Synthesis of Substituted Cyclooctenones: Substituent Effects in the [3,3]-Sigmatropic Rearrangement of Divinylcyclobutanols

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From cyclobutanone 1 12 divinylcyclobutanols were prepared. Substituent effects on the rate of oxy-Cope rearrangement to form cyclooctenones were monitored by NMR. Divinylcyclobutanols **2a**, **4a**, **5a**, **6a**, and **8a** gave first-order rate constants with the rates of rearrangements being in the order **4a** < **5a** < **2a** < **6a** < **3a** < **8a**. Cyclobutanols **7a**, **9a**, **10a**, and **12a** all rearranged too fast to isolate. The steric effects on the rate of rearrangement and the synthetic utility of this methodology are discussed.

As the number of known eight membered ring containing natural products has increased in recent years[1] so has an interest in the development of efficient methodology for their preparation.[2] The use of the oxy-Cope rearrangement of divinylcyclobutanols in the synthesis of eight membered ring containing natural products has recently received attention in these labs[3] as well as others.[4] The development of an efficient synthesis of the required cyclobutanone precursors[5] has offered further advantages for the use of this pathway. In light of these results we decided to investigate the range of substituted cyclooctenones which could be prepared. In the process we were also interested in studying what kind of substituents could be used in the rearrangement and what effect these substituents would have on the rate of rearrangement.

Extensive work on substituent effects of [3,3]-sigmatropic rearrangements has been reported by Gajewski and others in regards to the nature of the transition state and the mechanism.[6] Traditionally the reaction has been considered a concerted one. Two concerted but asynchronous pathways, however, might also be possible: one where bond breaking precedes bond making and one where bond making precedes bond breaking (diallyl and diyl, respectively, Figure 1). These possibilities must be kept in mind when considering substituent effects. In their investigation of the mechanism of the Cope rearrangement, Dewar and Wade reported the large rate enhancements of a phenyl[7] and naphthyl[8] groups in the 2 (C_2) and 2,5 (C_2, C_5) positions on hexa-1,5-diene, suggesting a diradical intermediate. Viola examined the effect of phenyl substituents on the oxy-Cope rearrangement and found that the rate ratios for two competing pathways (Cope and retroene) rules out a diradical pathway.[9] This result suggests that the presence of the hydroxyl group negates the radical stabilizing effect of the phenyl group.

An exhaustive study of the synthetic utility of substituent effects on the Cope rearrangement has not been reported to date, although the literature does provide numerous examples, and this is still an area of active interest. The most notable substituent effect is that of the anionic oxygen, giving a rate acceleration of 10^{10}–10^{17}, reported by Evans.[10,11] Curran has observed the accelerating effect of an electron donor at C_6 of a Claisen rearrangement and predicts that when resonance and bond-breaking energies work in concert a useful acceleration can be expected. Curran also suggests, for similar reasons, that an electron donor in the C_4 position would also have an accelerating effect.[12] In a recent paper by Wilcox the effect of alkyl substituents on the Claisen rearrangement was studied.[13] It was found that steric bulk at the C_5 position is rate accelerating, electron donation at C_5 is decelerating, and steric interaction between axial groups at C_1 and C_5 decelerates the rate. Berson also found that methyl–methyl interactions in dipropenylcyclobutanes caused a decline in the rate of rearrangement.[14] These results indicate that, not surprisingly, steric as well as electronic effects need to be taken into account when considering the use of a [3,3]-sigmatropic rearrangement. According to calculations by Delbecq,[15] substituents located on C_3 and C_1, facilitate C_1C_6 bond formation. Although Delbecq calculated that a substituent will enhance the rate irrespective of its donor or attractor character, steric factors are expected to play a significant role in our systems (vide infra).

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(1) Some of the classes of cyclooctane-containing natural products are as follows. (a) Ophiobolin: Nozoe, S.; Hirsi, K.; Tsuda, K. *Tetrahedron Lett.* **1966**, 2211. (b) Ceroplastol: Rios, T.; Quijano, L. *Tetrahedron Lett.* **1969**, 1317. (c) Cotylenol: Takeshi, S.; Akhisiro, T.; Tamutso, S. *Agric. Biol. Chem.* **1975**, *39*, 1929. (d) Fusiococcin: Ballio, A.; Chain, E. B.; DeLeo, P.; Erlanger, B. F.; Mauri, M.; Tonolo, A. *Nature (London)* **1964**, *203*, 297. (e) Pleuromutilin: Birch, A. *J. Proc. Chem. Soc.* **1962**, 3. Arigoni, D. *Gazz. Chim. Ital.* **1962**, *82*, 884. (f) Taxol: Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggan, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325.

(2) Some representative references of cyclooctane formation. (a) One-carbon ring expansion of cycloheptanes: Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*; Academic: New York, 1968. (b) Two-carbon ring expansion of cyclohexanes: Geetha, K. Y.; Rajagopalan, K.; Swaminathan, S. *Tetrahedron* **1978**, *34*, 2201. Dauben, W.; Hart, D. *J. Org. Chem.* **1977**, *42*, 922. (c) Fragmentation of bicyclic precursors: Reference 2a. Mehta, G.; Murthy, A. N. *J. Org. Chem.* **1987**, *52*, 2875. Oppolzer, W.; Bird, T. G. L. *Helv. Chim. Acta.* **1979**, *62*, 1199. Boeckman, R. K., Jr.; Bershas, J. P.; Clardy, J.; Solheim, B. *J. Org. Chem.* **1977**, *42*, 3630.

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(6) Gajewski, J. J.; Gilbert, K. E. *J. Org. Chem.* **1984**, *49*, 11. Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025. Gajewski, J. J. *Acc. Chem. Res.* **1980**, *13*, 142 and references cited therein. Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 6693.

(7) Dewar, M. J. S.; Wade, L. E. *J. Am. Chem. Soc.* **1973**, *95*, 290.

(8) Dewar, M. J. S., Wade, L. E. *J. Am. Chem. Soc.* **1977**, *99*, 4417.

(9) Viola, A.; Padilla, A. J.; Lennox, D. M.; Hecht, A.; Proverb, R. J. *J. Chem. Soc., Chem. Commun.* **1974**, 491. See also Thies (Thies, R. W. *J. Am. Chem. Soc.* **1972**, *94*, 7074) for a siloxy and oxy-Cope rearrangement which suggests a biradical intermediate.

(10) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. Evans, D. A.; Baillangeon, D. J.; Nelson, J. V. *Ibid.* **1978**, *100*, 2242. Evans, D. A.; Nelson, J. V. *Ibid.* **1980**, *102*, 774.

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(12) Curran, D. P.; Young-Ger, S. *J. Am. Chem. Soc.* **1984**, *106*, 5002 and references therein. See also: Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, O. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.

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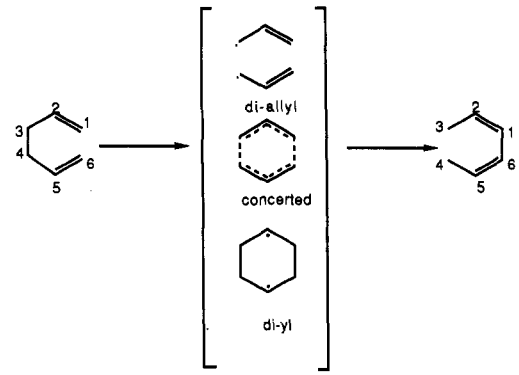
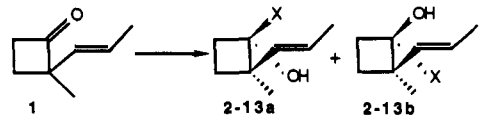
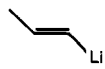
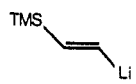
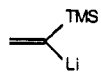
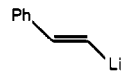
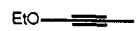


Figure 1. Possible transition states for a [3,3]-sigmatropic rearrangement.

Table I



cmpd	organometallic	ratio of steriproximal to distal (a:b)	% yield
2		2.0:1	85
3		1.8:1	64 (88)[b]
4		2.4:1	66
5		4.0:1	96
6		2.2:1	88
7		3.3:1	67
8		3.0:1	60
9		100[a]	61 (79)[b]
10		1.5:1	84
11		1.6:1	33[c]
12		2.2:1	64
13		100[a]	42

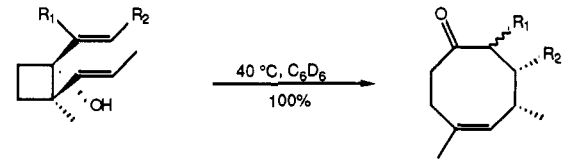
[a] No stereodistal product was isolated. [b] Yield including fraction from undesired halide (*cis*-bromopropene and *cis*-bromostyrene, respectively). [c] Products appeared to decompose rapidly.

We report here the variety of functionalization possible in eight-membered rings produced by the rearrangement of substituted 1,2-divinyl cyclobutanols. The rate of cyclooctenone formation is determined by monitoring the oxy-Cope rearrangement by NMR.

Results and Discussion

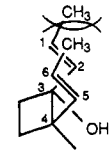
Cyclobutanone 1[16] (Table I) was selected since, at the outset, it appeared to form divinylcyclobutanols which rearranged slowly enough to monitor by NMR. Use of this cyclobutanone allowed the substituents to be varied at C_1 and C_2 while keeping C_4, C_5, and C_6 constant. Examination of **3a** indicates that steric interaction between a substituent at C_1 and C_6 would slow down the rearrangement by forcing double bonds apart, a factor discussed by Berson for *cis*-1,2-dialkenylcyclobutanes[14] and by Wilcox in the Claisen examples.[13] The ring strain present in our 1,2-dialkenylcyclobutanol systems also suggests that bond breaking between C_3 and C_4 would occur before bond making between C_1 and C_6.

Table II



cmpd	R_1	R_2	$t_{1/2}$, h	k_{rel}	cyclooctenone
2a	H	H	4.23	1.00	**14**
4a	CH_3	H	0.674	6.29	**16**
7a	TMS	H	<0.6	>7	**19**
10a	Ph	H	<0.6	>7	**22**
11a	OEt	H	*a*	*a*	**23**
13a	SPh	H	*b*	*b*	**25**
3a	H	CH_3	10.5	0.404	**15**
6a	H	TMS	7.12	0.593	**18**
9a	H	Ph	<0.6	>7	**21**

[a] Product was isolated impure and appeared to decompose rapidly. [b] Competitive fragmentation occurred along with [3,3] rearrangement.



3a

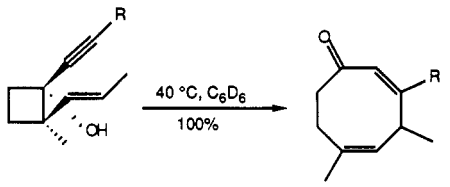
The results for addition of various organolithium reagents to **1** are shown in Table I. The favorable ratio of cis to trans ring substitution (stereoproximal to stereodistal[17]) can be attributed to the presence of the methyl group on the cyclobutanol; for example addition of vinyllithium to 2-*trans*-propenylcyclobutanone under the same conditions gave a proximal to distal ratio of 1:4.7, confirming the steric role of the methyl group. In all cases, the stereodistal isomer had a higher R_f than the stereoproximal in HPLC separation, with enough difference to give clean separation. The isomers could easily be differentiated by NMR where the stereoproximal methyl singlet was downfield from the stereodistal methyl singlet, this effect being reversed for the isolated alkynylcyclobutanols (**5**, **8**).

The rearrangements (Tables II and III) were followed by 400-MHz NMR, giving first-order rate constants in all cases. Rate constants were calculated by integration of the vinyl regions of the cyclobutanols and cyclooctenones. Plotting the natural log of the ratio of starting material over product versus time (in hours) gave a linear plot with slope = $-k_1$. Unfortunately, cyclobutanols **7a**, **9a**, **10a**, **11a**, and **12a** rearranged too fast at room temperature to isolate for the NMR rate study. Synthetically, however, this is an advantage since the cyclooctenone can be isolated in one step. Qualitatively, **7a** could be seen to rearrange more

(16) From (*E*)-3-penten-2-one, prepared by the procedure of: Font, J.; de March, P. *Tetrahedron* **1981**, *37*, 2391 and references therein.

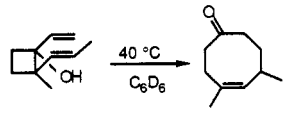
(17) Berson, J. A.: Dervan, P. B. *J. Am. Chem. Soc.* **1972**, *94*, 8949.

Table III



cmpd	R	$t_{1/2}$, h	k_{rel}[a]	cyclooctadienone
5a	H	2.42	1.75	**17**
8a	TMS	9[b]	0.48[b]	**20**
12a	OEt	<0.6	>7	**24**

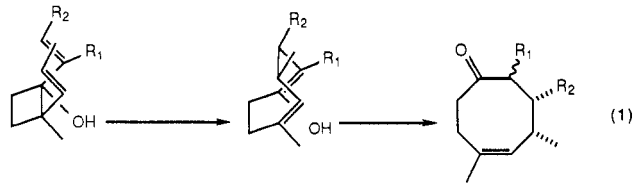
[a] k_{rel} = 1.00 for



[b] These are approximate values obtained at 70 °C.

slowly than **10a** during the HPLC separation. The large accelerating effect of the methyl group at C_2 (**4a**) is as predicted from electronics due to the electron donor ability of the methyl, and the decelerating effect at C_1 (**3a**) is due to the aforementioned steric factors. The corresponding TMS compound (**6a**) supports the argument of steric interaction since one would expect the longer C–Si bond length to remove some of the strain. The electronic accelerating effect, seen in **7a**, is not great enough to compensate for the decelerating steric interactions seen in **6a**.

Rearrangement of **4a**, **7a**, **10a**, **11a**, and **13a** would be expected to yield epimeric mixtures at the α carbon (eq 1). Indeed an approximate ratio of 3 to 1 by NMR in-



(1)

tegration is observed for rearrangements **4a** to **16**, **7a** to **19**, and **10a** to **22** (Table II). The isomers could be separated by using HPLC in the phenyl case (**22**). The major isomer had its methyne proton shifted upfield slightly in all three cases: 0.013 ppm (5.37 Hz) for **16**, 0.07 ppm (28.1 Hz) for **19**, and 0.051 ppm (20.26 Hz) for **22**. To confirm the stereochemical preference of one isomer over another the minor epimer (**22b**) was refluxed in methanol with base for 1.5 h. The NMR spectrum of the resulting product gave a ratio of 1.4/1 of **22b**/**22a**, indicating that **22b** was isomerizing toward the more favored **22a**.

The thermodynamically favored isomer of **16** (i.e., with the α methyl group) was determined from computer-generated structures by using Ringmaker and MM2 minimization on a Harris 1000 minicomputer. The lowest energy conformers had values of 15.30 kcal/mol for the 2- and 4-methyls being "cis" and 15.87 kcal/mol for the 2- and 4-methyls being "trans", suggesting that the former is the preferred isomer.

The oxy-Cope rearrangements yield only the desired eight-membered rings according to NMR analysis. Any impurities that may have been present in the divinylcyclobutanols were not affected during the rearrangement, indicating they originated prior to the sigmatropic rearrangement, most likely during the vinyllithium addition. The final products tend to be stable for long periods of time (>1 year) when stored in a freezer. Cyclobutanol **11b** and its cyclooctenone **23** (not listed in Table II) were exceptions. The cyclooctenone was isolated impure and appeared to decompose over a period of several days, as did **11b**.

Only the rearrangement of **13a** gave an observable competing fragmentation reaction, so that no accurate number for the rate could be determined. If such a substituent were needed on an eight-membered ring, conducting the rearrangement under anionic conditions would avoid the competing reaction.

The rate acceleration with acetylene as a substituent was reported and discussed by Viola[18] and is seen in **5a** (Table III). It is noteworthy that **8** did not rearrange at 40 °C and would only do so slowly at 70–75 °C. Strong steric interactions between the TMS group and the trans methyl group in **8** would be expected since the shorter alkyne carbon–carbon bond offsets the longer carbon–silicon bond. In contrast, the fast rearrangement of **12a** can be attributed to the resonance electron-donating character of the ethoxy group and its ability to avoid steric interaction with the opposite methyl group.

In conclusion, acceleration of the [3,3] sigmatropic rearrangement and the effect of steric bulk on the rate of rearrangement are demonstrated by these results. It seems that in absence of steric effects all substituents accelerate the rearrangement, in agreement with Delbecq's calculations. However, no conclusions can be made concerning the nature of the transition state as the substituents are changed. The substituent that can be appended on to an eight-membered ring in the α and β position by using this methodology is limited only by the type of substituted vinyl anion needed. In the case of **24**, a protected ketone was placed on the ring which might otherwise be difficult, thus facilitating further modification of the ring. Rearrangements proceed in high yield, and since the formation of the 1,2-divinylcyclobutanones also occurs in good yield this method offers a facile route to substituted cyclooctenones.

Experimental Section

General Methods. Dry tetrahydrofuran (THF) and diethyl ether (Et_2O) were obtained by distillation from sodium benzophenone. Hexanes and ethyl acetate were distilled before use. All inert atmosphere operations were done under dry nitrogen in oven- or flame-dried glassware.

Preparative HPLC separations were carried out by using a 25 cm × 1 cm Alltech column containing 10 μm silica gel. Thin-layer chromatography was carried out on silica gel plates by using radial elution in inexpensive radial TLC chambers.[19]

Proton nuclear magnetic resonance (NMR) spectra were measured on a Varian XL-400 spectrometer or, where specified, on a Varian EM-390 (90 MHz). Carbon nuclear magnetic resonance spectra were measured on a GE QE-300 (75.48 MHz) spectrometer. DEPT experiments were run on the GE QE-300, and the assignments are indicated in parentheses in the ^{13}C spectra. All proton shifts are reported downfield from an internal Me_4Si standard. All carbon shifts are reported by using the solvent as standard. Infrared (IR) spectra were taken with a Perkin-Elmer Model 283 spectrophotometer. Mass spectra (MS) were measured with a Hewlett-Packard HP 5985A GC/MS system. High-resolution mass spectra (EI 70 eV) were determined on a VG analytical 7070e spectrometer.

2-Methyl-2-*trans*-propen-1-ylcyclobutanone (1). Prepared by standard procedure[5] from (*E*)-3-penten-2-one.[16] Distilled through a short-path distillation apparatus: bp_{18} 64–67 °C, 76% yield as a clear colorless liquid. ^1H NMR ($CDCl_3$) δ 5.52 (m, 2 H), 3.03 (t, 2 H, J = 9 Hz), 2.0 (m, 2 H), 1.5 (d, 3 H, J = 5 Hz),

(18) Viola, A.; Collins, J. J.; Filipp, N. *Tetrahedron* 1981, *37*, 3765.
(19) Gadwood, R. C. *J. Chem. Educ.* 1985, *62*, 820.

1.28 (s, 3 H). ^{13}C NMR δ 212.78, 131.40, 124.60, 66.19, 42.46, 24.76, 21.73, 17.99. IR (neat) 2960 (s), 1780 (s), 1450 (m), 1155 (m), 960 (m) cm^{-1}.

General Procedure for 1,2-Divinylcyclobutanol Synthesis. To 25 mL of ether in a 50-mL round-bottomed flask was added 0.0116 mol of the halide, and then the solution was cooled to −78 °C. After addition of 5.69 mL of *tert*-butyllithium (0.0097 mol, Aldrich, 1.7 M in hexane) the solution was stirred for 15 min, and the cyclobutanone 1 (0.004 mol, 0.5 g, 0.58 mL) was added. The resulting solution was stirred for 20 min at −78 °C. The reaction was quenched with 0.58 mL (0.0102 mol, 0.61 g) of acetic acid at −78 °C. After the solution was warmed to 15 °C, 10 mL of saturated sodium bicarbonate solution was added and the solution stirred for several minutes. The layers were then separated, and the aqueous phase was extracted (3 × 20 mL of Et_2O). The combined organic layers were dried over $MgSO_4$ and filtered, and the ether was removed on a rotary evaporator. The product was then purified by HPLC using ethyl acetate/hexane as the solvent pair. In between injections the receiving and sample flasks were stored in the freezer at −20 °C to slow down rearrangement. The HPLC solvent was removed by rotary evaporator and then by vacuum pump to ensure the removal of all hexane. Unless noted, the substituted 1,2-divinylcyclobutanols were colorless liquids.

1-Ethenyl-2-methyl-2-*trans*-1-propenylcyclobutanol (2). A large excess of vinyl bromide (98%, Aldrich) was used. Ethyl acetate/hexane (7%) was used for the separation to give two fractions: **2a**, 0.350 g, and **2b**, 0.171 g. Total yield, 0.521 g, 85%. **2a**: ^1H NMR (C_6D_6) δ 6.00 (dd, 1 H, J = 18.1, 10.8 Hz), 5.50 (dd, 1 H, J = 15.1, 2 Hz), 5.22 (m, 2 H), 5.00 (dd, 1 H, J = 10.7, 2 Hz), 1.97 (m, 2 H), 1.68 (apparent q, 1 H, J = 9 Hz), 1.58 (dd, 3 H, J = 6.4, 1.5 Hz), 1.45 (ddd, 1 H, J = 10.9, 9, 3.5 Hz), 1.22 (s, 3 H). IR (neat) 3420 (s), 3020 (m), 2960 (s), 1640 (w), 1450 (m), 1240 (m), 960 (m), 920 (m), 785 (m) cm^{-1}. **2b**: 90-MHz ^1H NMR (CCl_4) δ 5.90 (dd, 1 H, J = 18, 10 Hz), 5.52 (m, 2 H), 5.10 (m, 2 H), 2.0–1.3 (m, 4 H), 1.75 (d, 3 H, J = 4 Hz), 1.05 (s, 3 H).

1,2-Di-*trans*-propenyl-2-methylcyclobutanol (3). 1-Bromo-1-propene (98%, Aldrich), consisting primarily of the cis isomer (based on 400-MHz NMR, the cis methyl group is downfield of the trans), was enriched in trans isomer by slowly distilling through a vacuum-jacketed column with glass rings in the dark.[20] HPLC separation of **3** using 7% ethyl acetate/hexane gave 0.241 g of proximal and 0.134 g of distal isomers from *trans*-bromopropene and 0.142 g of proximal and 0.0672 g of distal isomers from *cis*-bromopropene. Overall yield, 0.584 g (88%). **3a**: ^1H NMR ($CDCl_3$) δ 5.65 (m, 2 H), 5.45 (dd, 1 H, J = 15.6, 2 Hz), 5.30 (dq, 1 H, J = 15.6, 6.4 Hz), 2.07 (m, 2 H), 1.69 (m, 2 H), 1.72 (d, 3 H, J = 5.4 Hz), 1.66 (dd, 3 H, J = 6.4, 2.4 Hz), 1.54 (m, 1 H), 1.22 (s, 3 H). Decoupling the doublet at 1.72 ppm caused the multiplet at 5.65 ppm to collapse to two doublets (J = 15.6 Hz). Decoupling at 1.66 ppm caused the dd at 5.45 ppm to collapse to a doublet (J = 15.6 Hz) and the dq at 5.30 ppm to partially collapse to a doublet (J = 10.7 Hz). IR (neat) 3400 (m), 3000 (w), 2950 (d, s), 2860 (m), 1450 (m), 960 cm^{-1} (m). **3b**: ^1H NMR ($CDCl_3$) δ 5.75–5.53 (m, 4 H), 2.24 (m, 1 H), 2.06 (m, 1 H), 1.85 (m, 1 H), 1.77 (d, 3 H, J = 5.4 Hz), 1.73 (dd, 3 H, J = 6.4, 1.5 Hz), 1.68 (br s, 1 H), 1.46 (m, 1 H), 1.06 (s, 3 H).

1-(1-Methylethenyl)-2-methyl-2-*trans*-propenylcyclobutanol (4). 2-Bromopropene (99%, Aldrich) was freshly distilled (bp 47–49 °C). Cyclobutanol 4 was separated by using 7% ethyl acetate/hexane on HPLC to give 0.309 g of the stereoproximal and 0.128 g of the distal isomers for an overall yield of 0.437 g (66%). **4a**: ^1H NMR (C_6D_6) δ 5.60 (dq, 1 H, J = 16.4, 2.0 Hz), 5.32 (dq, 1 H, J = 15.6, 6.4 Hz), 4.87 (br apparent s, 1 H), 4.83 (apparent quintet, 1 H, J = 2.4 Hz), 2.34 (m, 1 H), 1.78–1.65 (m, 3 H), 1.69 (d, 3 H, J = 1.95 Hz), 1.59 (br s, 1 H), 1.59 (dd, 3 H, J = 6.4, 2.4 Hz), 1.27 (s, 3 H). IR (neat) 3460 (m), 3080 (w), 3020 (m), 2960 (s), 2860 (m), 1640 (w), 1450 (m), 960 (m), 885 cm^{-1} (m). **4b**: ^1H NMR (C_6D_6) δ 5.61 (br dq, 1 H, J = 15.6, 1.5 Hz), 5.44 (dq, 1 H, J = 15.6, 6.4 Hz), 4.89 (br apparent quintet, 1 H, J = 2.4 Hz), 4.84 (br apparent s, 1 H), 2.36 (m, 1 H), 2.21 (apparent q, 1 H, J = 9.8 Hz), 1.79 (s, 1 H), 1.70 (m, 1 H), 1.66 (s, 3 H), 1.56 (dd, 3 H, J = 6.4, 2.4 Hz), 1.31 (ddd, 1 H, J = 11, 9, 4 Hz), 1.04 (s, 3 H).

1-Ethynyl-2-methyl-2-*trans*-propenylcyclobutanol (5). According to the procedure of Midland,[21] acetylene (Matheson) was bubbled into 35 mL of THF at −78 °C for 20 min while being stirred with a magnetic stir bar. To the acetylene solution was then added 5.81 mL of *n*-BuLi (0.0090 mol, Aldrich, 1.55 M) with a syringe pump over a 16-min period while the needle was kept just above the surface of the THF or slightly submerged. After 10 min at −78 °C, 0.650 mL of **1** (0.0045 mol, 0.559 g) was added in 10 mL of THF at −78 °C via a stainless steel canula from a 25-mL pear flask. The flask was rinsed with 1 × 2 mL and 1 × 4 mL of THF, and these portions were also transferred via cannula to the reaction solution. After being stirred for 20 min, the reaction was warmed to −30 °C and quenched with 0.57 mL (0.01 mol) of acetic acid (some gas evolves). After the solution was warmed to 15 °C, 10 mL of saturated sodium bicarbonate was added slowly (vigorous gas evolution!). Layers were separated, and the aqueous phase was washed with 3 × 25 mL of Et_2O. The combined organic layers were dried over $MgSO_4$ (again much bubbling) and filtered, and the Et_2O was removed on a rotary evaporator. The resulting crude liquid was purified with HPLC using 10% ethyl acetate/hexane to give 0.524 g of proximal and 0.126 g of distal isomers for an overall yield of 0.651 g (96%). **5a**: ^1H NMR (C_6D_6) δ 5.89 (br apparent dq, 1 H, J = 15.6, 1.5 Hz), 5.35 (dq, 1 H, J = 15.6, 6.4 Hz), 2.25 (m, 1 H), 2.23 (s, 1 H), 2.11 (apparent q, 1 H, J = 10.25 Hz), 1.97 (br s, 1 H), 1.84 (apparent q, 1 H, J = 9.8 Hz), 1.66 (d, 3 H, J = 6.4 Hz), 1.44 (dt, 1 H, J = 9.8, 4.4 Hz), 1.2 (s, 3 H). IR (neat) 3400 (m), 3300 (m), 3000 (w), 2960 (d, s), 2860 (m), 2110 (vw), 1650 (w), 1450 (m), 990 (m), 865 cm^{-1} (m). **5b**: ^1H NMR (C_6D_6) δ 5.51 (br dq, 1 H, J = 15.6, 1.5 Hz), 5.40 (dq, 1 H, J = 15.6, 6.4 Hz), 2.30 (m, 1 H), 2.24 (s, 1 H), 2.03 (m, 2 H), 1.54 (dd, 3 H, J = 6.4, 1.5 Hz), 1.46 (m, 1 H), 1.40 (br s, 1 H), 1.33 (s, 3 H). IR (neat) 3420 (m), 3300 (m), 3000 (w), 2960 (s), 2860 (m), 2110 (vw), 1650 (m), 1445 (m), 965 cm^{-1} (m).

1-[2-(Trimethylsilyl)ethenyl]-2-methyl-2-*trans*-propenylcyclobutanol (6). (*trans*-2-Bromoethenyl)trimethylsilane was prepared by the method of Boeckmann and Bruza[22] in 62% yield. In this case 0.0106 mol (6.21 mL, 1.7 M) of *tert*-butyllithium, 0.0088 mol (1.58 g, 1.36 mL) of the halide, and 0.0030 mol (0.373 g, 0.43 mL) of **1** were used. HPLC separation using 4.5% ethyl acetate/hexane gave 0.410 of the stereoproximal (**6a**) and 0.183 of the distal (**6b**) isomers for a total yield of 0.593 g (88%). **6a**: ^1H NMR (C_6D_6) δ 6.34 (d, 1 H, J = 19.0 Hz), 5.91 (d, 1 H, J = 19.0 Hz), 5.47 (dq, 1 H, J = 15.6, 1.5 Hz), 5.24 (dq, 1 H, J = 16.1, 6.4 Hz), 2.06 (m, 2 H), 1.78 (apparent q, 1 H, J = 8.8 Hz), 1.62 (dd, 3 H, J = 6.3, 1.5 Hz), 1.58 (br s, 1 H), 1.49 (ddd, 1 H, J = 11.0, 8.5, 4.9 Hz), 1.28 (s, 3 H), 0.17 (s, 9 H). IR (neat) 3380 (m), 2950 (s), 2860 (m), 1615 (m), 1450 (m), 1243 (s), 990 (m), 860 (s), 835 cm^{-1} (s). **6b**: ^1H NMR (C_6D_6) δ 6.35 (d, 1 H, J = 19.1), 6.16 (d, 1 H, J = 19.0 Hz), 5.61 (dq, 1 H, J = 15.6, 2.4 Hz), 5.46 (dq, 1 H, J = 15.6, 6.4 Hz), 2.22 (m, 1 H), 2.05 (m, 1 H), 1.94 (m, 1 H), 1.89 (br s, 1 H), 1.59 (dd, 3 H, J = 6.4, 1.5 Hz), 1.44 (m, 1 H), 1.08 (s, 3 H), 0.18 (s, 9 H). IR (neat) 3460 (m), 2950 (s), 2860 (m), 1610 (w), 1450 (m), 1243 (s), 990 (m), 970 (m), 865 (s), 845 cm^{-1} (s).

1-[1-(Trimethylsilyl)ethenyl]-2-methyl-2-*trans*-propenylcyclobutanol (7). (1-Bromovinyl)trimethylsilane was prepared by the method of Boeckman et al.[23] Yield, 53% from vinyltrimethylsilane. The same quantities were used as for **6**. The proximal fraction could be seen to rearrange during the isolation on HPLC with 5% ethyl acetate/hexane. Overall yield, 0.454 g (67%), which consisted of 0.348 g of the rearranged stereoproximal isomer and 0.106 g of the distal isomer (containing some residual (1-bromovinyl)trimethylsilane. **7b**: ^1H NMR (C_6D_6) δ 6.11 (d, 1 H, J = 2.44 Hz), 5.85 (d, 1 H, J = 2.4 Hz), 5.62 (br dq, 1 H, J = 15.6, 1.5 Hz), 5.49 (dq, 1 H, J = 15.6, 6.4 Hz), 2.54 (apparent dd, 1 H, J = 8.8, 5.9 Hz), 2.42 (m, 1 H), 2.00 (m, 1 H), 1.73 (m, 1 H), 1.60 (dd, 3 H, J = 6.4, 1.5 Hz), 1.32 (m, 1 H), 1.02 (s, 3 H),

(20) Harwell and Hatch (Harwell, K.; Hatch, L. F. *J. Am. Chem. Soc.* **1955**, *77*, 1682) report boiling points of −18 and −13 °C for *cis*- and *trans*-bromopropene, respectively (low-temperature distillation). Nesmeianov et al. (Nesmeianov, A. N.; Borisov, A. E.; Novikova, N. V. *Akad. Sci. USSR Prov. (Chem. Sect.)* **1958**, *257*, 118) report boiling points of 57 and 62.5–63 °C for cis and trans isomers, respectively.

(21) Midland, M. *J. Org. Chem.* **1975**, *40*, 2250.

(22) Boeckmann, R.; Bruza, K. *J. Org. Chem.* **1979**, *44*, 4781.

(23) Boeckmann, R.; Blum, D. M.; Ganem, B.; Halvey, N. *Org. Synth.* **1978**, *58*, 152.

0.25 (s, 9 H). Impurities from the halide were visible in the upfield region of the NMR. IR (neat) 3530 (w), 2960 (s), 1660 (s), 1240 (s), 830 cm^{-1} (s).

1-[2-(Trimethylsilyl)ethynyl]-2-methyl-2-*trans*-propenylcyclobutanol (8). To 0.236 g (0.0024 mol, 0.339 mL) of (trimethylsilyl)acetylene (Aldrich, 98%) in 25 mL of THF at −78 °C was added 1.35 mL (0.0021 mol) of *n*-butyllithium (Aldrich, 1.55 M), and the solution was stirred for 15 min. The reaction flask was warmed to −30 °C for 5 min, and 0.289 mL (0.0020 mol) of **1** was added neat at −78 °C (the color of the solution changed from colorless to yellow). After 40 min at −78 °C the reaction was quenched with 0.14 mL (0.0025 mol) of acetic acid and worked up as usual. HPLC purification with 8% ethyl acetate/hexane gave two main fractions: stereoproximal **8a**, 0.200 g, and stereodistal **8b**, 0.0675 g. Total yield, 0.268 g (60%). **8a**: isolated as a colorless solid, mp 45–46 °C. ^1H NMR (C_6D_6) δ 5.94 (dq, 1 H, J = 15.6, 1.5 Hz), 5.40 (dq, 1 H, J = 15.1, 6.3 Hz), 2.33 (ddd, 1 H, J = 11, 9.0, 3.4 Hz), 2.16 (apparent q, 1 H, J = 11.2 Hz), 1.91 (q, 1 H, J = 10.7 Hz), 1.84 (br s, 1 H), 1.75 (dd, 3 H, J = 6.2, 1.8 Hz), 1.47 (apparent dt, 1 H, J = 11, 3.4 Hz), 1.24 (s, 3 H), 0.23 (s, 9 H). IR (KBr pellet) 3280 (s), 3020 (w), 2960 (s), 2160 (w), 1240 (s), 835 cm^{-1} (s). **8b**: ^1H NMR (C_6D_6) δ 5.55 (br dq, 1 H, J = 12.4, 1.2 Hz), 5.45 (dq, 1 H, J = 15.6, 6.1 Hz), 2.39 (m, 1 H), 2.08 (m, 2 H), 1.57 (dd, 3 H, J = 6.1, 1.2 Hz), 1.53 (m, 1 H), 1.42 (s, 3 H), 1.32 (br s, 1 H), 0.23 (s, 9 H). IR (neat) 3420 (m), 2960 (s), 2160 (m), 1450 (m), 1250 (s), 850 cm^{-1} (s).

1-(*trans*-2-Phenylethenyl)-2-methyl-2-*trans*-propenylcyclobutanol (9). β-Bromostyrene (99%, Aldrich) was found, by GC and NMR, to consist primarily of the trans isomer. *tert*-Butyllithium (0.0097 mol), 0.0116 mol of β-bromostyrene, and 0.0040 mol of **1** were used in this reaction. Separation on HPLC with 5% ethyl acetate/hexane gave two fractions of rearranged proximal isomers from *cis*- and *trans*-2-bromostyrene. There was insufficient quantity of the distal isomers to collect. Yield of the cyclooctenone from *trans*-β-bromostyrene, 0.562 g, from *cis*-β-bromostyrene, 0.159 g. Combined yield, 0.721 g (79%).

1-(1-Phenylethenyl)-2-methyl-2-*trans*-propenylcyclobutanol (10). α-Bromostyrene was prepared by the method of Taylor[24] in 73% yield from (1,2-dibromoethyl)benzene (97%, Aldrich). *tert*-Butyllithium (0.0061 mol), 1.33 g (0.0073 mol, 0.95 mL) α-bromostyrene, and 0.310 g (0.0025 mol, 0.361 mL) of **1** were used. Separation on HPLC with 7% ethyl acetate/hexane gave four fractions: two cyclooctenone isomers and **10a** and **10b**. Once all the solvent had been removed from **10a** there was little of the unrearranged cyclobutanol present. Yield of stereoproximal (both cyclooctenone isomers), 0.284 g, distal, 0.193 g. Total yield, 0.478 g (84%). **10b**: ^1H NMR (C_6D_6) δ 7.52 (apparent dd, 2 H, J = 9, 2 Hz), 7.10 (m, 3 H), 5.60 (br dq, 1 H, J = 15.6, 1.5 Hz), 5.34 (dq, 1 H, J = 15.6, 6.4 Hz), 5.19 (d, 1 H, J = 1.5 Hz), 5.07 (d, 1 H, J = 1.9 Hz), 2.37 (apparent q, 1 H, J = 8.3 Hz), 2.34 (m, 1 H), 2.04 (br s, 1 H), 1.86 (m, 1 H), 1.52 (dd, 3 H, J = 6.4, 2.4 Hz), 1.35 (m, 1 H), 1.06 (s, 3 H). IR (neat) 3480 (m), 3020 (m), 2960 (s), 2860 (m), 1620 (w), 1600 (w), 1490 (m), 1440 (m), 970 (m), 770 (m), 694 cm^{-1} (m).

1-(1-Ethoxyethenyl)-2-methyl-2-*trans*-propenylcyclobutanol (11). According to the procedure of Heathcock,[25] to 30 mL of THF was added 0.44 mL (0.0046 mol, 0.331 g) of ethyl vinyl ether (99%, Aldrich, distilled from sodium under N_2) and cooled to −78 °C. Upon addition of 0.0031 mol (1.8 mL, 1.7 M) of *tert*-butyllithium the solution turned yellow/orange. The solution was allowed to warm 15 °C, at which point the color dissipated. After the solution was again cooled to −78 °C, 0.0015 mol (0.221 mL, 0.180 g) of **1** was added. Following 10 min of stirring, the solution was warmed to −30 °C and then to 0 °C (no change in the TLC was observed from −78 to 0 °C) and then quenched with 10 mL of 20% (v/v of saturated) ammonium chloride. After the usual workup the product was purified via HPLC using 8% ethyl acetate/hexane to give three fractions: rearranged and partially decomposed **11a**, 0.0134 g; **11b**, 0.0666g (stereodistal); **11c**, 0.0193 g. **11c** appears to be decomposed **11b**; no further identification was attempted. Total yield, 0.0993 g (33%). The ^1H NMR (C_6D_6) of **11a** and **11b** contained too many impurities to report accurately.

1-(2-Ethoxyethynyl)-2-methyl-2-*trans*-propenylcyclobutanol (12). To 0.420 g (approximately 0.0030 mol) of ethoxyacetylene (Aldrich 50% in hexanes, distilled before use) in 25 mL of THF at −78 °C was added 1.67 mL (0.0026 mol) of *n*-butyllithium (Aldrich, 1.55 M) and the solution stirred for 15 min. The reaction flask was warmed to −30 °C for 5 min and 0.361 mL (0.0025 mol, 0.310 g) of **1** added neat at −78 °C (no color changes observed). After being stirred for 1 h at −78 °C the reaction was quenched with 0.172 mL (0.003 mol) of acetic acid and worked up as usual. HPLC separation with 16% ethyl acetate/hexane gave three fractions: rearranged **12a**, 0.144 g; **12b** (stereodistal), 0.0665 g; recovered cyclobutanone **1**, 0.0689g. Total yield (based on recovered **1**), 0.243 g (64%). **12b**: ^1H NMR (C_6D_6) δ 5.68 (br d, 1 H, J = 15.6 Hz), 5.47 (dq, 1 H, J = 15.6, 6.3 Hz), 3.60 (q, 2 H, J = 7.1 Hz), 2.36 (m, 1 H), 2.12 (m, 3 H), 1.59 (dd, 3 H, J = 6.3, 1.5 Hz), 1.56 (ddd, 1 H, J = 10, 8, 6 Hz), 1.39 (s, 3 H), 0.92 (t, 3 H). Note: this sample was not pure, due to apparent decomposition. IR (neat) 3420 (m), 2960 (s), 2250 (s), 1590 (s), 1445 (m), 1220 (m), 1045 (m), 1000 (m), 965 cm^{-1} (m).

1-[1-(Phenylthio)ethenyl]-2-methyl-2-*trans*-propenylcyclobutanol (13). According to the procedure of Magnus,[26] 1.56 mL of *n*-butyllithium (0.025 mol, 1.6 M) was added to 0.350 mL (0.0025 mol, 0.253 g) of diisopropylamine (99%, Aldrich, distilled over CaH) in 25 mL of THF at −78 °C. Phenyl vinyl sulfide (0.327 mL, 0.0025 mol, 0.341 g, 97% Aldrich) was then added slowly and the reaction stirred for 20 min. After several minutes the solution changed to a light yellow color. Upon addition of 0.289 mL (0.0020 mol, 0.248 g) of **1** most of the color disappeared instantly. The reaction was allowed to stir for 20 min at −78 °C and quenched with 0.172 mL (0.003 mol) of acetic acid and worked up as usual. HPLC separation with 7% ethyl acetate/hexane gave 0.1436 g of the proximal isomer and 0.0686 g of cyclooctenone. Total yield, 0.212 g (41%). **13a**: ^1H NMR (C_6D_6) δ 7.47 (apparent dd, 2 H, J = 8.3, 1.5 Hz), 7.00 (m, 3 H), 5.80 (dq, 1 H, J = 15.6, 2.4 Hz), 5.52 (dq, 1 H, J = 15.6, 7.3 Hz), 5.16 (s, 1 H), 4.84 (s, 1 H), 2.59 (br s, 1 H), 2.39 (m, 1 H), 2.29 (apparent q, 1 H, J = 8.8 Hz), 1.88 (m, 1 H), 1.58 (dd, 3 H, J = 6.4, 0.98 Hz), 1.34 (apparent m, 1 H), 1.28 (s, 3 H). IR (neat) 3500 (w), 3020 (w), 2950 (s), 2920 (s), 2860 (m), 1470 (m), 970 (m), 735 (m), 680 cm^{-1} (m).

General Method for the Rearrangement of Divinylcyclobutanols and the Calculation of Rate Constants. The stereoproximal isomer (50 mg) was placed in a NMR tube along with 0.6 mL of C_6D_6 (99.5% isotopic abundance, Aldrich and Stohler Isotope Chemicals) and the NMR tube heated in a constant temperature bath at 40.0 °C. When a spectrum was taken, the sample was removed from the water bath and quenched at −78 °C. The spectrum was recorded at probe temperature (~20 °C) and then returned to the water bath. The average time the sample spent out of the bath, at or below room temperature, was 8 min. A 5-mm proton probe was used on the Varian XL-400 NMR. The pulse sequence consisted of a 90° pulse (PW = 17), a 10-s delay, 2-s acquisition time, and 8 pulses (8 collected transients). The integral regions were identical throughout the experiment, as were the integral and vertical scales. The vinyl regions proved to be the cleanest for observation of the reactions. Integration of the disappearance of the 1,2-divinylcyclobutanol vinyl protons and growth of the cyclooctenone methyne proton were sufficient to give accurate results. The natural log of the ratio of the cyclobutanol integral number for 1 proton (SM) to SM plus the cyclooctenone integral number for 1 proton (SM_o) was then plotted versus time. Plots were done in a least-squares program on a Harris 1000 minicomputer and gave linear regressions between −0.999 98 and −0.984.

4,6-Dimethylcyclooct-4-enone (14). This rearrangement gave a first-order rate constant (k_1) of 4.55×10^{-5} s^{-1} and a half-life ($t_{1/2}$) of 4.23 h. ^1H NMR (C_6D_6) δ 4.88 (d, 1 H, J = 8.8 Hz), 2.49 (dt, 1 H, J = 13.7, 4.4 Hz), 2.27 (dt, 1 H, J = 13.7, 4.4 Hz), 2.14 (m, 3 H), 2.03 (ddd, 1 H, J = 11.5, 8.0, 4.4 Hz), 1.53 (s, 3 H), 1.49 (m, 1 H), 1.40 (m, 1 H), 1.24 (m, 1 H), 0.82 (d, 3 H, J = 6.8 Hz). IR (neat) 2950 (s), 2920 (s), 2860 (m), 1700 (s), 1450 (m), 1436 cm^{-1} (m). MS (70 eV), m/e 152 (M^+), 137, 124 (base), 109, 95, 82, 67.

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3,4,6-Trimethylcyclooct-5-enone (15). $k_1 = 1.84 \times 10^{-5}$ s^{-1}, $t_{1/2}$ 10.5 h. ^{1}H NMR (C_6D_6) δ 4.92 (d, 1 H, J = 9.28 Hz), 2.44 (dt, 1 H, J = 12.7, 4.4 Hz) 2.36 (m, 1 H), 2.25 (dt, 1 H, J = 14.2, 3.9 Hz), 2.18 (dd, 1 H, J = 11.2, 4.4 Hz), 2.15 (m, 1 H), 2.00 (dd, 1 H, J =11.2, 8.5 Hz), 1.76 (m, 1 H), 1.56 (d, 3 H, J = 2.93 Hz), 1.52 (m, 1 H), 0.85 (d, 3 H, J = 5.86 Hz), 0.76 (d, 3 H, J = 6.84 Hz). IR (neat) 2950 (s), 2920 (s), 2860 (s), 1700 (s), 1445 cm^{-1} (m). MS (70 eV), m/e 166 (M^+), 124, 95, 82 (base), 67, 41.

2,4,6-Trimethylcyclooct-5-enone (16). $k_1 = 2.86 \times 10^{-4}$ s^{-1}, $t_{1/2}$ 0.674 h. ^{1}H NMR (C_6D_6) δ 4.87 (d, 1 H, J = 10.2 Hz), 2.38 (m, 1 H), 2.22 (m, 2 H), 2.10 (m, 2 H), 1.63 (m, 1 H), 1.60 (s, 3 H), 1.58 (m, 1 H), 1.40 (dt, 1 H, J = 12.4, 5.1 Hz), 0.95 (d, 3 H, J = 7.3 Hz), 0.80 (d, 3 H, J = 6.4 Hz). The presence of another isomer of the cyclooctenone (3:1 ratio by integration) can be seen at the methyne proton (4.87 ppm) and methyl doublets at 0.93 and 0.84 ppm. IR (neat) 2955 (s), 2920 (s), 2860 (m), 1705 (s), 1450 (m), 1430 (m), 1370 cm^{-1} (m). MS (15 eV), m/e 166 (M^+), 151, 124 (base), 109, 95, 82, 67.

4,6-Dimethylcycloocta-2,5-dienone (17). $k_1 = 7.94 \times 10^{-5}$ s^{-1}, $t_{1/2}$ 2.42 h. ^{1}H NMR (C_6D_6) δ 5.89 (apparent ddd, 1 H, J = 12, 2.3, 1.4 Hz), 5.72 (dd, 1 H, J = 12.7, 4.9 Hz), 4.92 (d, 1 H, J = 5.9 Hz), 3.33 (br apparent q, 1 H, J = 6.8 Hz), 2.82 (ddd, 1 H, J = 13.7, 11.2, 4.4 Hz), 2.40 (dt, 1 H, J = 16.1, 4.9 Hz), 2.07 (dt, 1 H, J = 16.1, 4.9 Hz), 1.87 (ddd, 1 H, J = 14.5, 11.5, 4.9 Hz), 1.40 (s, 3 H), 0.83 (d, 3 H, J = 6.8 Hz). IR (neat) 3020 (w), 2960 (s), 2922 (s), 2870 (m), 1660 (s), 1450 (m), 1370 (m), 1200 cm^{-1} (m). MS (15 eV), m/e 150 (M^+), 135, 122, 108, 107, 94 (base), 93, 79, 57.

3-(Trimethylsilyl)-4,6-dimethylcyclooct-5-enone (18). $k_1 = 2.70 \times 10^{-5}$ s^{-1}, $t_{1/2}$ 7.12 h. ^{1}H NMR (C_6D_6) δ 5.08 (d, 1 H, J = 9.8 Hz), 2.59 (m, 1 H), 2.42 (br dt, 1 H, J = 13, 4.9 Hz), 2.24 (m, 3 H), 2.13 br dd, 1 H, J = 11, 5 Hz), 1.62 (s, 3 H), 1.60 (m, 1 H), 1.28 (m, 1 H), 1.00 (dd, 3 H, J = 6.8, 2.0 Hz), 0.07 (s, 9 H). ^{13}C NMR ($CDCl_3$) δ 217.03 (C), 134.22 (C), 131.01 (CH), 46.30 (CH_2), 42.61 (CH_2), 35.35 (CH), 30.89 (CH), 28.51 (CH_2), 24.55 (CH_3), 21.91 (CH_3), 0.52 (CH_3). IR (neat) 2960 (s), 1700 (s), 1455 (m), 1435 (m), 1245 (m), 865 (m), 830 (s), 750 cm^{-1} (m). MS (15 eV), m/e 224 (M^+), 209, 195, 169, 142, 127 (base), 124, 73. High-resolution mass spectrum, calcd for $C_{13}H_{24}OSi$ 224.1596, found 224.1615.

2-(Trimethylsilyl)-4,6-dimethylcyclooct-5-enone (19). Product was isolated as the cyclooctenone. ^{1}H NMR (C_6D_6) δ 4.96 (d, 1 H, J = 9.77 Hz), 2.40–2.20 (m, 4 H)8, 1.87 (dt, 2 H, J = 12.7, 5.9 Hz), 1.72 (dt, 1 H, J = 7, 3 Hz), 1.68 (d, 3 H, J = 1.5 Hz), 0.91 (d, 3 H, J = 6.4 Hz), 0.84 (dt, 1 H, J = 12.1, 4.4 Hz), 0.10 (s, 9 H). The presence of another isomer of the cyclooctenone (3.8:1 ratio by integration) can be seen at the methyne proton (4.96 ppm) and methyl doublet at 0.91 and 0.84 ppm. ^{13}C NMR (only the peaks from the major isomer are listed) δ 217.28, 132.78, 131.35, 46.81, 44.73, 32.14, 29.99, 24.95, 23.06, 21.29, -2.53. IR (neat) 2950 (s), 2920 (s), 2900 (s), 2860 (m), 1685 (s), 1450 (m), 1430 (m), 1243 (s), 850 (s), 835 cm^{-1} (s). MS (15 eV), m/e 224 (M^+), 209, 169, 142, 127 (base), 75, 73. High-resolution mass spectrum, calcd for $C_{13}H_{24}OSi$ 224.1596, found 224.1595.

3-(Trimethylsilyl)-4,6-dimethylcycloocta-2,5-dienone (20). Heating for 11 h at 40 °C gave no rearrangement. Warming the bath to 70 °C and heating for 3 h caused some change in the NMR and after ~11 h the reaction appeared to be close to its half-life. After the temperature was raised to 75 °C the reaction was still not complete after an additional 6 h so the NMR tube was heated "indefinitely" until there was almost no starting material present. Rate for the rearrangement at 70 °C is $k_1 = 2 \times 10^{-5}$ s^{-1}, half-life 9 h. Product is a colorless, viscous liquid. ^{1}H NMR (C_6D_6) δ 6.28 (s, 1 H), 5.12 (d, 1 H, J = 7.3 Hz), 3.72 (apparent quintet, 1 H, J = 6.8 Hz), 2.75 (ddd, 1 H, J = 13.7, 12.2, 3.9 Hz), 2.46 (m, 1 H), 2.15 (m, 1 H), 1.94 (m, 1 H), 1.52 (s, 3 H), 1.10 (d, 3 H, J = 6.4 Hz), 0.11 (s, 9 H). IR (neat) 2960 (s), 1670 (s), 1440 (m), 1245 (s), 830 (s), 750 cm^{-1} (m). MS (70 eV), m/e 222 (M^+), 207, 194, 117, 82, 75, 73 (base).

3-Phenyl-4,6-dimethylcyclooct-5-enone (21). Product was isolated as the cyclooctenone, as a thick oil which solidifies below room temperature. An analytical sample was prepared by preparative-scale TLC (Analtech, silica gel GF, 2000 μm, 5% ethyl acetate/hexane). ^{1}H NMR (C_6D_6) δ 7.10 (m, 5 H), 5.08 (d, 1 H, J = 10.3 Hz), 3.02 (dt, 1 H, J = 12.2, 5.2 Hz), 2.74 (t, 1 H, J = 11.9 Hz), 2.48 (m, 1 H), 2.26 (m, 4 H), 1.62 (s, 3 H), 1.58 (m, 1 H), 0.64 (d, 3 H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$) δ 214.7 (C), 141.0 (C), 135.7 (C), 129.0 (2 × CH), 128.4 (CH), 128.2 (2 × CH), 126.7 (CH), 47.5 (CH_2), 47.0 (CH_2), 46.5 (CH), 35.0 (CH), 29.7 (CH_2), 25.1 (CH_3), 19.3 (CH_3). IR (neat) 3040 (m), 2960 (s), 2920 (s), 2860 (m), 1700 (s), 1490 (w), 1450 (m), 970 (w), 770 (w), 740 (w), 695 cm^{-1} (m). MS (70 eV), m/e 228 (M^+), 133, 104, 82 (base), 77, 67. High-resolution mass spectrum calculated for $C_{16}H_{20}O$ 228.1514, found 228.1500. **21a**: This was generated from *cis*-bromostyrene and is a white solid, mp 66.5–68 °C. ^{1}H NMR (C_6D_6) δ 7.15 (m, 3 H), 6.95 (m, 2 H), 4.97 (d, 1 H, J = 7.8 Hz), 2.79 (m, 1 H), 2.67 (m, 2 H), 2.54 (m, 1 H), 2.34 (dt, 1 H, J = 13.2, 5.0 Hz), 2.18 (m, 2 H), 1.56 (s, 3 H), 1.56 (m, 2 H), 0.61 (dd, 3 H, J = 6.3, 2.2 Hz). Some of the other isomer is present in **21a**. ^{13}C NMR δ 211.7, 136.4, 132.3, 128.7, 128.0, 127.5, 126.5, 50.3, 48.9, 46.0, 38.3, 27.0, 23.0, 21.3. IR (neat, taken before solidification) 3030 (w), 3010 (m), 2940 (s), 2860 (m), 1700 (s), 1600 (m), 1490 (m), 1448 (s), 1375 (m), 1325 (m), 1015 (m), 745 (m), 695 cm^{-1} (s). MS (70 eV), m/e 228 (M^+), 133, 105, 104, 82 (base), 81, 77, 67. High-resolution mass spectrum, calcd for $C_{16}H_{20}O$ 228.1514, found 228.1516.

2-Phenyl-4,6-dimethylcyclooct-5-enone (22). Two isomers were isolated in a ratio of 1.7 (**22a**) to 1 (**22b**), the larger fraction having a shorter retention time (higher R_f) on HPLC. **22a**: ^{1}H NMR (C_6D_6) δ 7.45 (m, 2 H), 7.17 (m, 3 H), 4.91 (d, 1 H, J = 9.8 Hz), 3.70 (dd, 1 H, J = 12.2, 4.9 Hz), 2.22 (m, 4 H), 2.03 (dt, 1 H, J = 12.2, 4.9 Hz), 1.62 (d, 3 H, J = 1.5 Hz), 1.62 (m, 1 H), 1.07 (dt, 1 H, J = 11.7, 4.4 Hz), 0.82 (d, 3 H, J = 6.4 Hz). ^{13}C NMR δ 215.00 (C), 139.26 (C), 134.57 (C), 131.27 (CH), 128.50 (2 × CH), 128.41 (2 × CH), 127.07 (CH), 56.01 (CH), 45.55 (CH_2), 40.42 (CH_2), 31.62 (CH), 29.59 (CH_2), 24.81 (CH_3), 21.59 (CH_3). IR (neat) 3020 (w), 2950 (s), 2860 (m), 1706 (s), 1600 (w), 1490 (m), 1450 (m), 1430 (m),1100 (m), 1028 (w), 825 (w), 690 cm^{-1} (m). MS (70 eV), m/e 228 (M^+) 132, 131, 124, 117, 104, 91, 81, 77, 67 (base). High-resolution mass spectrum, calcd for $C_{16}H_{20}O$ 228.1514, found 228.1502. **22b**: ^{1}H NMR (C_6D_6) δ 7.35 (m, 2 H), 7.16 (m, 3 H), 4.97 (d, 1 H, J = 6.3 Hz), 3.71 (dd, 1 H, J = 12.7, 2.9 Hz), 2.67 (dt, 1 H, J = 12.2, 6.4 Hz), 2.26 (m, 4 H), 1.90 (apparent q, 1 H, J = 12.2 Hz), 1.56 (s, 3 H), 1.42 (dt, 1 H, J = 12.2, 3 Hz), 0.83 (d, 3 H, J = 6.8 Hz). **22b** contained some impurities, particularly in the aromatic region. In order to obtain conclusive evidence as to which isomer was the most stable, the HPLC fraction of partially rearranged proximal isomer (**10a**) was taken and heated in an oil bath at 40 °C for several hours. This gave a ratio of 2.6/1 of **22a**/**22b** (based on integration of the two proton aromatic multiplets). **22b** (0.075 g, 3.28×10^{-4} mol) was then taken and dissolved in 10 mL of methanol with an excess of K_2CO_3 (0.136 g, 9.84×10^{-4} mol) and refluxed for 1.5 h. The solution was allowed to cool to room temperature, then 50 mL of water added, and extracted with 3 × 25 mL of ether. The combined organic layers were washed with 20 mL of brine, dried over $MgSO_4$, and filtered, and the solvent was removed on a rotary evaporator. Yield after the removal of solvent, 0.0473 g (63%). NMR revealed the presence of isomer **22a** in a 1.4/1 ratio of **22b**/**22a**, thus showing that **22b** was isomerizing toward the more favored **22a**. On the basis of calculations for the corresponding methyl compounds (**16**) we would expect the cis-substituted conformer to be the most stable; thus **22a** is most likely to be the cis conformer.

2-Ethoxy-4,6-dimethylcyclooct-5-enone (23). Although HPLC indicated the sample to be pure the NMR spectrum showed a significant amount of impurities, possibly caused by decomposition. MS (15 eV), m/e 197, 196 (M^+, base), 181, 167, 139, 115, 96, 82, 81.

3-Ethoxy-4,6-dimethylcycloocta-2,5-dienone (24). Isolated as a white solid, mp 74 °C. ^{1}H NMR (C_6D_6) δ 5.46 (s, 1 H), 5.11 (d, 1 H), 5.11 (d, 1 H, J = 7.3 Hz), 4.14 (apparent quintet, 1 H, J = 6.8 Hz), 3.17 (q, 2 H, J = 6.4 Hz), 3.14 (m, 1 H), 2.58 (dt, 1 H, J = 13.2, 4.4 Hz), 2.11 (apparent q, 1 H, J = 13.7, 4.4 Hz), 2.02 (m, 1 H), 1.38 (s, 3 H), 1.08 (d, 3 H, J = 6.8 Hz), 0.85 (t, 3 H, J = 7.3 Hz). ^{13}C NMR δ 201.74, 178.22, 136.24, 128.28, 104.65, 64.64, 41.22, 33.89, 31.37, 26.55, 16.28, 14.20. IR (KBr pellet) 2975 (m), 2935 (m), 2900 (w), 1635 (s), 1590 (s), 1340 (m), 1220 (s), 1110 (m), 1040 (m), 810 cm^{-1} (m). MS (70 eV), m/e 194 (M^+), 166, 165, 152, 151, 137, 123, 109 (base), 95, 79, 69, 67. High-resolution mass spectrum, calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1302.

2-(Phenylthio)-4,6-dimethylcyclooct-5-enone (25). The rearrangement formed two products: one from the expected

oxy-Cope [3,3] rearrangement and the other from a fragmentation reaction. Thus the kinetic data could not be used for this compound since there were two competing reactions occurring at the same time. After the rearrangement the sample was separated via HPLC using 6% ethyl acetate/hexane. ^{1}H NMR (C_6D_6) δ 7.36 (apparent dd, 2 H, J = 8.3, 1.5 Hz), 6.95 (m, 3 H), 4.79 (d, 1 H, J = 8.3 Hz), 3.88 (dd, 1 H, J = 8.8, 4.9 Hz), 2.48 (m, 2 H), 2.27 (m, 1 H), 2.16 (ddd, 1 H, J = 14.0, 12.2, 3.9 Hz), 1.85 (ddd, 1 H, J = 13.1, 9.5, 3.9 Hz), 1.52 (m, 2 H), 1.46 (s, 3 H), 0.74 (d, 3 H, J = 5.9 Hz). IR (neat) 3060 (w), 2960 (s), 2930 (s), 2870 (m), 1700 (s), 1580 (w), 1450 (m), 1430 (m), 1090 (m), 730 (m), 680 cm^{-1} (m). MS (70 eV), m/e 260 (M^+), 151, 135, 124 (base), 109, 107, 81, 55. The fragmentation product was not conclusively identified.

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Internal Thioaldehyde Trapping by Enes and Dienes

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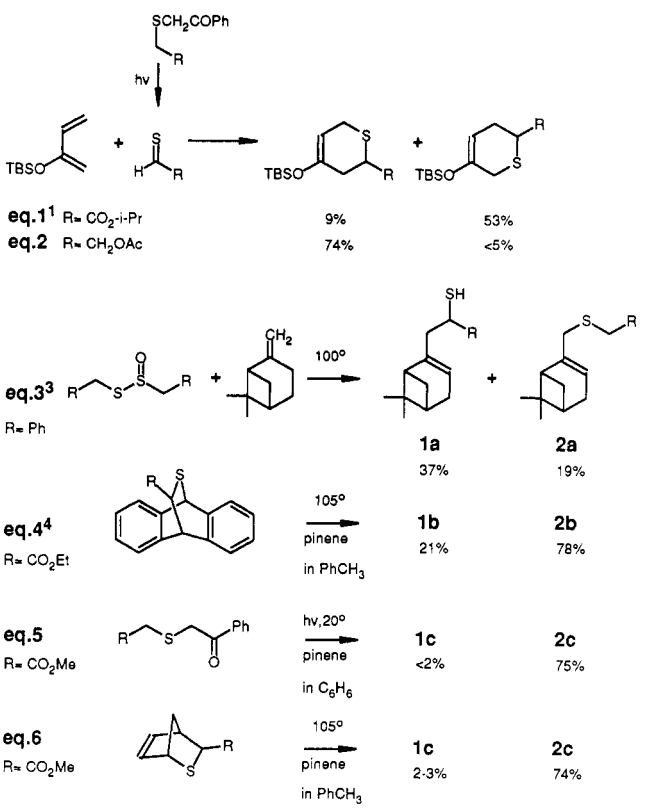
Intermolecular ene insertion of photochemically generated thioaldehyde $MeO_2CCH{=}S$ with β-pinene occurs at room temperature to give the sulfide **2c**. The internal ene insertion of thioaldehyde **6** affords a six-membered carbocycle **9** rather than the seven-membered sulfide **10** which would correspond to the regiochemistry of the intermolecular process (eq 5, 6). Likewise, internal Diels–Alder trapping occurs without a dominant role for the regiochemical preferences seen in intermolecular reactions. Desulfurization of typical internal adducts such as **25,26** or **29,30** affords **31** and **33,34**, respectively.

The synthetic potential of thioaldehydes as reactive carbon bond forming agents has been demonstrated in a variety of intermolecular Diels–Alder reactions.[1,2] There are also some isolated examples of internal Diels–Alder cyclizations, and of intermolecular ene insertions where the thioaldehyde is involved in the generation of carbon bonds.[3,4] We have been interested in the regiochemistry of these processes since the discovery that alkanethials undergo the Diels–Alder reaction with reversed selectivity compared to α-oxo thioaldehydes.[1,5] The typical examples in eq 1 and 2 (Chart I) show that the inherent preferences of electron-deficient thioaldehydes are markedly different from those of the alkanethials, properties that have been attributed to a reversal in LUMO polarization in the C=S group.[5] It was of interest to determine whether the same behavior would be observed in ene insertions as well as in Diels–Alder reactions, and how these preferences would respond to tethering the thioaldehyde and alkene units.

While this work was in progress, two groups reported examples of thermal thioaldehyde generation in the presence of ene substrates. Baldwin and Lopez described the insertion of thiobenzaldehyde into β-pinene (eq 3),[3] while Kirby et al. obtained an ene product from the thermolysis of an anthracene–thioaldehyde adduct (eq 4).[4]

Experiments in our laboratory had failed to detect any ene insertion products from the relatively stable thiopivaldehyde[6] with β-pinene. Likewise, photochemical generation of other alkanethials from phenacyl sulfides gave only decomposition products at room temperature.[1] On the other hand, ene insertion products were formed when the more reactive $CH_3O_2CCH{=}S$ was generated photochemically from the phenacyl sulfide (eq 5). This experiment gave 75% of the allyl sulfide **2c**, but the isomeric mercaptan **1c** was not formed (<2%). For comparison, we

Chart I



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