

Supporting Information for:

**Synthesis and evaluation of protein arginine
N-methyltransferase inhibitors designed to simultaneously occupy both substrate
binding sites**

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Utrecht Institute for Pharmaceutical Sciences, Utrecht University,
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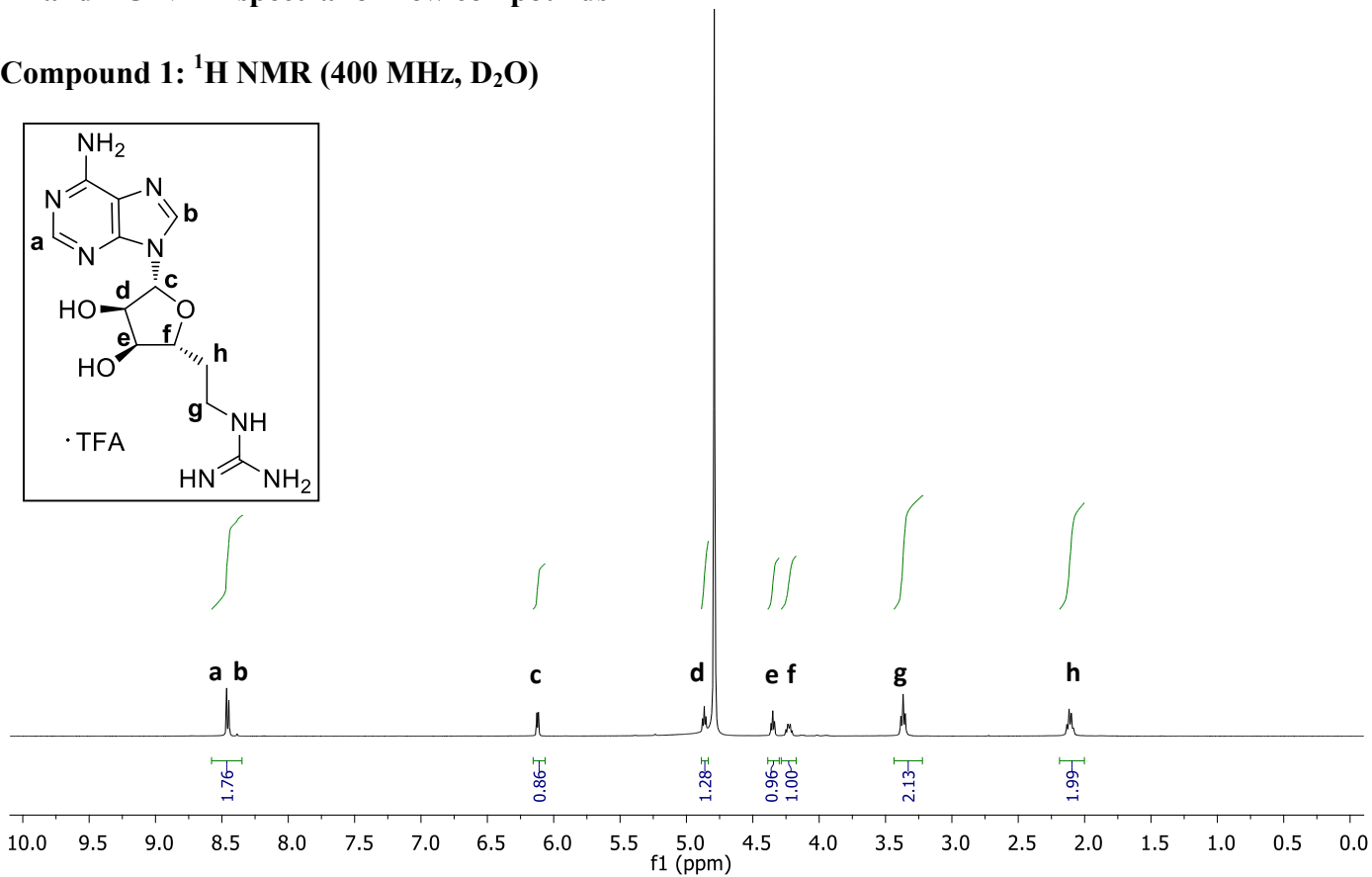
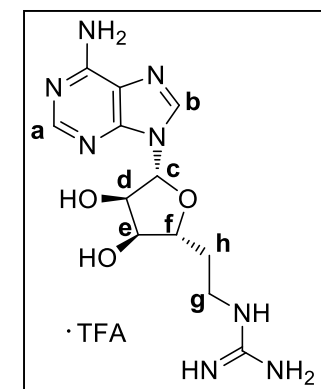
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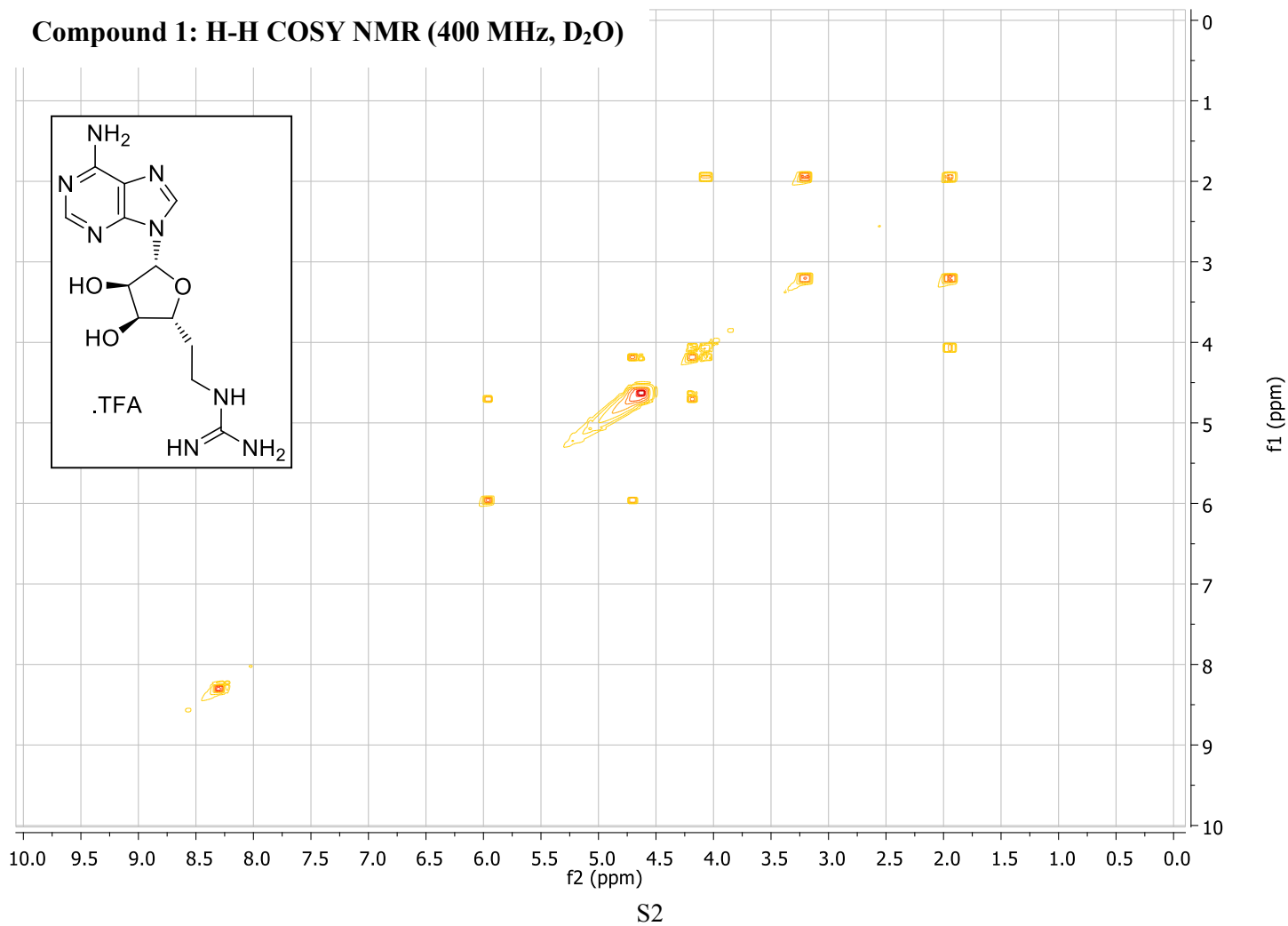
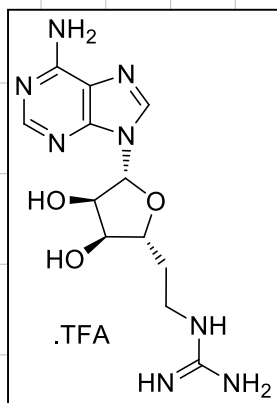
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S22-24	Analytical RP-HPLC traces for compounds 1-6
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^1H and ^{13}C NMR spectra for new compounds

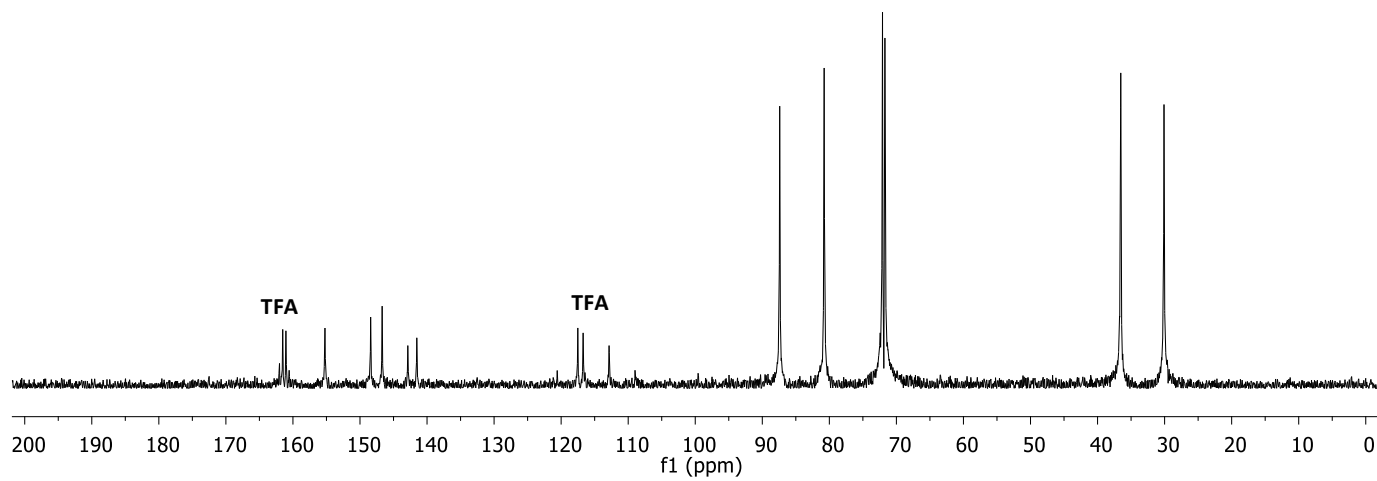
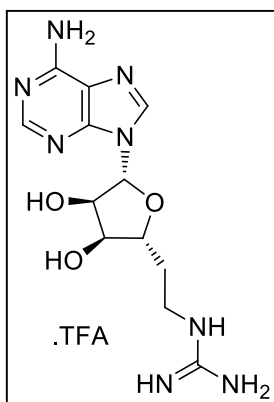
Compound 1: ^1H NMR (400 MHz, D_2O)



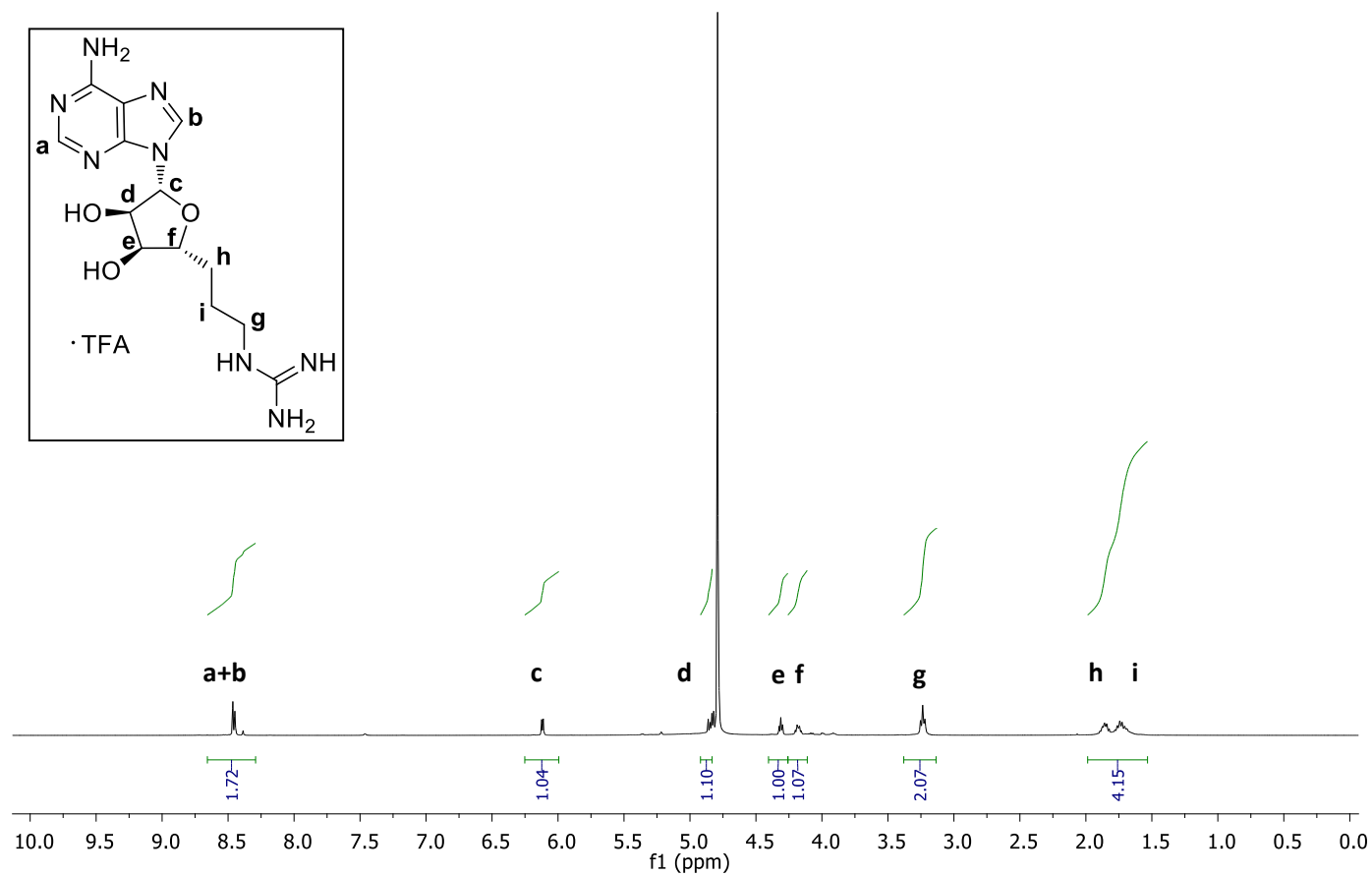
Compound 1: H-H COSY NMR (400 MHz, D_2O)



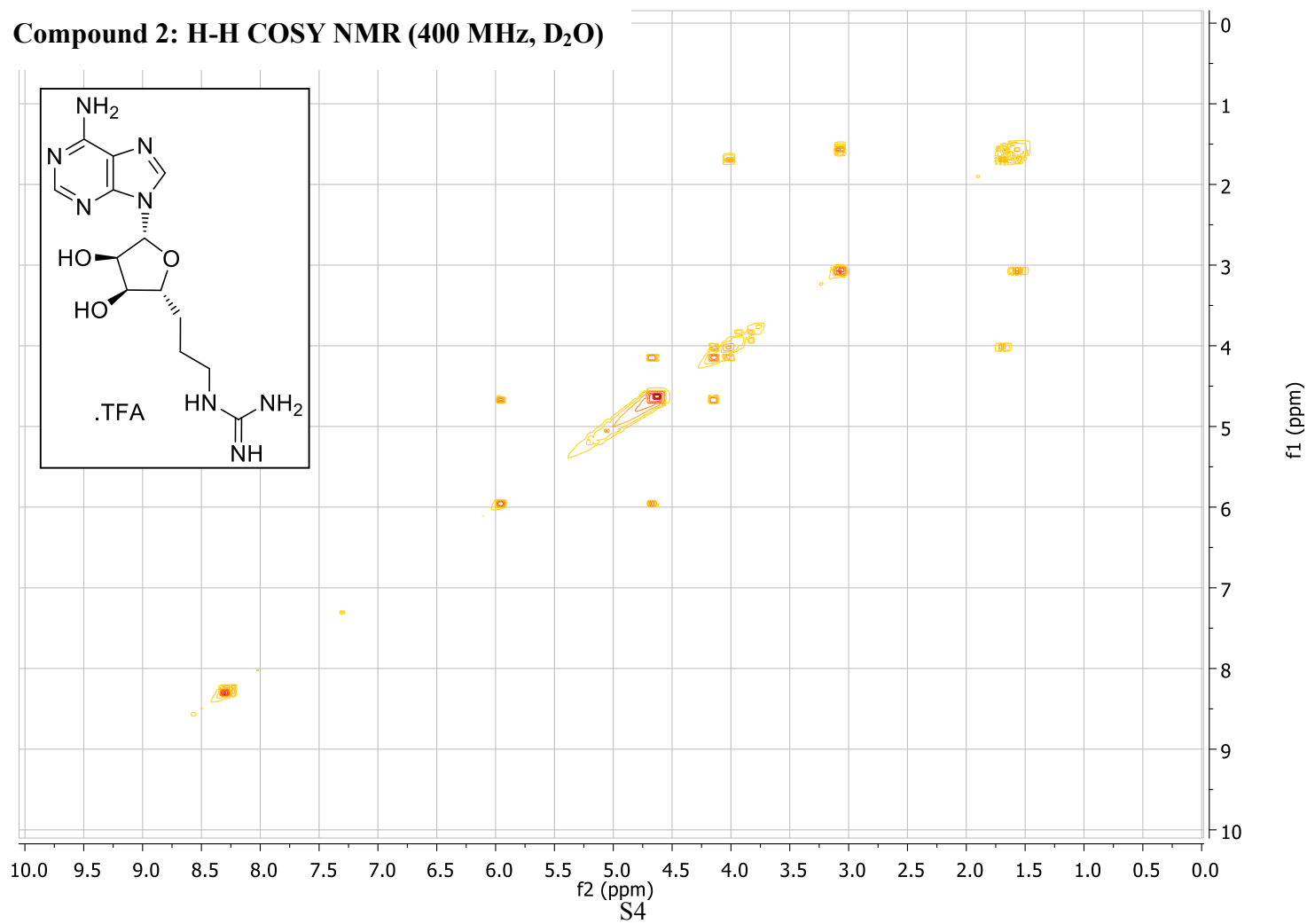
Compound 1: ^{13}C NMR (75 MHz, D_2O)



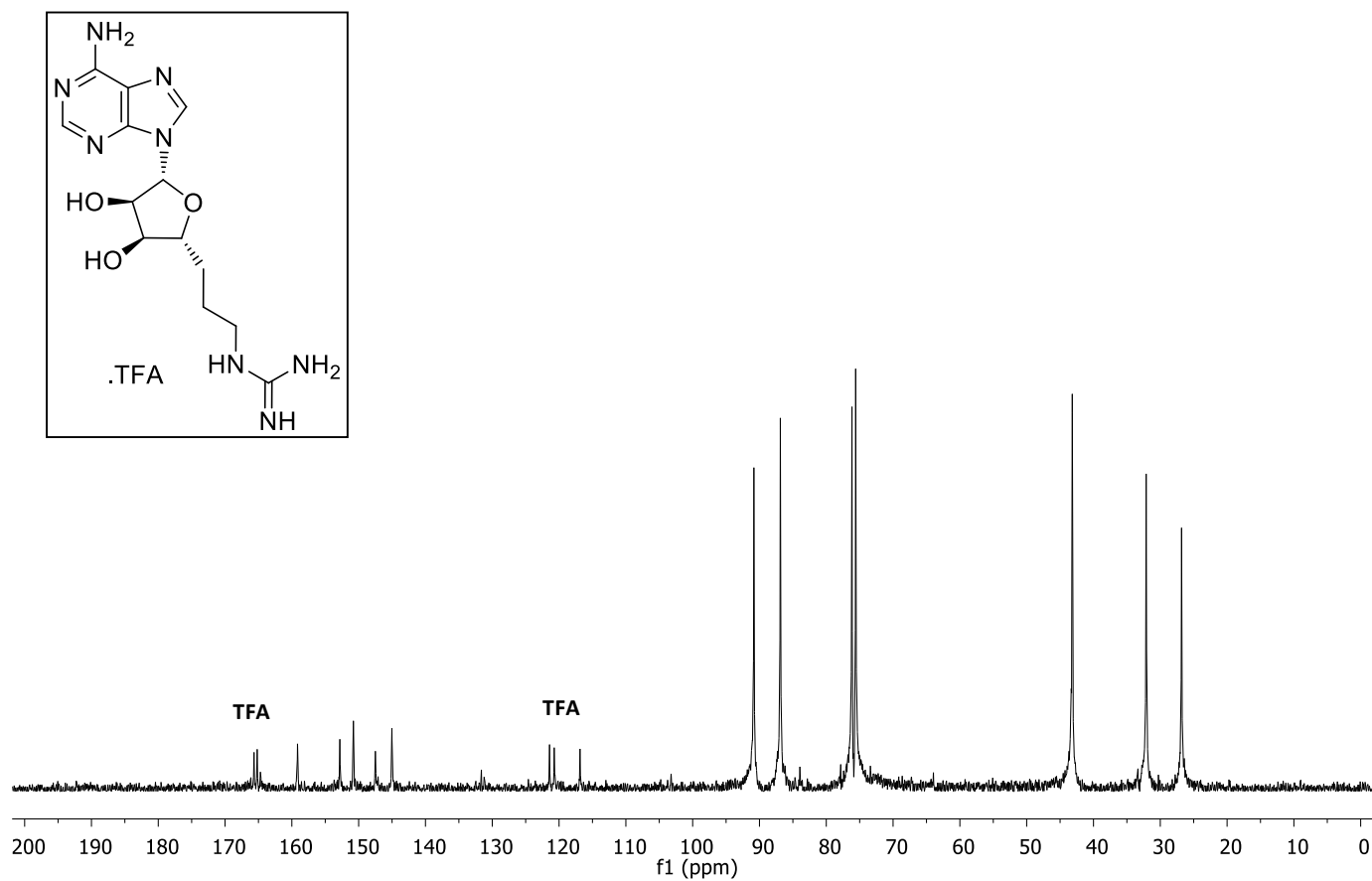
Compound 2: ^1H NMR (400 MHz, D_2O)



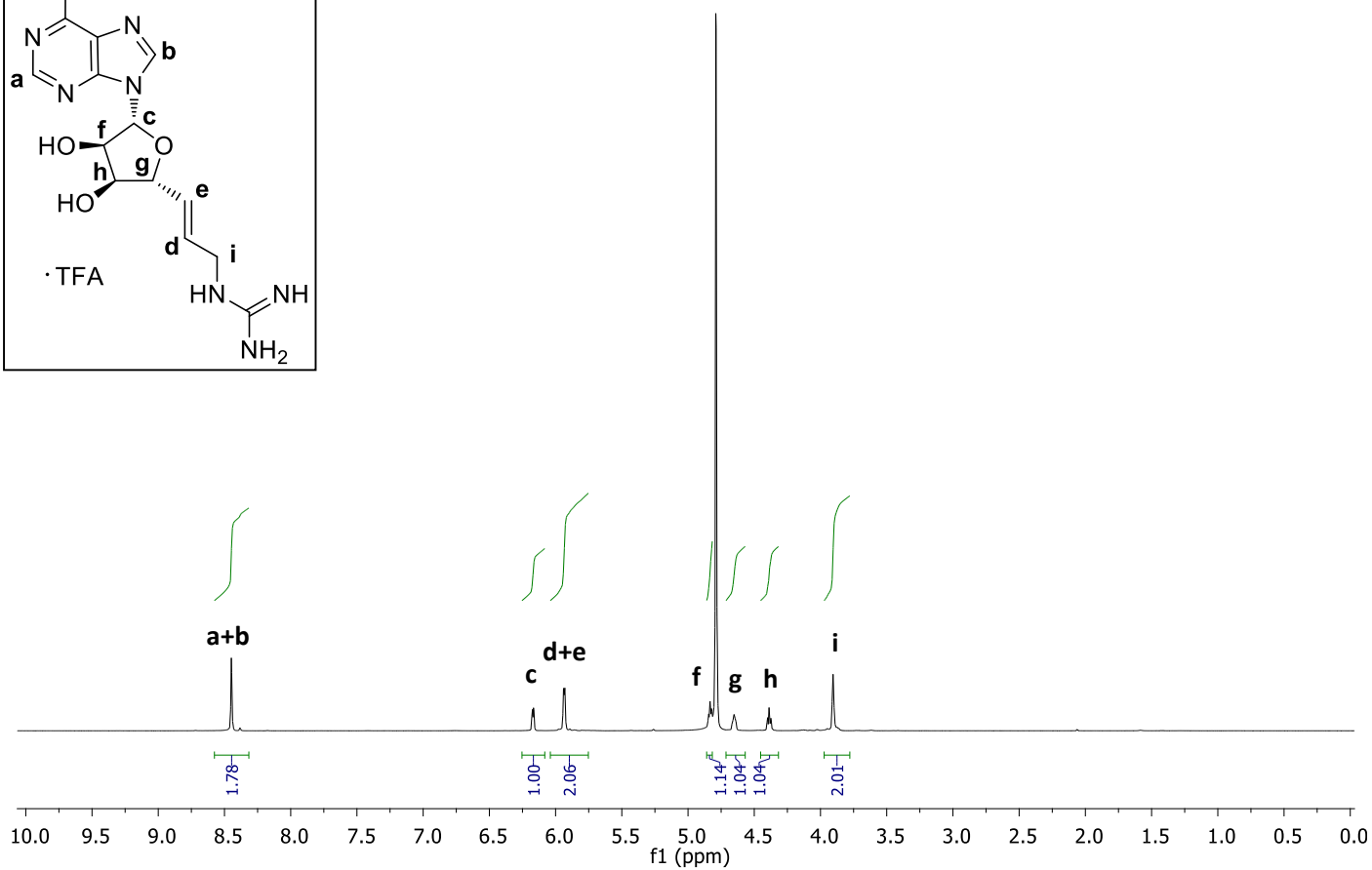
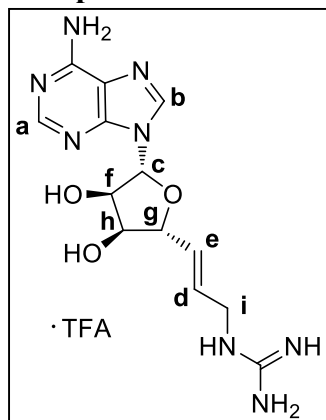
Compound 2: H-H COSY NMR (400 MHz, D_2O)



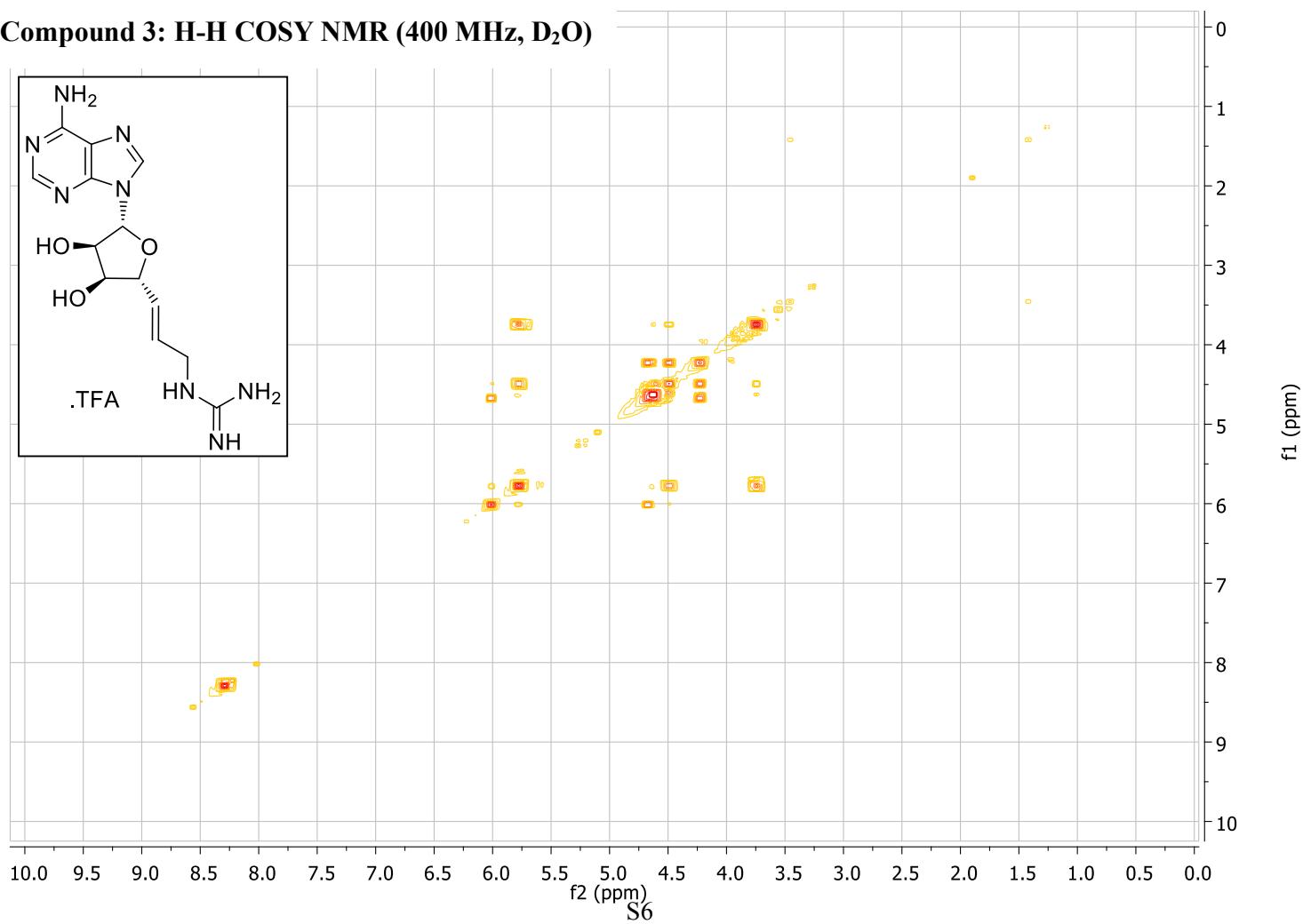
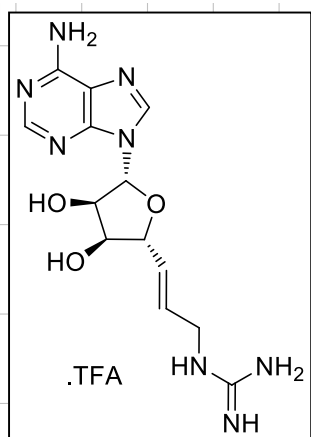
Compound 2: ^{13}C NMR (75 MHz, D_2O)



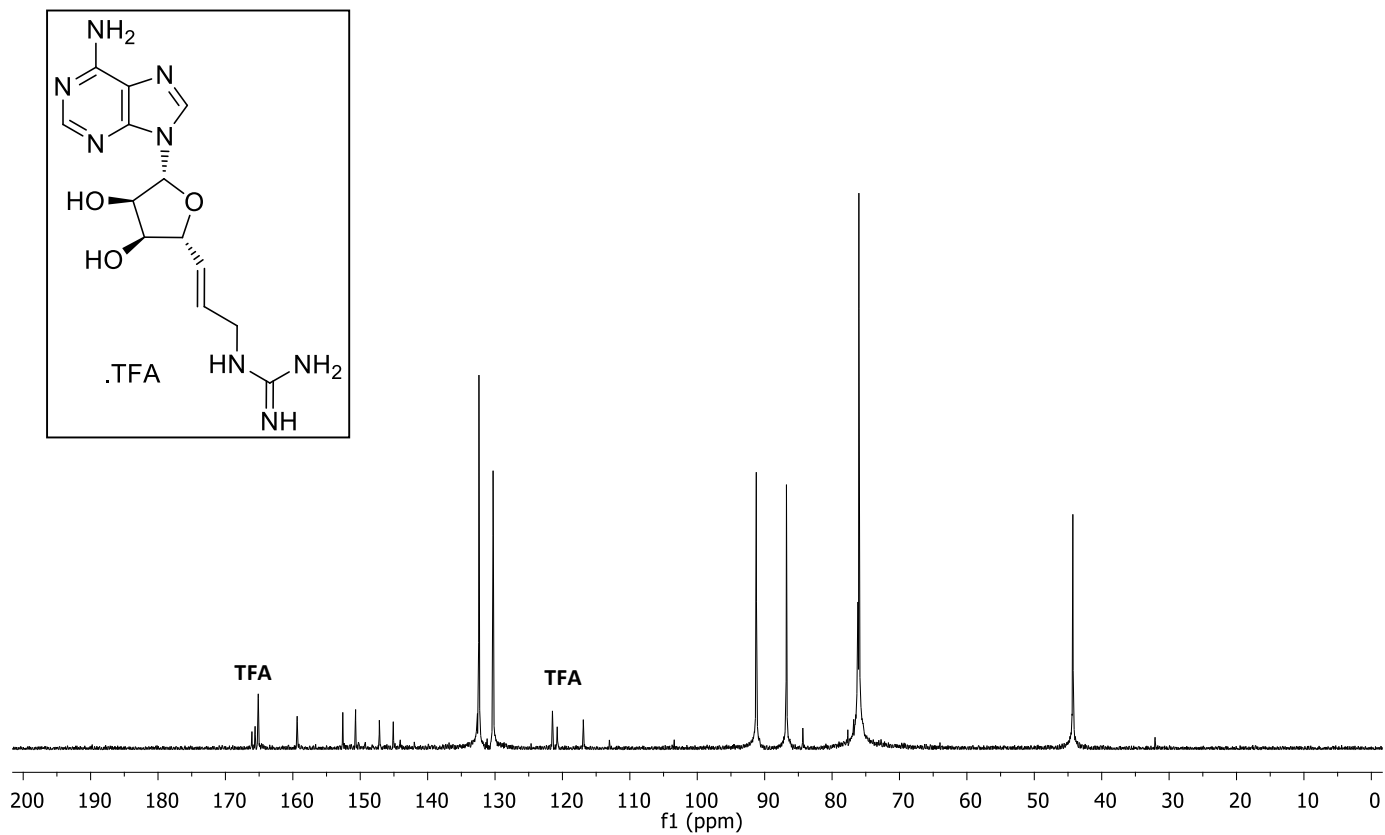
Compound 3: ^1H NMR (400 MHz, D_2O)



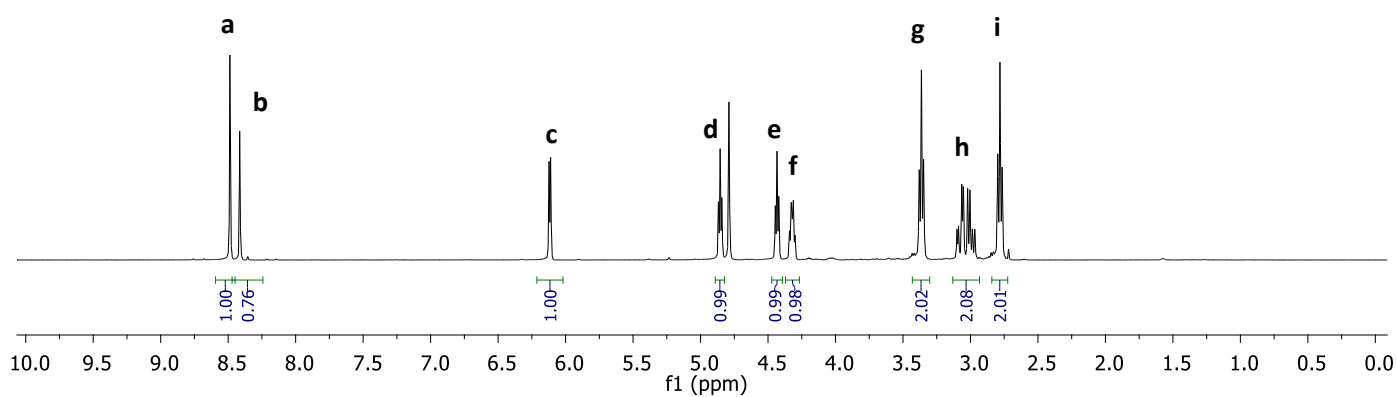
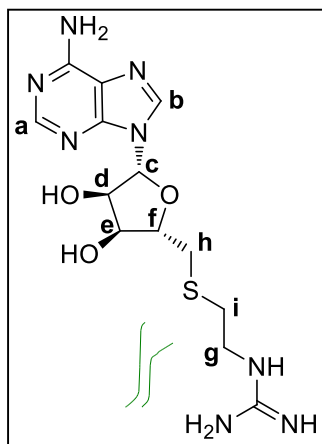
Compound 3: H-H COSY NMR (400 MHz, D_2O)



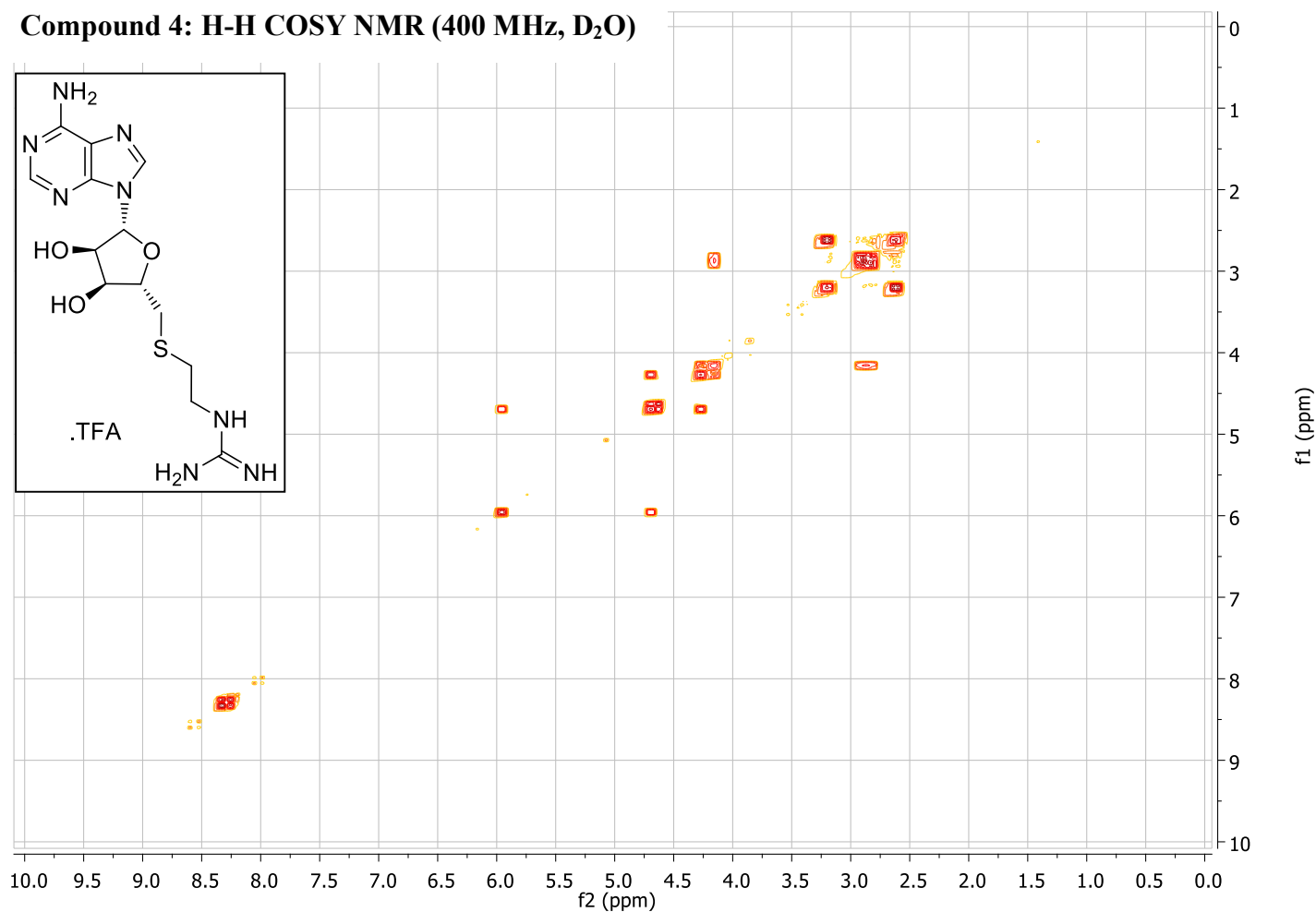
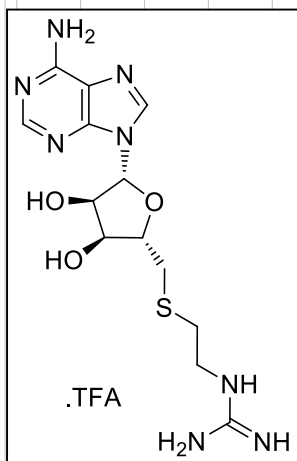
Compound 3: ^{13}C NMR (75 MHz, D_2O)



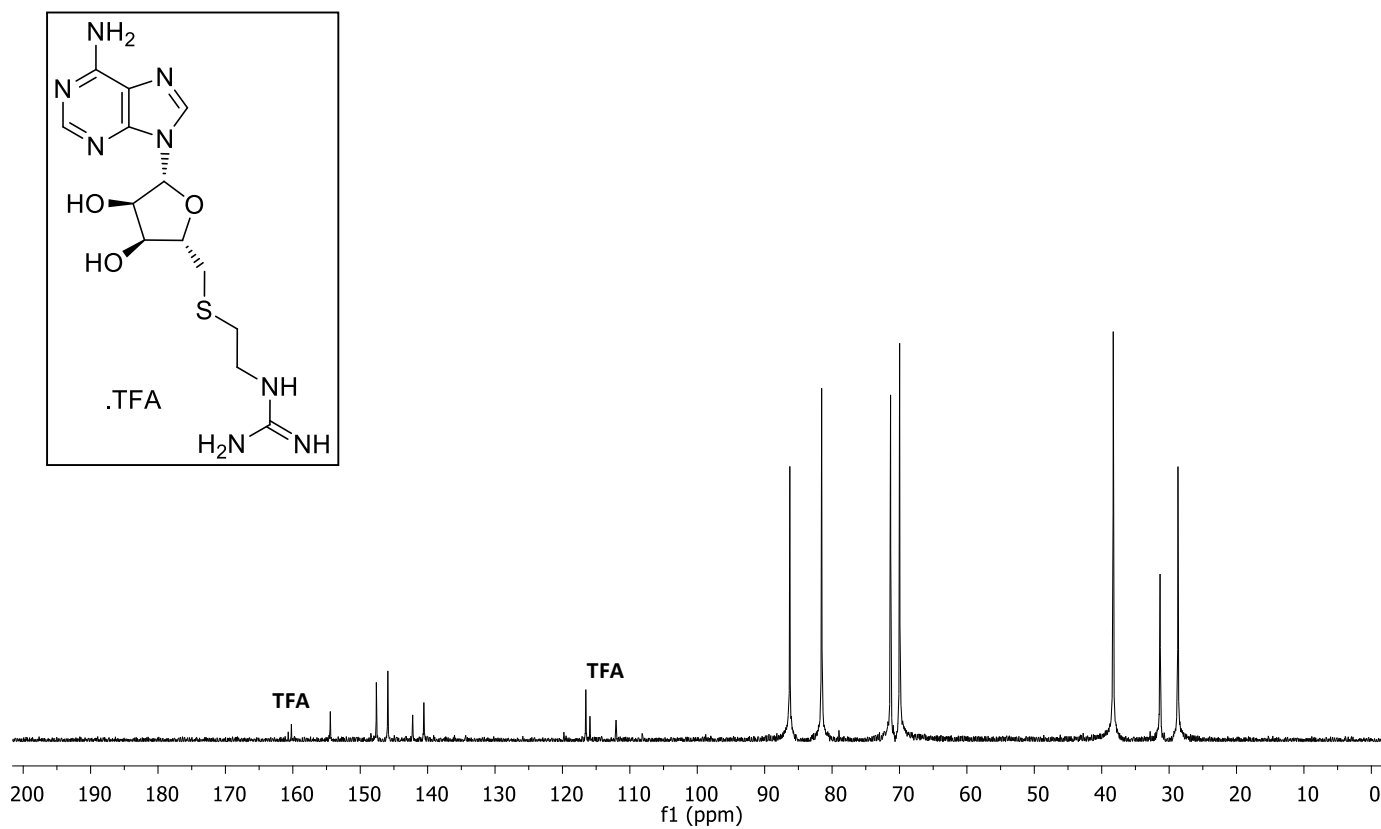
Compound 4: ^1H NMR (400 MHz, D_2O)



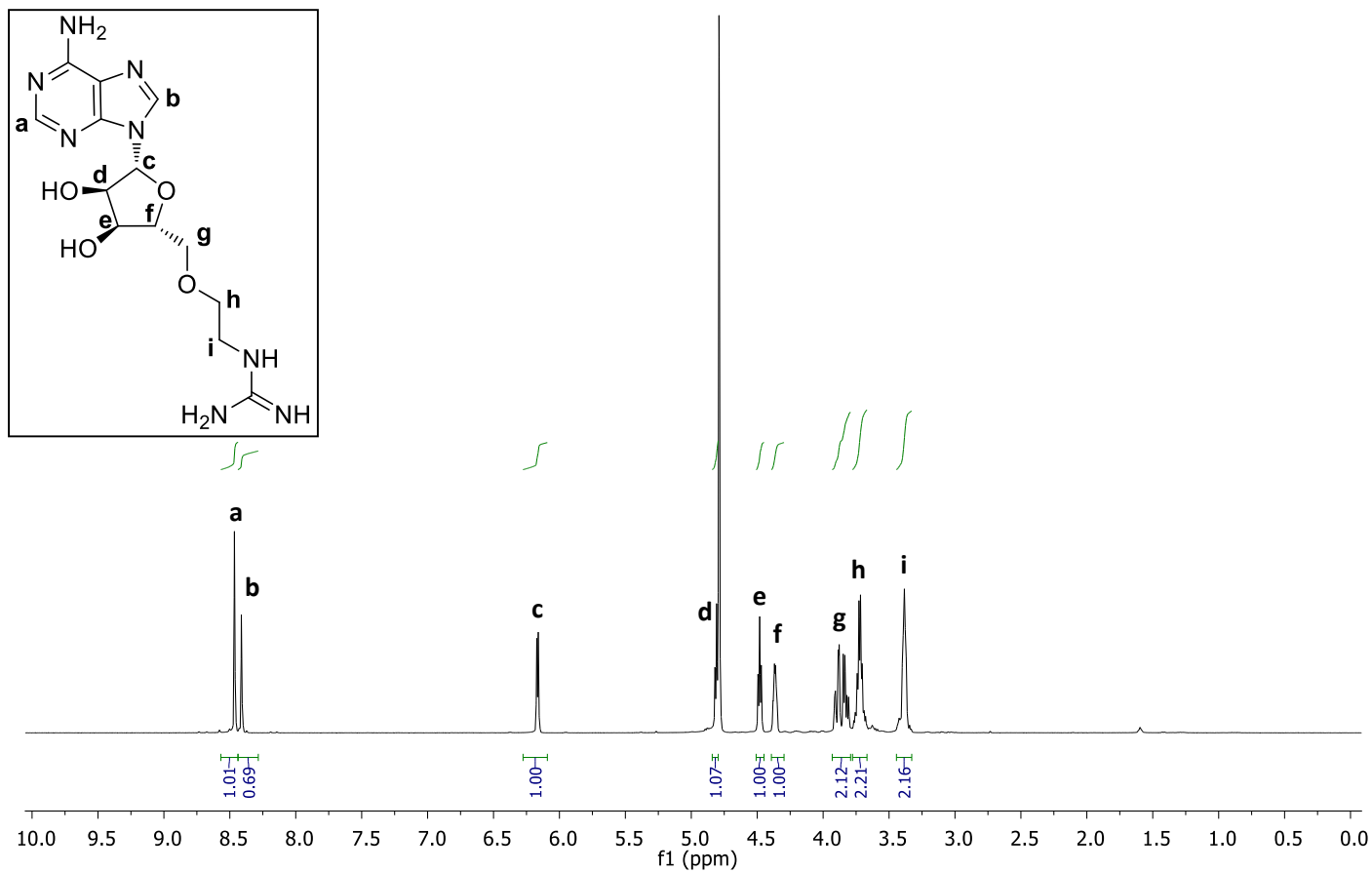
Compound 4: H-H COSY NMR (400 MHz, D_2O)



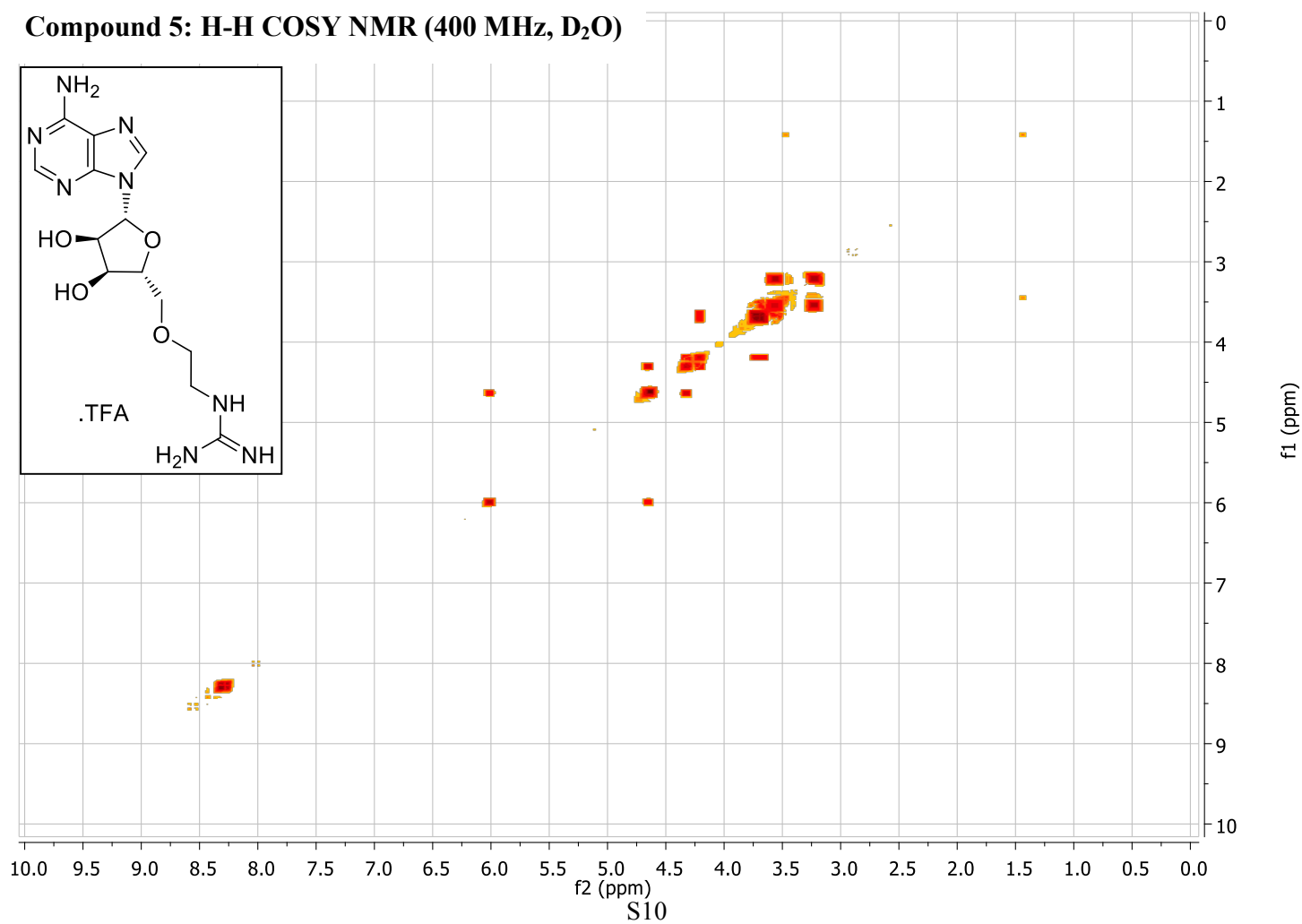
Compound 4: ^{13}C NMR (75 MHz, D_2O)



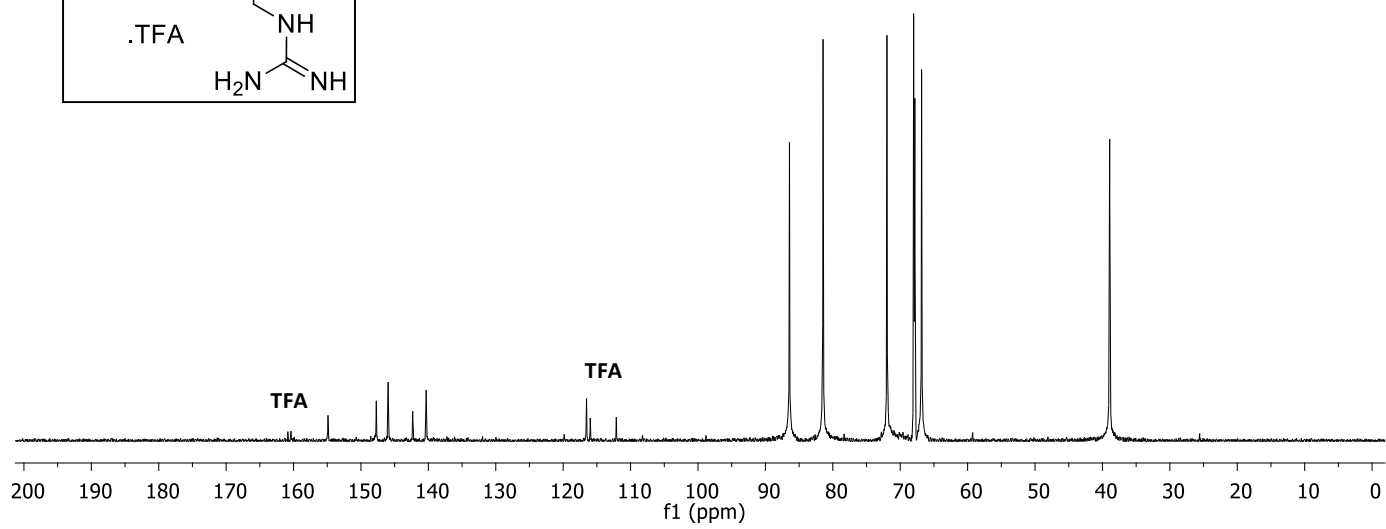
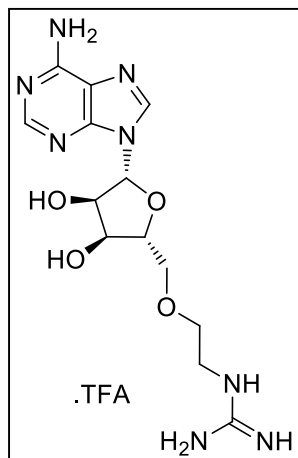
Compound 5: ^1H NMR (400 MHz, D_2O)



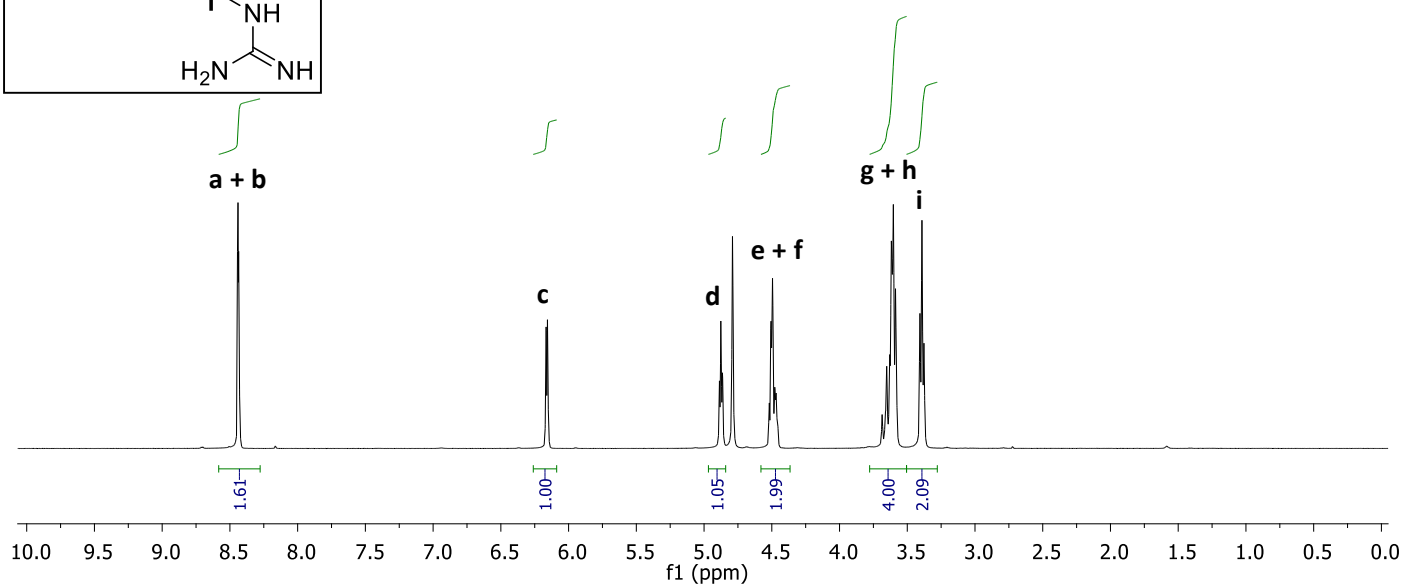
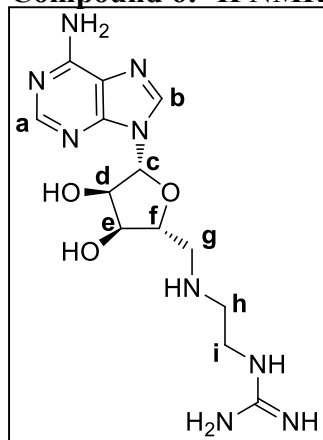
Compound 5: H-H COSY NMR (400 MHz, D_2O)



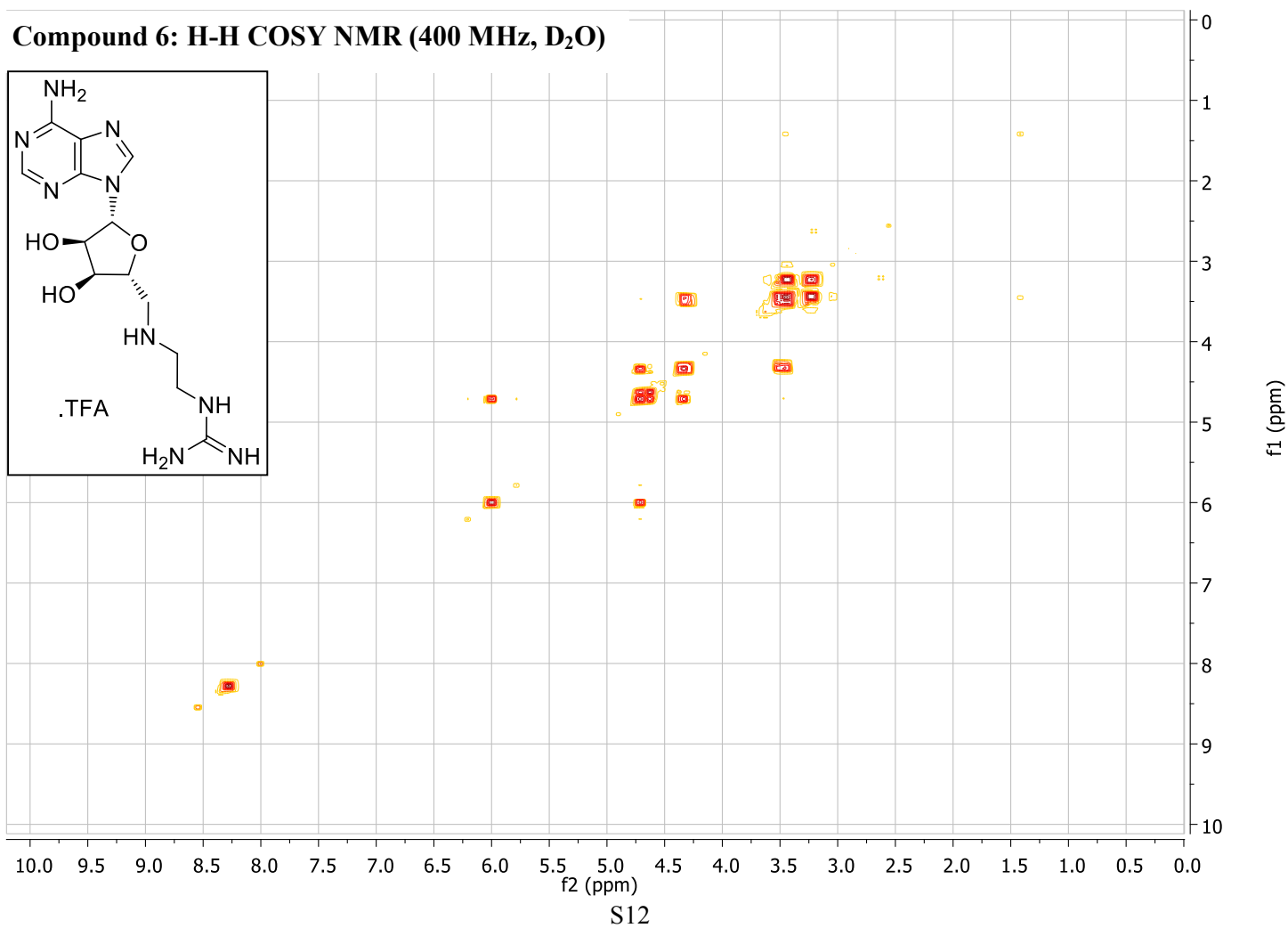
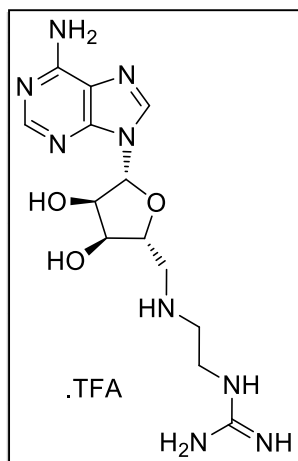
Compound 5: ^{13}C NMR (75 MHz, D_2O)



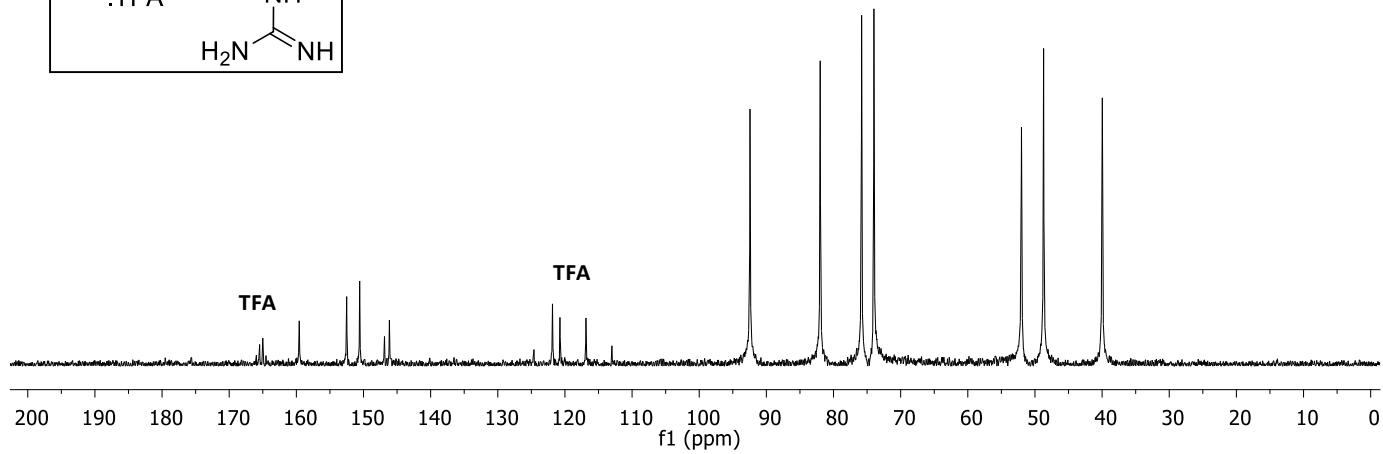
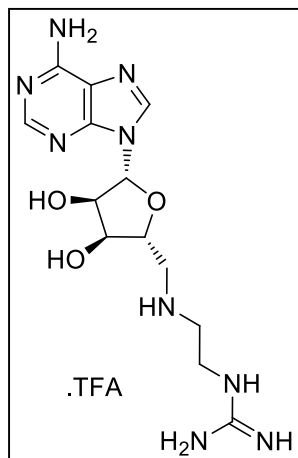
Compound 6: ^1H NMR (400 MHz, D_2O)



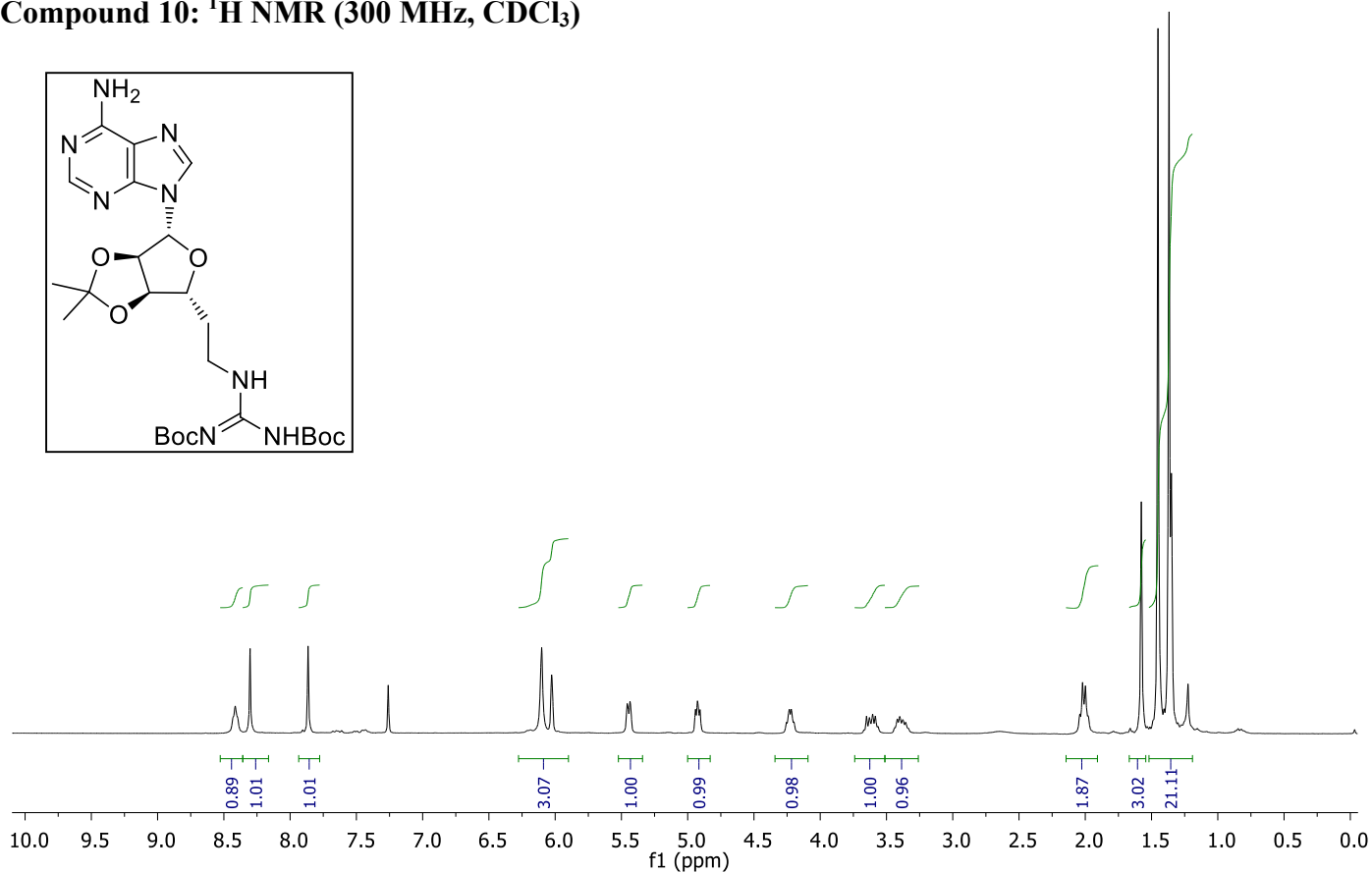
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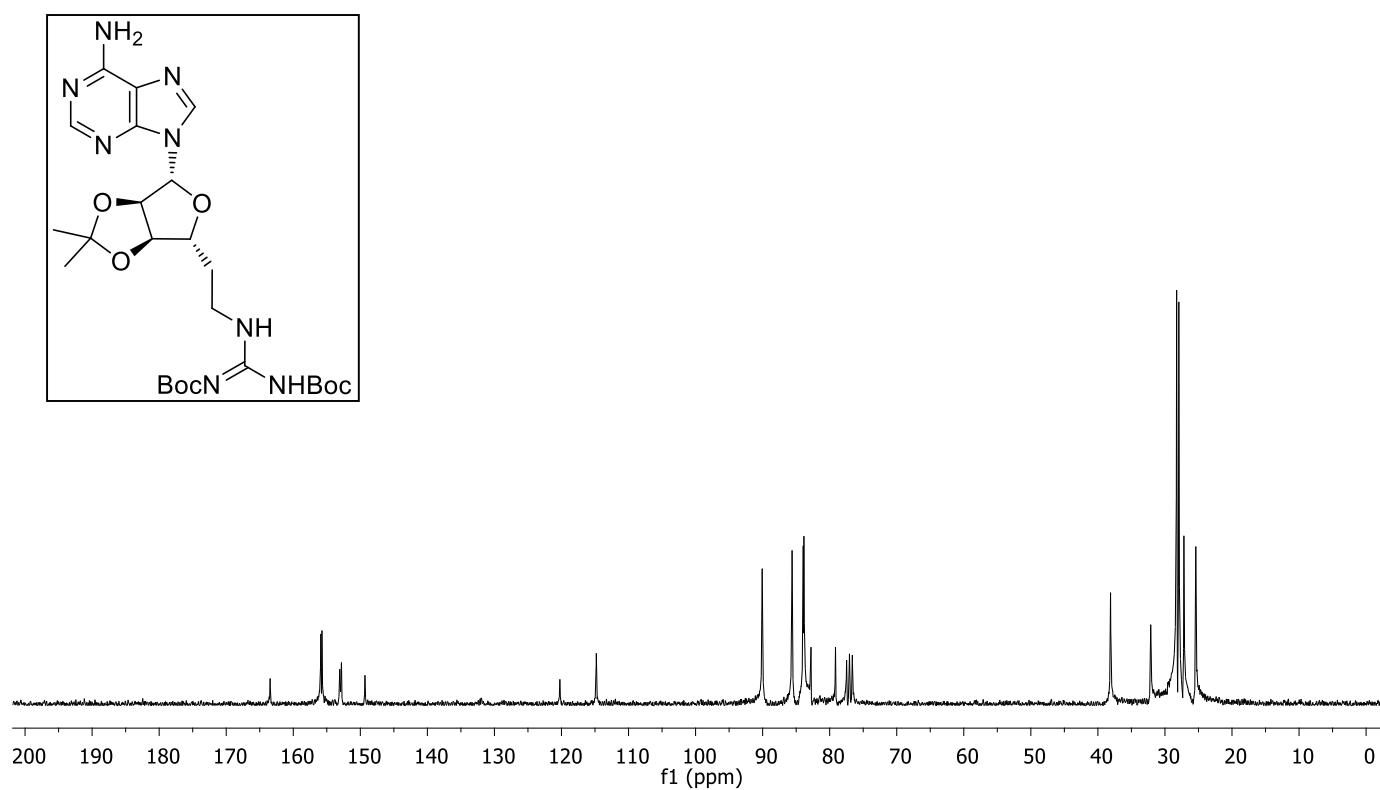
Compound 6: ^{13}C NMR (75 MHz, D_2O)



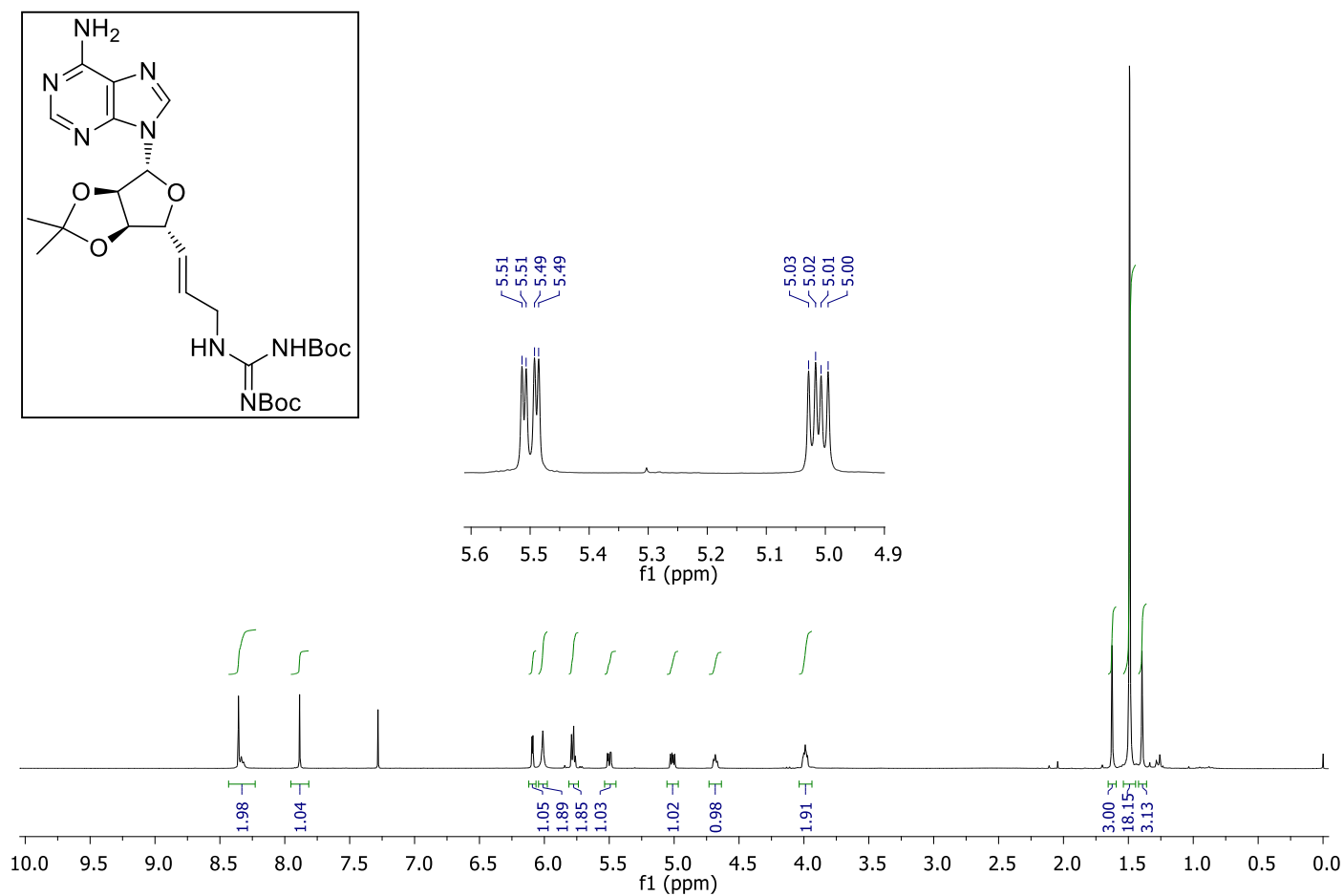
Compound 10: ^1H NMR (300 MHz, CDCl_3)



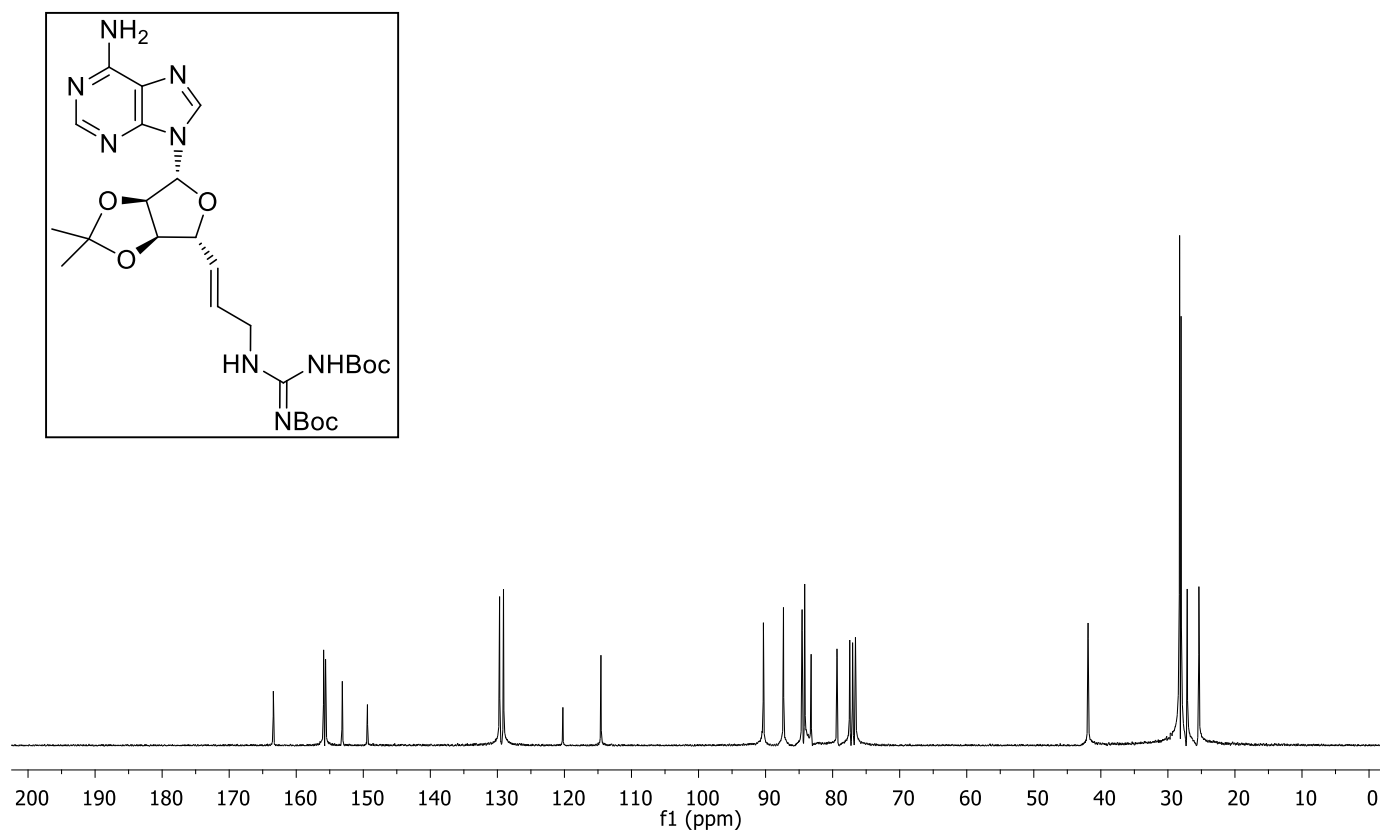
Compound 10: ^{13}C NMR (75 MHz, CDCl_3)



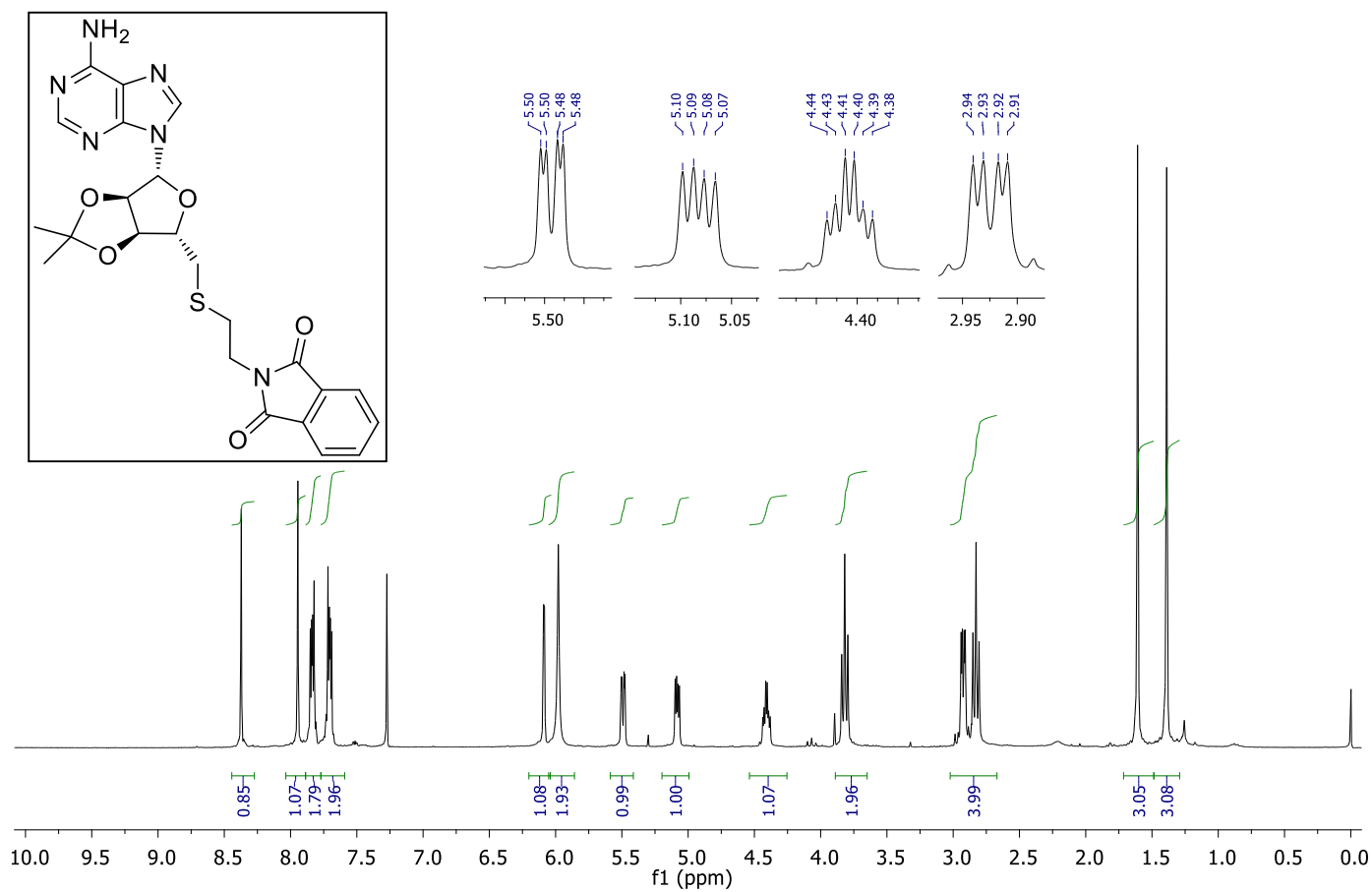
Compound 15: ^1H NMR (300 MHz, CDCl_3)



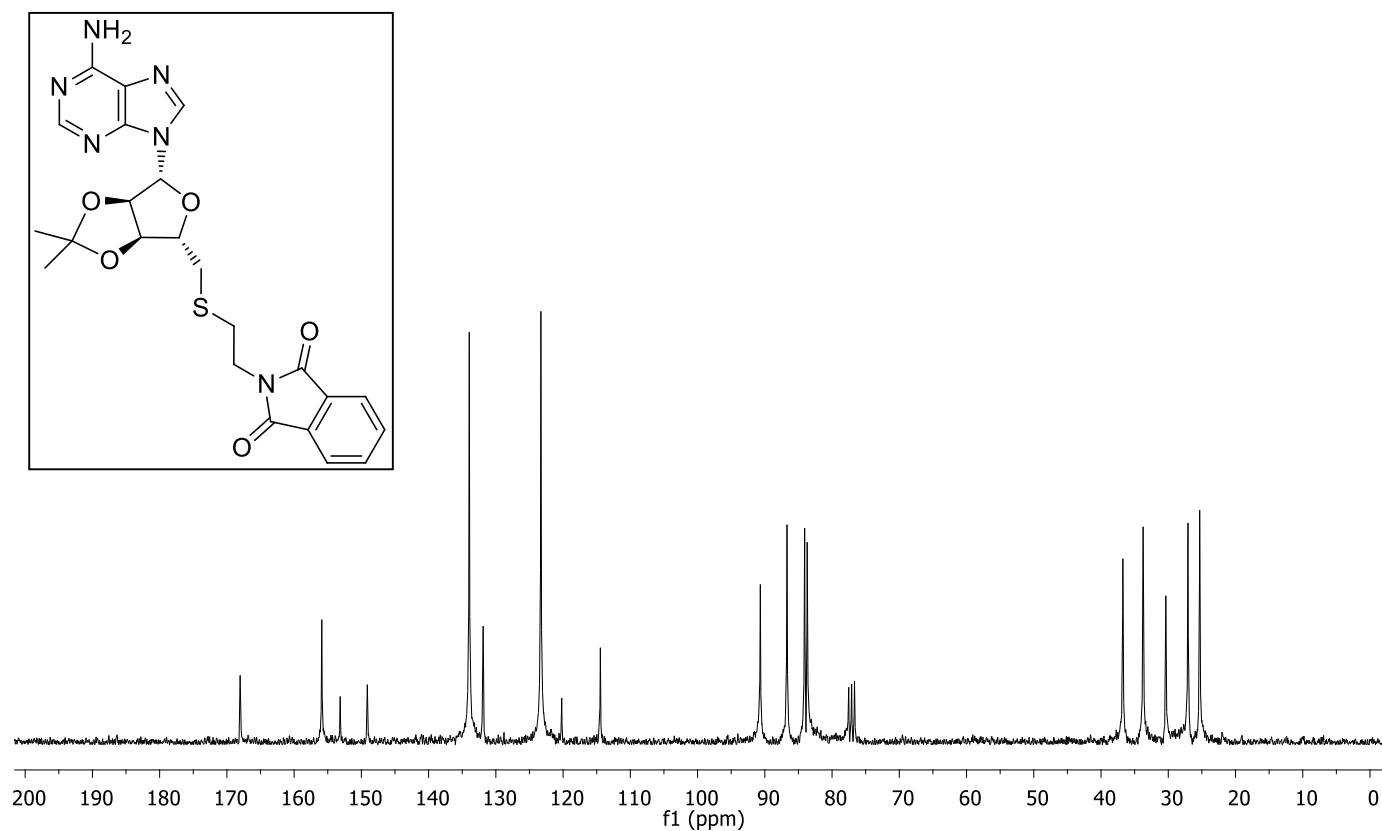
Compound 15: ^{13}C NMR (75 MHz, CDCl_3)



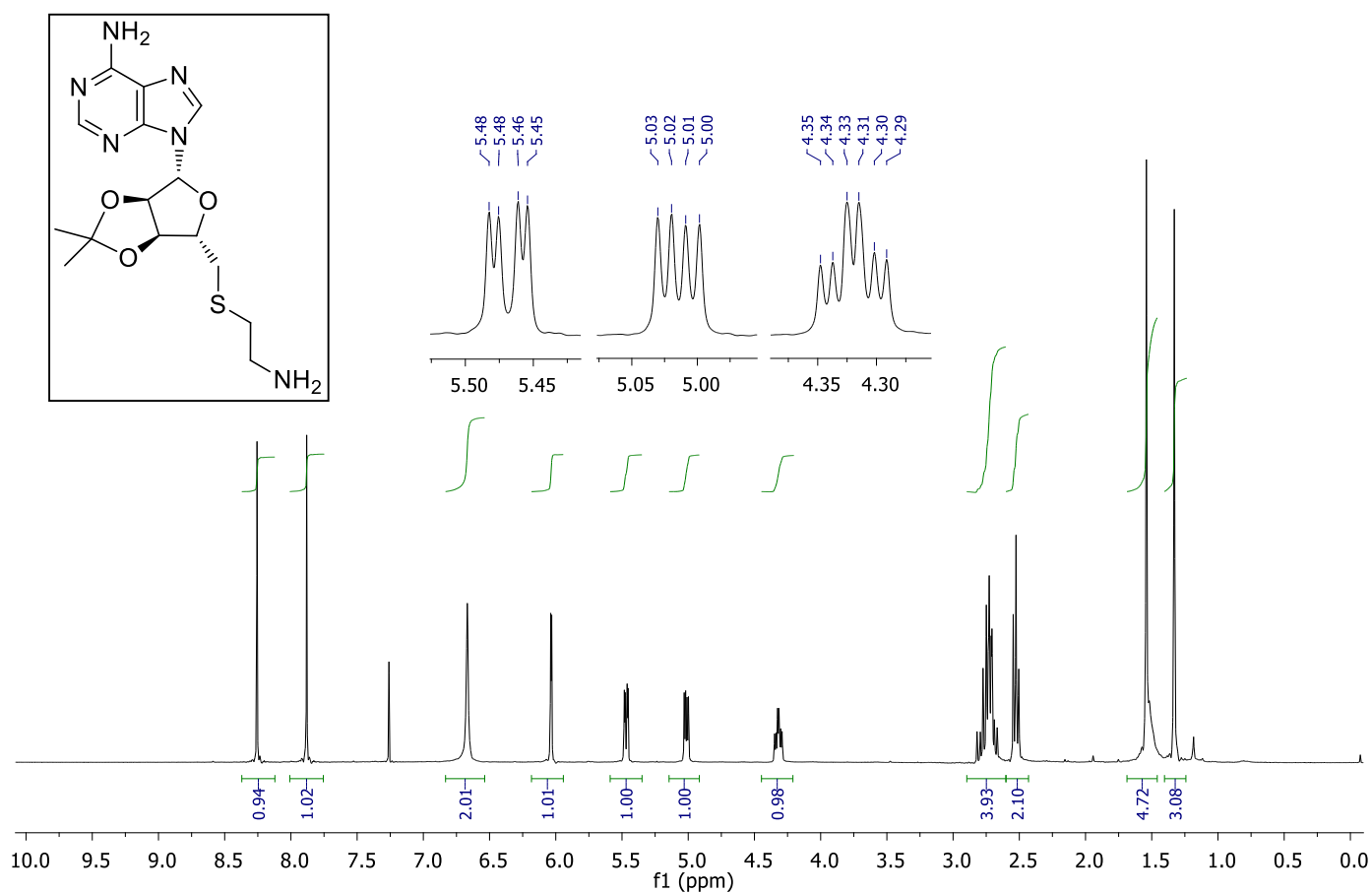
Compound 17: ^1H NMR (300 MHz, CDCl_3)



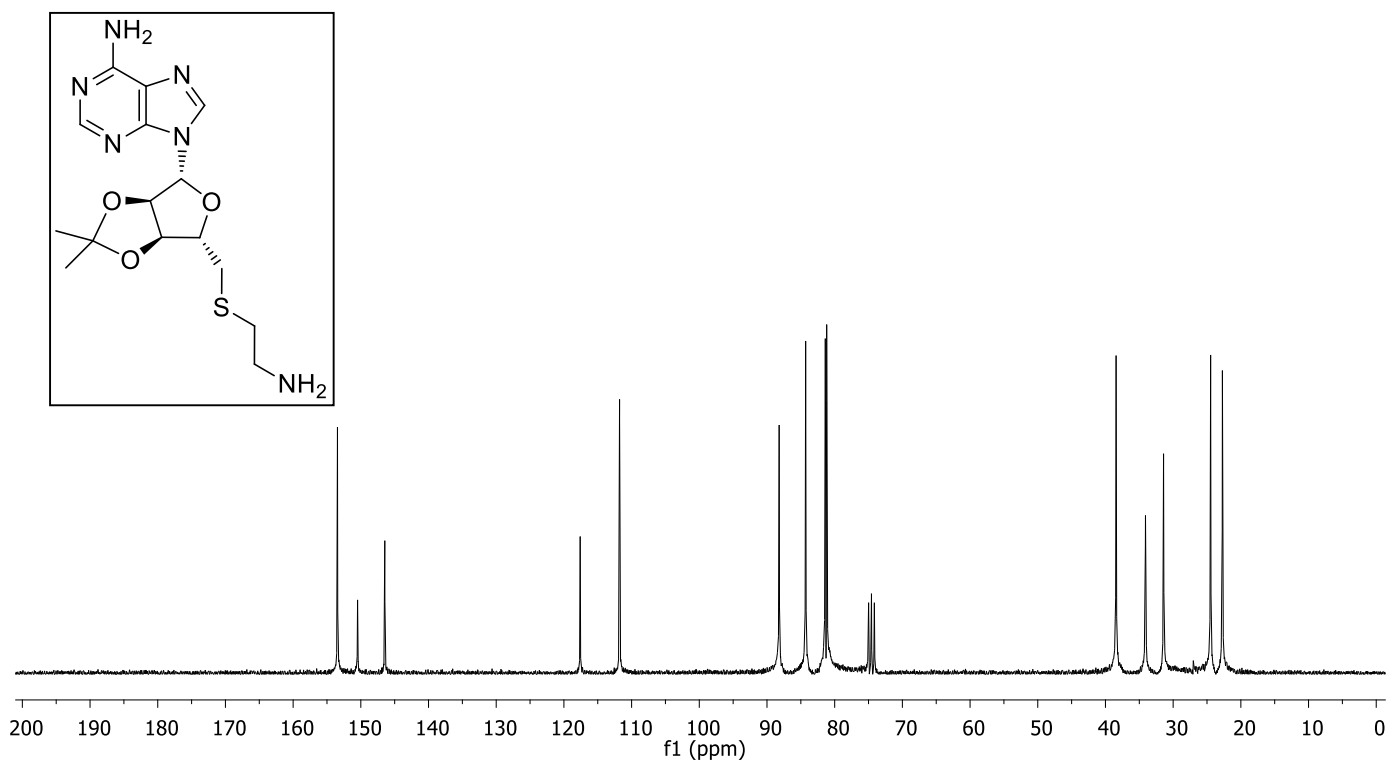
Compound 17: ^{13}C NMR (75 MHz, CDCl_3)



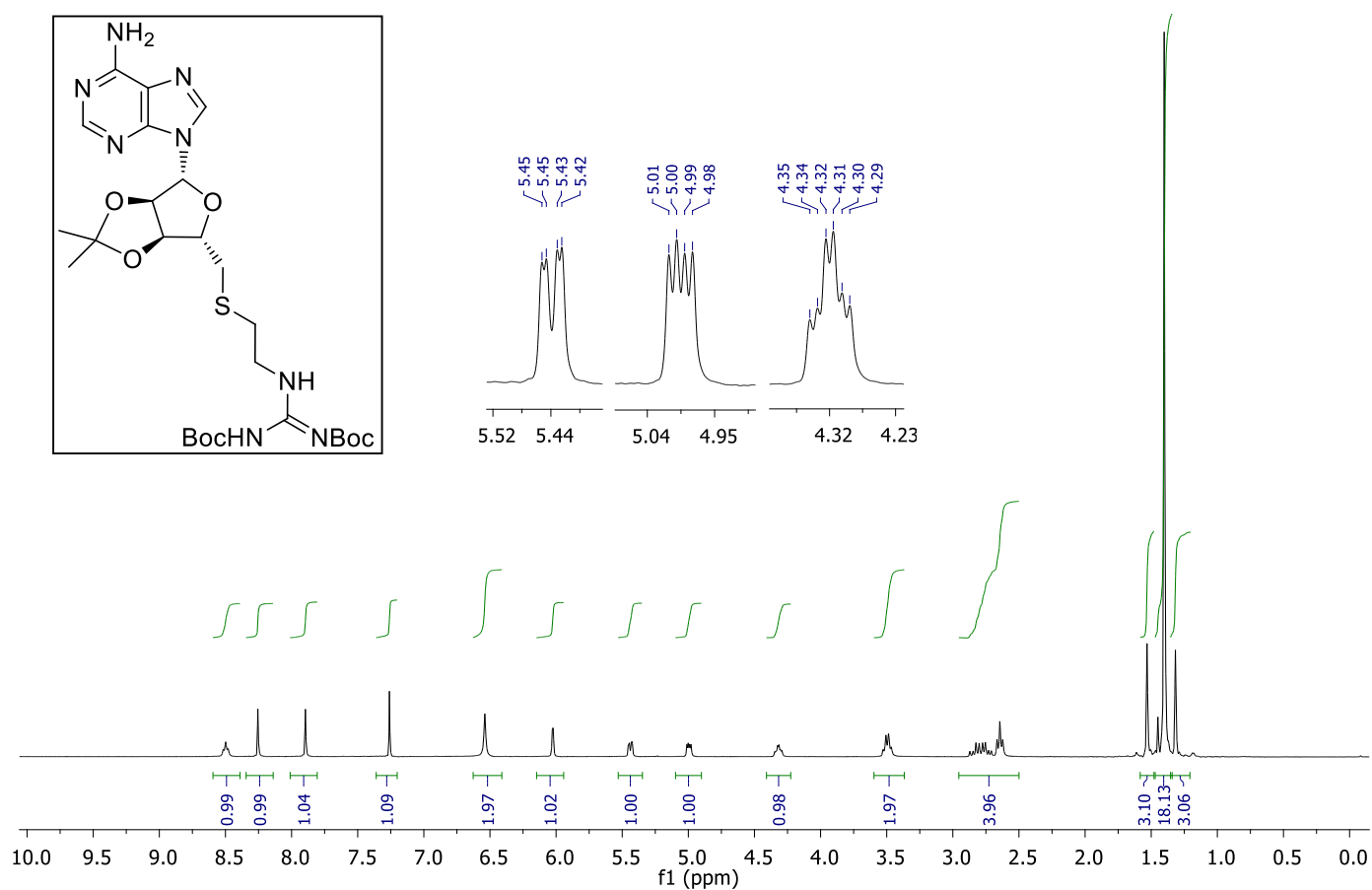
Compound 18: ^1H NMR (300 MHz, CDCl_3)



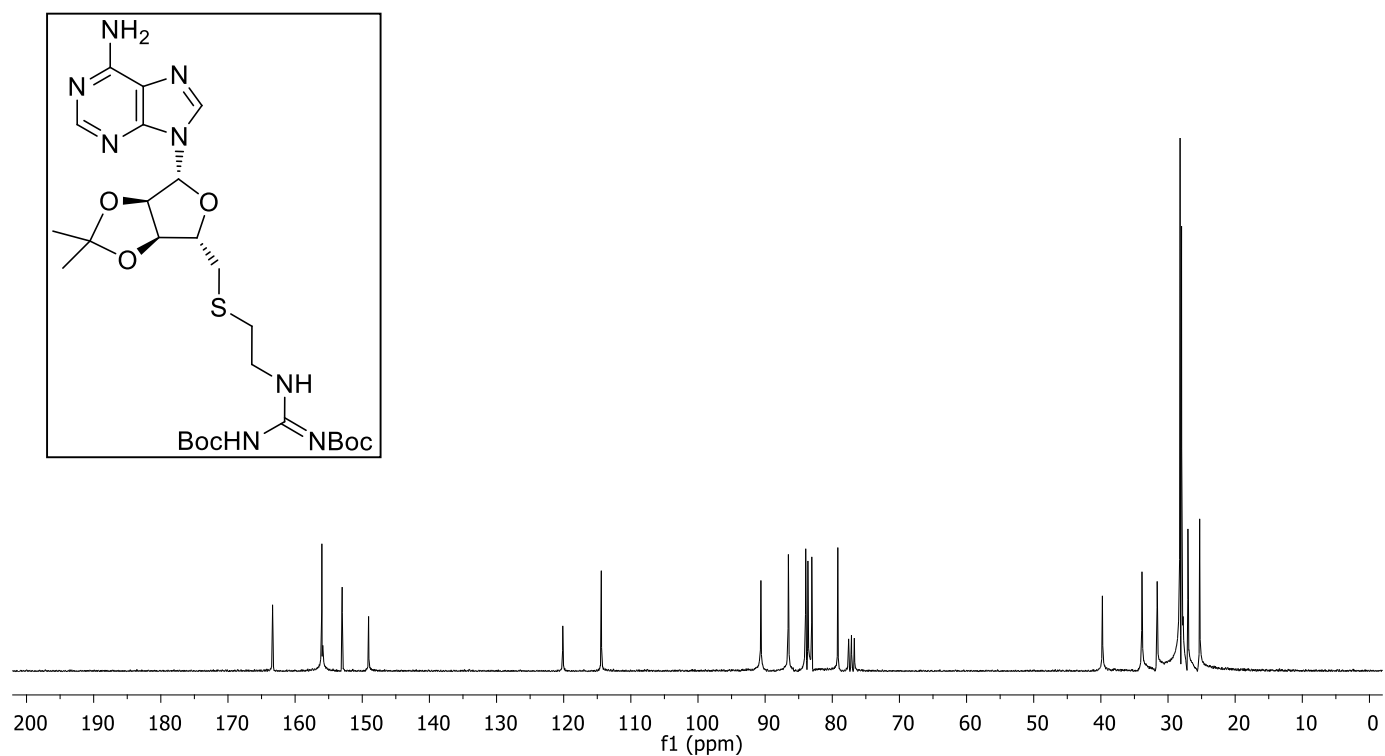
Compound 18: ^{13}C NMR (75 MHz, CDCl_3)



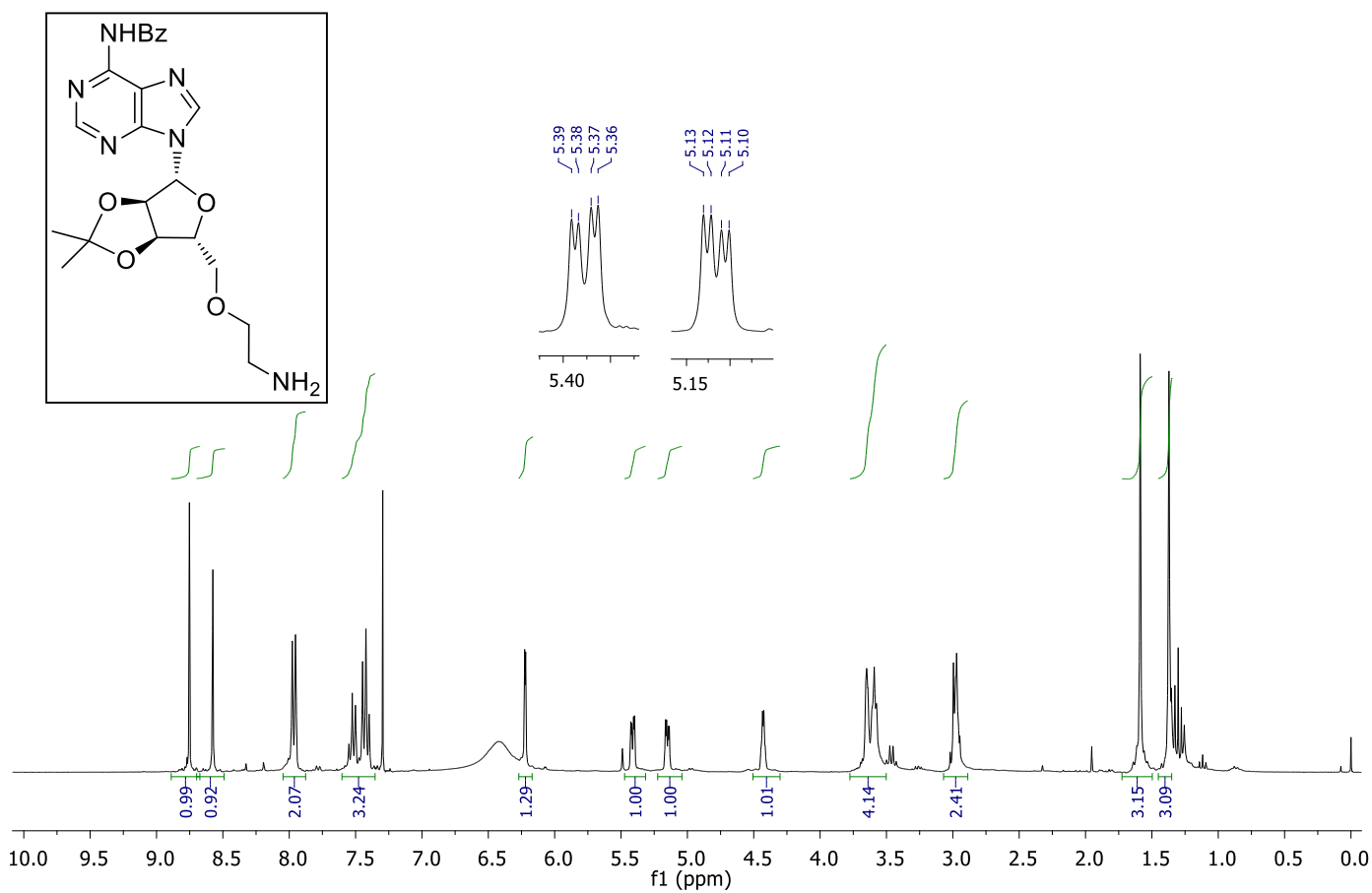
Compound 19: ^1H NMR (300 MHz, CDCl_3)



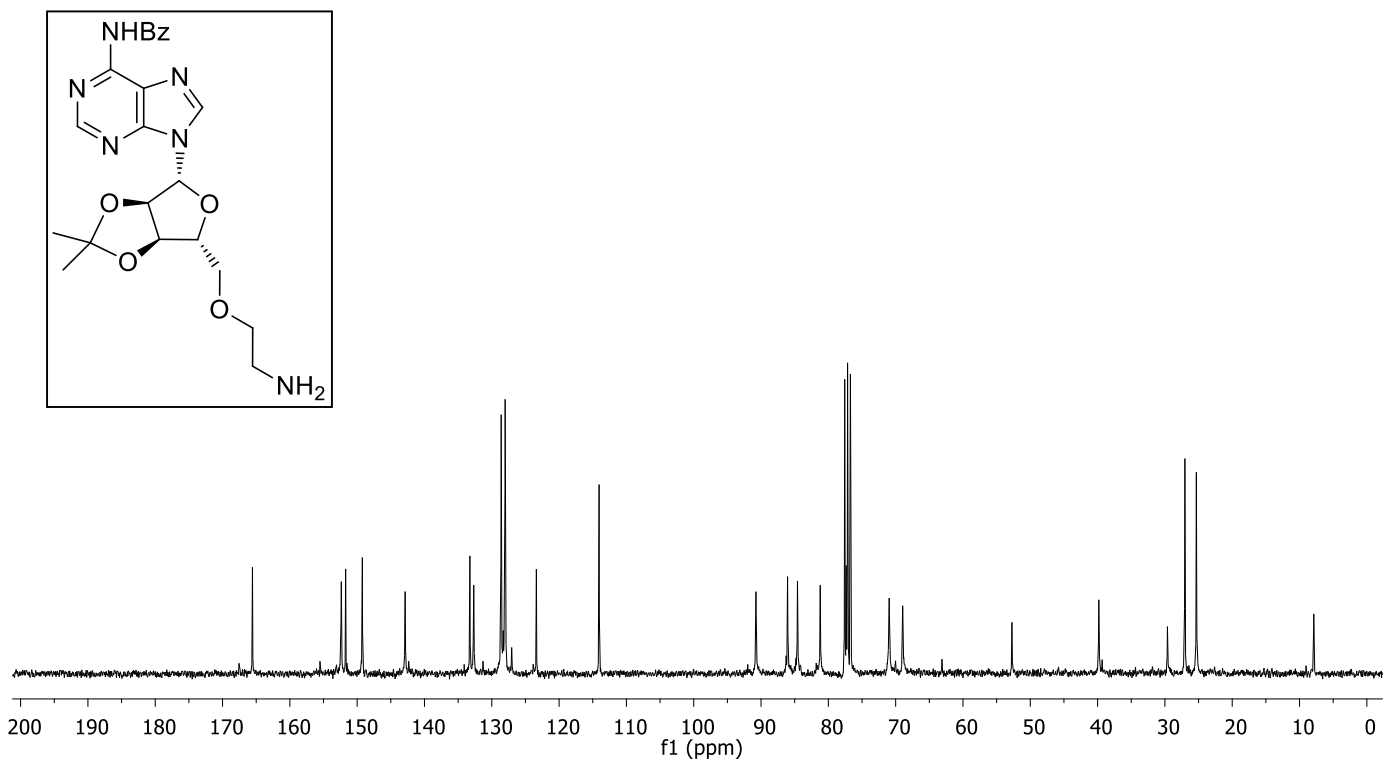
Compound 19: ^{13}C NMR (75 MHz, CDCl_3)



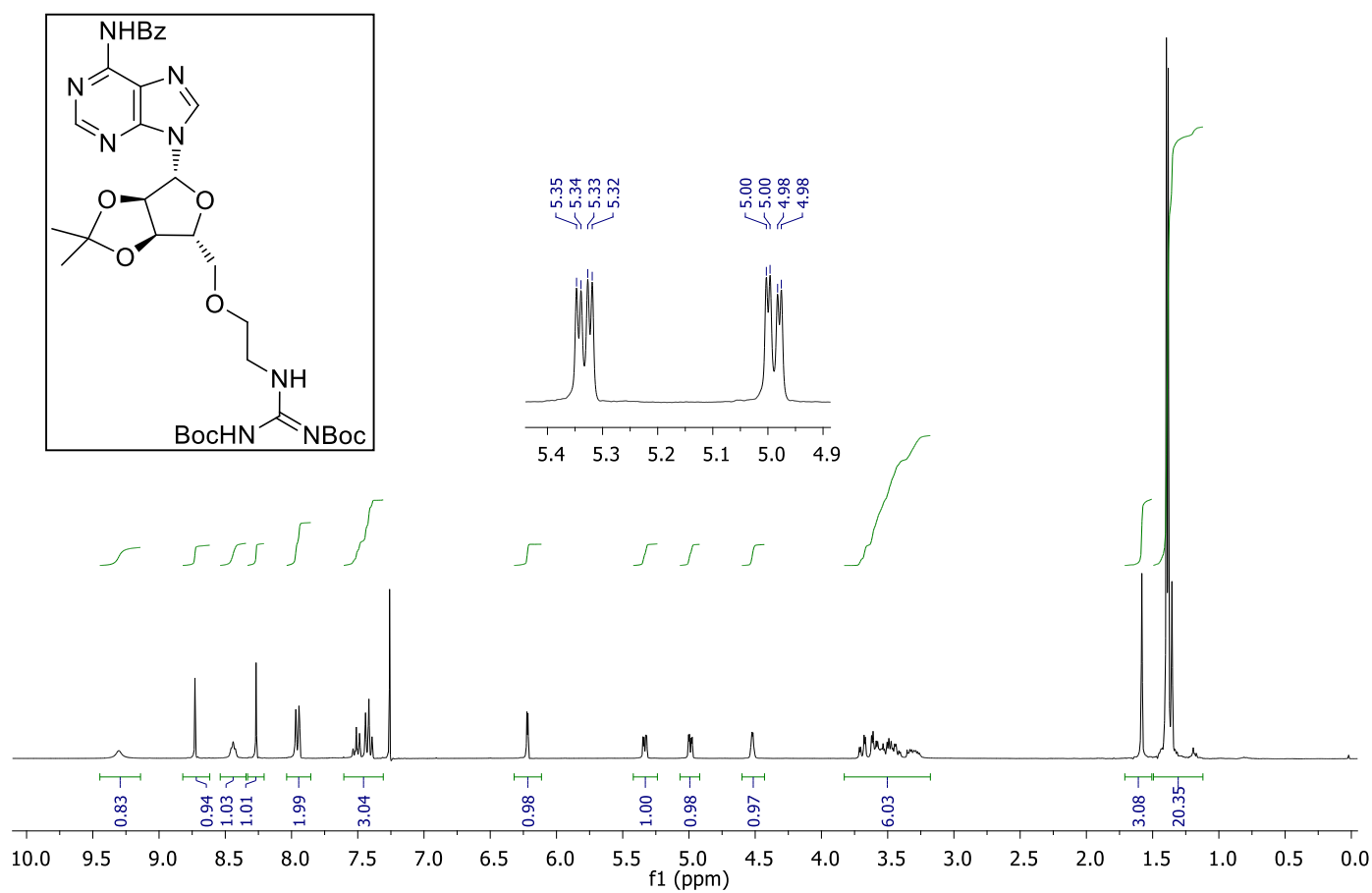
Compound 21: ^1H NMR (300 MHz, CDCl_3)



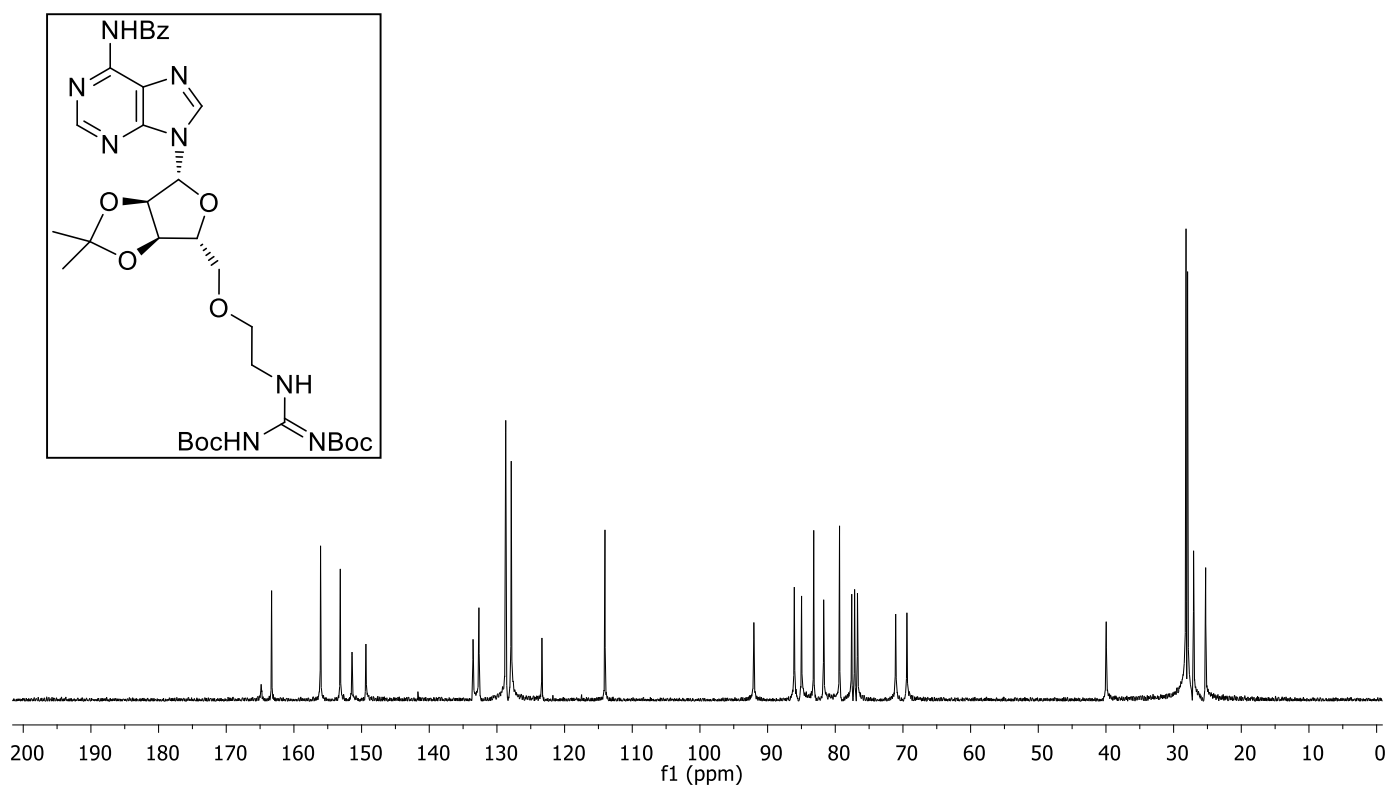
Compound 21: ^{13}C NMR (75 MHz, CDCl_3)



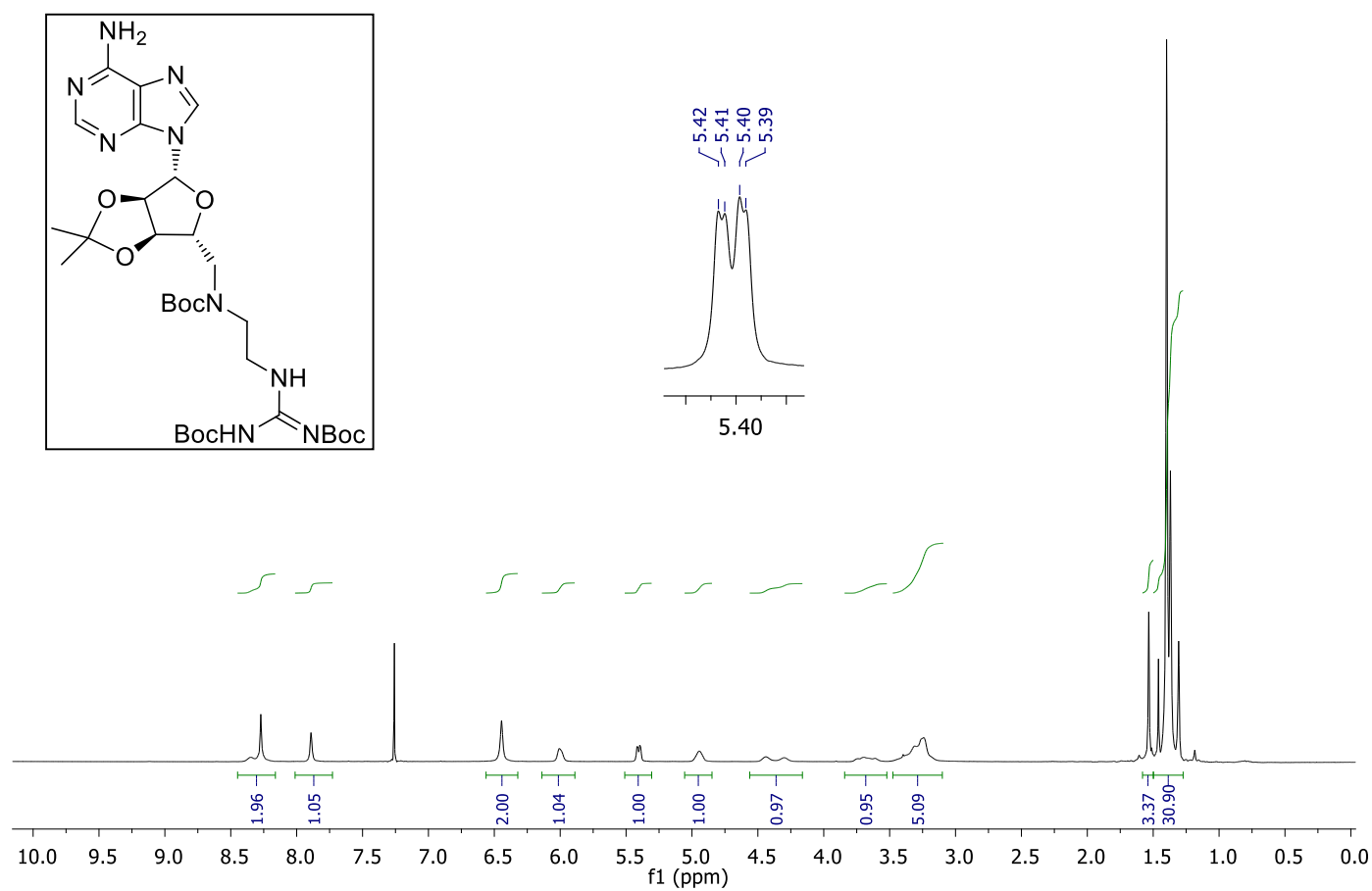
Compound 22: ^1H NMR (300 MHz, CDCl_3)



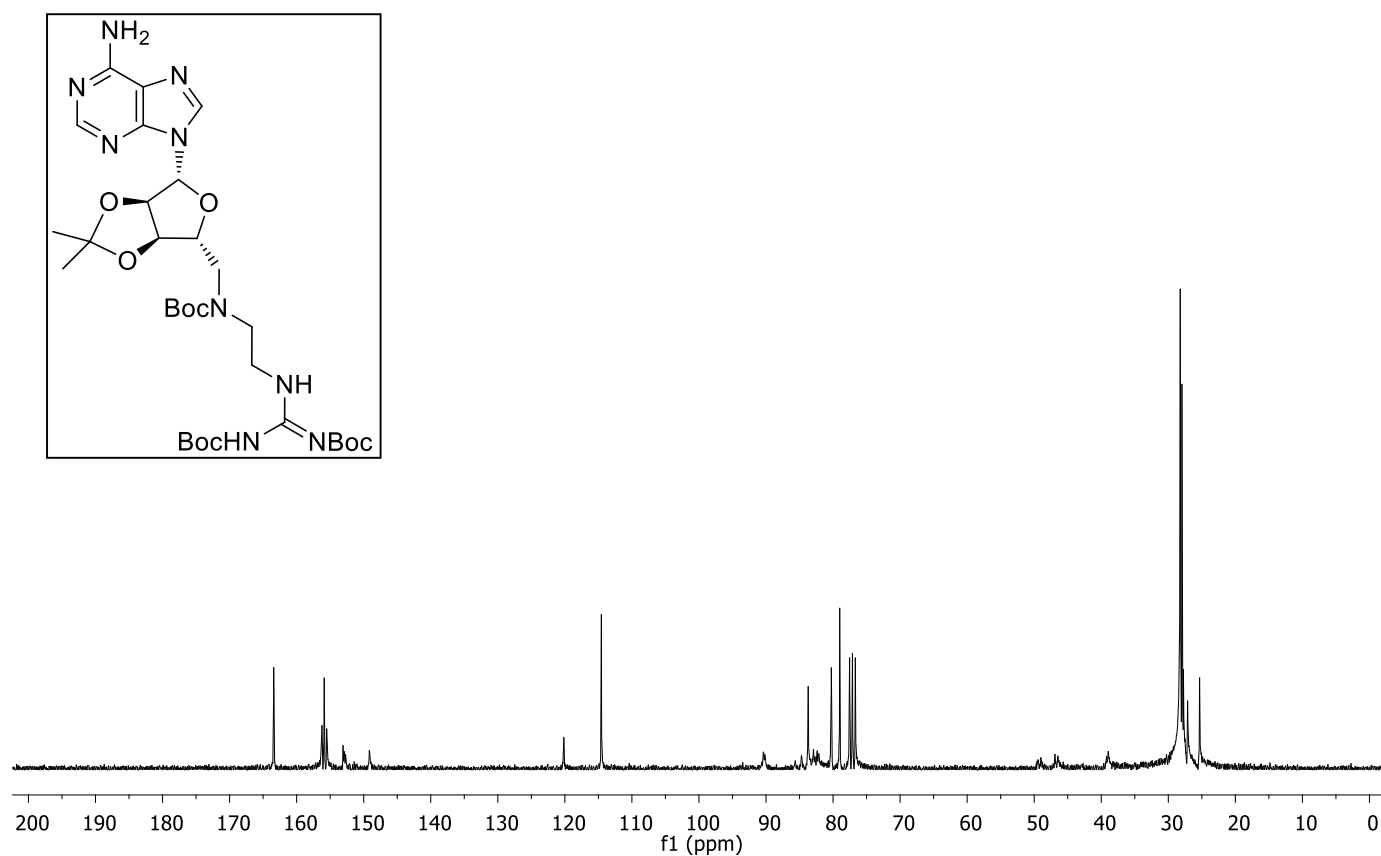
Compound 22: ^{13}C NMR (75 MHz, CDCl_3)



Compound 31: ^1H NMR (300 MHz, CDCl_3)

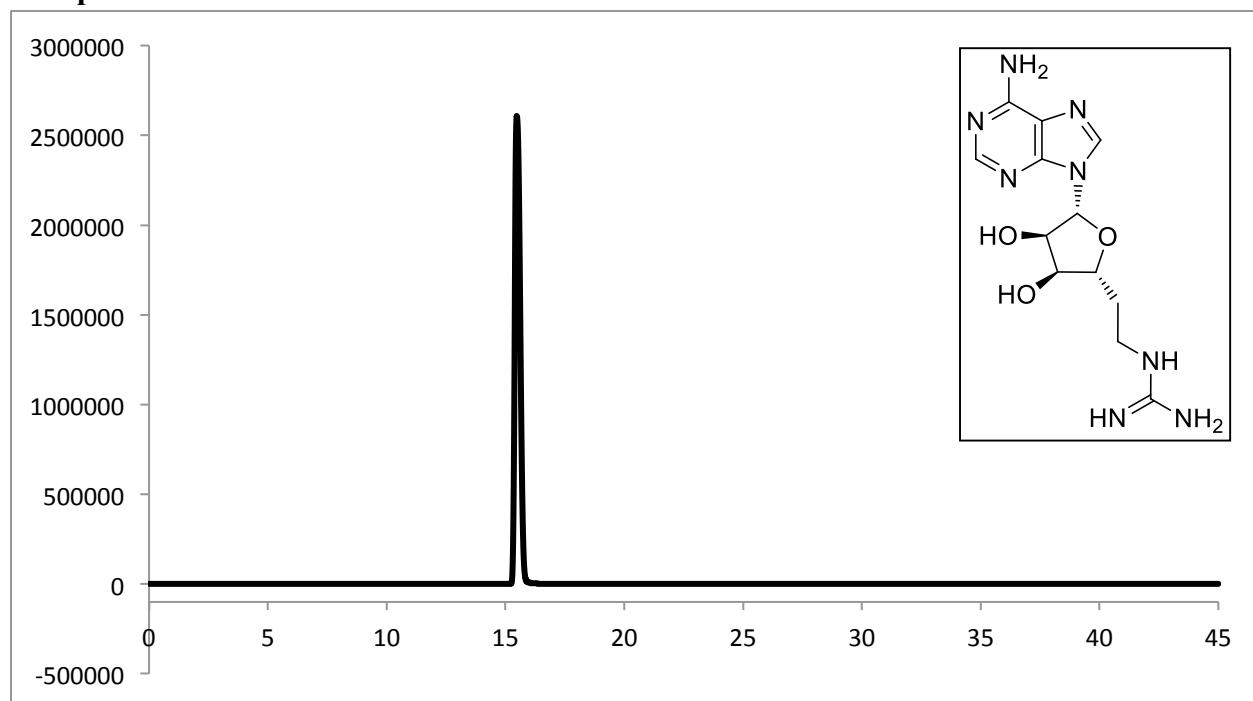


Compound 31: ^{13}C NMR (75 MHz, CDCl_3)

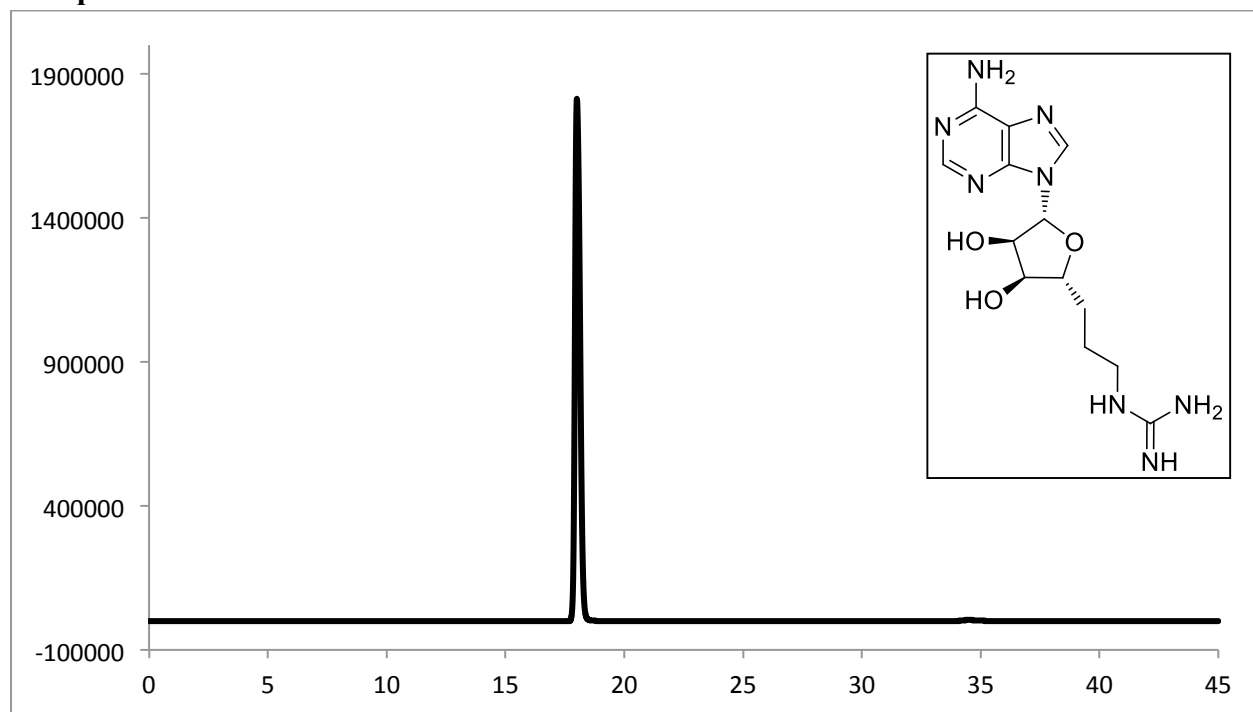


Analytical RP-HPLC traces for compounds 1-6

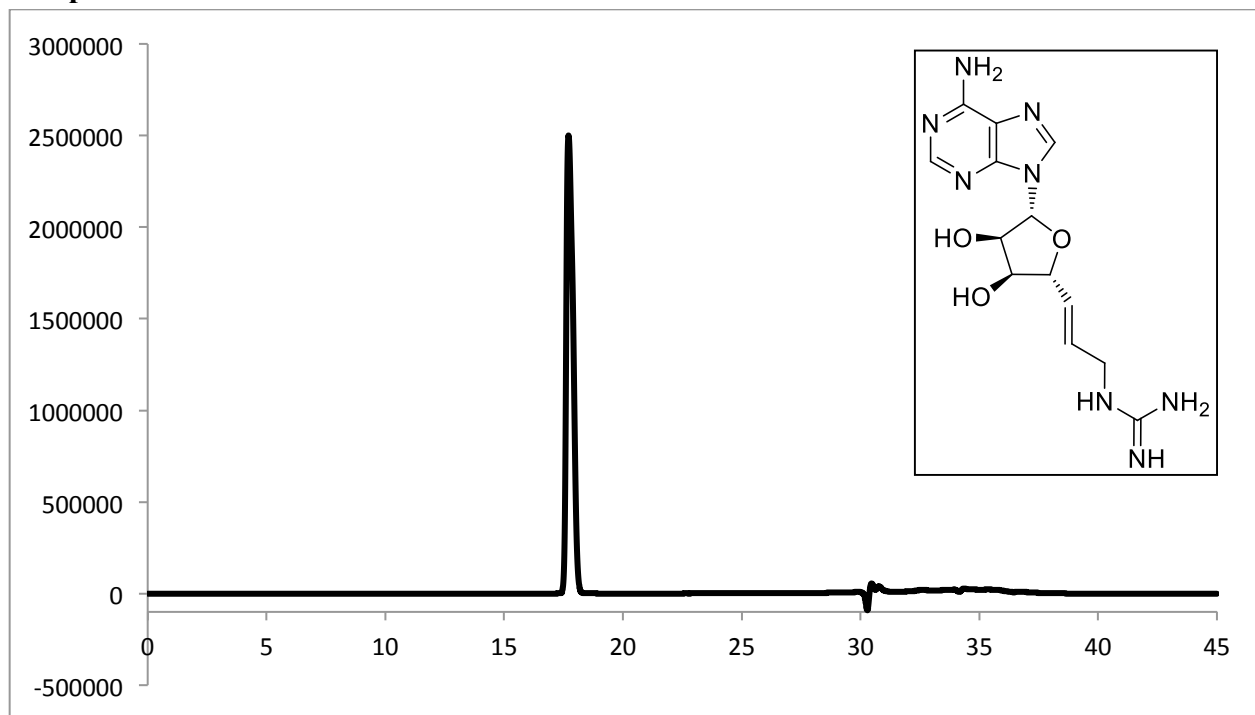
Compound 1



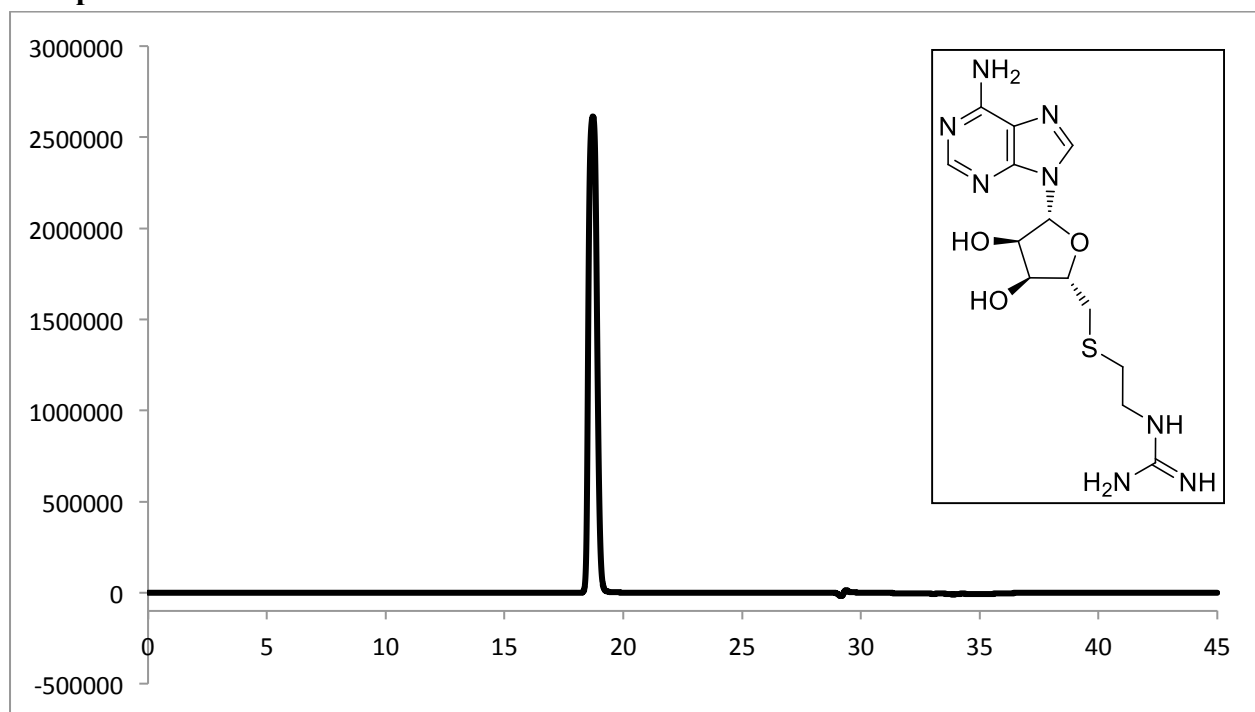
Compound 2



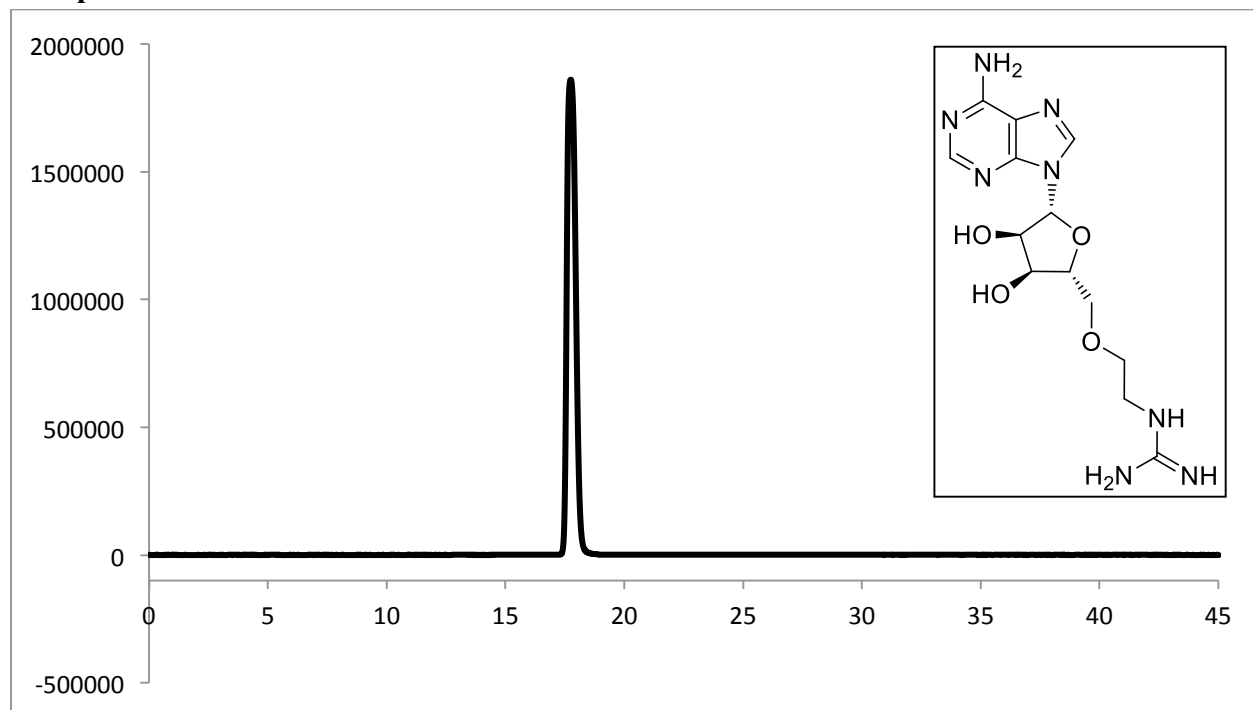
Compound 3



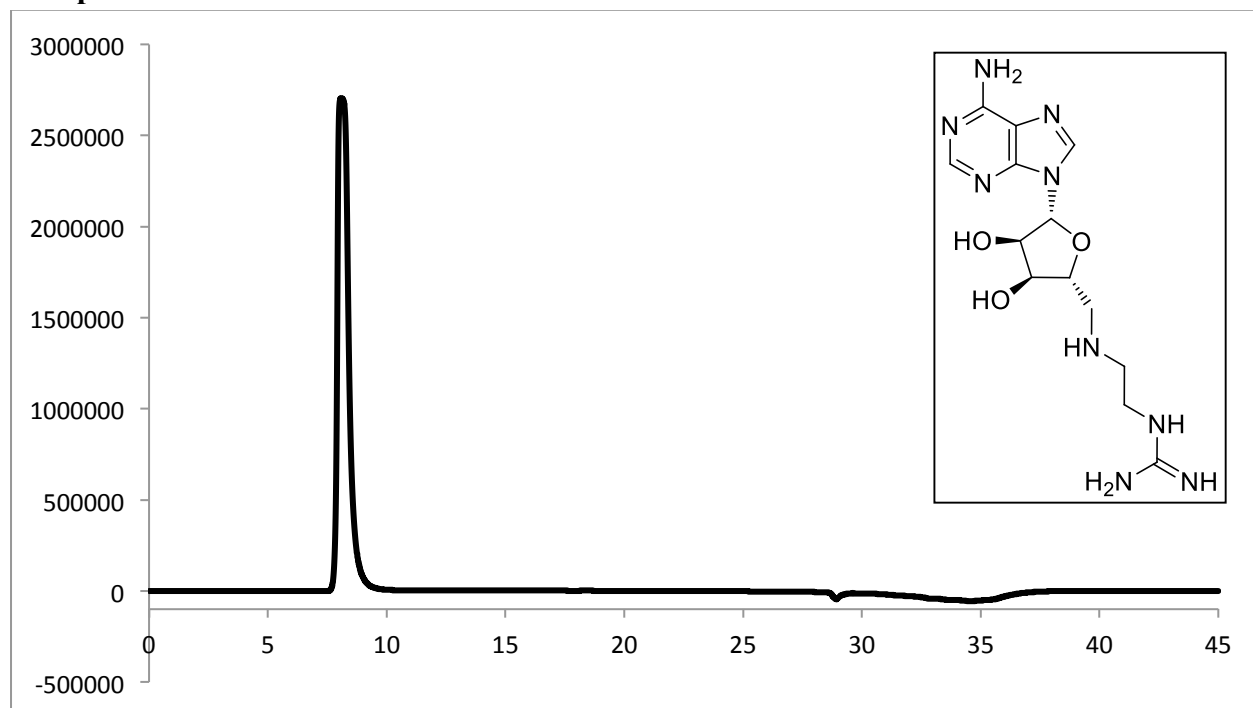
Compound 4



Compound 5

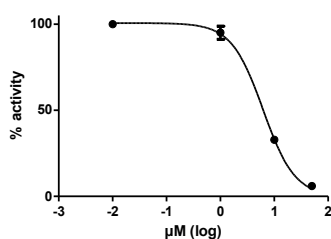


Compound 6



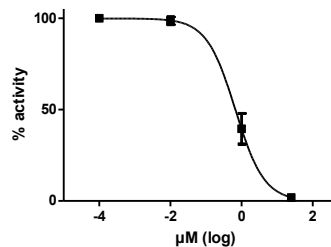
IC₅₀ curves of Compounds 1-6 and AdoHcy

AdoHcy - PRMT 1



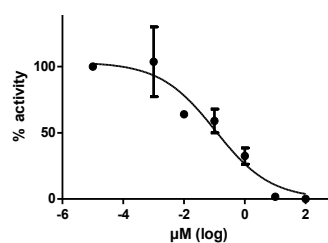
IC₅₀ = 6.21 ± 0.56 μM

AdoHcy - PRMT 4



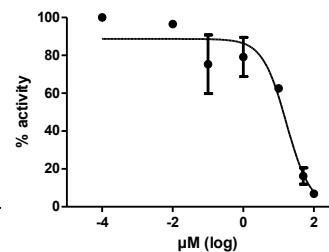
IC₅₀ = 0.67 ± 0.19 μM

AdoHcy - PRMT 6



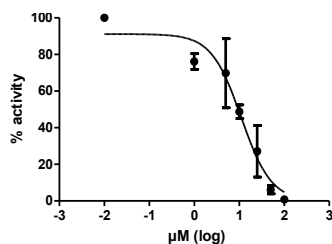
IC₅₀ = 0.20 ± 0.25 μM

AdoHcy - G9a



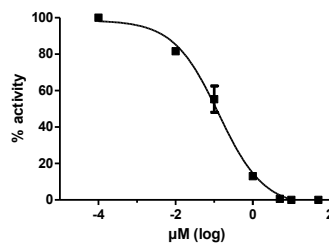
IC₅₀ = 16.64 ± 6.43 μM

Compound 1 - PRMT 1



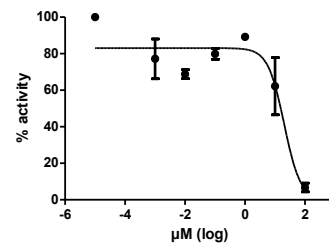
IC₅₀ = 11.09 ± 2.77 μM

Compound 1 - PRMT 4



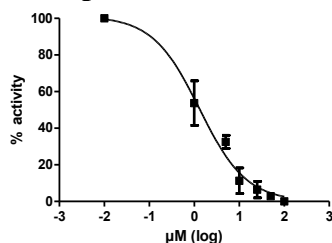
IC₅₀ = 0.12 ± 0.02 μM

Compound 1 - PRMT 6



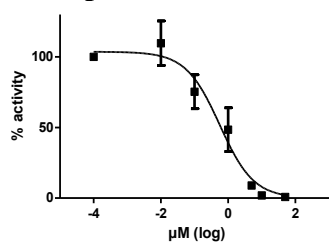
IC₅₀ = 20.23 ± 8.67 μM

Compound 2 - PRMT 1



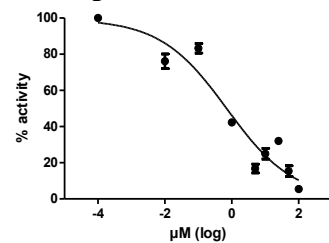
IC₅₀ = 1.30 ± 0.38 μM

Compound 2 - PRMT 4



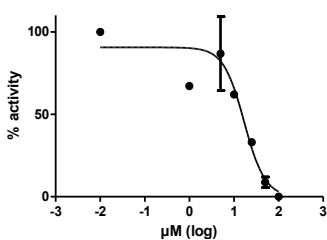
IC₅₀ = 0.56 ± 0.25 μM

Compound 2 - PRMT 6



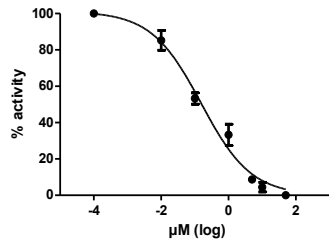
IC₅₀ = 0.72 ± 0.33 μM

Compound 3 - PRMT 1



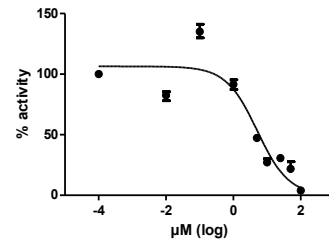
IC₅₀ = 16.96 ± 3.73 μM

Compound 3 - PRMT 4



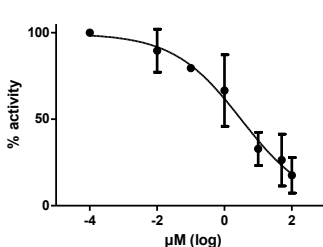
IC₅₀ = 0.15 ± 0.05 μM

Compound 3 - PRMT 6



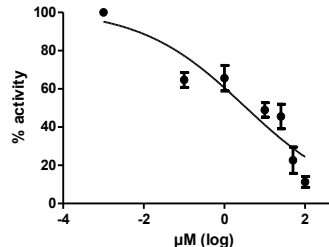
IC₅₀ = 5.15 ± 1.27 μM

Compound 4 - G9a



IC₅₀ = 3.18 ± 2.67 μM

Compound 6 - PRMT6



IC₅₀ = 3.20 ± 3.93 μM