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Supporting Information

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A Deep, Water-Soluble Cavitand Acts As A Phase-Transfer Catalyst For Hydrophobic Species

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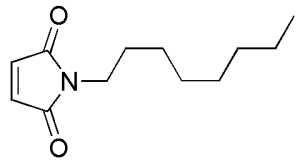
General Information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-600 spectrometer. Proton (^{1}H) chemical shifts, reported in parts per million (ppm), were indirectly referenced to external tetramethylsilane employing resonances due to trace monoprotio-solvent as an internal reference. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. High resolution electrospray ionization (ESI) TOF spectra were acquired on an Agilent ESI-TOF mass spectrometer. Anhydrous solvents were used as obtained from Acros Organics. N-cyclohexyl maleimide **8**, N-phenyl maleimide **9** and sodium 2-mercaptoethanesulfonate **2** were obtained from Aldrich Chemical Company, St. Louis, MO and were used as received. Cavitand **1** was synthesized according to the published procedure.[1] N-adamantyl maleimide **2**[2] and N-^{t}octyl maleimide **5**[3] were synthesized according to the published procedures.

Experimental Procedures

General Procedure for Phase-transfer Reactions.

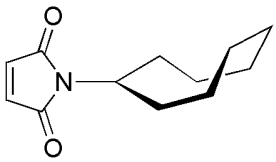
Sodium 2-mercaptoethanesulfonate **2** (6.4 mg, 0.039 mmol) and cavitand **1** (1.5 mg, 8 x 10^{-4} mmol) were dissolved in D_2O (0.75 mL) in a 1 dr vial with light sonication. Adamantyl maleimide **3** (6.0 mg, 0.026 mmol) was dissolved in CD_2Cl_2 and transferred to the aqueous solution. The two-phase mixture was stirred vigorously and the reaction monitored by TLC analysis of the organic layer. Time of completion was noted and the reaction repeated for yield determination. After the previously determined time, a 100 μL aliquot was removed from the aqueous layer and diluted with 500 μL of a 6.70 mM stock solution of benzenedisulfonic acid, dipotassium salt in D_2O. The solution was transferred to a 5mm NMR tube and a ^1H NMR spectrum taken (d1 = 5s). Integration of the representative peaks gave the proportion of product and standard, from which was calculated the yield displayed in Table 1.



Synthesis of N-octyl maleimide 7:

Maleic anhydride (358 mg, 3.65 mmol) was added to a 50 mL round-bottomed flask equipped with a magnetic stirbar followed by anhydrous ether (10 mL). Octylamine (500 μL, 391 mg, 3.02 mmol) was added dropwise via syringe and the mixture stirred for 3h, yielding a white precipitate of N-octyl maleamic acid, which was isolated by suction filtration and used in the next step without further purification.

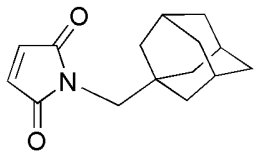
N-octylmaleamic acid (250 mg, 1.10 mmol) was added to a 100 mL round-bottomed flask equipped with a magnetic stirbar and condenser, followed by anhydrous 2-butanone. Acetic anhydride (1.67 mmol, 170 mg, 157 μL) and triethylamine (2.22 mmol, 224 mg, 449 μL) were sequentially added dropwise, via syringe. The reaction was heated to reflux and stirred for 3 days, then cooled to room temperature. CH_2Cl_2 (100 mL) and saturated aqueous ammonium chloride (20 mL) were added, and the mixture transferred to a separatory funnel. The layers were separated, and the aqueous layer extracted with CH_2Cl_2 (3 x 10 mL). The organic fractions were combined and washed with saturated brine (20 mL) and water (20 mL), dried ($MgSO_4$), filtered and the solvent removed by rotary evaporation. Column chromatography (SiO_2; hexanes/ether 9:1) gave N-octyl maleimide **7** (151 mg, 65%) as a white, crystalline solid. ^{1}H NMR (600 MHz, CD_3COCD_3) d 0.87 (t, J = 7.2 Hz, 3H); 1.24-1.33 (m, 10H); 1.55 (qn, J = 7.2 Hz, 2H); 3.46 (t, J = 7.2 Hz, 2H); 6.84 (s, 2H); ^{13}C NMR (150 MHz, CD_3COCD_3) d 15.3; 24.3; 28.4; 30.2; 30.8; 30.9; 33.5; 39.1; 136.1; 172.5; ESI-HRMS *m/z*: calcd for $C_{12}H_{19}NO_2$ ($M+H^+$) 210.1488; found 210.1496.



Synthesis of N-cyclooctyl maleimide 6:

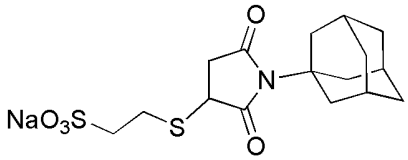
Cyclooctylamine was converted to N-cyclooctyl maleimide **6** on a 1.5 mmol scale using the procedure reported above for the synthesis of **7**, providing **6** as a white crystalline solid in 58% yield. ^{1}H NMR (600 MHz, CD_3COCD_3) d 1.47-1.80 (m, 12H); 2.12-2.20 (m, 2H); 4.14 (tt, J = 10.2, 3.6 Hz, 1H); 6.78 (s, 2H); ^{13}C NMR

(150 MHz, CD_3COCD_3) d 26.7; 27.6; 28.2; 33.2; 52.8; 135.9; 173.1; ESI-HRMS *m/z*: calcd for $C_{12}H_{17}NO_2$ ($M+H^+$) 208.1332; found 208.1338.



Synthesis of N-adamantylmethyl maleimide 4:

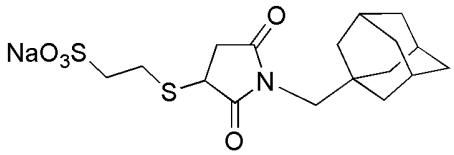
Adamantylmethylamine was converted to N-adamantylmethyl maleimide **4** on a 1.5 mmol scale using the procedure reported above for the synthesis of **7**, providing **4** as a white crystalline solid in 45% yield. ^1H NMR (600 MHz, CD_3COCD_3) d 1.49 (br s, 6H); 1.61 (br d, 3H, J = 11.4 Hz); 1.69 (br d, 3H, J = 11.4 Hz); 1.93 (br s, 3H); 3.13 (s, 2H); 6.88 (s, 2H); ^{13}C NMR (150 MHz, CD_3COCD_3) d 30.2; 36.7; 38.4; 42.4; 51.0; 136.0; 173.3; ESI-HRMS *m/z*: calcd for $C_{15}H_{19}NO_2$ ($M+H^+$) 246.1488; found 246.1488.



Characterization of sodium 2-(2,5-dioxo-1-adamantylpyrrolidin-3-ylthio) ethanesulfonate 10:

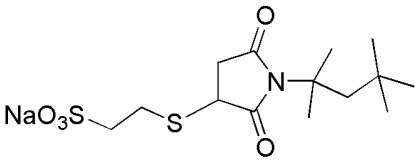
^1H NMR (600 MHz, D_2O) d 1.73 (br d, 3H, J = 12.6 Hz); 1.77 (br d, 3H, J = 12.6 Hz); 2.15 (br s, 3H); 2.41 (br s, 6H); 2.62 (dd, 1H, J = 3.6, 18.6 Hz); 3.08 (m, 1H); 3.16 (m, 2H); 3.25 (m, 2H); 3.91 (dd, 1H, J = 3.6, 9 Hz); ^{13}C NMR (150 MHz, D_2O) d 25.8; 30.0;

36.0; 36.6; 39.2; 40.8; 51.3; 62.6; 179.8; 180.8; ESI-HRMS *m/z*: calcd for $C_{16}H_{23}NNaO_5S_2$ ($M+H^+$) 396.0915; found 396.0920.



Characterization of sodium 2-(2,5-dioxo-1-adamantylmethylpyrrolidin-3-ylthio) ethanesulfonate 11:

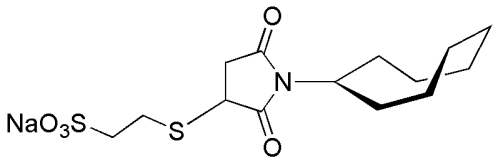
^{1}H NMR (600 MHz, D_2O) d 1.52 (br s, 6H); 1.65 (br d, 3H, J = 12.0 Hz); 1.73 (br d, 3H, J = 12.0 Hz); 1.97 (br s, 3H); 2.82 (br d, 1H, J = 19.2 Hz); 3.11 (m, 2H); 3.18-3.43 (m, 5H); 3.26 (s, 2H); 4.00 (m, 1H); ^{13}C NMR (150 MHz, D_2O) d 26.1; 28.4; 32.2; 35.5; 36.1; 36.5; 40.6; 51.1; 68.2; 179.5; 180.6; ESI-HRMS *m/z*: calcd for $C_{17}H_{25}NNaO_5S_2$ ($M+H^+$) 410.1066; found 410.1060.



Characterization of sodium 2-(2,5-dioxo-1-(2,4,4-trimethylpentan-2-yl)pyrrolidin-3-ylthio)ethanesulfonate 12:

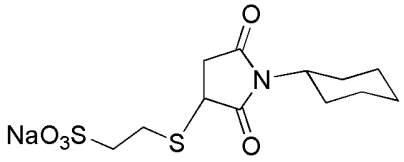
^{1}H NMR (600 MHz, D_2O) d 0.99 (s, 9H); 1.68 (s, 3H); 1.69 (s, 3H); 1.92 (d, 1H, J = 15 Hz); 1.99 (d, 1H, J = 15 Hz); 2.66 (dd, 1H, J = 4.2, 18.6 Hz); 3.12 (m, 1H); 3.24 (m, 4H); 4.00 (dd, 1H, J =

4.2, 9.6 Hz); ^{13}C NMR (150 MHz, D_2O) d 26.3; 29.0; 29.1; 31.0; 31.3; 36.7; 40.8; 49.9; 51.3; 63.7; 180.2; 181.2; ESI-HRMS *m/z*: calcd for $C_{14}H_{25}NNaO_5S_2$ ($M+H^+$) 374.1072; found 374.1066.



Characterization of sodium 2-(1-cyclooctyl-2,5-dioxopyrrolidin-3-ylthio)ethanesulfonate 13:

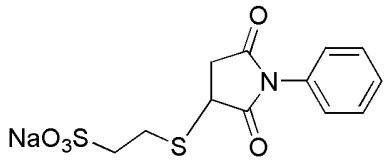
^{1}H NMR (600 MHz, D_2O) d 1.56 (m, 5H); 1.68 (m, 5H); 1.81 (m, 2H); 2.15 (m, 2H); 2.73 (dd, 1H, J = 3.6, 19.2 Hz); 3.09 (m, 1H); 3.18 (m, 1H); 3.26 (m, 2H); 3.31 (dd, 1H, J = 9, 19.2 Hz); 4.05 (dd, 1H, J = 3.6, 9 Hz); 4.26 (tt, 1H, 2.4, 10.2 Hz); ^{13}C NMR (150 MHz, D_2O) d 25.2; 25.9; 26.1; 30.8; 30.9; 36.3; 40.5; 51.3; 53.4; 178.7; 179.8; ESI-HRMS *m/z*: calcd for $C_{14}H_{23}NNaO_5S_2$ ($M+H^+$) 372.0915; found 372.0906.



Characterization of sodium 2-(1-cyclohexyl-2,5-dioxopyrrolidin-3-ylthio)ethanesulfonate 15:

^{1}H NMR (600 MHz, D_2O) d 1.21 (m, 1H); 1.35 (m, 2H); 1.68 (m, 3H); 1.86 (m, 2H); 2.04 (m, 2H); 2.74 (dd, 1H, J = 4.2, 18.6 Hz); 3.09 (m, 1H); 3.17 (m, 1H); 3.25 (m, 2H); 3.31 (dd, 1H, J = 9,

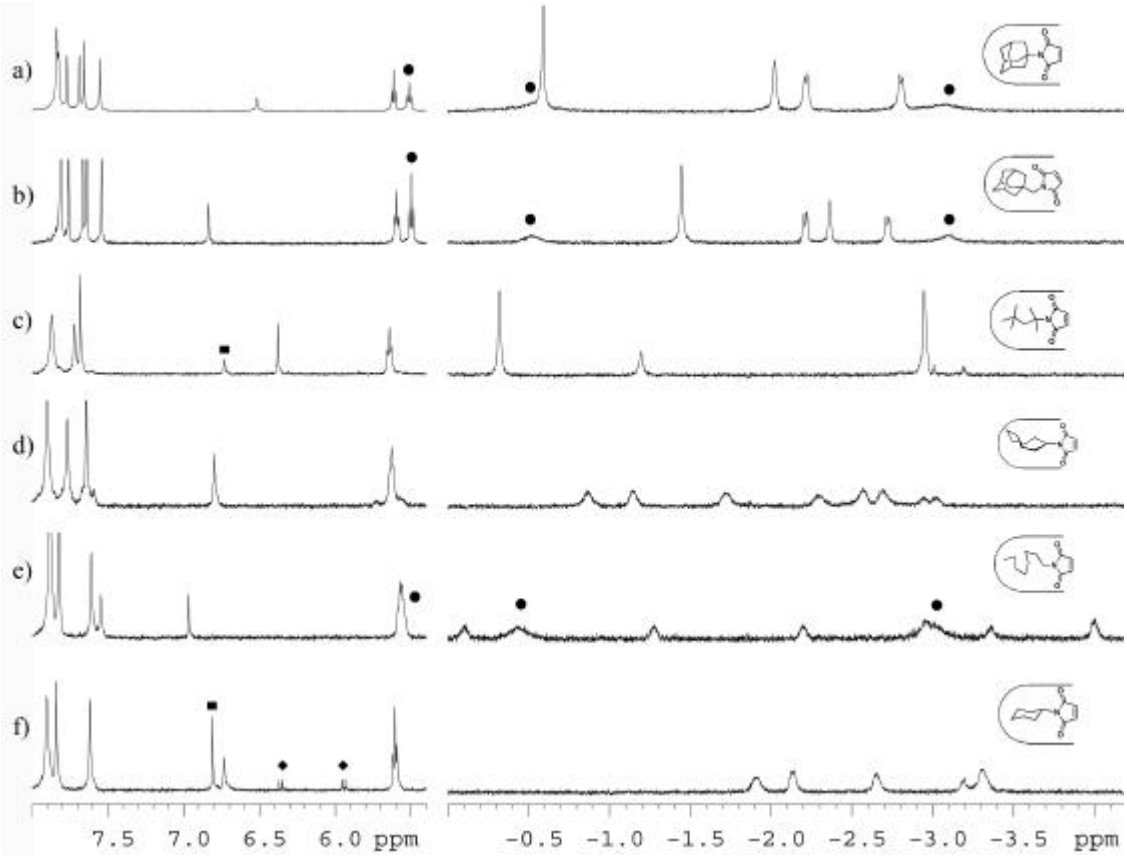
18.6 Hz); 3.99 (tt, 1H, 3, 12.6 Hz); 4.05 (dd, 1H, J = 4.2, 9 Hz); ^{13}C NMR (150 MHz, D_2O) d 25.2; 25.8; 28.6; 28.7; 36.3; 40.6; 51.3; 53.0; 179.0; 180.1; ESI-HRMS *m/z*: calcd for $C_{12}H_{19}NNaO_5S_2$ ($M+H^+$) 344.0602; found 344.0595.



Characterization of sodium 2-(2,5-dioxo-1-phenylpyrrolidin-3-ylthio)ethanesulfonate 16:

^{1}H NMR (600 MHz, D_2O) d 2.98 (dd, 1H, J = 4.2, 19.2 Hz); 3.19 (m, 1H); 3.27 (m, 2H); 3.31 (m, 2H); 3.56 (dd, 1H, J = 9, 19.2 Hz); 4.32 (dd, 1H, J = 4.2, 9 Hz); 7.36 (m, 2H); 7.62 (m, 3H); ^{13}C NMR (150 MHz, D_2O) d 26.4; 36.7; 41.1; 51.3; 127.4; 130.2; 130.3; 131.4; 178.3; 179.6; ESI-HRMS *m/z*: calcd for $C_{12}H_{13}NNaO_5S_2$ ($M+H^+$) 338.0133; found 338.0134.

^{1}H NMR Spectra of Host-Guest Complexes:



Supporting Figure 1. ^{1}H NMR spectra of the complexes of cavitand **1** (1 mM, D_2O) and a) *N*-adamantyl maleimide **3**, b) *N*-adamantylmethyl maleimide **4**, c) *N*-*tert*-octyl maleimide **5**, d) *N*-cyclooctyl maleimide **6**, e) *N*-octyl maleimide **7**, f) *N*-cyclohexyl maleimide **8**. (?) = peak from "free" cavitand **1** binding THF. (?) = peak from free maleimide. (¦) = peak from cyclohexylmaleamic acid formed upon complexation.

References

[1] S.M. Biros, E.C. Ullrich, F. Hof, L. Trembleau, J. Rebek, *J. Am. Chem. Soc.* **2004**, *126*, 2870-2876.

[2] A. L. Schwartz, L. M. Lerner, *J. Org. Chem.* **1974**, *39*, 21-23.

[3] Z. Y. Wang, *Synthetic Commun.* **1990**, *20*, 1607-1610.