Supporting Information

Enzyme-Like Catalysis of the Nazarov Cyclization by Supramolecular Encapsulation

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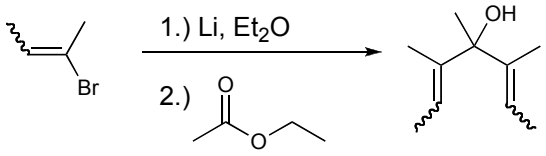
General Experimental Procedures. Unless otherwise noted, reactions and manipulations were performed using standard Schlenk and high-vacuum techniques at room temperature. All glassware was dried in an oven at 150 °C for at least 12 h or flame-dried under vacuum prior to use. Column chromatography was performed on a Biotage SP1 MPLC instrument using pre-packed silica gel columns.

Instrumentation. NMR spectra were obtained on Bruker Avance AV 300 (300 MHz), AV 400 (400 MHz), AV 500 (500 MHz), or AV 600 (600 MHz) spectrometers as indicated. Chemical shifts are reported as δ in parts per million (ppm) relative to residual protonated solvent resonances. In the case of D_2O samples, ^{13}C shifts were referenced to an internal standard of CH_3OH[1]. NMR data are reported in the following format: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; integration; coupling constant). The temperatures of the kinetics experiments carried out in a circulating oil bath were measured using a calibrated mercury thermometer and varied ±0.1 ºC. The temperatures of the kinetics and titration experiments carried out in an NMR probe were determined from the ^1H NMR chemical shifts of ethylene glycol and CH_3OH samples, and varied ±0.1 ºC. IR spectra were measured neat on a Nicolet iS10 FT-IR spectrometer with a diamond attenuated total reflective (ATR) accessory. Peak intensities are reported as broad (b), weak (w), medium (m), or strong (s). Only peaks in the functional group region (4000−1300 cm^{-1}) are reported. Mass spectral data were obtained at the QB3 Mass Spectrometry Facility operated by the College of Chemistry, University of California,

Berkeley. Fast atom bombardment mass spectra were recorded on a Micromass ZAB2-EQ magnetic sector instrument. Electron impact (EI) mass spectra were recorded on a Micromass ProSpec magnetic sector instrument equipped with an EI source.

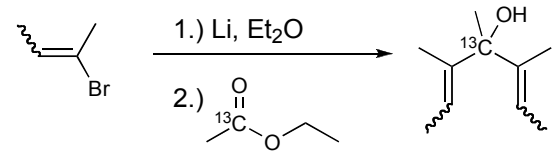
Materials. Unless otherwise noted, reagents were obtained from commercial suppliers and used without further purification. Ethyl ether (Et_2O), tetrahydrofuran (THF), and pentane were dried by passing through columns of activated alumina under nitrogen pressure and were sparged with nitrogen before use[2]. The two isomers of 2-bromo-2-butene could be separated by preparative gas chromatography (Varian Aerograph 970, using a 0.38" x 10' column packed 10% Carbowax chemically bonded to Chromsorb stationary phase). The helium flow rate was 60 mL/min, the column temperature was 60 ^{o}C, the injector temperature was 100 ^{o}C, and the detector temperature was 150 ^{o}C. Prior to injection, the *E* and *Z* isomers of 2-bromo-2-butene were passed through a column of basic alumina. Total recovery of the two isomers was approximately 45%, and both isomers were >99% pure by ^{1}H-NMR. Although the photoisomerization of pure (*E*)- or (*Z*)-2-bromo-2-butene has been reported[3], the pure compounds can tolerate ambient light for several minutes with no apparent erosion of stereochemical purity. As a precaution, however, all operations involving either pure compound were performed with as much light excluded as possible. The *E* and *Z* isomer of 2-bromo-2-butene are occasionally available commercially from Sigma-Aldrich. 1,2,3,4,7–pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide (**4**)[4] and $K_{12}Ga_4L_6$ (K_{12}**1**)[5] were prepared according to literature procedures.

Synthesis and Characterization of 3,4,5-Trimethyl-2,5-pentadien-4-ols: Attempts to separate the individual stereoisomers **2a**, **2b**, and **2c** from the mixture **2** were unsuccessful using silica chromatography, alumina chromatography, preparative gas chromatography, and reverse-phase HPLC. Compound **2a** could be prepared in reasonably high purity using commercially available (*E*)-2-bromo-2-butene. Although **2b** can be prepared from (*Z*)-2-bromo-2-butene, it can be obtained in higher purity via dienone **7b**. It was not possible to purchase (*Z*)-2-bromo-2-butene at the time of this work, so it was purified by preparative GC. Obtaining the necessary amount of (*Z*)-2-bromo-2-butene to prepare **2b** is very time-consuming, and the synthesis described here proved to be more convenient. The isomer **2c** was prepared via dienone **7c**. Attempts to synthesize **2c** directly from 3-methyl-3-penten-2-one and (*Z*)-2-bromo-2-butene were unsuccessful.



2

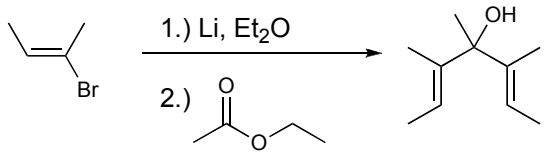
3,4,5-Trimethyl-2,5-pentadien-4-ol (2), mixture of stereoisomers. This procedure was adapted for a small scale (5-50 mmol) from a published procedure for the large-scale preparation of **2**[6]. A 2-necked round-bottomed flask equipped with a magnetic stir bar and a reflux condenser was charged with lithium wire (310 mg, cut into 1 cm lengths, 44.8 mmol) and 1.5 mL dry Et_2O. 2-bromo-2-butene was purified and dried immediately before use by passage through a pipette column of basic alumina. The first 1.0 mL of 2-bromo-2-butene (total of 2.3 mL, 22.4 mmol) was added to the stirred solution via syringe dropwise over the course of several minutes. At this point, the reaction initiated, as indicated by the evolution of heat and bubbling of the reaction mixture. An additional 15 mL of fresh Et_2O was added, and the remainder of the 2-bromo-2-butene was added slowly to keep the reaction at reflux. After the addition was complete, stirring was continued for one additional hour. The reaction mixture was then cooled to 0 ^oC in an ice bath and quenched by the slow addition of ethyl acetate (1.1 mL, 11.2 mmol) diluted to 50% with Et_2O. The reaction mixture was poured into saturated aqueous NH_4Cl and extracted five times with 20 mL Et_2O. The combined organic layers were washed with brine and dried over $MgSO_4$, and the solvent was removed by rotary evaporation to obtain the title compound (1.35 g, 8.75 mol) as a yellow liquid in 78% yield. This mixture contains **2a**, **2b**, and **2c** (*vide infra*) according to analysis by ^1H- NMR, $^{13}C\{^1H\}$-NMR and GC-MS.



2-^{13}C

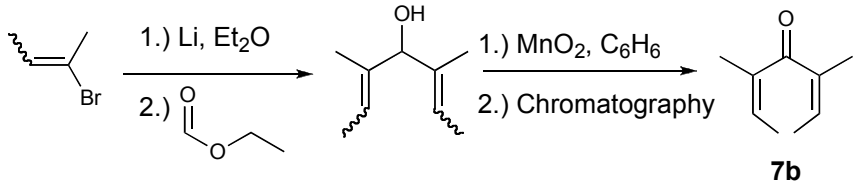
[4-^{13}C]3,4,5-Trimethyl-2,5-pentadien-4-ol (2-^{13}C), mixture of stereoisomers. The above procedure was followed using 313 mg lithium wire (45.2 mmol), 2.3 mL 2-bromo-2-butene (22.6 mmol), and 1.0 g ethyl acetate-1-^{13}C (11.3 mmol). The title compound was obtained as a yellow oil (1.40 g, 9.01 mmol) in 80% yield. This material is identical to **2** by ^1H

and $^{13}C\{^1H\}$-NMR, except that the following peaks are enriched: **$^{13}C\{^1H\}$-NMR** (125.8 MHz, $CDCl_3$): δ 78.9, 78.5, 76.4 ppm.



2a

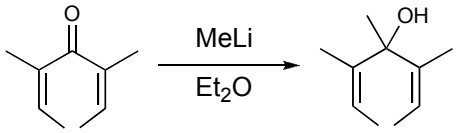
3,4,5-Trimethylhepta-2-*cis*-5-*cis*-dien-4-ol (2a). The above procedure for preparing **2** was followed using 192 mg lithium wire (27.7 mmol), 1.87 g (*E*)-2-bromo-2-butene (13.9 mmol), and 0.680 mL ethyl acetate (6.95 mmol). The title compound was obtained in 90% purity in 87% yield (928 mg, 6.0 mmol) as a yellow oil, with **2c** as the contaminant. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.55 (m, 2H, ^3J = 6.6 Hz, ^4J = 1.3 Hz), 1.56 (d, 6H, ^3J = 6.6 Hz), 1.43 (br, 6H), 1.32 (s, 3H) ppm; **$^{13}C\{^1H\}$ NMR** (125.8 MHz, $CDCl_3$): δ 139.7, 118.4, 78.9, 26.2, 13.7, 12.6 ppm; **IR**: 3459 (br), 2922 (s), 2859 (m), 1731 (w), 1452 (m), 1378 (s), 1366 (m), 1310 (w) cm^{-1}; **HRMS (EI)**: Exact mass calcd for $C_{10}H_{17}O$ $[M-H]^+$: 153.1279, found 153.1276.



7b

3,4,5-Trimethylhepta-2-*trans*-5-*trans*-dien-4-one (7b). The title compound was obtained in 11% overall yield. Purification of 2-bromo-2-butene was performed as described above. A 3-necked round-bottomed flask equipped with a magnetic stir bar, reflux condenser and addition funnel was charged with lithium wire (5.94 g, cut into 1 cm lengths, 0.86 mol) and 30 mL dry Et_2O. The first 1.5 mL of 2-bromo-2-butene (total of 43 mL, 0.43 mol) was added to the stirred solution via syringe in three 0.5 mL portions spaced at one minute intervals. At this point, the reaction initiated as indicated by the evolution of heat and bubbling of the reaction mixture. An additional 125 mL of fresh Et_2O was added, and the remainder of the 2-bromo-2-butene was added slowly via addition funnel to keep the reaction at reflux. After the addition was complete, the reaction mixture was stirred for one additional hour. The reaction mixture was cooled to 0 ^oC in an ice bath, and quenched slowly with ethyl formate (17 mL, 0.21 mol)

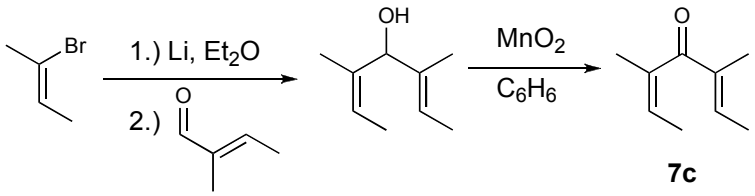
diluted to 50% with Et_2O, added via addition funnel. The reaction mixture was poured into saturated aqueous NH_4Cl and extracted five times with 100 mL Et_2O. The combined organic layers were washed with brine and dried over $MgSO_4$, and the solvent was removed by rotary evaporation to obtain the crude alcohol (22.36 g, 0.16 mol) as a red liquid. This material was used in the subsequent reaction without further purification. A round bottom flask equipped with a stir bar was charged with the crude alcohol (3.00 g, 21.4 mmol) and 200 mL pentane. To this mixture was added MnO_2 (37.0 g, 428 mmol), and the reaction mixture was stirred for one hour, at which point the reaction was complete as judged by TLC analysis (using 10% ethyl acetate in hexane as eluent). The reaction mixture was filtered through celite over a medium frit and concentrated by rotary evaporation to obtain compound **7b** as a mixture with the other two stereoisomers. Pure **7b** was obtained by automated column chromatography using a solvent gradient of 2 to 8% ethyl acetate in hexanes over 10 column volumes. The other two stereoisomers are copolar. The title compound was obtained as a yellow liquid in 31% yield (90.5 mg, 0.65 mmol). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.80 (q, 2H, ^3J = 7.3 Hz), 1.87 (s, 6H), 1.76 (d, 6H, ^3J = 7.3 Hz) ppm; **^{13}C{^{1}H} NMR** (125.8 MHz, $CDCl_3$): δ 203.1, 138.0, 131.0, 20.4, 15.3 ppm; **IR:** 2973 (m), 2921 (m), 1717 (m), 1640 (s), 1455 (s), 1378 (m) cm^{-1}; **HRMS (FAB)**: Exact mass calcd for $C_9H_{14}O$ $[M]^+$: 138.1045, found 138.1041.



7b **2b**

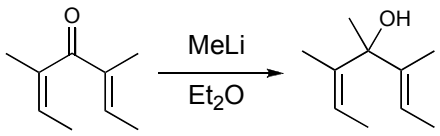
3,4,5-Trimethylhepta-2-*trans*-5-*trans*-dien-4-ol (2b). A flame-dried, 50 mL round-bottom flask was charged with 161 mg **7b** (1.16 mmol) and 25 mL Et_2O. The reaction mixture was cooled to -78 ^oC in a dry ice/acetone bath, at which point 0.91 mL methyllithium (1.6 M in pentane, 1.5 mmol) was added dropwise to the stirred solution by syringe. The reaction flask was removed from the cold bath and allowed to warm to room temperature, and the mixture was stirred for an additional two hours. The reaction mixture was quenched by addition to saturated aqueous NH_4Cl solution, and extracted with three portions of 50 mL Et_2O. The combined organic fractions were washed with three portions of brine and dried over $MgSO_4$, and the solvent removed by rotary evaporation to obtain 167 mg of the title compound (1.08 mmol) in

93% yield. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 5.27 (q, 2H, ^3J = 7.5 Hz), 1.81 (s, 6H), 1.58 (d, 6H, ^3J = 7.5 Hz), 1.35 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (125.8 MHz, $CDCl_3$): δ 141.8, 121.6, 76.4, 27.2, 22.1, 14.9 ppm; **IR:** 3480 (br), 2969 (s), 2941 (m), 2918 (m), 2860 (w), 1452 (m), 1376 (m) cm^{-1}; **HRMS (EI)**: Exact mass calcd for $C_{10}H_{17}O$ $[M-H]^+$: 153.1279, found 153.1280.



7c

3,4,5-Trimethylhepta-2-*cis*-5-*trans*-dien-4-one (7c). The procedure described above for preparing **7b** was followed using 1.3 mL (*Z*)-2-bromo-2-butene (12.8 mmol), 208 mg Li (30.0 mmol), and 1.35 mL tiglaldehyde (14.1 mmol) to quench the organolithium reagent in the first step. The resulting crude alcohol was oxidized without purification using 34 g MnO_2 (384 mmol). The resulting crude ketone was purified by automated chromatography using a 5% ethyl acetate in hexane. The title compound was obtained as a yellow liquid in 45% yield (862 mg). **^{1}H NMR** (600 MHz, $CDCl_3$): δ 6.72 (q, 1H, ^3J = 7.0 Hz), 5.52 (q, 1H, ^3J = 7.0 Hz), 1.86 (d, 3H, ^3J = 7.0 Hz), 1.81 (s, 3H), 1.79 (s, 3H), 1.47 (d, ^3J = 7.0 Hz) ppm; **^{13}C{^{1}H} NMR** (150.9 MHz, $CDCl_3$): δ 203.09, 142.27, 137.66, 137.11, 124.33, 21.67, 15.24, 15.18, 10.34 ppm; **HRMS (EI)**: Exact mass calcd for $C_9H_{14}O$ $[M]^+$: 138.1045, found 138.1044.



7c **2c**

3,4,5-Trimethylhepta-2-*trans*-5-*cis*-dien-4-ol (2c). The procedure described above for preparing **2b** was followed, using 100 mg **7c** (0.72 mmol) and 0.50 mL methyl lithium (1.6 M in diethyl ether, 0.79 mmol). The title compound was obtained in 81% yield (90 mg, 0.58 mmol) as a yellow liquid. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 5.62 (q, 1H, ^3J = 7.4 Hz), 5.32 (q, 1H, ^3J = 7.2 Hz), 1.70 (br, 6H), 1.65 – 1.61 (m, 9H), 1.43 (s, 3H) ppm; **^{13}C{^{1}H} NMR** (150.9 MHz, $CDCl_3$): δ 140.7, 140.0, 121.7, 118.0. 78.6, 26.8, 23.1, 14.5, 13.5, 12.8 ppm; **IR**: 3470 (br), 2969 (m),

2920 (m), 2862 (w), 1450 (s), 1378 (m), 1303 (m) cm^{-1}; **HRMS (EI)** : Exact mass calcd for $C_{10}H_{17}O$ $[M-H]^+$: 153.1279, found 153.1276.

General Procedure for Encapsulation Reactions:

The potassium salt of **1** (15.0 mg, 4.0 μmol) was dissolved in 0.6 mL D_2O (buffered to pD = 11.3 with 0.1 M K_2CO_3 to slow **1**-catalyzed reaction of guest), and the resulting solution was then mixed thoroughly with the guest (12.0 μmol). The solution was transferred to an NMR tube, and the spectrum of the host-guest complex was recorded within 20 minutes. The NMR resonances for the encapsulated guests are shifted upfield by 2 to 3 ppm because of shielding by the aromatic walls of the host. Due to the chirality of the host, diastereotopic atoms become inequivalent upon binding and two diastereomeric host-guest complexes were observed for the chiral guest **2c**. Quantitative guest binding was not observed in these experiments, so the reported binding efficiency represents the relative ^{1}H-NMR integrations of the guest to host peaks. Resonances corresponding to encapsulated guests were not observed by $^{13}C\{^1H\}$-NMR after obtaining hundreds of scans unless ^{13}C-enriched material is used. However, host resonances in the $^{13}C\{^1H\}$-NMR are easily observed. The unencapsulated guest is sparingly soluble in D_2O, and only broad resonances were observed. Encapsulated peaks were assigned by 2-D NMR Exchange Spectroscopy (EXSY) experiment acquired using an optimized 90^o pulse and a 150 msec mixing time.

K_{12}[2a ⊂ 1]. Host-guest complex prepared as above with a binding efficiency of 47%. **^{1}H NMR** (500 MHz, D_2O): δ 7.81 (br, 12H, Ar-*H*), 7.78 (d, 12H, ^3J = 8.7 Hz, Ar-*H*), 7.27 (d, 12H, ^3J = 8.7 Hz, Ar-*H*), 6.95 (t, 12H, ^3J = 7.0 Hz, Ar-*H*), 6.73 (d, 12H, ^3J = 7.1 Hz, Ar-*H*), 6.57 (t, 12H, ^3J = 7.6 Hz, Ar-*H*), -0.48 (br, 6H, encaps.), -1.22 (br, 3H, encaps.), -1.47 (br, 3H, encaps.), -1.71 (br, 3H, encaps.) ppm.

K_{12}[2b ⊂ 1]. Host-guest complex prepared as above with a binding efficiency of 86%. **^{1}H-NMR** (400 MHz, D_2O): δ 7.91 (d, 12H, ^3J = 6.3 Hz, Ar-*H*), 7.80 (d, 12H, ^3J = 8.1 Hz, Ar-*H*), 7.32 (d, 12H, ^3J = 7.6 Hz, Ar-*H*), 7.01 (t, 12H, ^3J = 7.5 Hz, Ar-*H*), 6.74 (d, 12H, ^3J = 6.8 Hz, Ar-*H*), 6.59

(t, 12H, ^3J = 7.4 Hz, Ar-*H*), -0.99 (s, 3H, encaps.), -1.04 (s, 3H, encaps.), -1.16 (br, 6H, encaps.), -1.94 (s, 3H, encaps.) ppm.

K_{12}[2c ⊂ 1]. Host-guest complex prepared as above with a binding efficiency of 83%. A 1:1 mixture of two diastereomeric host-guest complexes is formed. **^{1}H-NMR** (500 MHz, D_2O): δ 7.86 (br, 12H, Ar-*H*), 7.79 (d, 12H, ^3J = 8.5 Hz, Ar-*H*), 7.28 (d, 12H, ^3J = 7.9 Hz, Ar-*H*), 7.00 (t, 12H, ^3J = 8.0 Hz, Ar-*H*), 6.73 (d, 12H, ^3J = 7.1 Hz, Ar-*H*), 6.57 (t, 12H, ^3J = 7.8 Hz, Ar-*H*), -0.69 (s, 6H, encaps.), -0.85 (s, 6H, encaps.), -0.97 (s, 3H, encaps.), -1.03 (s, 3H, encaps.), -1.20 (s, 3H, encaps.), -1.40 (s, 3H, encaps.), -1.61 (s, 6H, encaps.) ppm.

K_{12}[2-^{13}C ⊂ 1]. The host-guest complex was prepared as above. By ^{1}H-NMR analysis, peaks corresponding to **2b** ⊂ **1** and **2c** ⊂ **1** are observed. The weaker-binding **2a** is not encapsulated in the presence of the other two stereoisomers. **^{13}C{^{1}H} NMR** (150.9 MHz, $CDCl_3$): δ 170.1, 167.0, 158.9, 155.0, 133.7, 127.3, 126.3, 119.8, 118.4, 115.9, 115.2, 114.9, 75.8 (encaps.), 73.6 (encaps.) ppm. The encapsulated peaks are not present in the ^{13}C{^{1}H} NMR of **K_{12}[2 ⊂1]** (prepared in an analogous fashion), which is otherwise identical by ^{1}H and ^{13}C{^{1}H} NMR.

Kinetic Analysis of Catalyzed Reactions:

General procedure for kinetic runs: 2.0 mg substrate alcohol (13.0 μmol), 3.5 mg K_{12}**1** (0.9 μmol), 2.0 mg maleimide (20.6 μmol), and 3.0 mg sodium *p*-toluenesulfonate (15.4 μmol, added as an integration standard) were dissolved in 0.3 mL DMSO-d_6 and 0.3 mL D_2O (buffered with 100 mM phosphate buffer, adjusted to pD = 8.0). The solution was transferred to an NMR tube and inserted into the NMR probe preheated to 45 ^{o}C. After allowing the sample temperature to equilibrate for two minutes, ^{1}H-NMR spectra were acquired every 20 seconds (for **2b** and **2c**) or every 240 seconds (for **2a**) until >95% of the starting material was consumed. Concentration versus time plots for the **1**-catalyzed reactions of **2a**, **2b**, and **2c** are given in Figure S1, Figure S2, and Figure S3 respectively.

Rate constants are calculated from initial rate data (first 15% conversion) using the Michaelis-Menten equation:

$d[P]/dt = (k_{cat}[\mathbf{1}]_{tot}[SM])/([SM] + K_M)$, where [SM] is the average starting material concentration and $K_M = (k_{cat} + k_{-1})/k_1$.

Since guest exchange is fast in this system, the reciprocal of the dissociation constant ($1/K_d$) of the host-guest complex is substituted for K_M. In the case of substrate **2b**, the concentration of host-guest complex **2b** ⊂ **1** can be measured during the kinetic run, and the K_d is calculated from the observed concentration of **1**, **2b**, and **2b** ⊂ **1**. In the case of substrates **2a** and **2c**, concentrations of the respective host-guest complexes are too low to measure under the reaction conditions of the kinetic runs. The K_d for **2c** ⊂ **1** can be determined by preparing samples that are more highly concentrated than those used for the kinetic runs, and buffered to a higher pD to slow the **1**-catalyzed Nazarov reaction. The K_d for **2a** ⊂ **1** could not be determined using this method. Standard errors are given in parentheses.

Typical procedure for binding constant determination: 22.0 mg K_{12}**1** (5.8 μmol), 3.0 mg substrate alcohol (19.4 μmol), and 3.0 mg sodium *p*-toluenesulfonate (15.4 μmol, added as an integration standard) were dissolved in 0.3 mL DMSO-d_6 and 0.3 mL D_2O (buffered with 100 mM carbonate buffer, adjusted to pD = 11.0). The solution was transferred to an NMR tube and inserted into the NMR probe preheated to 45 °C. A single scan ^{1}H-NMR spectrum was obtained using a calibrated 90° pulse and a 6.0 second relaxation time.

Substrate	Initial d[P]/dt (M/s)	K_d (M^{-1})	k_{cat} (s^{-1})	k_{obs} (s^{-1})
2a	$4.0(5) \times 10^{-7}$	-	-	$5.1(1) \times 10^{-5}$
2b	$7.6(2) \times 10^{-6}$	24(1)	$1.6(1) \times 10^{-2}$	$4.2(1) \times 10^{-4}$
2c	$1.64(4) \times 10^{-5}$	11(1)	$5.7(1) \times 10^{-2}$	$1.08(2) \times 10^{-3}$

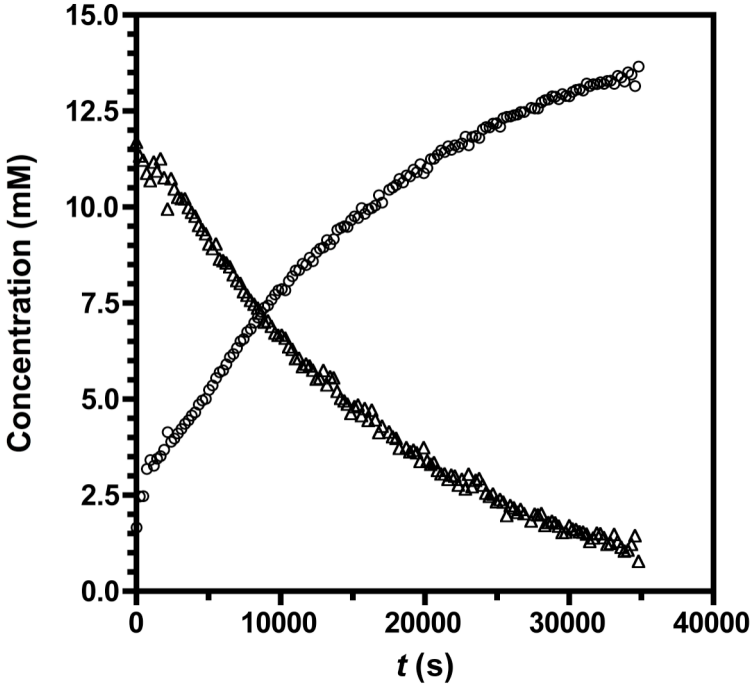


Figure S1: Concentration vs. time plot of the reaction of substrate **2a** (△) to form **4** (○), catalyzed by 1.5 mM **1** at 45 ^{o}C with added maleimide.

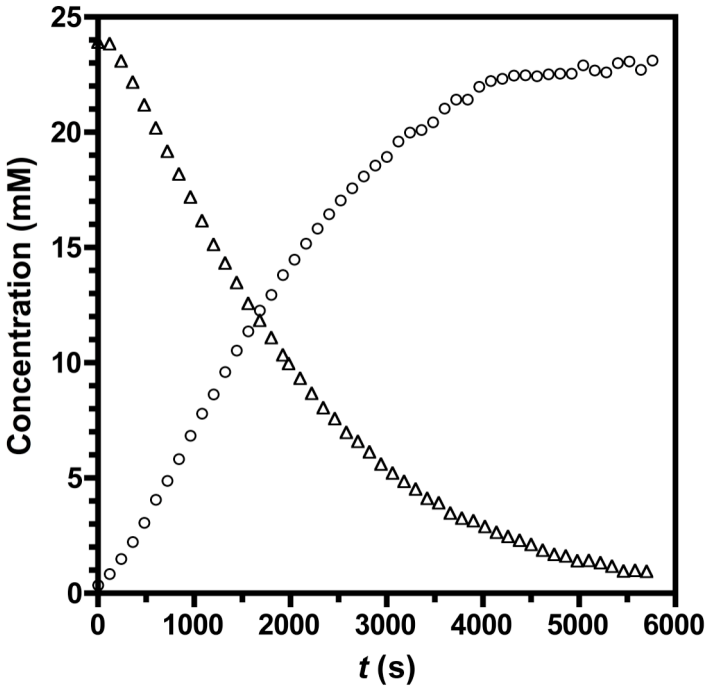


Figure S2: Concentration vs. time plot of the reaction of substrate **2b** (△) to form **4** (○), catalyzed by 1.5 mM **1** at 45 °C with added maleimide.

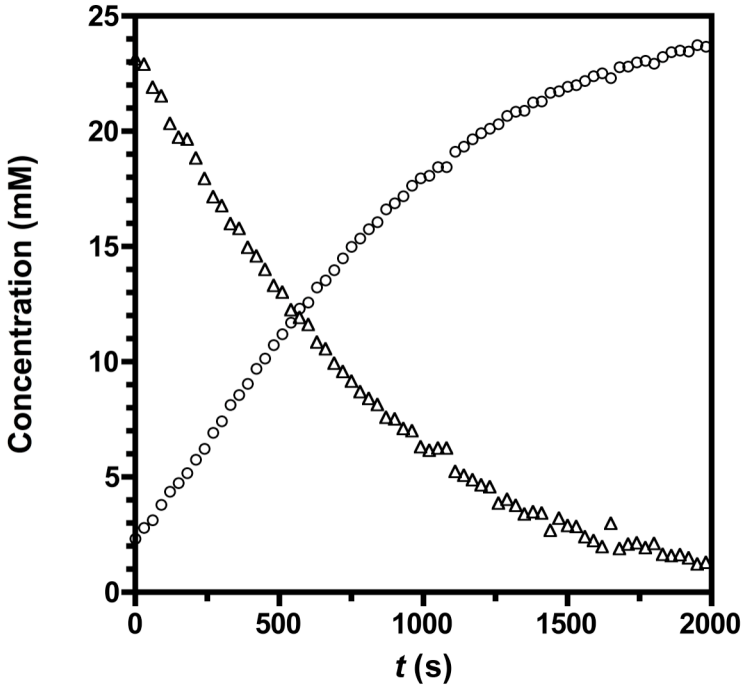


Figure S3: Concentration vs. time plot of the reaction of substrate **2c** (△) to form **4** (○), catalyzed by 1.5 mM **1** at 45 °C with added maleimide.

Kinetic Analysis of Uncatalyzed Reactions:

The procedure for sample preparation is analogous to that used for the catalyzed reaction, except that **1** is omitted. The sample is sealed under vacuum in a thin-walled NMR tube and heated at 45 °C in circulating oil bath. During initial attempts to measure the uncatalyzed reaction rate of **2a**, the data obtained were erratic, exhibiting an apparent induction period (e.g., there was little or no reaction for a period of time, followed by a decrease in substrate concentration). A likely explanation is that the glass from the NMR tube is slowly (over the course of days) acidifying the reaction mixture, at which point the reaction proceeds more rapidly. The measurements were repeated using silylated NMR tubes, in which the acidic

functional groups on the interior glass surface are protected as silyl ethers. The rate data collected in silylated tubes were very erratic, and we suspected that the hydrophobic substrate was adsorbing to the silylated surface in the upper portion of the tube, which is outside of the NMR probe during measurement. Partially silylated tubes, in which only the portion of the NMR tube that contacts the reaction mixture was silylated and the remainder is unmodified, were prepared. This modification yielded consistent results, and over the course of many weeks low but reproducible levels of conversion of all three Nazarov substrates was observed. By treating the initial reaction rate as the derivative of a first-order process, the rate constant is calculated from the equation $d[SM]/dt = - k_{uncat} [SM]$. The reported values are the average of two or more experiments.

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