Electronic Supplementary Material (ESI) for Chemical Communications.

Supporting Information

The "Chaperone" Effect in Microwave-Driven Reactions

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Heating curves for solutes of interest in tridecane.

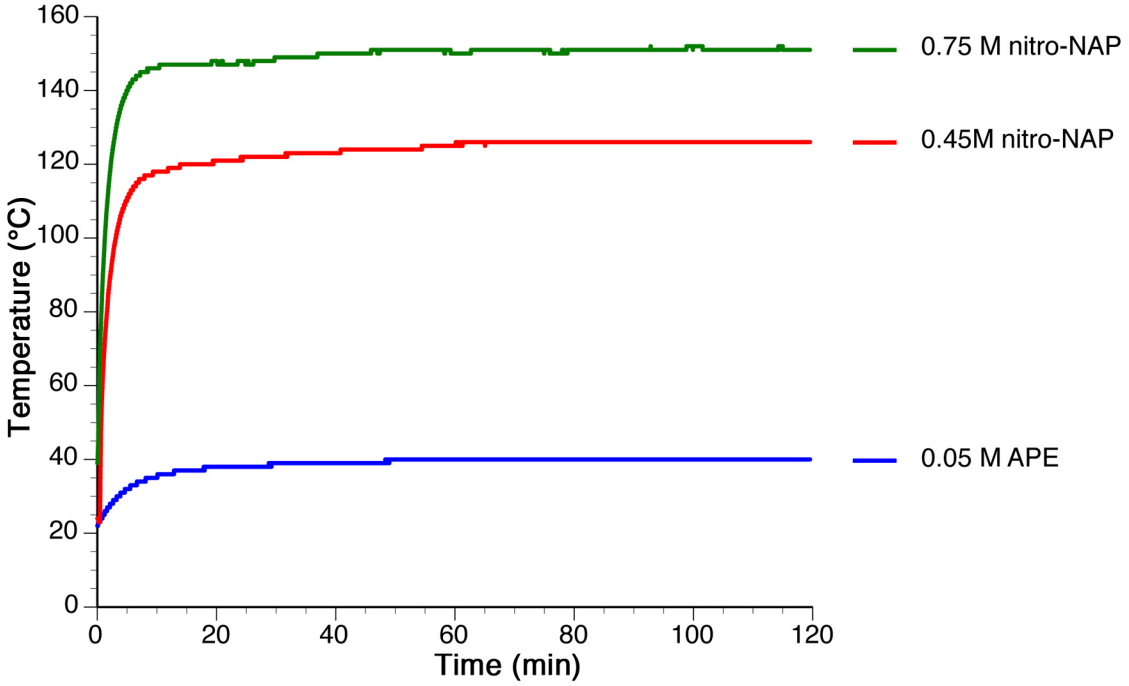

Figure S1. Microwave heating curves for (blue) 0.05 M APE and (red) 0.45 and (green) 0.75 nitro-NAP at 50 W constant power.

Aggregation of nitro-NAP and APE in tridecane.

General NMR experimental information:

All materials were purchased from Sigma-Aldrich and used without further purification. ^{1}H-NMR was performed on a 400 MHz spectrometer using cyclohexane-d^{12} (C_6D_{12}) as the deuterated solvent. The chemical shifts (**δ**) are reported in parts per million (ppm) relative to the residual solvent peak (1.38 ppm for ^{1}H-NMR). All samples were made by dissolving the appropriate amount of either allyl phenyl ether, 1-nitronaphthalene or both, in 1 mL of a 1:1 (v:v) mixture of tridecane and cyclohexane-d12.

Among several methods for determining the presence and degree of molecular association in solution, perhaps the simplest and most common is to analyze for concentration-dependent changes in chemical shift by ^{1}H NMR spectroscopy. Observed changes in chemical shift with the concentration of nitro-NAP and APE will provide support for aggregation.

Self-Aggregation of 1-Nitro-Naphthalene (nitro-NAP):

The chemical shifts of the protons on nitro-NAP in tridecane as function of concentration are given in Table S1 and shown in Figure S2. As can be seen, there is an upfield chemical shift with increasing concentration, consistent with aggregation. The observed chemical shift changes are smaller than what was observed in larger conjugated systems and strongly interacting biological molecules.[1-3] Estimates of the association constants, K, obtained from equation 1 in reference [1] yielded values of 0.055> K <.003 for the protons in Table S1. While it is likely the nitro-NAP system is more weakly interacting than systems typically studied by this method, there are other factors that compromise the quantitative result. In particular, we are not able to duplicate the conditions under which the microwave experiment was carried out. Specifically, at the low temperatures used in the experiment the concentration of nitro-NAP used, due to solubility, lower (≤.21 M) than was used under reaction conditions. Moreover, to obtain lock we used a 1:1 mixture of tridecane and cyclohexane-d12. For these reasons we think this represents a lower estimate of the association. Regardless, concentration-dependent changes in chemical shifts are consistent with solute aggregation in solution.

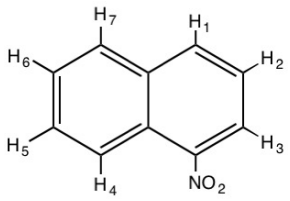

Table S1: Observed NMR shifts of 1-Nitronaphthalene at Different Concentrations

Total Concentration (M)	H_4	H_3	H_1	H_7	H_5	H_6	H_2
0.01	8.703	8.218	8.055	7.924	7.707	7.604	7.509
0.03	8.697	8.213	8.052	7.922	7.703	7.602	7.506
0.09	8.679	8.199	8.042	7.913	7.692	7.593	7.494
0.15	8.664	8.187	8.032	7.903	7.682	7.586	7.483
0.21	8.646	8.174	8.022	7.893	7.671	7.578	7.472

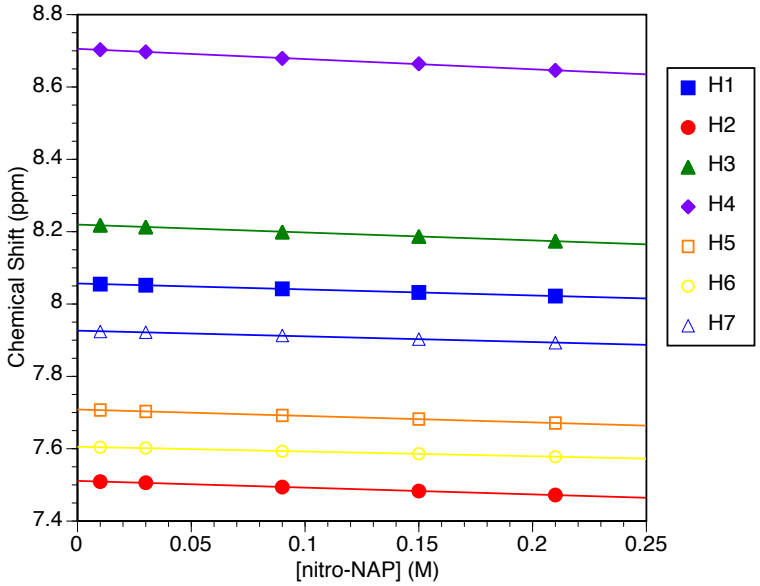

Figure S2. Chemical shift as a function of nitro-NAP concentration in tridecane/cyclohexane-d12.

Association of Allyl Phenyl Ether (APE) with nitro-Nap:

The association of APE with nitro-NAP is also observable by tracking changes in APE chemical shifts at progressively higher concentrations of nitro-NAP (Table S2). Plots of the chemical shift are shown in Figure S3. As can be seen, the complex changes in the proton chemical shift for APE exhibit upfield or downfield chemical shifts, depending on the peak. These changes reflect differential impacts on the various APE protons as a function of aggregation between APE and the chaperone molecule (nitro-NAP). We perceive the magnitude of the chemical shift changes to be small, indicative of relatively weak interactions under the experimental conditions. H6 and H7 of APE showed almost no change, H4 and H5 shifted upfield, and H1 and H2 shifted downfield with increasing nitro-NAP concentration. Similar observations have been made in other binary associating systems and were ascribed to specific orientations of the molecules relative to each other.[4] In this case, dipole-dipole interactions may enforce preferential orientation of the APE that causes some protons to be shield and other deshielded. With respect to the results reported here, the chemical shift changes serve to indicate that some degree of aggregation between the APE and the nitro-NAP is observed.

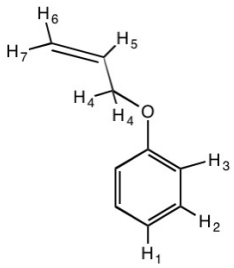

Table S2 Observed NMR shifts of APE at Different Concentrations

Total Concentration (M)	$H_{1,3}$*	H_2	H4	H5	H6	H7
0.01	6.890	7.237	4.5206	6.0885	5.439	5.255
0.03	6.891	7.237	4.5198	6.0883	5.439	5.255
0.09	6.892	7.239	4.5177	6.0881	5.439	5.255
0.15	6.893	7.241	4.5161	6.0877	5.439	5.255
0.21	6.894	7.243	4.5139	6.0874	5.440	5.255

*Chemical shifts of H_1 and H_3 are not distinguishable from each other

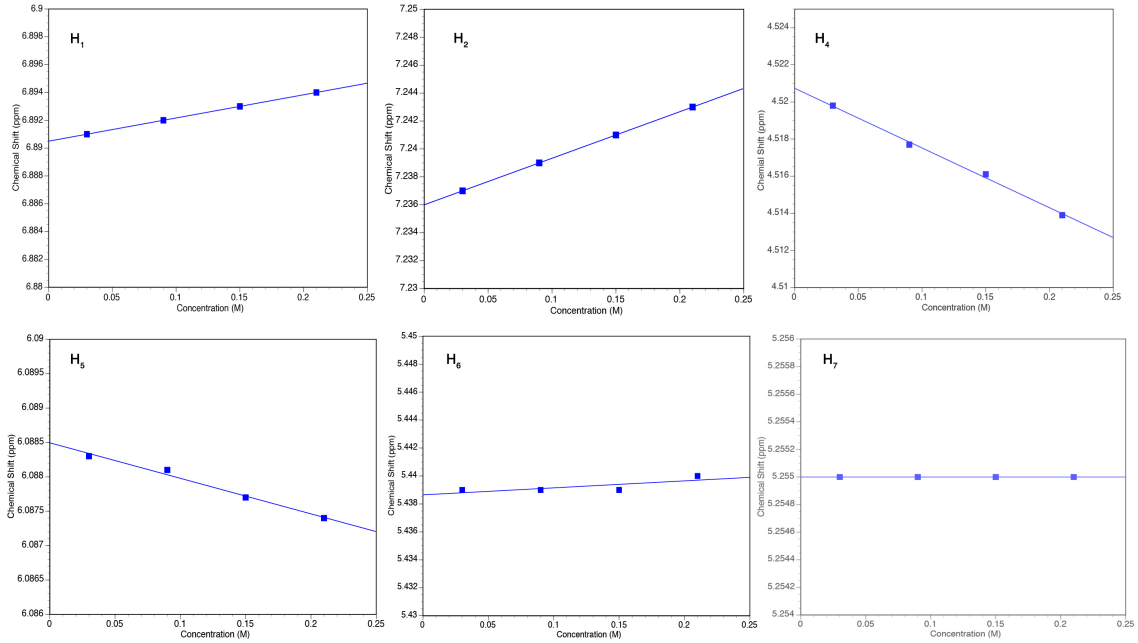

Figure S2 Chemical shift of APE protons as a function of nitro-NAP concentration in tridecane/cyclohexane-d12.

Microwave Kinetic Determinations.

To obtain kinetics data under microwave conditions for the reaction of APE in the presence of a chaperone (i.e. 1-nitro-naphthalene or dimethylsulfoxide), four independent samples of 0.05 M APE solution in tridecane at the desired concentration of chaperone were used for *each* of the reaction times of the

experiment. So, for example, for a reaction solution whose concentration was to be determined at 2, 3, 4 and 5 hrs in a kinetics run, four independent samples of APE in tridecane with the desired concentration of chaperone were reacted for 2 hours, and the concentration of each determined. Four fresh samples taken from the same stock solution were then reacted for 3 hours and the concentrations determined; this procedure was repeated for the other times. Once reacted and allowed to cool, 300 μL of the solution were transfer to a 10 mL volumetric flask, to which was added enough 1 M naphthalene in toluene solution to fill a 10mL volumetric flask (naphthalene is the internal standard for gas chromatography (GC) measurement, toluene is the solvent for GC samples). This was done to minimize the inherent difficulty in quantitatively withdrawing aliquots of a solution from the heat source. In addition it removes the effect of cooling and then reheating with applied microwave power to reestablish the temperature that would necessarily result from trying to take multiple aliquots from the same sample.

Conversion of Allyl phenyl ether (APE) to 2-Allylphenol in the presence of 1-Nitronaphthalene

In the microwave reaction a fixed starting concentration of 0.05 mol/L of APE is used. For a 1 : 9 APE : nitro-NAP solution, 0.234 g nitro-naphthalene was dissolved in 3 mL of 0.05 mol/L APE in tridecane solution to form 0.45 mol/L nitro-NAP solution. A sealed quartz tube containing the 1 : 9 chaperone solution was placed in the microwave (CEM SP) equipped with a stirring bar. Temperature was determined internally using a fiber optic that was independent calibrated to a NIST traceable thermocouple. Using an applied power of 250 W, four identical samples were irradiated for periods of 2, 3, 4 and 5 hrs respectively. Following the protocol described above, the concentration of APE over time was determined. The same procedure was used for the other APE:nitro-NAP ratios: 1 : 15 (0.05 M APE, 0.75 M nitro-NAP) and 1 : 6 (0.05 M APE, 0.30 M nitro-NAP). For each of these reaction solutions, different powers were used to reach similar steady-state solution temperatures (see main text). The kinetics exhibited the expected first order decay as can be seen in the plots in Figures S3-S5. The rate constants were determined by least squares fitting of the decay using the Stata statistical program. The rate constants and least squares fitting parameters are given in Table S3.

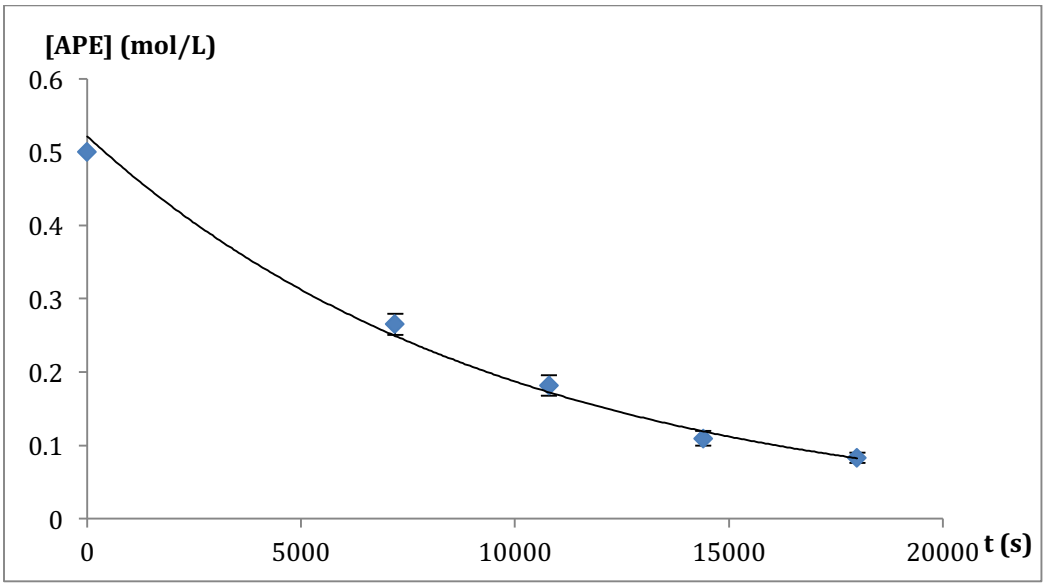

Figure S3. Kinetic plot of 1:9 APE :nitro-NAP microwave Claisen rearrangement.

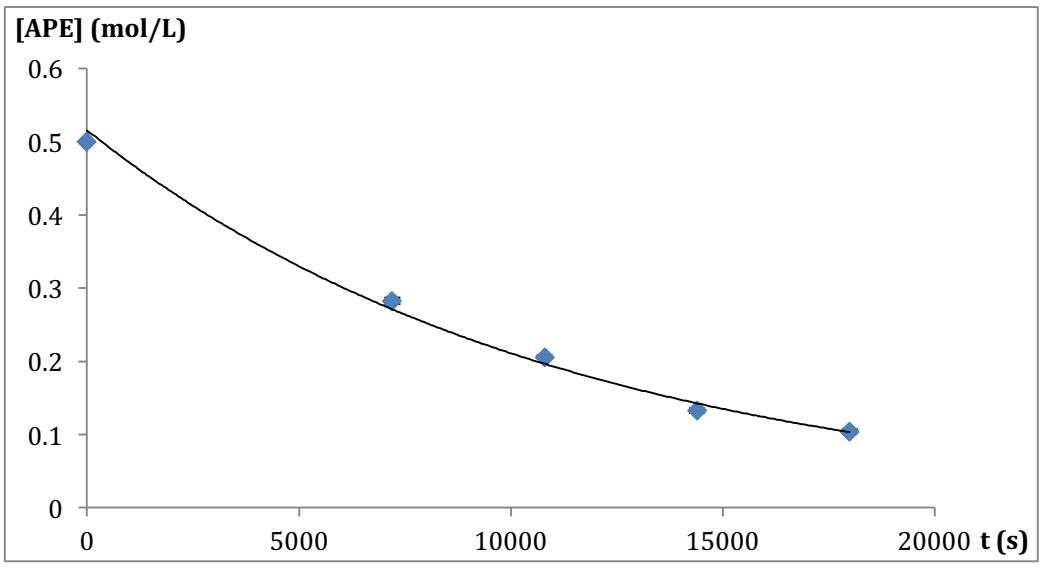

Figure S4. Kinetic plot of 1 : 15 APE : nitro-NAP microwave Claisen rearrangement.

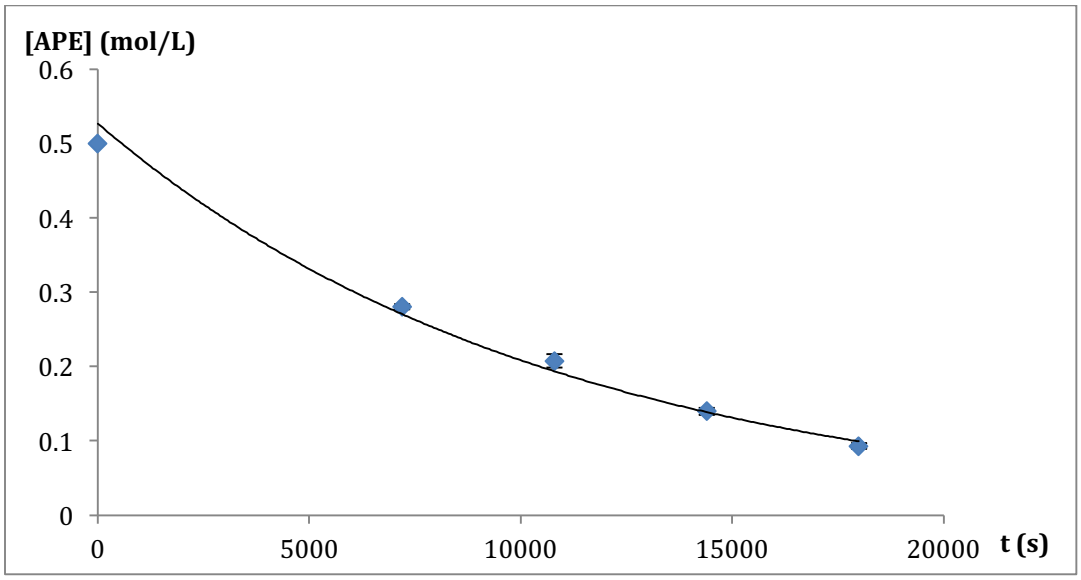

Figure S5. Kinetic plot of 1 : 6 APE : nitro-NAP microwave Claisen rearrangement.

Table S3 Rate constants and Least squares fitting of APE decay in the microwave

Power (W)	[nitro-NAP]	k (min^{-1})	std error	R^2	90 % confidence
120	0.75	.00536	.000258	0.9937	-.0061412 -.0045704
250	0.45	.00615	.000310	0.9925	-.0071333 -.0051628
300	0.75	.00557	.000288	0.9920	-.0064805 -.0046492

Conversion of Allyl phenyl ether (APE) to 2-Allylphenol in the presence of dimethyl sulfoxide (DMSO)

In this reaction, 213 μL DMSO is added to form 1 : 20 APE : DMSO in tridecane solution (0.05 M APE : 1 M DMSO), the solution was irradiated in the microwave at 300 W constant power and the concentration of APE over time was determined as decribed above.

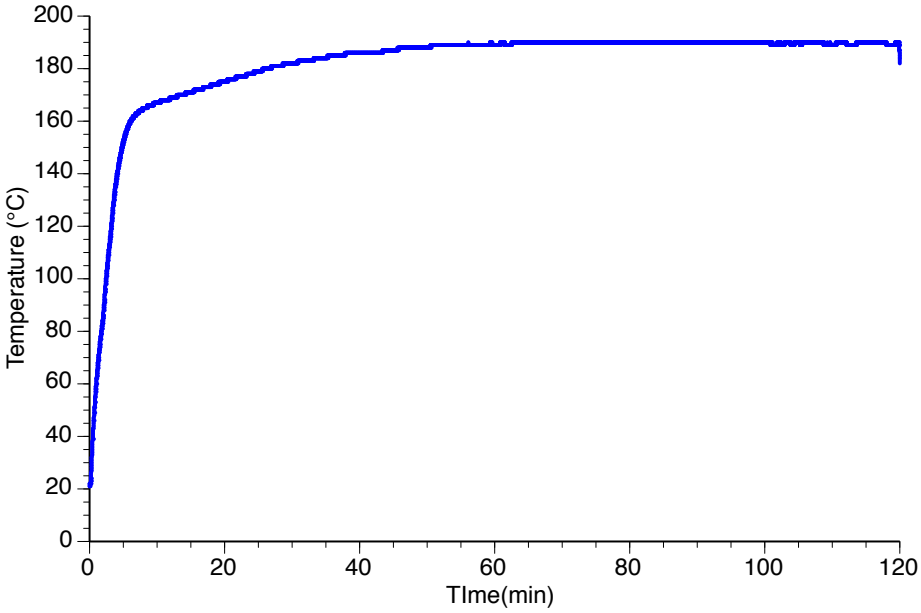

Figure S6 Heating curve for 1.0 M DMSO in tridecane.

Plots of the data showed first-order kinetics. S7

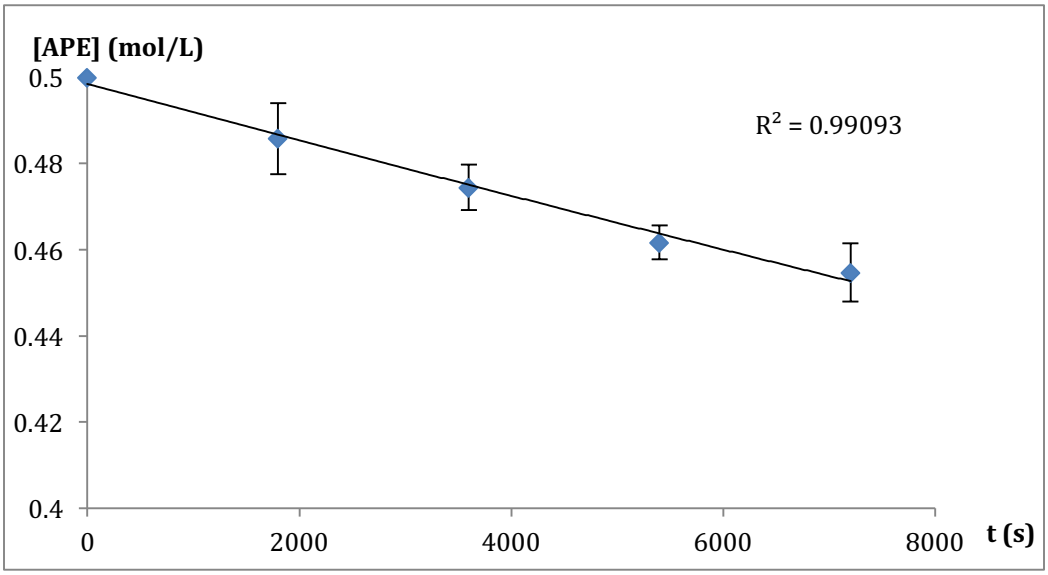

Figure S7 Kinetic plot of 1 : 20 APE : DMSO microwave Claisen rearrangement.

Thermal Conversion of Allyl phenyl ether (APE) to 2-Allylphenol

Table S4. Rate constants for the disappearance of APE in tridecane as a function of temperature

Rate Constant (min^{-1})	200 °C	205 °C	210 °C	215 °C
k1	.00228	.00281	.00379	.00459
k2	.00222	.00272	.00389	.00439
k3	.00237	.00301	.00370	.00475
k4	.00235	.00283	.00389	.00476
k_{avg}	.00230(±0.00006)	.00284 (±.00010)	.00382(±.00008)	.00462((±.00010)

The thermal reaction of APE in tridecane was carried out in an insulated mineral oil bath, heated on a temperature controlled hotplate with the temperature controlled to within 1 °C by an integrated controller. The reactions were carried out in the same 10 mL quartz cells that were used in the microwave reaction. In the kinetic runs, the sample was inserted into the oil bath, which had been preheated to the desired temperature. Kinetic data was collected for four different temperatures between 200 and 215°C in 5°C increments over a period of 120 minutes. At each temperature, four independent rate determinations were made. Kinetic plots of the time dependent concentration data collected at different temperatures is shown in Figure S-6. The rate constants were obtained from linear squares fit of the linearized (Ln(APE) vs time) data. The rate constants determined from the fits and the average value of the rate constant at each temperature are given in Table S4. The natural log of the average rate constants at each temperature were plotted against 1/T(K) to create an Arrhenius plot shown in Figure S8. Least squares fit of the data is given in Table S5.

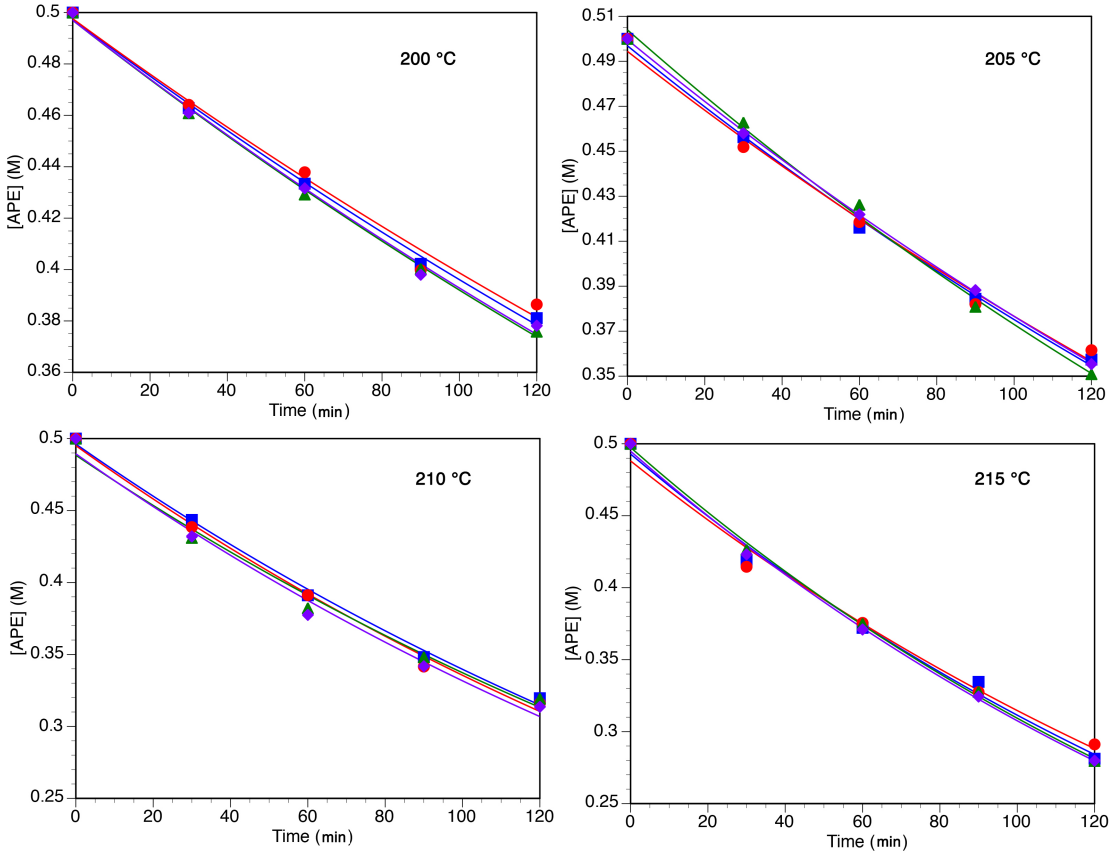

Figure S8. Disappearance of APE in tridecane as a function of temperature.

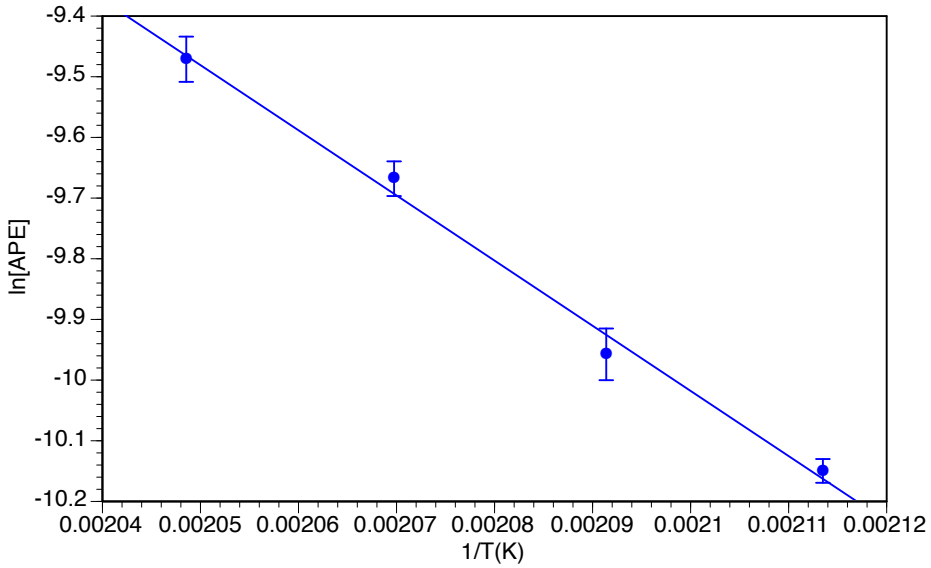

Figure S9 Arrhenius plot of APE in tridecane.

Table S5. Least square result for Arrhenius analysis of APE rearrangement

	Coefficient.	Std. Err.	[95% Conf. Interval]
Slope	-10739.33	629.6542	-13448.52 – -8030.149
Intercept	12.53475	1.310272	6.897109 – 18.1724
R-squared = 0.9932			
Ea = 89.2 kJ/mol, std. dev.= 10			

Thermal Conversion of Allyl phenyl ether (APE) to 2-Allylphenol in the presence of nitro-Nap

In this reaction, 0.05 M APE solution is made by dispensing 0.137 mL APE into a 20 mL vial which is then brought up to 20 mL with tridecane. 3 mL of the 0.5 M APE-tridecane solution is then transferred by pipet into a 10 mL Pyrex tube equipped with a magnetic stir bar. For 1 : 9 APE : nitro-NAP solution, 0.234 g of 1-nitronaphthalene are then added to the 3 mL APE in tridecane solution to form 0.45 mol/L nNAP solution. Four of these solutions were used in the kinetic runs. The four samples were placed in preheated silicone oil baths at 210°C. One Pyrex tube was removed every 30 min (30 min, 60 min, 90 min, 120 min) and allowed to cool to room temperature. 300 μL of the reaction solution was transferred to a 10 mL volumetric flask, containing 1 M naphthalene in toluene solution (naphthalene is the internal standard for gas chromatography (GC) measurement, toluene is the solvent for GC samples) Analysis was carried out by GC. The first-order kinetic plot is shown in Figure S9. Least squares fit yielded a rate constant of 1.71 (±.03) $x10^{-3}$ min-1.

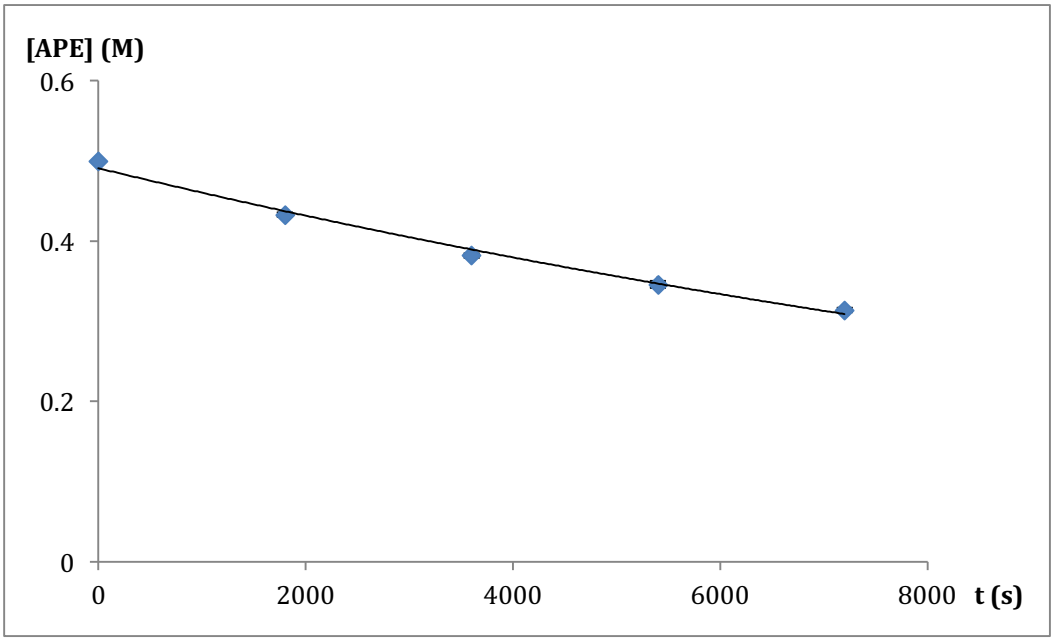

Figure S10. First-order kinetic plot of 1 : 9 APE : nitro-NAP thermal Claisen rearrangement.

References

1. S. Lahiri, J. L. Thompson and J. S. Moore, *J. Am. Chem. Soc.*, 2000, **122**, 11315-11319.
2. P. R. Mitchell and H. Sigel, *European Journal of Biochemistry*, 1978, **88**, 149-154.
3. A. Pérez, D. de Saá, A. Ballesteros, J. L. Serrano, T. Sierra and P. Romero, *Chemistry – A European Journal*, 2013, **19**, 10271-10279.
4. J. L. Dimicoli and C. Helene, *J. Am. Chem. Soc.*, 1973, **95**, 1036-1044.