Cooperativity in Multiply H-bonded Complexes

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Spectroscopic Data

Carbamate 1b

^{1}H NMR (250 MHz, $CDCl_3$) δ_H = 7.17 (d, 2H, J = 8), 7.00 (d, 2H, J = 8), δ 3.31 (m, 4H), 2.36 (s, 3H), 1.76 (m, 2H), 1.38 (m, 16H), 0.93 (m, 12H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C = 155.50, 149.40, 134.52, 129.69, 121.37, 51.02, 50.79, 38.08, 37.36, 30.56, 28.72, 23.91, 23.76, 23.09, 20.84, 14.08, 10.67; MS (EI+) m/z (%) = 268 (65),375 (10) [M+]; HRMS (EI+): calcd for $C_{24}H_{41}NO_2$: 375.3134; found 375.3134; FT-IR (thin film) ν_{max}/cm^{-1} 2958, 2928, 2872, 1713, 1512, 1462, 1417, 1379, 1214, 1199.

Carbamate 2b

^{1}H NMR (250 MHz, $CDCl_3$) δ_H = 7.19 (d, 4H, J = 9), δ 7.02 (d, 4H, J = 9), 3.97 (s, 2H), 3.28 (m, 8H), 1.76 (m, 4H), 1.32 (m, 32H), 0.93 (m, 24H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C = 155.36, 149.93, 137.67, 129.68, 121.60, 51.06, 50.85, 40.59, 38.08, 37.38, 30.57, 28.77, 23.91, 23.77, 23.25, 14.11, 10.68; MS (ES+) m/z (%) = 736 [M+H$^+$] (100),758 (50) [M+Na$^+$]; HRMS (ES+): calcd for $C_{47}H_{79}N_2O_4$: 735.6040 ; found 735.6069 ; FT-IR (thin film) ν_{max}/cm^{-1}. 2956, 2922, 2862, 1714, 1510, 1459, 1412, 1378, 1196, 1162.

Carbamate 3b

^{1}H NMR (250 MHz, $CDCl_3$) δ_H = 7.09 (d, 6H, J = 9), δ 6.98 (d, 6H, J = 9), 3.29 (m, 12H), 2.13 (s, 3H), 1.75 (m, 6H), 1.32 (m, 48H), 0.92 (m, 36H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ_C = 155.29, 149.68, 145.51, 129.56, 120.92, 51.05, 38.05, 37.38, 30.95, 30.57,28.73, 23.91, 23.11, 14.10, 10.68; MS (ES+) m/z (%) = 1109 [M+H$^+$] (100); HRMS (ES+): calcd for $C_{71}H_{118}N_3O_6$: 1108.9021 ; found 1108.9064 ; FT-IR (thin film) ν_{max}/cm^{-1} 2956, 2922, 2862, 1714, 1505, 1459, 1417, 1378, 1204, 1170.

Carbamate 4b

^{1}H NMR (250 MHz, $CDCl_3$) δ_H = 9.07 (s, 1H), 8.97 (s, 1H), δ 8.05 (m, 1H), 7.89 (s, 1H), δ 7.74 (dd, 1H, J = 8, J = 8), δ 7.58 (d, 1H, J = 8), 3.38 (m, 4H), 1.80 (m, 2H), 1.32 (m, 16H), 0.93 (m, 12H), -2.85 (s, 0.5H); MS (ES+) m/z (%) = 1747 (80), 1748 [M+H$^+$] (100), 1749 (80); HRMS (ES+) [M+H$^+$]: calcd for $C_{112}H_{163}N_8O_8$: 1748.2594 ; found 1748.2643; UV/Vis ($CHCl_3$) λ_{max}/nm (ε/mol^{-1}cm^{-1}) 420 (ε=1.9*10^5), 515 (ε=4.7*10^4), 547 (ε=5.7*10^3), 587 (ε=2.1*10^3), 644 (ε=7.2*10^2).

^{1}H NMR Experiments

^{1}H NMR Titrations

^{1}H NMR titrations thermostated at 298 K were carried out by preparing a 3 ml sample of host (**1a** or **2a**) at known concentration (1-50 mM). Then, 0.6 ml of this solution was removed, and a ^{1}H NMR spectrum was recorded. A 2 ml volumetric solution of guest (10-150 mM) in the host solution was prepared (so that the concentration of host remained constant throughout the titration). Aliquots of guest solution were added successively to the NMR tube containing the host, and the NMR spectrum was recorded after each addition. Changes in chemical shift for the host signals were analyzed by using a 1:1 binding isotherm in Microsoft Excel. All experiments were repeated at least twice.

^{1}H NMR Dilutions

^{1}H NMR dilution studies thermostated at 298 K were carried out by preparing 3 ml samples of guest (**3b** or **4b)** at known concentrations (0.1-1mM). A saturated solution of host (**3a** or **4a)** respectively was then prepared using the guest solution. The stock solution was filtered to remove any undissolved host. 0.6 ml of carbon tetrachloride was placed in an NMR tube and a ^{1}H NMR spectrum was recorded. Aliquots of the stock solution were added to the NMR tube, and after each addition a ^{1}H NMR spectrum was recorded. The concentration of the carbamate guest is known, and the concentration of host could be determined by integration. Changes in the chemical shift for the host were analyzed using a 1:1 binding isotherm in Microsoft Excel. All experiments were repeated at least twice.

The changes in chemical shift were analysed using purpose-written software to fit the data to the equations for a 1:1 binding isotherm (see below) to yield the association constant, the bound chemical shift and, if required, the free chemical shift.

$$[\mathrm{HG}] = \frac{1 + K([\mathrm{H}]_0 + [\mathrm{G}]_0) - \sqrt{\left(1 + K([\mathrm{H}]_0 + [\mathrm{G}]_0)\right)^2 - 4K^2[\mathrm{H}]_0[\mathrm{G}]_0}}{2K} \qquad (1)$$

$$[\mathrm{H}] = [\mathrm{H}]_0 - [\mathrm{HG}] \qquad (2)$$

$$\delta_{\mathrm{obs}} = \frac{[\mathrm{HG}]}{[\mathrm{H}]_0}\,\delta_{\mathrm{b}} + \frac{[\mathrm{H}]}{[\mathrm{H}]_0}\,\delta_{\mathrm{f}} \qquad (3)$$

where $[\mathrm{H}]_0$ is the total concentration of host
$[\mathrm{G}]_0$ is the total concentration of guest
[H] is the concentration of unbound free host
[HG] is the concentration of host•guest complex
K is the association constant for formation of the host•guest complex
δ_{f} is the free chemical shift of the host
δ_{b} is the limiting bound chemical shift of the host•guest complex

Example titration and dilution data

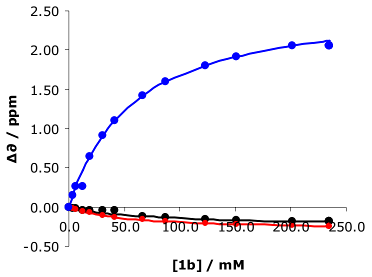

Figure 1. ^{1}H NMR titration of **1a** and **1b** to give **1a●1b** in carbon tetrachloride at 298 K. The lines are the best fit to the 1:1 binding isotherm.

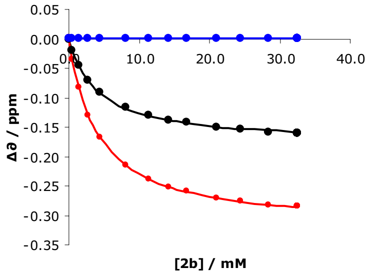

Figure 2. ^{1}H NMR titration of **2a** and **2b** to give **2a●2b** in carbon tetrachloride at 298 K. The lines are the best fit to the 1:1 binding isotherm.

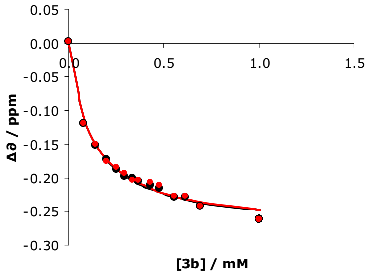

Figure 3. ^{1}H NMR dilution of **3a** and **3b** to give **3a●3b** in carbon tetrachloride at 298 K. The lines are the best fit to the 1:1 binding isotherm.

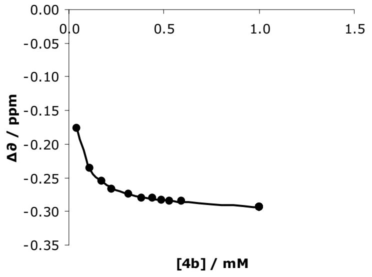

Figure 4. ^{1}H NMR dilution of **4a** and **4b** to give **4a●4b** in carbon tetrachloride at 298 K. The lines are the best fit to the 1:1 binding isotherm.