Supporting Online Material for

Stabilization of Labile Carbonyl Addition Intermediates by a Synthetic Receptor

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Stabilization of Labile Carbonyl Addition Intermediates by a Synthetic Receptor

Supplementary Information

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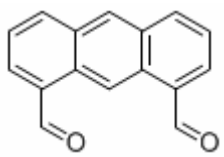
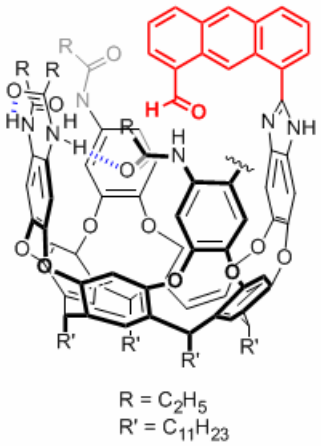
General Information

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX-600 spectrometer with a 5mm QNP probe. 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. ESI-HRMS data were recorded on an Agilent Electrospray TOF Mass Spectrometer. Hexamide-diamino cavitand **1** was synthesized according to the published procedures.(*S1*)

Experimental Procedures



Anthracene-1,8-dicarbaldehyde, 3 (*S2)*: To a suspension of anthracene-1,8-diyldimethanol (250 mg, 1.1 mmol) in dichloromethane (25 mL) was added MnO_2 (383 mg, 4.4 mmol). After stirring for 1 h at room temperature, 44 equivalent of MnO_2 (3.8 g, 44 mmol) was added. After additional stirring overnight, the reaction mixture was filtered through a pad of silica gel and celite to afford a yellow solution. The solution was evaporated off to give pure **3** (220 mg, 85%). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 11.2 (s, 1H), 10.6 (s, 2H, C*H*O), 8.56 (s, 1H), 8.30 (d, *J* = 8.4 Hz, 2H), 8.11 (dd, *J* = 6.6 Hz, 1.8 Hz, 2H), 7.69 (dd, *J* = 8.4 Hz, 1,8 Hz, 2H). All the other analytical data are identical to the literature.



Introverted Aldehyde, 1 (*S3*)**:** To a 50 mL sealed tube charged with the diamine **2** (174 mg, 0.094 mmol) and the dialdehyde **3** (22 mg, 0.094 mmol) was added 1,4-dioxane (0.8 mL). Immediately, the tube was soaked into a pre-heated oil-bath (100 ºC). After stirring for 24 h, the reaction mixture was allowed to cool to ambient temperature and the volatiles were evaporated off. The residue was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 20/1 ~ 9/1) to afford **1**. (124 mg, 64% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 11.8 (s, 1H, *H* of the imidazole ring), 10.5 (s, 1H, 9-positioned *H* of anthracene part), 10.4 (s, 1H, C*H*O), 9.87 (s, 1H, *H* of amide), 9.82 (s, 1H, *H* of amide), 9.34 (s, 1H, *H* of amide), 9.21 (s, 1H, *H* of amide), 8.77 (s, 1H, *H* of amide), 8.68 (s, 1H, *H* of amide), 8.58 (s, 1H), 8.30 (d, *J* = 8.4 H, 1H), 8.13 (dd, *J* = 7.2 Hz, 1.8 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 1H), 7.99 (s, 1H), 7.85 (s, 1H), 7.81 (s, 1H), 7.71 (s, 1H), 7.69 (dd, *J* = 8.4 Hz, 1.8 Hz, 1H), 7.63 (s, 1H), 7.55 (s, 1H), 7.48 (s, 1H), 7.44 (s, 1H), 7.43 (m, 1H), 7.29 (s, 2H), 7.244 (s, 1H), 7.236 (s, 1H), 7.224 (s, 1H), 7.217 (s, 1H), 7.19 (s, 1H), 7.157 (s, 1H), 7.151 (s, 1H), 5.78 (t, *J* = 8.4 Hz, 1H), 5.76 (t, *J* = 8.4 Hz, 1H), 5.74 (t, *J* = 8.4 Hz, 1H), 5.66 (t, *J* = 8.4 Hz, 1H), 2.51 – 2.20 (m, 14H), 1.49 – 1.19 (m, 81H), 1.08 (t, *J* = 7.8 Hz, 3H), 0.91 – 0.87 (12H, m), 0.62 (t, *J* = 8.4 Hz, 3H), 0.31 (t, *J* = 8.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 192.9 (*C*HO), 175.5, 174.5, 174.2, 172.8 (two peaks are overlapped), 172.2, 157.4, 156.3, 155.4, 155.0, 154.7, 154.6, 154.3, 151.7, 150.7, 150.6, 150.2, 149.9, 149.6, 149.1, 140.5, 138.4, 135.8, 135.51, 135.48, 135.33, 135.29, 134.9, 132.3, 132.0, 131.74, 131.71, 130.8, 130.6, 130.2, 129.5, 128.7, 128.5, 128.2, 127.9, 127.8, 127.1, 125.9, 125.0, 124.6, 124.1, 123.9, 123.4, 122.9, 122.7, 121.6, 121.4, 121.0, 119.1, 117.3, 116.9, 116.2, 116.0, 113.1, 106.5, 33.6, 33.33, 33.27, 33.0, 32.8, 32.3 – 32.1 (many peaks are overlapped), 31.9, 30.6, 29.9 – 29.7 (many peaks are overlapped), 29.4, 28.10, 28.07, 22.7, 14.1, 10.7, 10.0, 9.53, 9.10. HRMS (ESI, *m/z*, MH^+) Calcd For $C_{130}H_{159}N_8O_{15}$: 2072.1919. Found: 2072.1859.

General Procedure for Imine Formation

Aldehyde **1** (1.8 mg, 9 x 10^{-4} mmol) was dissolved in mesitylene-d_{12} (600 µL) and added to a 5 mM high-field NMR tube. Amine (1.25 µL in 25 µL mesitylene-d_{12}) was added *via* syringe, the NMR tube shaken to allow mixing and the mixture analyzed by ^{1}H NMR. After completion, the imines were analyzed by ^{1}H NMR and ESI-HRMS. The ^{1}H NMR spectra (containing excess amine) for each product are shown below, as are stacked plots of the buildup and loss of intermediates in each case.

ESI-HRMS analysis for imine **6** (from **1** and isobutylamine): calc. for $C_{134}H_{168}N_9O_{14}$ ($M+H^+$): 2127.2705; found 2127.2715.

ESI-HRMS analysis for imine ***S*-1** (from **1** and isopropylamine): calc. for $C_{133}H_{166}N_9O_{14}$ ($M+H^+$): 2113.2548; found 2113.2518

ESI-HRMS analysis for imine ***S*-2** (from **1** and *n*-propylamine): calc. for $C_{133}H_{166}N_9O_{14}$ ($M+H^+$): 2113.2548; found 2113.2562.

ESI-HRMS analysis for imine ***S*-3** (from **1** and *n*-butylamine): calc. for $C_{134}H_{168}N_9O_{14}$ ($M+H^+$): 2127.2705; found 2127.2717.

NMR Spectra:

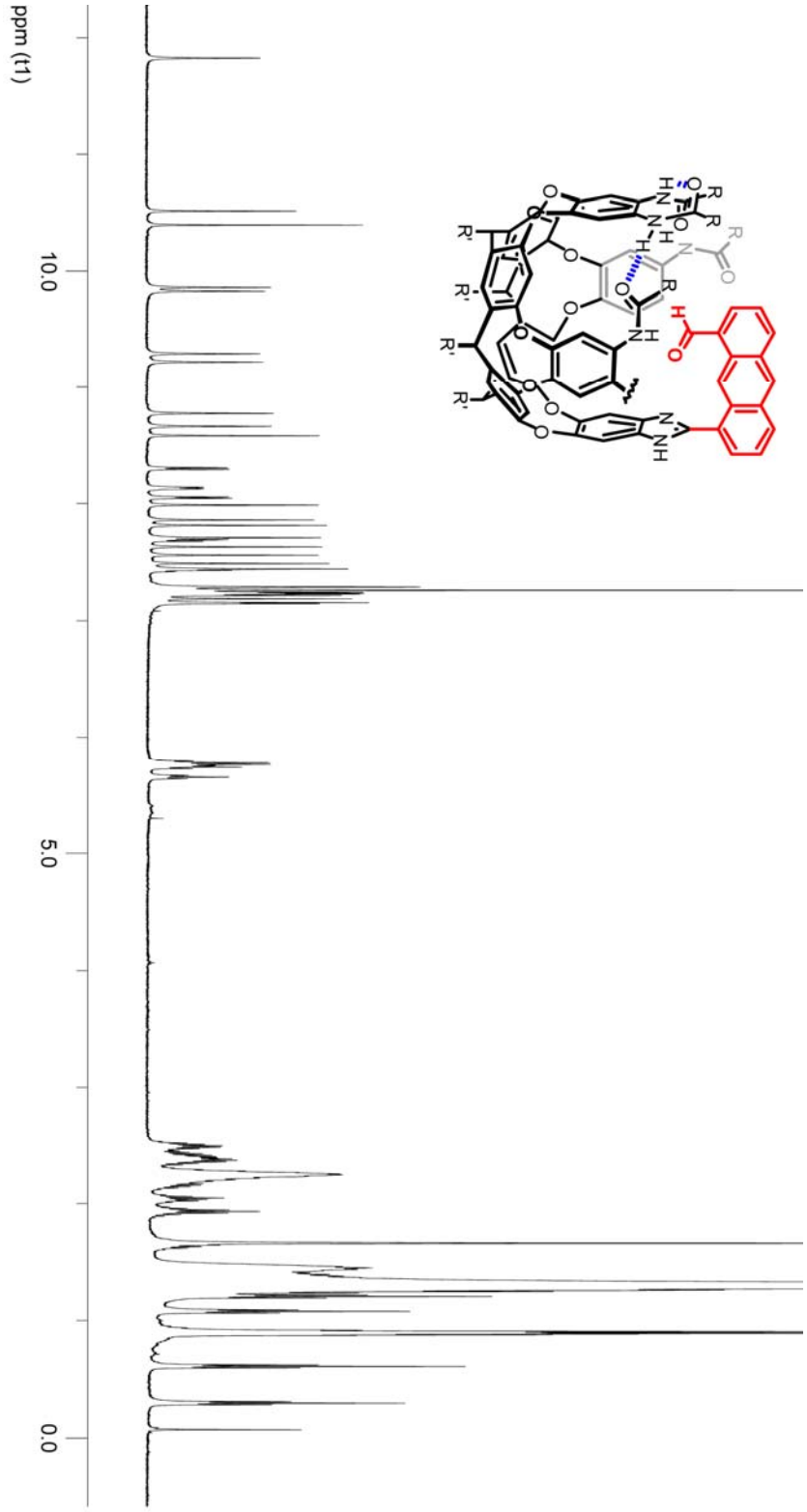


Figure *S*-1. ^{1}H NMR spectrum of cavitand **1** (600 MHz, $CDCl_3$, 300K)

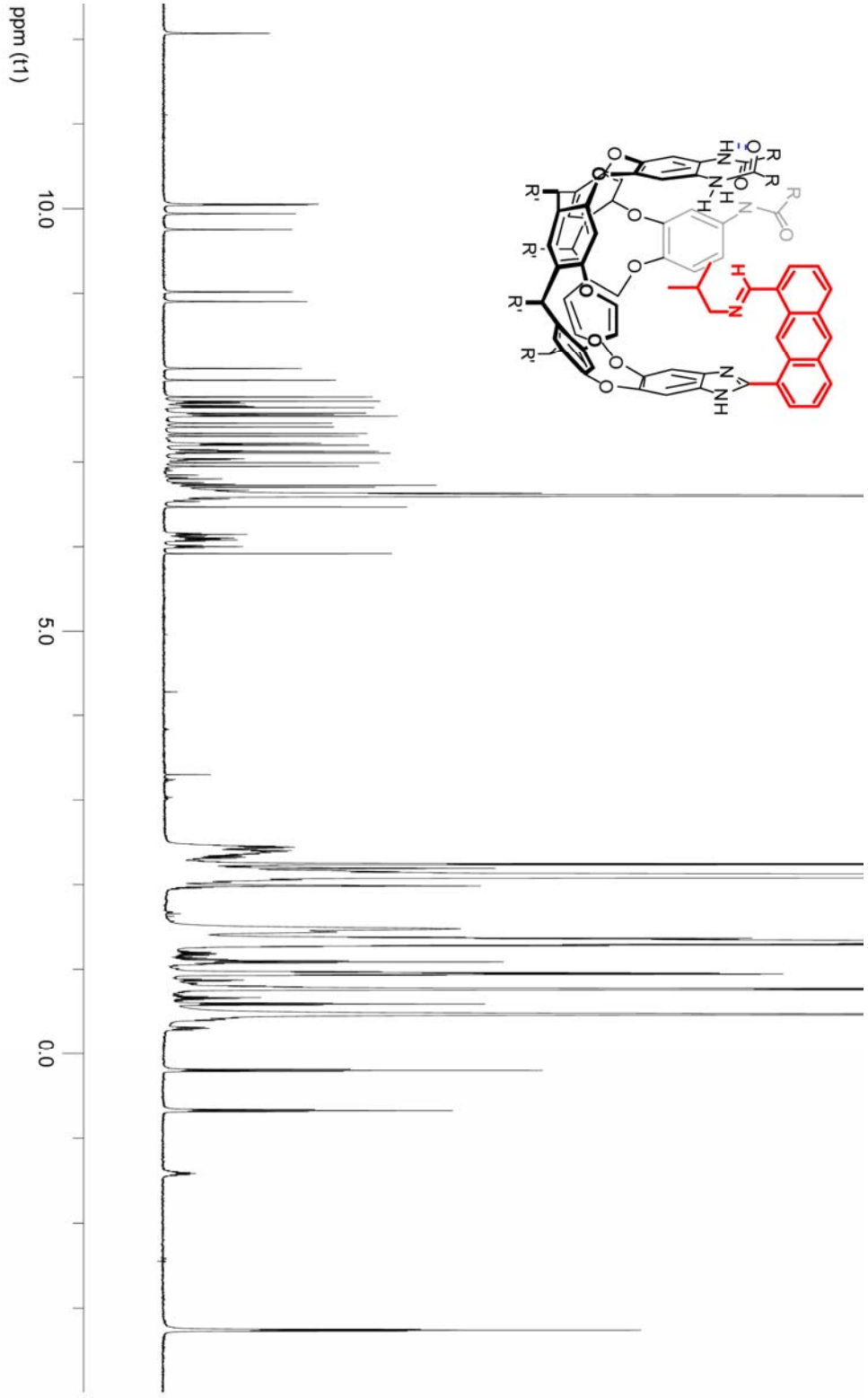


Figure *S*-2. ^{1}H NMR spectrum of imine generated from exposure of cavitand **1** to isobutylamine (600 MHz, mesitylene-d_{12}, 300K)

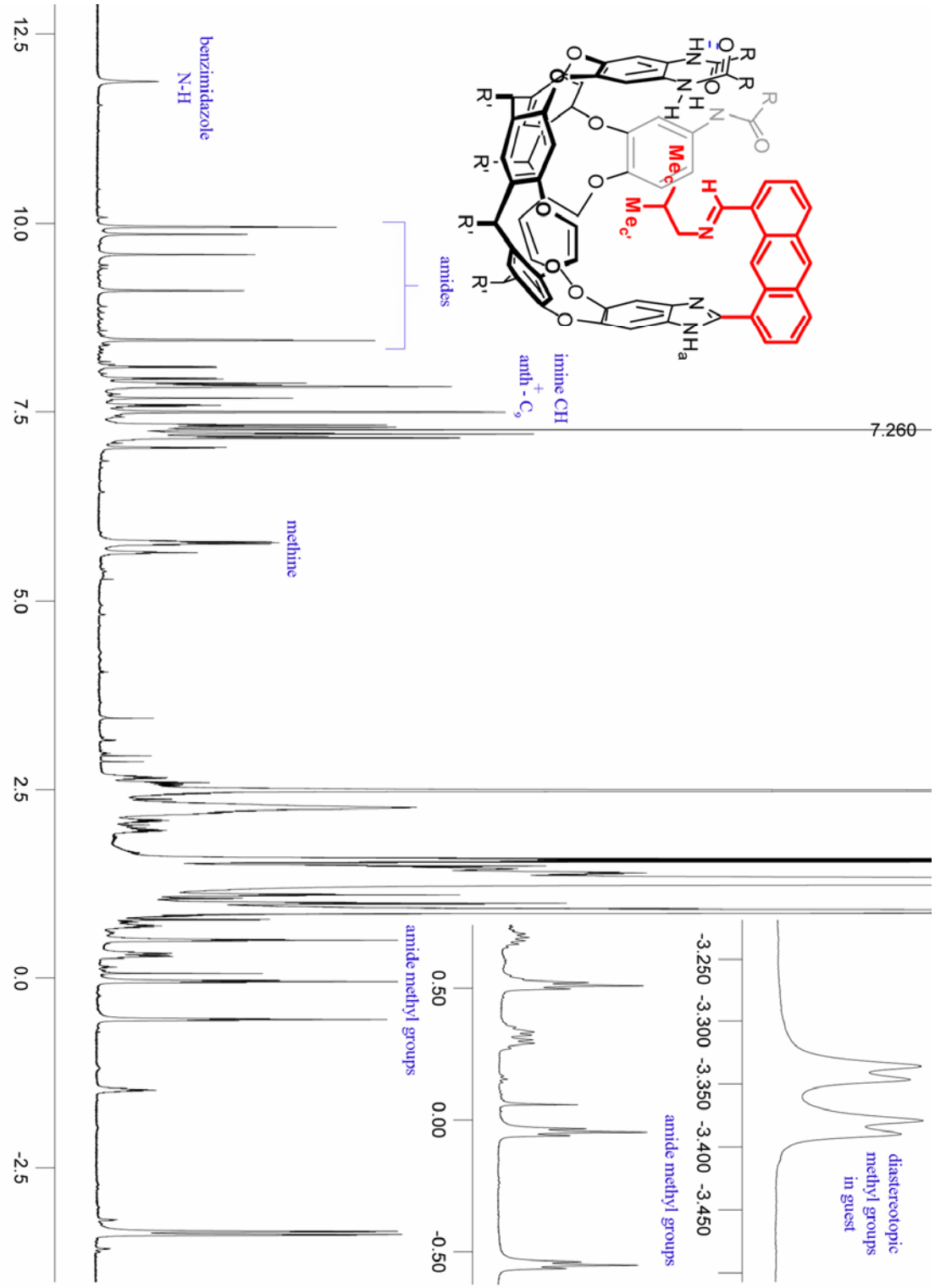


Figure *S*-2b. Partially assigned ^{1}H NMR spectrum of imine generated from exposure of cavitand **1** to isobutylamine (600 MHz, mesitylene-d_{12}, 300K).

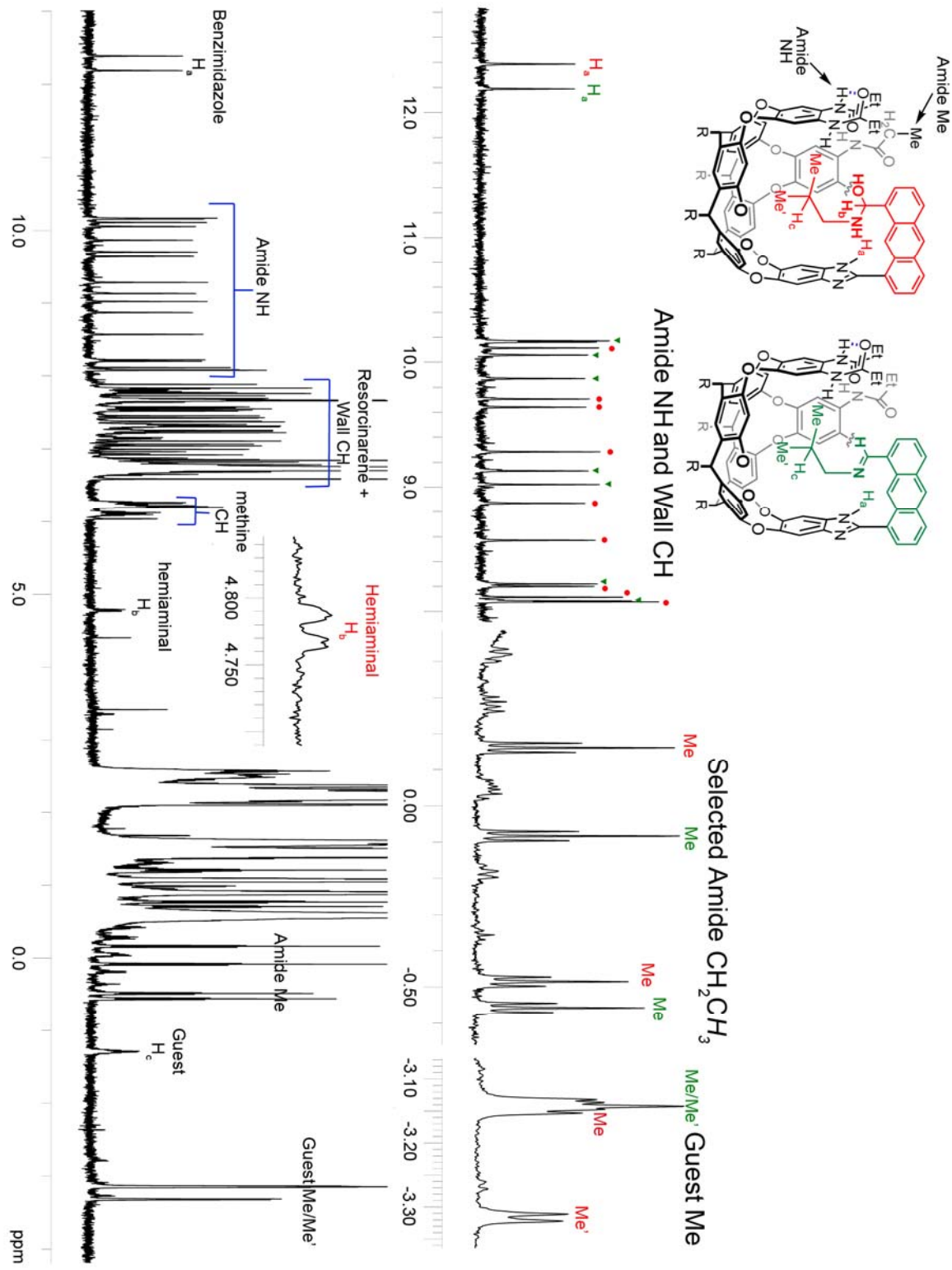


Figure *S*-2c. Partially assigned ^{1}H NMR spectrum (with expansions) of hemiaminal/imine mixture generated from exposure of cavitand **1** to isobutylamine for 30 min (600 MHz, mesitylene-d_{12}, 300K); Green annotation = imine product peaks. Red annotation = hemiaminal intermediate peaks.

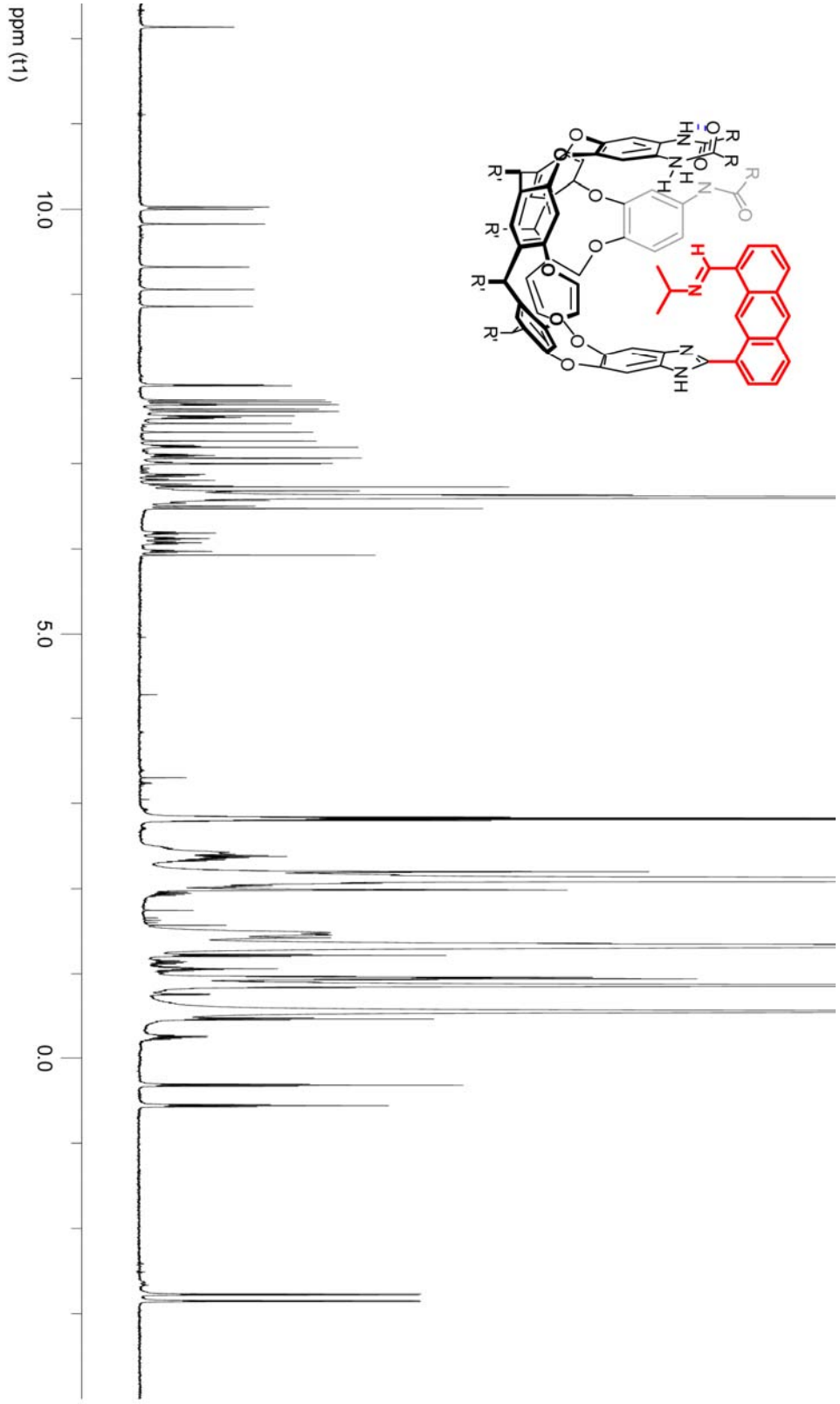


Figure *S*-3. ^{1}H NMR spectrum of imine generated from exposure of cavitand **1** to isopropylamine (600 MHz, mesitylene-d_{12}, 300K)

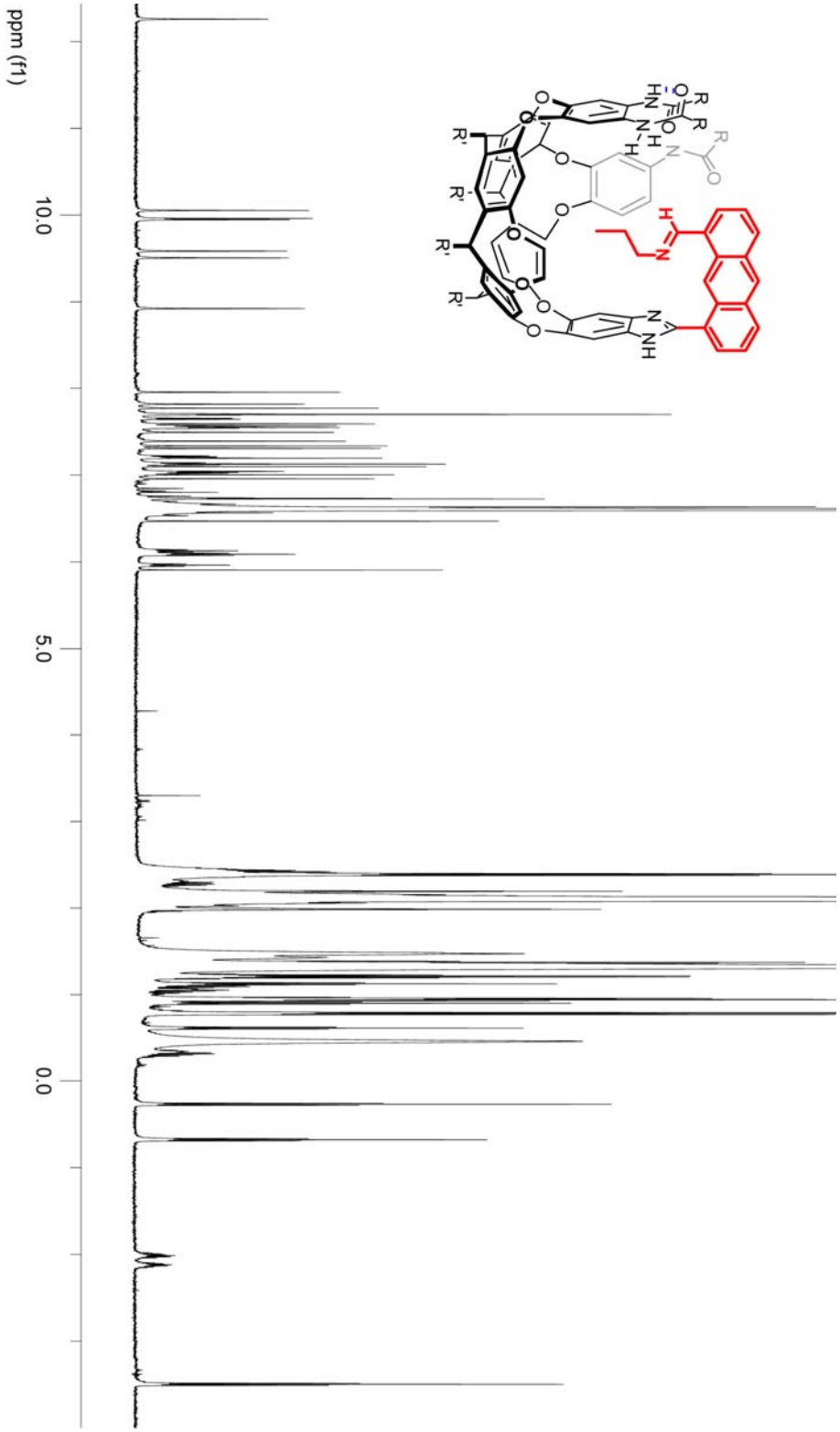


Figure *S*-4. ^{1}H NMR spectrum of imine generated from exposure of cavitand **1** to *n*-propylamine (600 MHz, mesitylene-d_{12}, 300K)

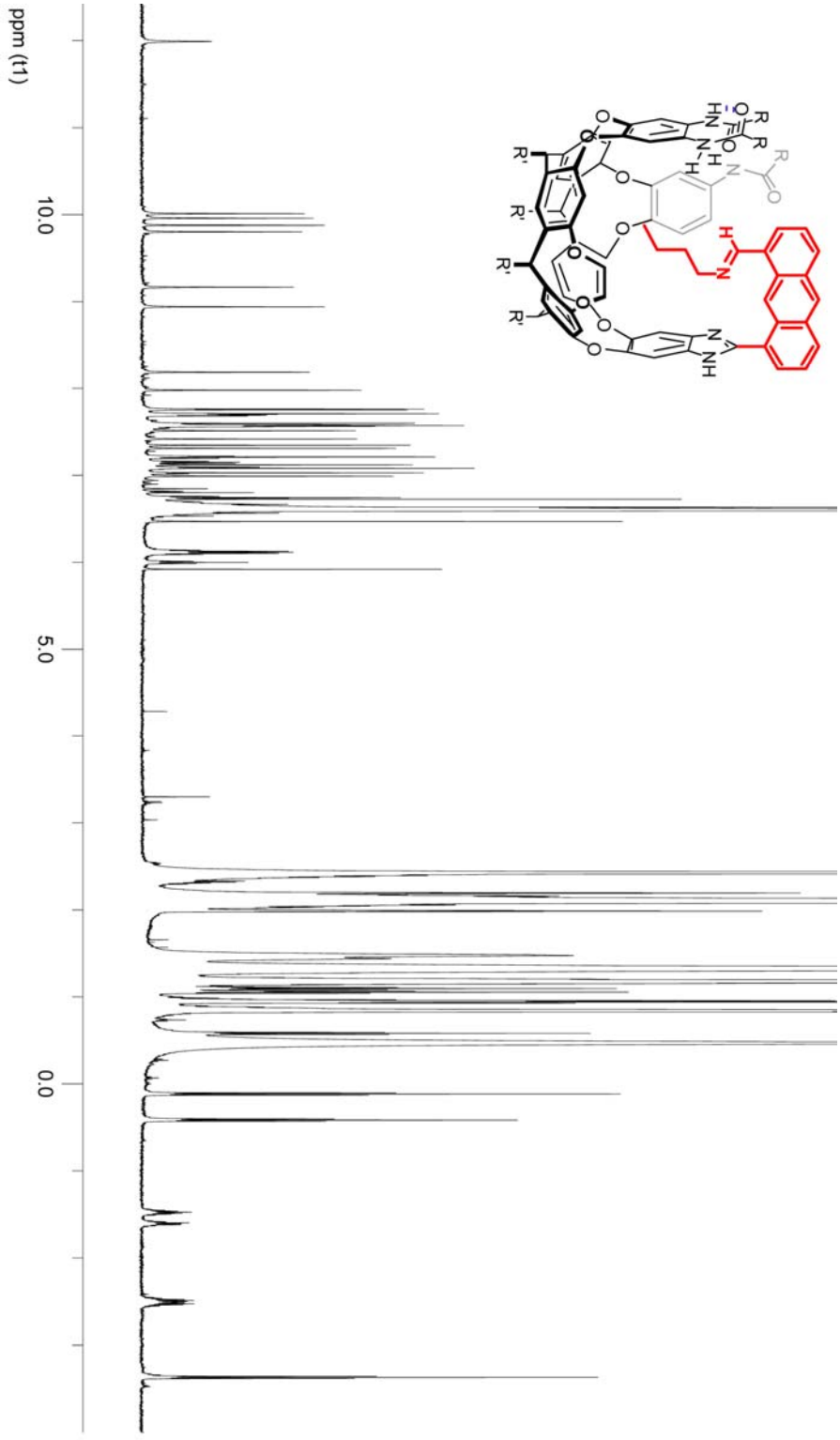


Figure *S*-5. ^{1}H NMR spectrum of imine generated from exposure of cavitand **1** to *n*-butylamine (600 MHz, mesitylene-d_{12}, 300K)

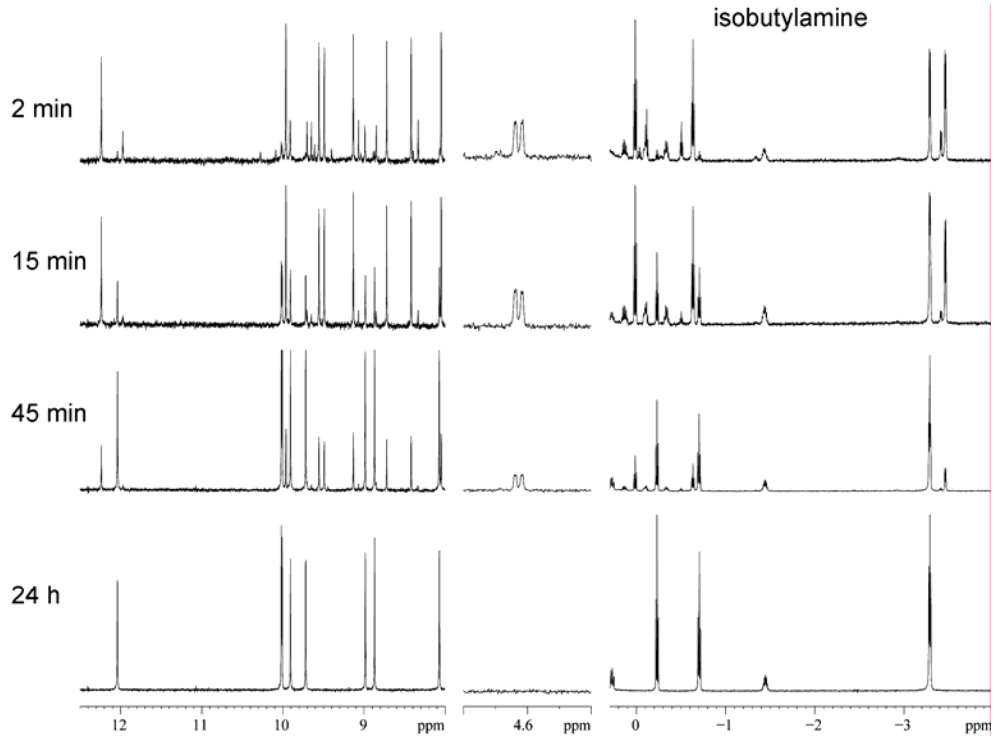


Figure *S*-6. Sections of ^{1}H NMR spectra of the reaction of cavitand **1** with isoutylamine over time (600 MHz, mesitylene-d_{12}, 300K).

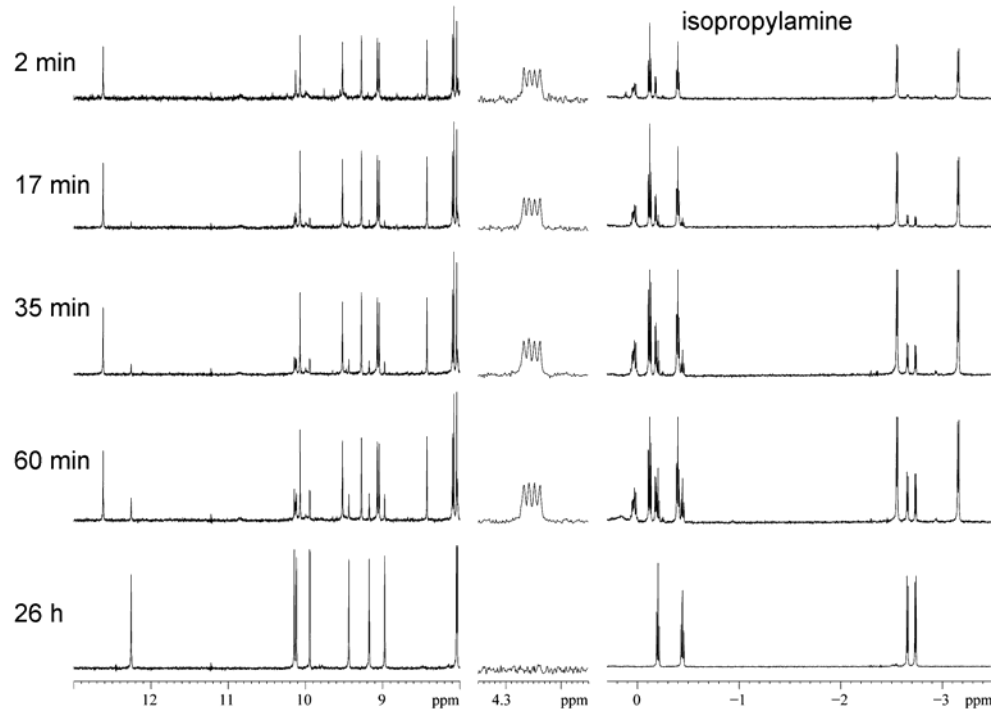


Figure *S*-7. Sections of ^{1}H NMR spectra of the reaction of cavitand **1** with isopropylamine over time (600 MHz, mesitylene-d_{12}, 300K).

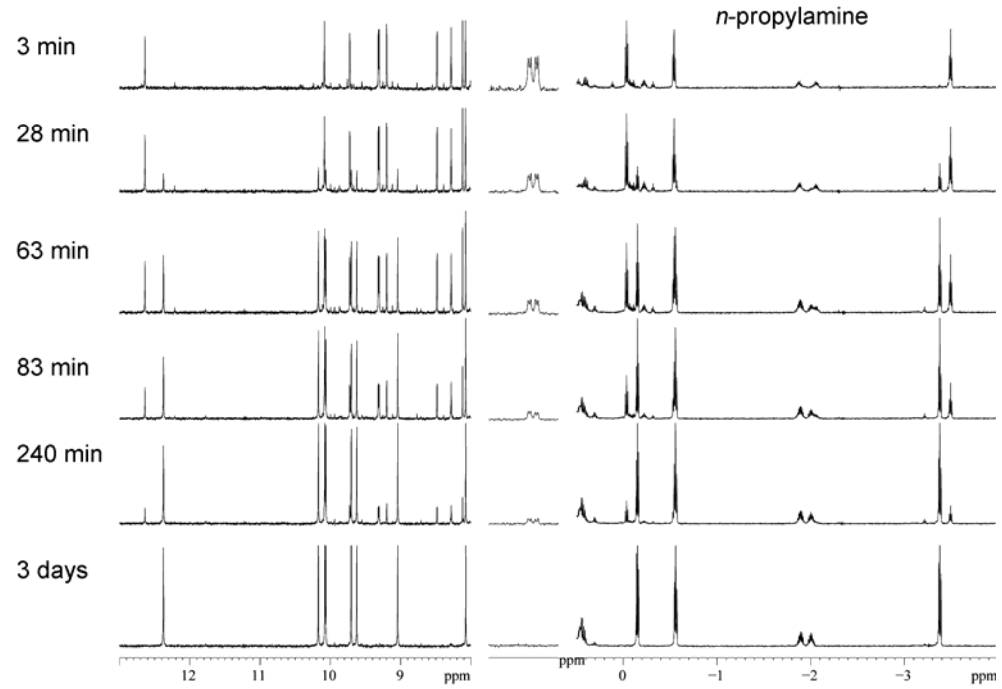


Figure *S*-8. Sections of ^{1}H NMR spectra of the reaction of cavitand **1** with *n*-propylamine over time (600 MHz, mesitylene-d_{12}, 300K).

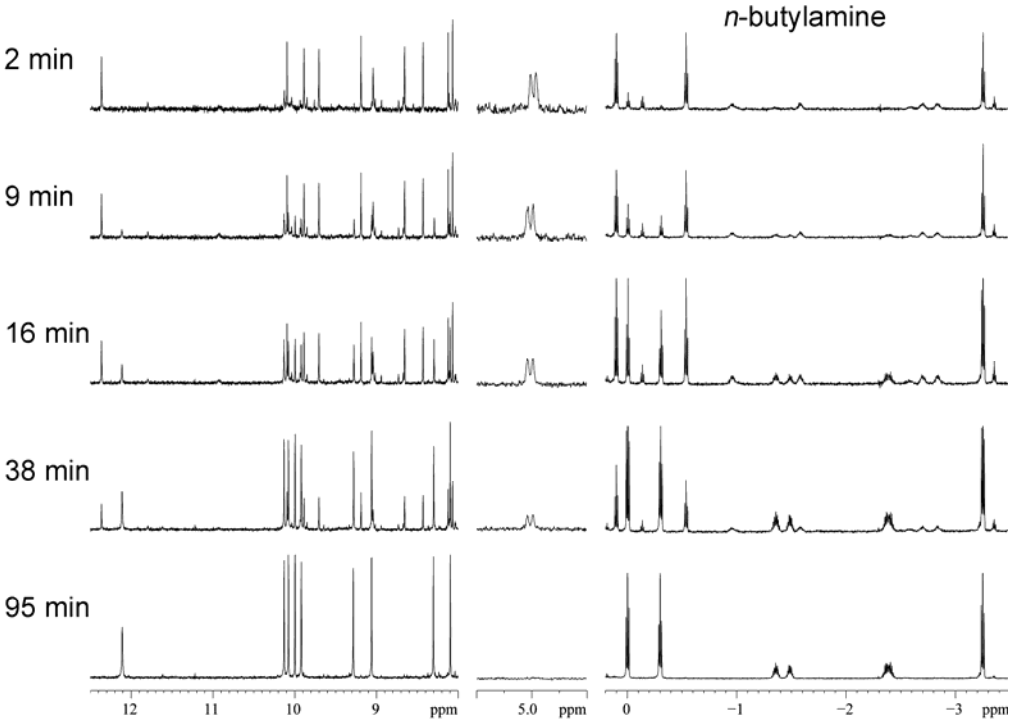


Figure *S*-9. Sections of ^{1}H NMR spectra of the reaction of cavitand **1** with *n*-butylamine over time (600 MHz, mesitylene-d_{12}, 300K).

Kinetics Plot for Formation of 6:

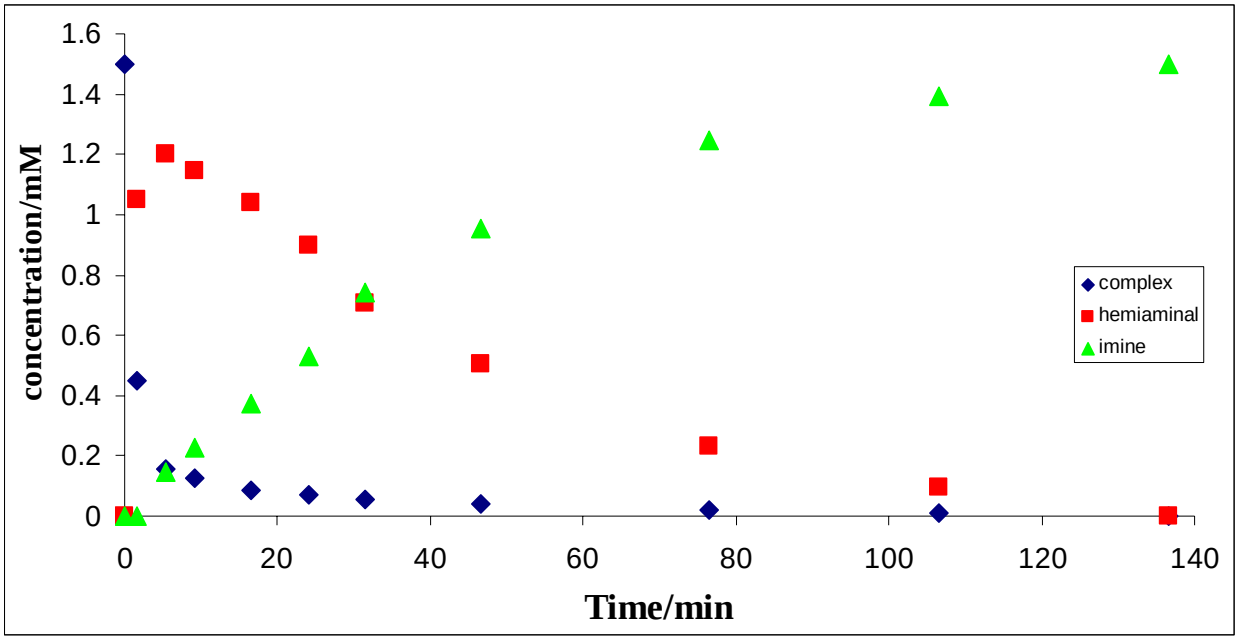


Figure *S*-10. Distribution of species in the cavitand with respect to time for the reaction of **1** (1.5 mM) with isobutylamine (10 mM) in mesitylene-d_{12}..

References

(*S1*) A. R. Renslo, F.C. Tucci, D. M. Rudkevich, J. Rebek, Jr. *J. Am. Chem. Soc.* **122**, 4573-4582 (2000).

(*S2*) T. Wada, K. Tsuge, K. Tanaka, *Inorg. Chem.* **40**, 329 – 337 (2001).

(*S3*) S. Lin, L. Yang, *Tetrahedron Lett.* **46**, 4315 – 4319 (2005).