Supporting Information

For

"Synthesis and Thermodynamic Studies of Oligodeoxynucleotides Containing Tandem Lesions of Thymidine Glycol and 8-oxo-2'-Deoxyguanosine"

by

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Synthesis of 8-oxo-2'-deoxyguanosine Phosphoramidite Building Block

The title compound was synthesized according to reported procedures[1-3].

8-bromo-2'-deoxyguanosine[1]

8-Bromo-2'-deoxyguanosine was prepared according to the procedure reported by Scharer et al. [1]

^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 10.78 (s, 1H, N1-H), 6.48 (s, 2H), 6.15 (t, J = 7.8 Hz), 4.39 (m, 1H), 3.80 (m, 1H), 3.60 (dd, J = 5.2, 11.8 Hz, 1H), 3.50 (dd, J = 5.9, 11.6 Hz, 1H), 3.16 (m, 1H), 2.09 (m, 1H); ESI-MS: *m/z* 343.9 $[M - H]^-$.

8-benzyloxy-2'-deoxyguanosine[2]

The title compound was synthesized using the procedure reported by Kumar et al. [2]

^{1}H NMR (500 MHz, DMSO-d_6): δ (ppm) 10.55 (s, 1H, N-H), 7.31-7.49 (m, 5H), 6.31 (s, 2H), 6.08 (t, J = 7.2 Hz), 5.40 (dd, J = 11.9, 17.3 Hz, 2H), 5.16 (d, J = 4.3 Hz, 1H), 4.77 (5, J = 6.0 Hz, 1H), 4.23 (m, 1H), 3.70 (m, 1H), 3.43 (m, 1H), 3.36 (m, 1H), 3.08 (br, 1H), 2.85 (m, 1H), 2.02 (m, 1H), 1.17 (t, J = 7.2 Hz, 1H); ESI-MS: *m/z* 372.1 $[M - H]^-$.

8-oxo-2'-deoxyguanosine[2]

The title compound was synthesized using the procedure reported by Kumar et al. [2]

^{1}H NMR (300 MHz, DMSO-d_6): δ (ppm) 10.80 (br, 1H, N-H); 10.68 (s, 1H), 6.45 (br, 2H), 6.02(t, J = 7.4 Hz, 1H), 4.85 (br, 2H), 4.32 (m, 1H), 3.74 (m, 1H), 3.56 (dd, J = 5.5, 11.7 Hz, 1H), 3.43 (dd, J = 5.5, 11.7 Hz, 1H), 2.97(m, 1H), 1.92 (m, 1H); ESI-MS: *m/z* 282.1 $[M - H]^-$.

2-*N*-(phenoxyacetyl)-8-oxo-2'-deoxyguanosine[3]

Phenoxyacetyl-protected 8-oxodeoxyguanosine was prepared according to the procedure described by Cadet et al. [3]

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm) 11.88 (br, 1H), 11.68 (br, 1H, N-H), 11.30 (s, 1H), 7.31 (t, J = 8.9 Hz, 2H), 6.98 (m, 3H), 6.08 (t, J = 7.3 Hz, 1H), 5.15 (d, J = 4.1 Hz, 1H), 4.85 (s, 2H), 4.70 (t, J = 5.5 Hz, 1H), 4.37 (m, 1H), 3.75 (m, 1H), 3.57 (m, 1H), 3.44 (m, 1H), 3.05 (m, 1H), 1.99 (m, 1H); ESI-MS: *m/z* 418.0 $[M+H]^+$.

5'-*O*-(4,4'-dimethoxytrityl)-2-*N*-(phenoxyacetyl)-8-oxo-2'-deoxyguanosine-3'-*O*-[(2-cyanoethyl)-*N,N*-diisopropyl-phosphoramidite (7)

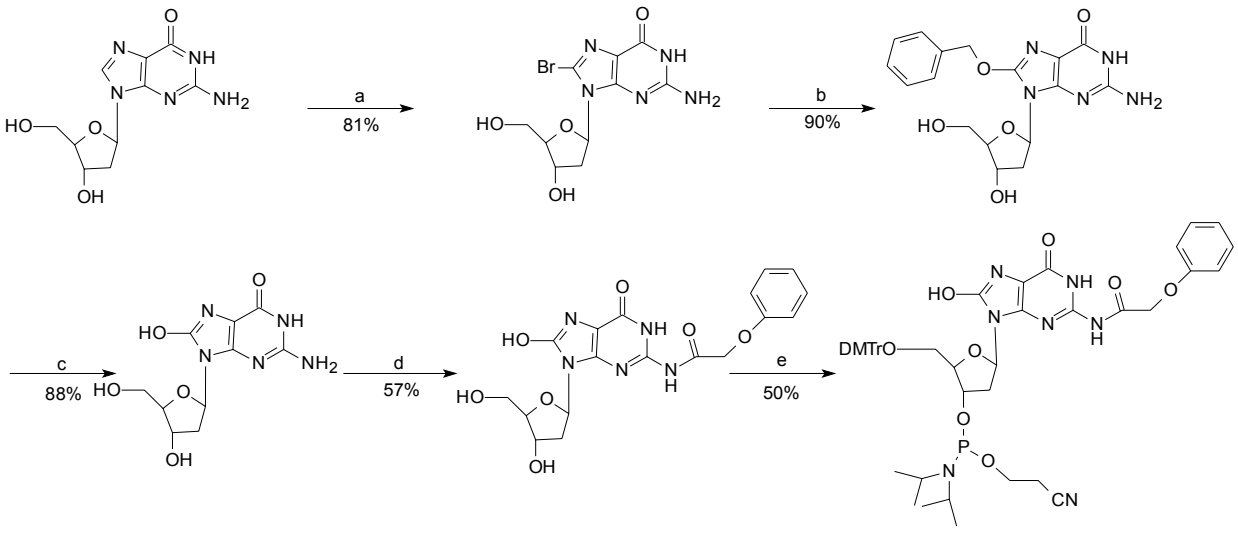
Compound **7** was prepared according to the procedure described by Cadet et al.[3]

^{31}P-NMR (400 MHz, $CDCl_3$): 149.56, 149.66. ESI-MS: *m/z* 942.3 $[M+Na]^+$.

References:

1. Gillet, L. C. J.; Scharer, O. D., Preparation of C8-Amine and Acetylamine Adducts of 2'-Deoxyguanosine Suitably Protected for DNA Synthesis. *Org. Lett.* **2002,** 4, (24), 4205-4208.
2. Nampalli, S.; Kumar, S., Efficient synthesis of 8-Oxo-dGTP: A mutagenic nucleotide. *Bioorg. Med. Chem. Lett.* **2000,** 10, (15), 1677-1679.
3. Bourdat, A.-G.; Gasparutto, D.; Cadet, J., Synthesis and enzymic processing of oligodeoxynucleotides containing tandem base damage. *Nucleic Acids Res.* **1999,** 27, (4), 1015-1024.

Scheme S1 Synthesis of 8-oxodG phosphoramidite building block



Reagents: (a) NBS/CH_3CN/H_2O; (b) Na/BnOH/DMSO; (c) 1.0 M HCl/CH_3OH; (d) i, TMS/Pyridine; ii, Phenoxyacetyl chloride; (e) i, DMTrCl/Pyridine, ii, $NC(CH_2)_2OP(Cl)N(iPr)_2$/DIEA/CH_2Cl_2

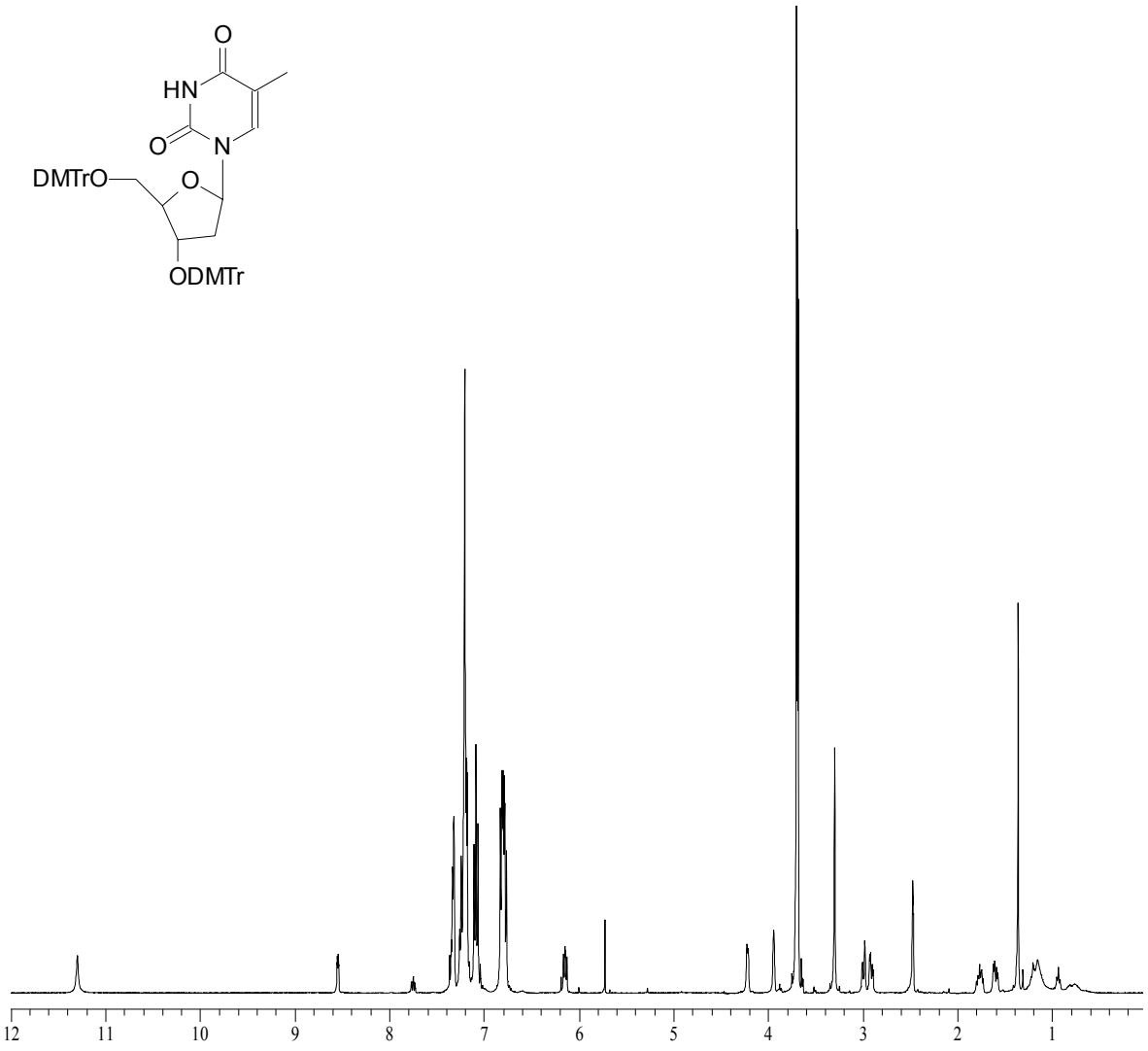


Figure S1. ^{1}H NMR spectrum of **1** (400 MHz, DMSO-d_6).

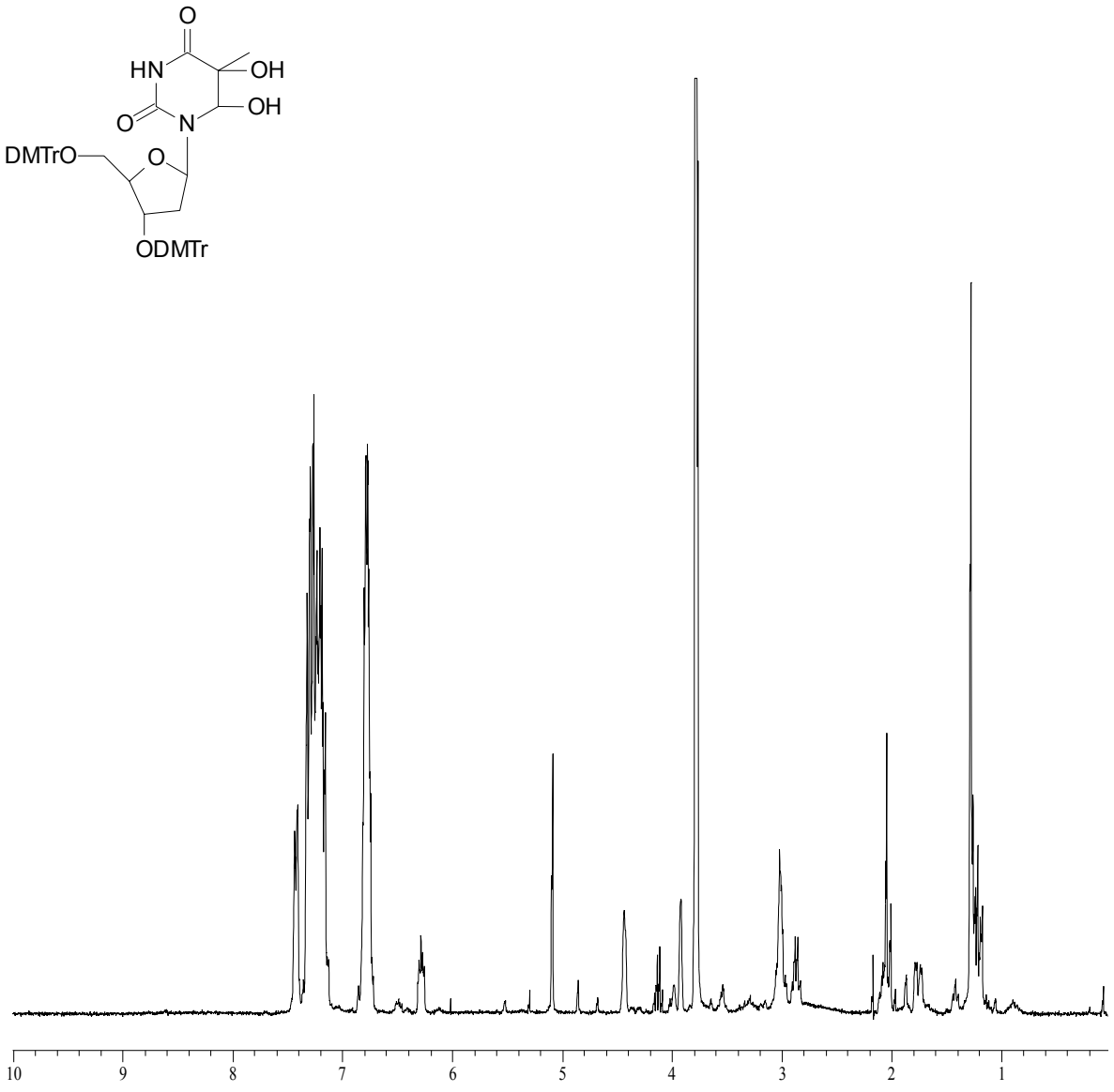


Figure S2. ^{1}H NMR spectrum of **2** (300 MHz, $CDCl_3$).

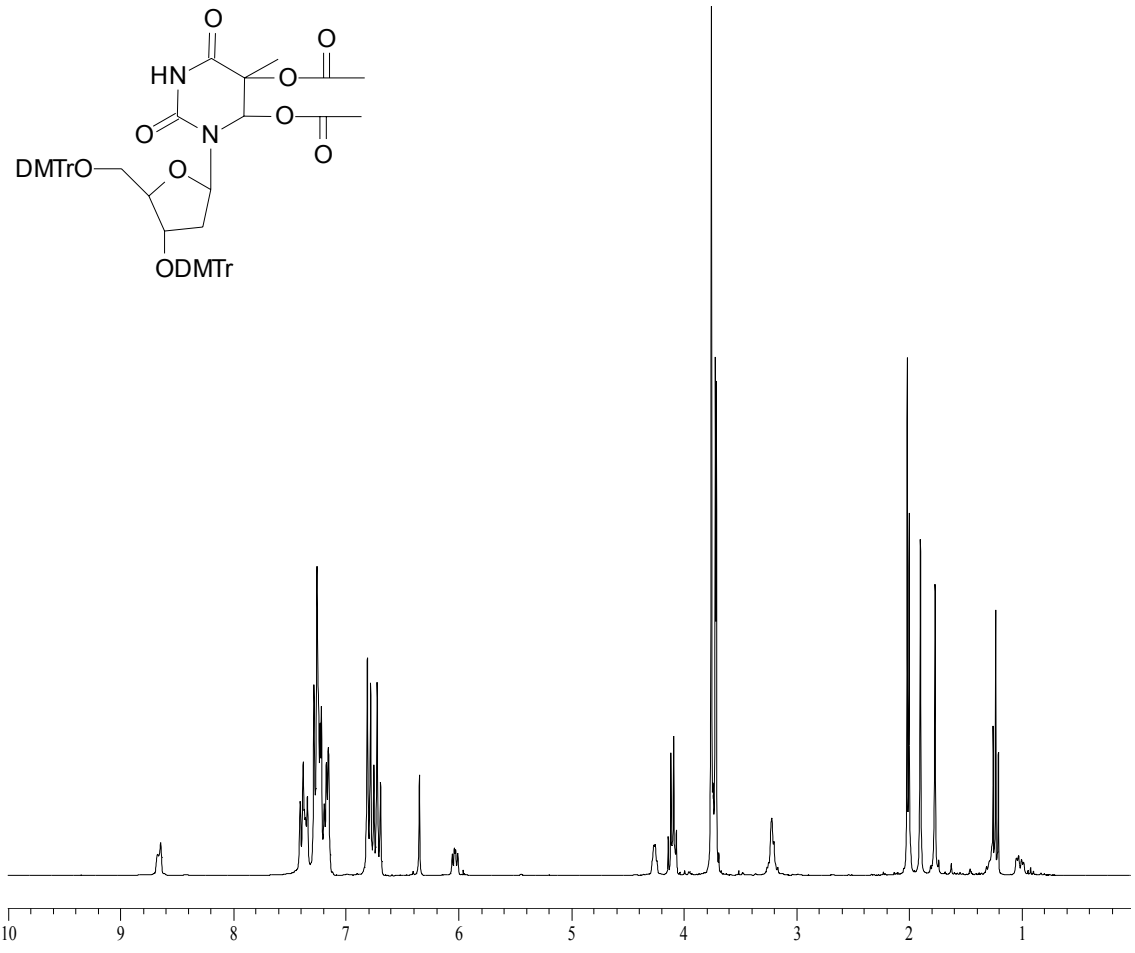


Figure S3. ^{1}H NMR spectrum of **3** (400 MHz, $CDCl_3$).

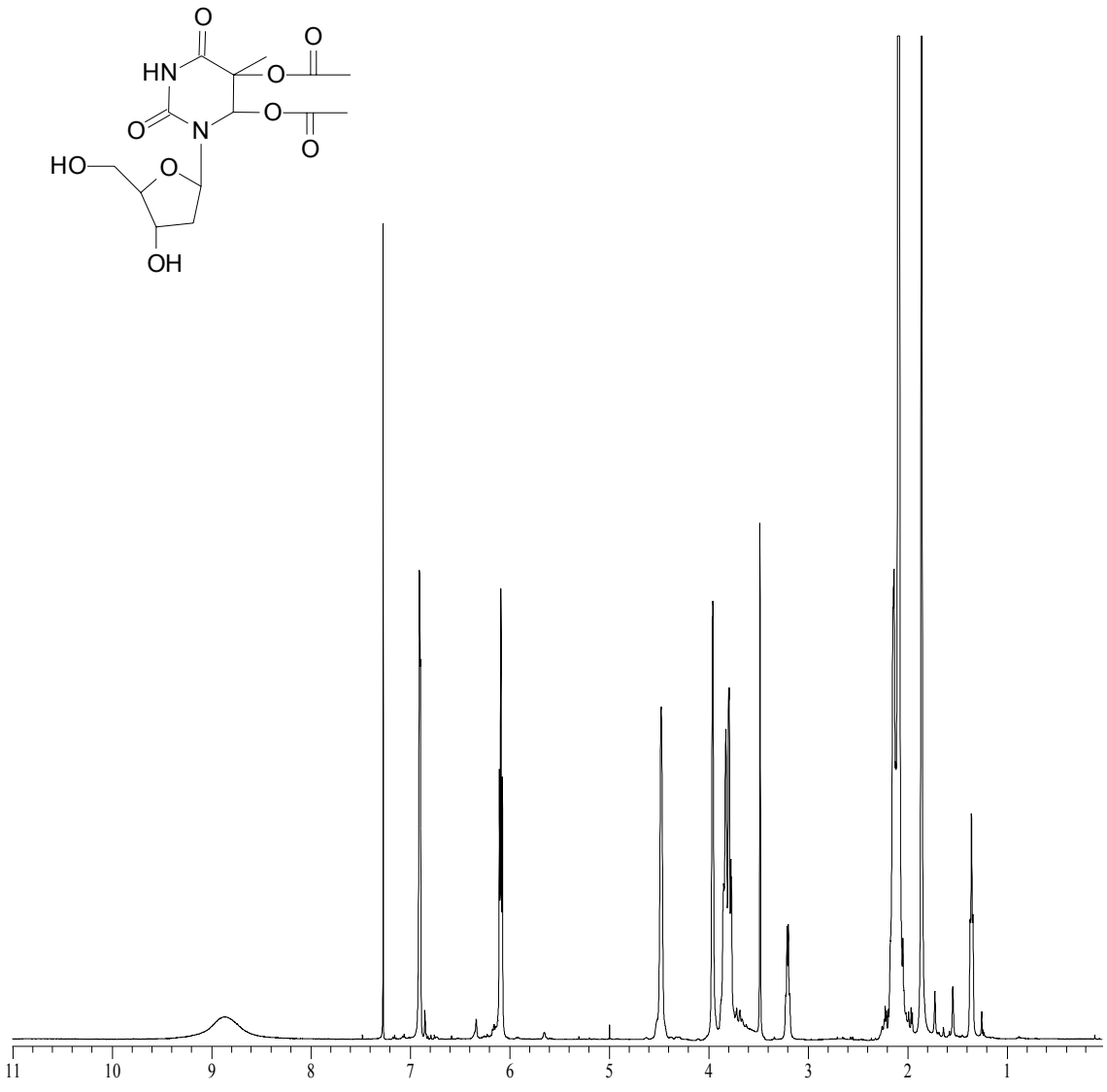


Figure S4. ^{1}H NMR spectrum of **4** (400 MHz, $CDCl_3$).

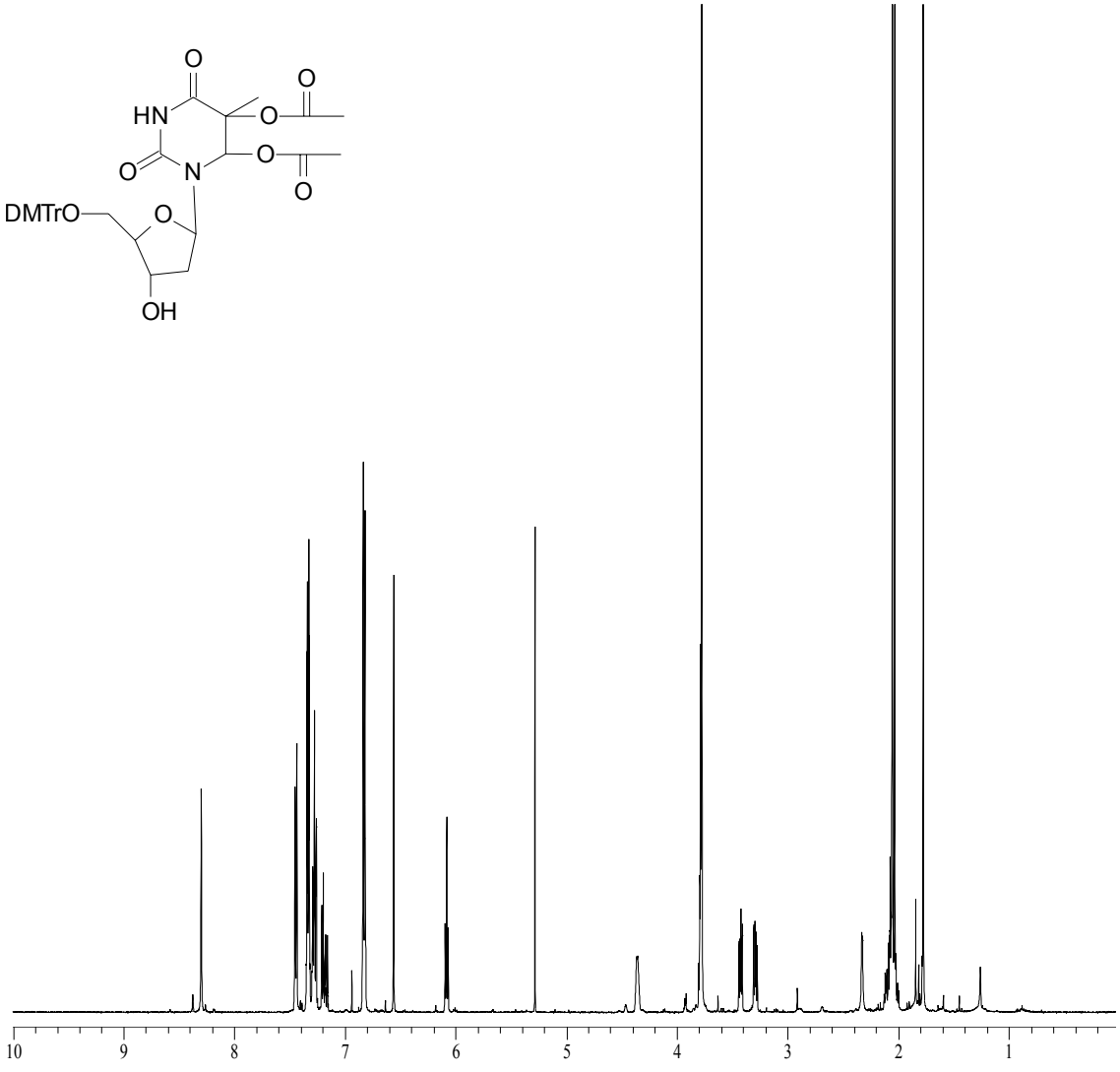


Figure S5. ^{1}H NMR spectrum of **5** (400 MHz, $CDCl_3$).

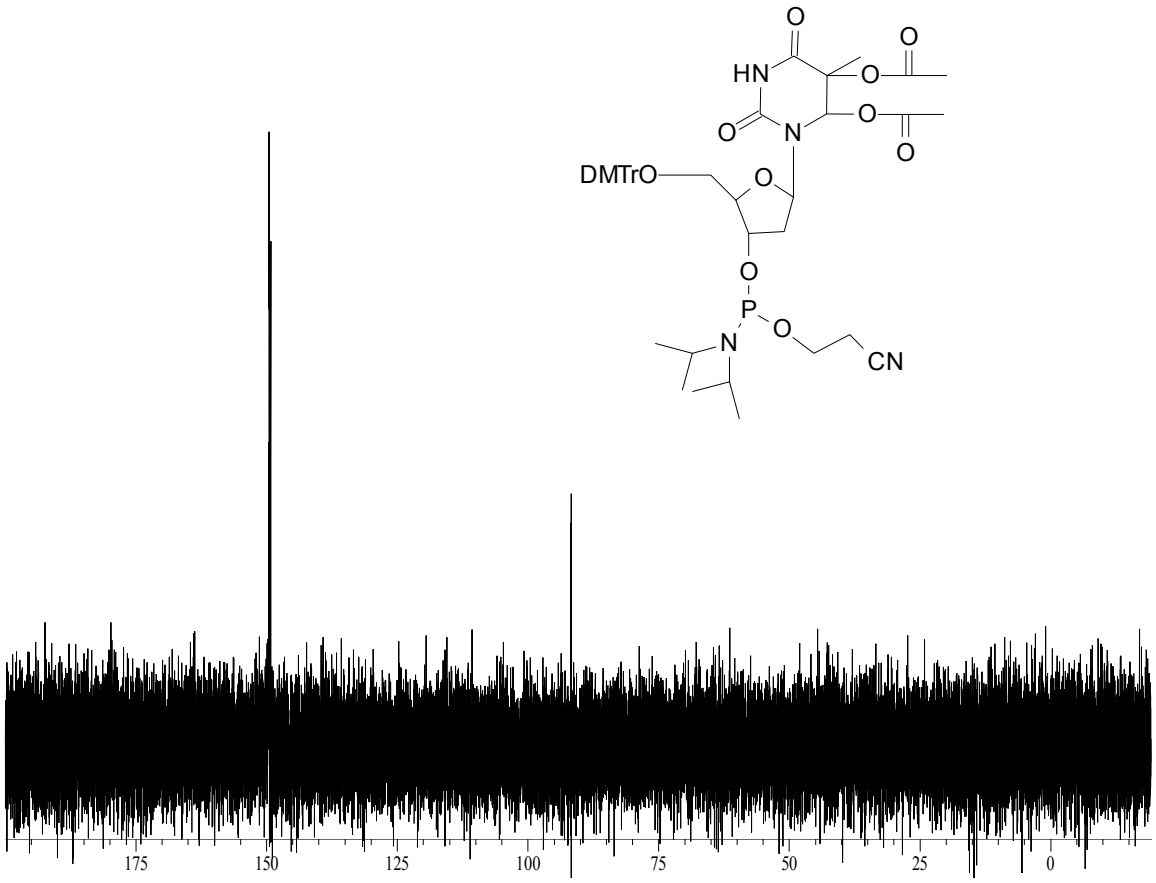


Figure S6. ^{31}P NMR spectrum of **6** (400 MHz, $CDCl_3$).

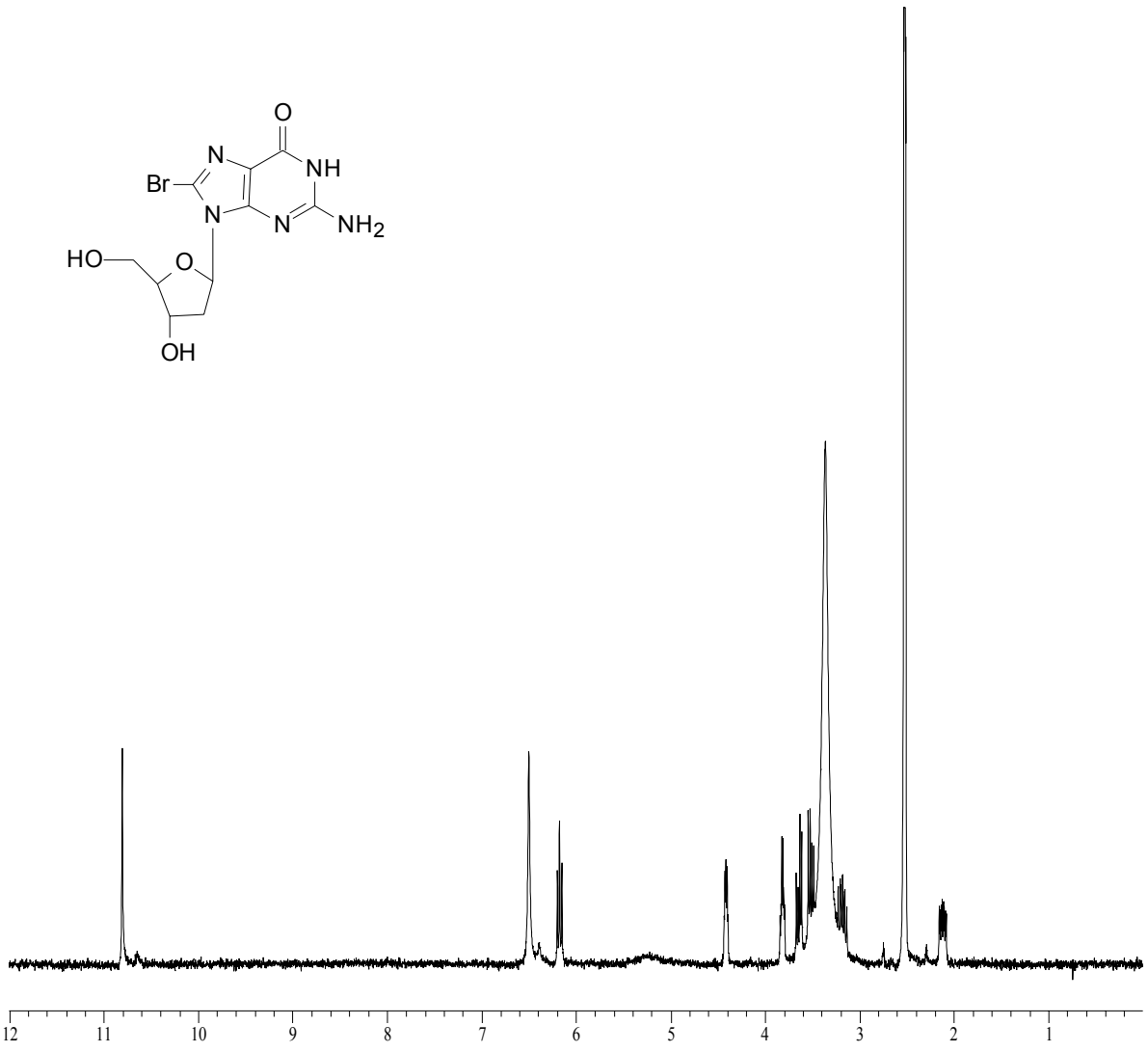


Figure S7. ^{1}H NMR spectrum of 8-bromo-2'-deoxyguanosine (300 MHz, DMSO-d_6).

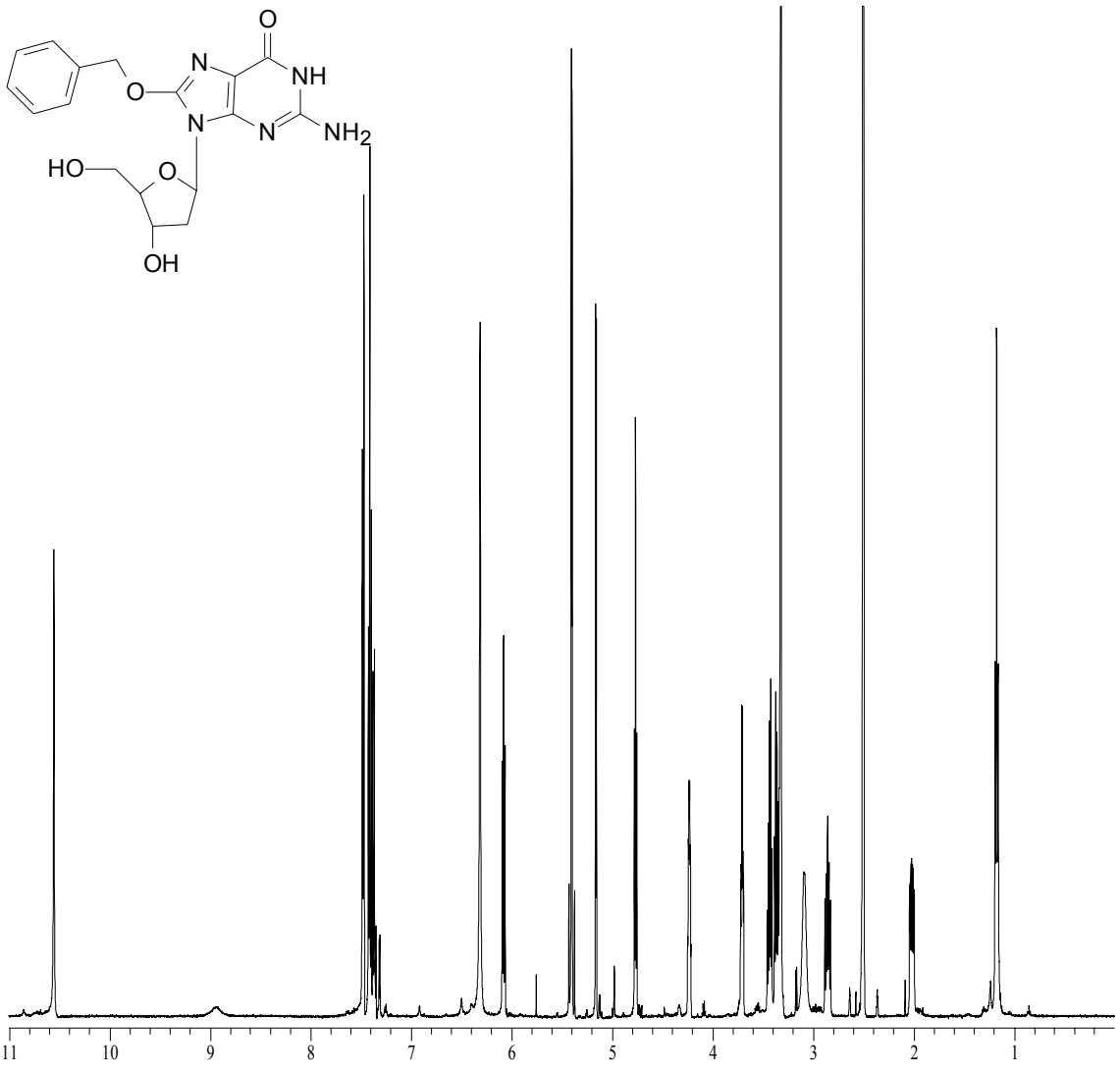


Figure S8. ^{1}H NMR spectrum of 8-benzyloxy-2'-deoxyguanosine (500 MHz, DMSO-d_6).

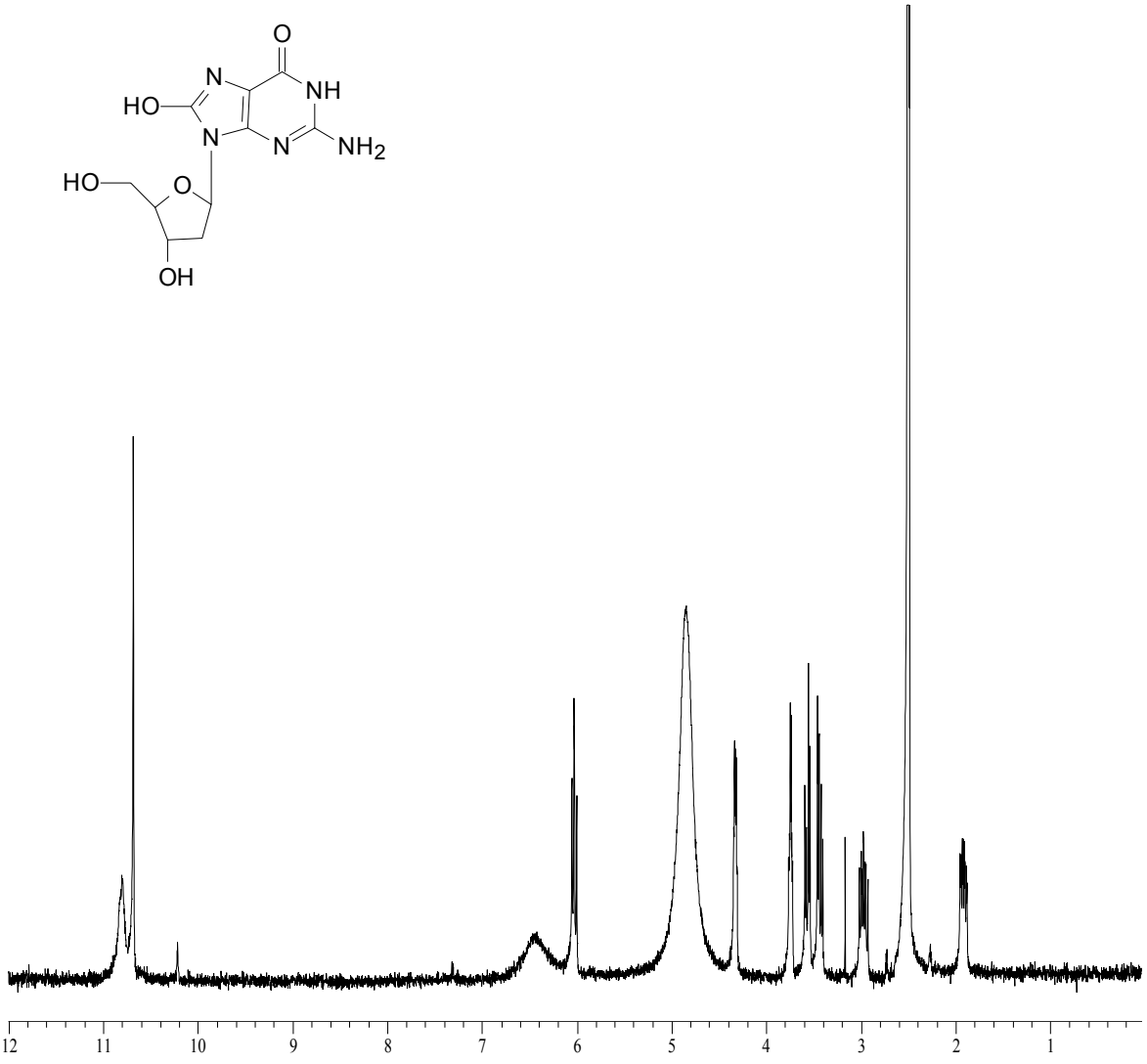


Figure S9. ^{1}H NMR of 8-oxo-2'-deoxyguanosine (300 MHz, DMSO-d_6).

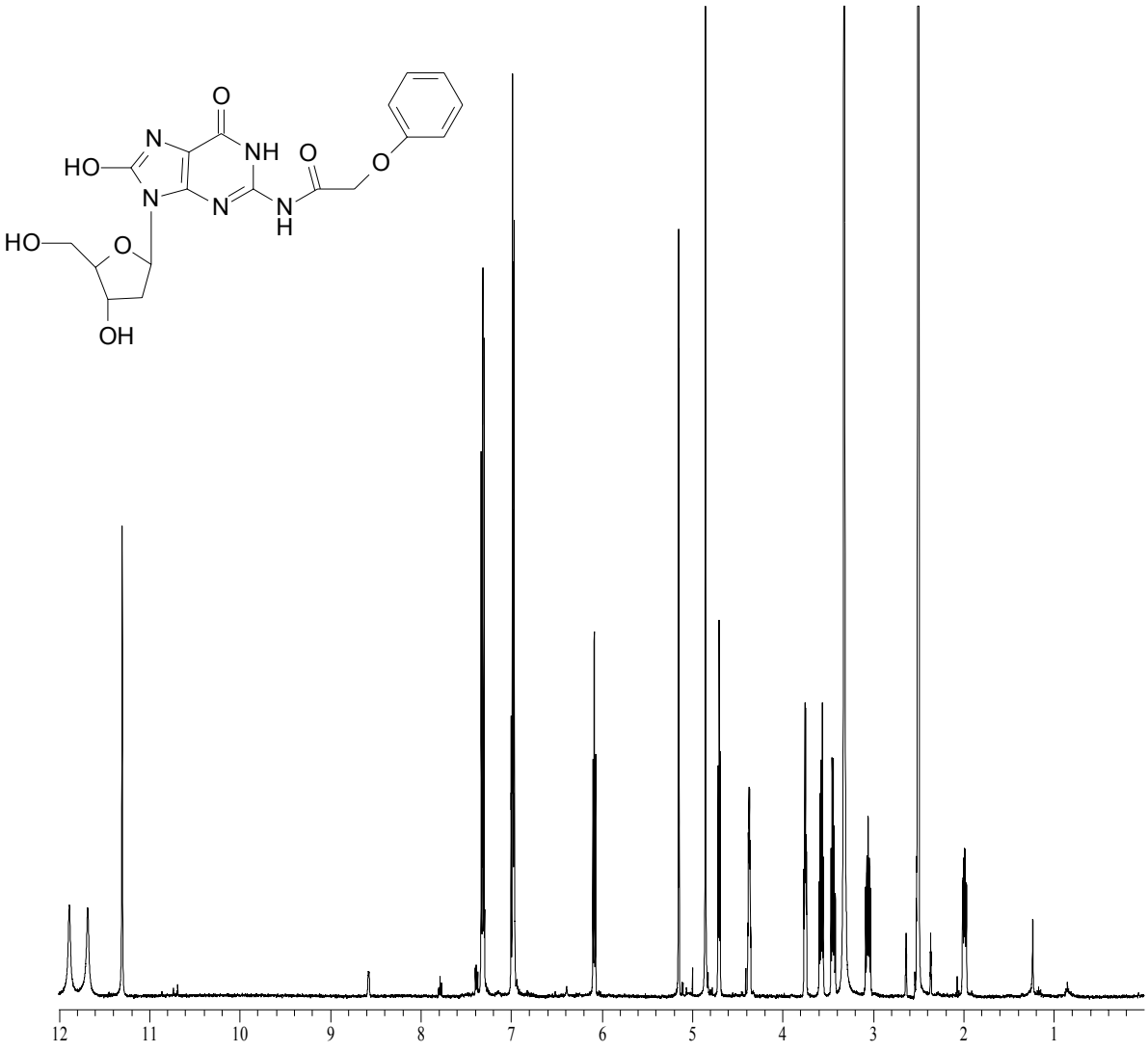


Figure S10. ^{1}H NMR of 2-N-(phenoxyacetyl)-8-oxo-2'-deoxyguanosine (500 MHz, DMSO-d_6).

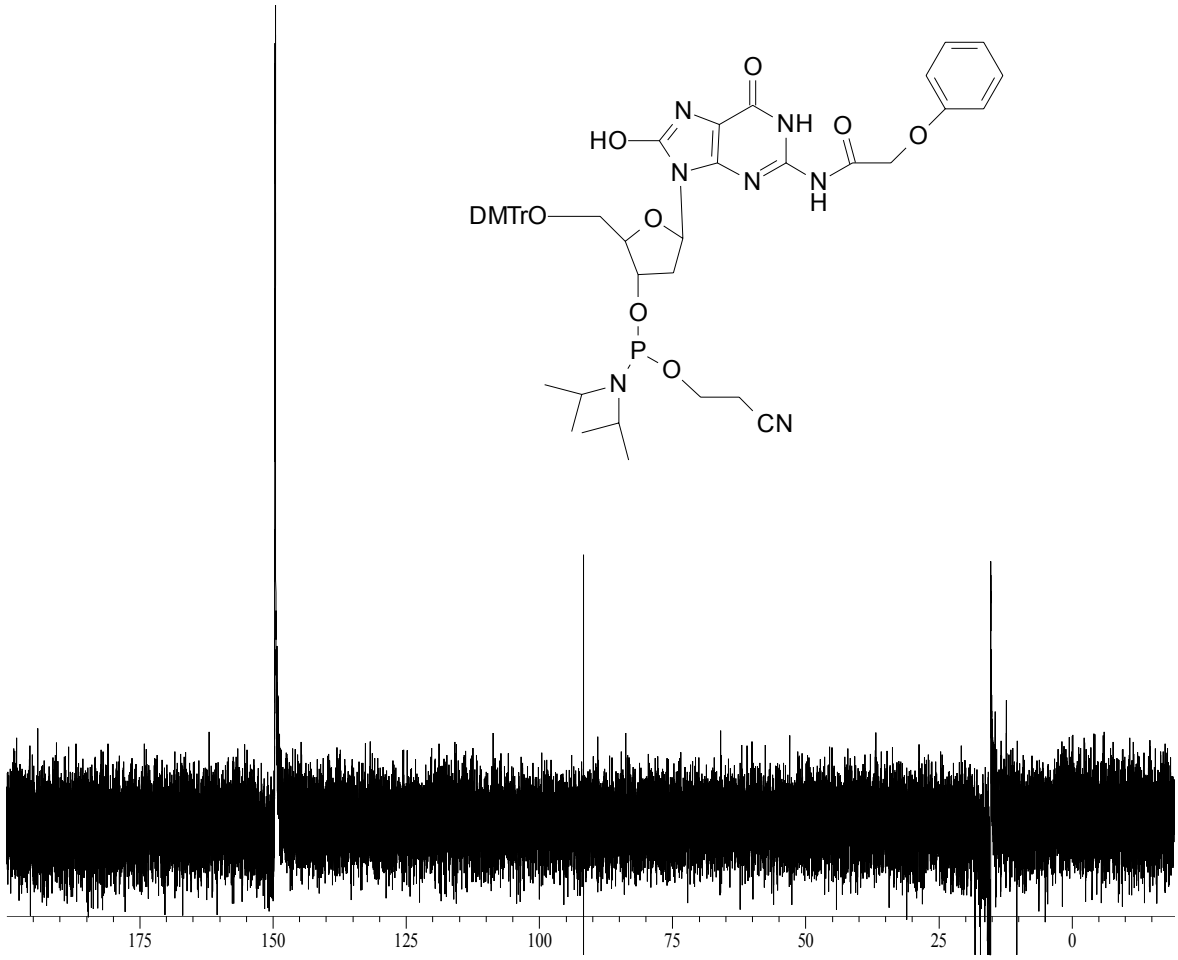


Figure S11. ^{31}P NMR of **7** (400 MHz, $CDCl_3$).

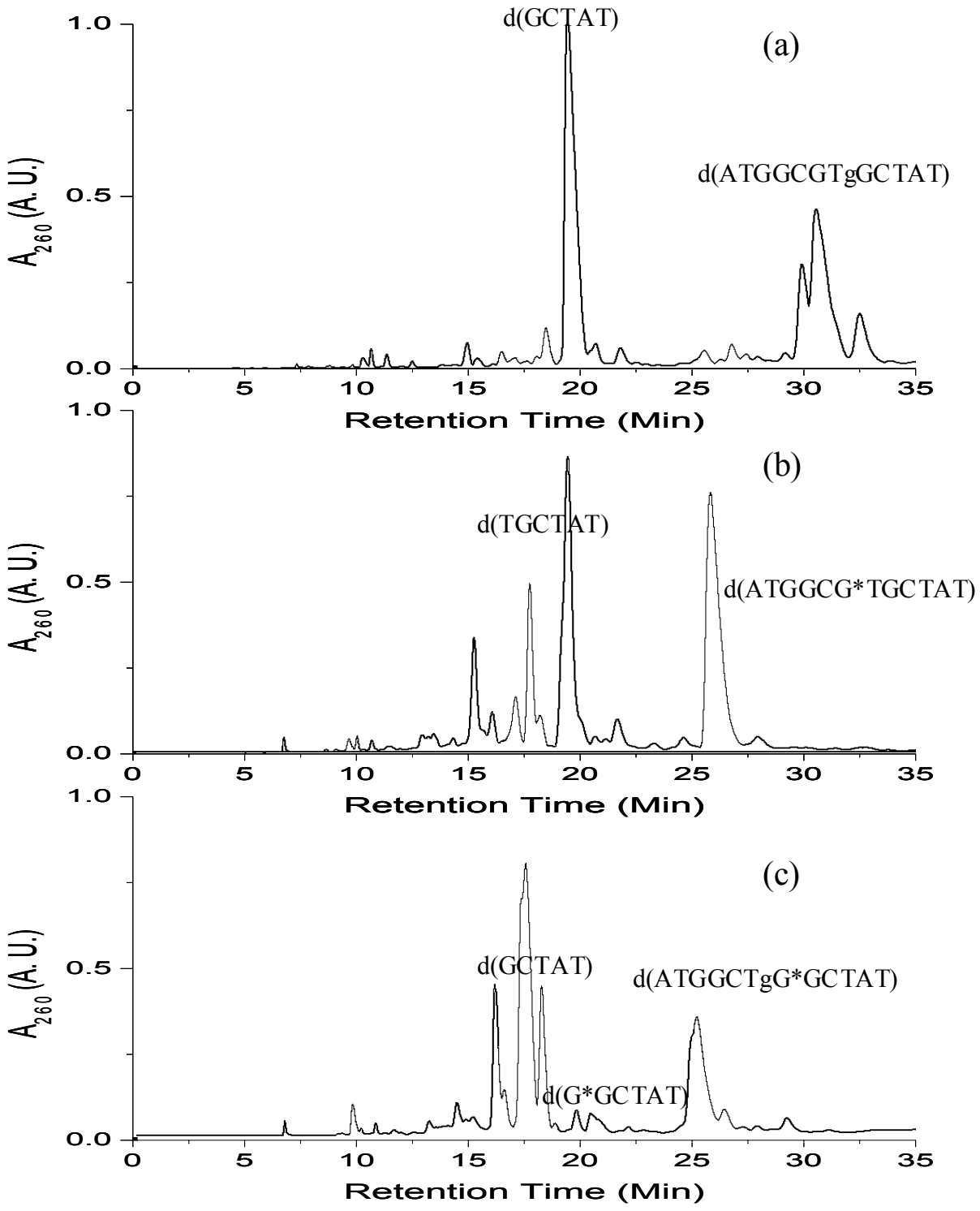


Figure S12. HPLC traces for the separation of the synthesized ODNs: (a) d(ATGGCGTgGCTAT); (b) d(ATGGCG*TGCTAT), (c) d(ATGGCTgG*GCTAT).

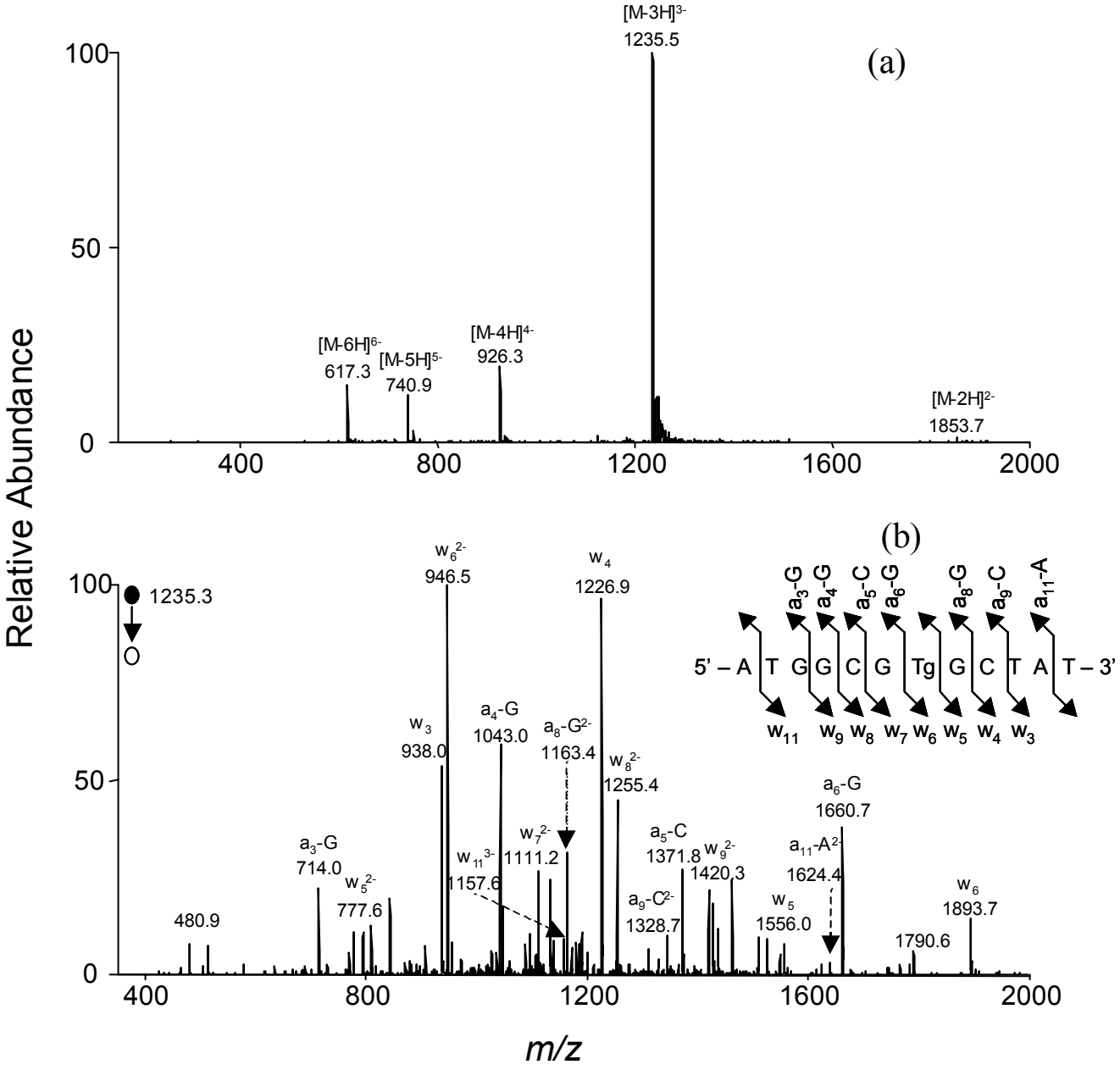


Figure S13. ESI-MS & MS/MS characterizations of d(ATGGCGTgGCTAT). (a) Negative-ion ESI-MS; (b) product-ion spectrum of the $[M - 3H]^{3-}$ ion (*m/z* 1235).

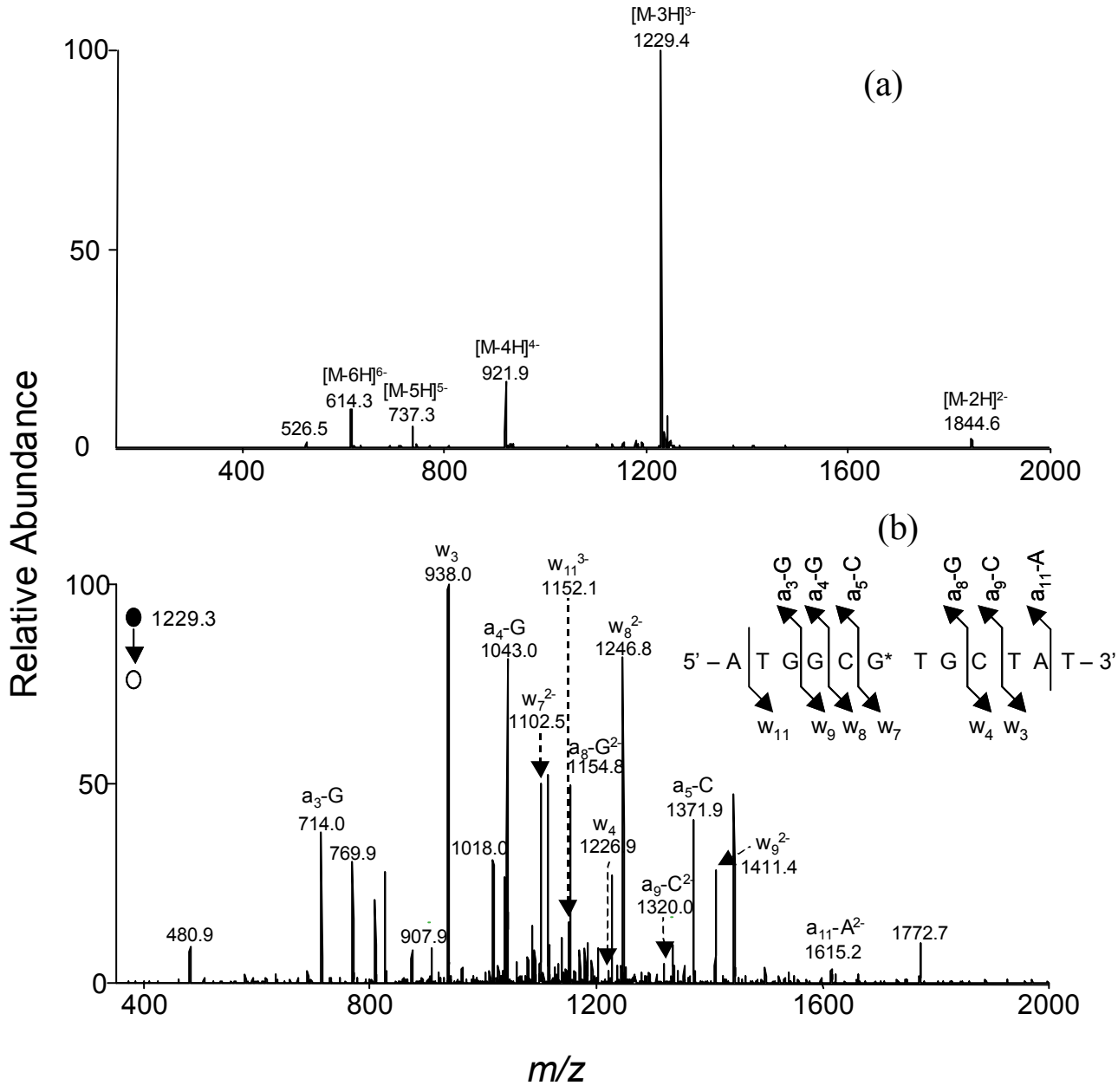


Figure S14. ESI-MS & MS/MS characterizations of d(ATGGC*GTGCTAT). (a) Negative-ion ESI-MS; (b) product-ion spectrum of the $[M - 3H]^{3-}$ ion (*m/z* 1229).

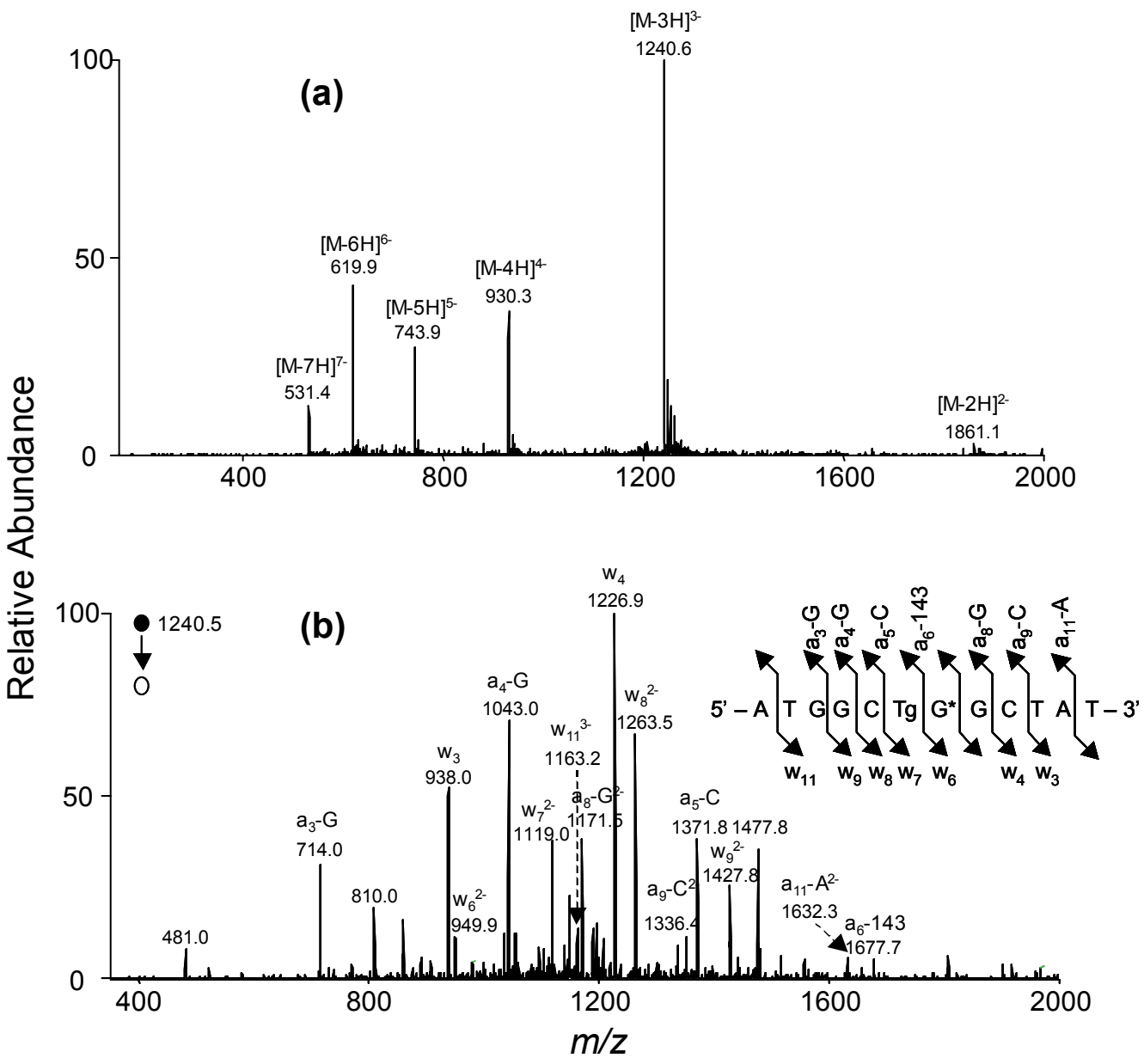


Figure S15. ESI-MS & MS/MS characterizations of d(ATGGCTgG*GCTAT): (a) Negative-ion ESI-MS; (b) product-ion spectrum of $[M–3H]^{3–}$ ion (*m/z* 1241).

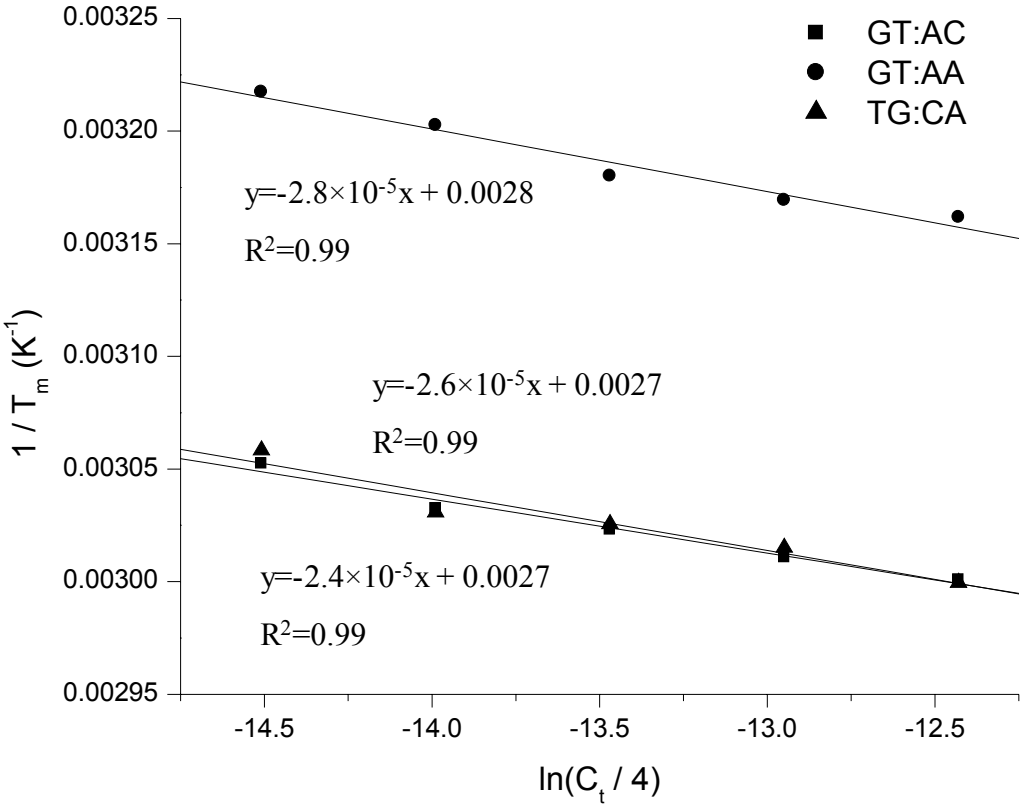


Figure S16. Plot of $1/T_m$ vs $\ln(C_t/4)$ for the unmodified duplexes. The duplex is d(ATGGCXYGCTAT)/d(ATAGCMNGCCAT), where XY/MN represents GT/AC(■), GT/AA(●), TG/CA(▲).

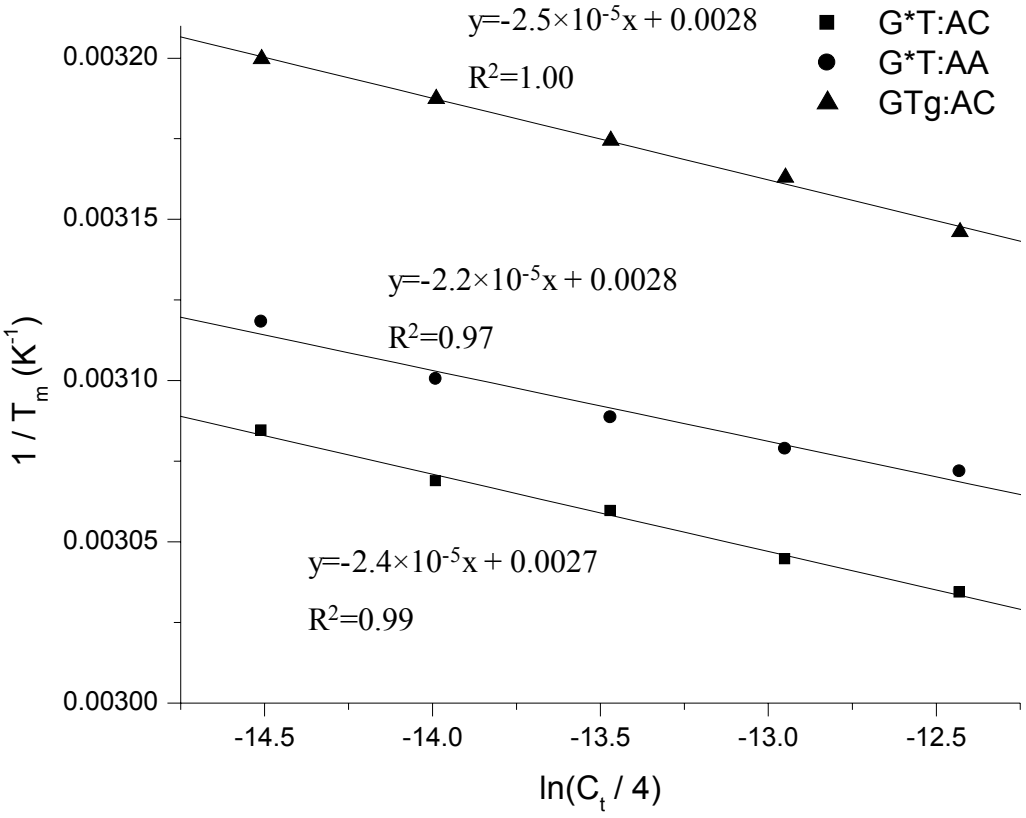


Figure S17. Plot of $1/T_m$ vs $\ln(C_t/4)$ for the duplexes including single damaged lesion. The duplex is d(ATGGCXYGCTAT)/d(ATAGCMNGCCAT), where XY/MN represents G*T/AC(■), G*T/AA(●), GTg/AC(▲).