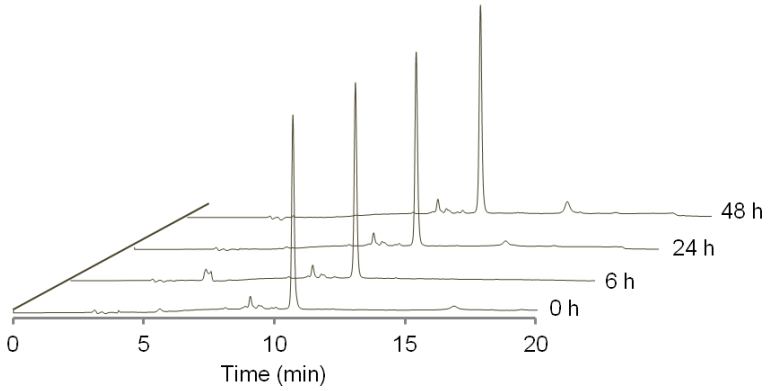
Experimental

·General

All air sensitive reactions were carried out under argon in oven-dried glassware using standard syringe and septa techniques, unless otherwise noted. The ^{1}H and ^{13}C NMR were recorded on a Bruker 400 (400 MHz for 1H and 100 MHz for 13C) spectorometer using Chloroform (1H, δ = 7.26) and $CDCl_3$ (13C, δ = 77.0) as an internal standards. 31P NMR were recorded on a Bruker 400 (162 MHz for 31P) using H_3PO_4 (85%) as an external standard. Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, m = multiplet, br = broad. High resolution mass analyses (HRSM) were recorded using a MicrOTOFQII mass spectrometer. MALDI-TOF mass spectra were measured by using autoflex speed mass spectrometer and the laser at 337 nm by negative mode using 3-hydroxypicolinic acid as the matrix. Thin-layer chromatography was performed on Merck 60 F254 precoated silica gel plates. Merck 60 F254 precoated silica gel on glass in a thickness of 0.9 mm was used for preparative TLC. column chromatography was performed on silica gel (Silica Gel 60 N; 63−210 mesh, KANTO CHEMICAL CO., INC. or 40 − 50 mesh, KANTO CHEMICAL CO., INC.). The ultraviolet-visible (UV-vis) absorption spectra were recorded by a BECKMAN COULTER DU800. ODN synthesis was carried out by the use of an automated DNA synthesizer (ABI, 392 DNA/RNA synthesizer) following the standard phosphoramidite chemistry. High performance liquid chromatography (HPLC) was performed using nacalai tesque cosmosil 5C18MS (4.6 or 10 × 250 mm) as the columns, JASCO PU-986 as the pump, JASCO 2075 as the UV monitoring, and JASCO 2067 as the column oven. pH measurements were measured performed on Mettler Toledo Seven Easy pH meter using ORION 8220BNWP as the electrode. Densitometric analysis of the gel was carried out on the 20% denaturing polyacrylamide gel plates, and visualized, quantified with use of a FLA-5100 Fluor Imager. Commercial available reagents were obtained from Wako Pure Chemical Industries Ltd., KANTO CHEMICAL CO., INC. and used without further purification. DNA and RNA oligomer was purchased from Japan Bio Services Co., LTD. (Saitama, JAPAN), buffers and salts from Nacalai tesque.

HPLC profile for ON1



HPLC profile for ON2

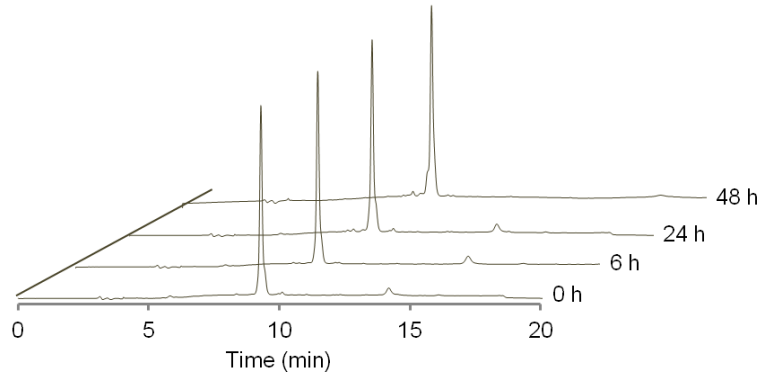


Fig S1 HPLC analysis for the stability confirmation of **ON1** and **ON2**. 10 μM of **ON1** or **ON2** was incubated in 100 mM NaCl, 50 mM MES, pH 7 at 37 ºC and analyzed by HPLC at indicated time

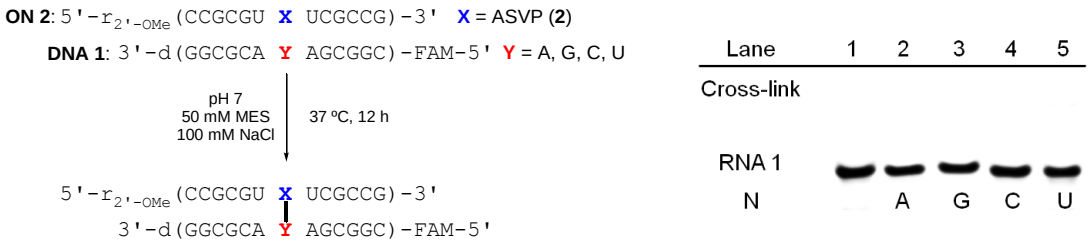


Fig S2 The gel electrophoresis for the cross-link reaction of **ON 2** with **RNA 1**.The reaction was performed with 10 μM **ON 2** and 5 μM **RNA1** in 100 mM NaCl, 50 mM MES, pH 7 at 37 ºC for 12 h

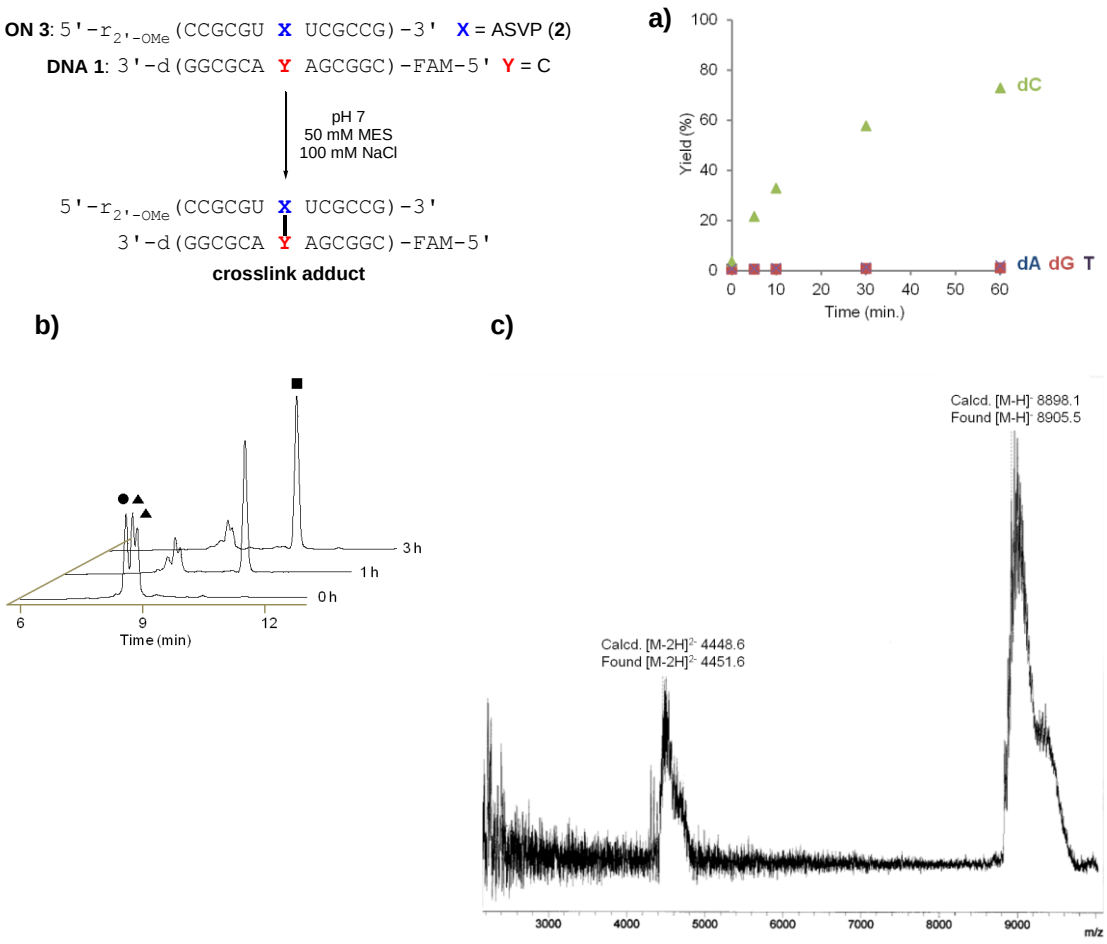


Fig S3 Crosslink reaction of **ON 3** with **DNA 1**. a) The summary for the time course of the crosslink yield, Y = A; ♦, Y = G;■, Y = C;▲, Y = U;●. b) HPLC analysis of the crosslink reaction between **ON 3** (▲: diastereomers) and **DNA 1** (●,N = C).■ referred as cross-link adduct. The aliquot of the reaction mixture was collected at each indicated time and injected to HPLC. The analysis was performed with reverse-phase HPLC with C-18 column (nacalai tesque: COSMOSIL 5C18-MS-II, 4 × 250 mm) by a linear gradient of 10-40%/20 min of acetonitrile in 0.1 M TEAA buffer at a flow rate of 1 ml/min and monitored by UV absorbance at λ = 255 nm. c) MALDI-spectrum of isolated crosslink adduct

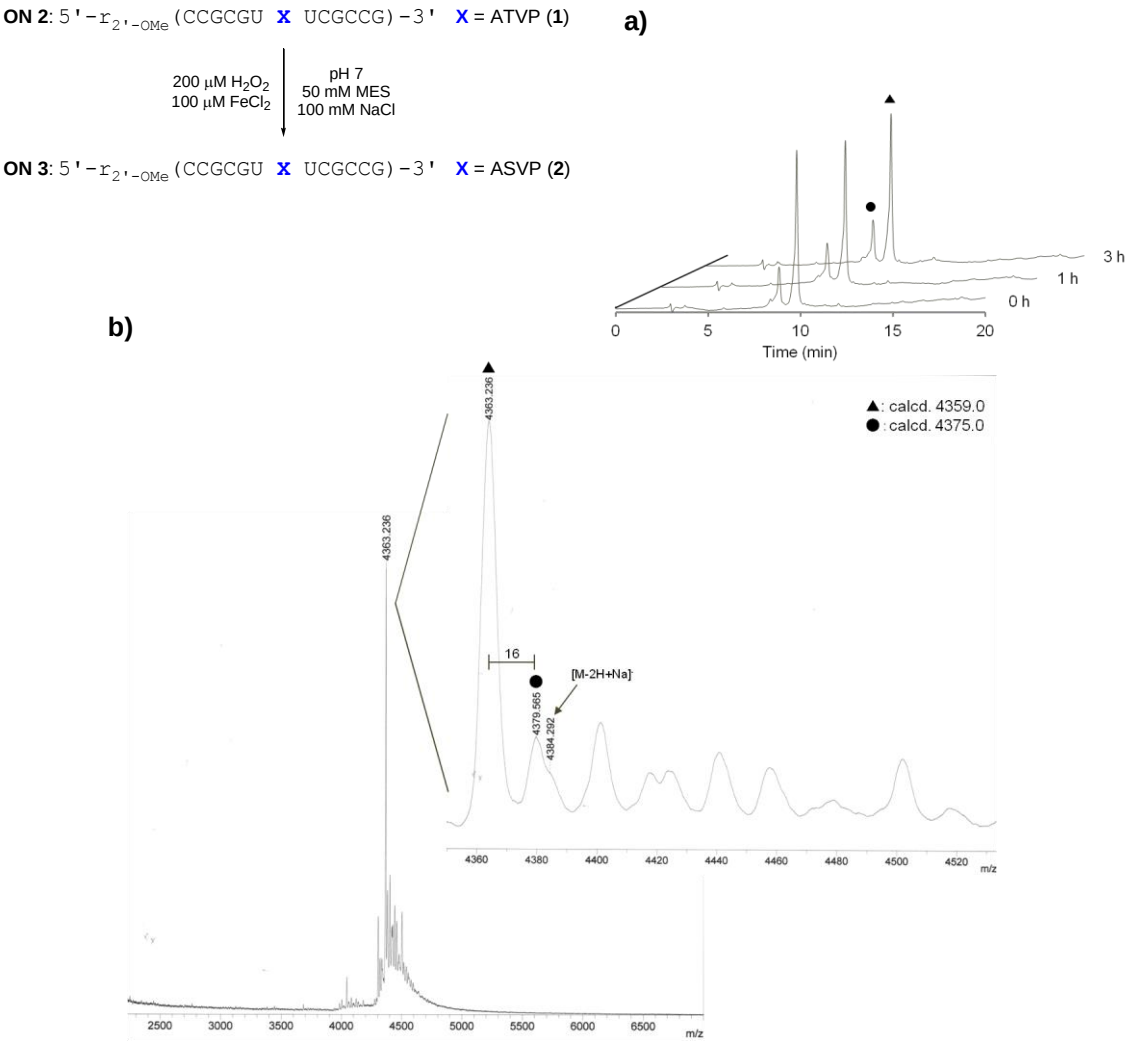


Fig S4 Oxidation of **ON 2** by H_2O_2 and $FeCl_2$. a) HPLC analysis for the oxidation reaction of **ON 2** (▲). ● referred as oxidized product **ON 3**. The aliquot of the reaction mixture was collected and injected to HPLC at indicated time. b) MALDI-TOF spectroscopy of the reaction mixture for the oxidation of **ON 2**. The mixture was treated with Zip-tip treatment thereafter MALDI-TOF mass spectroscopy was measured. All reactions were performed with 10 μM **ON 2** in the presence of 100 μM of $FeCl_2$ and 200 μM of H_2O_2.

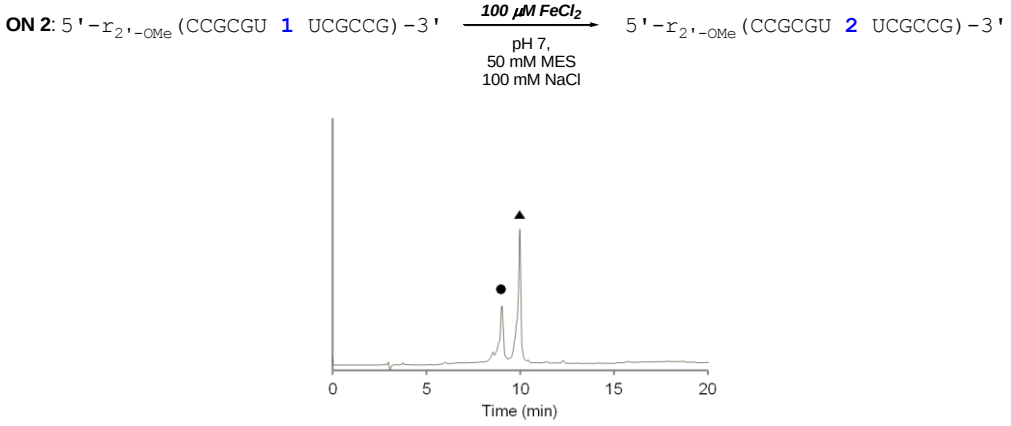
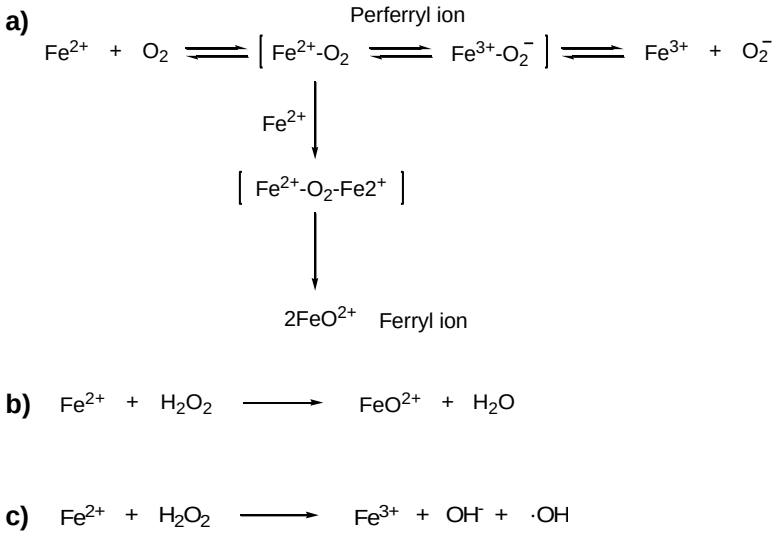


Fig. S5 HPLC profile for the oxidation of **ON 2** (▲) with 100 μM $FeCl_2$. ● referred as oxidized product **ON 3**.The reaction was performed with 10 μM **ON 2** in 100 mM in 100 mM NaCl, 50 mM MES at pH 7



Scheme S1 Generation of ferryl ion from Fe^{2+} (a and b) and Fenton reaction (c)

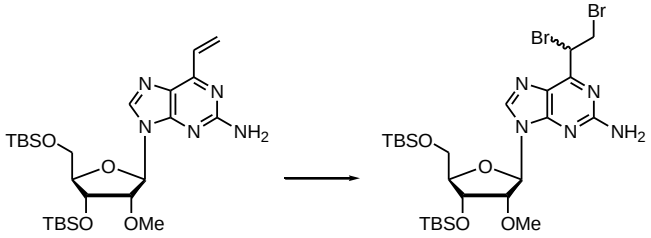
It is thought that ferryl ion is generated from Fe^{2+} in two pathways.[1] The first route to ferryl ion is by the reaction of perferryl ion which is an intermediate product produced through Fe^{2+}-O_2 or Fe^{3+}-O_2^-, with another Fe^{2+} (**Scheme S1a**). The second route relies on H_2O_2 to generate ferryl ion (**Scheme S1b**). It is reported that Fenton reagents (Fe^{2+} and H_2O_2) produce ferryl ion rather than ·OH (**Scheme S1c**) under proper conditions such as pH and buffer.[2] The condition employed in the crosslink reaction might be preferred for the formation of ferryl ion than ·OH, because sodium formate did not influence the crosslink reaction. Thus, high-level generation of ferryl ion in the presence of H_2O_2 explains that higher crosslink yield was observed when H_2O_2

and $FeCl_2$ are used as an oxidant than $FeCl_2$ alone. Furthermore, it is suspected that potassium iodide and sodium ascorbate prohibit the generation of ferryl ion by quenching $^3O_2$ and high oxidation potential iron species respectively, and that O_2^- generated form Fe^{2+} (**Scheme S1a**) would be relatively low therefore the influence of SOD for the crosslink reaction was small. Nevertheless, how sodium azide inhibit the oxidation reaction of **ON 2** is indecisive.

1) Qian, S. Y.; Buettner, G. R. *Free Radic. Biol. Med.* **1999**, *26*, 1447-1456.

2) Barbusinski, K. *Ecol. Chem. Eng.* **2009**, *16*, 347–358.

· Synthesis of 9-[4-(tert-Butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxymethyl)-3-methoxy-tetrahydro-furan-2-yl]-6-(1,2-dibromo-ethyl)-9*H*-purin-2-ylamine

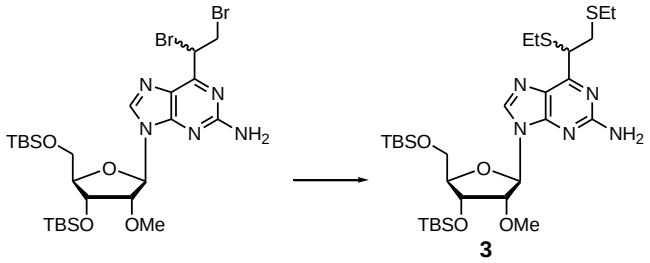


2

To a solition of **3** (216 mg, 0.403 mmol) in $CHCl_3$ (12 ml), was dropwised 2% bromine water (6.4 ml) using dropping funnel at 0 °C. After stirred 6 h at 0 °C, 0.5 M $Na_2S_2O_3$ aq. was added to the reaction mixture. The mixture was extracted with $CHCl_3$. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by silica gel column chromatography (Hexane-AcOEt, 15:1 to 5:1) to afford described product (180 mg, 64%, 1:1 mixture of diastereomer) as a pale orange foam.

^{1}H NMR (400 MHz, $CDCl_3$ for 1:1 mixture of diastereomer) δ 0.086 (s, 6H), 0.089 (s, 6H), 0.12 (s, 6H), 0.14 (s, 6H), 0.92 (s, 18 H), 0.93 (s, 18 H), 3.46 (s, 3H), 3.47 (s, 3H), 3.77 (dd, *J* = 4.2, 11.6 Hz, 1H), 3.92 (dd, *J* = 2.0, 11.6 Hz, 1H), 3.93 (dd, *J* = 2.0, 11.6 Hz, 1H), 4.00 (dd, *J* = 3.2, 4.8 Hz, 1H), 4.03 (dd, *J* = 3.2, 4.8 Hz, 1H), 4.08 (ddd, *J* = 2.0, 2.0, 4.2 Hz, 1H), 4.13 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.14 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.52 (dd, *J* = 2.0 Hz, *J* = 4.8 Hz, 1H), 4.53 (dd, *J* = 2.0, 4.8 Hz, 1H), 4.59 (dd, *J* = 9.6, 11.2 Hz, 1H), 4.63 (dd, *J* = 9.6, 11.2 Hz, 1H), 5.25 (brs, 2H), 5.26 (brs, 2H), 5.66 (dd, *J* = 4.8, 11.2 Hz, 1H), 5.69 (dd, *J* = 4.8, 11.2 Hz, 1H), 6.05 (d, *J* = 4.8, 1H), 8.08 (s, 1H), 8.10 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.4, -5.3, -4.7, -4.6, 18.2, 18.5, 25.8, 26.0, 43.3, 43.5, 58.5, 62.0, 62.1, 69.9, 70.0, 83.5, 83.6, 85.2, 85.9, 86.0, 126.0, 126.1, 140.8, 153.8, 153.9, 156.3, 156.3, 159.8, 159.58; HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{45}N_5O_4Si_2Br_2$, 694.1450; found, 694.1441.

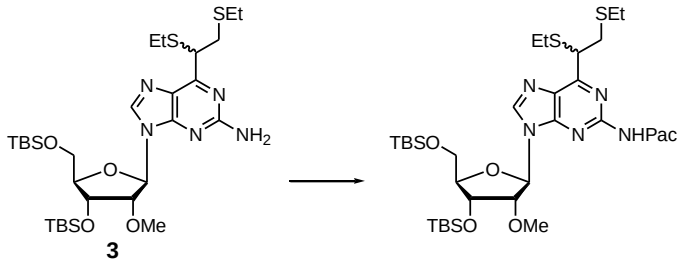
· Synthesis of 6-(1,2-Bis-ethylsulfanyl-ethyl)-9-[4-(tert-butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxymethyl)-3-methoxy-tetrahydro-furan-2-yl]-9*H*-purin-2-ylamine (4)



To a solution of **4** (78 mg, 0.112 mmol) in CH_2Cl_2 (0.10 M), was added DBU (42 μL, 0.280 mmol) at 0 °C. After stirred 1 hour at 0 °C, EtSH was added to the reaction mixture and stiired for additional s hours. The reaction mixture was directly applied to silica gel column chromatography ($CHCl_3$-AcOEt, 1:0 to 10:1) to afford **5** (41.7 mg, 57%) as a pale yellow foam.

^{1}H NMR (400 MHz, $CDCl_3$ for 1:1 mixture of diastereomer) δ 0.065 (s, 6H), 0.078 (s, 6H), 0.12 (s, 6H), 0.13 (s, 6H), 0.90 (s, 9 H), 0.93 (s, 9 H), 1.18-1.23 (m, 6H), 2.50-2.65 (m, 4H), 3.16 (dd, *J* = 4.8, 12.8 Hz, 1H), 3.45 (s, 3H), 3.45 (s, 3H), 3.46-3.52 (m, 1H), 3.75 (dd, *J* = 2.8, 11.2 Hz, 1H), 3.76 (dd, *J* = 2.8, 11.2 Hz, 1H), 3.92 (dd, *J* = 3.6, 11.2 Hz, 1H), 4.05-4.08 (m, 1H), 4.16 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.17 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.52 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.58 (dd, *J* = 4.8, 4.8 Hz, 1H), 4.61 (dd, *J* = 4.8, 4.8 Hz, 1H), 5.11 (brs, 2H), 5.12 (brs, 2H), 6.01 (d, *J* = 4.8, 1H), 6.02 (d, *J* = 4.8, 1H), 7.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.5, -5.4, -5.3, -4.7, -4.6, 14.6, 14.7, 18.2, 18.4, 18.5, 25.8, 25.9, 26.0, 26.0, 26.3, 26.4, 34.3, 34.4, 44.7, 44.9, 58.4, 62.1, 70.0, 76.7, 77.1, 77.4, 83.2, 83.3, 85.0, 85.0, 86.0, 126.8, 126.7, 139.9, 140.0, 152.9, 153.0, 159.7, 159.7, 161.3, 161.4; HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{56}N_5O_4S_2Si_2$, 658.3307; found, 658.3315.

· Synthesis of *N*-{6-(1,2-Bis-ethylsulfanyl-ethyl)-9-[4-(tert-butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxymethyl)-3-methoxy-tetrahydro-furan-2-yl]-9*H*-purin-2-yl}-2-phenoxy-acetamide

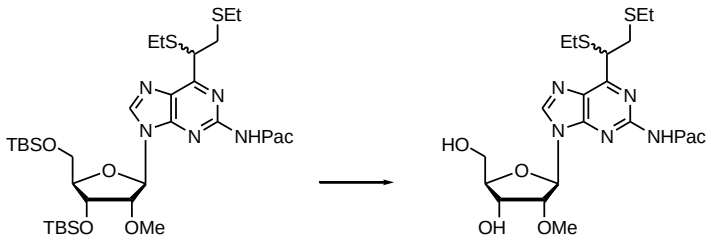


To a solution of **5** (203 mg, 0.310 mmol) in pyridine (0.10 M), was added PacCl (106 μL, 0.774 mmol) at 0 °C. After stirred 1 hour at 0 °C, the reaction mixture was allowed to warm up to room temperature. After stirred 23 h at room temperature, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$ and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in

vacuo. The residue was purified with silica gel column chromatography (Hexane-AcOEt, 10:1 to 4:1) to afford **6** (234 mg, 96%) as a pale yellow foam.

^{1}H NMR (400 MHz, $CDCl_3$ for 1:1 mixture of diastereomer) δ 0.097 (s, 6H), 0.10 (s, 6H), 0.11 (s, 6H), 0.12 (s, 6H), 0.92 (s, 9 H), 1.18-1.25 (m, 6H), 2.51-2.70 (m, 4H), 3.12 (dd, *J* = 4.2, 13.6 Hz, 1H), 3.56 (s, 3H), 3.58 (s, 3H), 3.52-3.59 (m, 1H), 3.78 (dd, *J* = 2.8, 11.2 Hz, 1H), 4.04 (dd, *J* = 3.6, 11.2 Hz, 1H), 4.10-4.11 (m, 1H), 4.35-4.38 (m, 1H), 4.51 (dd, *J* = 4.2, 4.2 Hz, 1H), 4.52 (dd, *J* = 4.4, 4.4 Hz, 1H), 4.68 (dd, *J* = 1.6, 4.2 Hz, 1H), 4.71 (dd, *J* = 1.6, 4.2 Hz, 1H), 4.77 (brs, 2H), 6.13 (d, *J* = 3.6, 1H), 6.15 (d, *J* = 3.6, 1H), 7.02 (d, *J* = 8.4, 3H), 7.32 (dd, *J* = 8.4, 8.4, 2H), 7.33 (d, *J* = 8.4, 8.4, 2H), 8.31 (s, 1H), 8.92 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.39, -5.37, -5.31, -4.74, -4.60, 14.6, 14.6, 18.2, 18.5, 18.5, 25.8, 26.0, 26.1, 26.4, 34.2, 34.3, 44.6, 44.7, 58.5, 61.8, 68.0, 69.6, 82.3, 85.1, 86.9, 87.1, 115.0, 122.3, 129.8, 143.1, 143.1, 151.7, 151.7, 151.7, 161.6, 161.2; HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{37}H_{61}N_5O_6S_2Si_2$, 792.3675; found, 792.3629.

· **Synthesis of *N*-[6-(1,2-Bis-ethylsulfanyl-ethyl)-9-(4-hydroxy-5-hydroxymethyl-3-methoxy-tetrahydro-furan-2-yl)-9*H*-purin-2-yl]-2-phenoxy-acetamide (5)**

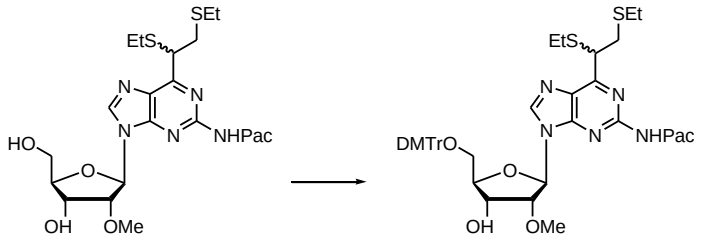


4

To a solution of **6** (234 mg, 0.295 mmol) in THF (0.10 M), was added TBAF (1 M THF solution, 890 μL, 0.886 mmol) at room temperature. After stirred 90 minutes at room temperature, the reaction mixture was diluted with EtOAc and washed with H_2O and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified with silica gel column chromatography ($CHCl_3$-MeOH, 1:0 to 25:1) to afford **7** (171 mg, quant.) as a pale yellow foam.

^{1}H NMR (400 MHz, $CDCl_3$ for 1:1 mixture of diastereomer) δ 1.17-1.23 (m, 6H), 2.50-2.67 (m, 4H), 3.19 (dd, *J* = 4.8, 13.6 Hz, 1H), 3.20 (dd, *J* = 4.8, 13.6 Hz, 1H), 3.41 (s, 3H), 3.51 (d, *J* = 13.6 Hz, 1H), 3.54 (d, *J* = 13.6 Hz, 1H), 3.82 (d, *J* = 12.8 Hz, 1H), 3.99 (d, *J* = 12.8 Hz, 1H), 4.25 (brs, 1H), 4.26 (brs, 1H), 4.64-4.72 (m, 5H), 5.96 (brs, 1H), 5.97 (brs, 1H), 7.00-7.04 (m, 3H), 7.33 (d, *J* = 8.4, 8.4, 2H), 8.14 (s, 1H), 8.15 (s, 1H), 9.22 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 14.4, 14.5, 14.5, 25.9, 26.1, 26.2, 33.9, 34.0, 44.4, 44.5, 58.6, 62.3, 67.6, 69.6, 77.2, 85.2, 86.8, 88.3, 88.4, 114.8, 122.2, 129.7, 144.3, 151.2 , 151.2, 151.2, 151.3, 156.8, 162.3, 166.5; HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{25}H_{33}N_5O_6S_2$, 564.1945; found, 564.1876.

· **Synthesis of *N*-(6-(1,2-Bis-ethylsulfanyl-ethyl)-9-{5-[bis-(4-methoxy-phenyl)-phenyl-methoxy methyl]-4-hydroxy-3-methoxy-tetrahydro-furan-2-yl}-9*H*-purin-2-yl)-2-phenoxy-acetamide**

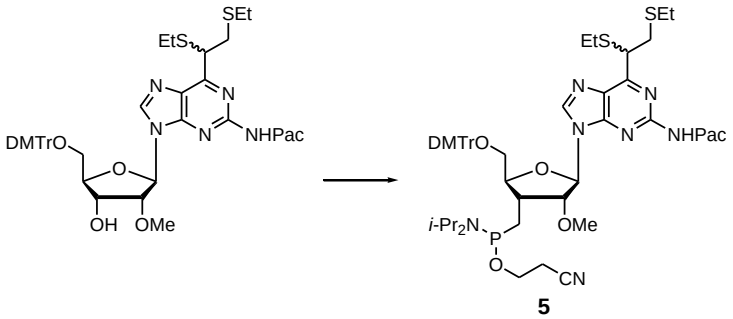


4

To a solution of **7** (71.4 mg, 0.127 mmol) in pyridine (0.10 M), was added DMTrCl (88.2 μL, 0.260 mmol) at 0 °C. After stirred 90 minutes at 0 °C, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$ and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified with silica gel column chromatography (Hexane-AcOEt, 2:1 to 1:2) to afford **8** (93.3 mg, 85%) as a pale yellow foam.

^{1}H NMR (400 MHz, $CDCl_3$ for 1:1 mixture of diastereomer) δ 1.20-1.27 (m, 6H), 2.52-2.71 (m, 4H), 3.51 (d, *J* = 6.4 Hz, 1H), 3.24 (dd, *J* = 5.2, 13.2 Hz, 1H), 3.25 (dd, *J* = 5.2, 13.2 Hz, 1H), 3.45-3.61 (m, 3H), 3.68 (s, 3H), 3.70 (s, 3H), 3.77 (s, 6H), 4.18-4.21 (m, 1H), 4.45-4.46 (m, 1H), 4.56-4.72 (m, 4H), 6.18 (d, *J* = 3.2, 1H), 6.19 (d, *J* = 3.6, 1H), 6.80 (d, *J* = 8.8, 4H), 7.01-7.06 (m, 3H), 7.19-7.24 (m, 4H), 7.32-7.36 (m, 5H), 7.42-7.43 (m, 2H), 8.20 (s, 1H), 8.24 (s, 1H), 8.93 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 14.5, 14.6, 26.0, 26.1, 26.2, 26.2, 34.1, 44.6, 55.1, 58.9, 62.8, 63.0, 67.9, 69.4, 69.5, 77.2, 82.9, 83. 0, 83.7, 86.4, 86.7, 113.1, 114.8, 122.2, 126.8, 127.8, 128.1, 130.0, 135.5, 135.7, 142.4, 142.5, 144.5, 151. 5, 151.6, 157.1, 158.4, 158.4, 161.8; HRMS-ESI (*m/z*): $[M+H]^+$ calcd for $C_{46}H_{51}N_5O_8S_2$, 866.3252; found, 866.3185.

· **Synthesis of Diisopropyl-phosphoramidous acid 5-[6-(1,2-bis-ethylsulfanyl-ethyl)-2-(2-phenoxy-acetylamino)-purin- 9-yl]-2-[bis-(4-methoxy-phenyl)-phenyl-methoxymethyl]-4-methoxy-tetrahydro -furan-3-yl ester 2-cyano- ethyl ester (6)**



5

To a solution of **8** (93.3 mg, 0.107 mmol) and DIPEA (110 μL, 0.646 mmol) in CH_2Cl_2 (0.05 M), was added phophitylation reagent (88.2 μL, 0.260 mmol) at 0 °C. After stirred 70 minutes at 0 °C, the reaction mixture was diluted with CH_2Cl_2 and washed with sat. $NaHCO_3$ and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified with silica gel

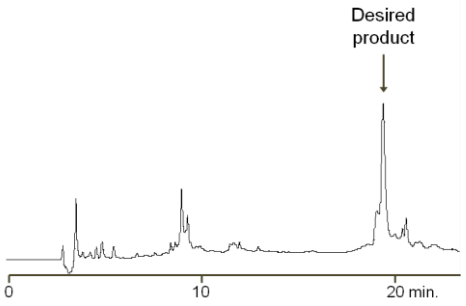
column chromatography (Hexane-AcOEt, 2:1 to 1:1 + 1% Et_3N) to afford **9** (89.8 mg, 79%) as a pale yellow foam.

^{31}P NMR (162 MHz, $CDCl_3$ for four diastereomers) δ 150.4, 150.9, 151.0,

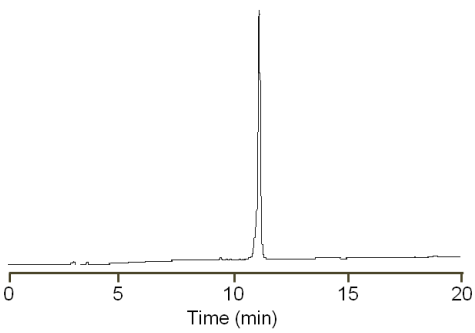
· Synthesis, Cleavage and purification of oligonucletide

All ONs were synthesized at a 1 μmol scale on ABI 392 DNA/RNA synthesizer with standard β-cyanoethyl phosphoramidite chemistry. 5'-terminal dimethoxytrityl bearing ONs were removed from the solid support by treatment with 28% NH_3 (0.5 ml) and evaporated under reduced pressure. The crude product was purified by reverse-phase HPLC with C-18 column (nacalai tesque: COSMOSIL 5C18-MS-II, 10 × 250 mm) by a linear gradient of 10-40%/20 min of acetonitrile in 0.1 M TEAA buffer at a flow rate of 4 ml/min. Dimethoxytrityl group of the purified ON was removed with 10% AcOH and the mixture was additionally purified by ethanol precipitation to afford ON **1**; MALDI-TOF MS (*m*/*z*): $[M-H]^-$ calcd 4422.1; found 4421.0.

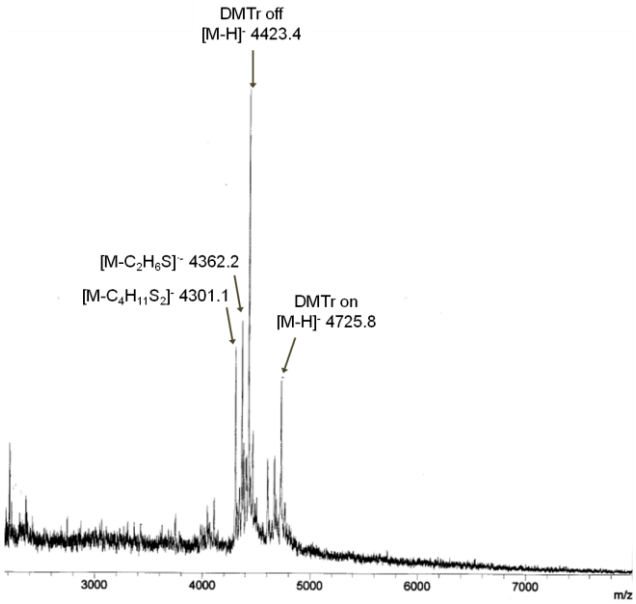
HPLC profile of crude product



HPLC profile of **ON 1** after purification



MALDI-TOF MS spectrum of crude product



· Synthesis of thiovinyl oligo (ON 2)

To a solution of **ON 1** (30 μL, 5.0 nmol), was added NaOH (4 M, 10 μL). After incubation for 14 h at room temparature, AcOH (25 μL) was added to the reaction mixture to neutralize. Subsequently, the reaction mixture was purified by HPLC to afford **ON 2** (thiovinyl); MALDI-TOF MS (*m*/*z*): $[M-H]^-$ calcd 4359.0; found 4359.6.

· Synthesis of sulfinylvinyl oligo (ON 3)

To a solution of ON **2** (26.8 μL, 3.0 nmol), was added a solution of magnesium monoper-phthalate (MMPP) (3 μl, 15 nmol) in carbonate buffer adjusted to pH 10 at room temperature. After 30 minutes at room temperature, the thiovinyl was completely converted to sulfinyl vinyl that was confirmed by MALDI TOF-MS and HPLC analysis. The product was not enough stabale to isolate, therefore that was used for each assy without purification; MALDI-TOF MS (*m*/*z*): $[M-H]^-$ calcd 4375.0; found 4378.5.

·General procedure of the crosslink reaction

The reaction was performed with 10 μM of **ON 2**, **3** or **5** and 5 μM of the target DNA or RNA labeled by fluorescein at 5'-end in a buffer of 100 mM or 500 mM NaCl and 50 mM MES at pH 7.0. The reaction mixture was incubated at 37 °C. The aliquot of the reaction mixture was reaction was collected at each indicated time and quenched with the addition of loading dye (95% formamide, 20 mM EDTA, 0.05% xylene cyanol, and 0.05% bromophenol blue). The cross-linked products were analyzed by a denaturing 20% polyacrylamide gel electrophoresis containing urea (7 M) with TBE buffer at 300 V for 1 h. The labeled bands were visualized and quantified with use of a FLA-5100 Fluor Imager.

· Crosslink reaction with H_2O_2 and metal ion

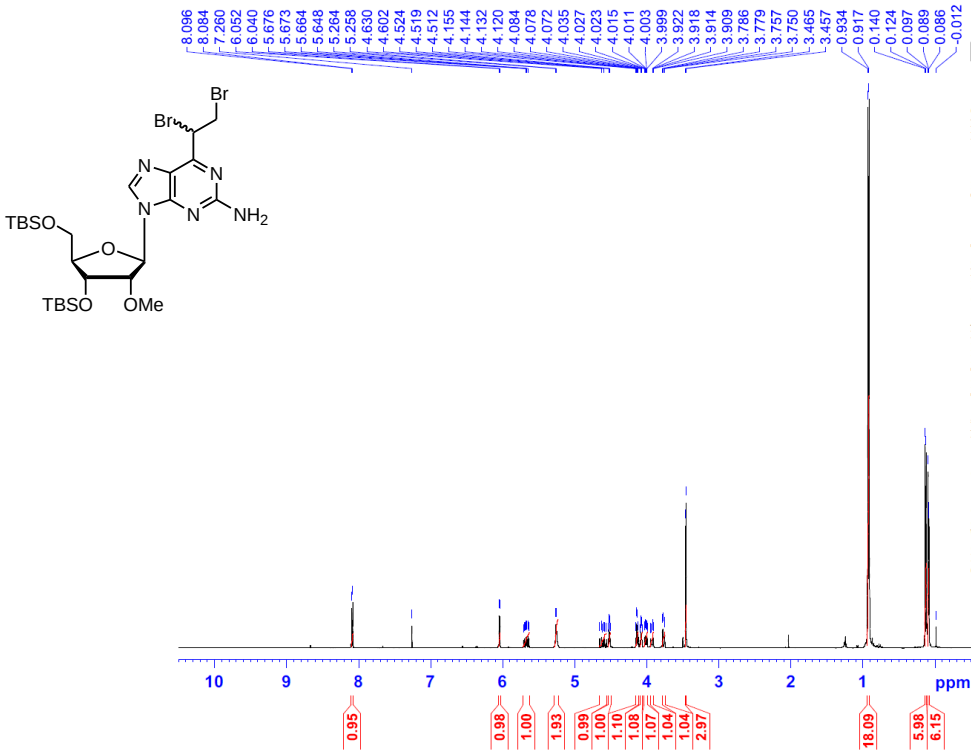
To the duplex solution of **ON 2** and **RNA 1** in a buffer of MES containing NaCl and H_2O_2, was added an aqueous solution of metal ion as to be the indicated final concentration. The reaction mixture was incubated at 37 °C for 1 hour and analyzed in the same manner described above.

· Crosslink reaction with H_2O_2 and $FeCl_2$ in the presence of scavenger

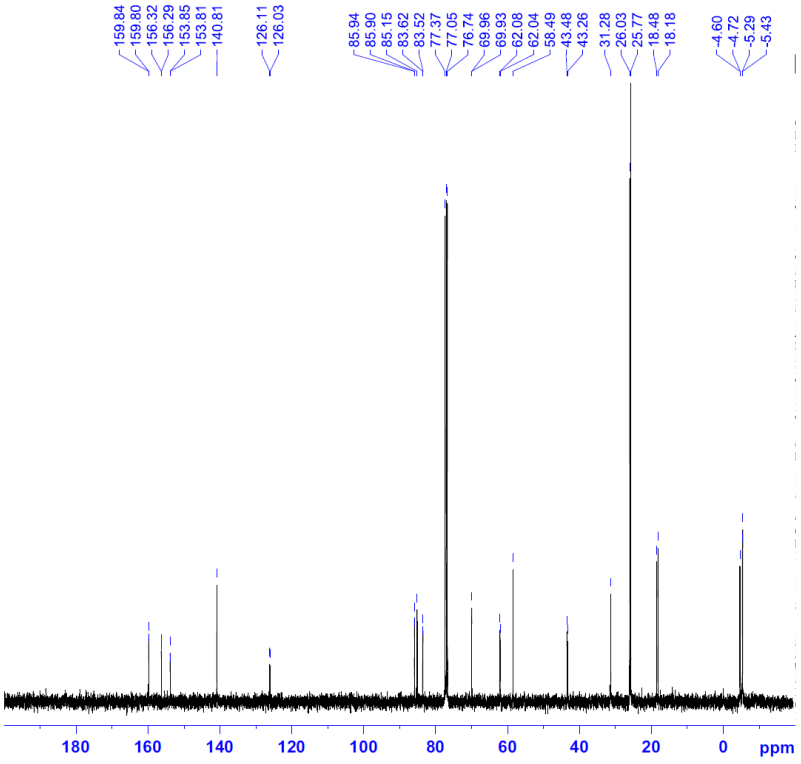
The scavenger was added to the duplex solution of **ON 2** and **RNA 1** in a buffer of MES containing NaCl before the addition of H_2O_2 and $FeCl_2$. After the addition of the H_2O_2 and $FeCl_2$, the reaction mixture was incubated at 37 °C for 1 hour and analyzed in the same manner described above.

9-[4-(tert-Butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxymethyl)-3-methoxy-tetrahydro-furan-2-yl]-6-(1,2-dibromo-ethyl)-9*H*-purin-2-ylamine

^{1}H NMR: (400 MHz, $CDCl_3$)

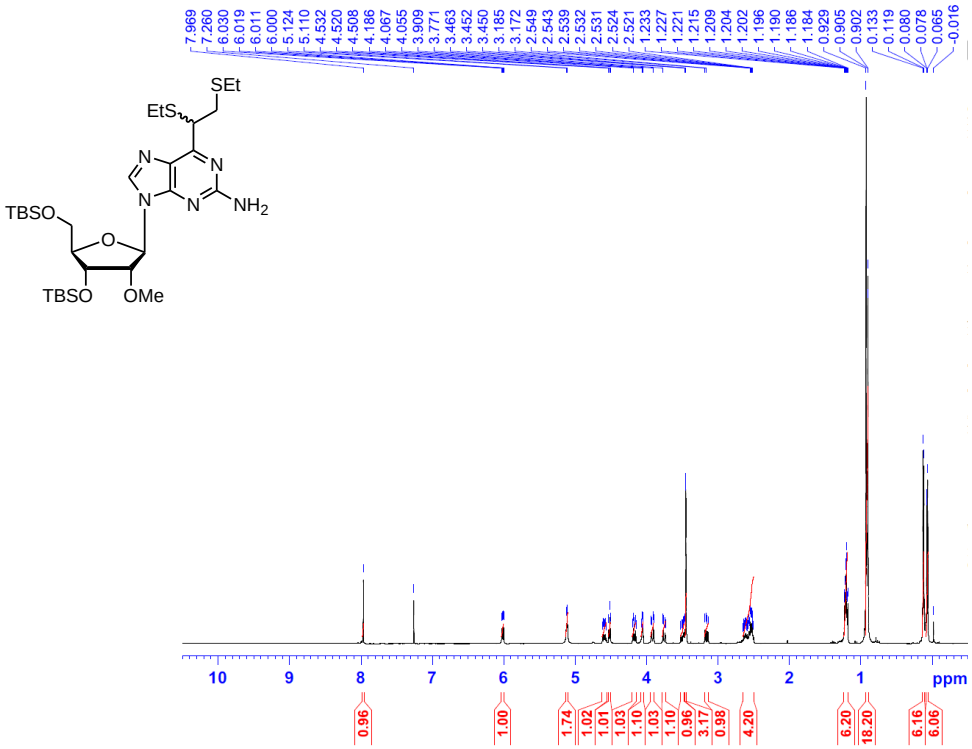


^{13}C NMR: (100 MHz, $CDCl_3$)

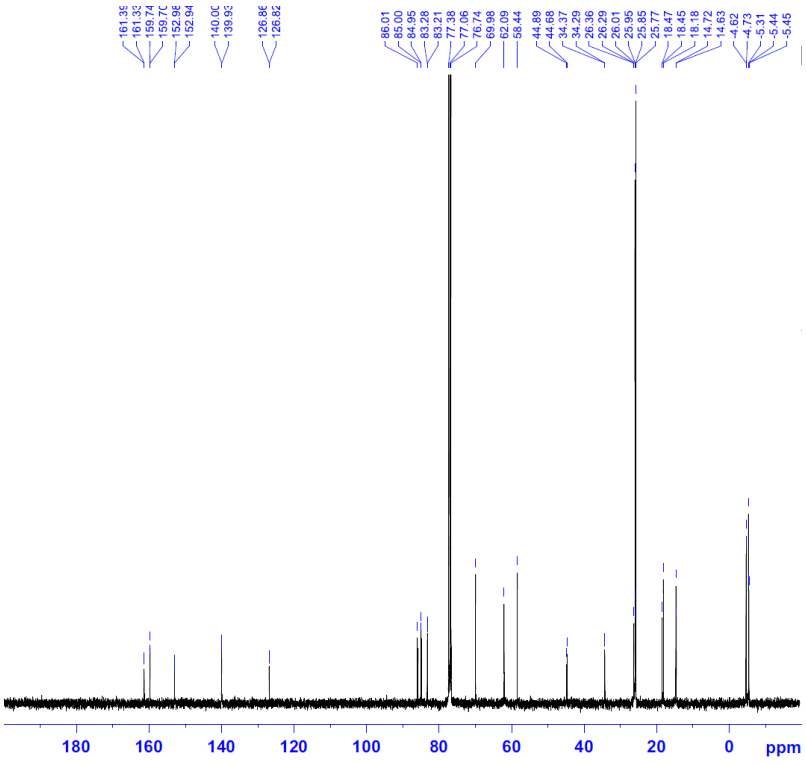


6-(1,2-Bis-ethylsulfanyl-ethyl)-9-[4-(tert-butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxymethyl)-3-methoxy-tetrahydro-furan-2-yl]-9*H*-purin-2-ylamine (**4**)

^{1}H NMR: (400 MHz, $CDCl_3$)

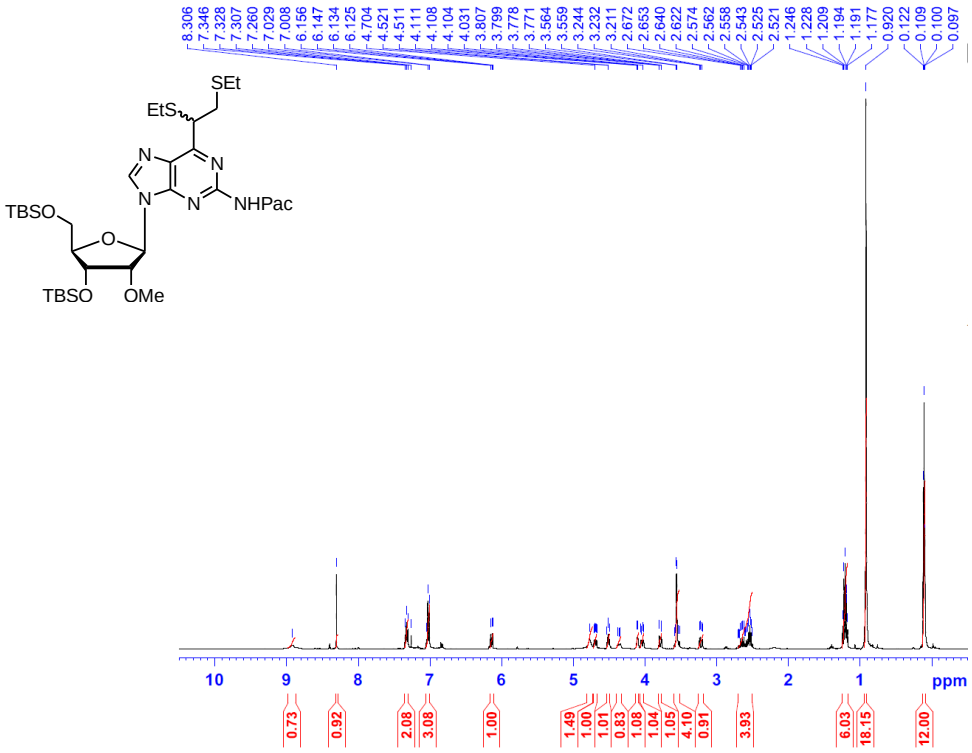


^{13}C NMR: (100 MHz, $CDCl_3$)

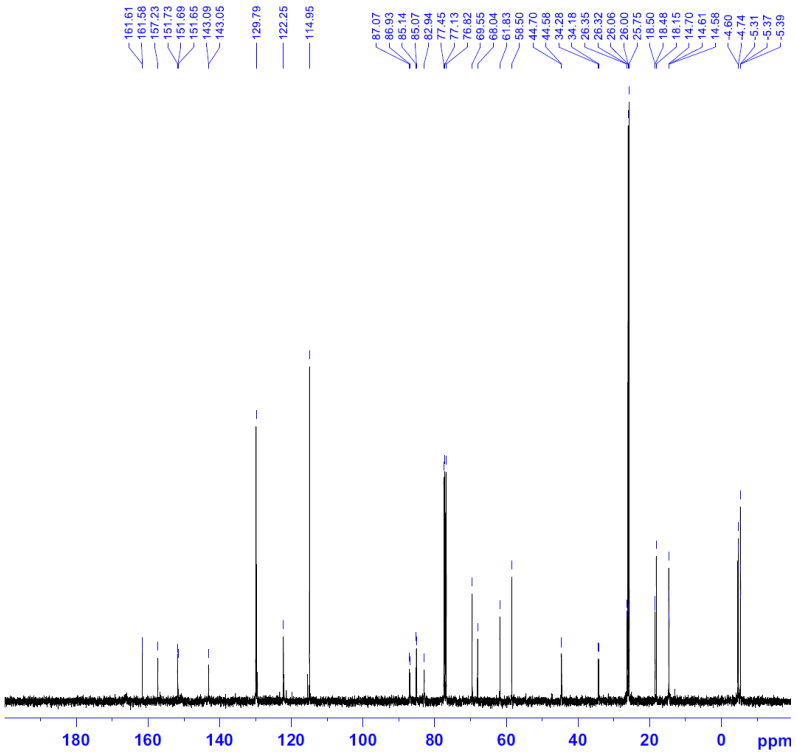


N-{6-(1,2-Bis-ethylsulfanyl-ethyl)-9-[4-(tert-butyl-dimethyl-silanyloxy)-5-(tert-butyl-dimethyl-silanyloxy methyl)-3-methoxy-tetrahydro-furan-2-yl]-9*H*-purin-2-yl}-2-phenoxy-acetamide

^{1}H NMR: (400 MHz, $CDCl_3$)

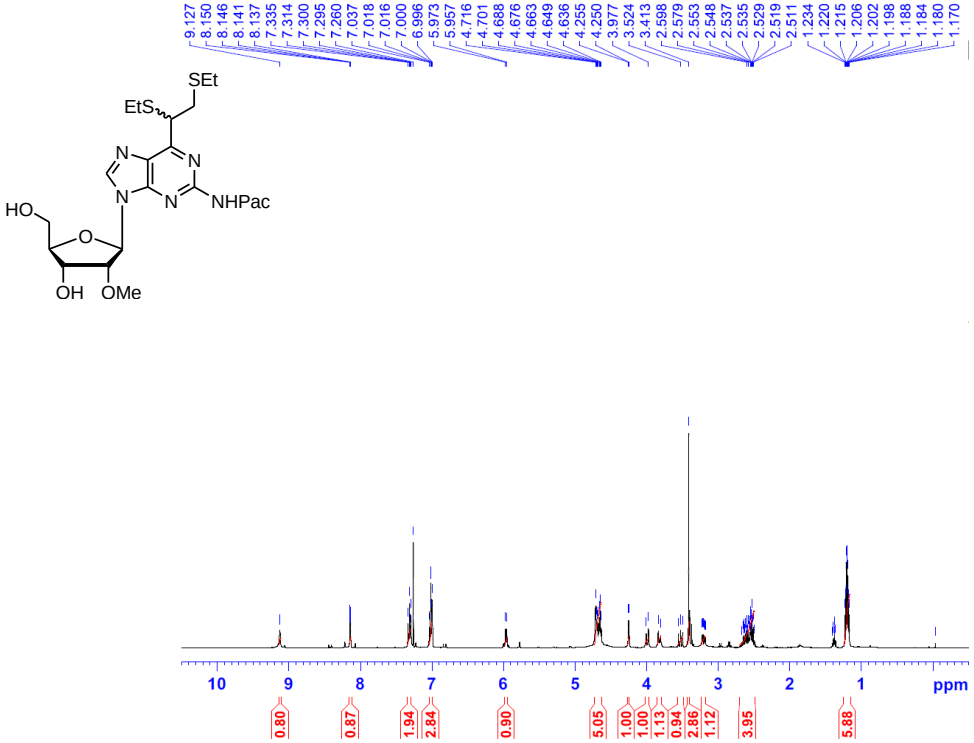


^{13}C NMR: (100 MHz, $CDCl_3$)

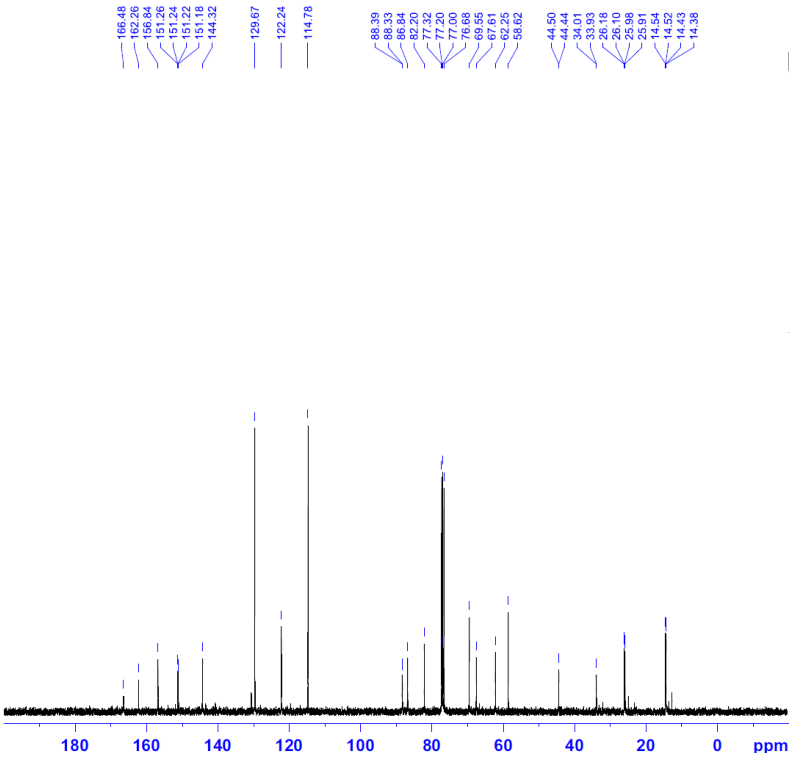


N-[6-(1,2-Bis-ethylsulfanyl-ethyl)-9-(4-hydroxy-5-hydroxymethyl-3-methoxy-tetrahydro-furan-2-yl)-9*H*-purin-2-yl]-2-phenoxy-acetamide (**5**)

^{1}H NMR: (400 MHz, $CDCl_3$)

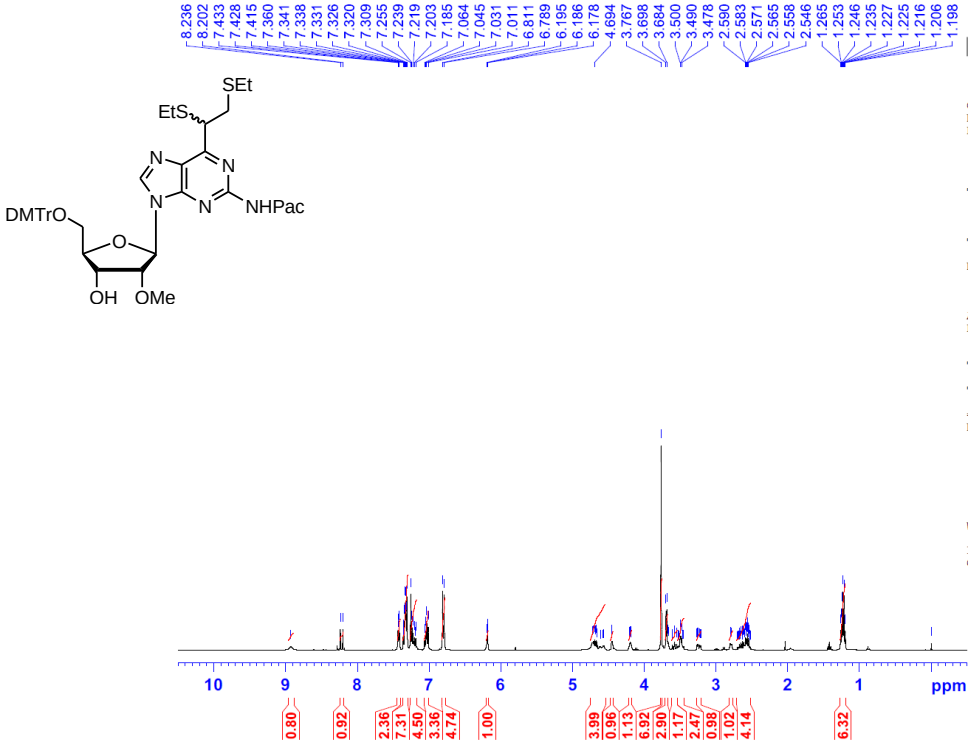


^{13}C NMR: (100 MHz, $CDCl_3$)

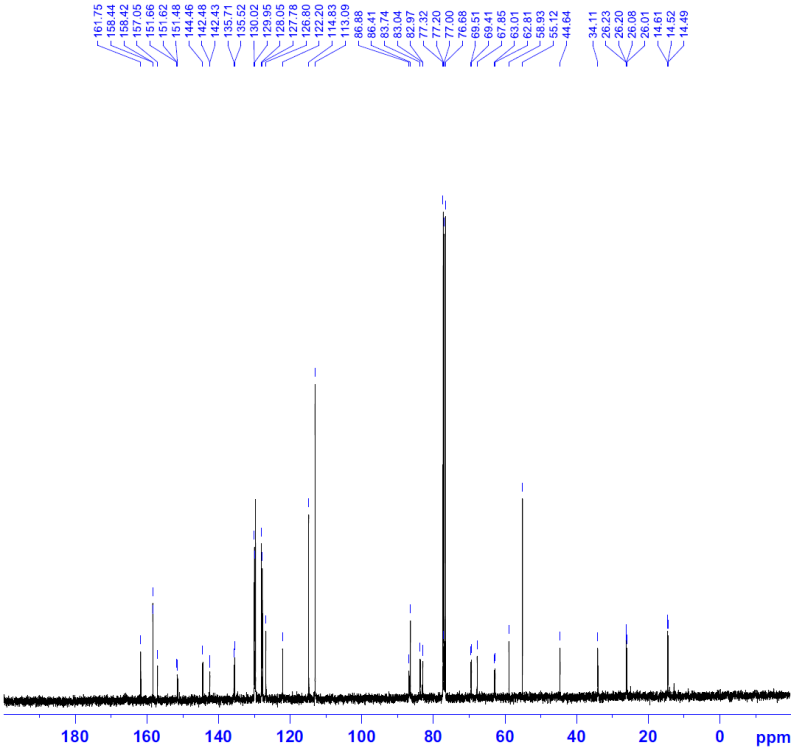


N-(6-(1,2-Bis-ethylsulfanyl-ethyl)-9-{5-[bis-(4-methoxy-phenyl)-phenyl-methoxymethyl]-4-hydroxy-3-methoxy-tetrahydro-furan-2-yl}-9H-purin-2-yl)-2-phenoxy-acetamide

^{1}H NMR: (400 MHz, $CDCl_3$)

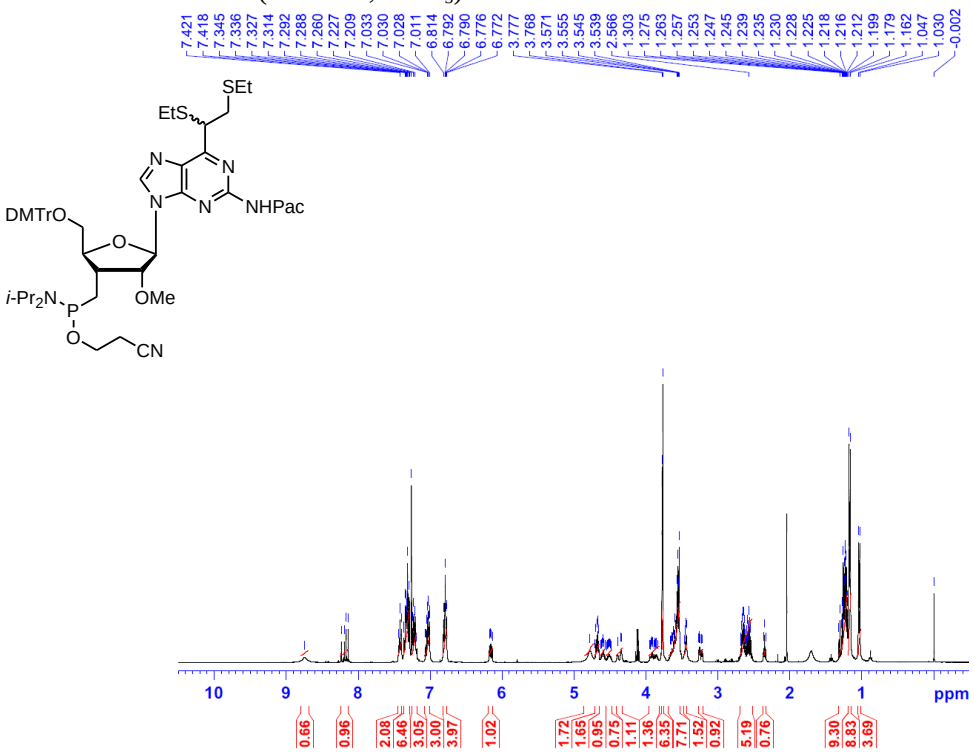


^{13}C NMR: (100 MHz, $CDCl_3$)



Diisopropyl-phosphoramidous acid 5-[6-(1,2-bis-ethylsulfanyl-ethyl)-2-(2-phenoxy-acetylamino)-purin-9-yl]-2-[bis-(4-methoxy-phenyl)-phenyl-methoxymethyl]-4-methoxy-tetrahydro-furan-3-yl ester 2-cyano-ethyl ester (**6**)

^{1}H NMR: (400 MHz, $CDCl_3$)



^{31}P NMR: (162 MHz, $CDCl_3$)