Supporting information

for the article

Mono- and diamination of 4,6-dichloropyrimidine, 2,6-dichloropyrazine and 1,3-dichloroisoquinoline with adamantane-containing amines

by
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Study of prototropic tautomerism of adamantine-containing 4-amino-6-chloropyrimidines

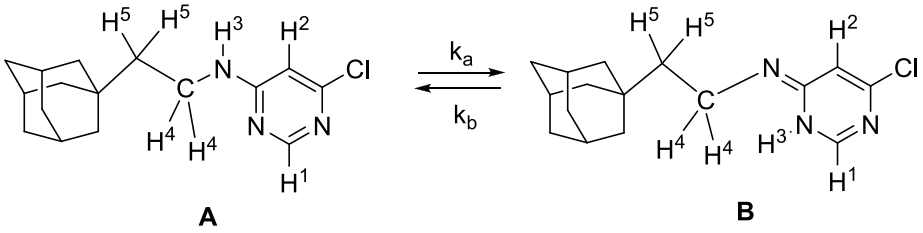
General information.

^{1}H NMR spectra were registered at Agilent 400-MR spectrometer (400 MHz) in $CDCl_3$. The spectra were fitted using WinDNMR software. Kinetic parameters were calculated from the dependence of the chemical shift of the proton in position 2 of the pyrimidine core on the temperature. As a result rate constant ($k = k_a + k_b$) and equilibrium constant ($K = k_a / k_b$) were calculated from the tautomer ratio for each temperature. $\Delta H^{\neq}$ and $\Delta S^{\neq}$ were calculated using Eyring equation (1) .

$$\ln\frac{k}{T} = \frac{-\Delta H^{\dagger}}{R}\frac{1}{T} + \ln\frac{k_B}{h} + \frac{\Delta S^{\ddagger}}{R} \quad (1)$$

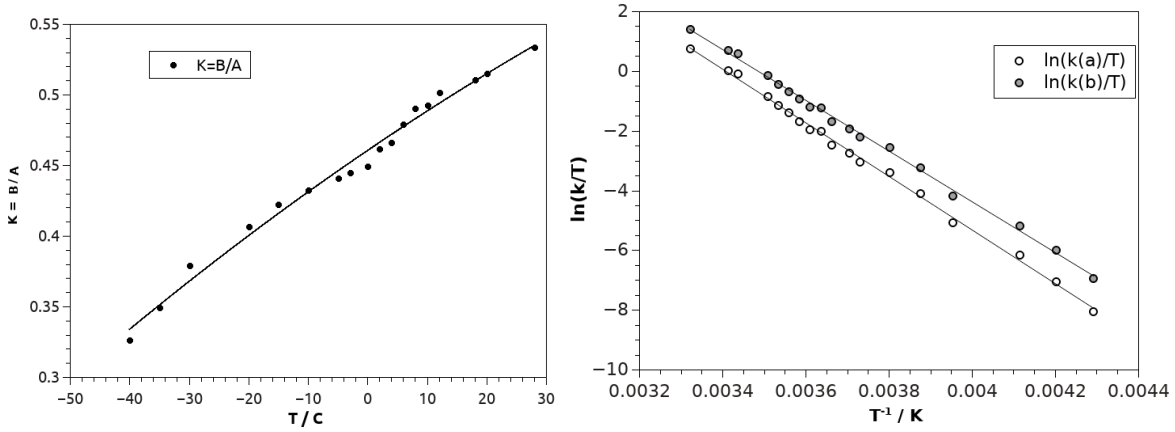
The standard deviation of the coefficients determined is ±2.5%

Compound 5g



The ^{1}H NMR spectra were registered at temperatures in the range 243-308 K. The chemical shifts of proton signals at 243 K and 308 K are given in the table S1.

Table S1. Selected chemical shifts of proton signals at 243 K and 308 K for **5g**			
Proton	T = 243 K		T = 308 K
	A (major)	**B** (minor)	Average
H_1	8.21	8.33	8.28
H_2	6.27	6.33	6.27
H_3	6.91	5.56	5.18
H_4	3.08	3.35	3.25
H_5	1.36	1.35	1.36

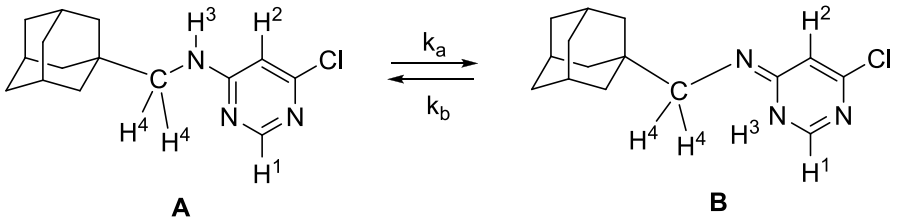


(a) **(b)**

Figure S1. (a) Dependence B/A ratio on the temperature for **5g**. **(b)** Dependence of ln (k/T) on 1/T for **5g**.

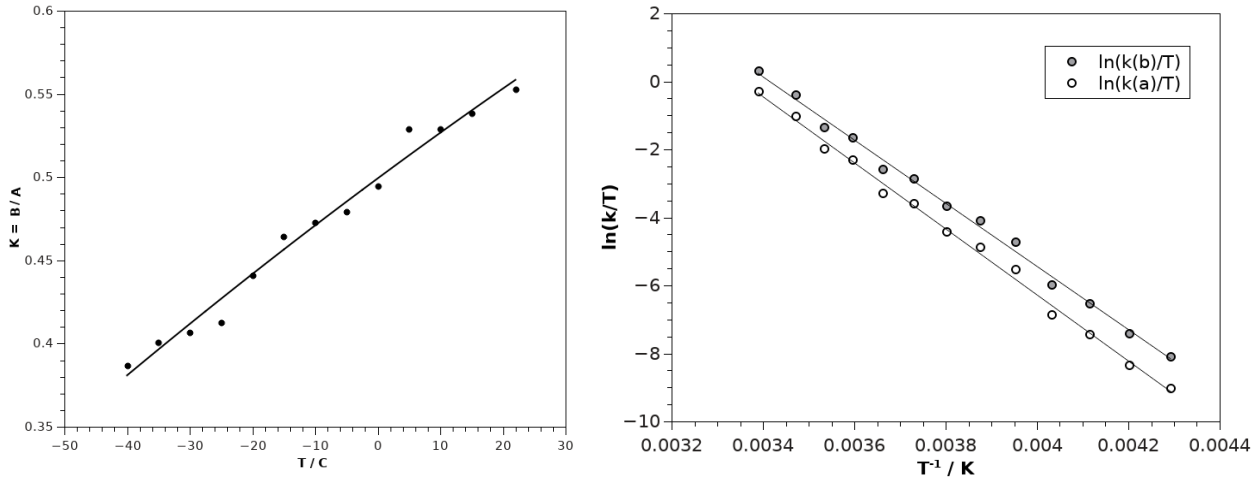
Table S2. The activation energy characteristics of prototropic transformation of **5g**		
	k_a (A → B)	k_b (B → A)
$\Delta H^{\neq}$ (kcal*mol^{-1})	17.84	16.89
$\Delta S^{\neq}$ (cal*mol^{-1}*T^{-1})	13.58	11.65
$\Delta G^{\neq}_{(273\ K)}$ (kcal*mol^{-1})	14.24	13.81

Compound 5b



The ^{1}H NMR spectra were registered at temperatures in the range 233-303 K. The chemical shifts of proton signals at 233 K and 303 K are given in the table S3.

Table S3. Selected chemical shifts of proton signals at 233 K and 303 K for **5b**			
Proton	T = 233 K		T = 303 K
	A (major)	**B** (minor)	Average
H_1	8.19	8.28	8.25
H_2	6.35	6.48	6.33
H_3	7.09	6.27	5.45
H_4	2.80	3.13	2.95

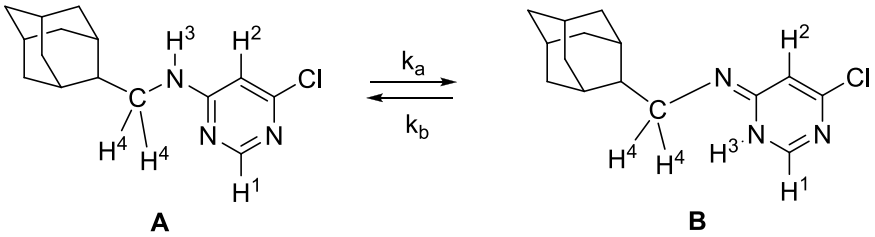


(a) **(b)**

Figure S2. (a) Dependence B/A ratio on the temperature for **5b**. **(b)** Dependence of ln (k/T) on 1/T for **5b**.

Table S4. The activation energy characteristics of prototropic transformation of **5b**		
	k_a (A → B)	k_b (B → A)
$\Delta H^{\neq}$ (kcal*mol^{-1})	19.30	18.46
$\Delta S^{\neq}$ (cal*mol^{-1}*T^{-1})	17.51	15.81
$\Delta G^{\neq}_{(273\ K)}$ (kcal*mol^{-1})	14.67	14.29

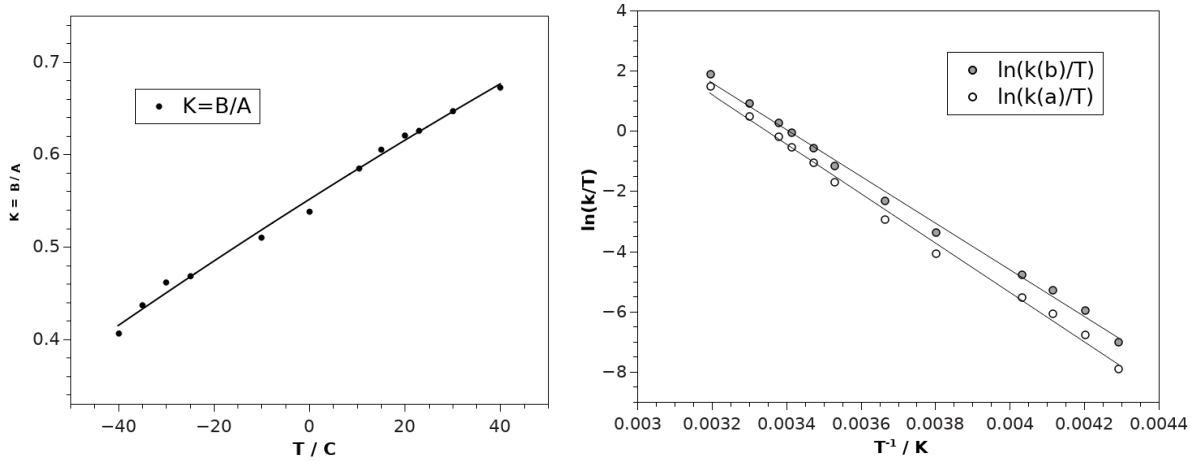
Compound 5c



A B

The ^{1}H NMR spectra were registered at temperatures in the range 233-313 K. The chemical shifts of proton signals at 233 K and 313 K are given in the table S5.

Table S5. Selected chemical shifts of proton signals at 233 K and 313 K for **5c**			
Proton	T = 233 K		T = 313 K
	A (major)	**B** (minor)	Average
H_1	8.16	8.27	8.25
H_2	6.28	6.35	6.29
H_3	7.45	6.35	5.53
H_4	3.54	4.26	3.97

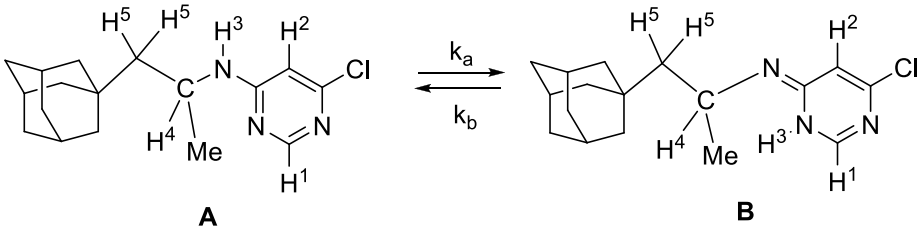


(a) **(b)**

Figure S3. (a) Dependence B/A ratio on the temperature for **5c**. **(b)** Dependence of ln (k/T) on 1/T for **5c**.

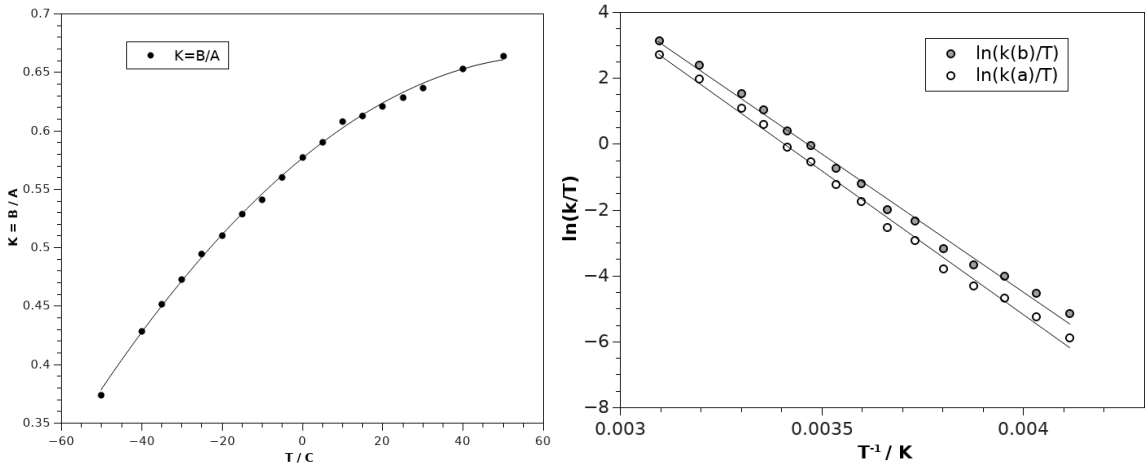
Table S6. The activation energy characteristics of prototropic transformation of **5c**		
	k_a (A → B)	k_b (B → A)
$\Delta H^{\neq}$ (kcal*mol^{-1})	16.31	15.42
$\Delta S^{\neq}$ (cal*mol^{-1}*T^{-1})	7.38	5.30
$\Delta G^{\neq}_{(273\ K)}$ (kcal*mol^{-1})	14.48	14.15

Compound 5f



The ^{1}H NMR spectra were registered at temperatures in the range 223-323 K. The chemical shifts of proton signals at 223 K and 323 K are given in the table S7.

Table S7. Selected chemical shifts of proton signals at 223 K and 323 K for **5f**			
Proton	T = 223 K		T = 323 K
	A (major)	**B** (minor)	Average
H_1	8.24	8.33	8.29
H_2	6.32	6.31	6.26
H_3	6.84	5.65	4.96
H_4	3.17	3.47	3.36
H_5	1.25	1.25	1.28



(a) **(b)**

Figure S4. (a) Dependence B/A ratio on the temperature for **5f**. **(b)** Dependence of ln (k/T) on 1/T for **5f**.

Table S8. The activation energy characteristics of prototropic transformation of **5f**		
	k_a (A → B)	k_b (B → A)
$\Delta H^{\neq}$ (kcal*mol^{-1})	17.36	16.69
$\Delta S^{\neq}$ (cal*mol^{-1}*T^{-1})	11.90	10.59
$\Delta G^{\neq}_{(273\ K)}$ (kcal*mol^{-1})	14.26	13.96

NMR spectra

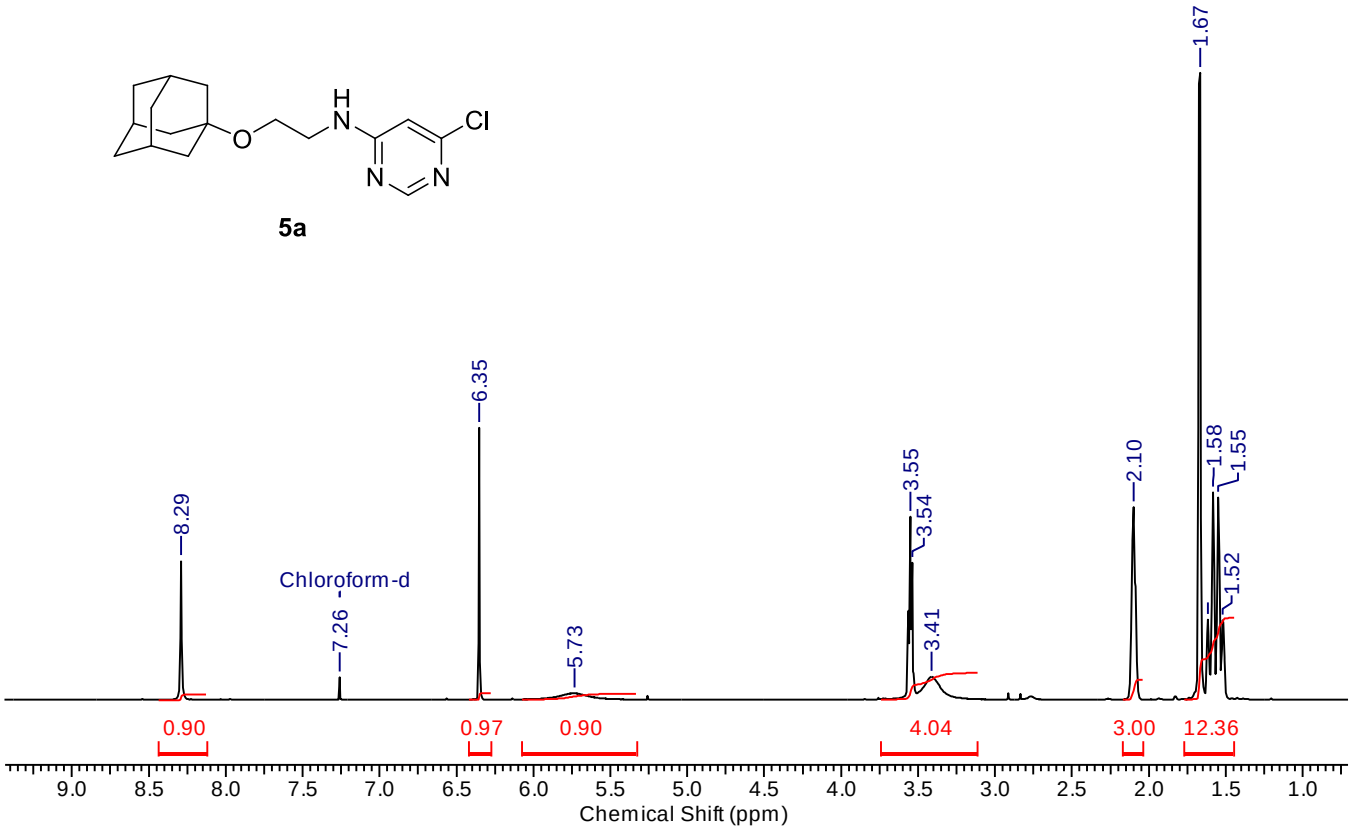


Figure S5. ^{1}H NMR spectrum of **5a** ($CDCl_3$, 400MHz, 300K).

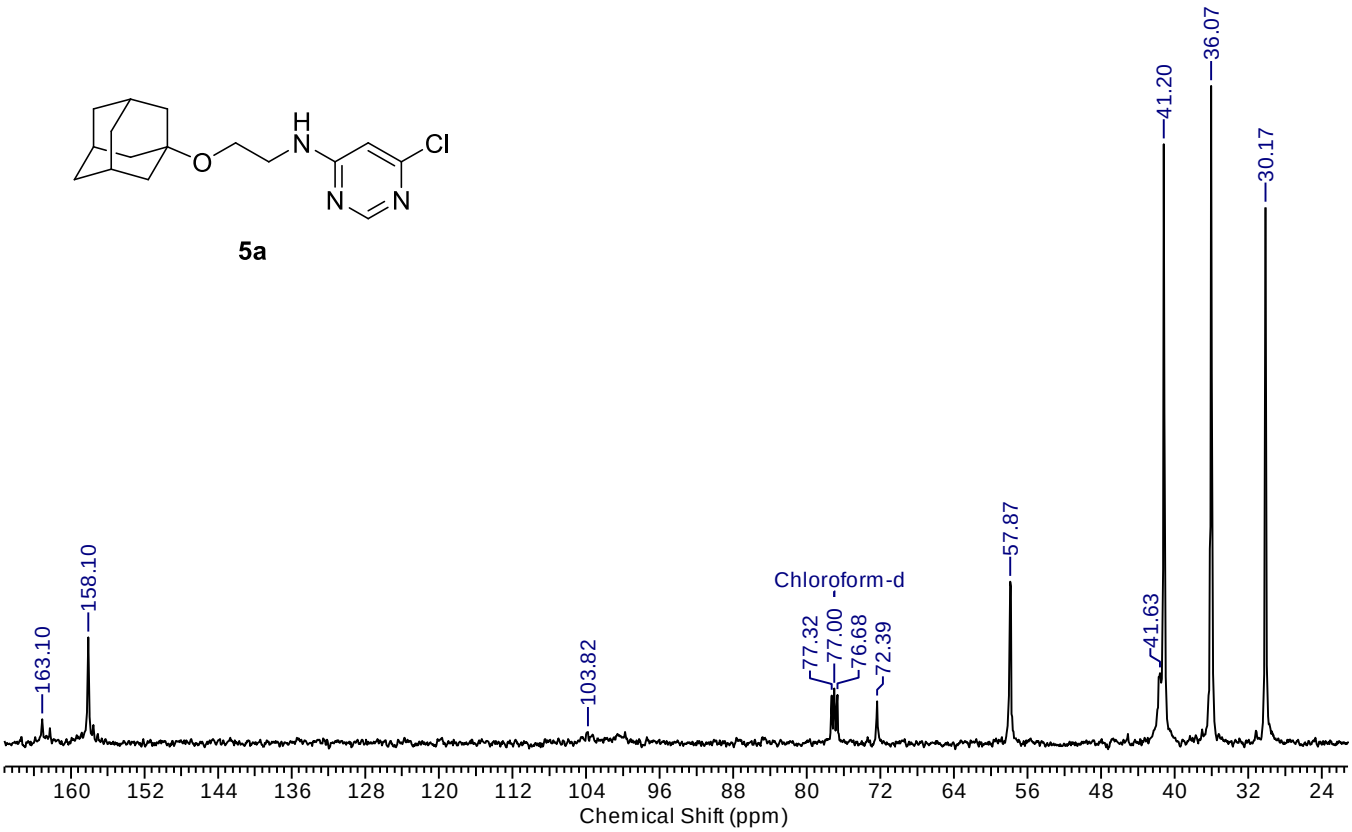


Figure S6. ^{13}C NMR spectrum of **5a** ($CDCl_3$, 100.6 MHz, 300K).

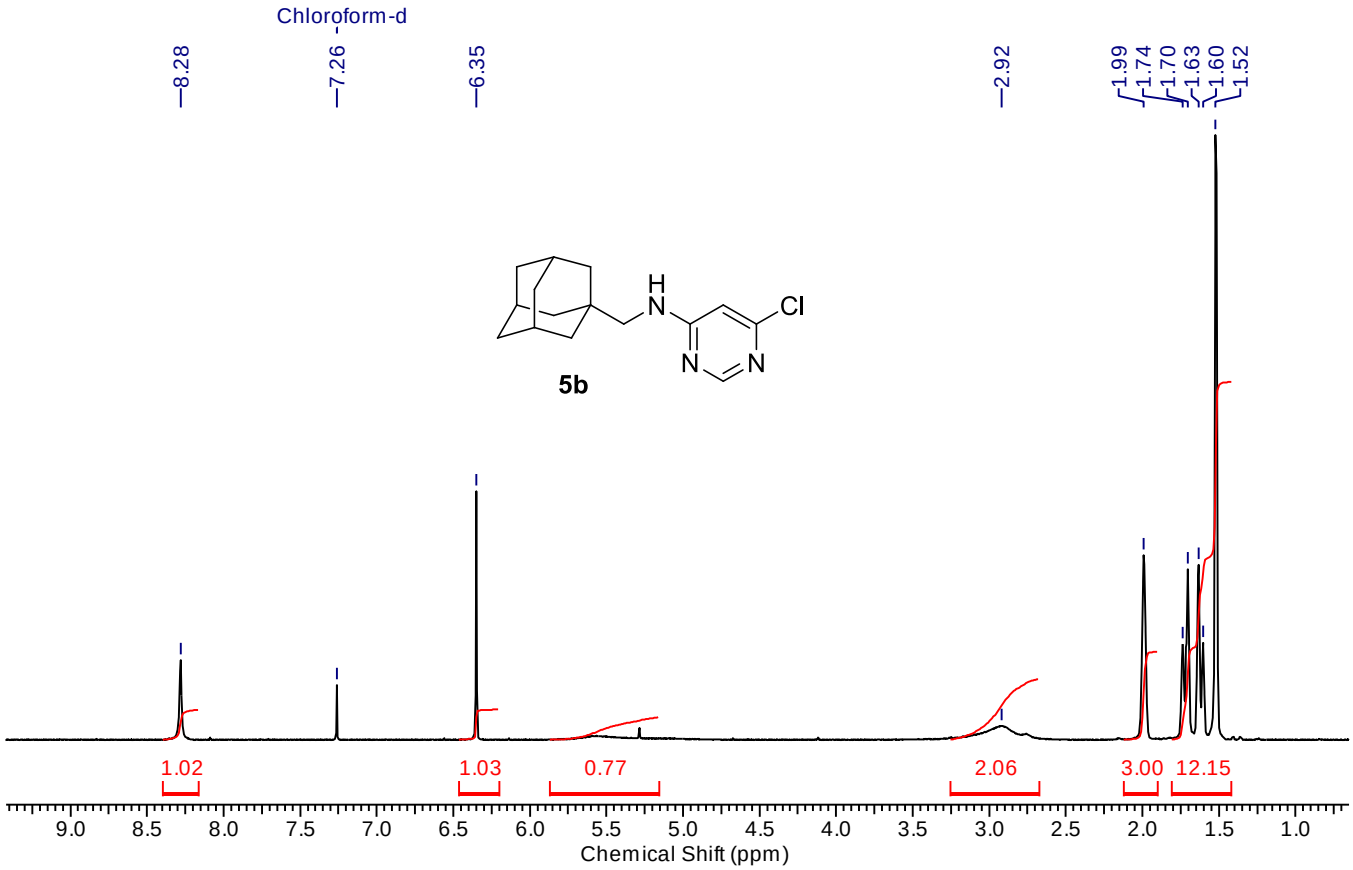


Figure S7. ^{1}H NMR spectrum of **5b** ($CDCl_3$, 400MHz, 300K).

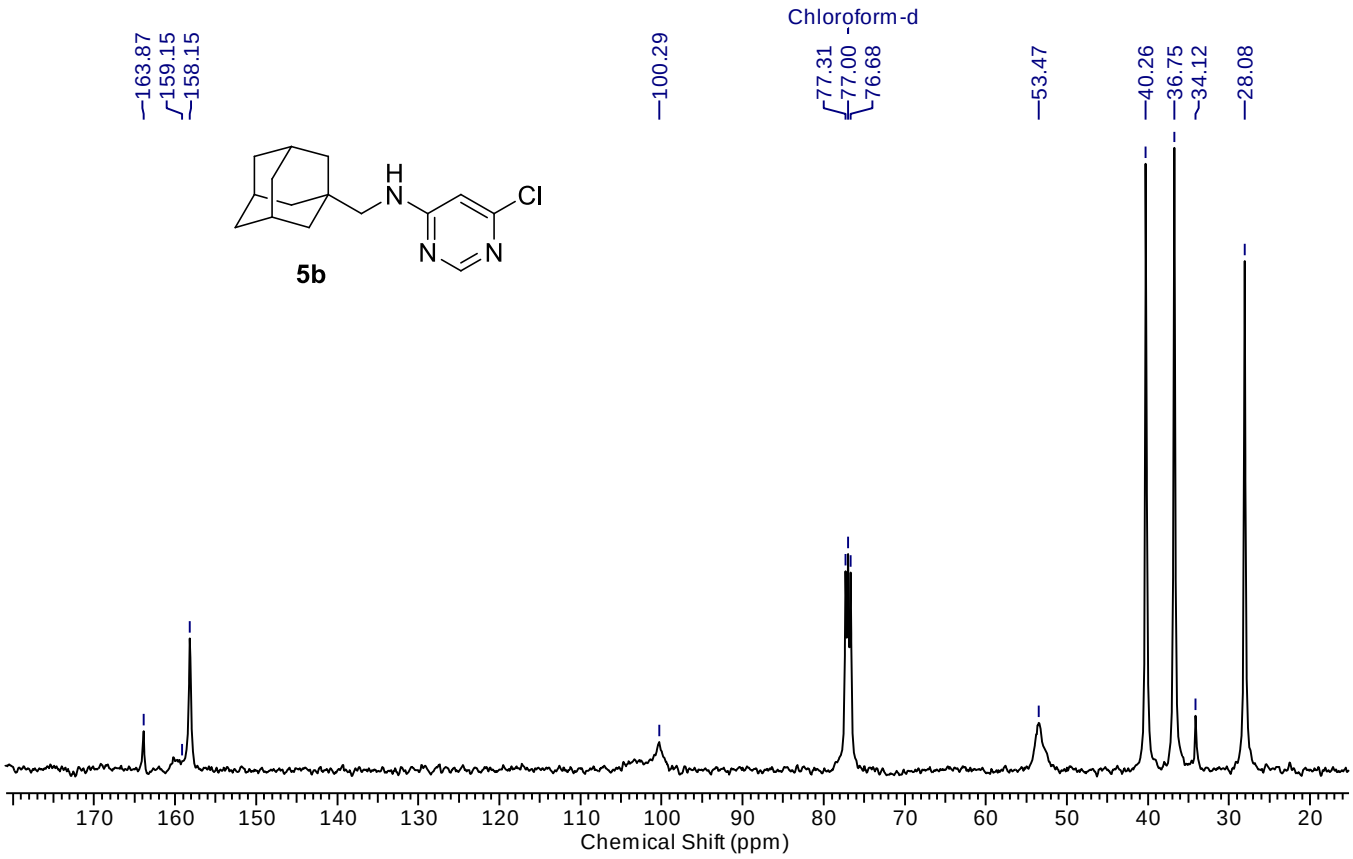


Figure S8. ^{13}C NMR spectrum of **5b** ($CDCl_3$, 100.6 MHz, 300K).

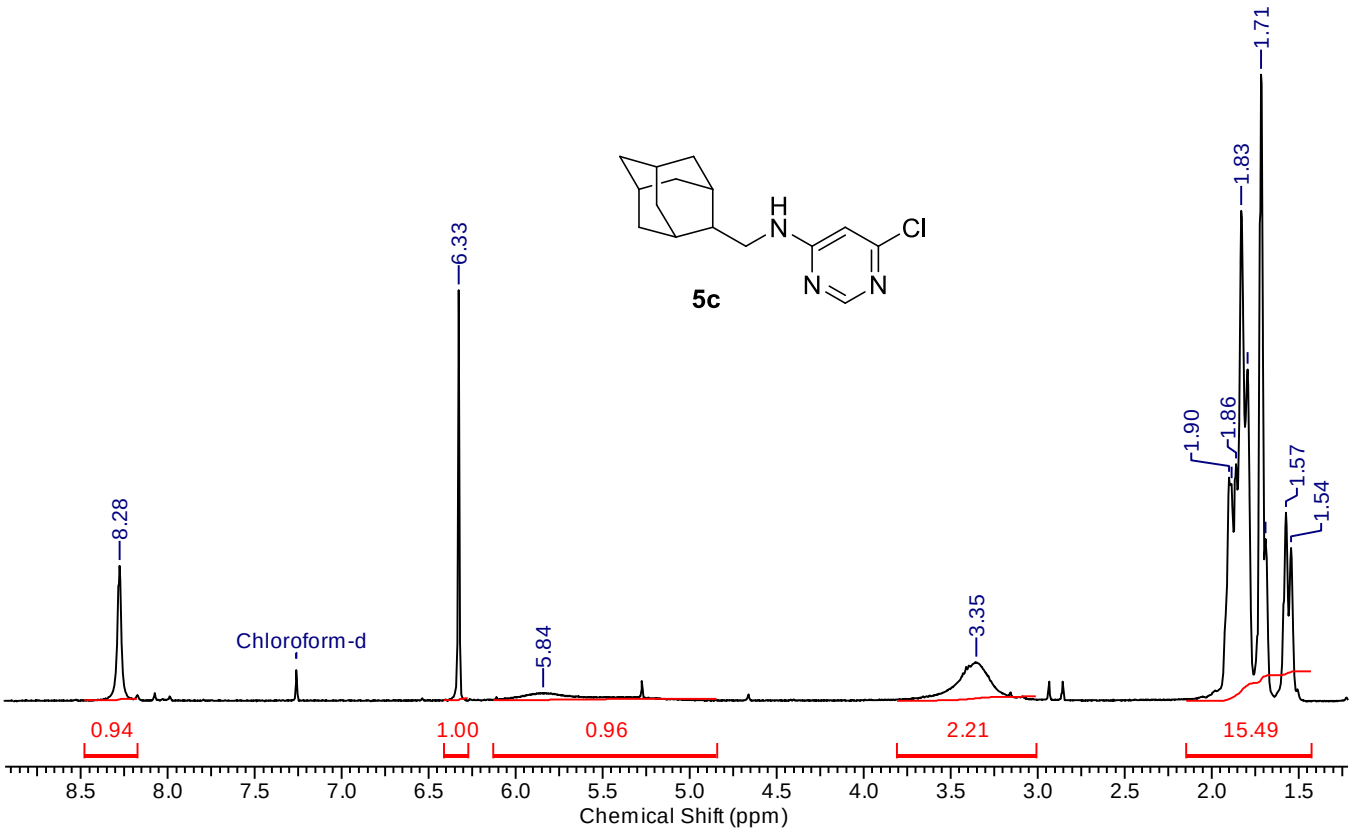


Figure S9. ^{1}H NMR spectrum of **5c** ($CDCl_3$, 400MHz, 300K).

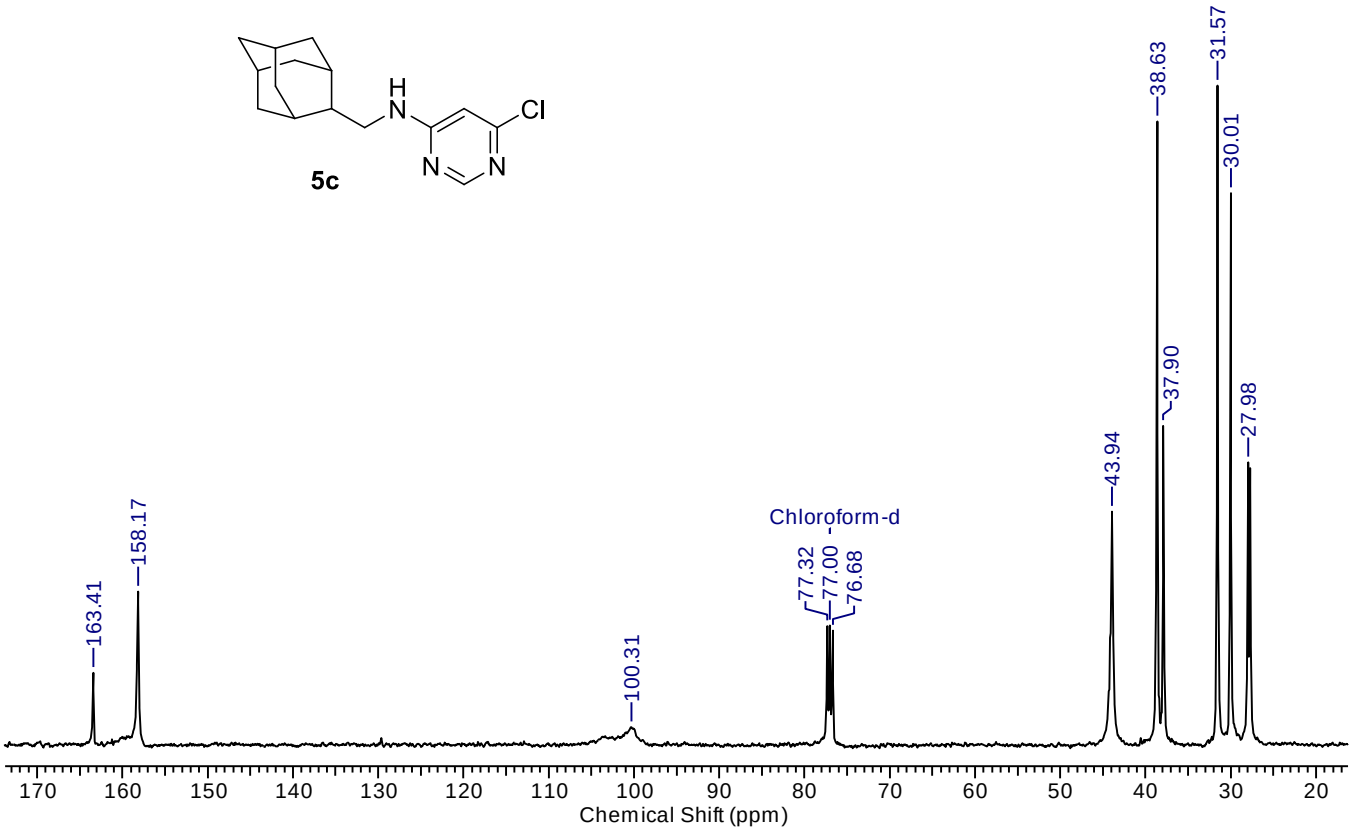


Figure S10. ^{13}C NMR spectrum of **5c** ($CDCl_3$, 100.6 MHz, 300K).

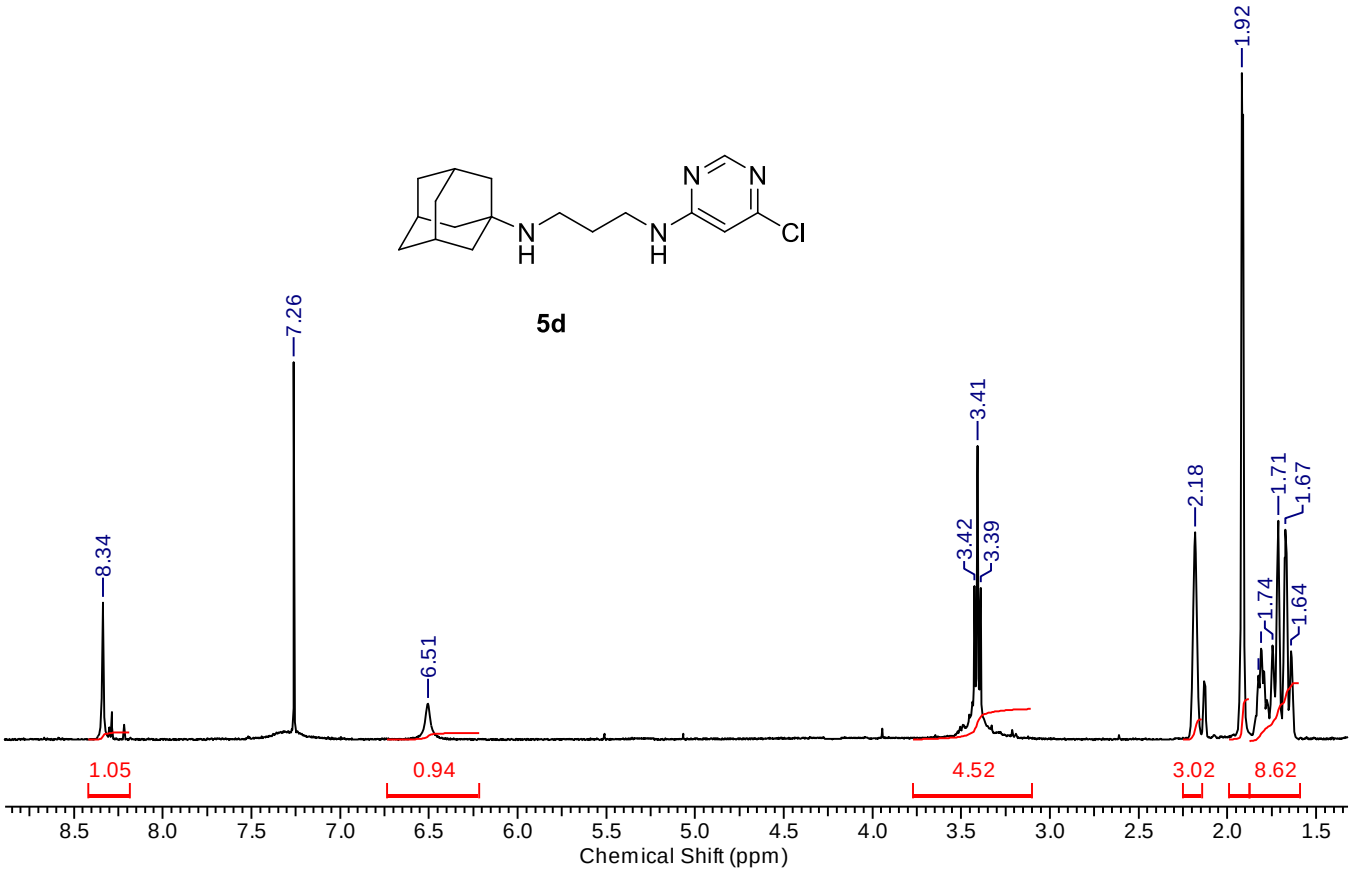


Figure S11. ^{1}H NMR spectrum of **5d** ($CDCl_3$, 400MHz, 300K).

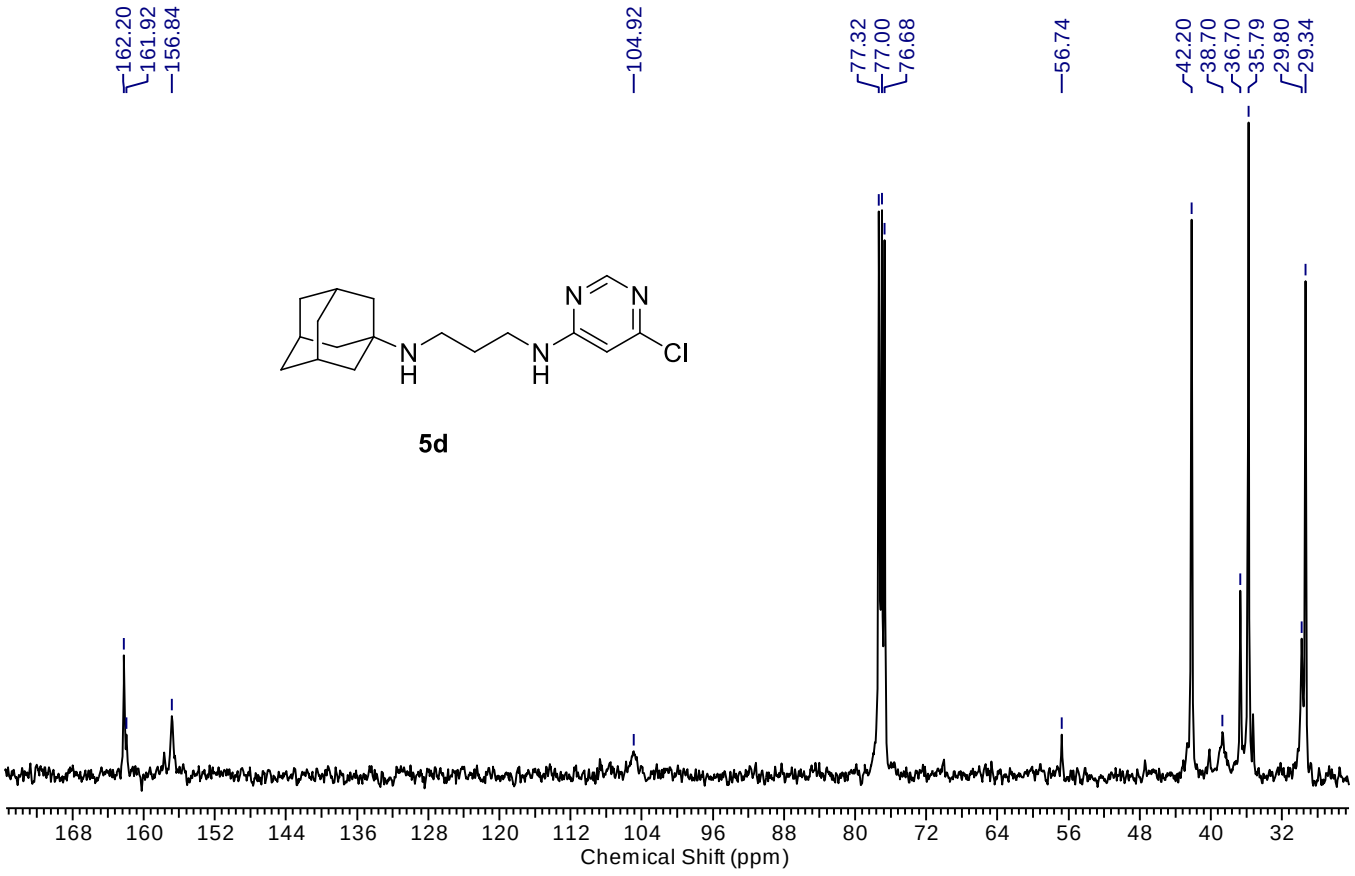


Figure S12. ^{13}C NMR spectrum of **5d** ($CDCl_3$, 100.6 MHz, 300K).

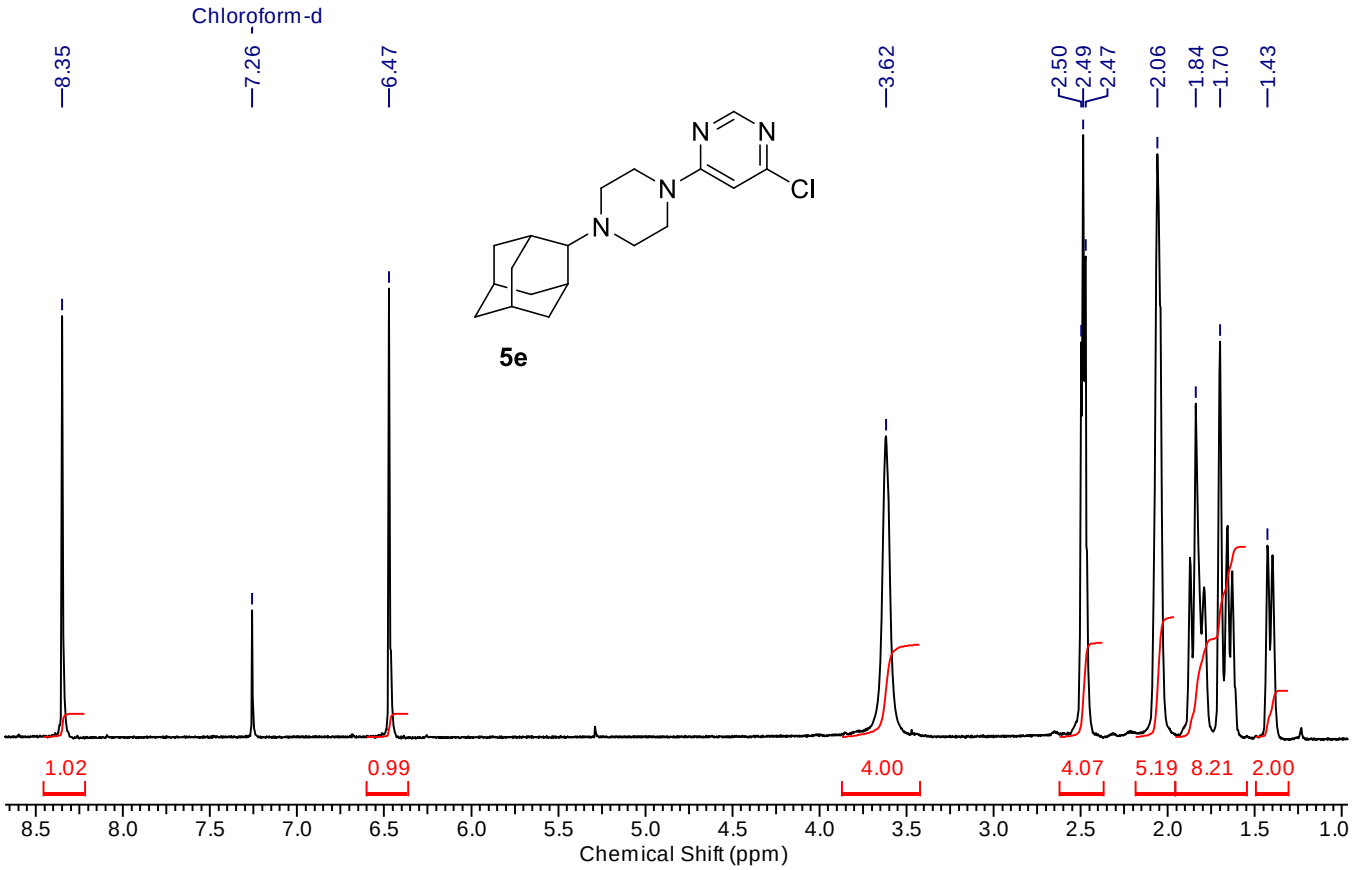


Figure S13. ^{1}H NMR spectrum of **5e** ($CDCl_3$, 400MHz, 300K).

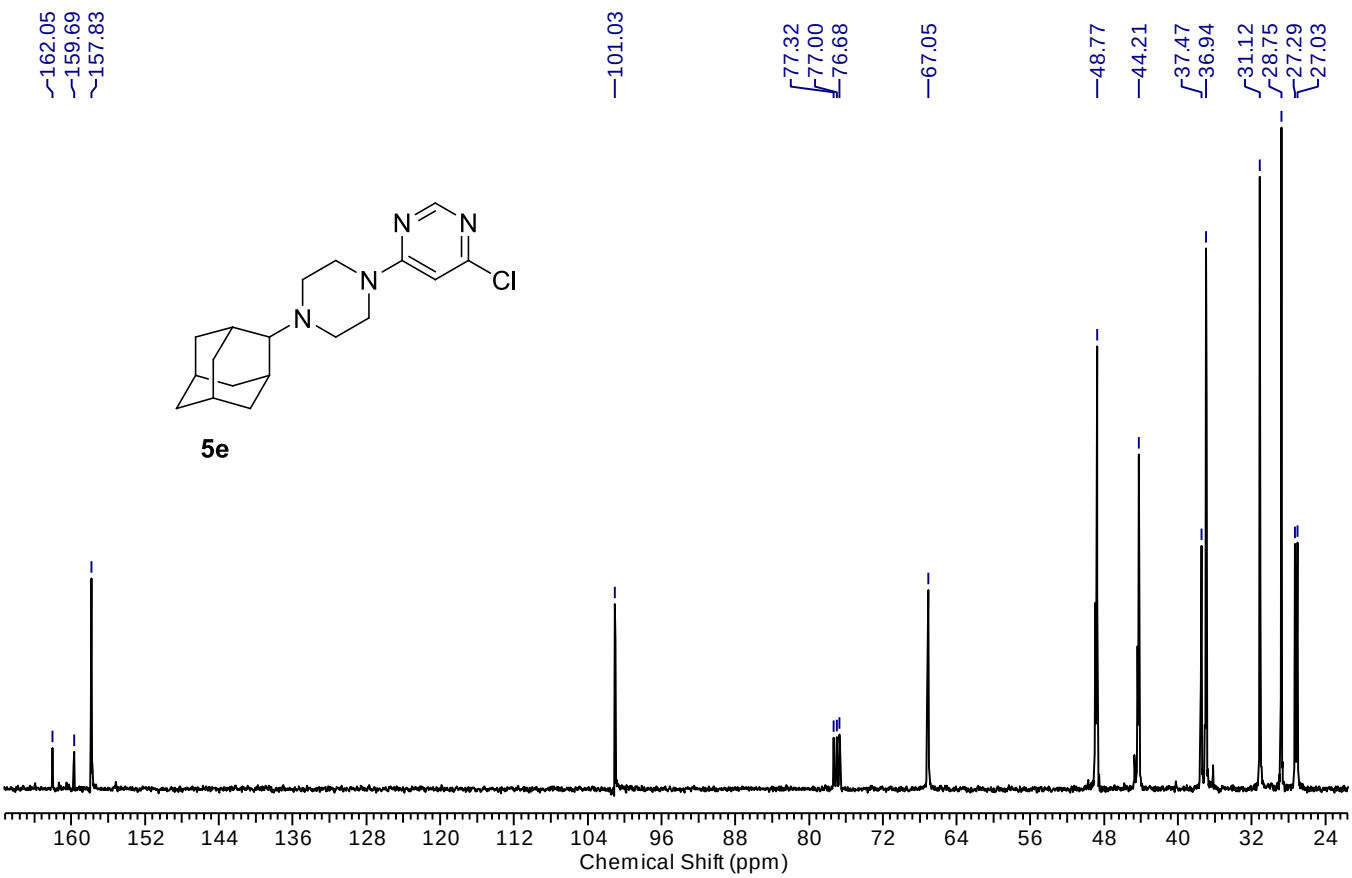


Figure S14. ^{13}C NMR spectrum of **5e** ($CDCl_3$, 100.6 MHz, 300K).

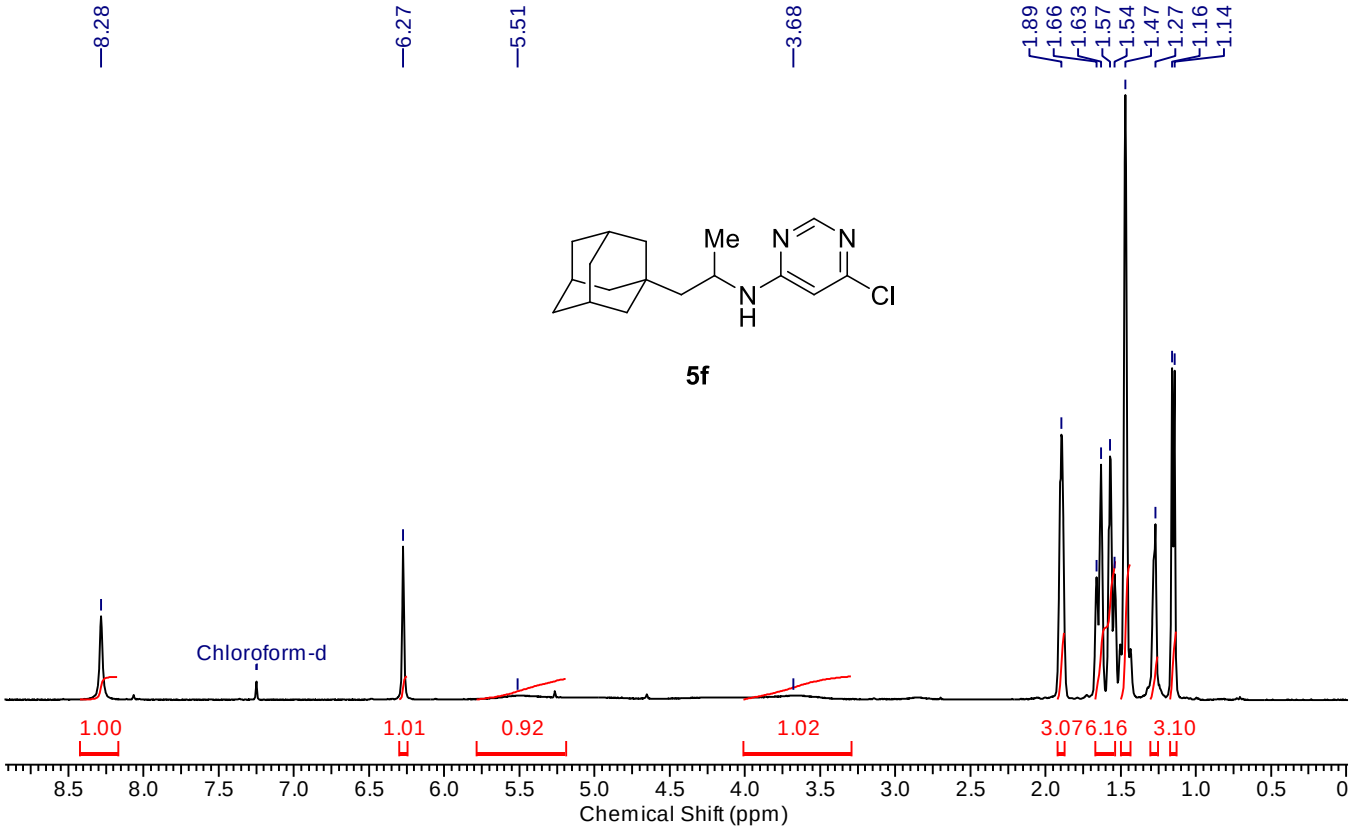


Figure S15. ^{1}H NMR spectrum of **5f** ($CDCl_3$, 400MHz, 300K).

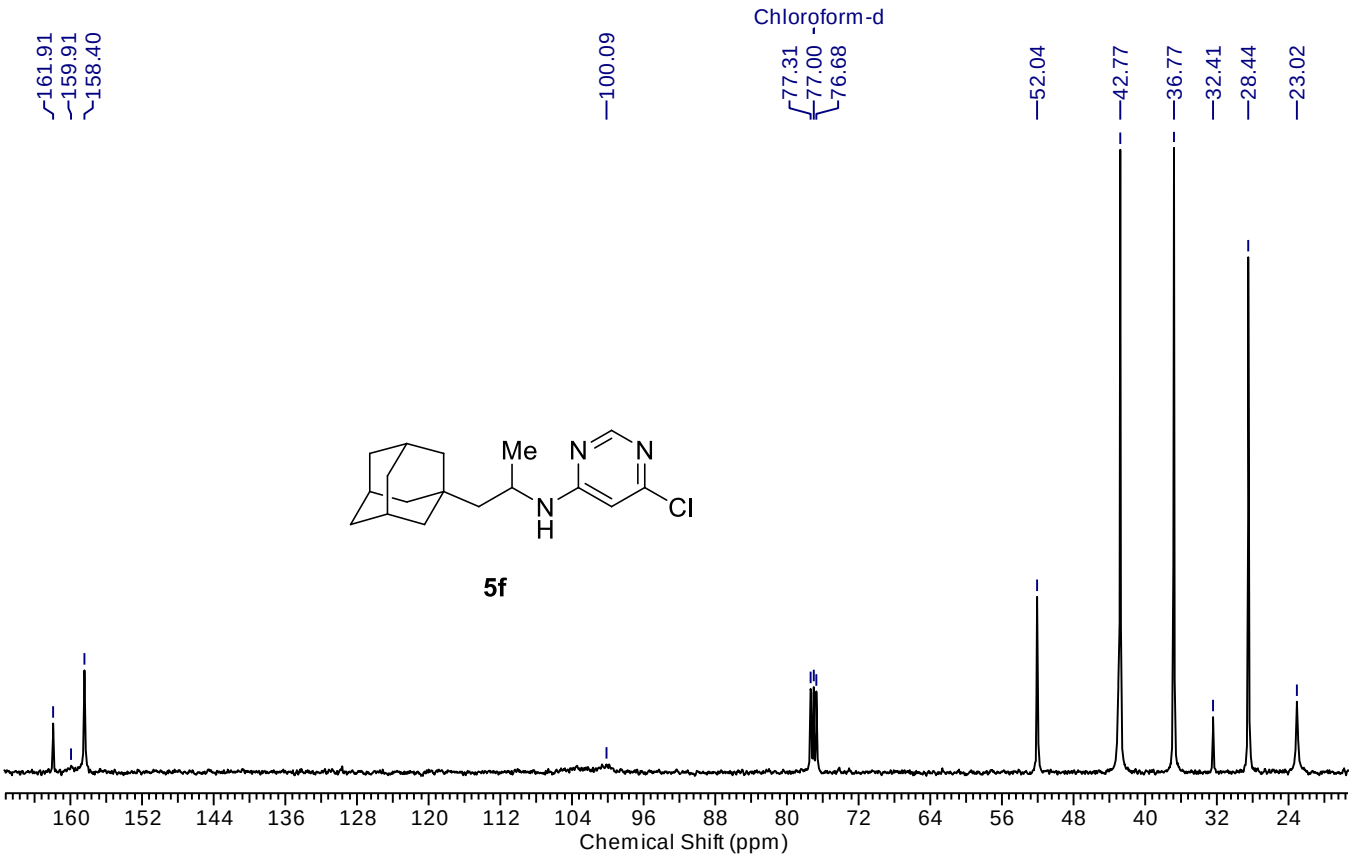


Figure S16. ^{13}C NMR spectrum of **5f** ($CDCl_3$, 100.6 MHz, 300K).

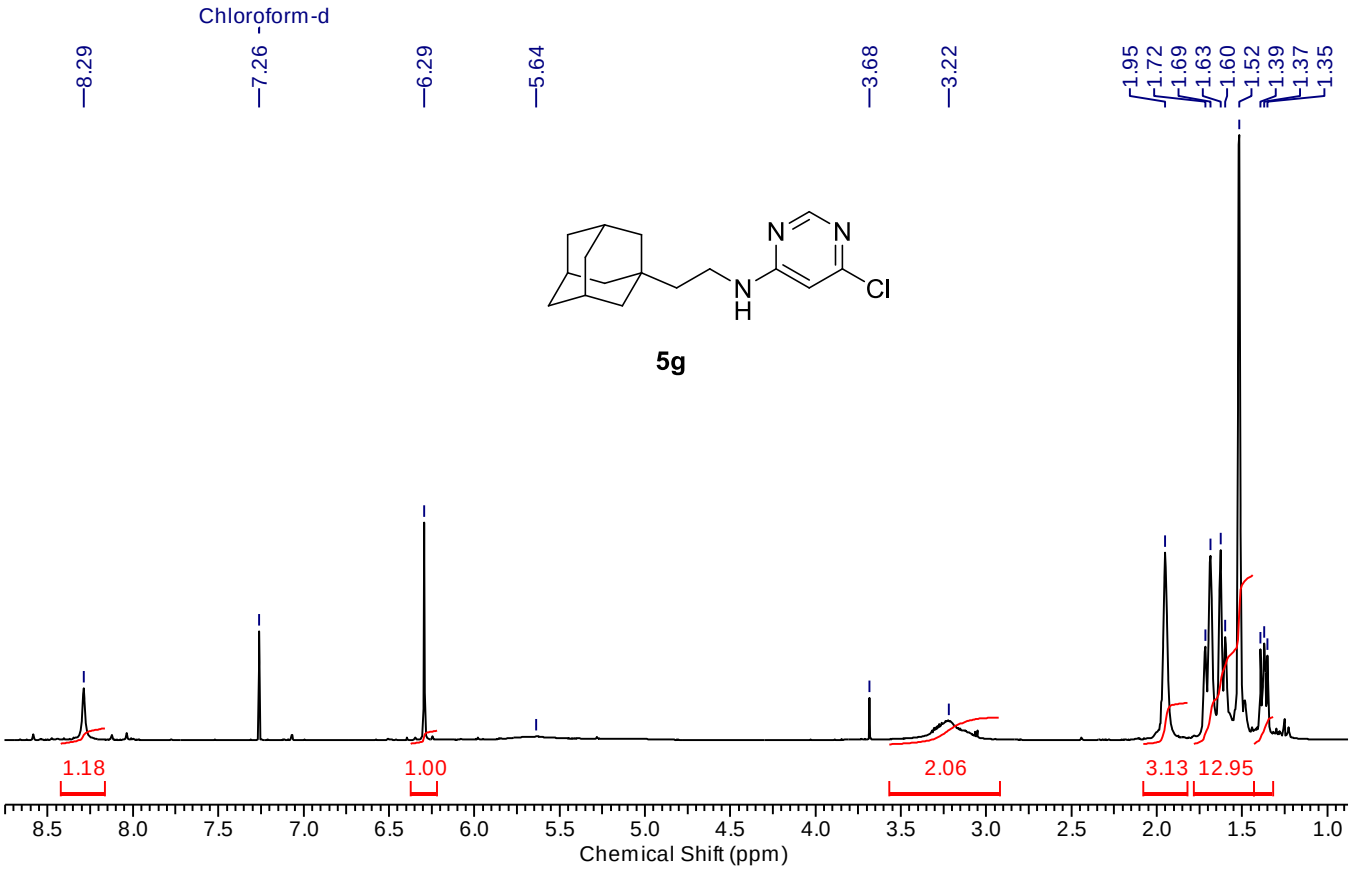


Figure S17. ^{1}H NMR spectrum of **5g** ($CDCl_3$, 400MHz, 300K).

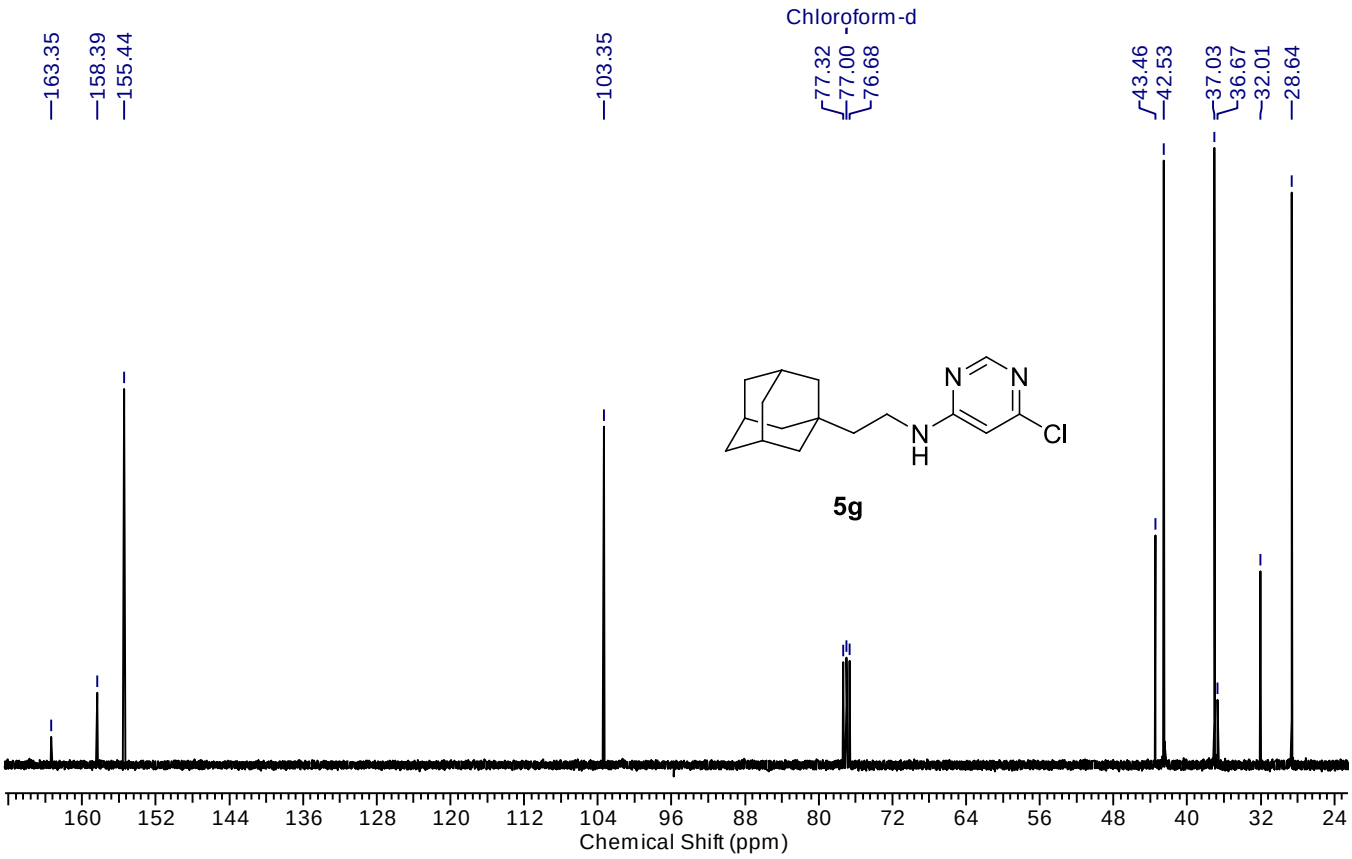


Figure S18. ^{13}C NMR spectrum of **5g** ($CDCl_3$, 100.6 MHz, 300K).

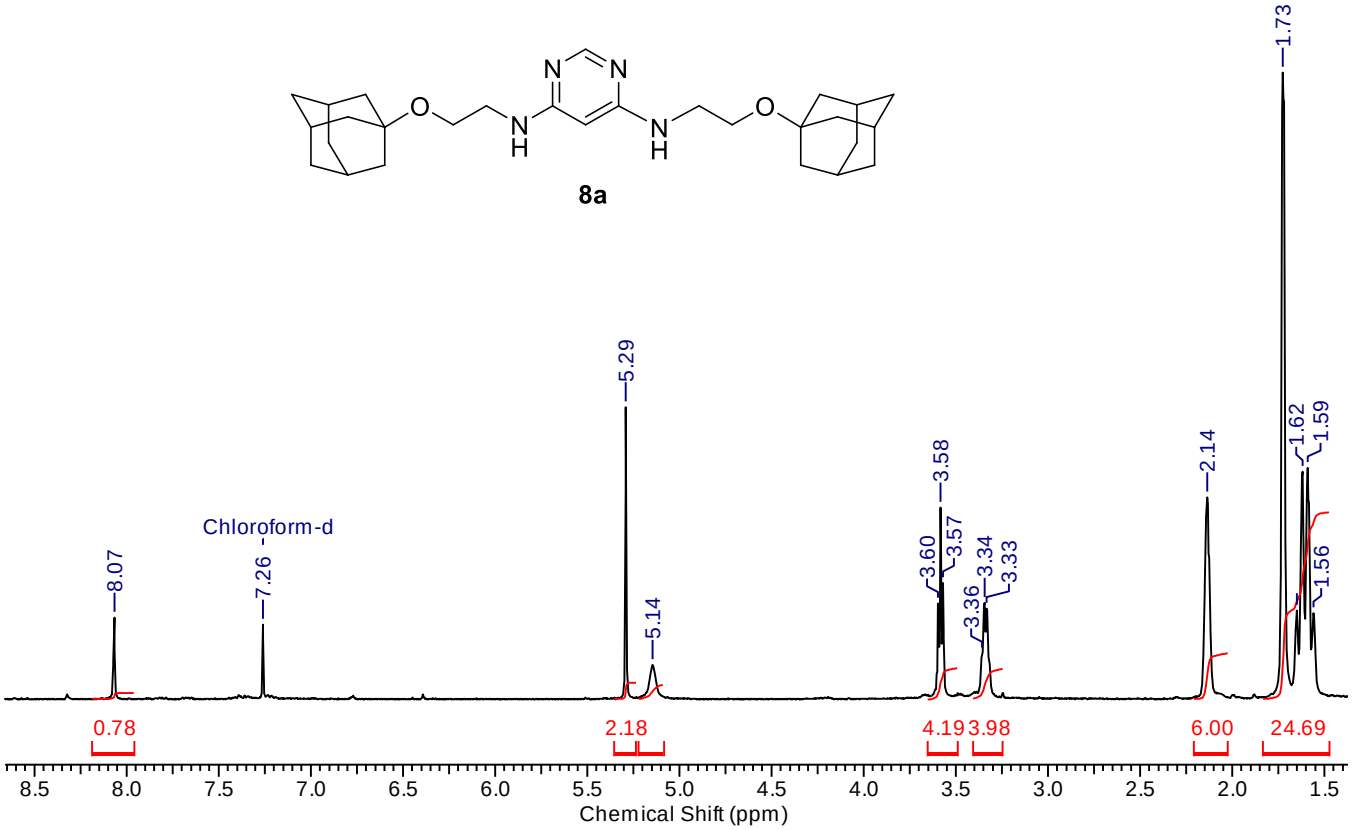


Figure S19. ^{1}H NMR spectrum of **8a** ($CDCl_3$, 400MHz, 300K).

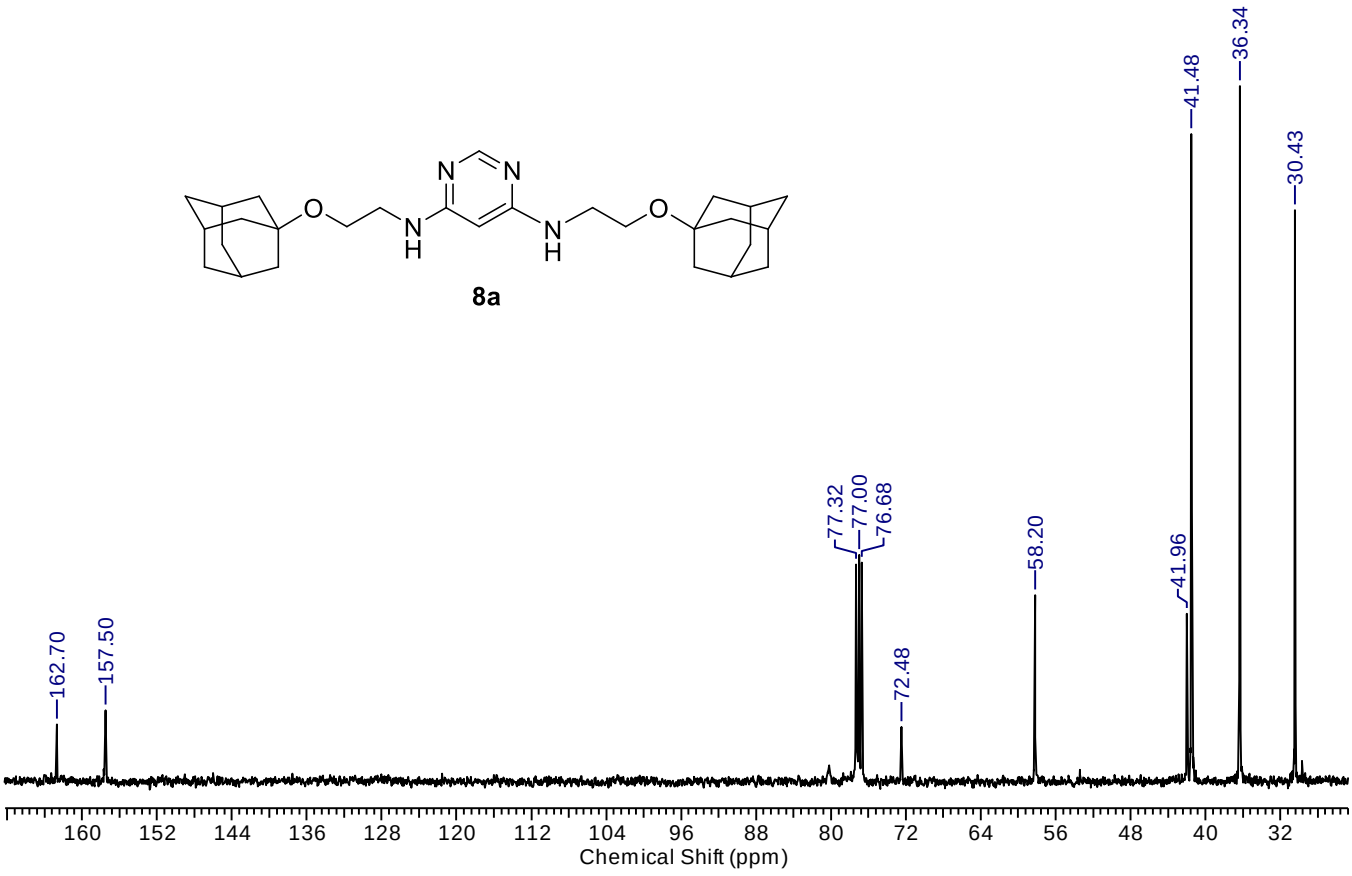


Figure S20. ^{13}C NMR spectrum of **8a** ($CDCl_3$, 100.6 MHz, 300K).

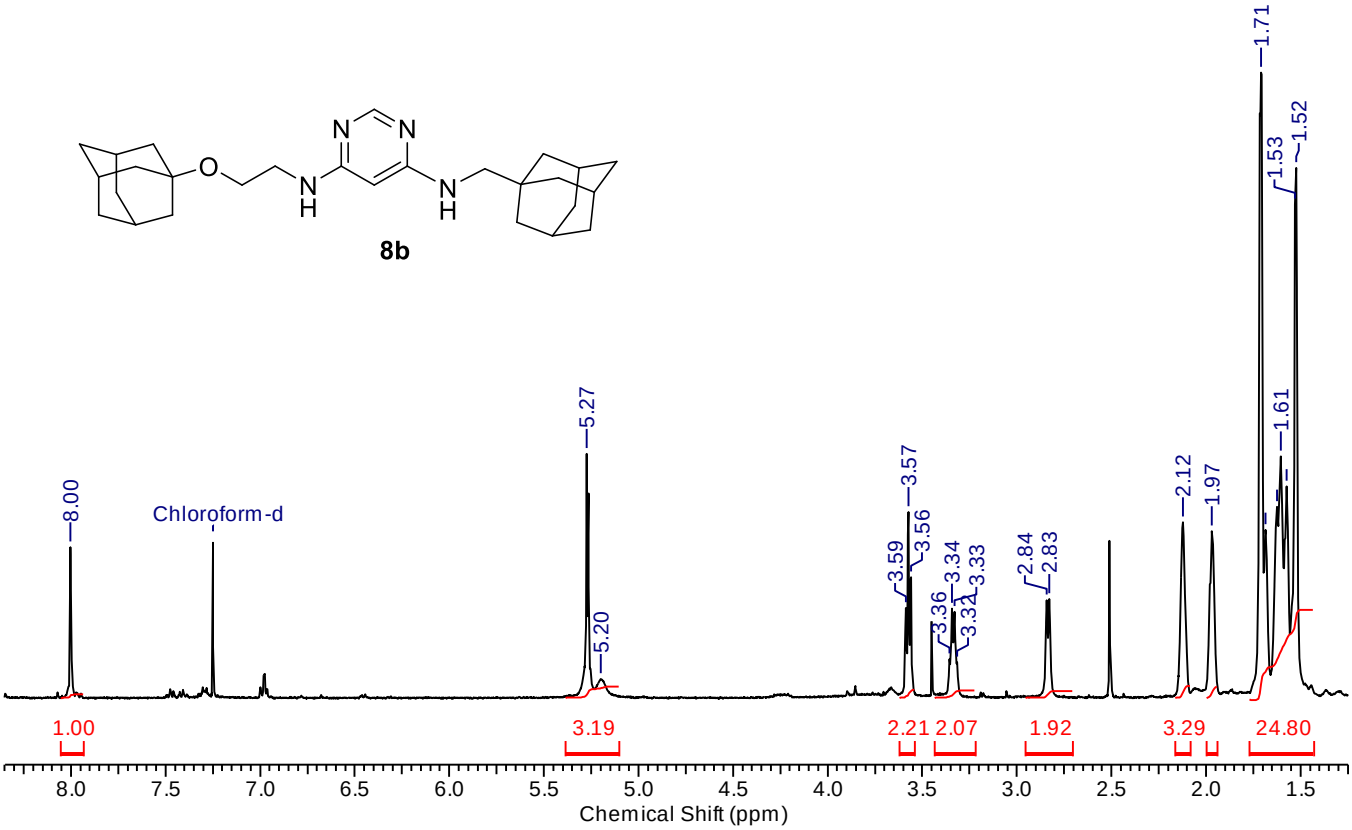


Figure S21. ^{1}H NMR spectrum of **8b** ($CDCl_3$, 400MHz, 300K).

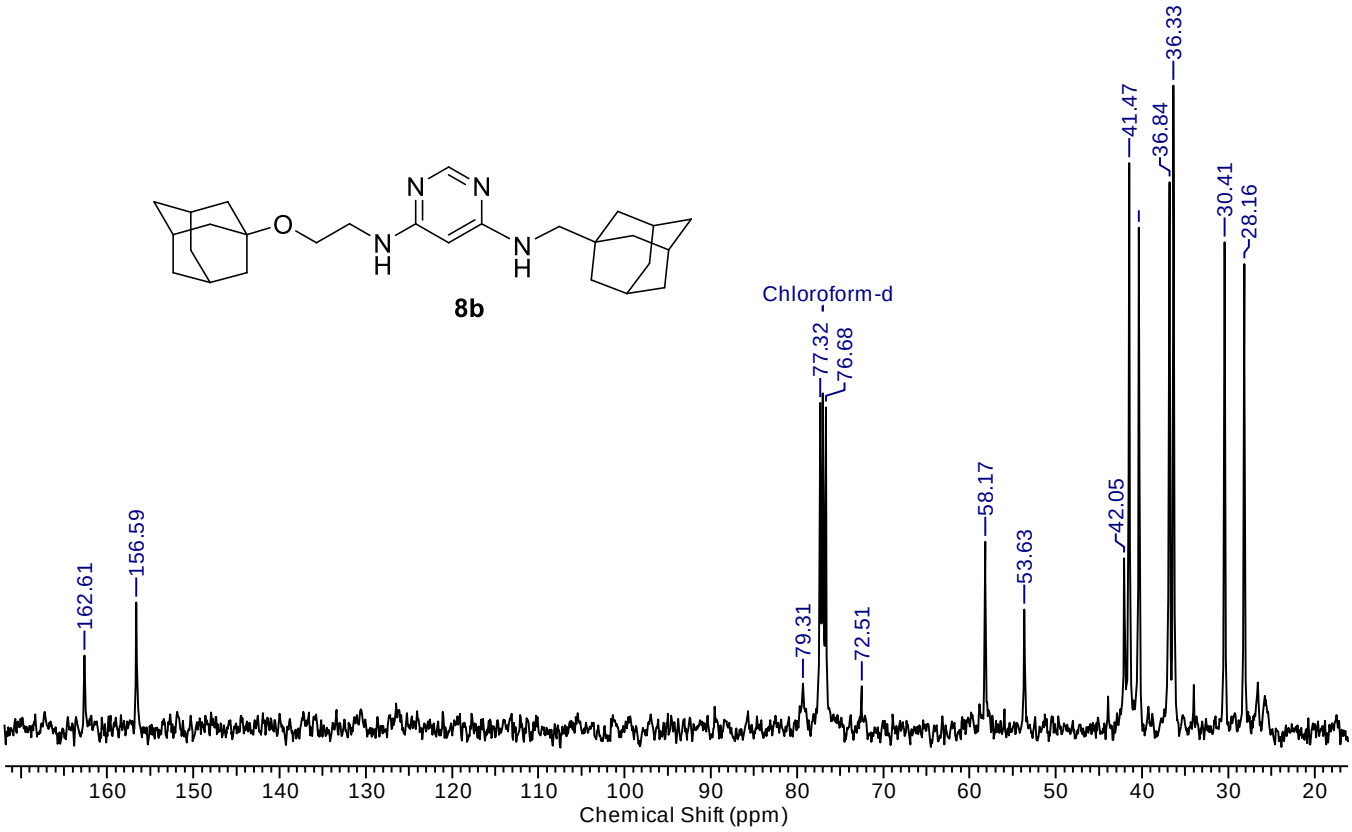


Figure S22. ^{13}C NMR spectrum of **8b** ($CDCl_3$, 100.6 MHz, 300K).

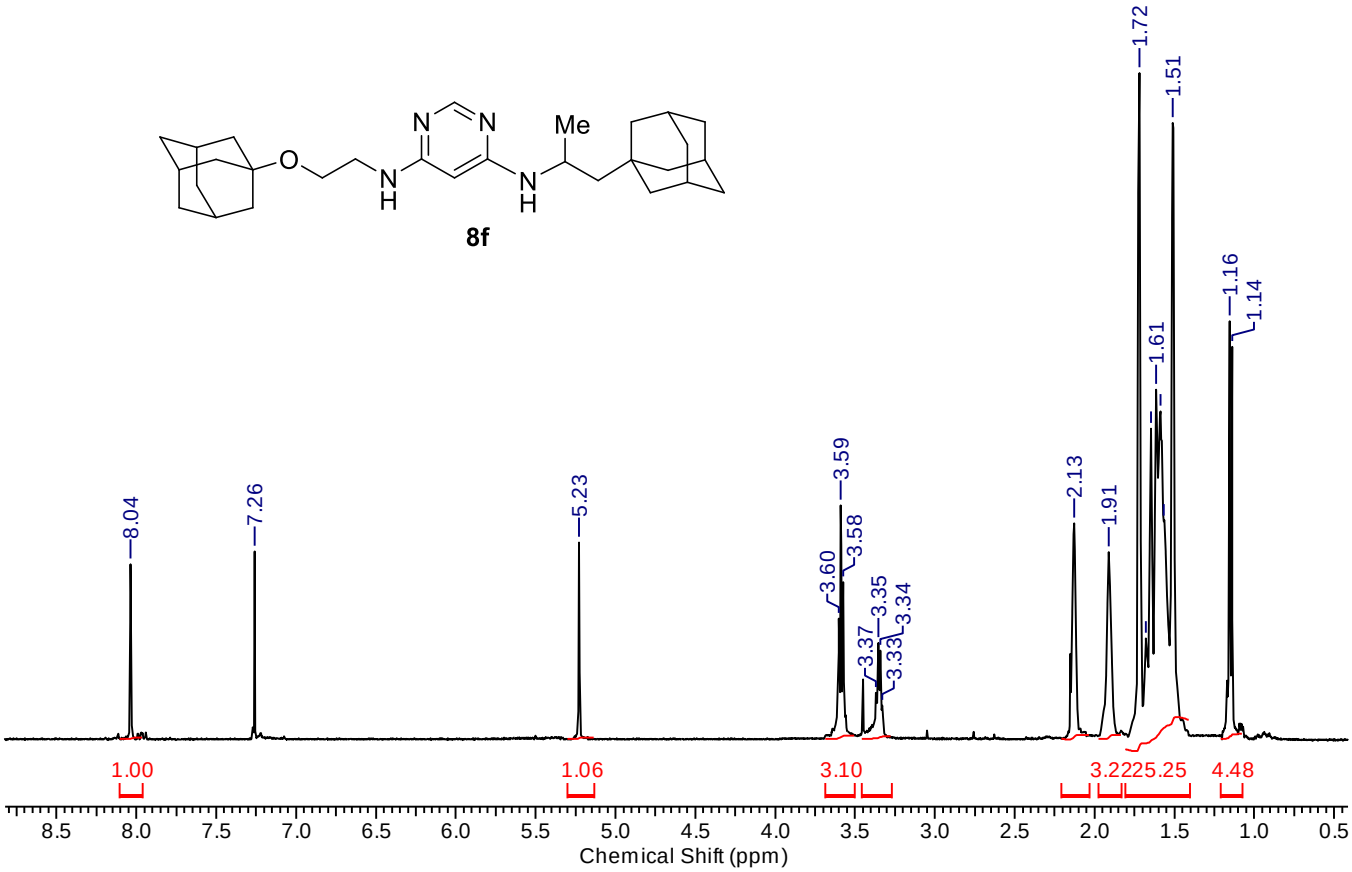


Figure S23. ^{1}H NMR spectrum of **8f** ($CDCl_3$, 400MHz, 300K).

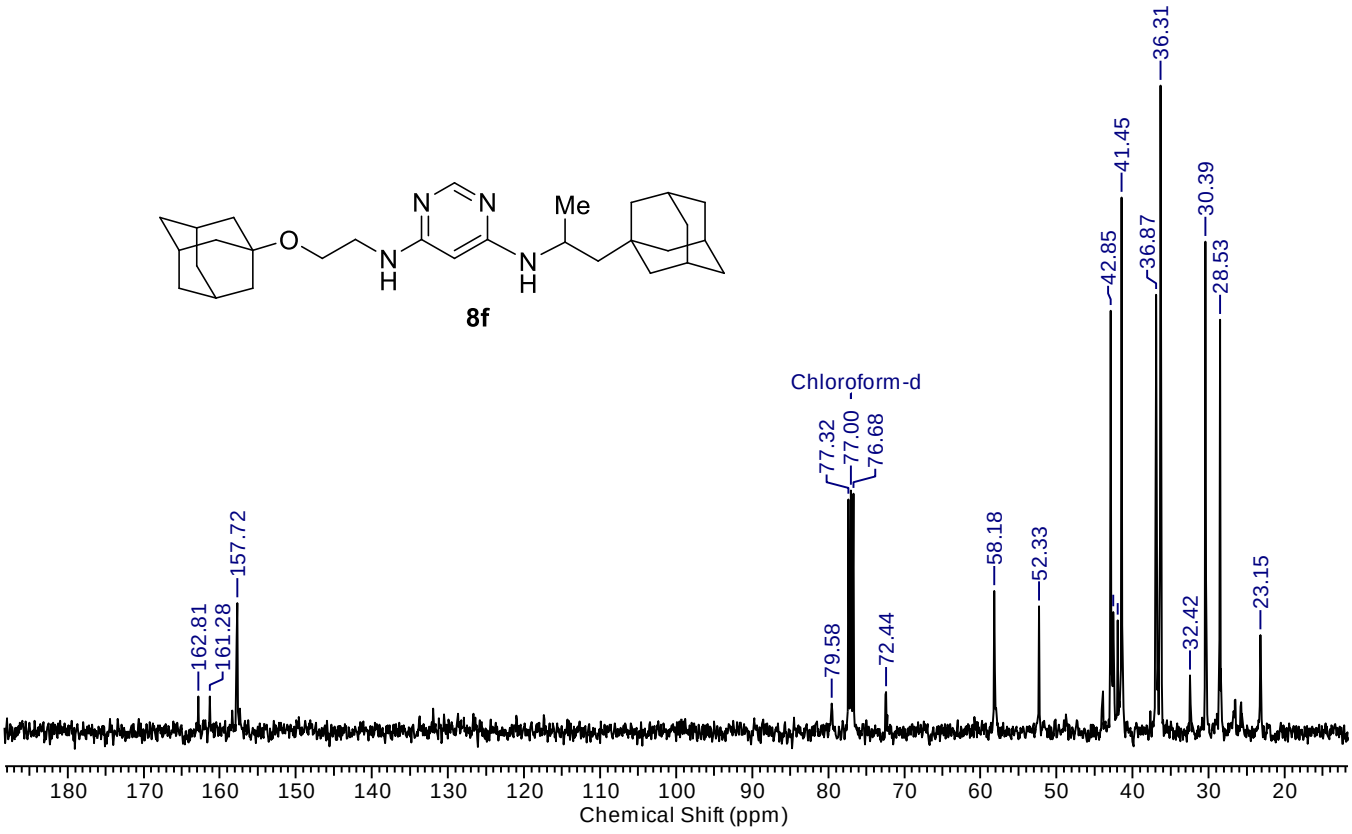


Figure S24. ^{13}C NMR spectrum of **8f** ($CDCl_3$, 100.6 MHz, 300K).

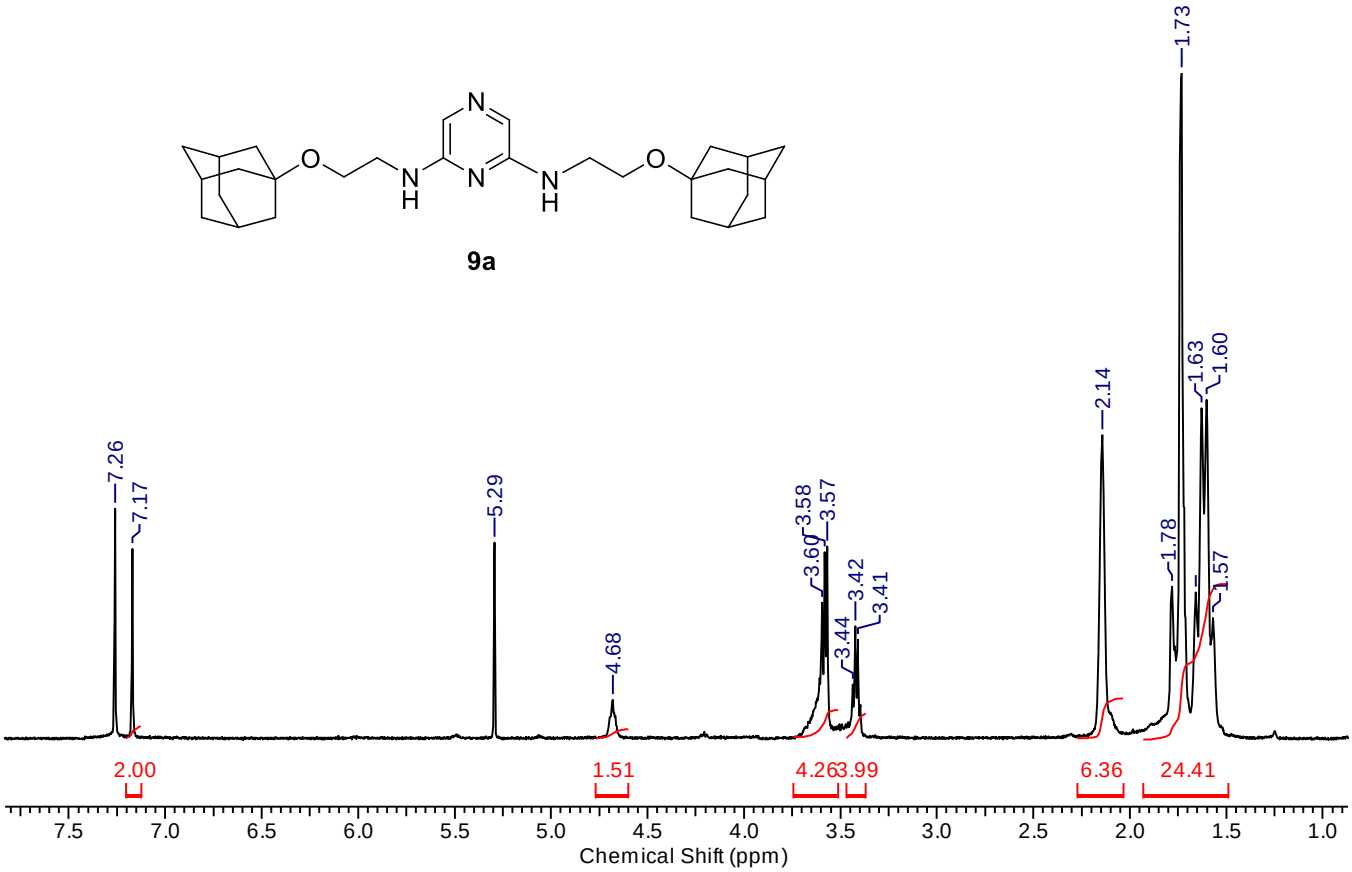


Figure S25. ^{1}H NMR spectrum of **9a** ($CDCl_3$, 400MHz, 300K).

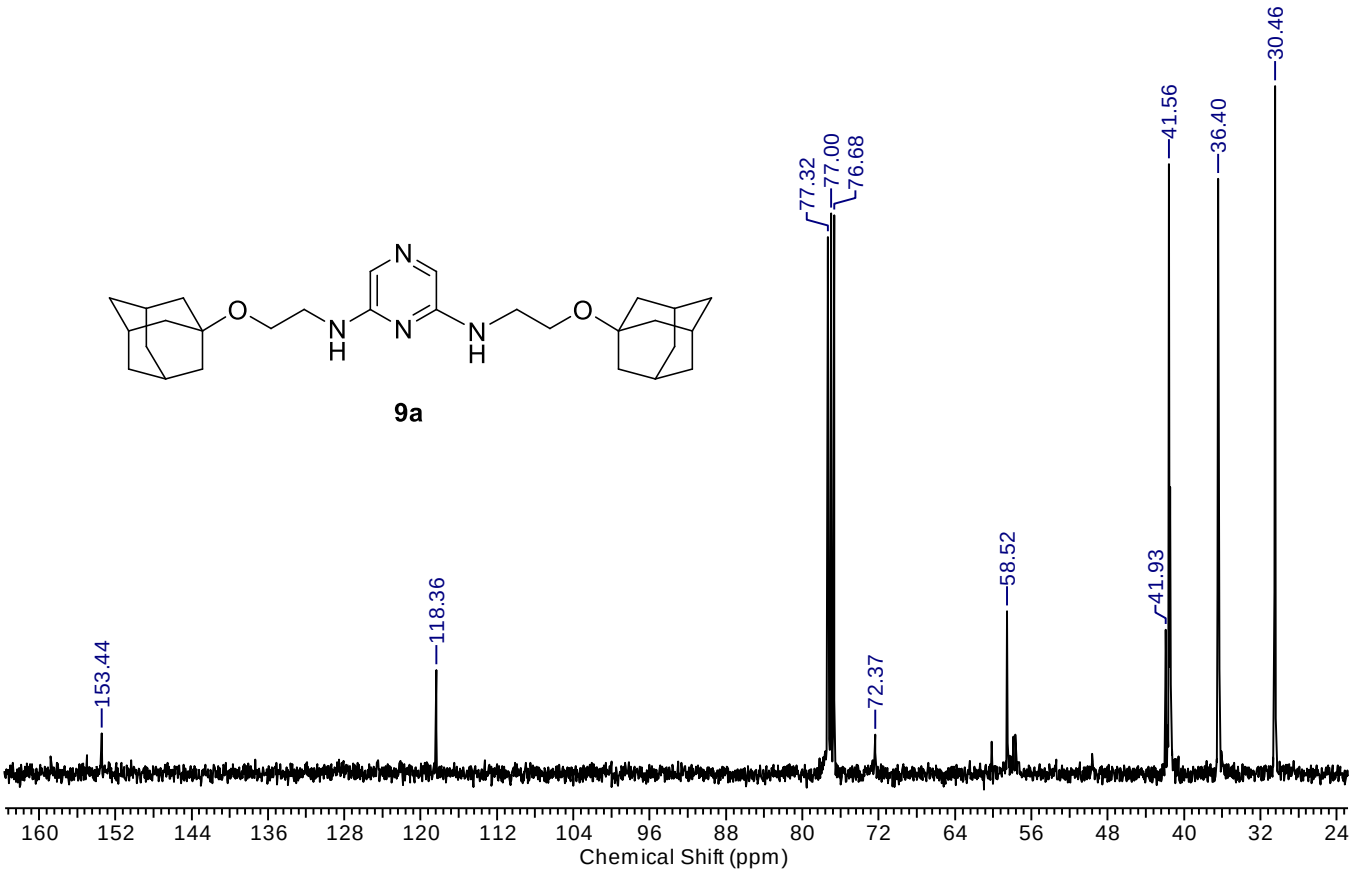


Figure S26. ^{13}C NMR spectrum of **9a** ($CDCl_3$, 100.6 MHz, 300K).

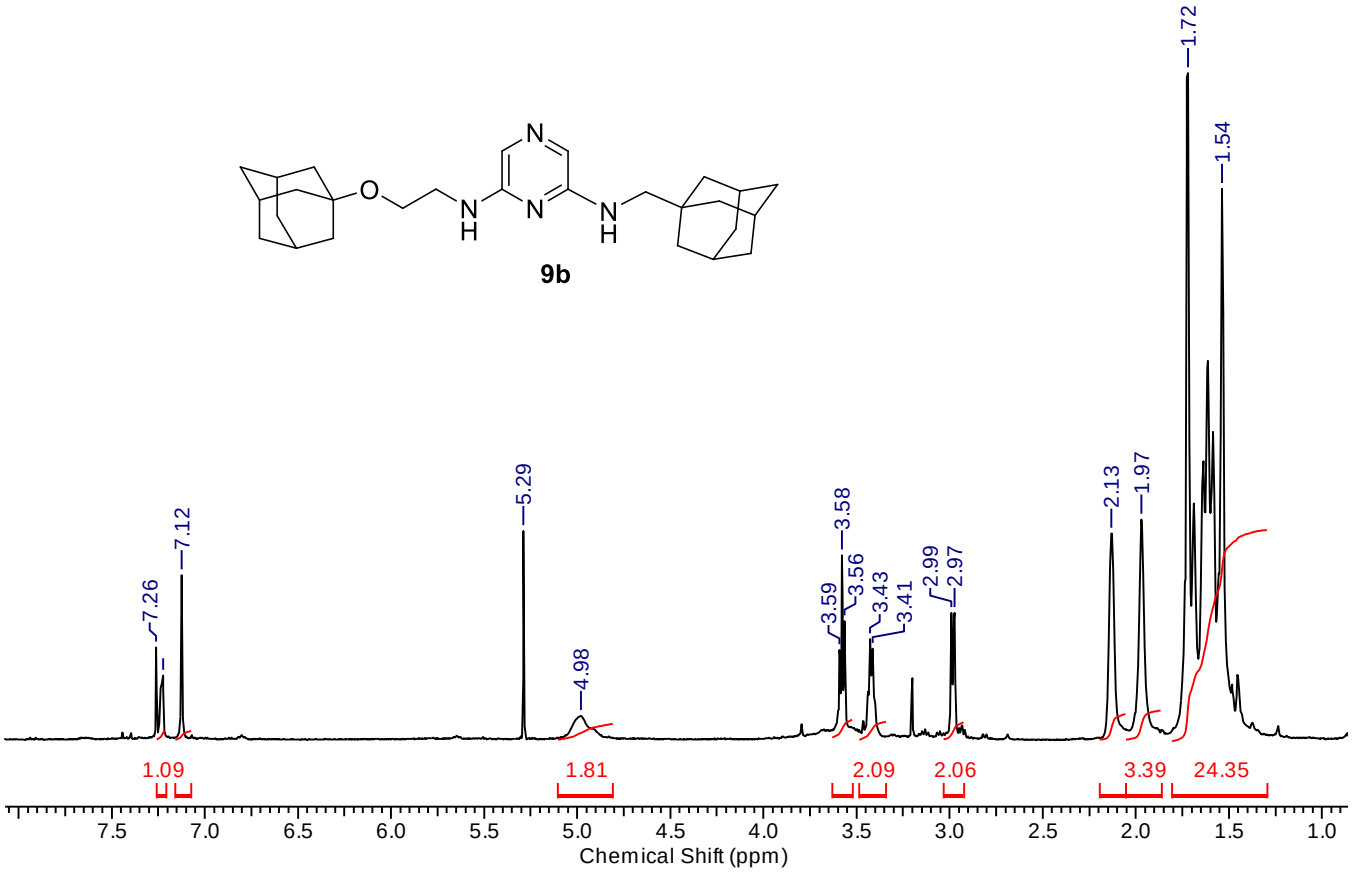


Figure S27. ^{1}H NMR spectrum of **9b** ($CDCl_3$, 400MHz, 300K).

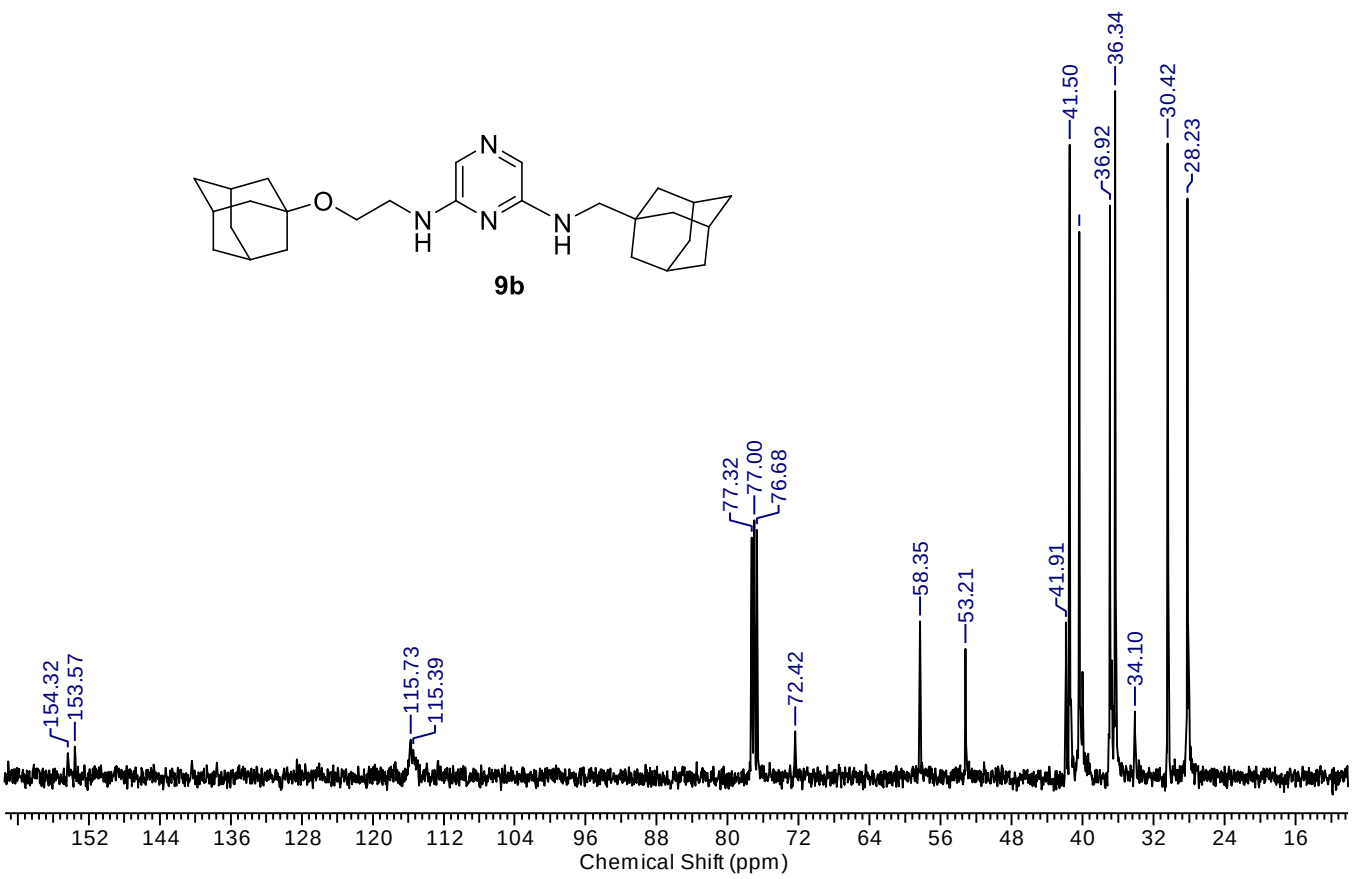


Figure S28. ^{13}C NMR spectrum of **9b** ($CDCl_3$, 100.6 MHz, 300K).

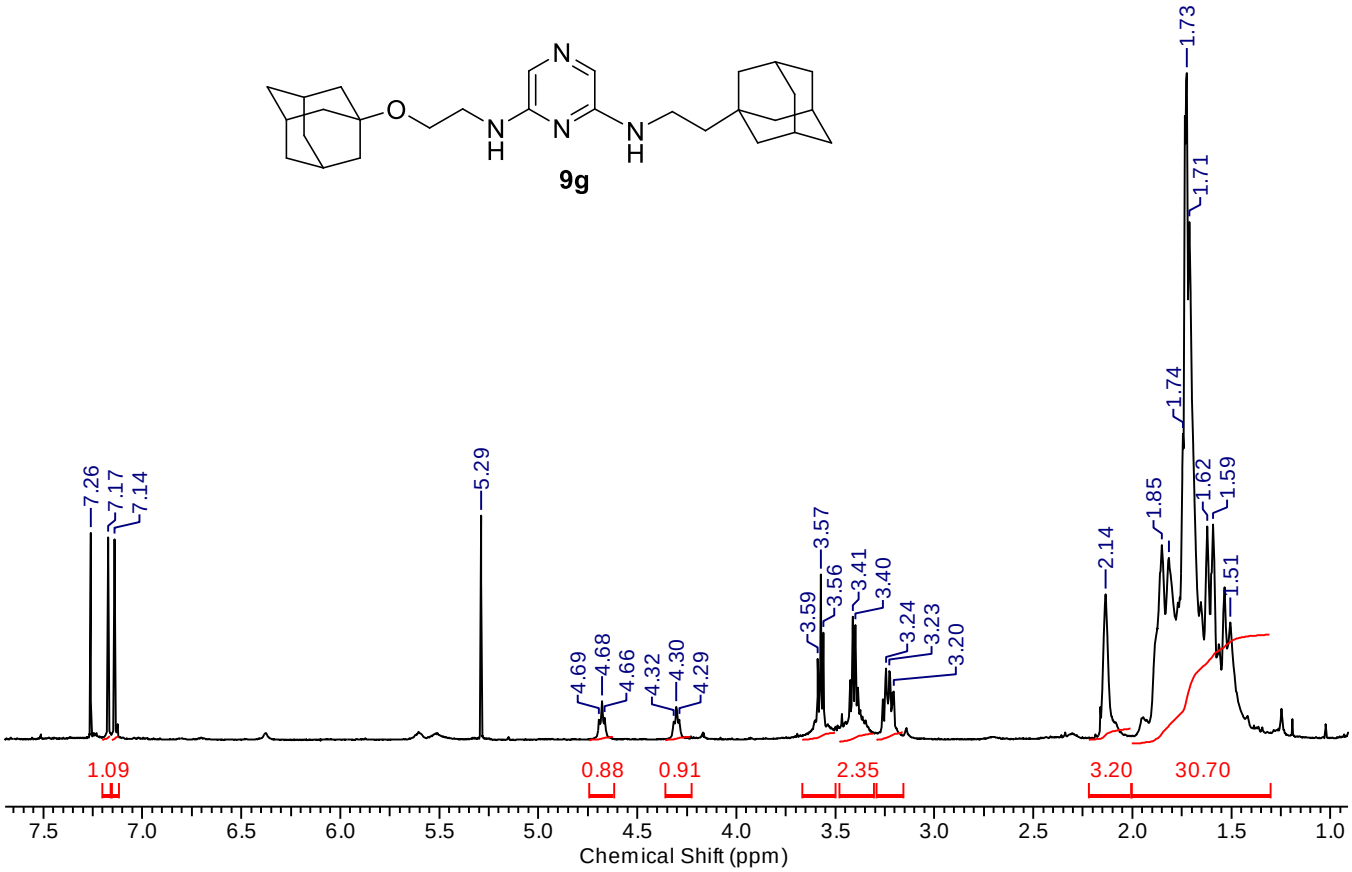


Figure S29. ^{1}H NMR spectrum of **9g** ($CDCl_3$, 400MHz, 300K).

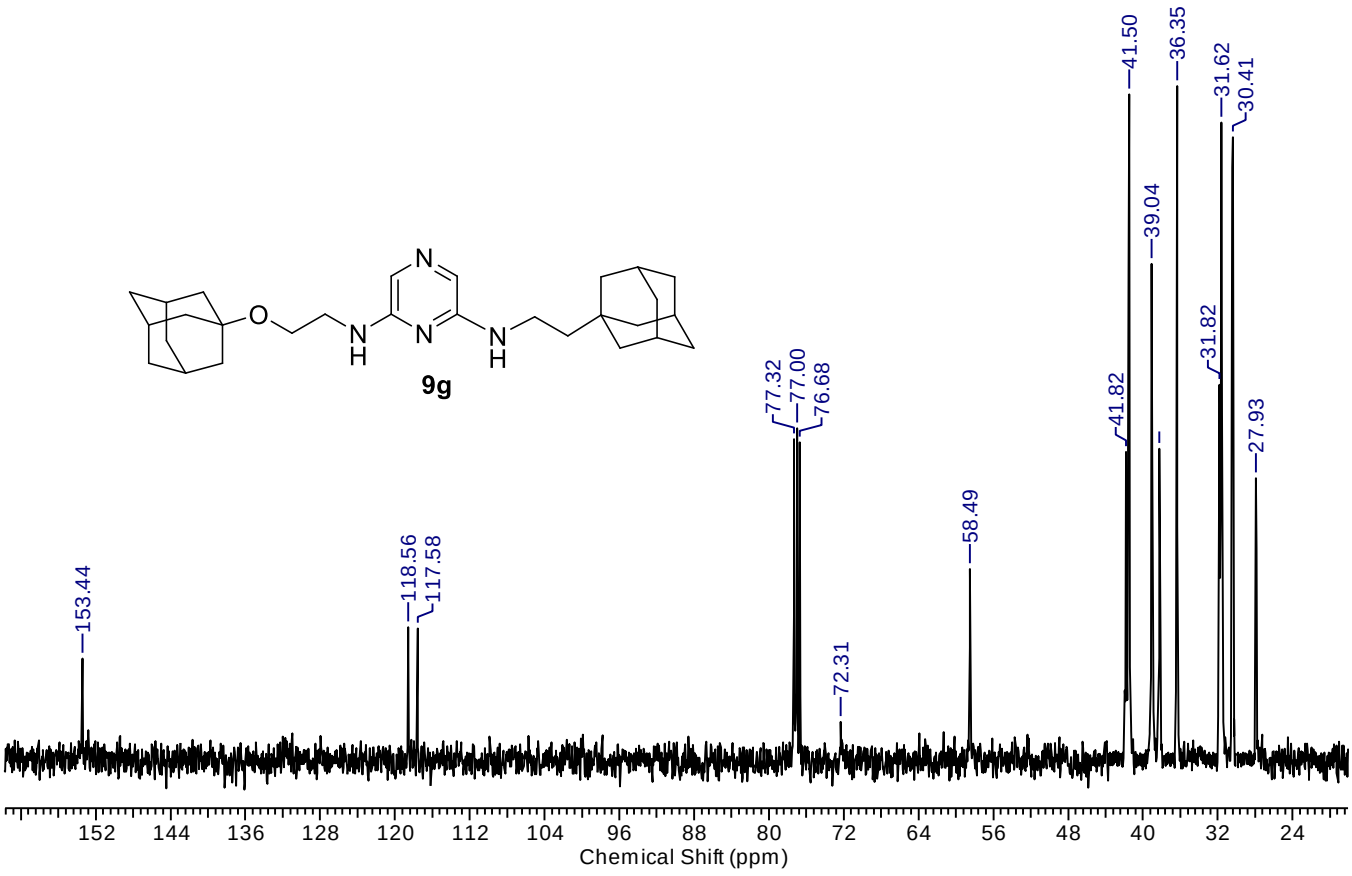


Figure S30. ^{13}C NMR spectrum of **9g** ($CDCl_3$, 100.6 MHz, 300K).

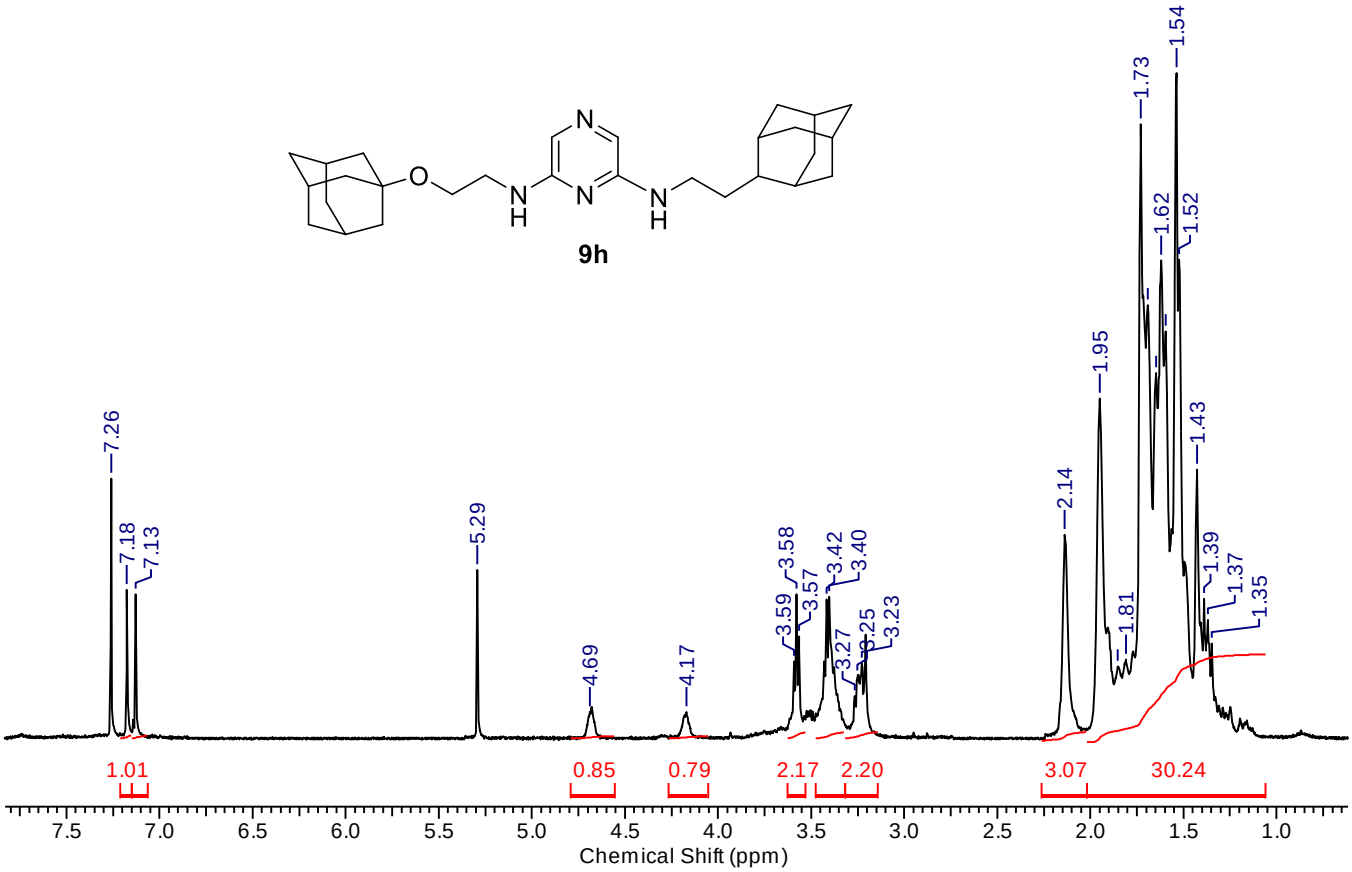


Figure S31. ^{1}H NMR spectrum of **9h** ($CDCl_3$, 400MHz, 300K).

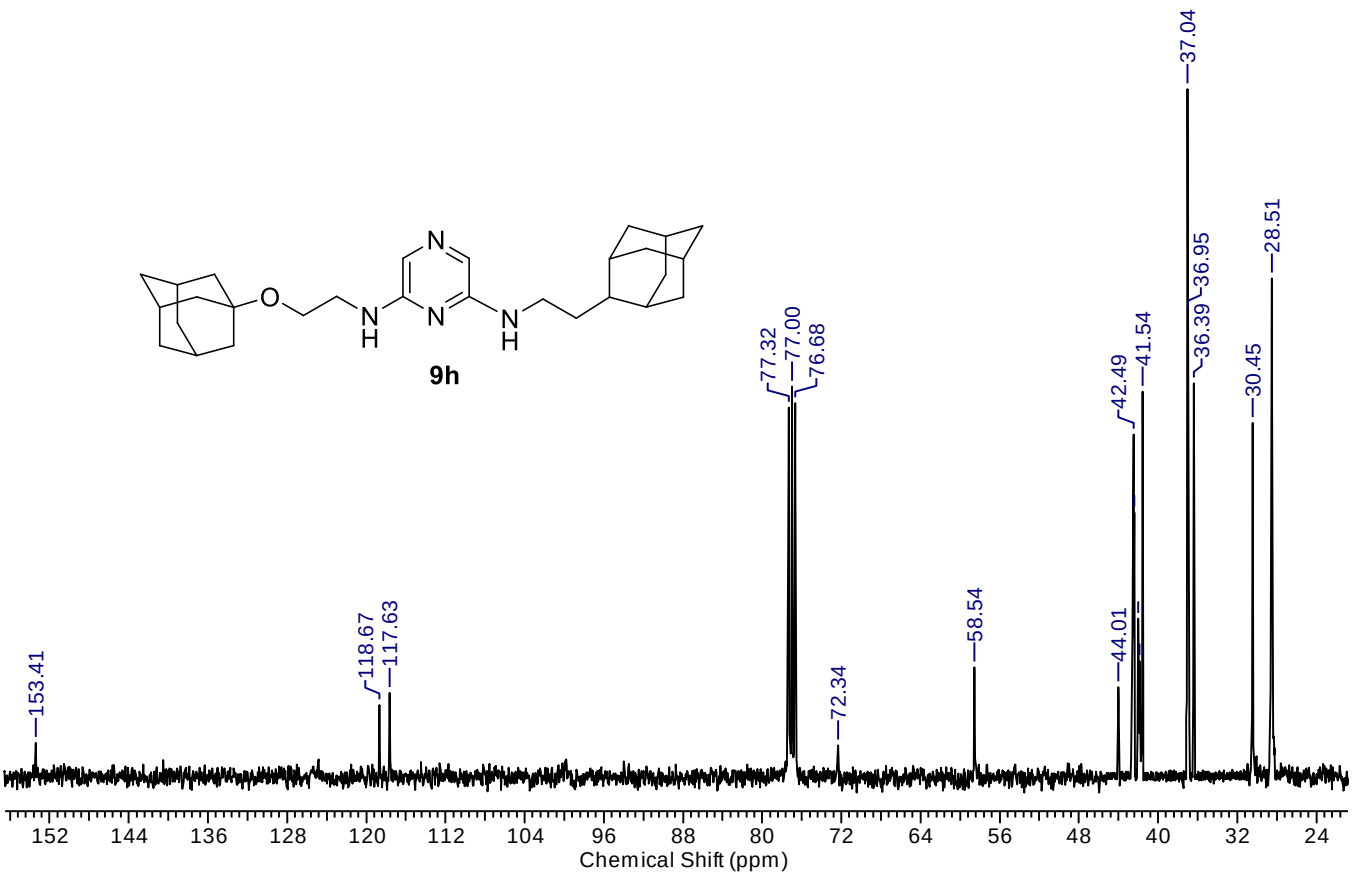


Figure S32. ^{13}C NMR spectrum of **9h** ($CDCl_3$, 100.6 MHz, 300K).

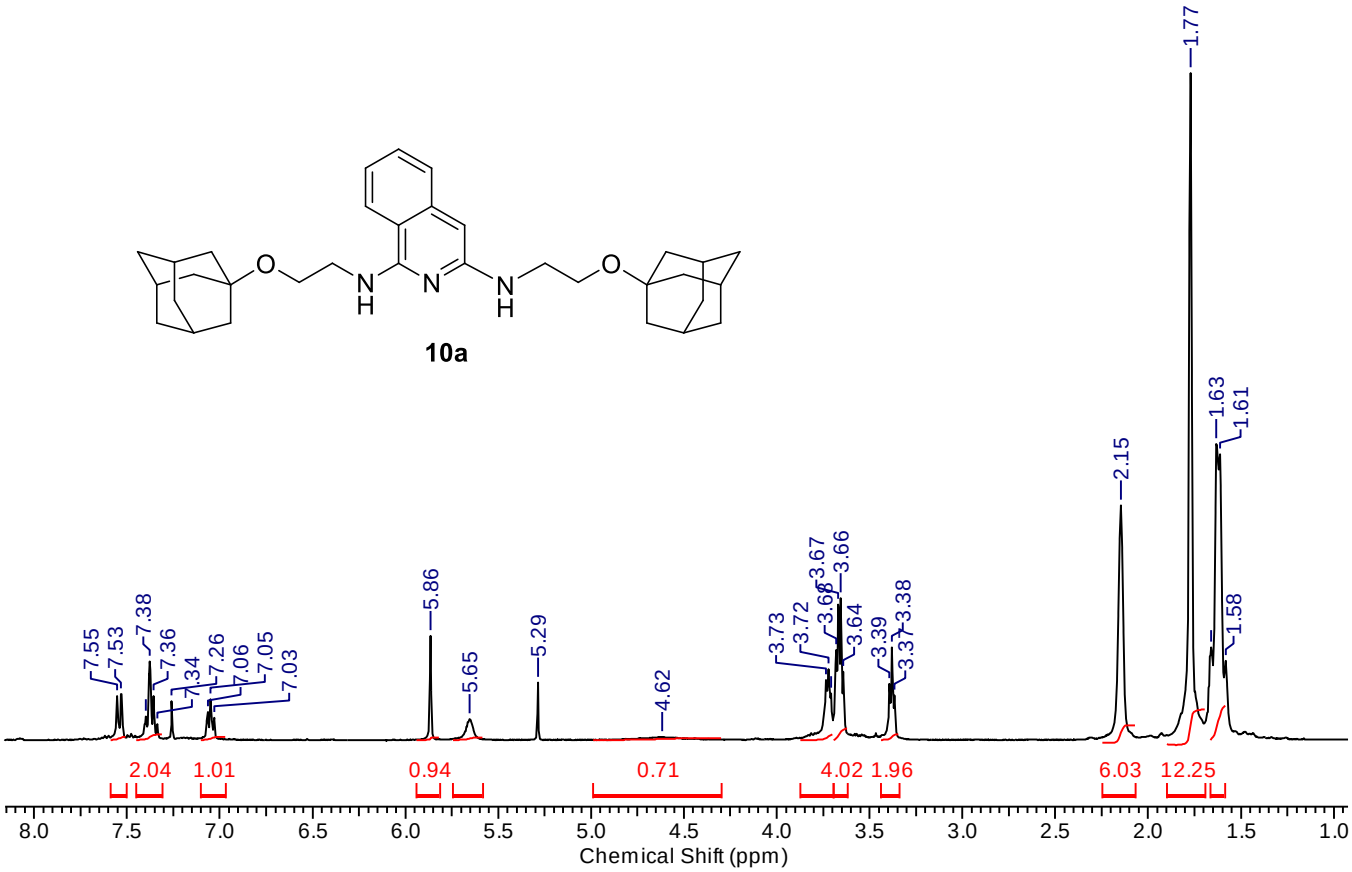


Figure S33. ^{1}H NMR spectrum of **10a** ($CDCl_3$, 400MHz, 300K).

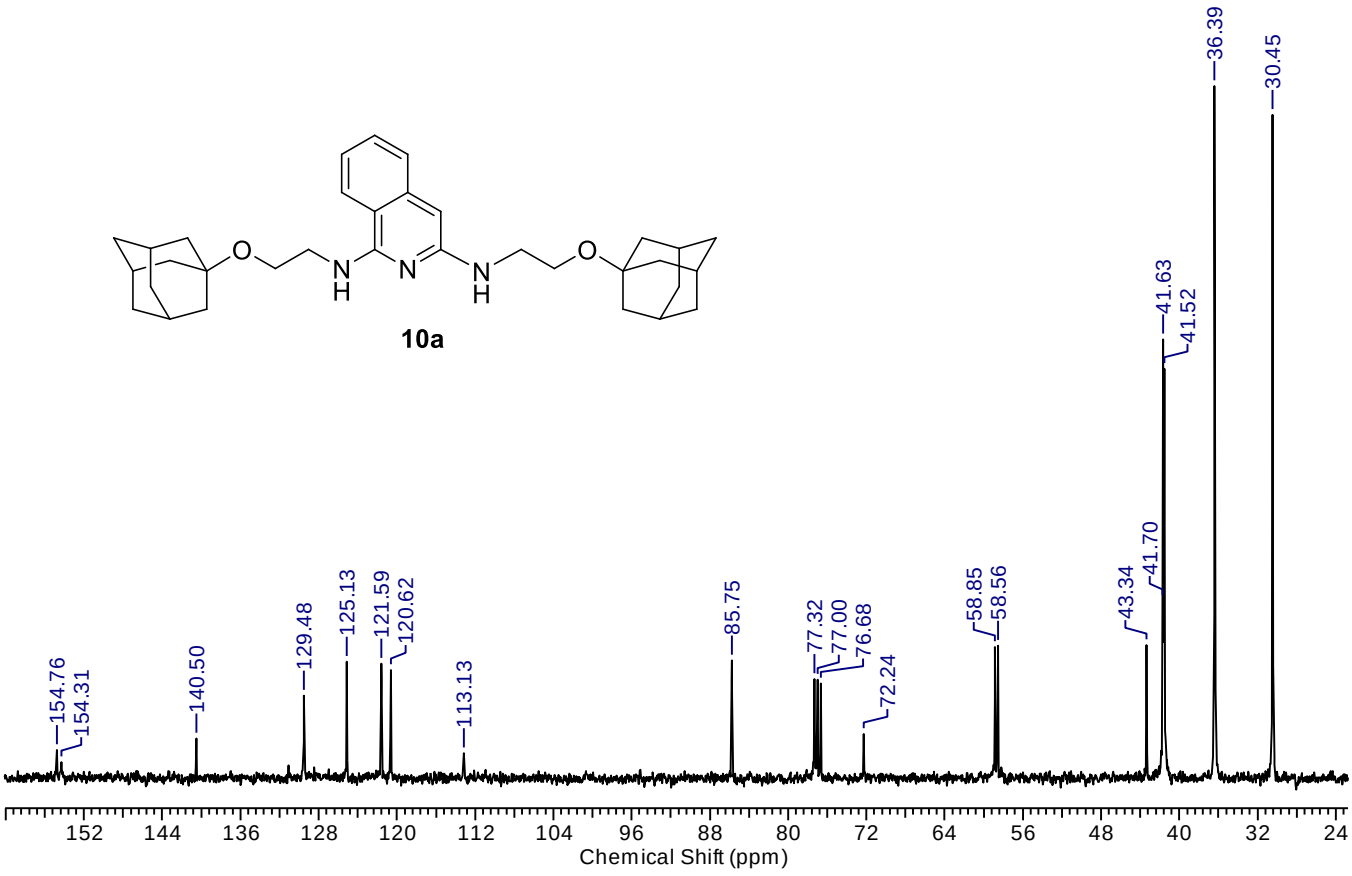


Figure S34. ^{13}C NMR spectrum of **10a** ($CDCl_3$, 100.6 MHz, 300K).

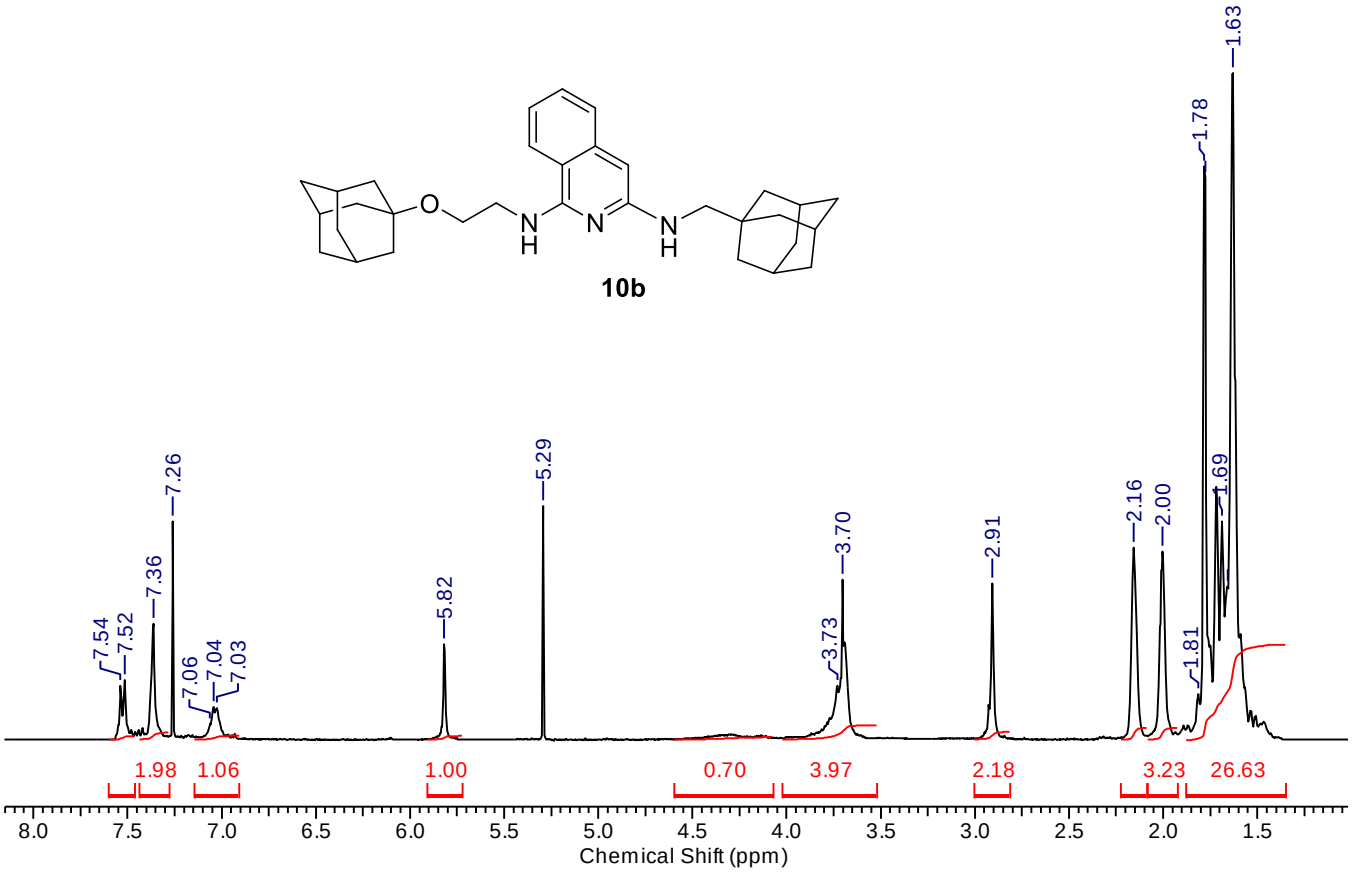


Figure S35. ^{1}H NMR spectrum of **10b** ($CDCl_3$, 400MHz, 300K).

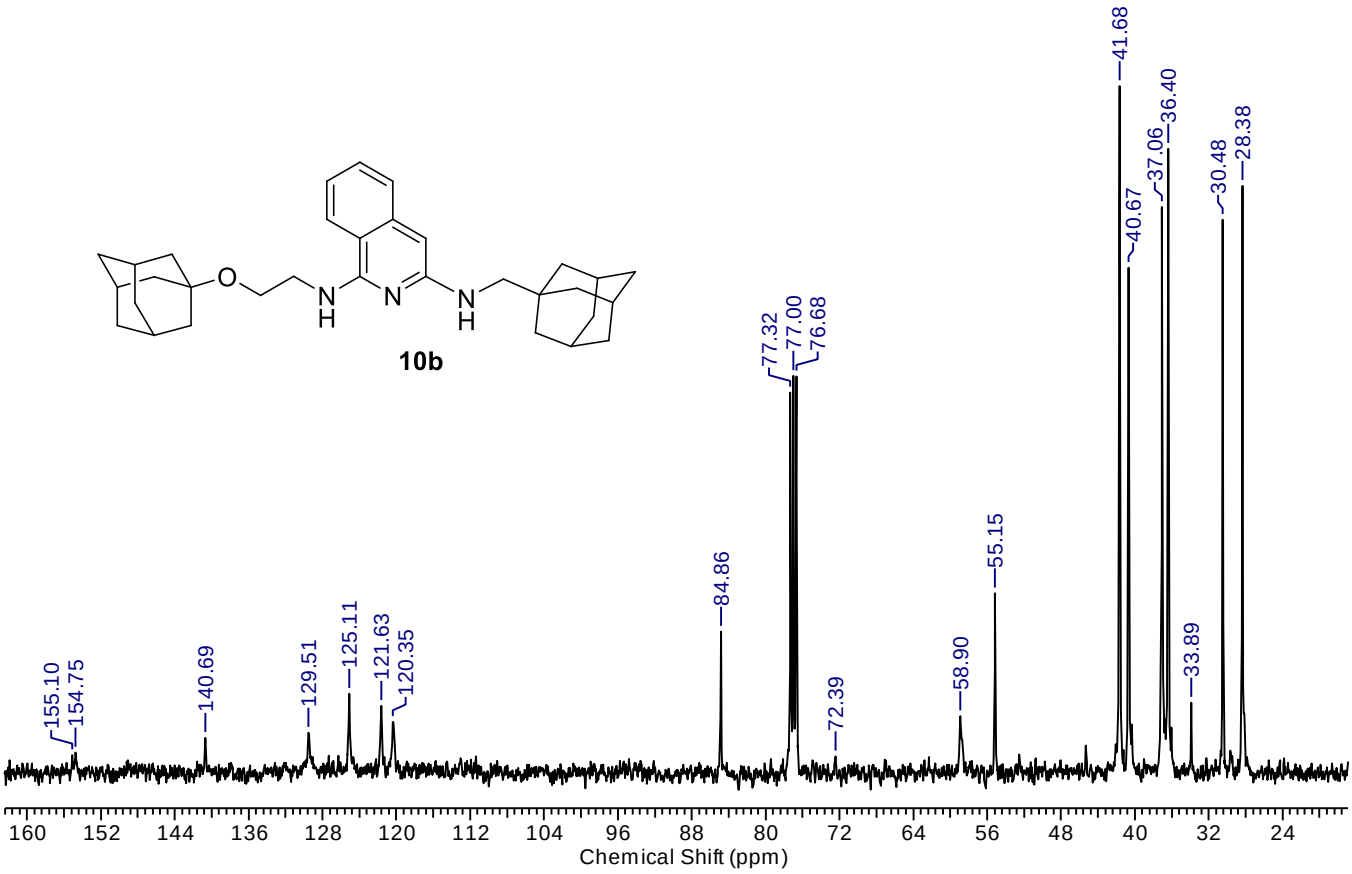


Figure S36. ^{13}C NMR spectrum of **10b** ($CDCl_3$, 100.6 MHz, 300K).

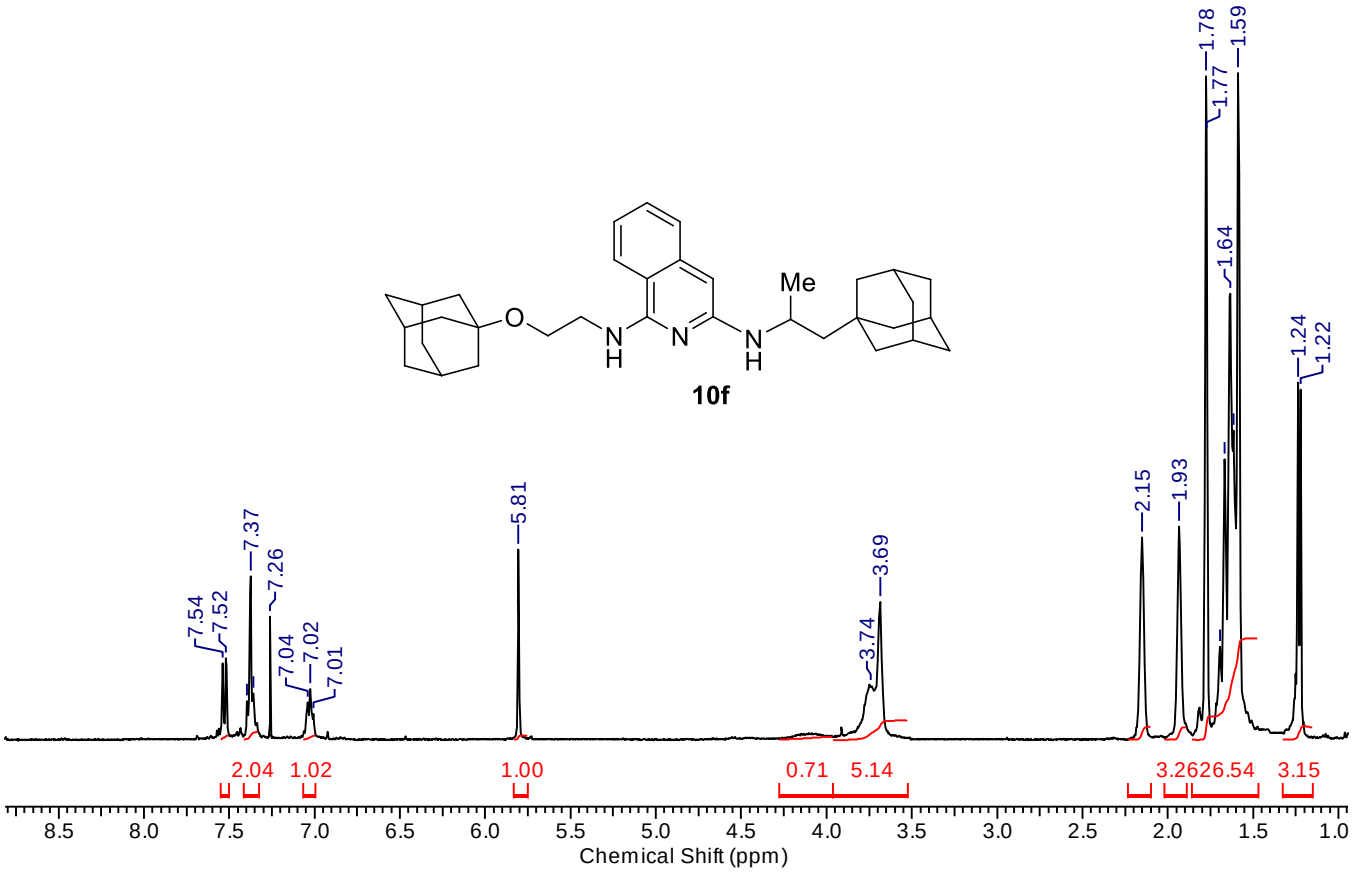


Figure S37. ^{1}H NMR spectrum of **10f** ($CDCl_3$, 400MHz, 300K).

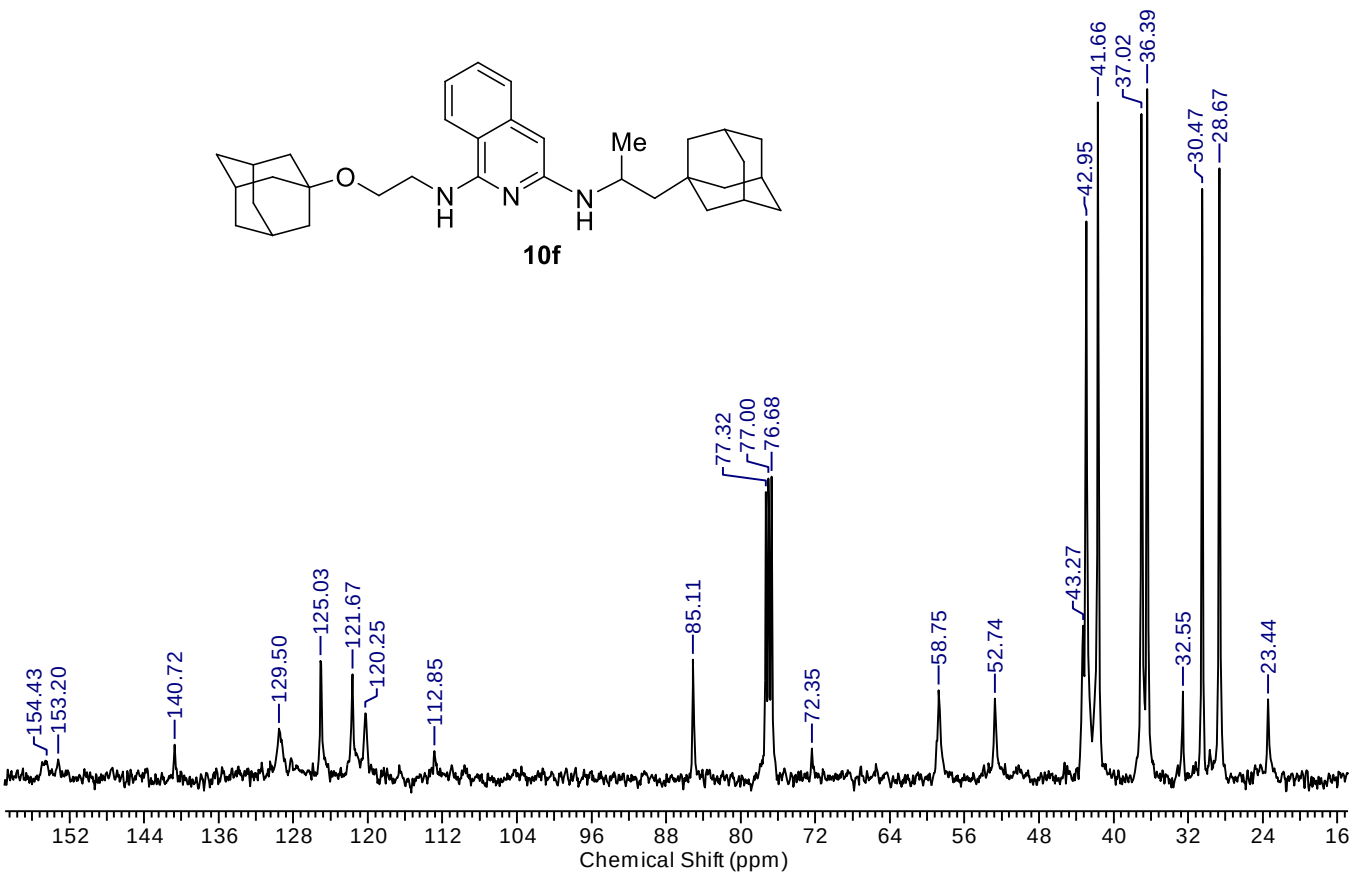


Figure S38. ^{13}C NMR spectrum of **10f** ($CDCl_3$, 100.6 MHz, 300K).

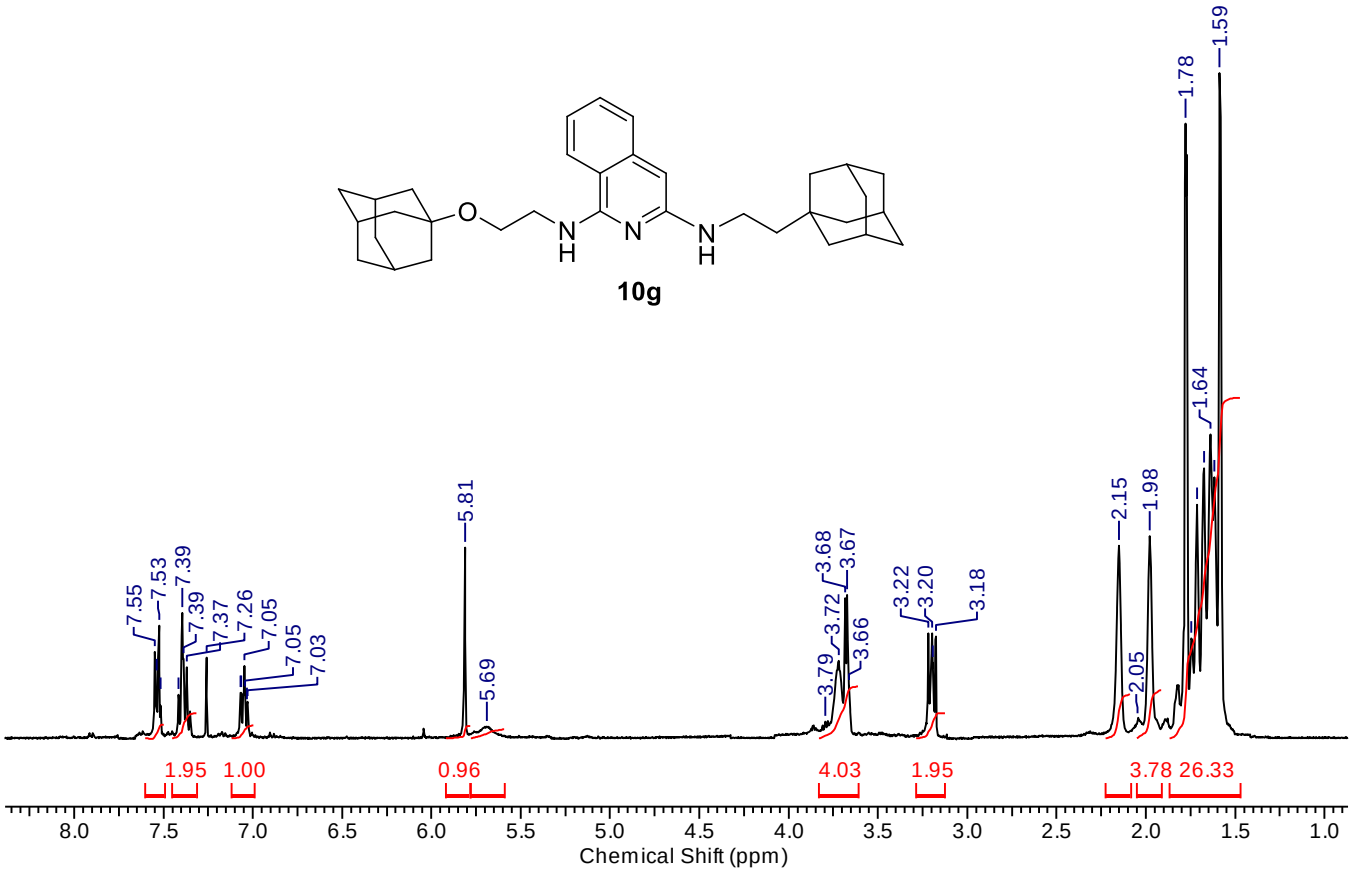


Figure S39. ^{1}H NMR spectrum of **10g** ($CDCl_3$, 400MHz, 300K).

MALDI-TOF spectra

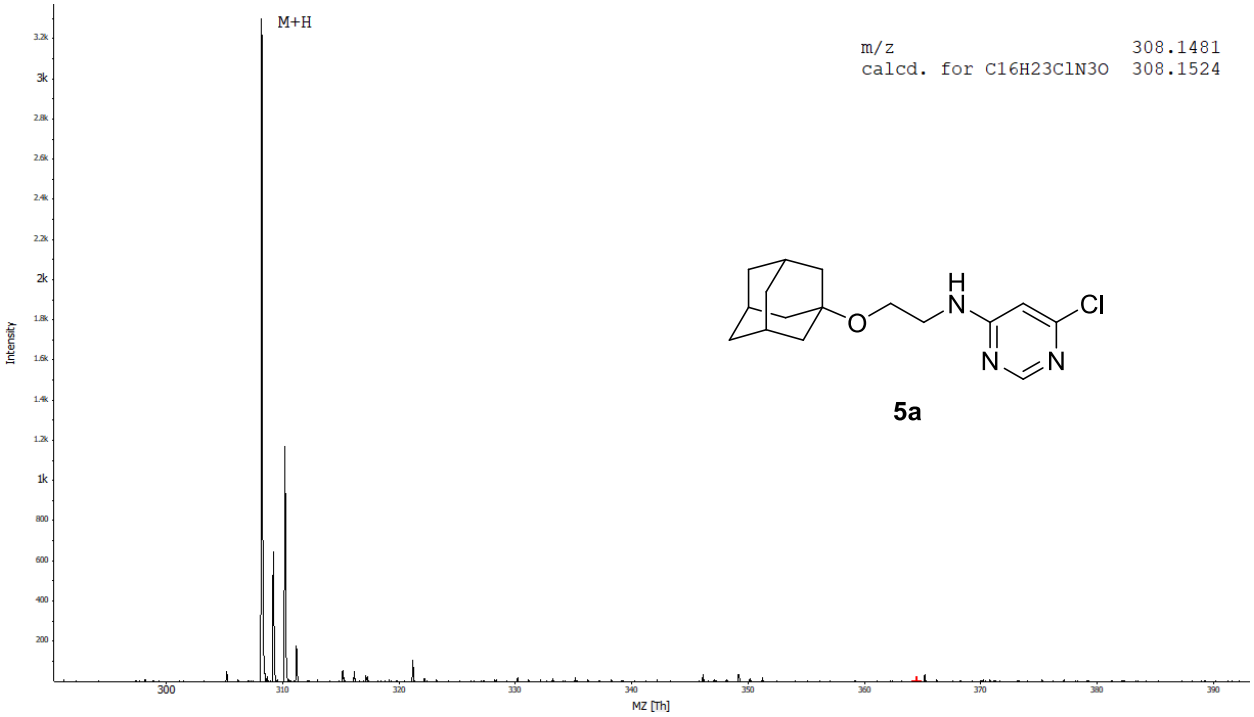


Figure S40. MALDI-TOF spectra of the compound **5a**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

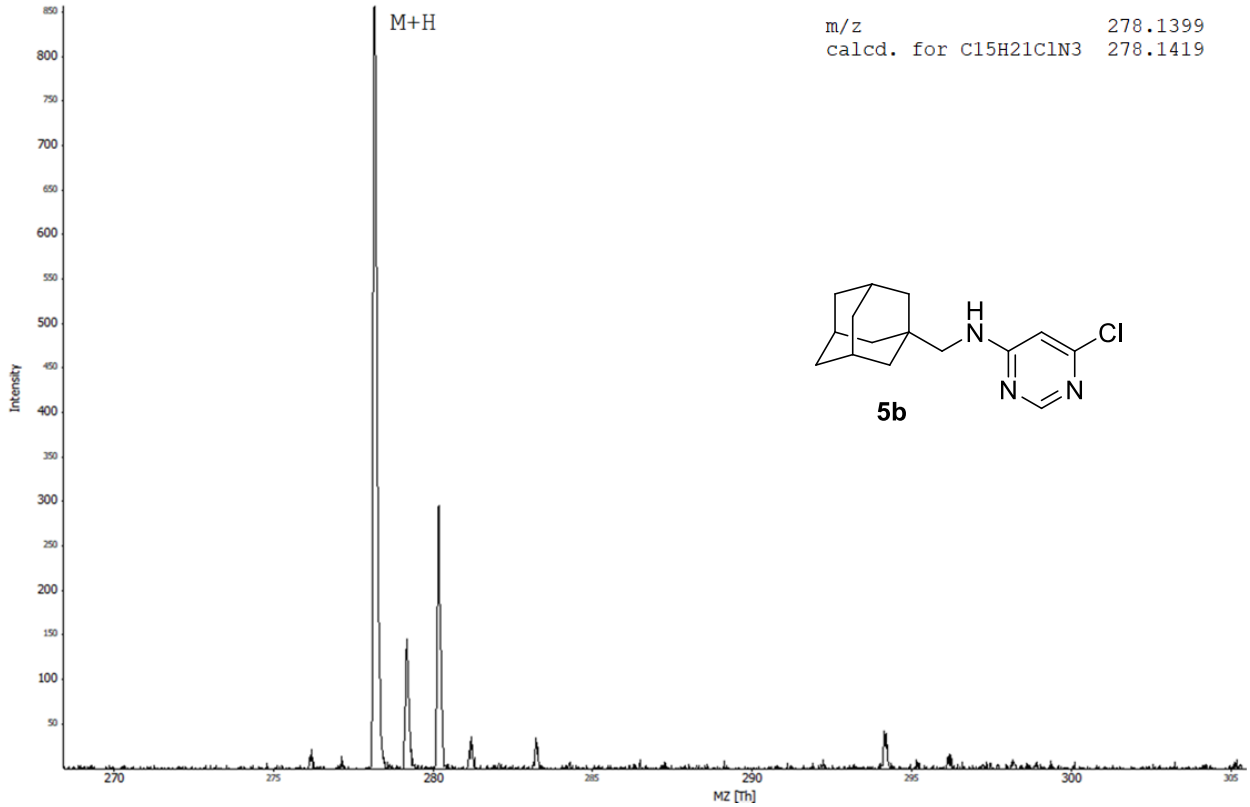


Figure S41. MALDI-TOF spectra of the compound **5b**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

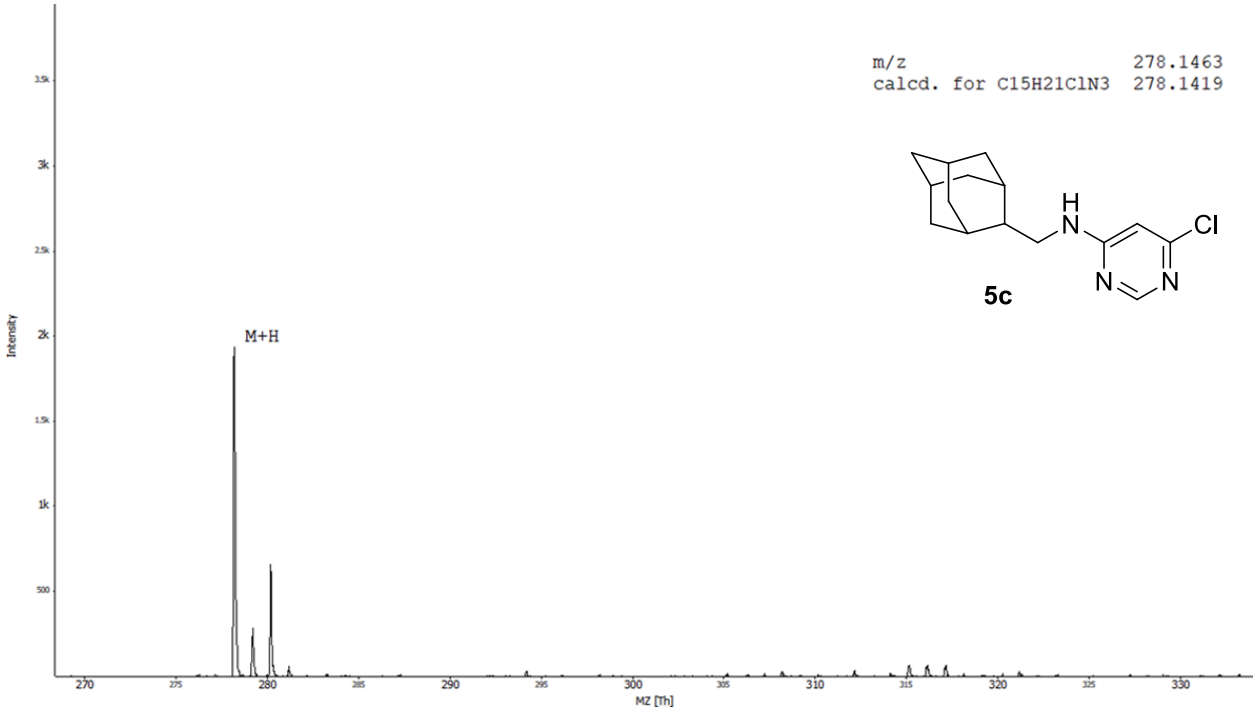


Figure S42. MALDI-TOF spectra of the compound **5c**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

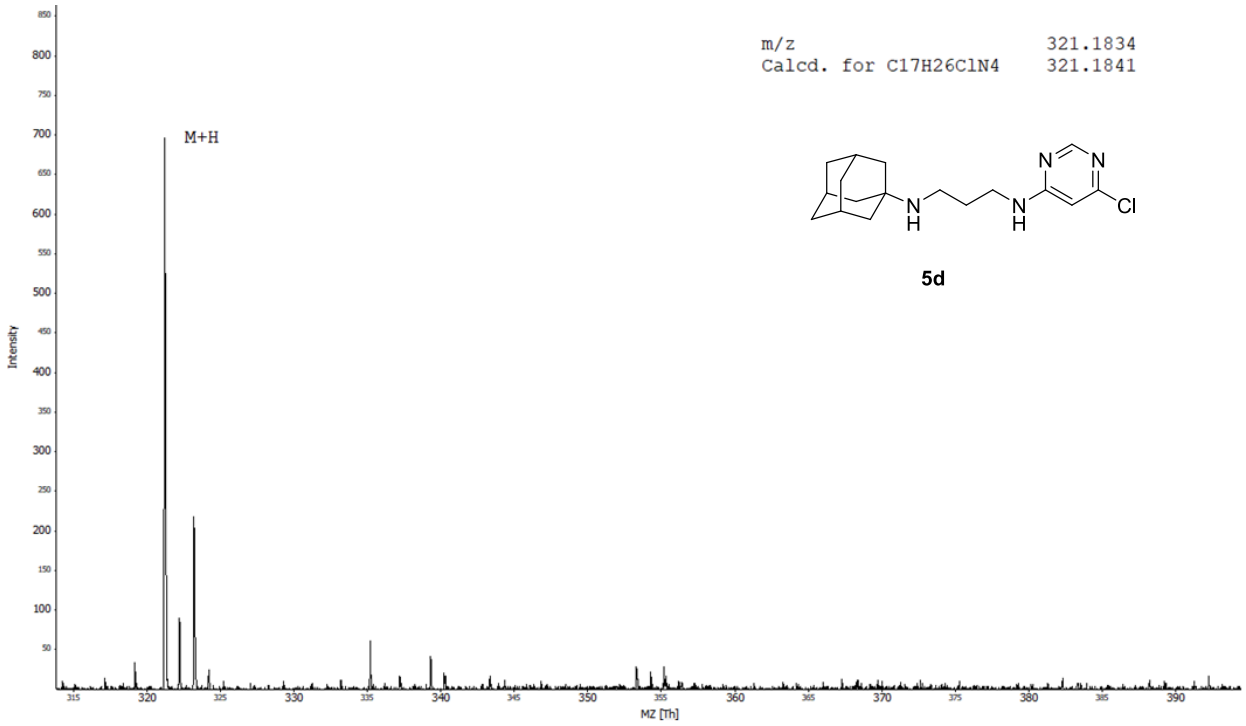


Figure S43. MALDI-TOF spectra of the compound **5d**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

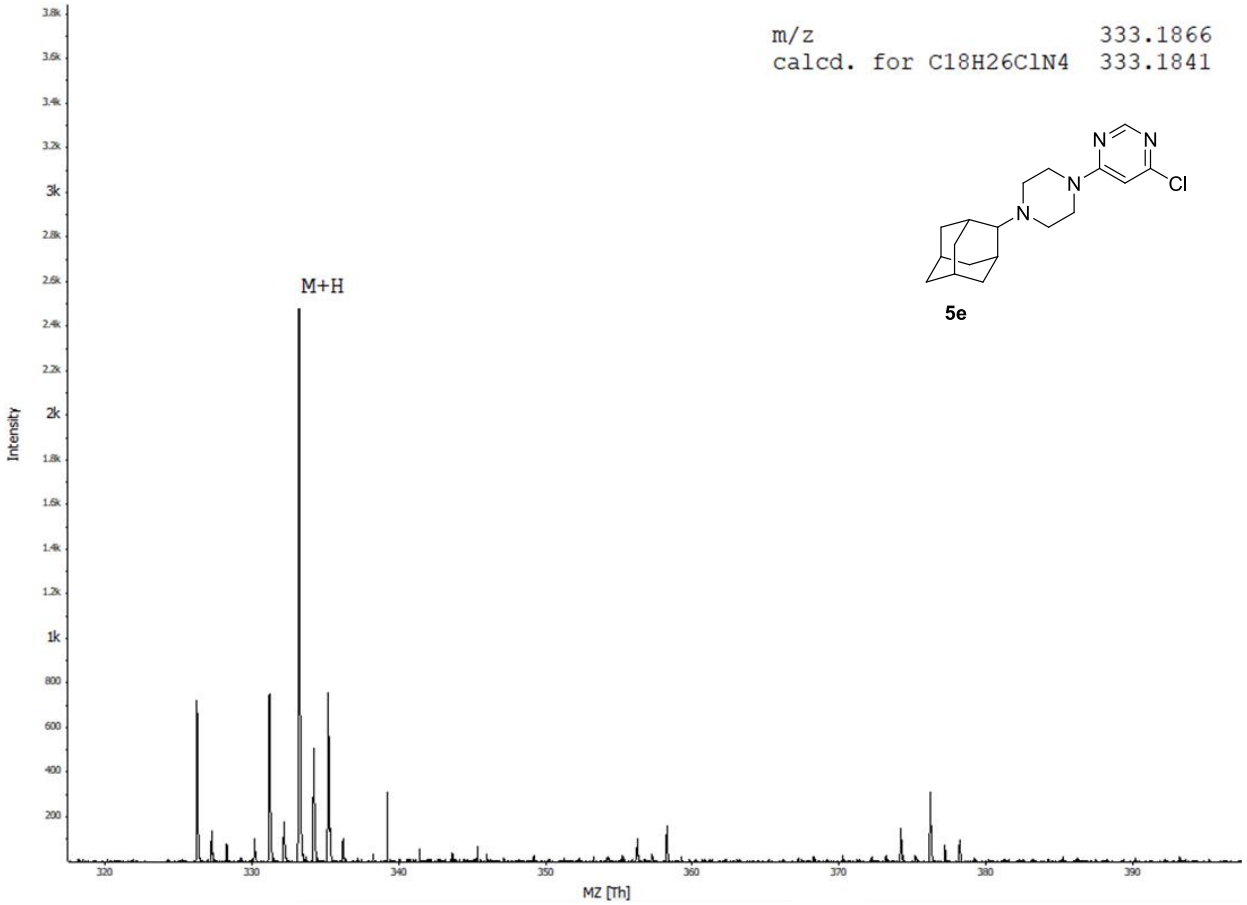


Figure S44. MALDI-TOF spectra of the compound **5e**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

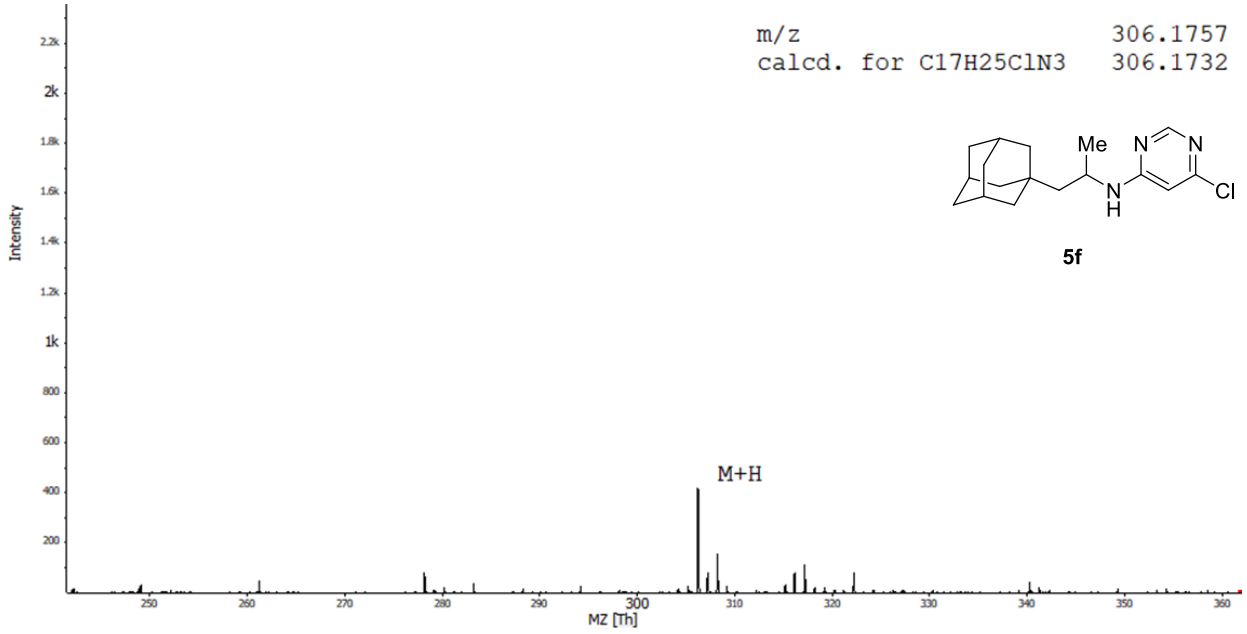


Figure S45. MALDI-TOF spectra of the compound **5f**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

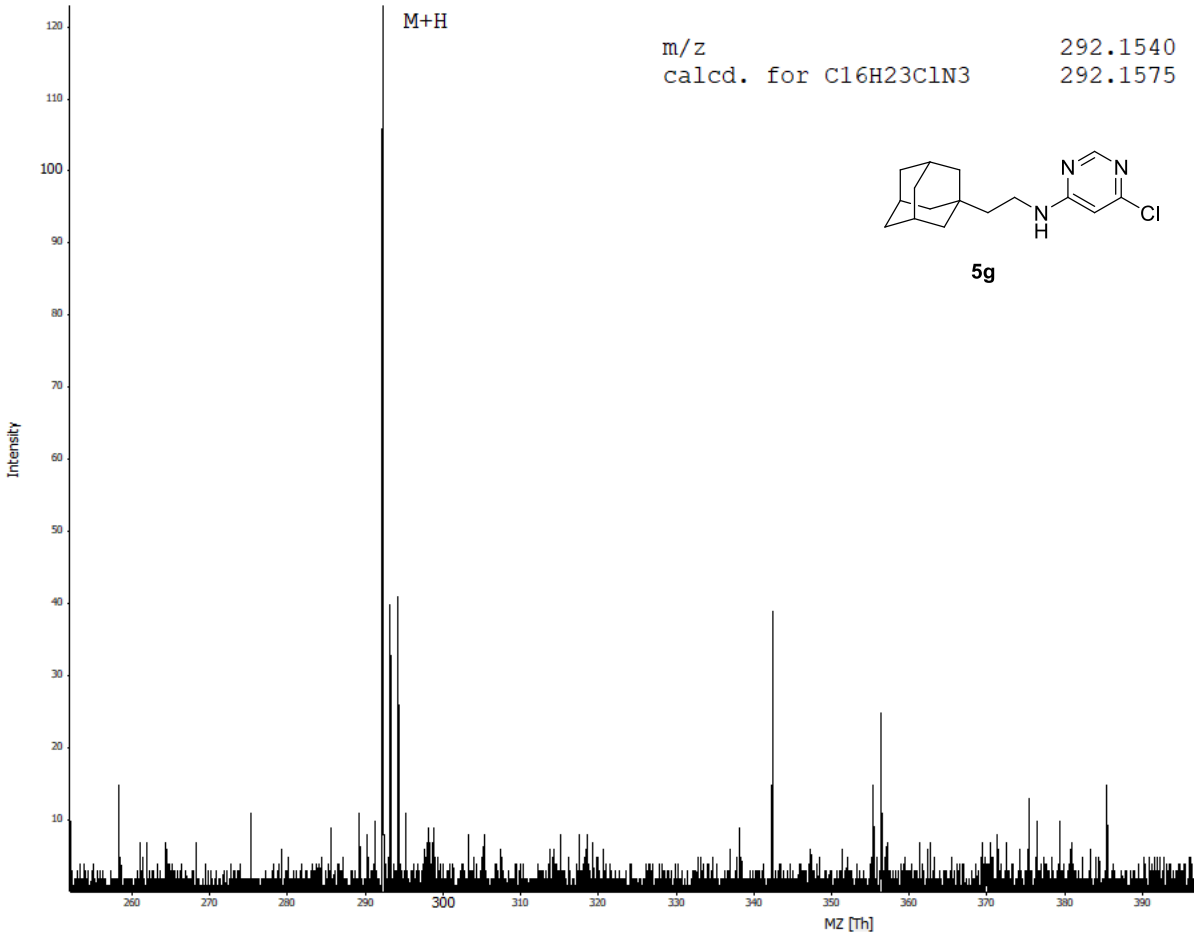


Figure S46. MALDI-TOF spectra of the compound **5g**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-300.

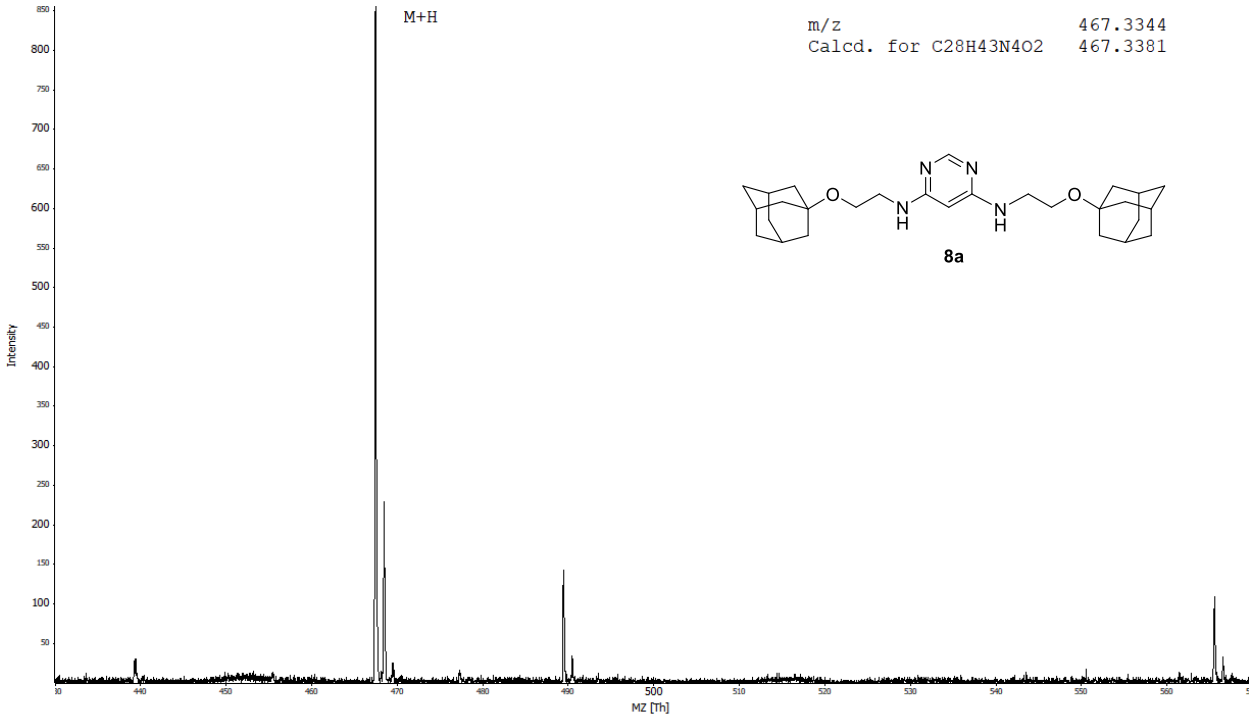


Figure S47. MALDI-TOF spectra of the compound **8a**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

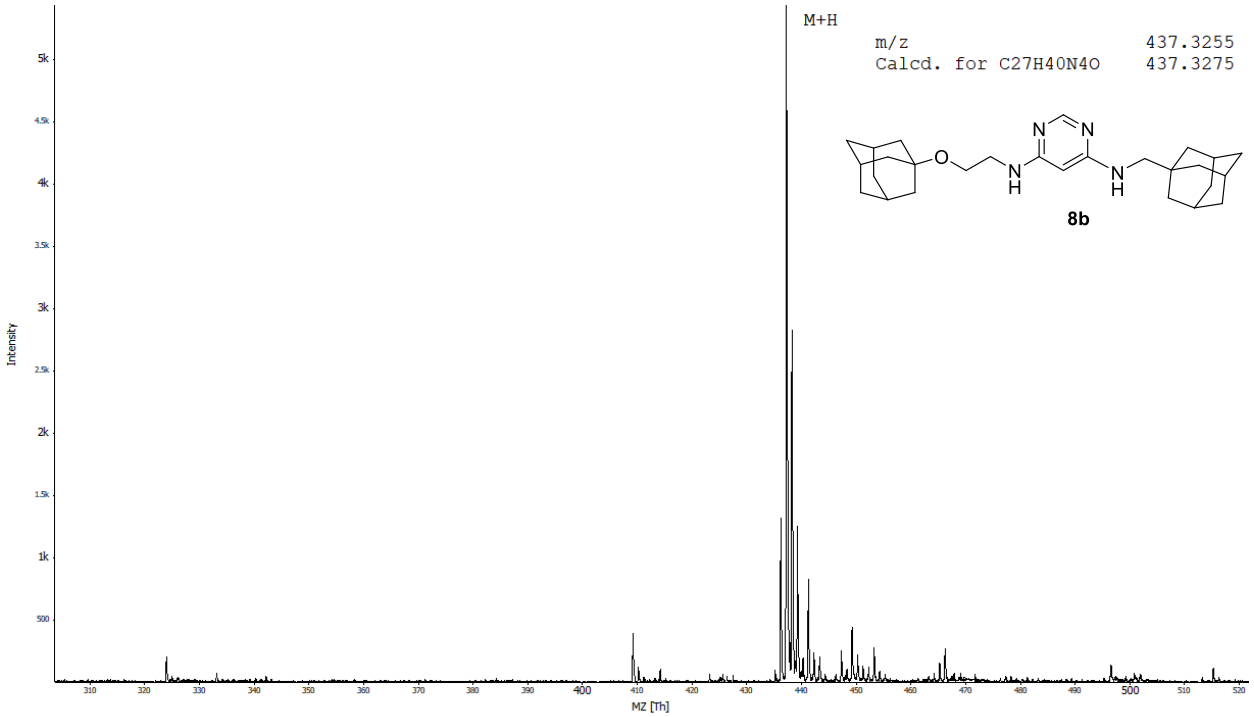


Figure S48. MALDI-TOF spectra of the compound **8b**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

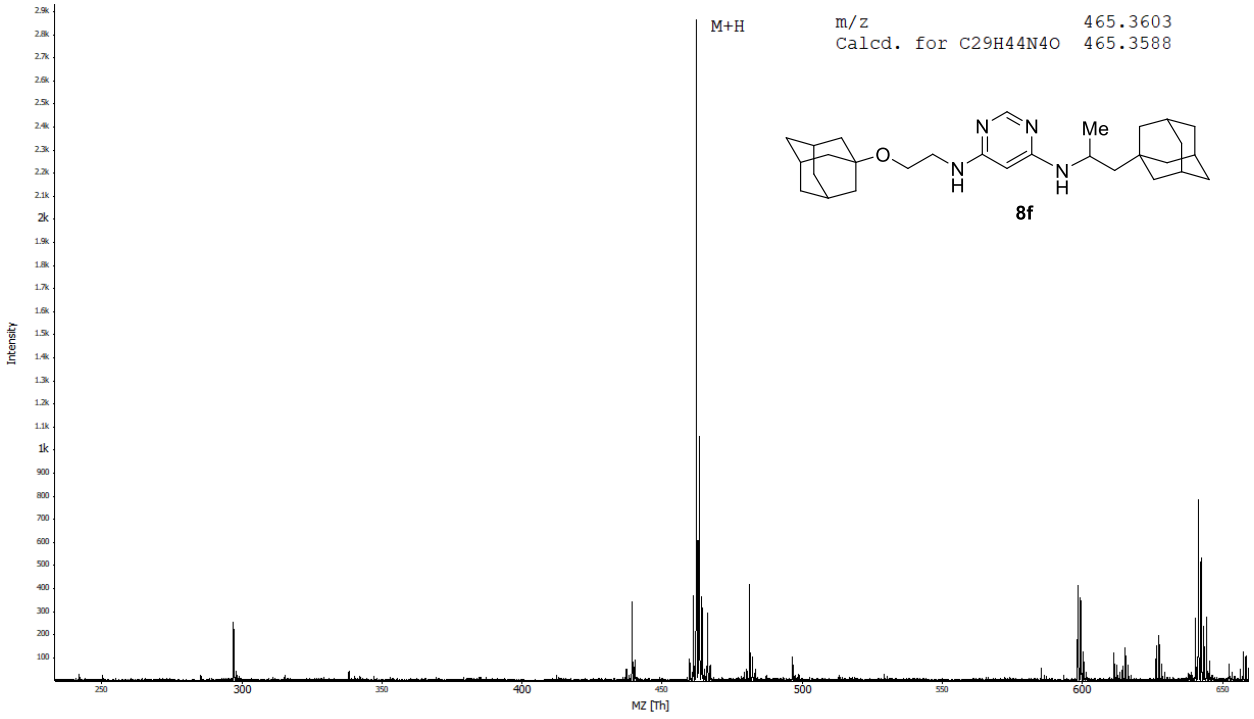


Figure S49. MALDI-TOF spectra of the compound **8f**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

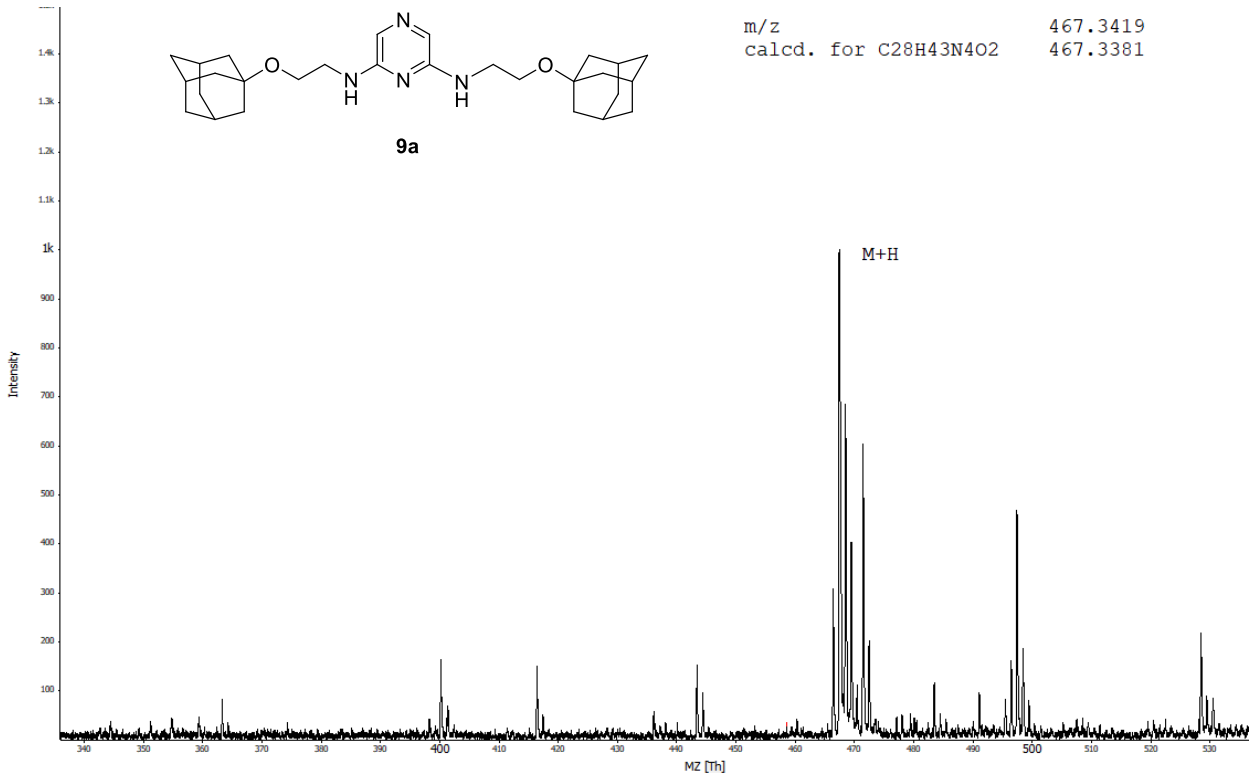


Figure S50. MALDI-TOF spectra of the compound **9a**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

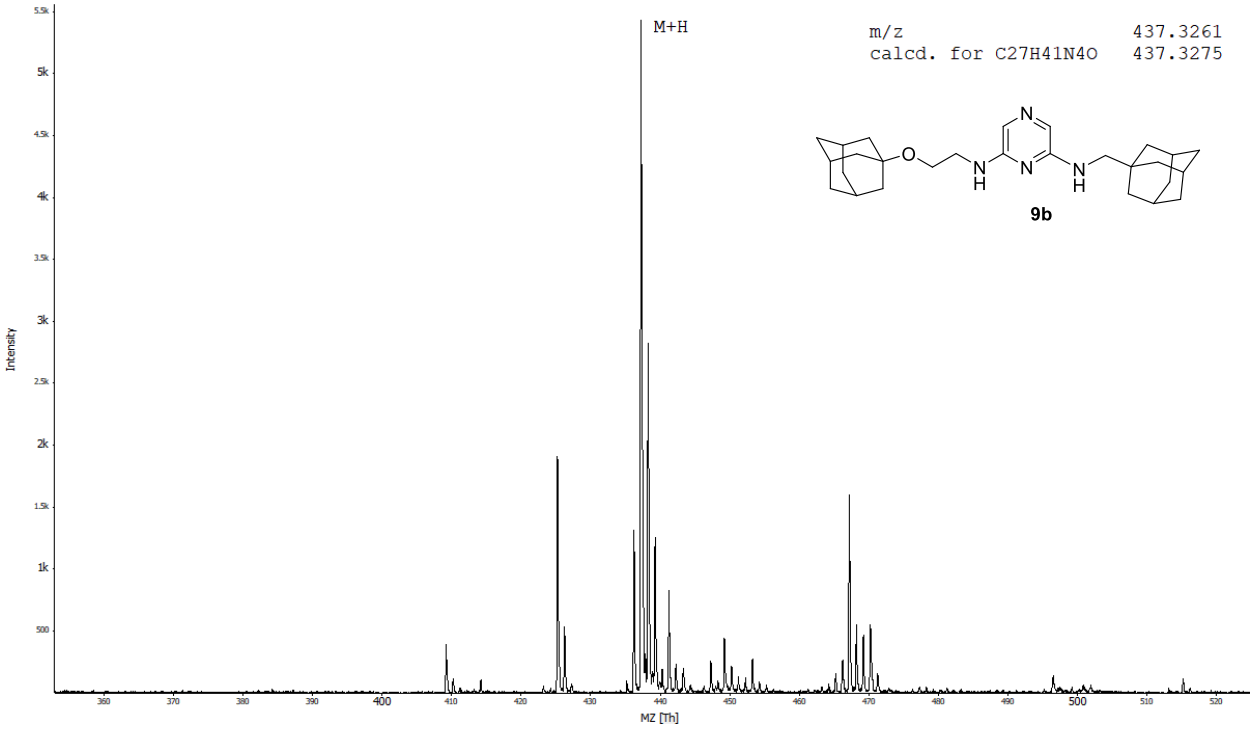


Figure S51. MALDI-TOF spectra of the compound **9b**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

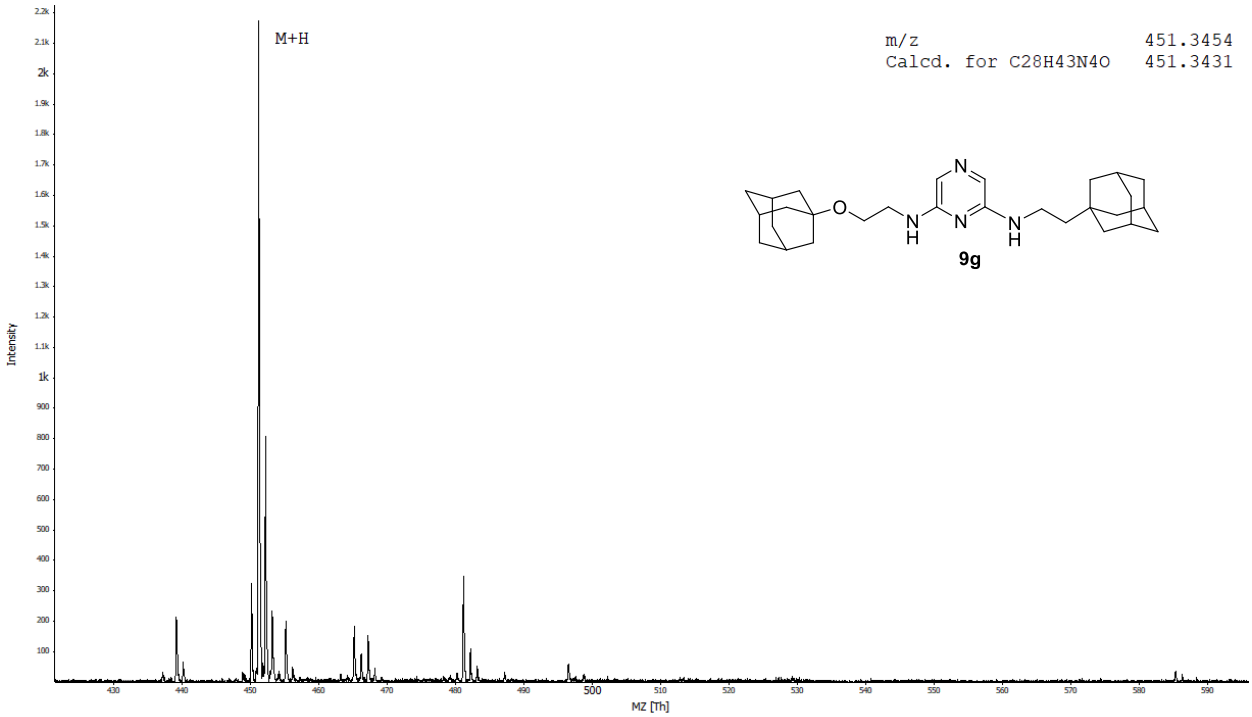


Figure S52. MALDI-TOF spectra of the compound **9g**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

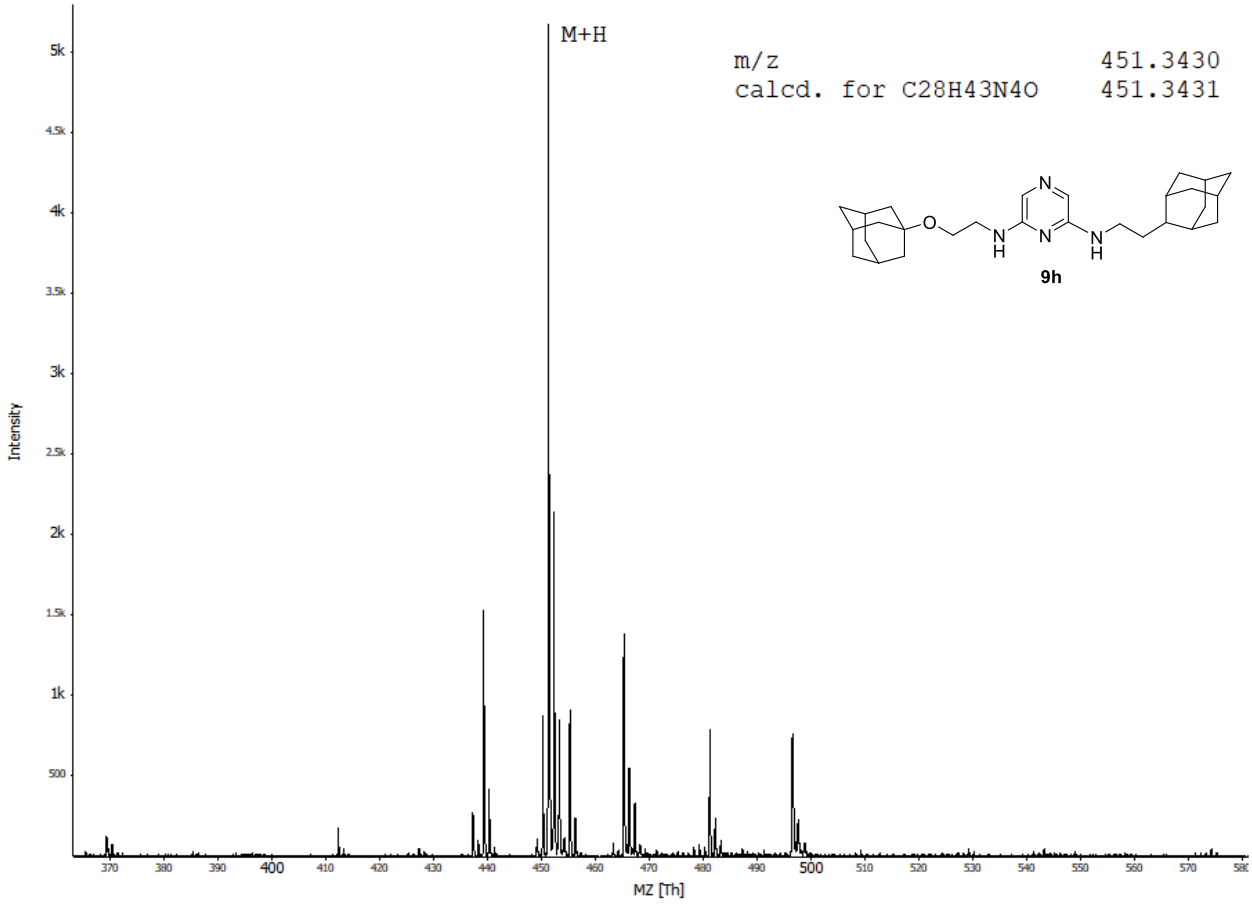


Figure S53. MALDI-TOF spectra of the compound **9h**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

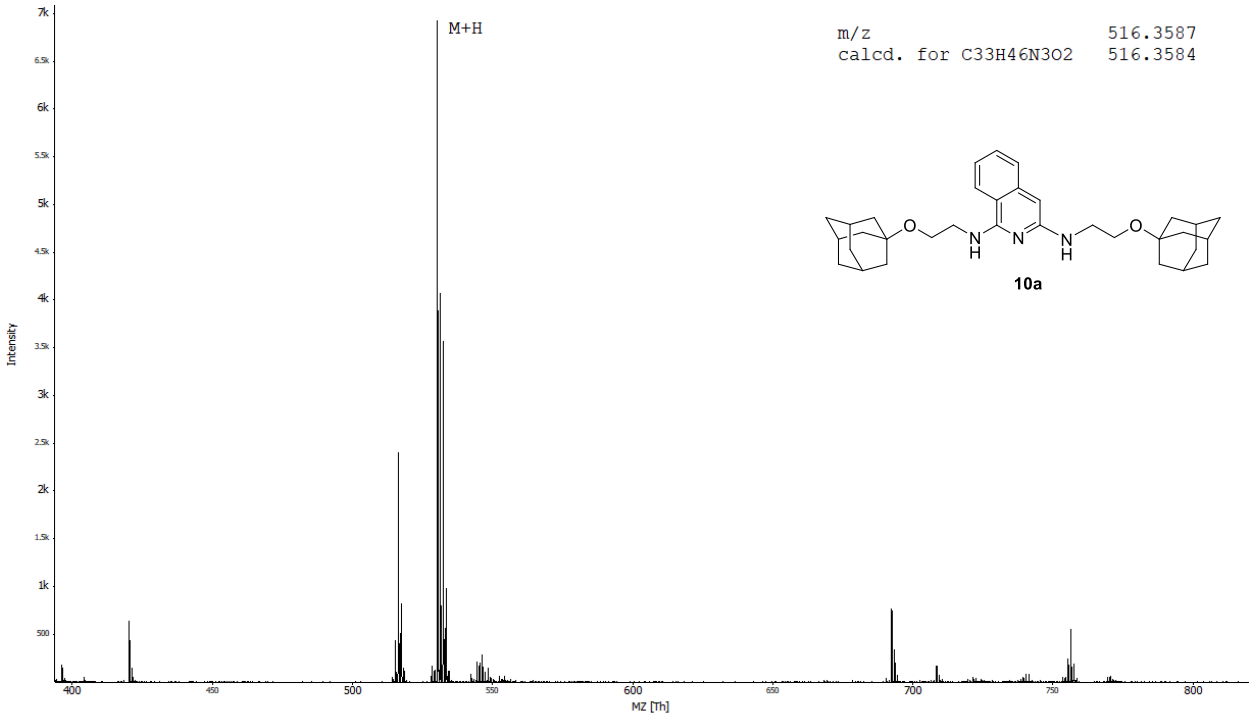


Figure S54. MALDI-TOF spectra of the compound **10a**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400+ PEG-600.

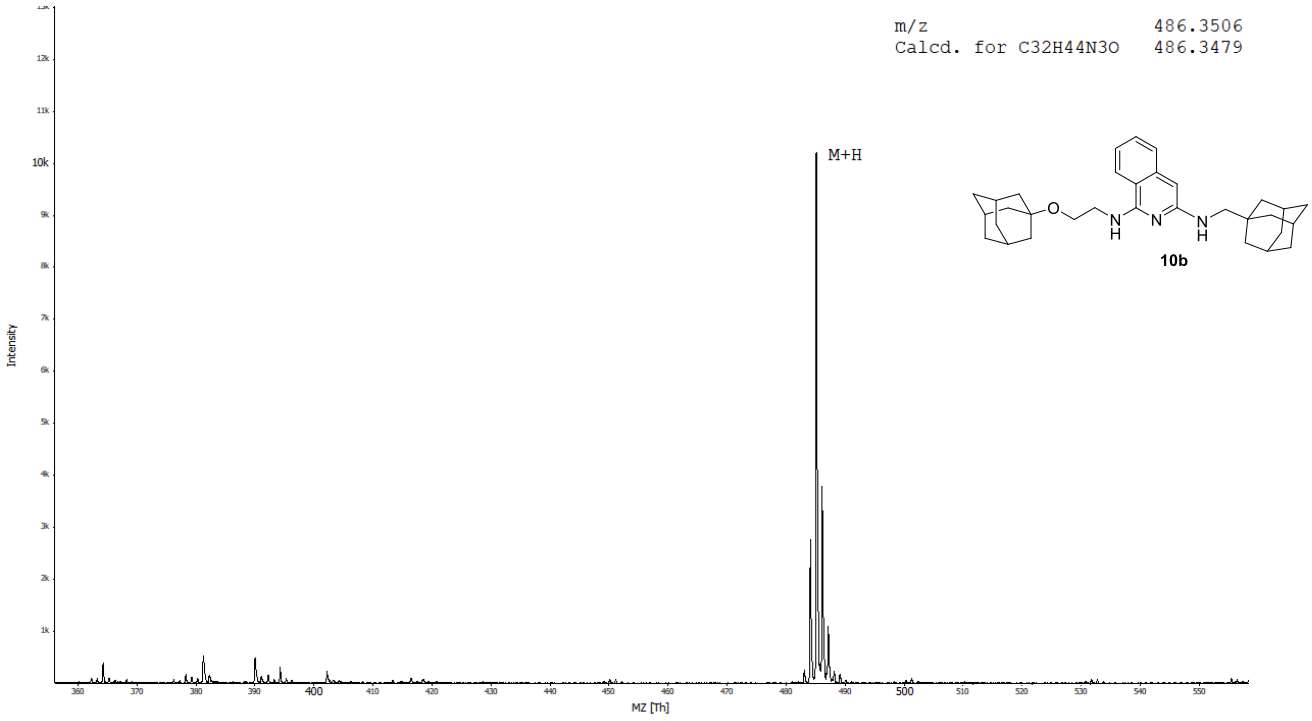


Figure S55. MALDI-TOF spectra of the compound **10b**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400.

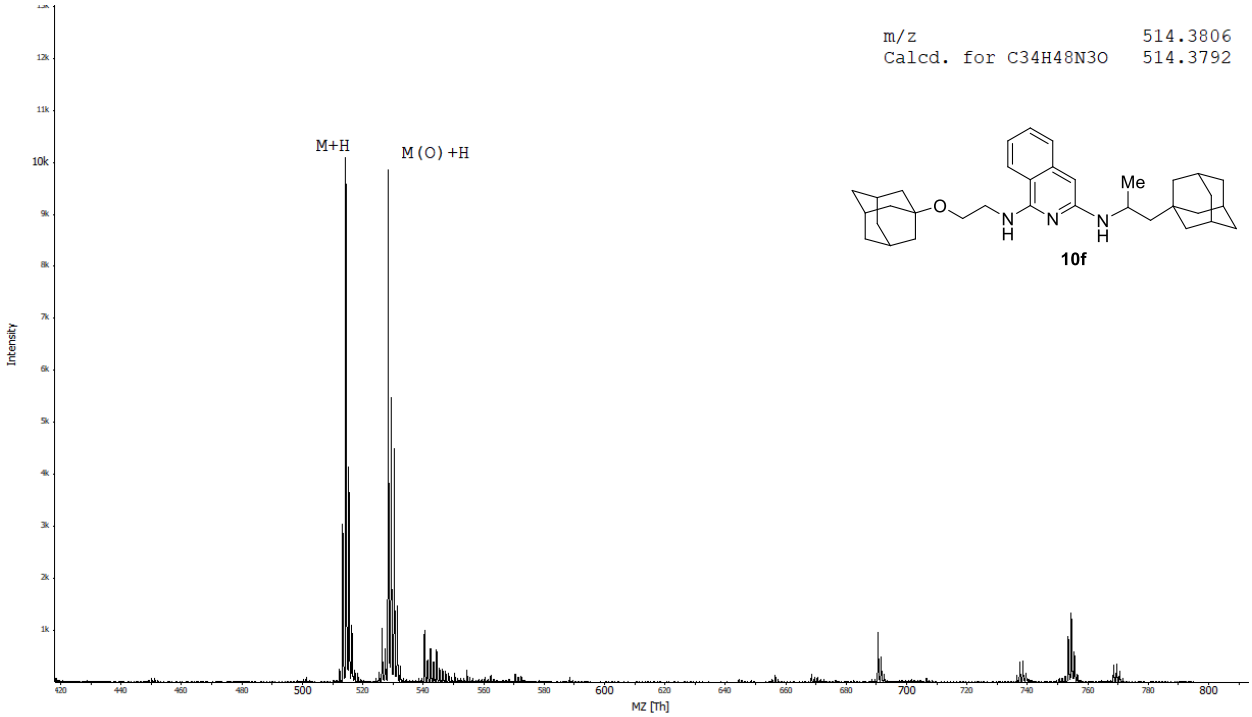


Figure S56. MALDI-TOF spectra of the compound **10f**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400+ PEG-600.

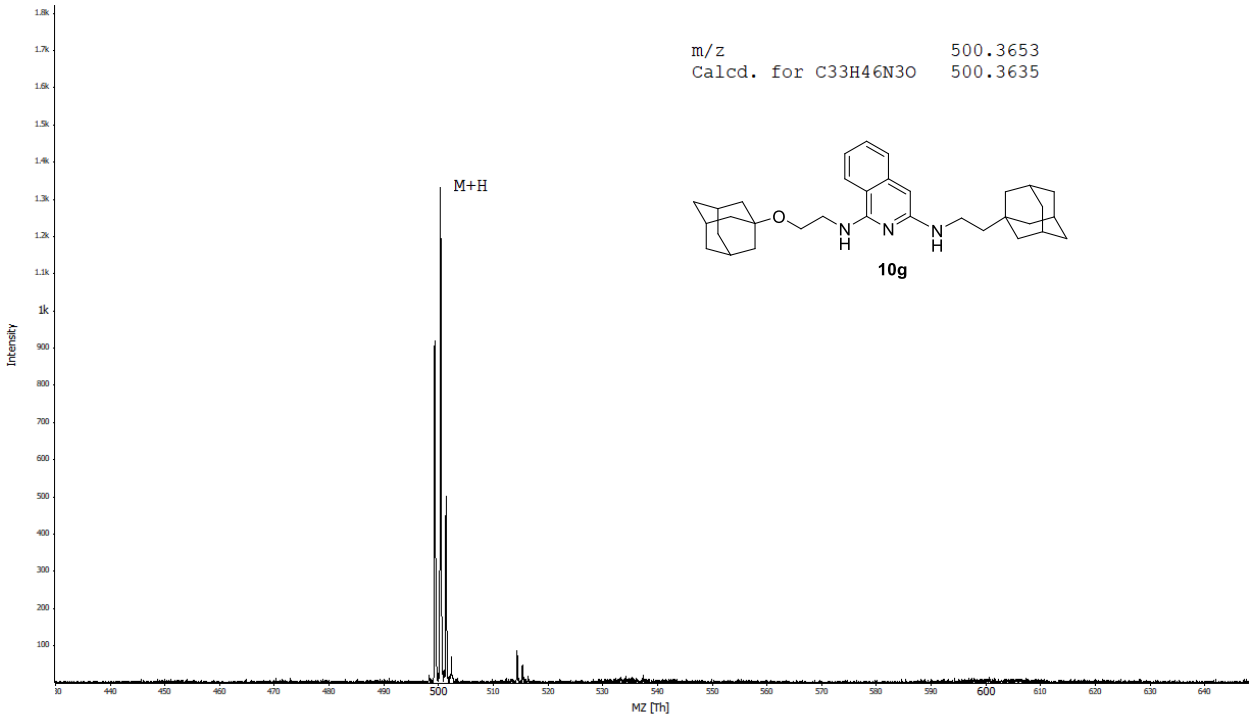


Figure S57. MALDI-TOF spectra of the compound **10g**. Matrix: 1,8,9-trihydroxyanthracene. Calibration standard: PEG-400+ PEG-600.