In Vitro Selectivity of an Acyclic Cucurbit[n]uril Molecular Container towards Neuromuscular Blocking Agents Relative to Commonly Used Drugs

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Supporting Information

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**General experimental details.** Drugs used for measuring binding constants with 2 were purchased from commercial suppliers and used without further purification. Compound 2 was prepared according to the literature procedure.¹ ¹H NMR spectra were measured on commercial spectrometers operating at 400 or 600 MHz. UV-Vis absorbance was measured on a Varian Cary 100 UV spectrophotometer.

**Determination of Kₐ between Host 2 with various drugs using UV/Vis spectroscopy.** Kₐ values up to 10⁴ M⁻¹ can be measured reliably by ¹H NMR spectroscopic methods. For values that exceed this level it is necessary to use other techniques such as UV/Vis, fluorescence, or isothermal titration calorimetry. UV/Vis spectroscopy was used in this work.

The Kₐ between 2 and 4 (tetracycline, UV/Vis active drug) was determined by direct titration of a fixed concentration of 4 with increasing concentrations of 2. The Kₐ value was determined by fitting the change in absorbance as a function of host concentration to a 1:1 binding model. In order to determine the Kₐ value for 2 toward guests which were not UV/Vis active, an indicator displacement assay involving the addition of guest to a solution of 2 and dye Rhodamine 6G was used. The change in UV/Vis absorbance as a function of guest concentration was fitted to a competitive binding model which allowed determination of the Kₐ values based on the known total concentrations of 2, Rhodamine 6G, and drug. The known Kₐ value of the 2•Rhodamine 6G complex (2.3 x 10⁶ M⁻¹) was used as input in the competitive binding model.²

Binding Models Used to Determine Values of \( K_a \) with Micromath Scientist

**1:1 Binding Model for UV/Vis.**

// Micromath Scientist Model File
// 1:1 Host:Guest binding model
// This model assumes the guest concentration is fixed and host concentration is varied
IndVars: ConcHostTot
DepVars: SpectroscopicSignal
Params: \( K_a \), ConcGuestTot, SpectroscopicSignalMin, SpectroscopicSignalMax

\[ K_a = \frac{\text{ConcHostGuest}}{\text{ConcHostFree} \times \text{ConcGuestFree}} \]

\[ \text{ConcHostTot} = \text{ConcHostFree} + \text{ConcHostGuest} \]

\[ \text{ConcGuestTot} = \text{ConcGuestFree} + \text{ConcHostGuest} \]

\[ \text{SpectroscopicSignal} = \text{SpectroscopicSignalMin} + \left( \text{SpectroscopicSignalMax} - \text{SpectroscopicSignalMin} \right) \times \left( \frac{\text{ConcHostGuest}}{\text{ConcGuestTot}} \right) \]

// Constraints
0 < ConcHostFree < ConcHostTot
0 < \( K_a \)
0 < ConcGuestFree < ConcGuestTot
0 < ConcHostGuest < ConcHostTot

**Competitive Binding (Indicator Displacement) Models.**

**Competitive Model Fitting Absorbance at One Wavelength.**

// MicroMath Scientist Model File

IndVars: ConcAntot
DepVars: Absorb
Params: ConcHtot, ConcGtot, Khg, Kha, AbsorbMax, AbsorbMin

\[ \text{Khg} = \frac{\text{ConcHG}}{\text{ConcH} \times \text{ConcG}} \]

\[ \text{Kha} = \frac{\text{ConcHAn}}{\text{ConcH} \times \text{ConcAn}} \]

\[ \text{Absorb} = \text{AbsorbMin} + \left( \text{AbsorbMax} - \text{AbsorbMin} \right) \times \left( \frac{\text{ConcHG}}{\text{ConcGtot}} \right) \]

\[ \text{ConcHtot} = \text{ConcH} + \text{ConcHG} + \text{ConcHAn} \]

\[ \text{ConcGtot} = \text{ConcHG} + \text{ConcG} \]

\[ \text{ConcAntot} = \text{ConcAn} + \text{ConcHAn} \]

0 < ConcHG < ConcHtot
0 < ConcH < ConcHtot
0 < ConcG < ConcGtot
0 < ConcAn < ConcAntot

***

**Competitive Model Fitting Absorbance at Two Wavelengths.**

// MicroMath Scientist Model File

IndVars: ConcAntot
DepVars: Absorb1, Absorb2
Params:Khg, Kha, AbsorbMax1, AbsorbMin1, AbsorbMax2, AbsorbMin2

\[ \text{Khg} = \frac{\text{ConcHG}}{\text{ConcH} \times \text{ConcG}} \]
\( K_{ha} = \frac{\text{ConcHAn}}{(\text{ConcH} \times \text{ConcAn})} \)
\( \text{Absorb}_1 = \text{AbsorbMin}_1 + (\text{AbsorbMax}_1 - \text{AbsorbMin}_1)(\text{ConcHG}/0.00001) \)
\( \text{Absorb}_2 = \text{AbsorbMin}_2 + (\text{AbsorbMax}_2 - \text{AbsorbMin}_2)(\text{ConcHG}/0.00001) \)
\( 0.00001 = \text{ConcH} + \text{ConcHG} + \text{ConcHAn} \)
\( 0.00001 = \text{ConcHG} + \text{ConcG} \)
\( \text{ConcAntot} = \text{ConcAn} + \text{ConcHAn} \)
\( 0 < \text{ConcHG} < 0.00001 \)
\( 0 < \text{ConcH} < 0.00001 \)
\( 0 < \text{ConcG} < 0.00001 \)
\( 0 < \text{ConcAn} < \text{ConcAntot} \)

***
Figure S1. (A) UV/Vis spectra from the titration of 2 (0–610 µM) with guest 4 (57.3 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₃₉₀ as a function of the concentration of 2. The solid line represents the best non-linear fit of the data to a 1:1 binding model ($K_d = (2.3 \pm 0.2) \times 10^3$ M$^{-1}$).
Figure S2. (A) UV/Vis spectra from the titration of 2 (5.07 µM) and Rhodamine 6G (5.01 µM) with guest 8 (0 – 6.08 mM) in 20 mM NaH2PO4 buffer (pH = 7.4); (B) plot of the A550 as a function of the concentration of 8. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (5.9 \pm 0.5) \times 10^3$ M$^{-1}$).
Figure S3. (A) UV/Vis spectra from the titration of 2 (10.1 µM) and Rhodamine 6G (9.96 µM) with guest 10 (0 – 4.32 mM) in 20 mM NaH2PO4 buffer (pH = 7.4); (B) plot of the A550 as a function of the concentration of 10. The solid line represents the best non-linear fit of the data to a competitive binding model (K_a = (8.6 ± 0.8) × 10^3 M^{-1}).
Figure S4. (A) UV/Vis spectra from the titration of 2 (9.98 µM) and Rhodamine 6G (9.96 µM) with guest 12 (0 – 1.11 mM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 12. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (2.1 ± 0.2) × 10⁶ M⁻¹).
Figure S5. (A) UV/Vis spectra from the titration of 2 (10.2 µM) and Rhodamine 6G (9.96 µM) with guest 14 (0 – 447 µM) in 20 mM NaH$_2$PO$_4$ buffer (pH = 7.4); (B) plot of the A$_{550}$ as a function of the concentration of 14. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (4.4 \pm 0.3) \times 10^4$ M$^{-1}$).
Figure S6. (A) UV/Vis spectra from the titration of 2 (9.92 µM) and Rhodamine 6G (10.0 µM) with guest 15 (0 – 2.05 mM) in 20 mM NaH$_2$PO$_4$ buffer (pH = 7.4); (B) plot of the A$_{550}$ as a function of the concentration of 15. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (4.8 \pm 0.3) \times 10^4$ M$^{-1}$)
Figure S7. (A) UV/Vis spectra from the titration of 2 (9.92 µM) and Rhodamine 6G (10.0 µM) with guest 16 (0 – 1.32 mM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 16. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (8.3 ± 0.6) × 10⁴ M⁻¹).
Figure S8. (A) UV/Vis spectra from the titration of 2 (10.1 µM) and Rhodamine 6G (9.96 µM) with guest 17 (0 – 486 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 17. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (1.9 ± 0.1) × 10⁵ M⁻¹).
Figure S9. (A) UV/Vis spectra from the titration of 2 (10.2 µM) and Rhodamine 6G (9.96 µM) with guest 18 (0 – 686 µM) in 20 mM NaH$_2$PO$_4$ buffer (pH = 7.4); (B) plot of the A$_{550}$ as a function of the concentration of 18. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (1.9 \pm 0.6) \times 10^5$ M$^{-1}$).
Figure S10. (A) UV/Vis spectra from the titration of 2 (10.2 µM) and Rhodamine 6G (10.3 µM) with guest 19 (0 – 510 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 19. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (2.5 ± 0.7) × 10⁵ M⁻¹).
Figure S11. (A) UV/Vis spectra from the titration of 2 (5.07 µM) and Rhodamine 6G (5.01 µM) with guest 20 (0 – 107 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 20. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (5.3 ± 0.4) × 10⁵ M⁻¹).
Figure S12. (A) UV/Vis spectra from the titration of 2 (12.5 μM) and Rhodamine 6G (12.4 μM) with guest 21 (0 –131μM) in 20mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 21. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (5.9 ± 0.7) \times 10^5$ M⁻¹).
Figure S13. (A) UV/Vis spectra from the titration of 2 (9.92 µM) and Rhodamine 6G (10.0 µM) with guest 22 (0 – 968 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 22. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (8.0 ± 0.7) × 10⁵ M⁻¹).
Figure S14. (A) UV/Vis spectra from the titration of 2 (5.07 µM) and Rhodamine 6G (5.01 µM) with guest 23 (0 – 616 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 23. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (8.2 \pm 0.9) \times 10^5 \text{ M}^{-1}$).
Figure S15. (A) UV/Vis spectra from the titration of 2 (5.07 μM) and Rhodamine 6G (5.01 μM) with guest 24 (0 – 237 μM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 24. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (9.3 ± 0.9) × 10⁵ M⁻¹).
Figure S16. (A) UV/Vis spectra from the titration of 2 (10.1 μM) and Rhodamine 6G (9.96 μM) with guest 25 (0 – 345 μM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 25. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (9.7 ± 1.1) × 10⁵ M⁻¹).
Figure S17. (A) UV/Vis spectra from the titration of 2 (10.1 µM) and Rhodamine 6G (9.96 µM) with guest 26 (0 – 450 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 26. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (9.8 ± 0.5) × 10⁵ M⁻¹).
Figure S18. (A) UV/Vis spectra from the titration of 2 (9.92 µM) and Rhodamine 6G (10.0 µM) with guest 27 (0 – 552 µM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 27. The solid line represents the best non-linear fit of the data to a competitive binding model (Kₐ = (2.8 ± 0.1) × 10⁶ M⁻¹).
Figure S19. (A) UV/Vis spectra from the titration of 2 (9.92 µM) and Rhodamine 6G (10.0 µM) with guest 28 (0 – 1.21 mM) in 20 mM NaH₂PO₄ buffer (pH = 7.4); (B) plot of the A₅₅₀ as a function of the concentration of 28. The solid line represents the best non-linear fit of the data to a competitive binding model ($K_a = (3.3 ± 0.5) \times 10^6$ M⁻¹).
Figure S20. (A) UV/Vis spectra from the titration of 2 (5.07 µM) and Rhodamine 6G (5.01 µM) with guest 29 (0 – 14.2 µM) in 20 mM NaH$_2$PO$_4$ buffer (pH = 7.4); (B) plot of the A$_{550}$ as a function of the concentration of 29. The solid line represents the best non-linear fit of the data to a competitive binding model (K$_a$ = (4.5 ± 0.7) × 10$^6$ M$^{-1}$).
1:1 Binding Models for NMR

Model Fitting Absorbance at One Chemical Shift.
// Micromath Scientist Model File
// 1:1 Host:Guest binding model for NMR
// This model assumes the guest concentration is fixed and host concentration is varied
IndVars: ConcHostTot
DepVars: Deltaobs
Params: Ka, ConcGuestTot, Deltasat, Deltazero
Ka = ConcHostGuest/(ConcHostFree*ConcGuestFree)
ConcHostTot=ConcHostFree + ConcHostGuest
ConcGuestTot=ConcGuestFree + ConcHostGuest
Deltaobs = Deltazero + (Deltasat - Deltazero) * (ConcHostGuest/ConcGuestTot)
// Constraints
0 < ConcHostFree < ConcHostTot
0 < Ka
0 < ConcGuestFree < ConcGuestTot
0 < ConcHostGuest < ConcHostTot
***

Model Fitting Absorbance at Two Chemical Shifts.
// Micromath Scientist Model File
IndVars: ConcHost
DepVars: CSA, CSB
Params: Ka, CSAzero, CSAsat, CSBzero, CSBsat
Ka = ConcHG/(ConcHfree*ConcGfree)
ConcHost=ConcHfree+ConcHG
0.0001=ConcGfree+ConcHG
CSA = CSAzero + ((CSAsat-CSAzero)*(ConcHG/0.0001))
CSB = CSBzero + ((CSBsat-CSBzero)*(ConcHG/0.0001))
0<ConcHfree<ConcHost
0<ConcGfree<0.0001
Figure S21. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (0.104 mM) with guest 3 (0 - 1.03 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.67 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (2.0 \pm 0.4) \times 10^3$ M$^{-1}$).
Figure S22. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (0 - 4.5 mM) with guest 5 (1.86 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 1.46 ppm as a function of host concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (3.0 \pm 0.4) \times 10^3$ M$^{-1}$).
Figure S23. (A) $^1$H NMR (400 MHz) stack plot of the titration of 2 (0.976 mM) with guest 6 (0 - 7.24 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.17 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (3.0 \pm 0.6) \times 10^3$ M$^{-1}$).
Figure S24. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (0.199 mM) with guest 7 (0 - 1.26 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.69 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (4.6 \pm 0.5) \times 10^3$ M$^{-1}$).
Figure S25. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (1.50 mM) with guest 9 (0 - 2.7 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.15 and 7.72 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (5.9 \pm 1.8) \times 10^3$ M$^{-1}$).
Figure S26. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (0.150 mM) with guest 11 (0 - 1.3 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.12 and 7.68 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (1.4 \pm 0.4) \times 10^4$ M$^{-1}$).
Figure S27. (A) $^1$H NMR (600 MHz) stack plot of the titration of 2 (0.150 mM) with guest 13 (0 - 1.26 mM) in 20 mM NaH$_2$PO$_4$ buffered D$_2$O (pH = 7.4); (B) plot of the chemical shift at 7.12 and 7.68 ppm as a function of guest concentration. The solid line represents the best non-linear fit of the data to a 1:1 model ($K_a = (3.3 \pm 1.0) \times 10^4$ M$^{-1}$).
Figure S28. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 3, b) 2, c) an equimolar mixture of 2 and 3 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 3 (10 mM).
Figure S29. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 4, b) 2, c) an equimolar mixture of 2 and 4 (12.5 mM), and d) a 1:2 mixture of 2 (12.5 mM) and 4 (25 mM).
Figure S30. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 5, b) 2, c) an equimolar mixture of 2 and 5 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 5 (10 mM).
Figure S31. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 6, b) 2, c) an equimolar mixture of 2 and 6 (12.5 mM), and d) a 1:2 mixture of 2 (12.5 mM) and 6 (25 mM).
Figure S32. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 7, b) 2, c) an equimolar mixture of 2 and 7 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 7 (10 mM).
Figure S33. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 8, b) 2, c) an equimolar mixture of 2 and 8 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 8 (10 mM).
Figure S34. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 9, b) 2, c) an equimolar mixture of 2 and 9 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 9 (10 mM).
Figure S35. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 10, b) 2, c) an equimolar mixture of 2 and 10 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 10 (8 mM).
Figure S36. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 11, b) 2, c) an equimolar mixture of 2 and 11 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 11 (8 mM).
Figure S37. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 12, b) 2, c) an equimolar mixture of 2 and 12 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 12 (8 mM).
Figure S38. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 13, b) 2, c) an equimolar mixture of 2 and 13 (12.5 mM), and d) a 1:2 mixture of 2 (4 mM) and 13 (8 mM).
Figure S39. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 14, b) 2, c) an equimolar mixture of 2 and 14 (4 mM), and d) a 1:2 mixture of 2 (1 mM) and 14 (2 mM).
Figure S40. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 15, b) 2, c) an equimolar mixture of 2 and 15 (12.5 mM), and d) a 1:2 mixture of 2 (12.5 mM) and 15 (25 mM).
Figure S41. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 16, b) 2, and c) an equimolar mixture of 2 and 16 (2 mM), and d) a 1:2 mixture of 2 (0.7 mM) and 16 (1.3 mM).
Figure S42. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 17, b) 2, and c) an equimolar mixture of 2 and 17 (4 mM).
Figure S43. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 18, b) 2, c) an equimolar mixture of 2 and 18 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 18 (8 mM).
Figure S44. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 19, b) 2, c) an equimolar mixture of 2 and 19 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 19 (8 mM).
Figure S45. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 20, b) 2, c) an equimolar mixture of 2 and 20 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 20 (10 mM).
Figure S46. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 21, b) 2, and c) an equimolar mixture of 2 and 21 (4 mM), and d) a 1:2 mixture of 2 (2 mM) and 21 (4 mM).
Figure 47. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 22, b) 2, c) an equimolar mixture of 2 and 22 (12.5 mM), and d) a 1:2 mixture of 2 (6.25 mM) and 22 (12.5 mM).
Figure S48. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 23, b) 2, c) an equimolar mixture of 2 and 23 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 23 (10 mM).
Figure S49. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 24, b) 2, c) an equimolar mixture of 2 and 24 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 24 (10 mM).
Figure S50: $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 25, b) 2, and c) an equimolar mixture of 2 and 25 (2 mM), and d) a 1:2 mixture of 2 (0.7 mM) and 25 (1.3 mM).
Figure S51. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 26, b) 2, c) an equimolar mixture of 2 and 26 (4 mM), and d) a 1:2 mixture of 2 (4 mM) and 26 (8 mM).
Figure S52. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 27, b) 2, c) an equimolar mixture of 2 and 27 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 27 (10 mM).
Figure S53. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 28, b) 2, c) an equimolar mixture of 2 and 28 (12.5 mM), and d) a 1:2 mixture of 2 (12.5 mM) and 28 (25 mM).
Figure S54. $^1$H NMR spectra recorded (400 MHz, RT, D$_2$O) for a) 29, b) 2, c) an equimolar mixture of 2 and 29 (5 mM), and d) a 1:2 mixture of 2 (5 mM) and 29 (10 mM).
Figure S55. Job plot establishing 1:1 binding of 6 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).

Figure S56. Job plot establishing 1:1 binding of 7 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).
Figure S57. Job plot establishing 1:1 binding of 13 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).

Figure S58. Job plot establishing 1:1 binding of 15 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).
**Figure S59.** Job plot establishing 1:1 binding of 20 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).

**Figure S60.** Job plot establishing 1:1 binding of 21 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).
Figure S61. Job plot establishing 1:1 binding of 22 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).

Figure S62. Job plot establishing 1:1 binding of 23 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).
Figure S63. Job plot establishing 1:1 binding of 28 (0 - 1 mM) with 2 (0 - 1 mM) based on change in chemical shift of $^1$H NMR (400 MHz, D$_2$O).
Figure S64. Three dimensional surface plot of the equilibrium mole fraction of AChR•vecuronium versus log [Drug] and log $K_3$ for vecuronium at [Vecuronium] = [AChR] = 27 μM, [2] = 54 μM (2 eqv.), $K_1 = 10^5$ M$^{-1}$, $K_2 = 1.6 \times 10^9$ M$^{-1}$. The red dots mark the points corresponding to each of the 27 drugs (2 – 29).

Figure S65. Three dimensional surface plot of the equilibrium mole fraction of AChR•cisatracurium versus log [Drug] and log $K_3$ at [Cisatracurium] = [AChR] = 18 μM, [2] = 576 μM (32 eqv.), $K_1 = 10^5$ M$^{-1}$, $K_2 = 4.8 \times 10^6$ M$^{-1}$. The red dots mark the points corresponding to each of the 27 drugs (2 – 29).
Figure S66. Three dimensional surface plot of the equilibrium mole fraction of AChR•cistracurium versus log [Drug] and log $K_3$ at [Cisatracurium] = [AChR] = 18 µM, [2] = 288 µM (16 eqv.), $K_1 = 10^5$ M$^{-1}$, $K_2 = 4.8 \times 10^6$ M$^{-1}$. The red dots mark the points corresponding to each of the 27 drugs (2 – 29).