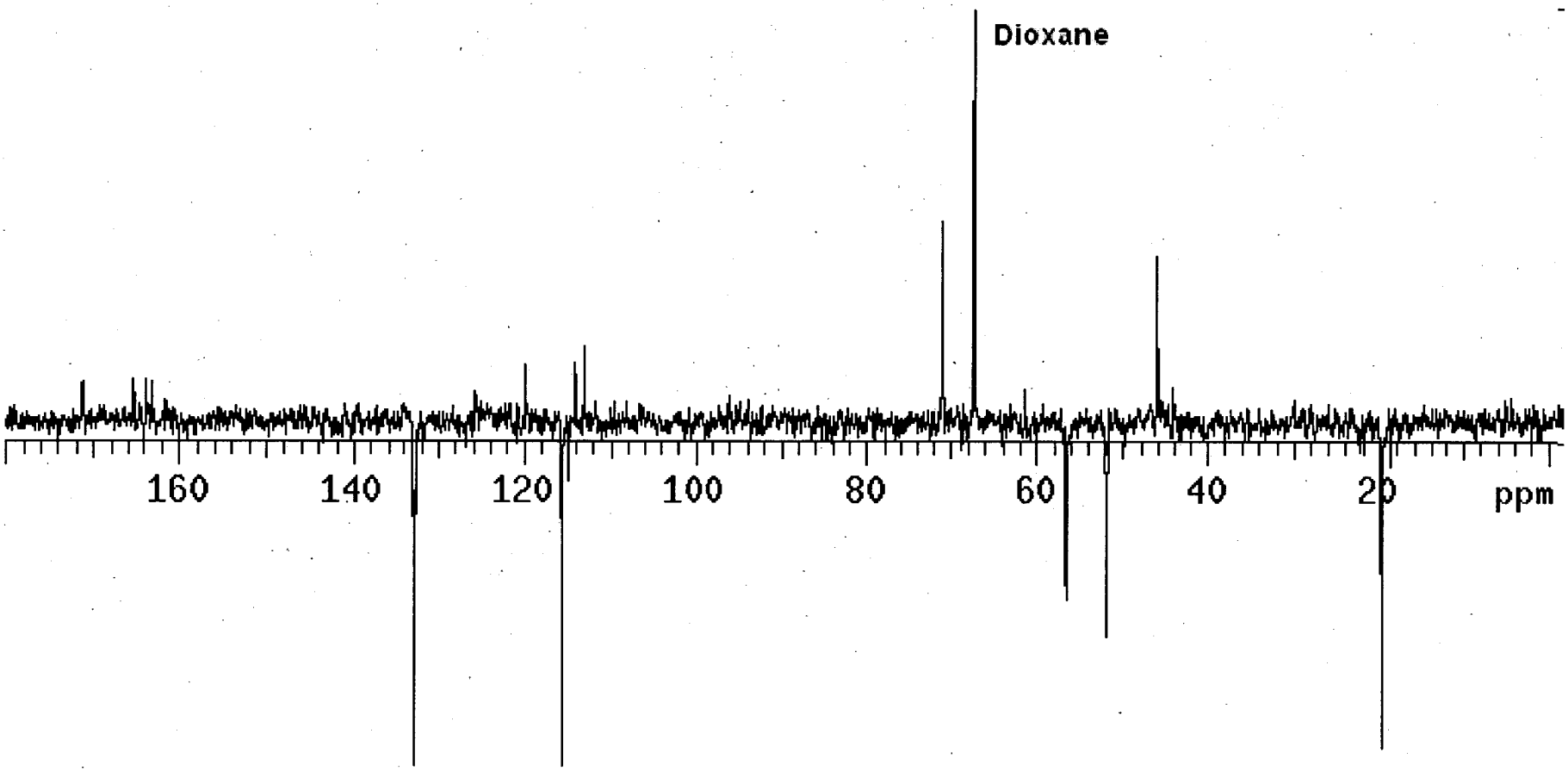


Figure S9. ^{1}H NMR Spectrum of HPLC-purified Compound **47** trifluoroacetate in 1% TFA–D_2O.

Figure S10. ^{13}C NMR (APT) Spectrum of HPLC-purified Compound **47** trifluoroacetate in 1% TFA–D_2O.



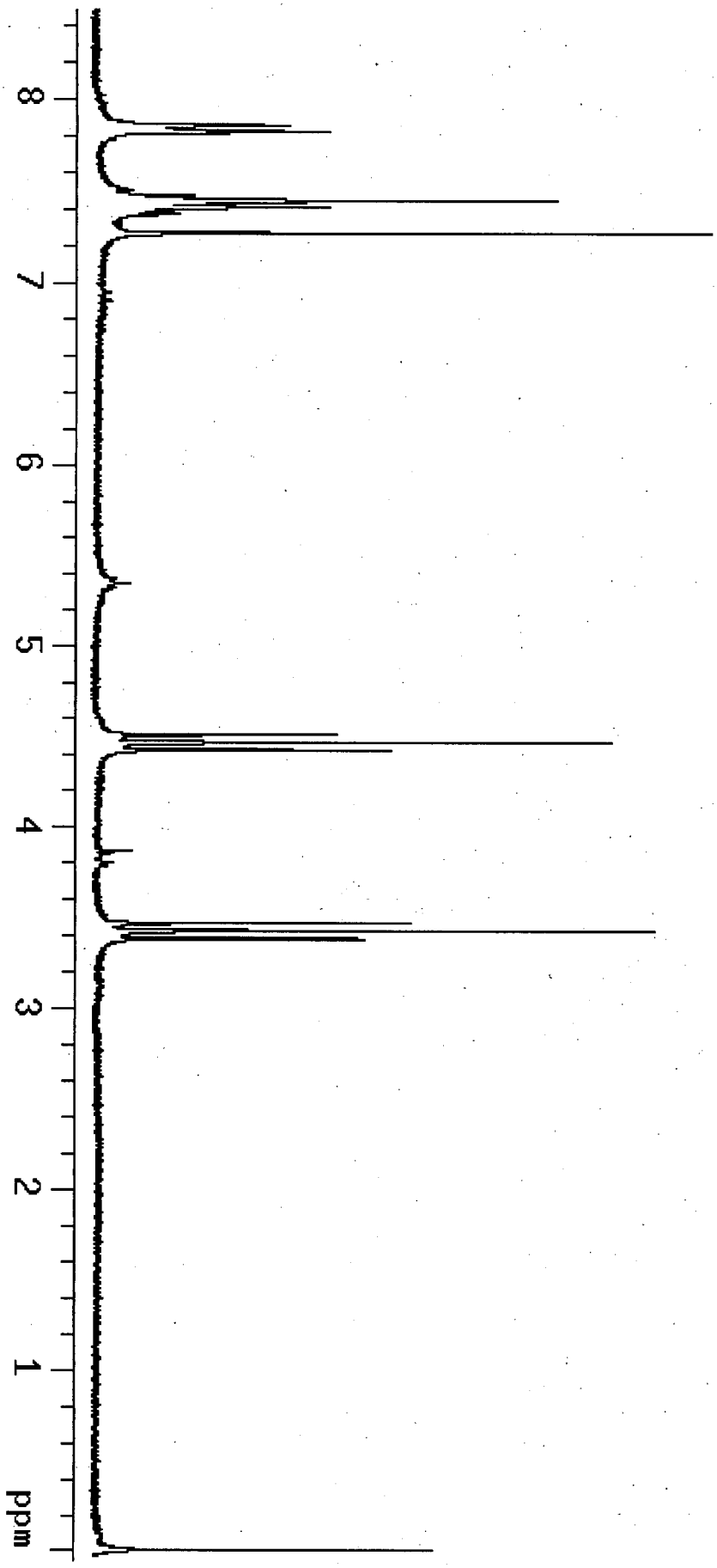
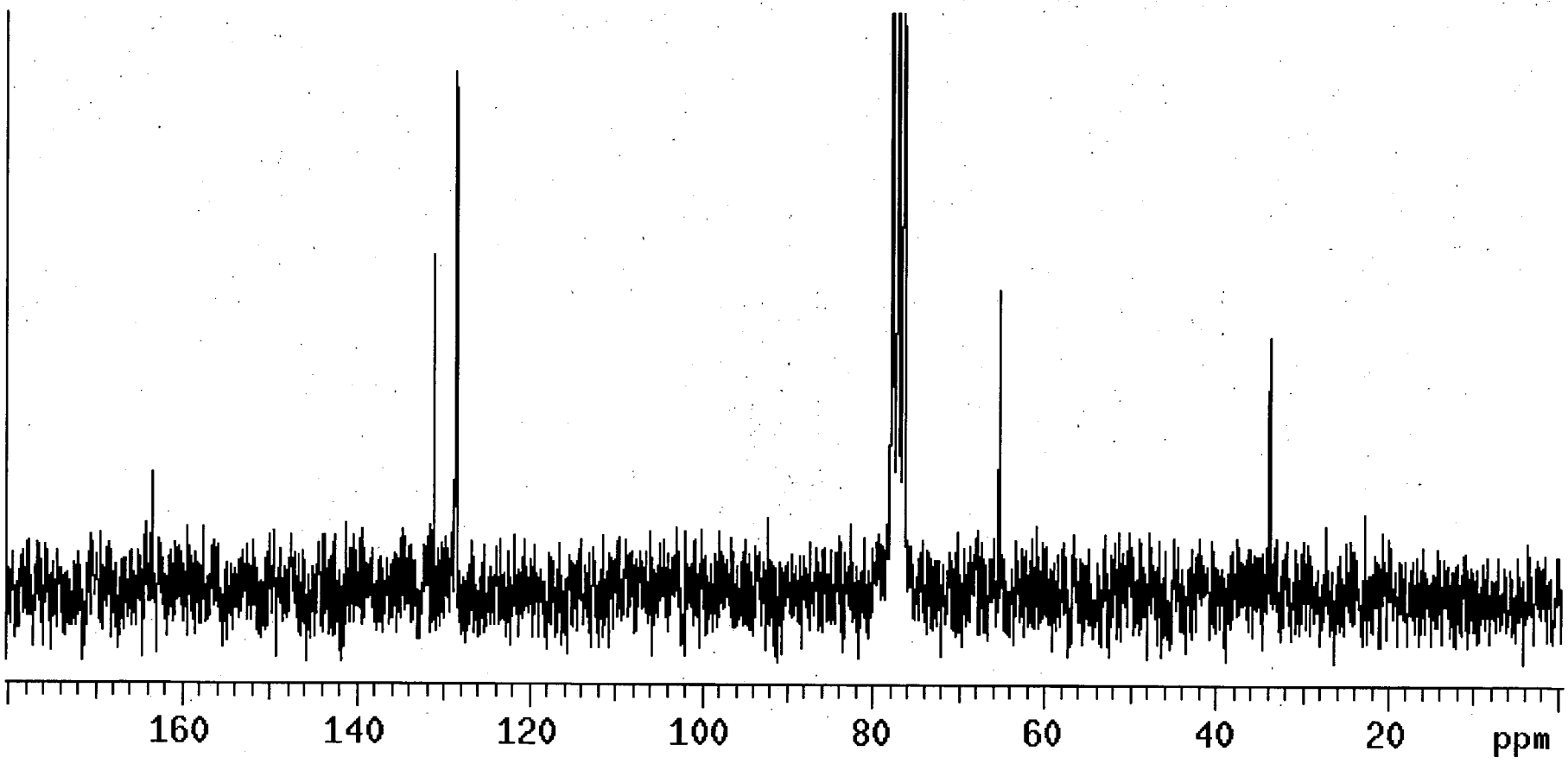


Figure S11. ^{1}H NMR Spectrum of Crude 2–Phenyl–2–thiazoline **59** in $CDCl_3$.

Figure S12 ^{13}C NMR Spectrum of Crude 2–Phenyl–2–thiazoline **59** in $CDCl_3$.



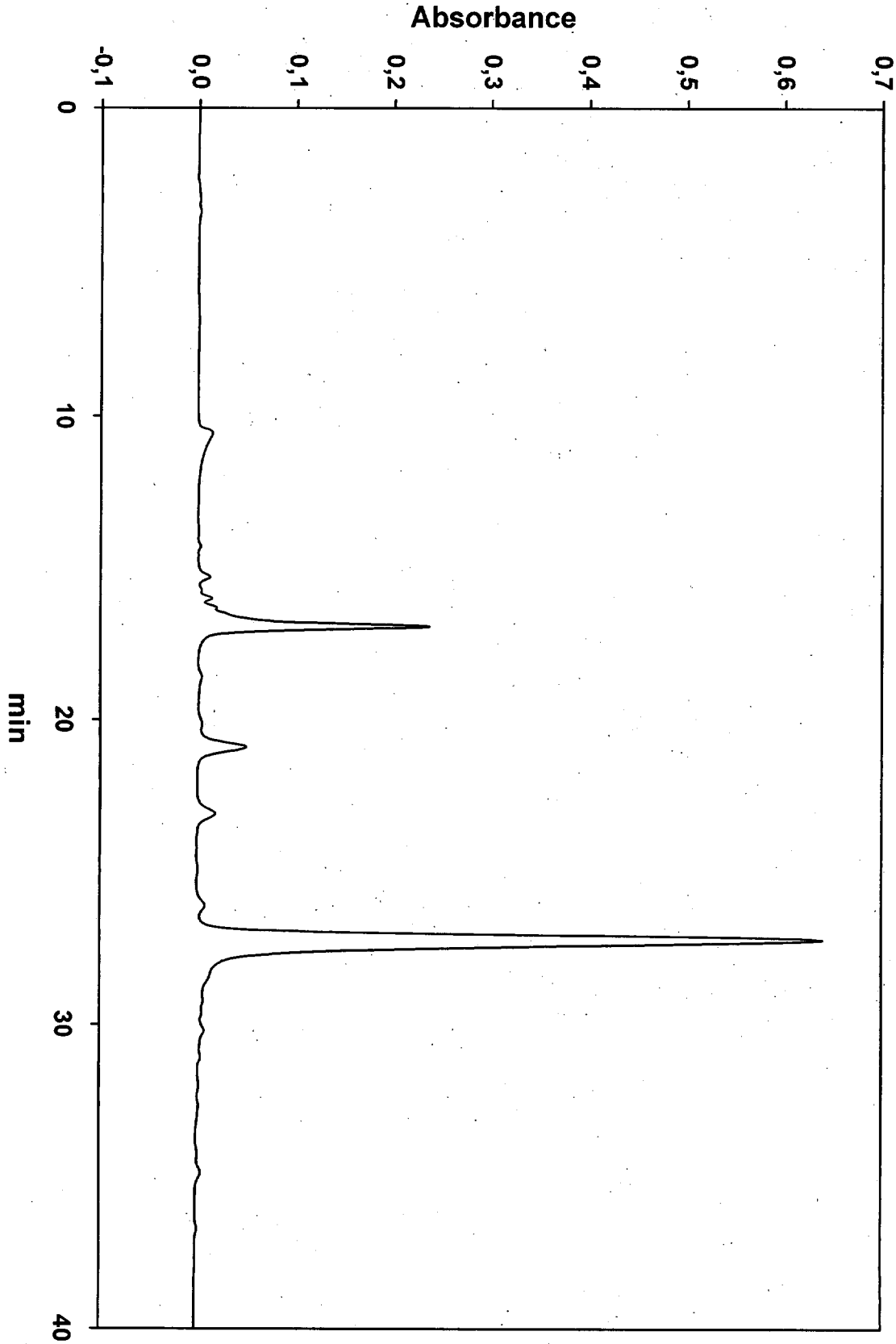
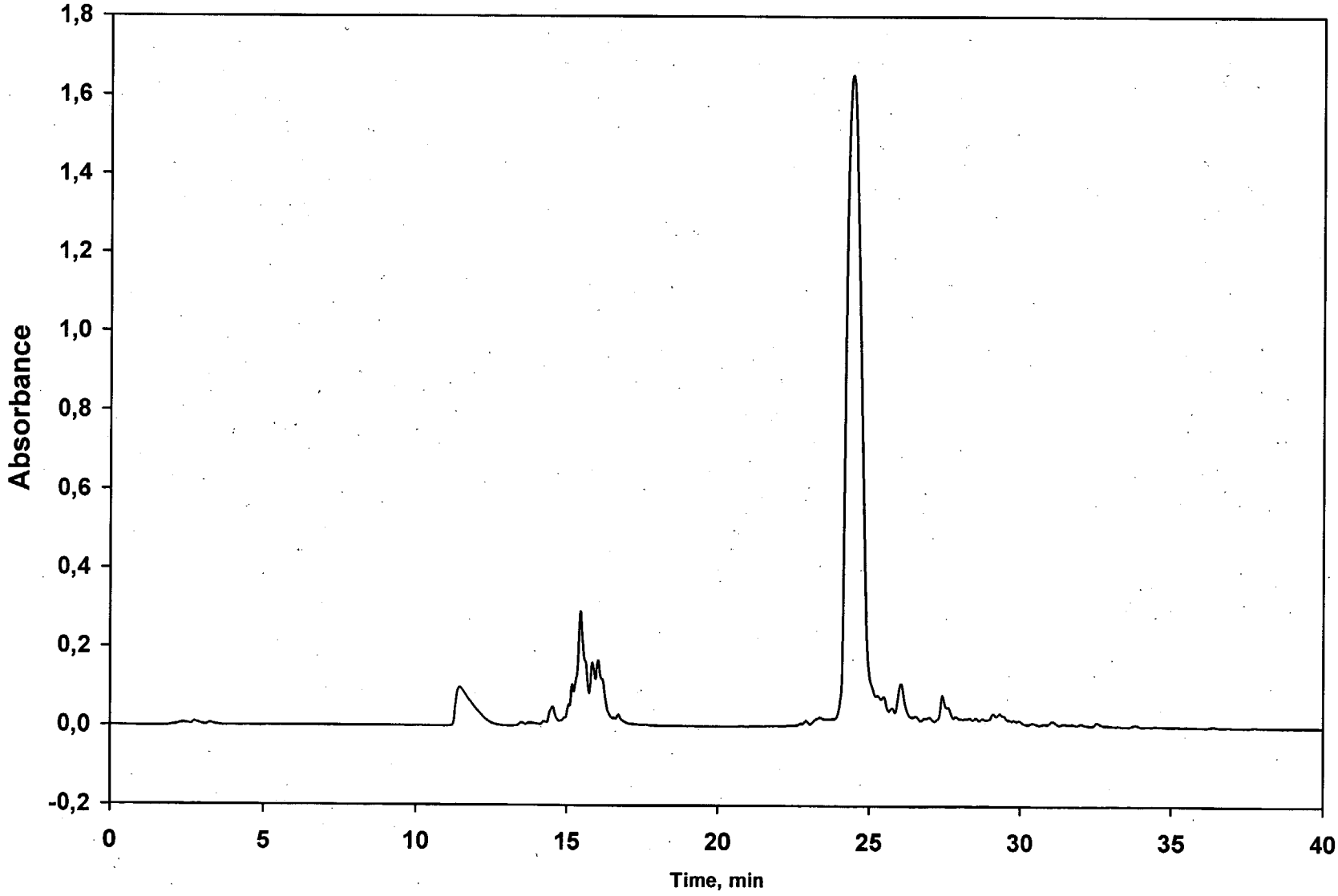


Figure S13. Reverse Phase HPLC Profile for Oligonucleotide DMT–**69** (Crude Deprotection Mixture).

Figure S14. Reverse Phase HPLC Profile for Oligonucleotide DMT–**70** (Crude Deprotection Mixture).



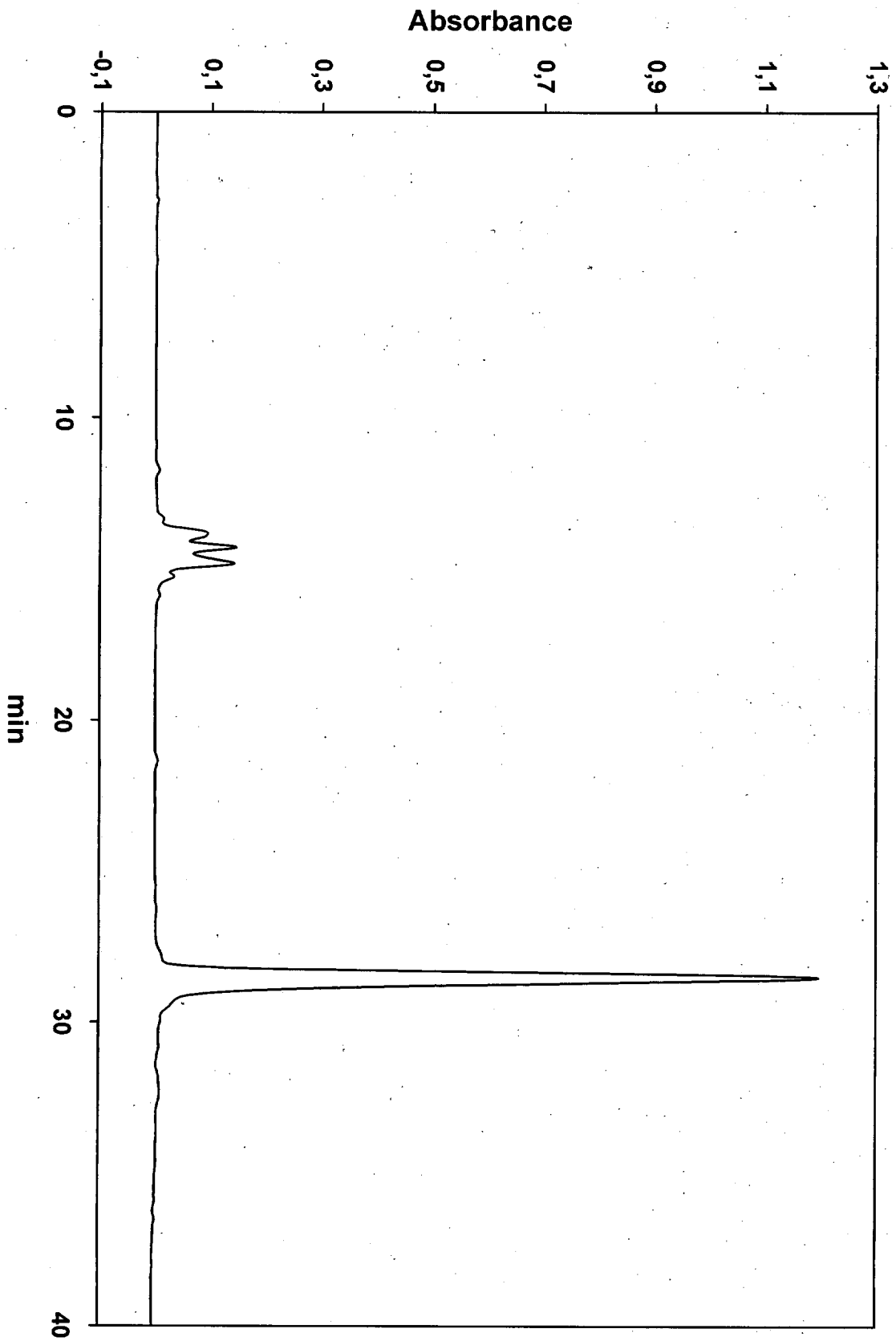


Figure S15. Reverse Phase HPLC Profile for Oligonucleotide DMT–71 (Crude Deprotection Mixture).

Figure S16. Reverse Phase HPLC Profile for Oligonucleotide DMT–**72** (Crude Deprotection Mixture).

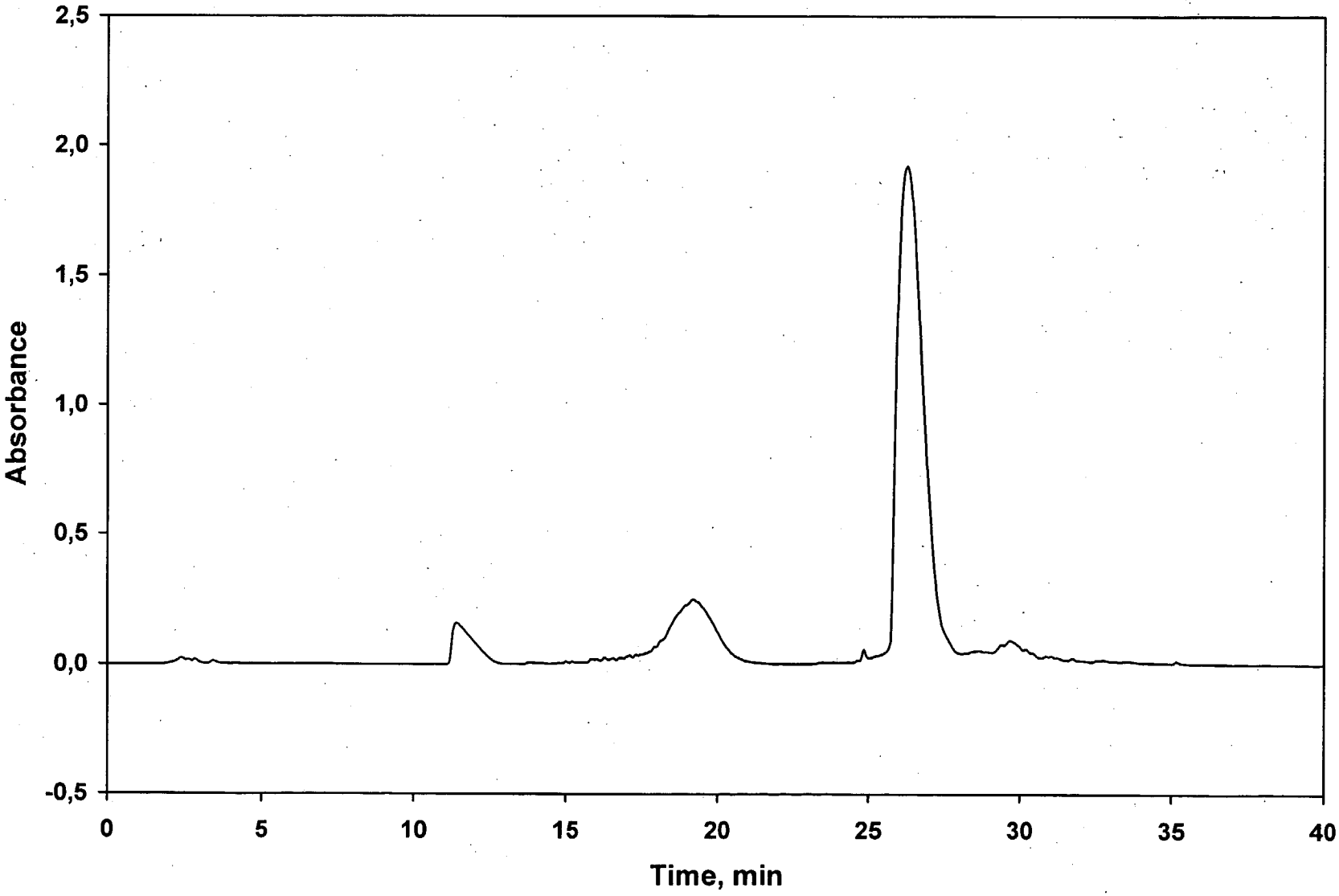


Figure S17. Reverse Phase HPLC Profile for Oligonucleotide DMT–**73** (Crude Deprotection Mixture).

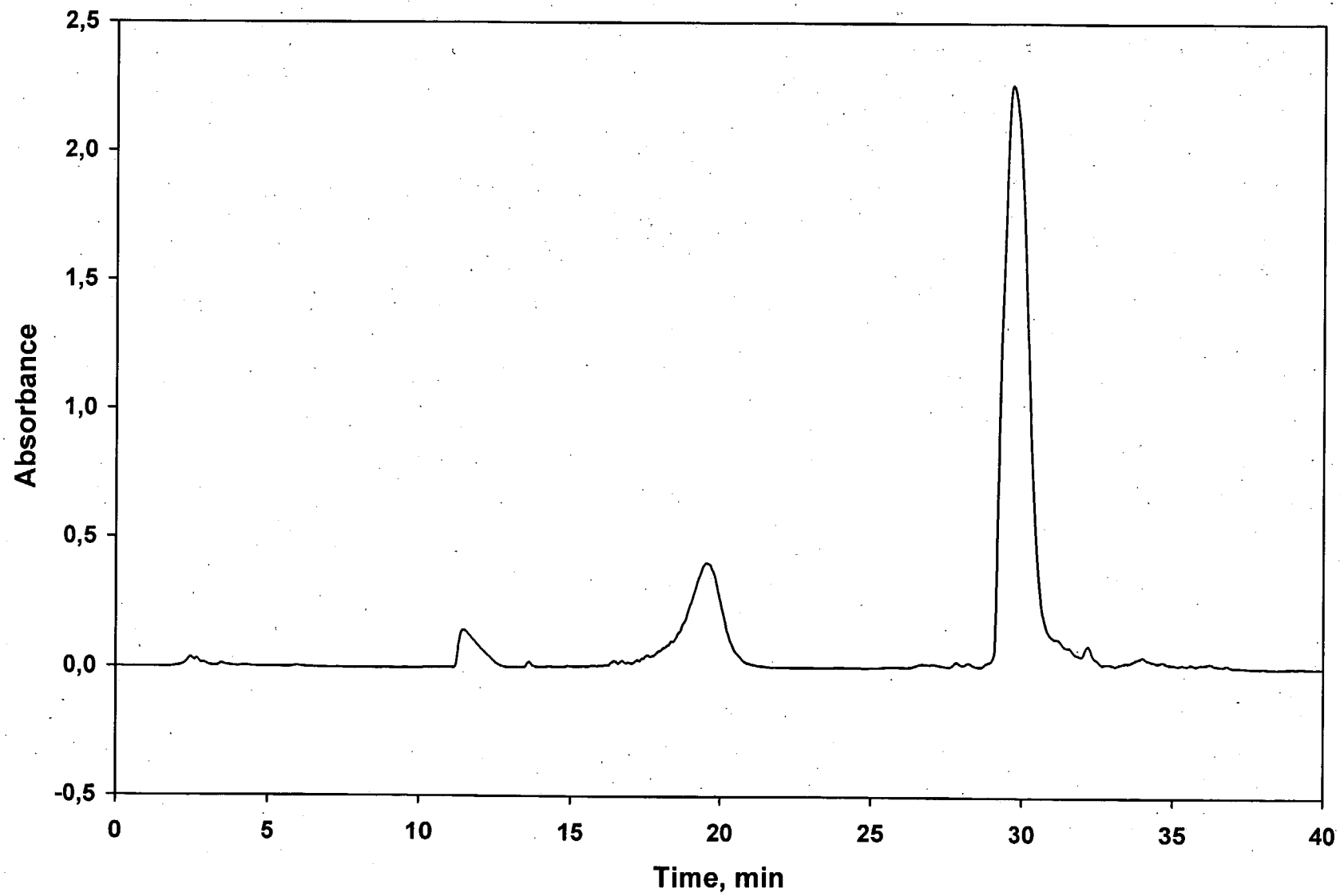


Figure S18. Reverse Phase HPLC Profile for Oligonucleotide DMT–**74** (Crude Deprotection Mixture).

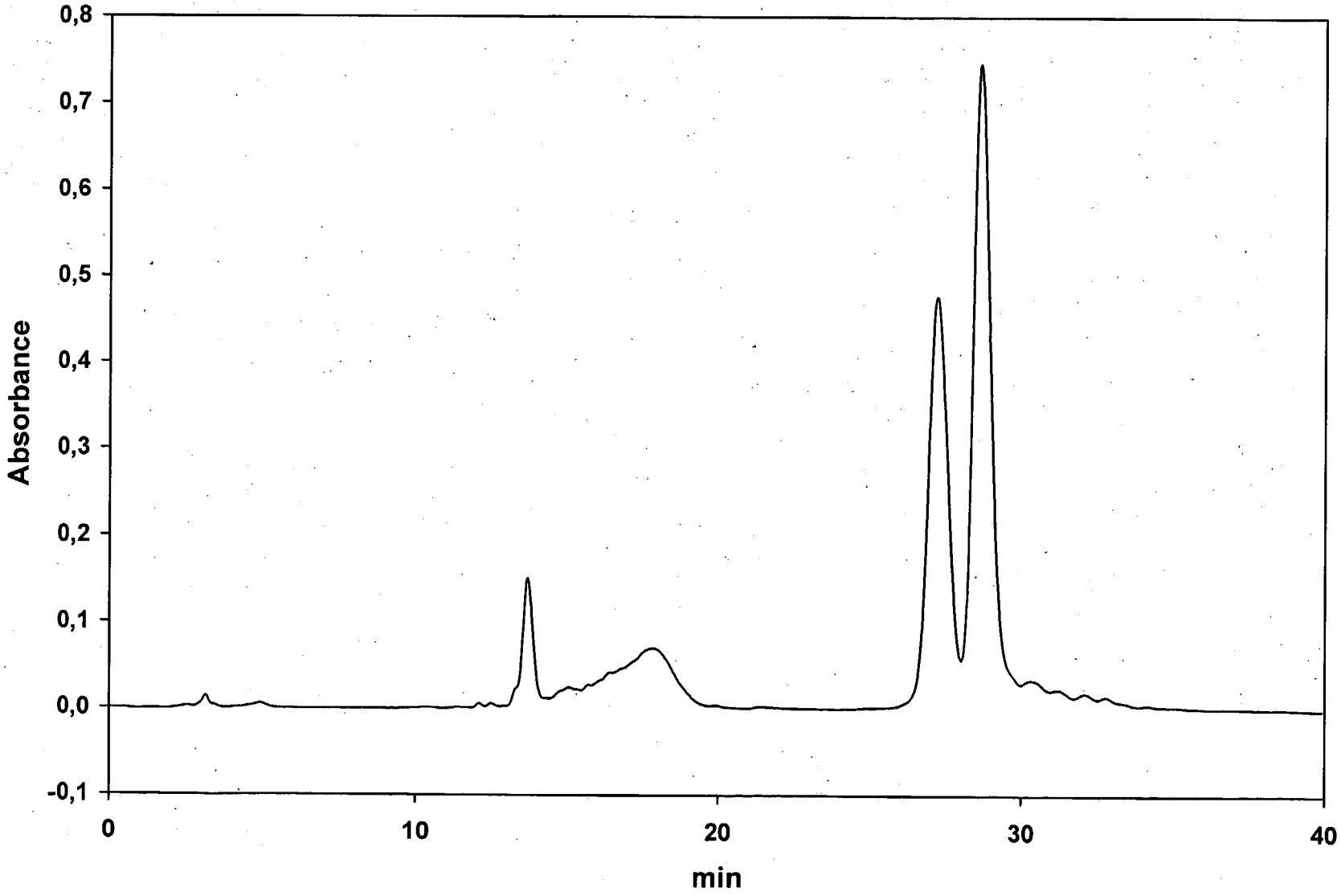
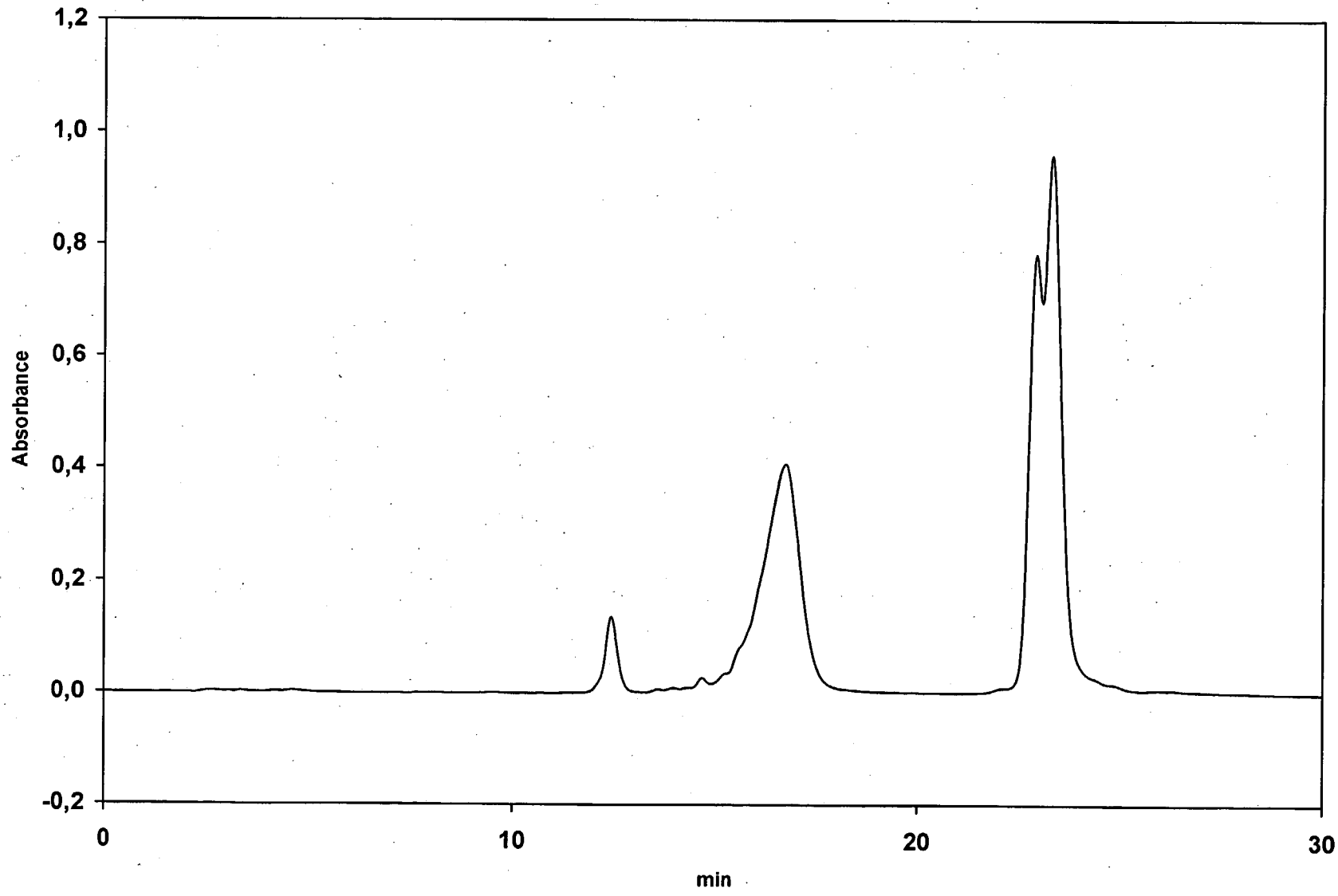


Figure S19. Reverse Phase HPLC Profile for Oligonucleotide DMT–**75** (Crude Deprotection Mixture).



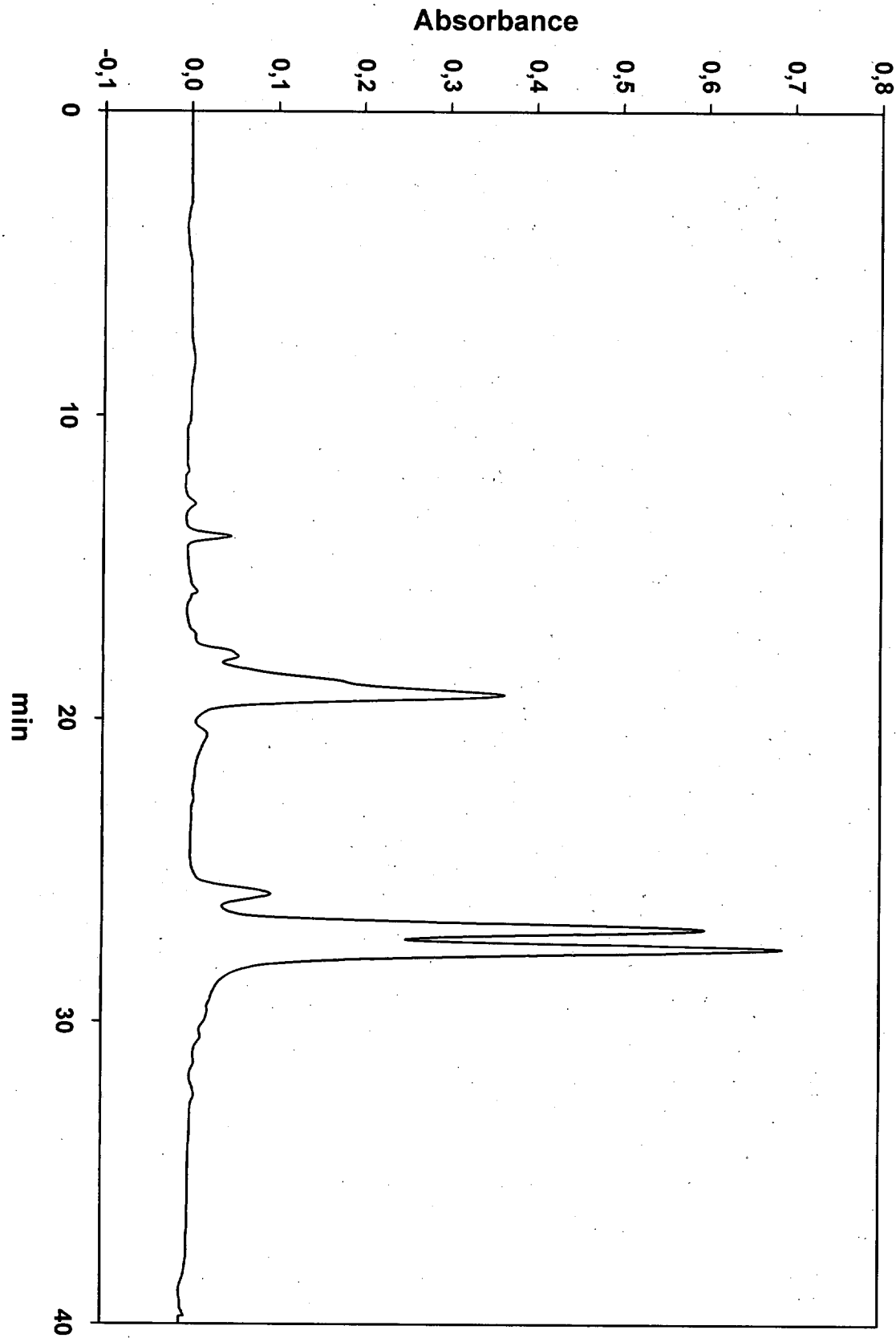


Figure S20. Reverse Phase HPLC Profile for Oligonucleotide DMT–**76** (Crude Deprotection Mixture).