

Oxathiaphospholane Approach to N- and O- Phosphorothioylation of Amino Acids

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SUPPLEMENTARY MATERIAL (page 1 of 9)

Experimental procedure and ^{31}P NMR spectra for compounds **12a**, **12c** and **12f** obtained in DBU catalyzed reactions of L-**3a**, D,L-**3a**, L-**3c**, D,L-**3c**, L-**3f** and D,L-**3f** with AZT. All spectra were recorded on a 500 MHz spectrometer using CDCl_3 as solvent

General Procedure for the Synthesis of 3'-Azido-3'-Deoxythymidine-5'-(Methoxyaminoacidophosphorothioamidate) (12).

Compound **3** (1 mmol) was dissolved in dry acetonitrile (5ml) and into this solution was dropped a solution of AZT (1mmol) and DBU (1.1 mmol) in dry acetonitrile (6ml). The reaction mixture was stirred at room temperature for 3h, then concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (0→15% methanol in chloroform).

3'-Azido-3'-Deoxythymidine-5'-(Methoxyalaninylphosphorothioamidate)(12a): yield 73%; ³¹P NMR (202 MHz, CDCl₃) δ: 62.96, 62.22; ¹H NMR (500 MHz, CDCl₃) δ: 7.88* and 7.86* (s, 2H), 6.43-6.40* and 6.38-6.35* (t, 1H, *J* = 6.8 Hz), 4.63-4.61* and 4.57-4.55* (m, 1H), 4.23-4.17 (m, 4H), 3.86* and 3.84* (s, 3H), 3.33-3.29 (q, 1H, *J* = 7.3 Hz), 2.57-2.46 (m, 2H), 2.13-2.12 (d, 3H), 1.51-1.47 (dd, 3H, *J* = 7.3 Hz); ¹³C NMR (125 MHz, CDCl₃) δ: 178.35, 177.83, 166.66, 152.67, 138.19, 113.25, 113.13, 86.57, 86.30, 85.02, 84.95, 69.98, 66.12, 65.91, 63.09, 62.98, 53.89, 53.78, 52.75, 52.23, 22.37 (*J* = 3.5 Hz), 22.13 (*J* = 4.0 Hz), 13.82, 13.77; FAB-MS *m/z*: (M-1) 447.

3'-Azido-3'-Deoxythymidine-5'-(Methoxyleucinylphosphorothioamidate)(12c): yield 80%; ³¹P NMR (202 MHz, CDCl₃) δ: 60.14, 59.85; ¹H NMR (500 MHz, CDCl₃) δ: 7.83* and 7.81* (s, 1H), 6.26-6.20 (m, 1H), 4.48-4.45 (m, 1H), 4.08* and 4.06* (s, 3H), 4.01-3.92 (m, 1H), 3.70-3.68 (m, 3H), 3.34-3.10 (d, 1H), 2.50-2.32 (m, 2H), 1.99 (s, 3H), 1.82-1.73 (m, 1H), 1.51-1.47 (m, 2H), 0.95-0.89 (m, 6H); ¹³C NMR (125 MHz, CDCl₃) δ: 178.77, 177.72, 166.15, 152.30, 138.25, 113.22, 86.12, 85.93, 85.14, 84.80, 68.17, 67.12, 65.19, 63.25, 62.73, 52.94, 52.80, 51.93, 51.75, 44.15 (*J* = 6.0 Hz), 25.15, 23.00, 22.15, 13.83, 13.70; FAB-MS *m/z*: (M-1) 489.

3'-Azido-3'-Deoxythymidine-5'-(Dimethoxyglutamicphosphorothioamidate)(12f): yield 77%; ³¹P NMR (202 MHz, CDCl₃) δ: 63.06, 62.90; ¹H NMR (500 MHz, CDCl₃) δ: 7.82 (bs, 1H), 6.39-6.368* and 6.35-6.32* (t, 1H, *J* = 6.2 Hz), 4.61-4.59* and 4.58-4.52* (m, 1H), 4.50-4.24 (m, 2H), 4.21-4.18 (m, 3H), 3.86* and 3.84* (s, 3H), 3.80* and 3.78* (s, 3H), 2.62-2.48 (m, 4H), 2.23-2.15 (m, 1H), 2.11-

2.10 (d, 3H), 2.07-2.01 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ : 177.15, 176.71, 166.59, 152.54, 138.10, 113.11, 86.68, 86.41, 84.88, 84.81, 65.93, 62.77, 56.45, 55.89, 53.96, 53.85, 53.47, 53.39, 31.79, 31.64, 31.12, 30.83, 13.79, 13.74; FAB-MS m/z : (M-1) 519.

Figure S1. 3'-Azido-3'-deoxythymidine-5'-(methoxyalaninylphosphorothioamidate) (**12a**) obtained in DBU-catalyzed reaction of L-**3a** with AZT.

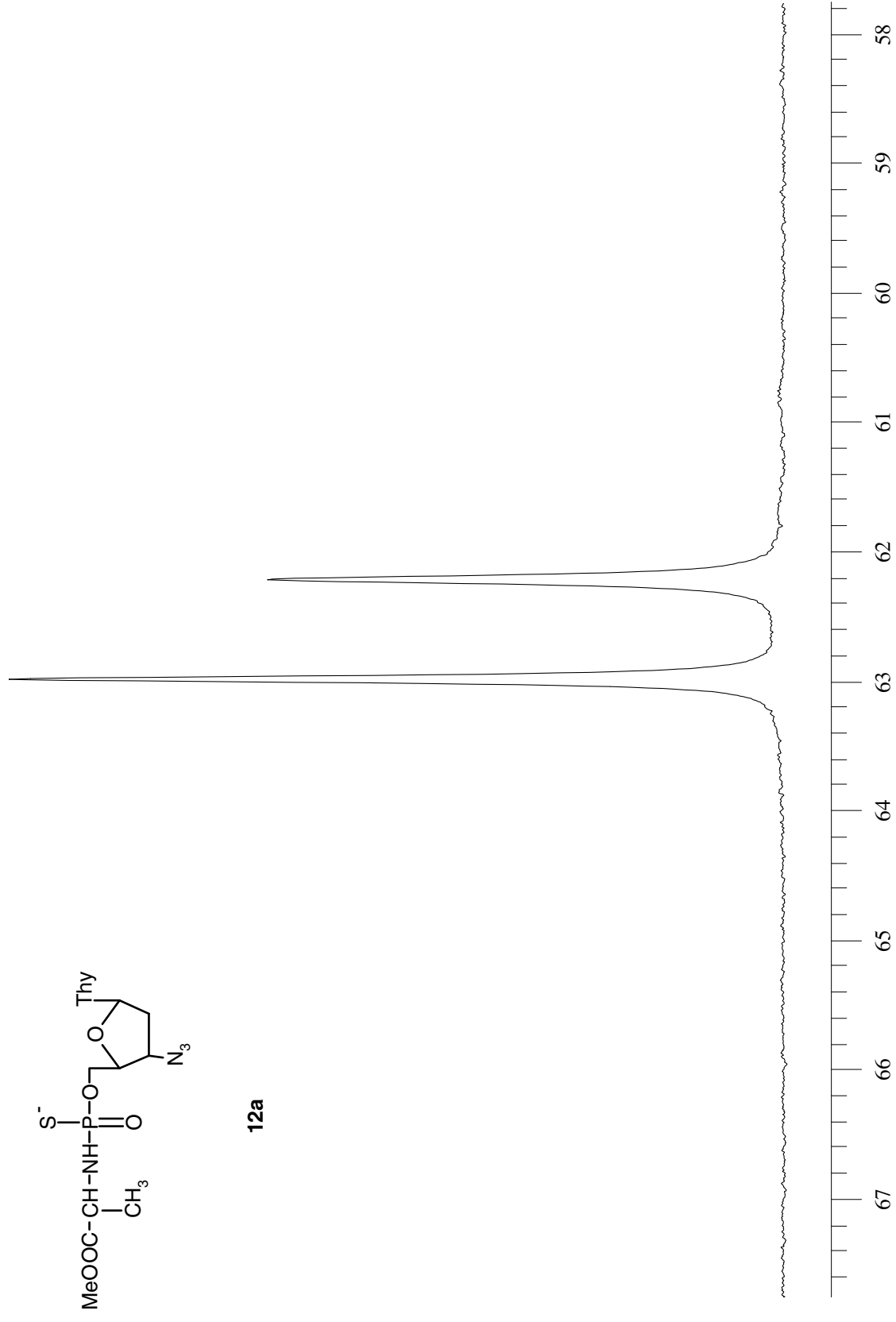


Figure S2. 3'-Azido-3'-deoxythymidine-5'-(methoxyalanyl)phosphorothioamidate (**12a**) obtained in DBU-catalyzed reaction of D,L-**3a** with AZT.

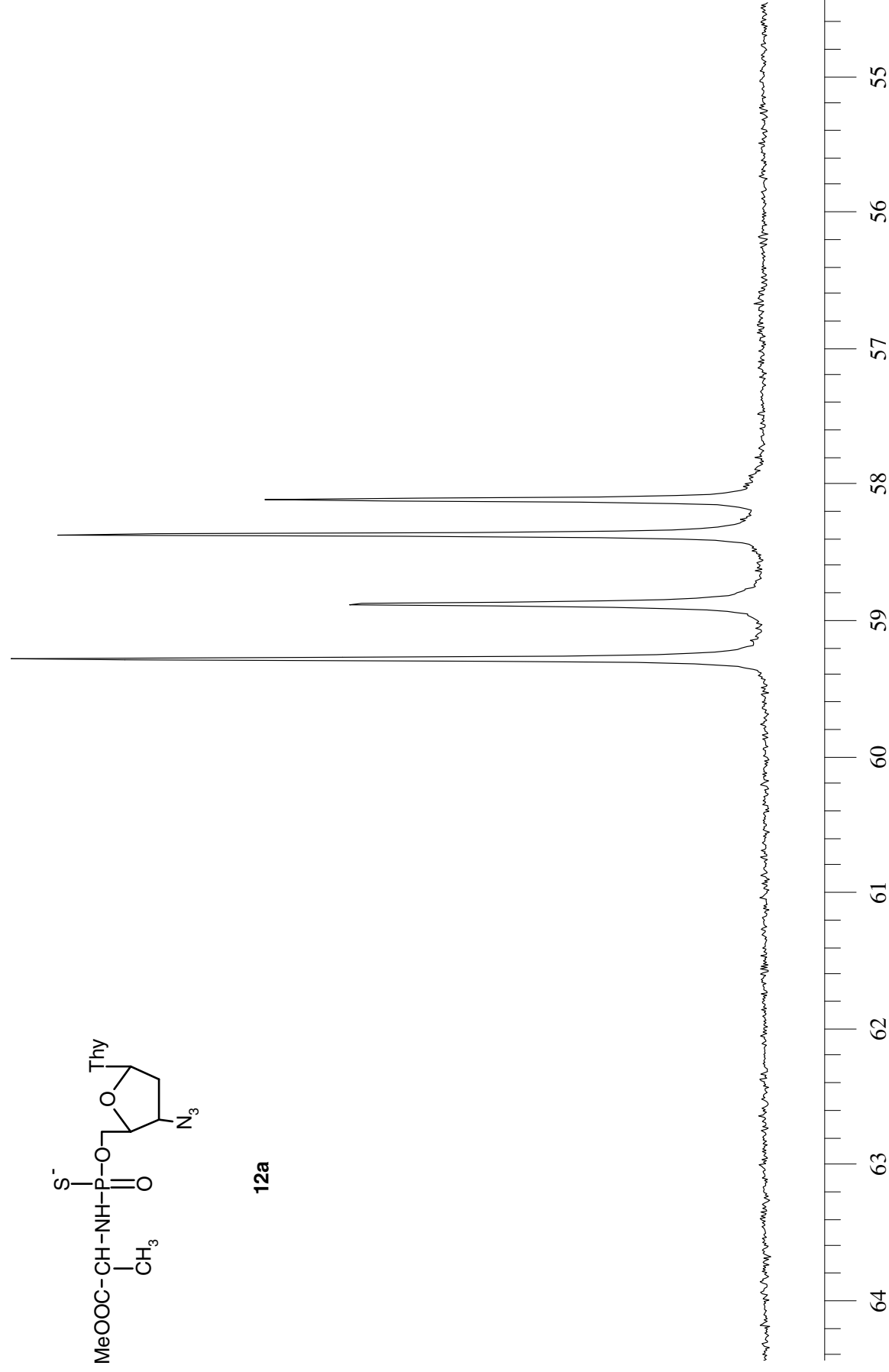


Figure S3. 3'-Azido-3'-deoxythymidine-5'-(methoxy)leucinylphosphorothioamidate (**12c**) obtained in DBU-catalyzed reaction of L-**3c** with AZT.

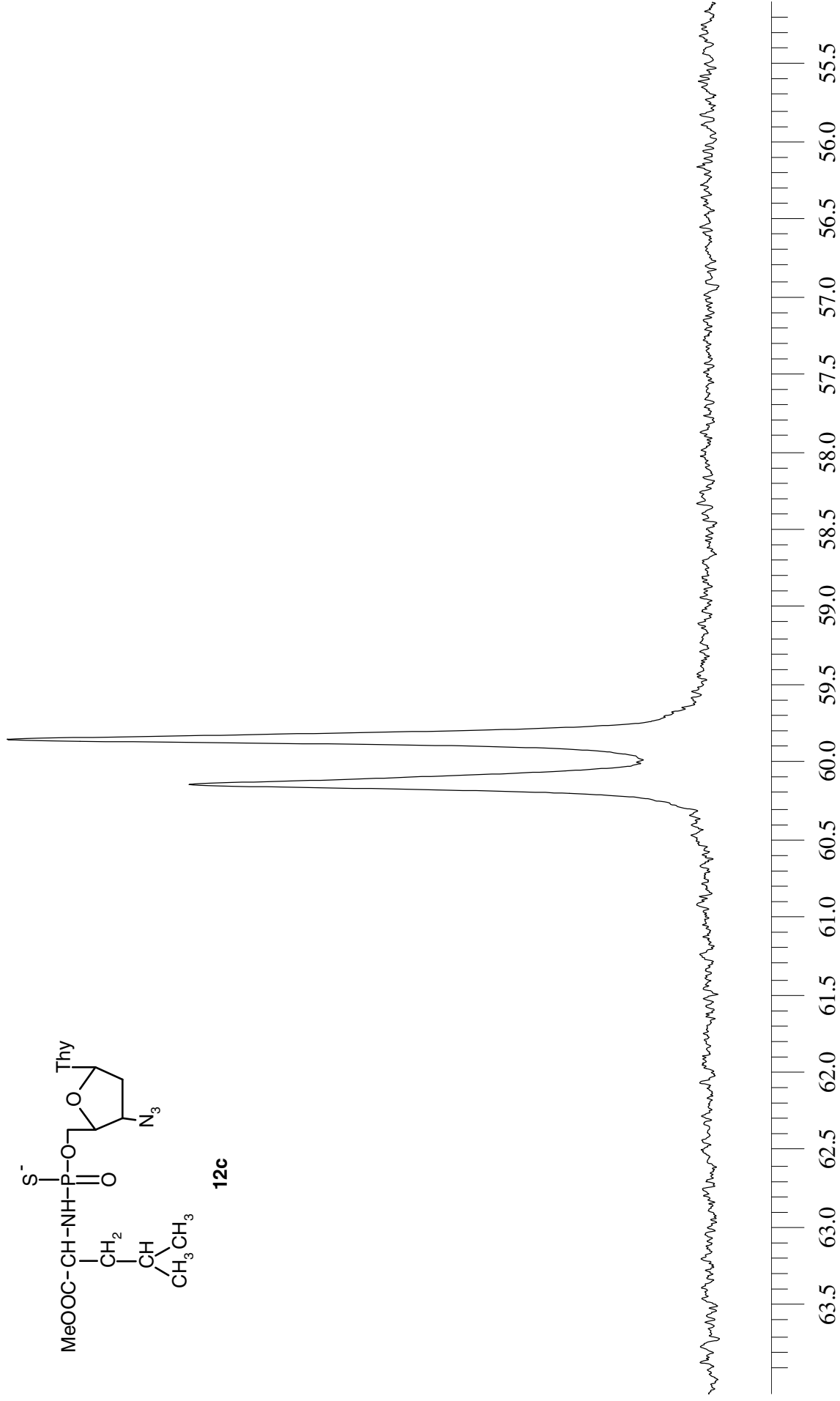


Figure S4. 3'-Azido-3'-deoxythymidine-5'-(methoxy)leucinylphosphorothioamide) (**12c**) obtained in DBU-catalyzed reaction of D,L-**3c** with AZT.

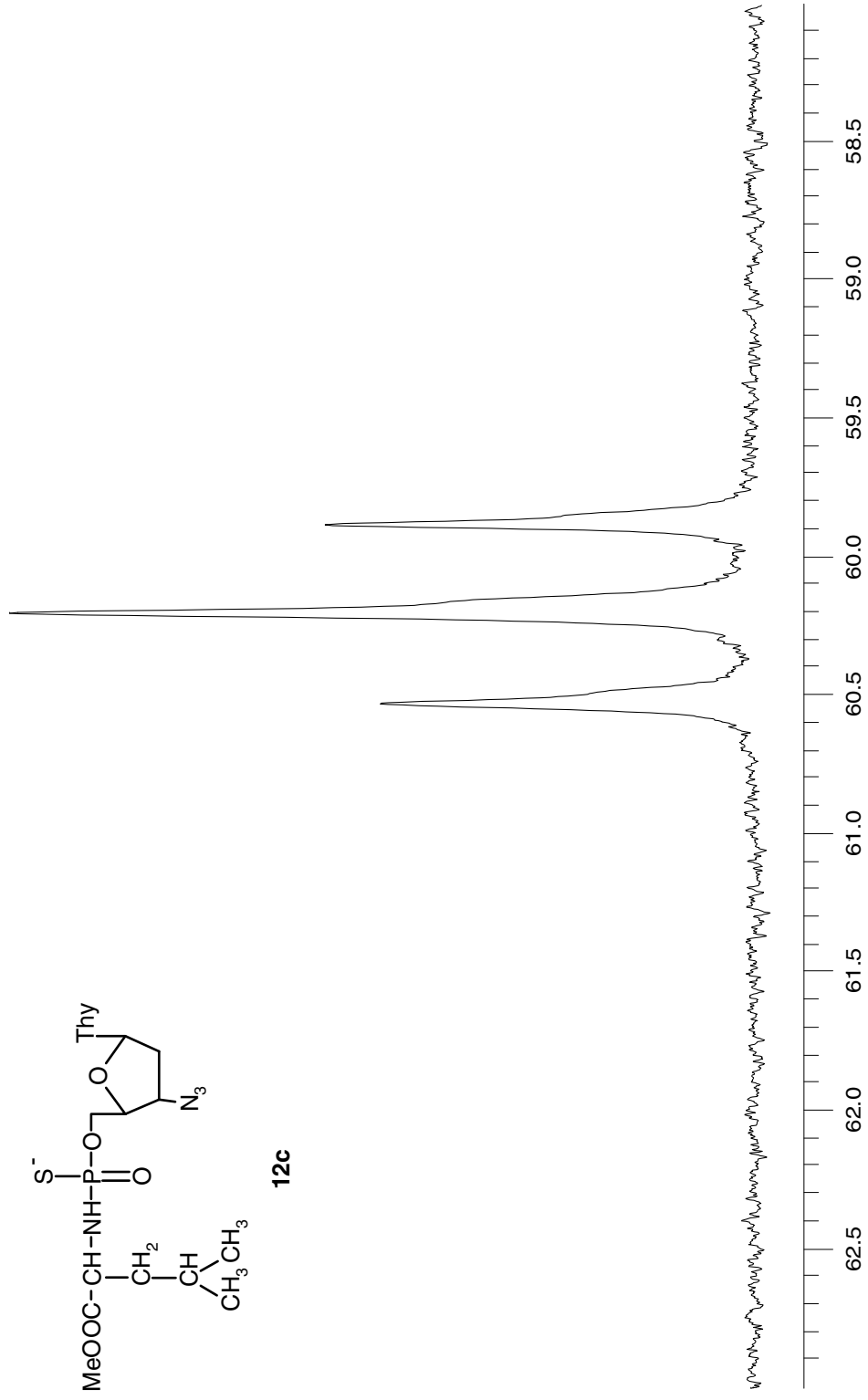
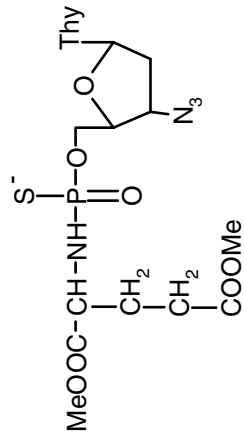


Figure S5. 3'-Azido-3'-deoxythymidine-5'-(dimethoxyglutamicphosphorothioamidate) (**12f**) obtained in DBU-catalyzed reaction of L-**3f** with AZT.



12f

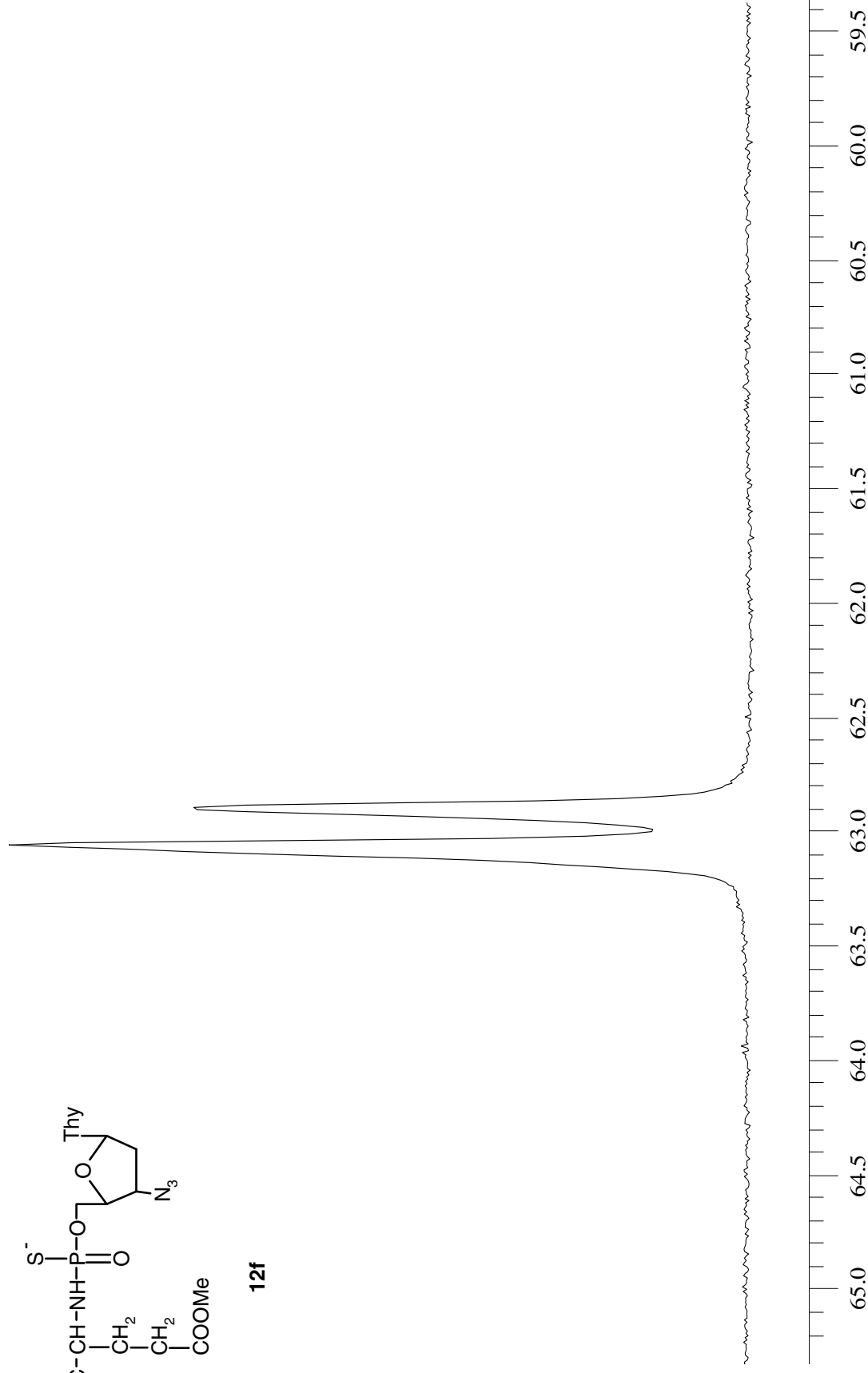
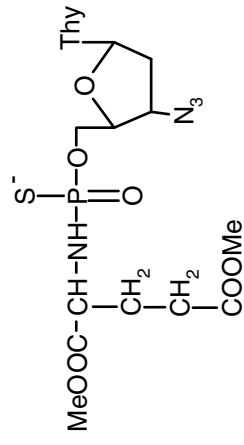


Figure S6. 3'-Azido-3'-deoxythymidine-5'-(dimethoxyglutamamicphosphorothioamidate) (**12f**) obtained in DBU-catalyzed reaction of D,L-**3f** with AZT.



12f

