

## Supplementary Information

### 8-Fluoro-*N*-2-isobutyryl-2'-deoxyguanosine: synthesis and stability

Andrei Solodin, James Helm, Samuel Ollivier, Hongbin Yan

Department of Chemistry, Brock University, 1812 Sir Isaac Brock Way, St. Catharines, Ontario  
L2S 3A1, Canada

#### List of figures

**Figure S1.**  $^1\text{H}$  NMR of **6** in  $\text{CDCl}_3$ .

**Figure S2.**  $^{13}\text{C}$  NMR of **6** in  $\text{CDCl}_3$ .

**Figure S3.** COSY NMR of **6** in  $\text{CDCl}_3$ .

**Figure S4.** HSQC NMR of **6** in  $\text{CDCl}_3$ .

**Figure S5.** HMBC NMR of **6** in  $\text{CDCl}_3$ .

**Figure S6.**  $^1\text{H}$  NMR of **7** in  $\text{CDCl}_3$ .

**Figure S7.**  $^{13}\text{C}$  NMR of **7** in  $\text{CDCl}_3$ .

**Figure S8.**  $^{19}\text{F}$  NMR of **7** in  $\text{CDCl}_3$ .

**Figure S9.** COSY NMR of **7** in  $\text{CDCl}_3$ .

**Figure S10.** HSQC NMR of **7** in  $\text{CDCl}_3$ .

**Figure S11.** HMBC NMR of **7** in  $\text{CDCl}_3$ .

**Figure S12.**  $^1\text{H}$  NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S13.**  $^{13}\text{C}$  NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S14.**  $^{19}\text{F}$  NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S15.** COSY NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S16.** HSQC NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S17.** HMBC NMR of **4** in  $\text{DMSO-d}_6$ .

**Figure S18.**  $^1\text{H}$  NMR of **10** in  $\text{CDCl}_3$ .

**Figure S19.**  $^{13}\text{C}$  NMR of **10** in  $\text{CDCl}_3$ .

**Figure S20.**  $^{19}\text{F}$  NMR of **10** in  $\text{CDCl}_3$ .

**Figure S21.** COSY NMR of **10** in  $\text{CDCl}_3$ .

**Figure S22.** HSQC NMR of **10** in  $\text{CDCl}_3$ .

**Figure S23.** HSQC NMR of **10** in  $\text{CDCl}_3$ .

**Figure S24.**  $^1\text{H}$  NMR of **11** in  $\text{CDCl}_3$ .

**Figure S25.**  $^{31}\text{P}$  NMR of **10** in  $\text{CDCl}_3$ .

**Figure S26.**  $^{19}\text{F}$  NMR of **10** in  $\text{CDCl}_3$ .

**Figure S27.** COSY NMR of **10** in  $\text{CDCl}_3$ .

**Figure S28.** HPLC profile of the product where compound **4** was treated with concentrated aqueous ammonium hydroxide at  $55^\circ\text{C}$  overnight (as described in Scheme 3). The mixture was eluted off a Dionex Polar Advantage-2 C18 reverse phase column ( $4.6 \times 150$  mm) with a linear gradient of water–acetonitrile (100:0 to 60:40, v/v over 10 min) at 0.7 ml/min.

**Figure S29.** Mass spectra of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at  $55^\circ\text{C}$  overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. a). Electrospray detected for positive ions (1.9-2.1min, background subtracted); b). zoomed-in portion, electrospray detected for positive ions (1.9-2.1min, background subtracted); c).

electrospray detected for negative ions (2.6-2.8 min, background subtracted); d). high-resolution EI analysis on m/z 265.

**Figure S30.**  $^1\text{H}$  NMR of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at  $55^\circ\text{C}$  overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. The spectrum was recorded in  $\text{DMSO-d}_6$  at 400.2 MHz.

**Figure S31.** COSY NMR of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at  $55^\circ\text{C}$  overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. The spectrum was recorded in  $\text{DMSO-d}_6$  at 400.2 MHz.

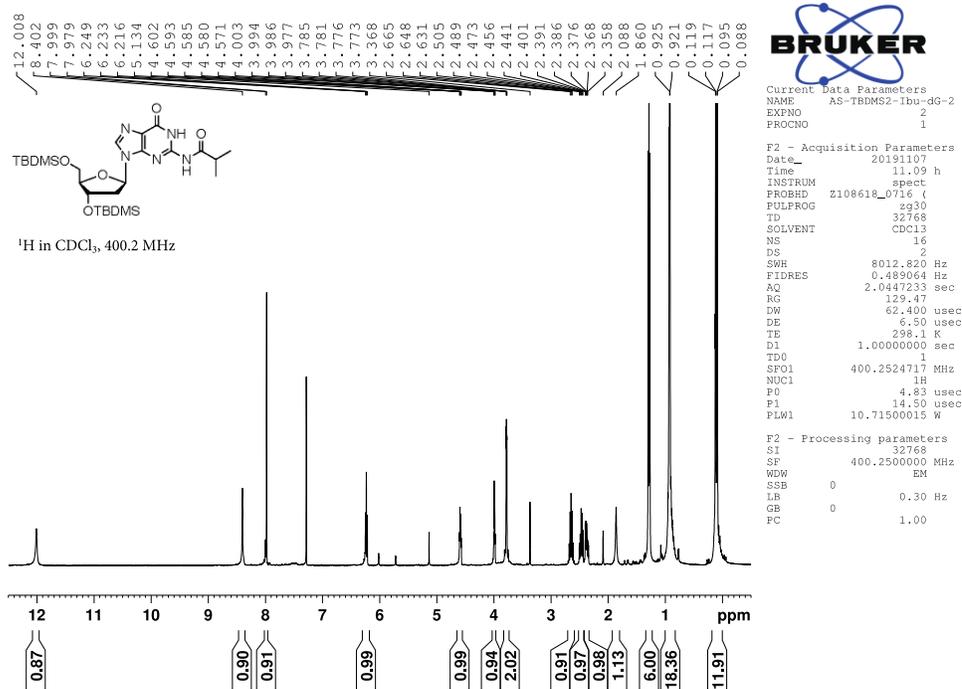


Figure S1. <sup>1</sup>H NMR of 6 in CDCl<sub>3</sub>.

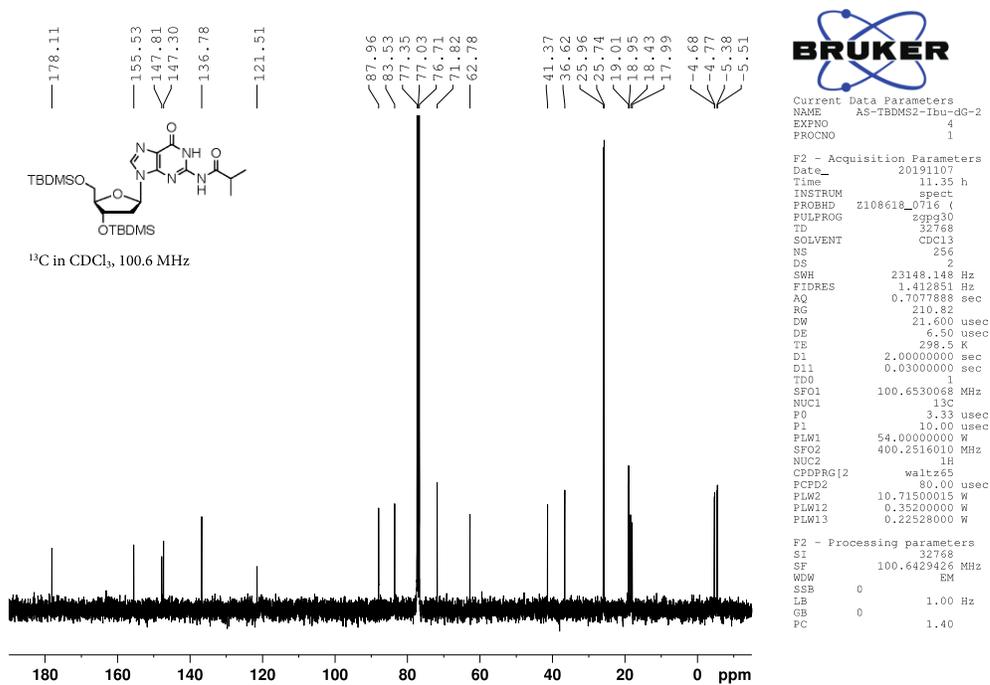


Figure S2. <sup>13</sup>C NMR of 6 in CDCl<sub>3</sub>.

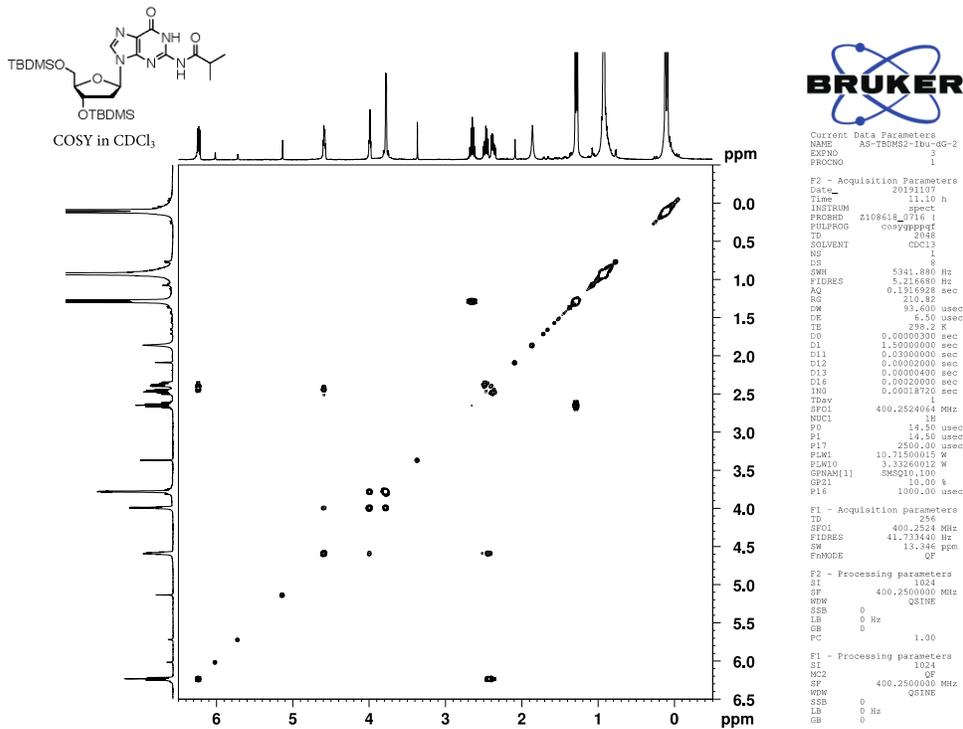


Figure S3. COSY NMR of **6** in CDCl<sub>3</sub>.

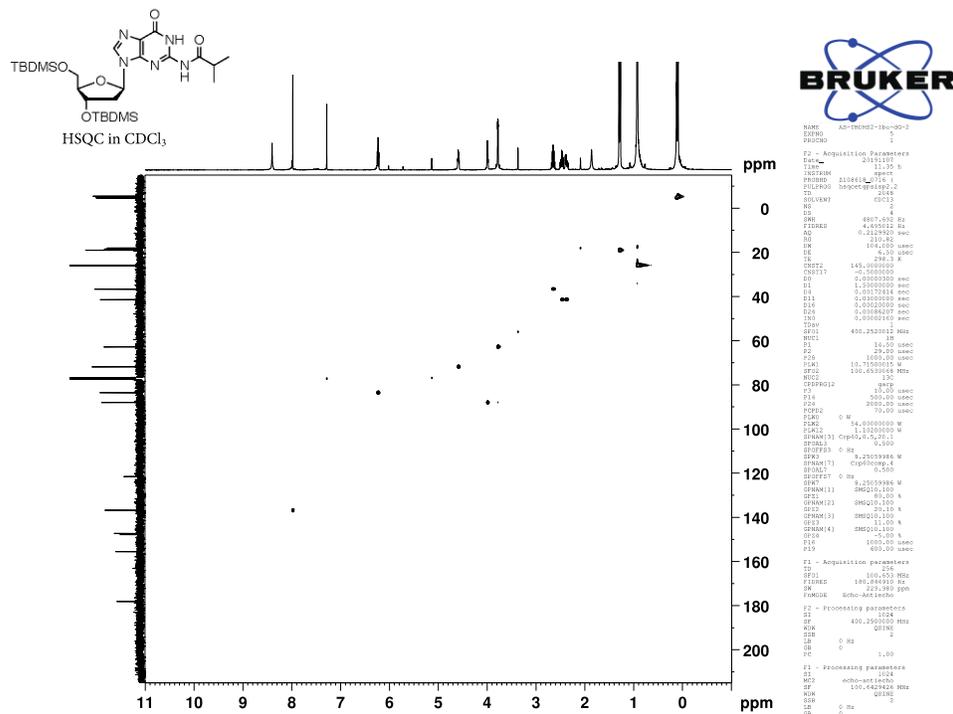


Figure S4. HSQC NMR of **6** in CDCl<sub>3</sub>.

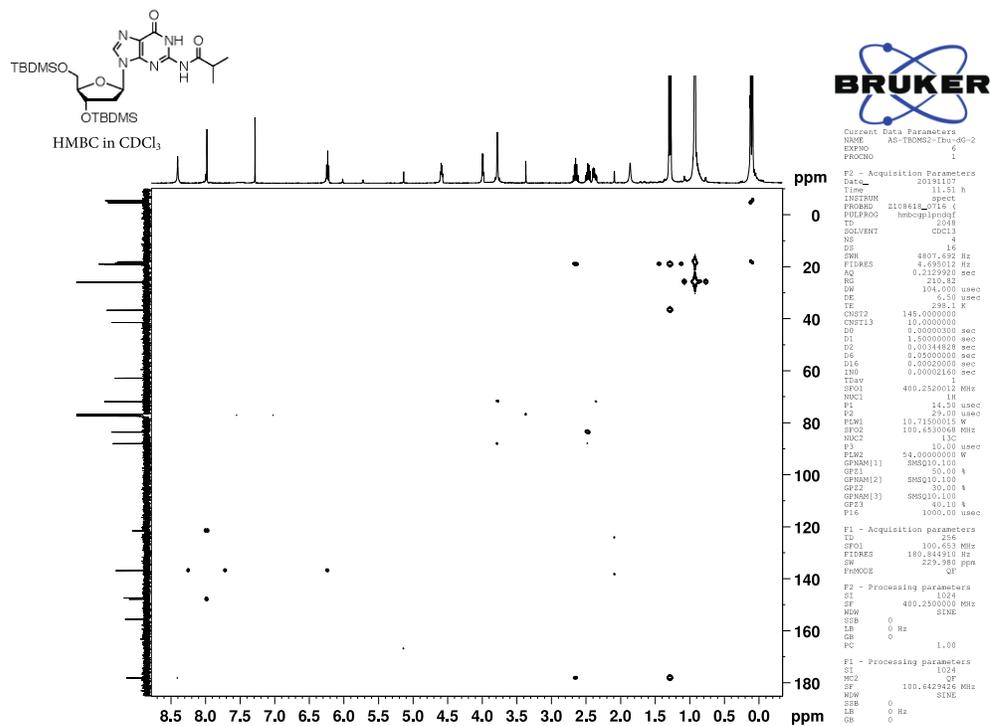


Figure S5. HMBC NMR of **6** in CDCl<sub>3</sub>.

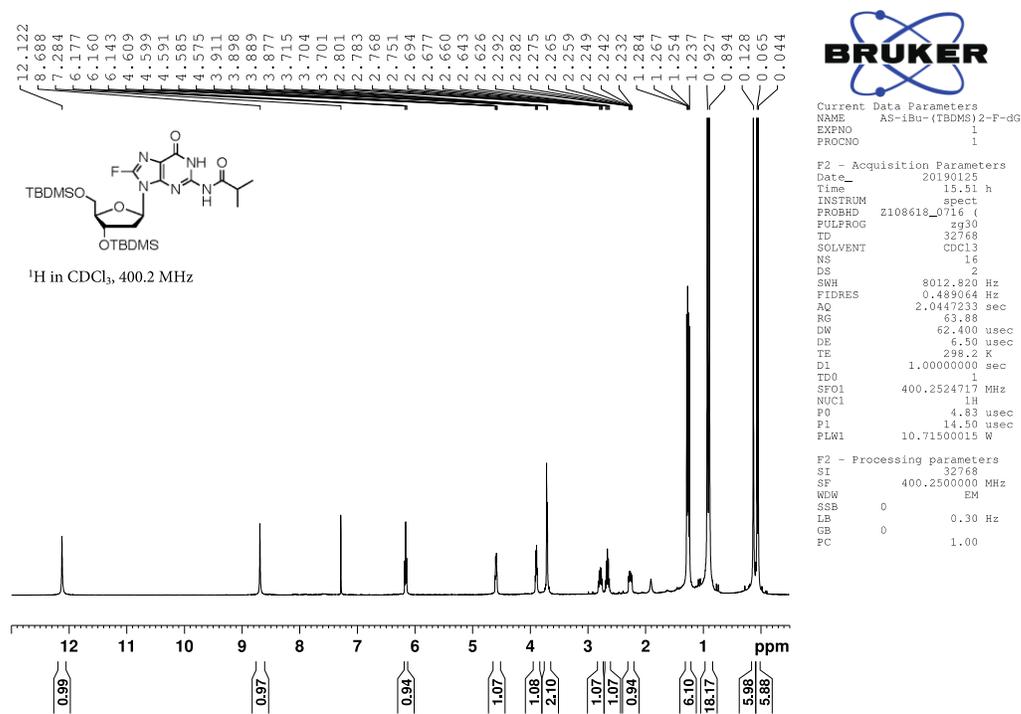


Figure S6. <sup>1</sup>H NMR of **7** in CDCl<sub>3</sub>.

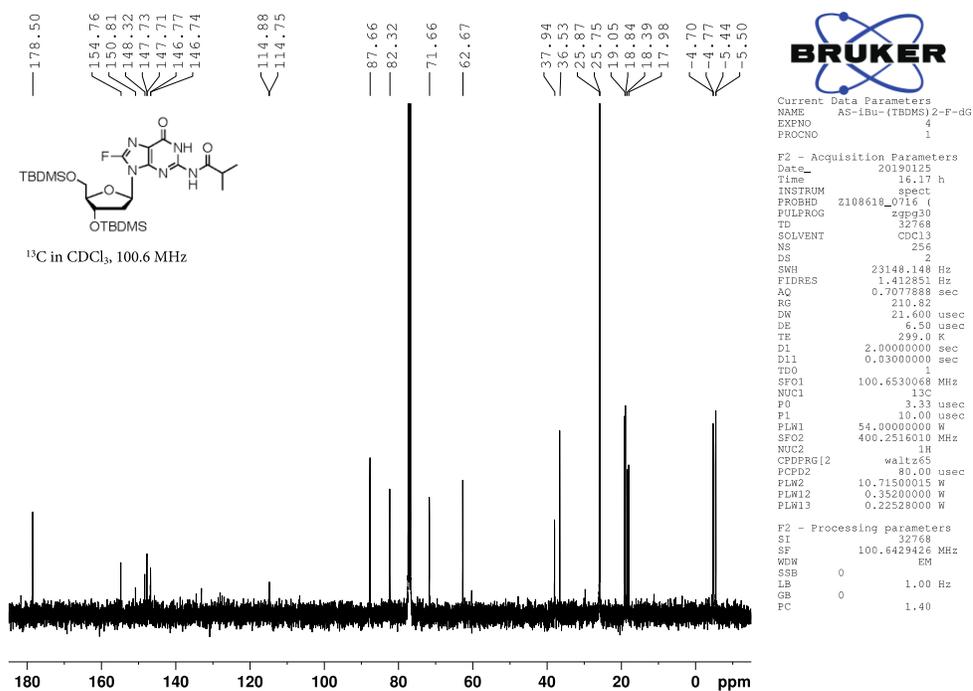


Figure S7. <sup>13</sup>C NMR of 7 in CDCl<sub>3</sub>.

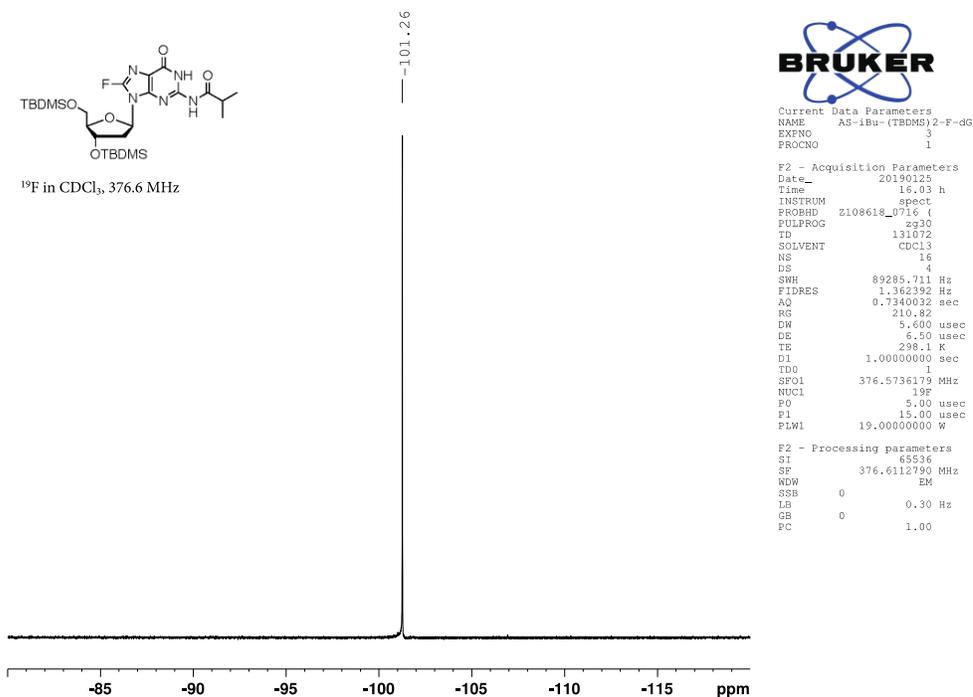


Figure S8. <sup>19</sup>F NMR of 7 in CDCl<sub>3</sub>.

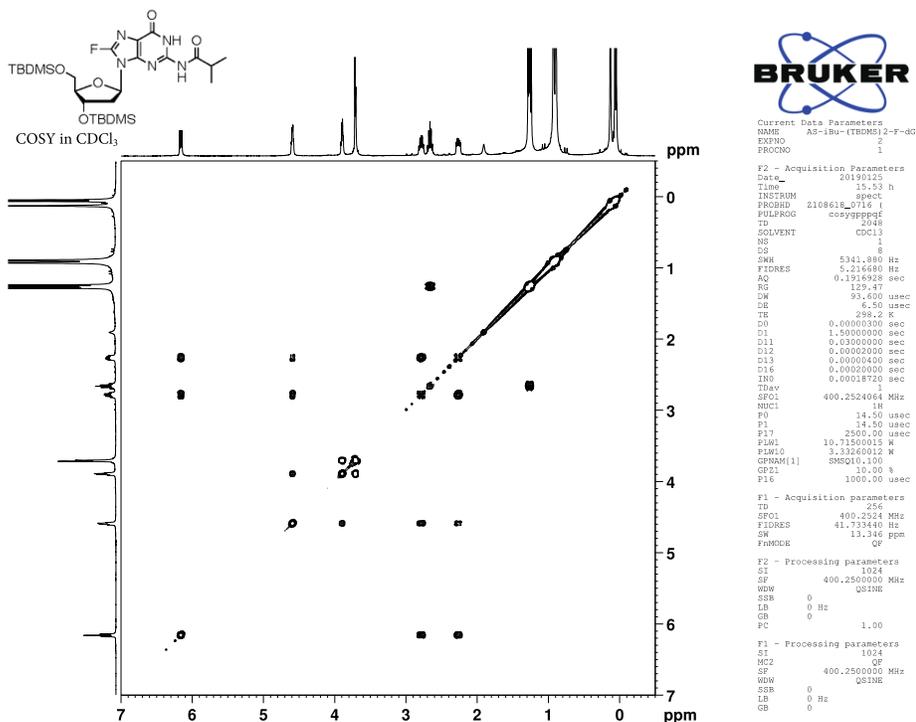


Figure S9. COSY NMR of 7 in CDCl<sub>3</sub>.

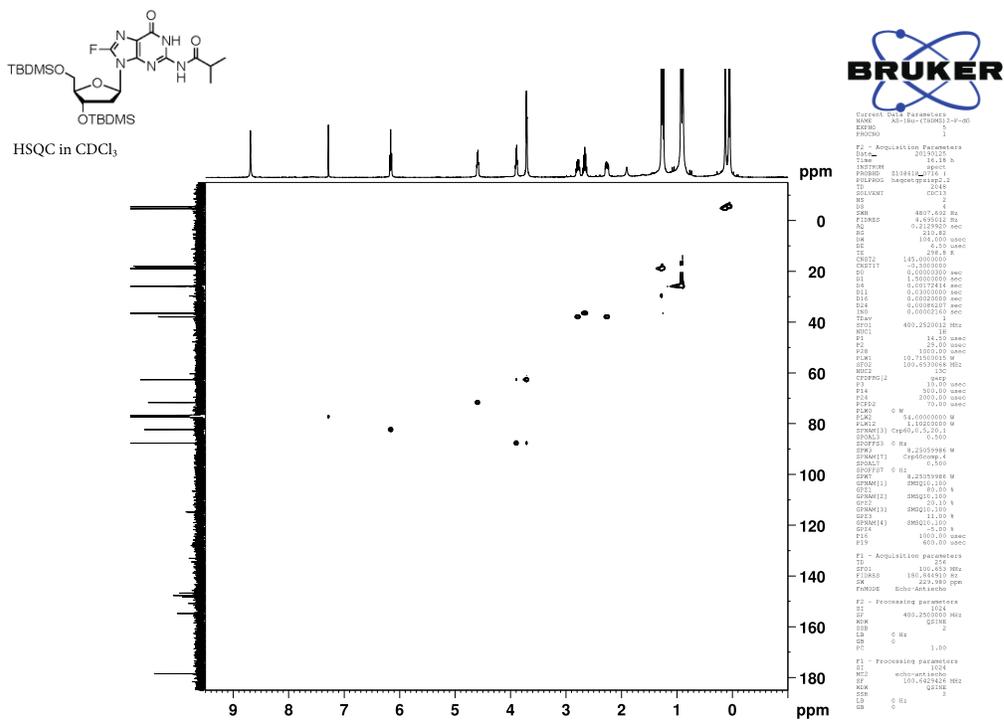


Figure S10. HSQC NMR of 7 in CDCl<sub>3</sub>.

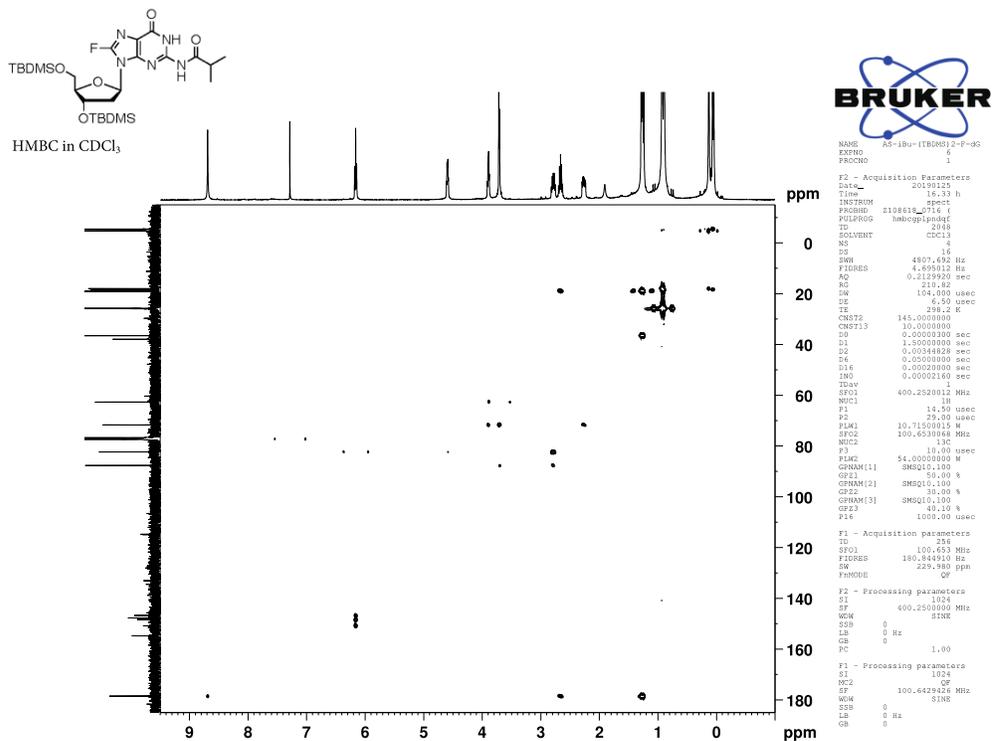


Figure S11. HMBC NMR of **7** in CDCl<sub>3</sub>.

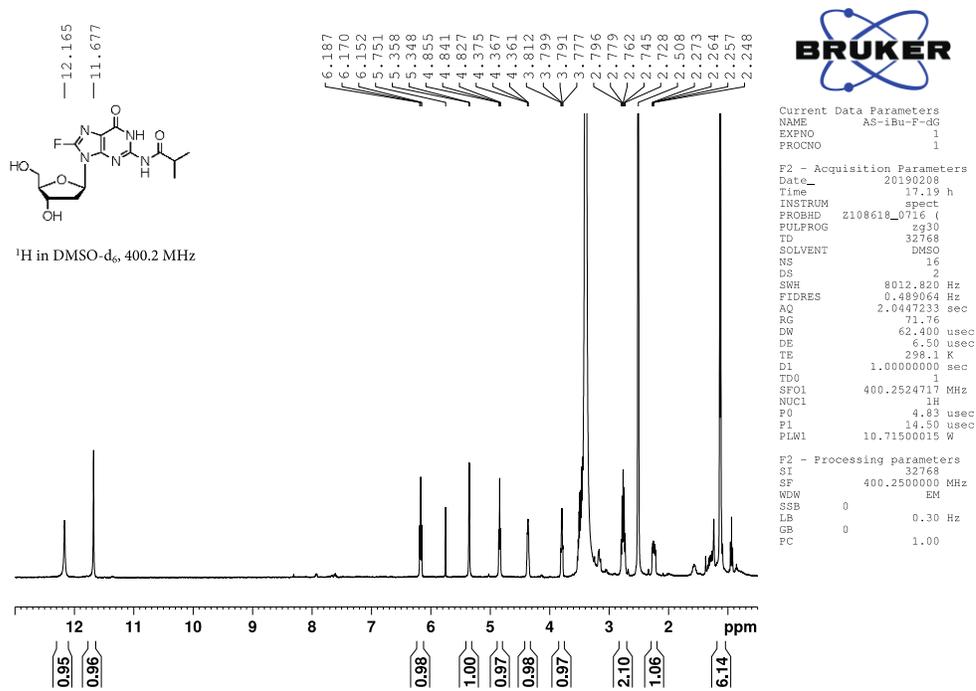


Figure S12. <sup>1</sup>H NMR of **4** in DMSO-d<sub>6</sub>.

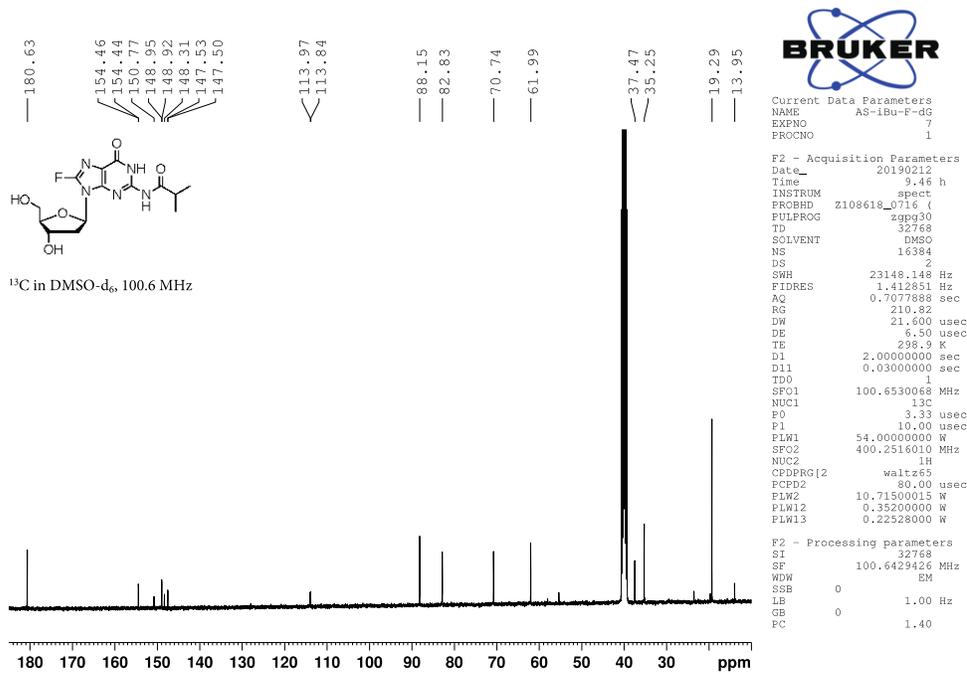


Figure S13. <sup>13</sup>C NMR of 4 in DMSO-d<sub>6</sub>.

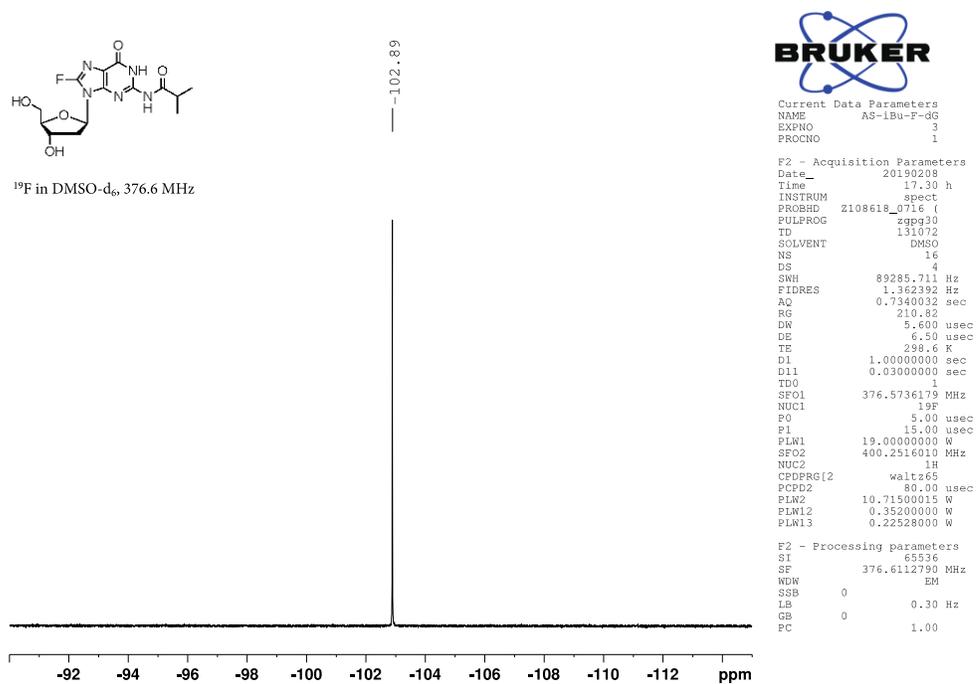
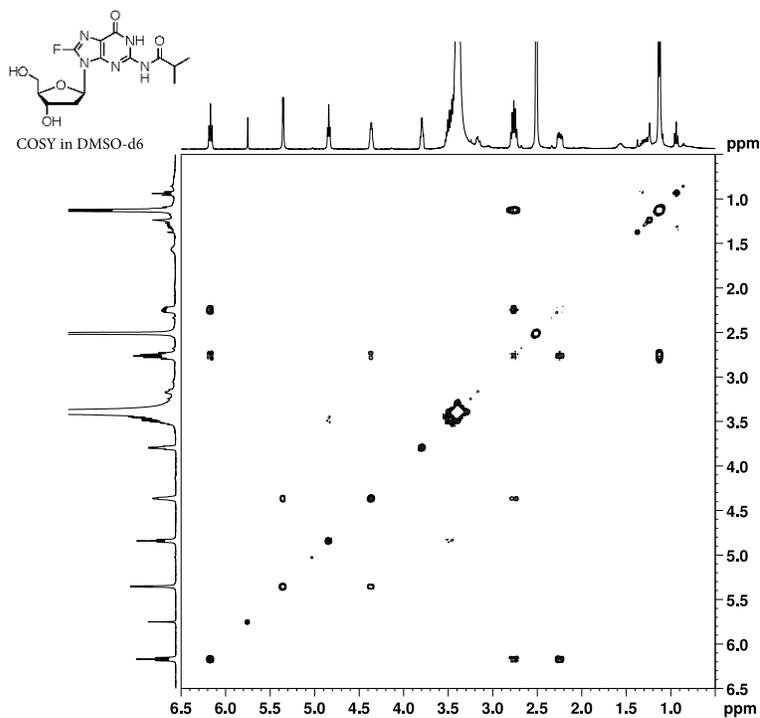


Figure S14. <sup>19</sup>F NMR of 4 in DMSO-d<sub>6</sub>.



```

Current Data Parameters
NAME AS-18u-F4C
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190208
Time 17.20 h
INSTRUM spect
PROBHD zgpg30
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1
DS 1
SWH 5341.880 Hz
FIDRES 5.2146880 Hz
AQ 0.1119928 sec
RG 189.38
DW 93.600 usec
DE 6.30 usec
TE 298.2 K
D1 0.03000000 sec
D11 0.03000000 sec
D12 0.00020000 sec
D13 0.00004000 sec
D14 0.00020000 sec
IN0 0.00018720 sec
TD0V 1
SFO1 400.252464 MHz
NUC1 1H
PC 14.50 usec
PI 14.50 usec
P17 2500.00 usec
PLM1 10.71500015 W
PLM10 3.3324012 W
GPM11 SMSQ1.100
SF1 10.00 %
P16 1000.00 usec

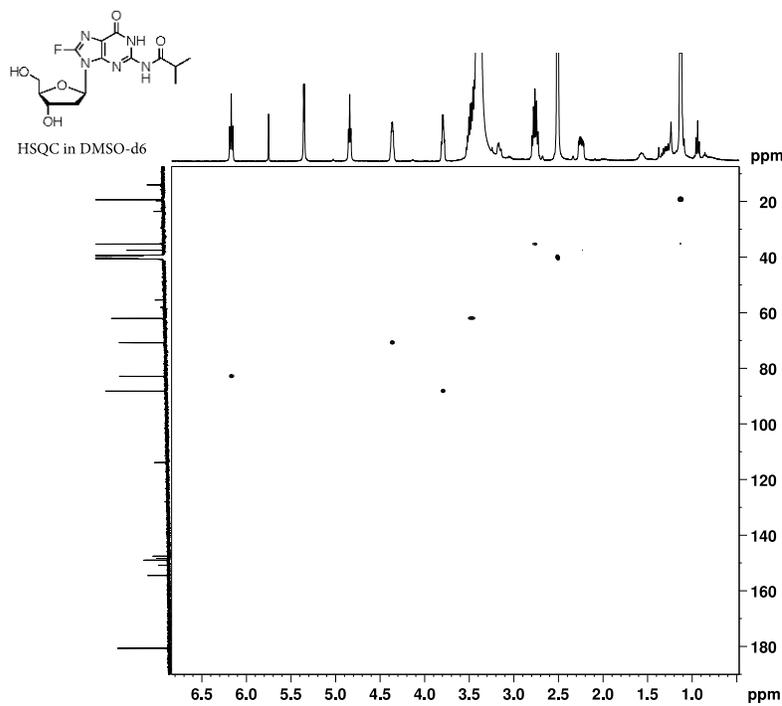
F1 - Acquisition parameters
TD 256
SFO1 400.2524 MHz
FIDRES 41.733440 Hz
SW 13.346 ppm
FMODE QF

F2 - Processing parameters
SI 1024
SF 400.2500000 MHz
WDW Q
SSB 0
LB 0 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
SF 400.2500000 MHz
WDW Q
SSB 0
LB 0 Hz
GB 0

```

Figure S15. COSY NMR of 4 in DMSO-d<sub>6</sub>.



```

Current Data Parameters
NAME AS-18u-F4C
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190208
Time 17.46 h
INSTRUM spect
PROBHD zgpg30
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 1
DS 1
SWH 8897.400 Hz
FIDRES 4.695012 Hz
AQ 0.1220000 sec
RG 189.38
DW 93.600 usec
DE 6.30 usec
TE 298.2 K
D1 0.03000000 sec
D11 0.03000000 sec
D12 0.00020000 sec
D13 0.00004000 sec
D14 0.00020000 sec
IN0 0.00018720 sec
TD0V 1
SFO1 400.252464 MHz
NUC1 1H
PC 14.50 usec
PI 14.50 usec
P17 2500.00 usec
PLM1 10.71500015 W
PLM10 3.3324012 W
GPM11 SMSQ1.100
SF1 10.00 %
P16 1000.00 usec

F1 - Acquisition parameters
SI 1024
SF 400.2500000 MHz
WDW Q
SSB 0
LB 0 Hz
GB 0
PC 1.00

F2 - Processing parameters
SI 1024
SF 400.2500000 MHz
WDW Q
SSB 0
LB 0 Hz
GB 0

```

Figure S16. HSQC NMR of 4 in DMSO-d<sub>6</sub>.

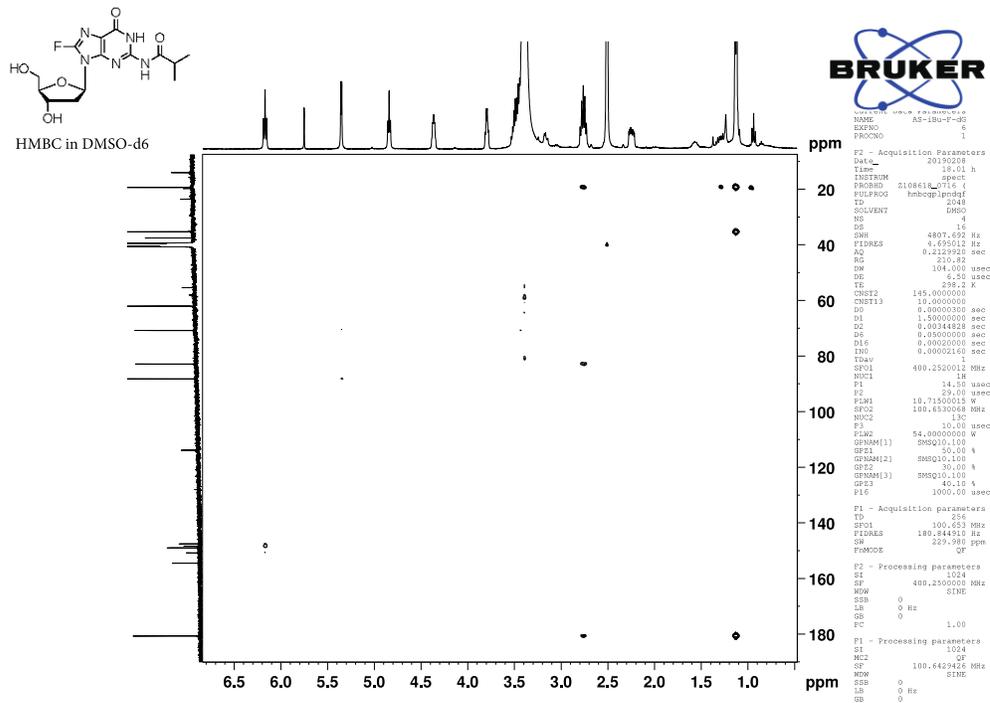


Figure S17. HMBC NMR of **4** in DMSO-d<sub>6</sub>.

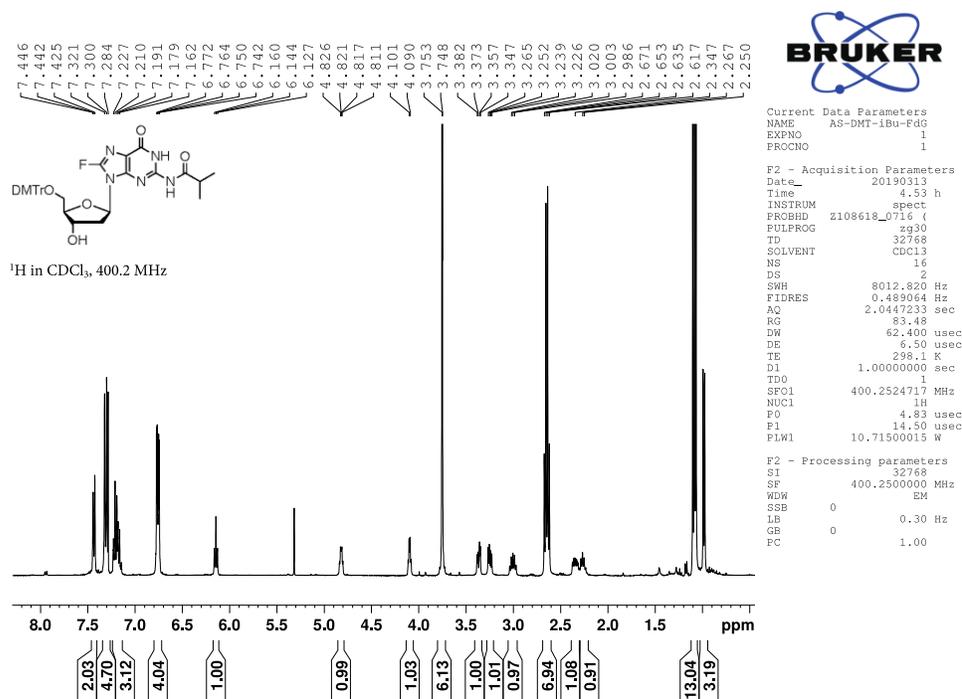


Figure S18. <sup>1</sup>H NMR of **10** in CDCl<sub>3</sub>.

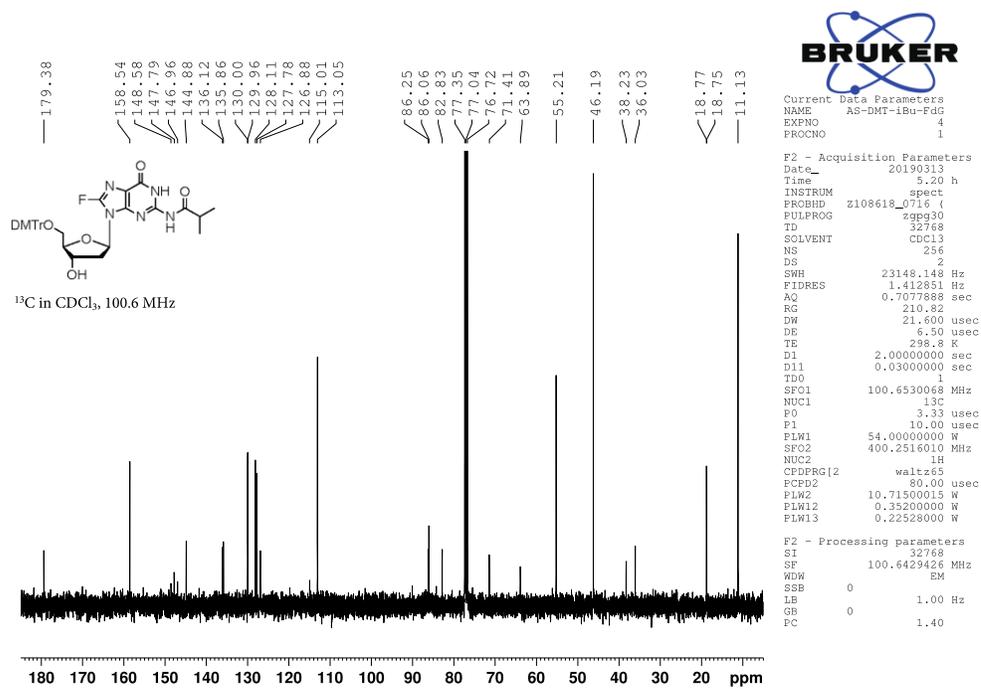


Figure S19. <sup>13</sup>C NMR of **10** in CDCl<sub>3</sub>.

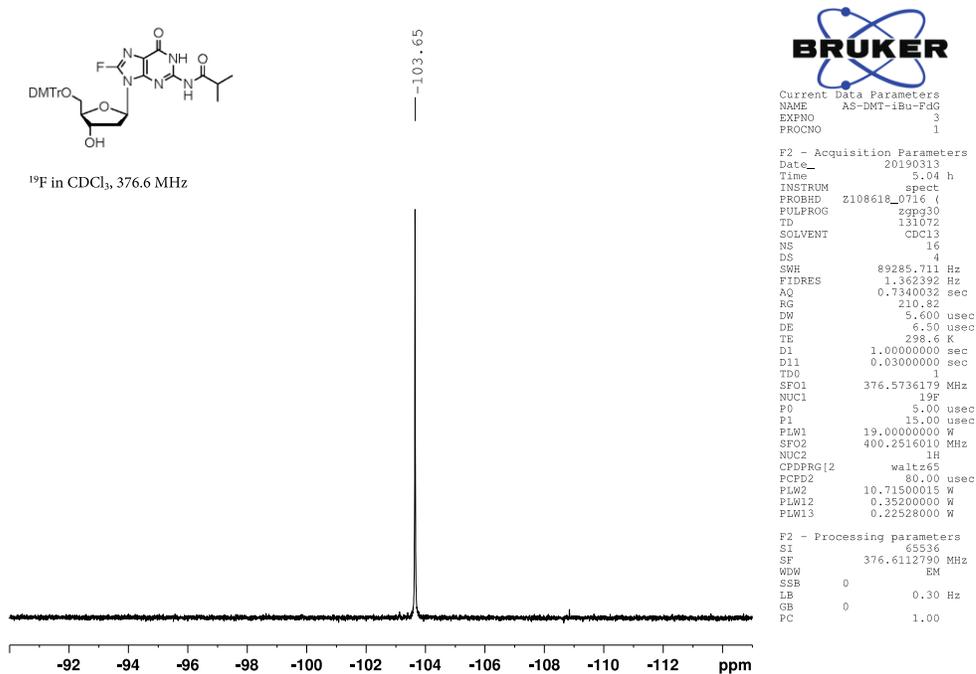


Figure S20. <sup>19</sup>F NMR of **10** in CDCl<sub>3</sub>.

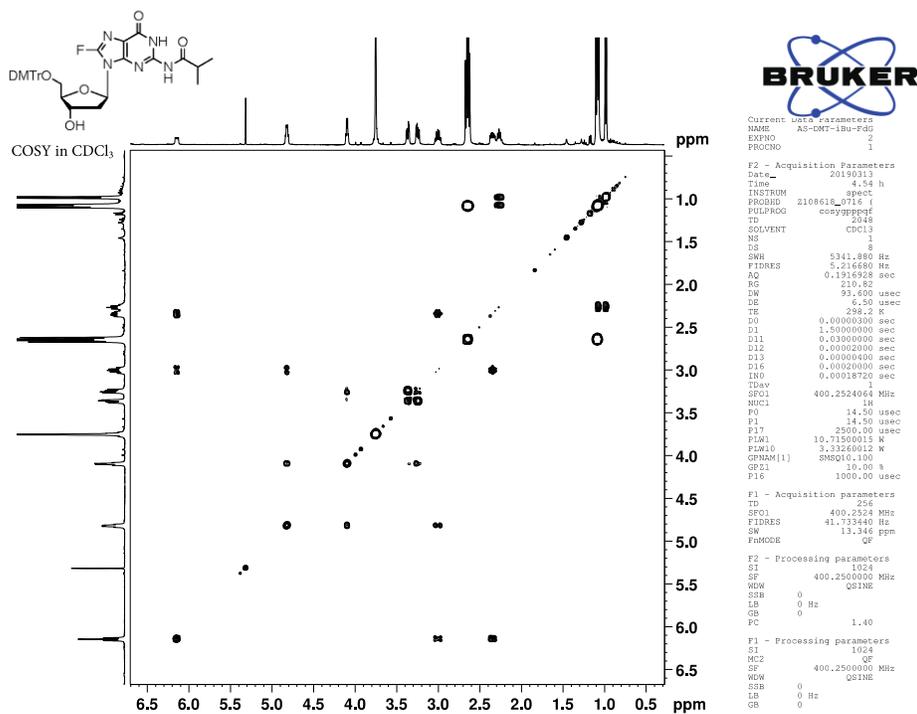


Figure S21. COSY NMR of **10** in CDCl<sub>3</sub>.

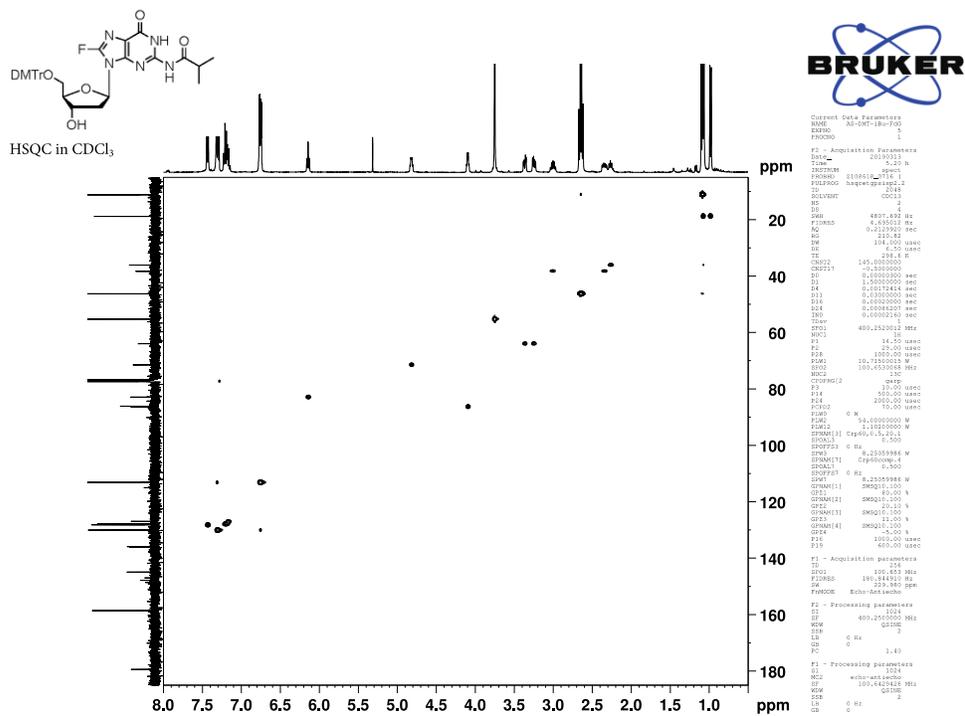
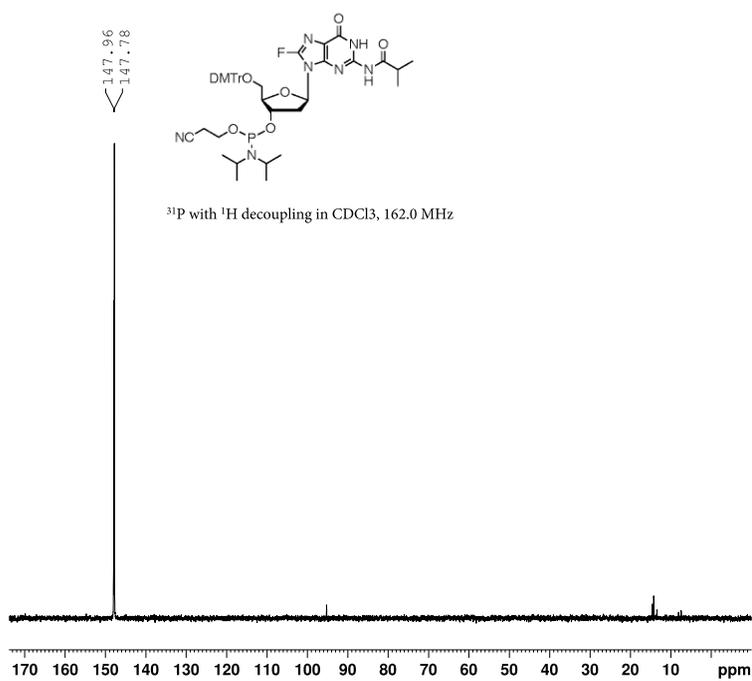


Figure S22. HSQC NMR of **10** in CDCl<sub>3</sub>.



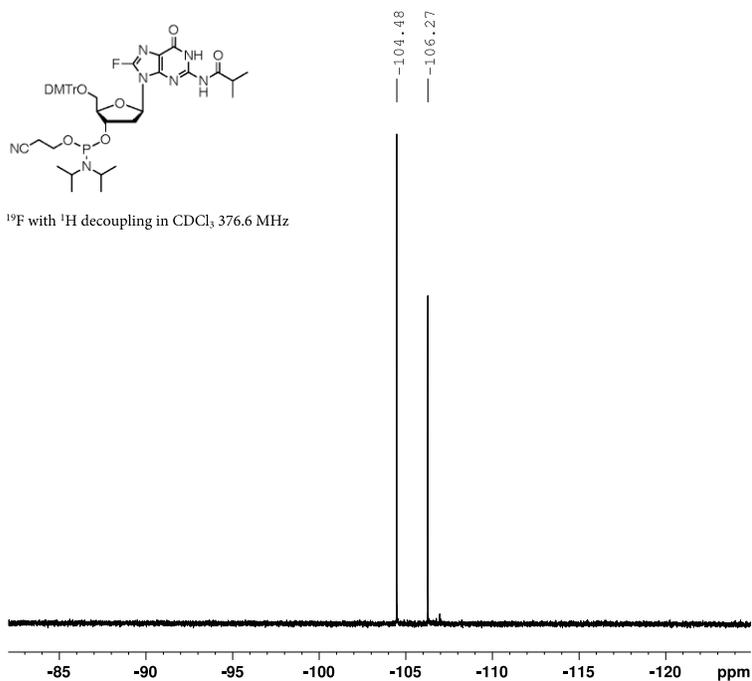


Current Data Parameters  
NAME AS-DMT-1Bu-FdG phosph  
EXPNO 3  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20190321  
Time 19:59 h  
INSTRUM spect  
PROBHD z108618\_0716 ( )  
PULPROG zgpg30  
TD 65536  
SOLVENT CDCl3  
NS 64  
DS 4  
SWH 64102.562 Hz  
FIDRES 1.956255 Hz  
AQ 0.5111808 sec  
RG 210.82  
DW 7.800 usec  
DE 6.50 usec  
TE 298.1 K  
D1 2.0000000 sec  
D11 0.0300000 sec  
TD0 1  
SFO1 162.0241700 MHz  
NUC1 31P  
PO 4.94 usec  
P1 14.82 usec  
PLW1 14.0000000 W  
SFO2 400.2516010 MHz  
NUC2 1H  
CPDPRG2 waltz16  
PCPD2 80.00 usec  
PLW2 10.71500015 W  
PLW12 0.35200000 W  
PLW13 0.22528000 W

F2 - Processing parameters  
SI 32768  
SF 162.0241699 MHz  
WDW EM  
SSB 0  
LB 3.00 Hz  
GB 0  
PC 1.40

Figure S25.  $^{31}\text{P}$  NMR of **10** in  $\text{CDCl}_3$ .



Current Data Parameters  
NAME AS-DMT-1Bu-FdG phosph  
EXPNO 4  
PROCNO 1

F2 - Acquisition Parameters  
Date\_ 20190321  
Time 20:04 h  
INSTRUM spect  
PROBHD z108618\_0716 ( )  
PULPROG zgpg30  
TD 131072  
SOLVENT CDCl3  
NS 16  
DS 4  
SWH 89285.711 Hz  
FIDRES 1.362392 Hz  
AQ 0.7340032 sec  
RG 210.82  
DW 5.600 usec  
DE 6.50 usec  
TE 298.3 K  
D1 1.0000000 sec  
D11 0.0300000 sec  
TD0 1  
SFO1 376.5736179 MHz  
NUC1 19F  
PO 5.00 usec  
P1 15.00 usec  
PLW1 19.0000000 W  
SFO2 400.2516010 MHz  
NUC2 1H  
CPDPRG2 waltz65  
PCPD2 80.00 usec  
PLW2 10.71500015 W  
PLW12 0.35200000 W  
PLW13 0.22528000 W

F2 - Processing parameters  
SI 85536  
SF 376.6112790 MHz  
WDW EM  
SSB 0  
LB 0.30 Hz  
GB 0  
PC 1.00

Figure S26.  $^{19}\text{F}$  NMR of **10** in  $\text{CDCl}_3$ .

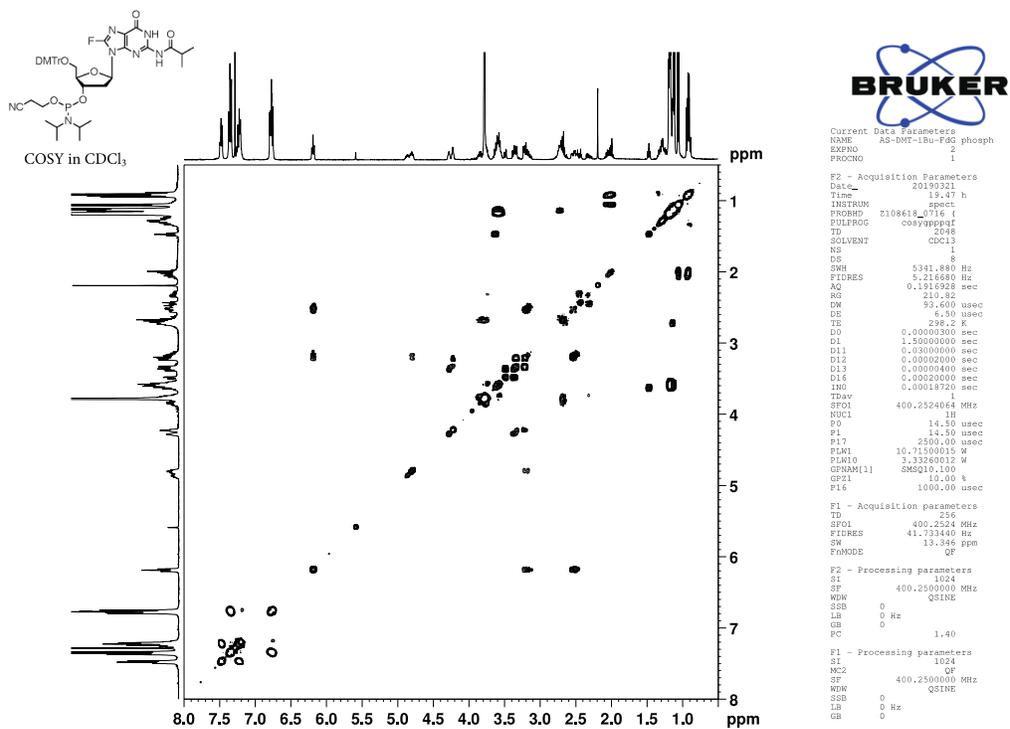


Figure S27. COSY NMR of **10** in CDCl<sub>3</sub>.

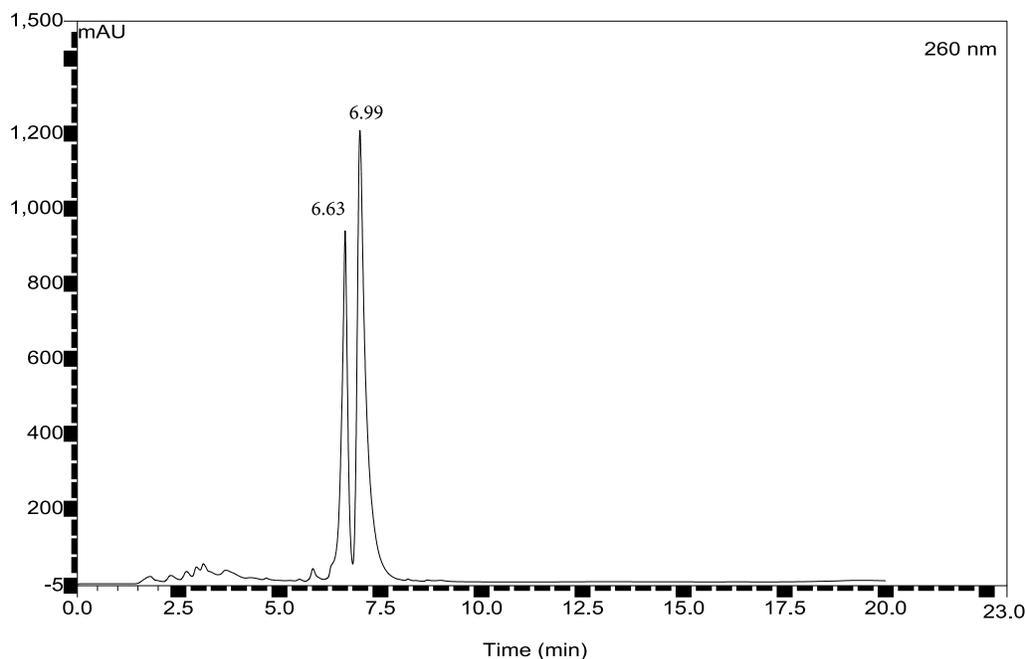
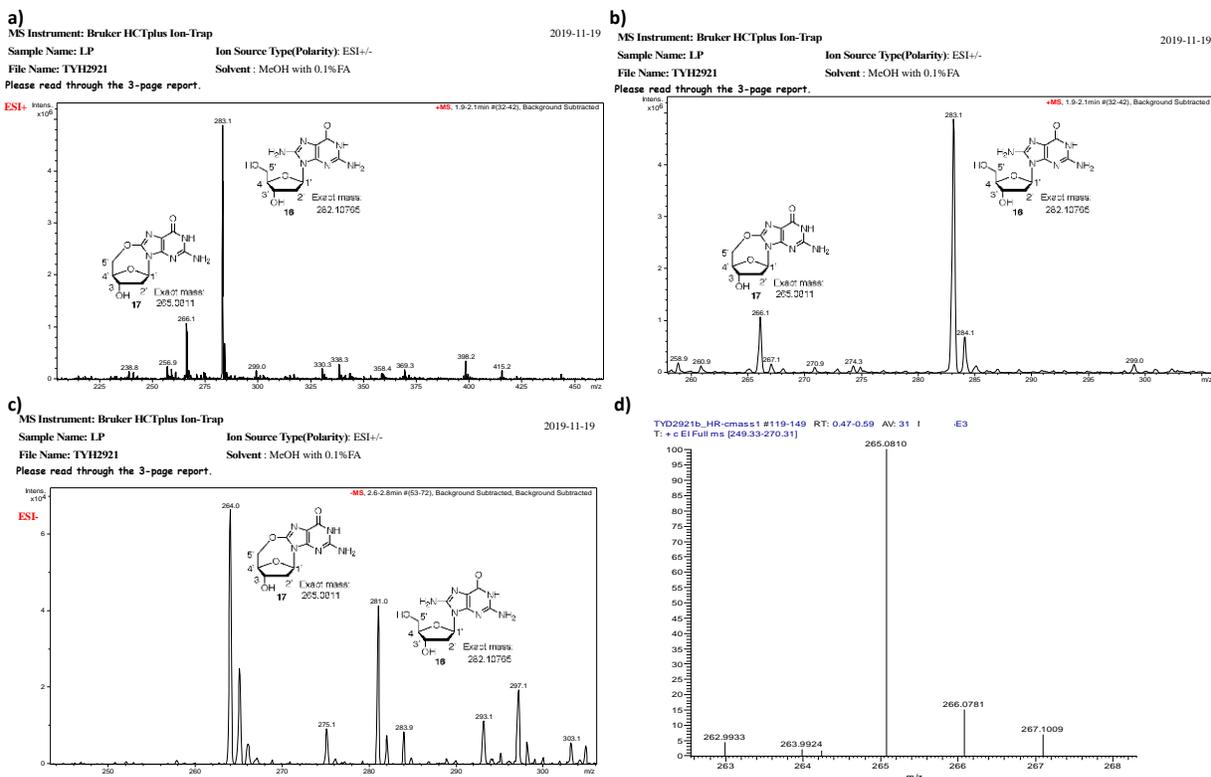
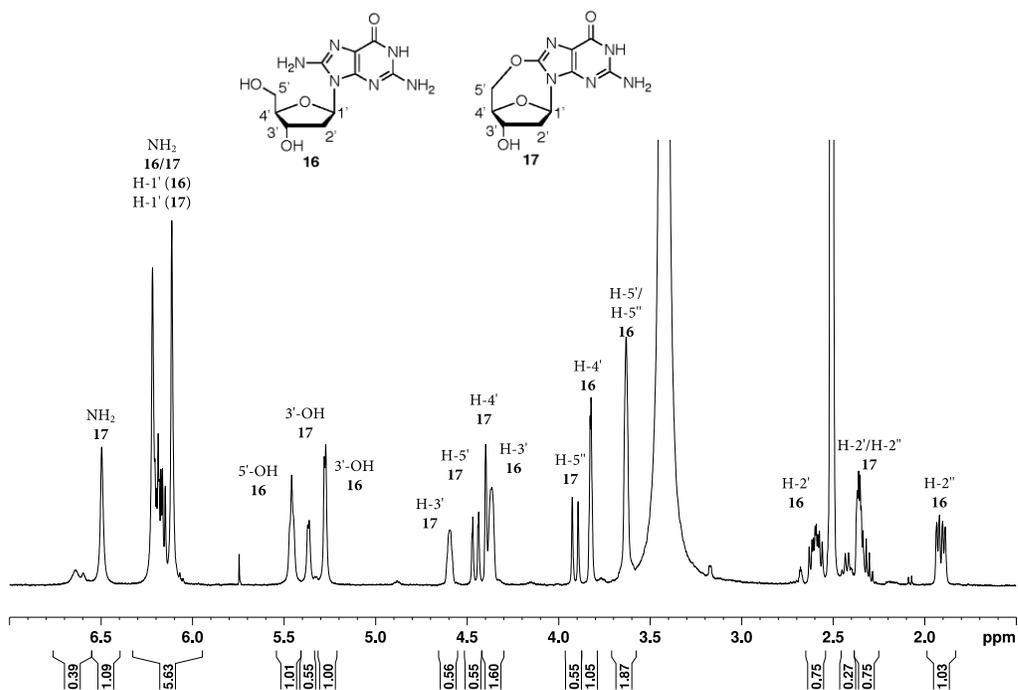


Figure S28. HPLC profile of the product where compound **4** was treated with concentrated aqueous ammonium hydroxide at 55°C overnight (as described in Scheme 3). The mixture was eluted off a Dionex Polar Advantage-2 C18 reverse phase column (4.6×150 mm) with a linear gradient of water–acetonitrile (100:0 to 60:40, v/v over 10 min) at 0.7 ml/min.

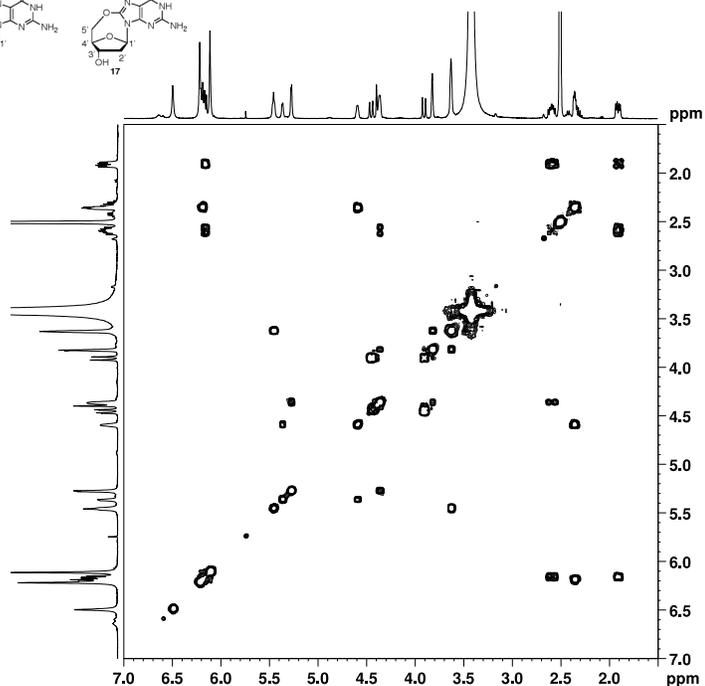
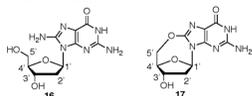


**Figure S29.** Mass spectra of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at 55°C overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. a). Electrospray detected for positive ions (1.9-2.1min, background Subtracted); b). zoomed-in portion, electrospray detected for positive ions. (1.9-2.1min, background Subtracted); c). electrospray detected for negative ions (2.6-2.8 min, background Subtracted); d). high-res analysis on m/z 265.



**Figure S30.**  $^1\text{H}$  NMR of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at  $55^\circ\text{C}$  overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. The spectrum was recorded in DMSO- $d_6$  at 400.2 MHz.

COSY in DMSO-d<sub>6</sub>



```

Current Data Parameters
NAME      AS-FDG-Less Polar
EXPNO    1
PROCNO   1

F2 - Acquisition Parameters
Date_    20191115
Time     11.53 h
INSTRUM  spect
PROBHD   2108618_0716 (
PULPROG  cosygpppg4f
TD       2048
SOLVENT  DMSO
NS       8
DS       8
SWH      5341.880 Hz
FIDRES   9.215680 Hz
AQ       0.1916928 sec
RG       145.6
DW       93.600 usec
DE       6.50 usec
TE       298.2 K
D0       0.0000000 sec
D1       1.5000000 sec
D11      0.0300000 sec
D12      0.0002000 sec
D13      0.0000400 sec
D16      0.0002000 sec
IN0      0.0001872 sec
TDav     400.2524064 MHz
NUC1     1H
P0       14.50 usec
P1       14.50 usec
P17      2500.00 usec
PLW1     10.7130015 W
PLW10    3.33260012 W
CPDPRG1  sngp01_100
GP21     10.00 s
P16      1000.00 usec

F1 - Acquisition parameters
TD       2048
SFO1     400.2524 MHz
FIDRES   41.733440 Hz
SWH      13.346 ppm
F0MODE   QF

F2 - Processing parameters
SI       1024
SF       400.2500000 MHz
WDW      QSI
SSB      0
LB       0 Hz
GB       0
PC       1.00

F1 - Processing parameters
SI       1024
SF       400.2500000 MHz
WDW      QSI
SSB      0
LB       0 Hz
GB       0
  
```

**Figure S31.** COSY NMR of products from the treatment of compound **4** with concentrated aqueous ammonium hydroxide at 55°C overnight. After the reaction mixture was cooled, it was lyophilized and purified by preparative C18-reverse phase column chromatography. The spectrum was recorded in DMSO-d<sub>6</sub> at 400.2 MHz.