High-Rate Accelerations in Oxy-Cope Rearrangements Induced by Sulfur Substitution: Kinetic Study Involving Electronically and Geometrically Differentiated 1-Alkenyl-2-(*Z*-1-propenyl)-7,7-dimethyl-*exo*-norbornan-2-ols

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Abstract: The rates of anionically promoted oxy-Cope rearrangement of five structurally related exo-norbornanols have been determined. A critical difference in the substitution pattern of these substrates is the presence or absence of oxygen or sulfur functionality at the terminal carbon of the bridgehead vinyl group and the geometric nature of the olefinic center. The results convincingly establish that although an OPMP substituent exerts, at best, a very modest decelerative kinetic effect, the presence of the PhS substituent causes rearrangement to occur approximately 10^3 times faster by lowering the activation energy to the extent of 3−4 kcal/mol. This remarkable divergence in behavior is shown to correlate well with the highly dissociative nature of the transition state that is predicted computationally.

The development of synthetic strategies that incorporate one or more [3,3] sigmatropic rearrangements for achieving fully stereocontrolled structural elaboration holds special value in modern organic synthesis. While the Cope[1] and Claisen rearrangements[2] have been important mainstays for several decades since their early discovery, variants thereof have more recently outdistanced the parent reactions in their ability to serve with increasingly encouraging success in utilitarian C−C bond construction schemes. The oxy-Cope rearrangement, discovered in 1964,[3] is an outstanding case in point. The simple placement of an OH group at C3 or C4 of a 1,5-diene results after thermal isomerization in the stereoselective production of a dienol. The subsequent tautomerism gives rise irreversibly in most cases[4] to an enone that is amenable to further chemical manipulation. A major shortcoming of this process is the concomitant operation of a retro ene fragmentation whenever geometrically possible.[5] This complication can, however, be skirted by preliminary *O*-alkylation[6] or acylation[7] or by making recourse to *N*-methylpyrrolidinone as the reaction medium.[8]

These advances have become overshadowed by the remarkable finding that rate enhancements of 10^{10}−10^{17} can be achieved by conversion to the respective potassium alkoxides,[9] most notably in the presence of an equivalent of 18-crown-6. This tremendous kinetic acceleration, which is believed to originate from alkoxide-induced weakening of the C3−C4 sigma

bond,[10] allows for the possibility of bringing about these rearrangements at or below 0 °C.[11] As a consequence, sensitive functionality is well-tolerated, thereby enabling the oxyanionic Cope rearrangement to serve broadly in the preparation of structurally intricate ketonic products.[12] A particularly advantageous feature of this reaction is its adoption of highly ordered cyclic transition states such that the new stereogenic centers are formed stereospecifically and double bond geometry is

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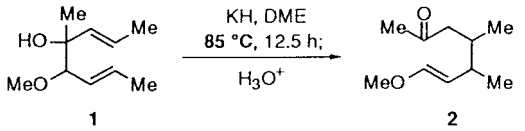
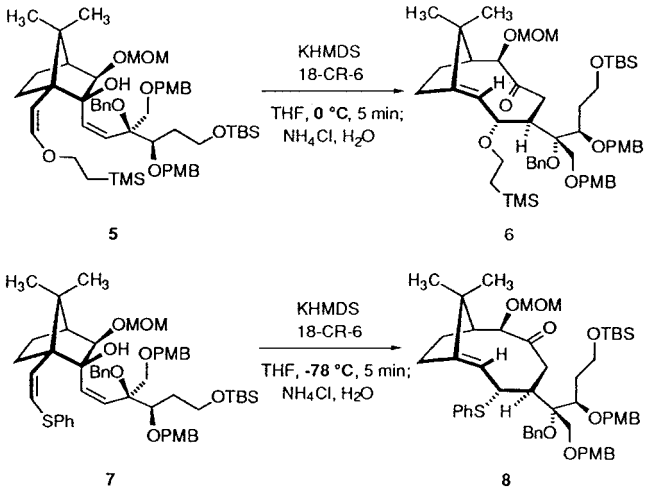
introduced with high fidelity. In short, the level of asymmetric transmission is unparalleled.

Remarkably, these developments have not initiated an intensive search for additional stereoelectronic effects on oxyanionic sigmatropy. Amino-Cope rearrangements have been accorded scant attention.[13,14] A few examples of anionic oxy-Cope rearrangement involving 1,5-diene-3-alkoxides carrying either a 4-methoxy (**1**) or a 4-thiophenoxy group (**3**) have been reported.[15] Note was taken of the fact that **1** isomerized at a

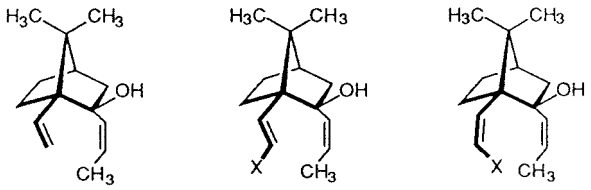


much slower rate than **3**. More recently, the discovery was made that a PhS substituent at the C6 position of bicyclic divinyl carbinol **7** significantly accelerated rearrangement, whereas an alkoxy group at the same position (as in **5**) caused deceleration.[16]



An early simple model of substituent effects predicted that both donor and acceptor groups at saturated carbons C3 and C4 in **A** should increase the rate.[17] The application of density functional theory to this problem has, however, revealed otherwise.[18] By means of this computational method, a SMe group at C4 or C6 was found to cause acceleration, which is likely because of adoption of a homolytic cleavage pathway in order to take advantage of a strong stabilizing effect by divalent sulfur. In contrast, an OCH_3 substituent at either of the same critical sites impedes heterolytic cleavage and slows the concerted sigmatropic rearrangement.

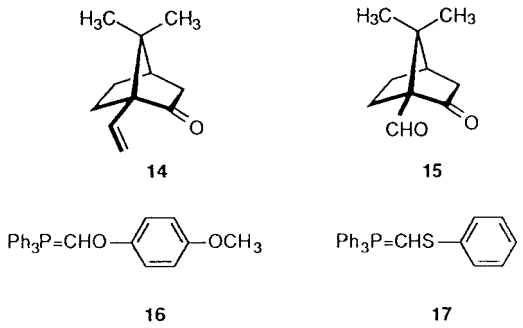
These differing electronic influences hold potentially useful applications. For example, proper selection of the group Y in **A** can serve to modulate matters such that one proceeds smoothly to conversion to **B** or induces the fragmentation of **A**. Regioselective intramolecular competitions should also be possible. Whatever the case, the quantification of these effects would prove highly desirable. In this paper, we present a kinetic and theoretical analysis of the response of the isomeric carbinol pairs **10**/**12** and **11**/**13** as their potassium salts to anionic



sigmatropy.[19] The purpose of the simpler vinyl derivative **9** is to play a calibrative role. The large magnitude of the rate enhancements exhibited by the sulfur derivatives **11** and **13** is quite impressive.

Results and Discussion

Synthetic Considerations. Enantiopure bicyclic ketone **14**, which is readily available from D-camphor-10-sulfonyl chloride,[20] offers several advantages as a starting material for this investigation: (1) it is amenable to conversion to keto aldehyde **15** by direct ozonolysis;[21] (2) the latter can be chemoselectively



olefinated with the *p*-methoxy-phenoxy (OPMP) ylide **16**[22] and its sulfur equivalent **17**[23] with generation of chromatographically separable *E*/*Z* isomer pairs; (3) the presence of apical methyl groups in **14** and its homologues serves to relegate entry of (*Z*)-1-propenylmagnesium bromide[24] (necessarily in the presence of anhydrous cerium trichloride in order to deter enolization[25]) exclusively to the endo surface; and (4) the structural features of **9**−**13** were expected to lend themselves to [3,3] sigmatropic rearrangement exclusively via an endo-chair transition state[21]

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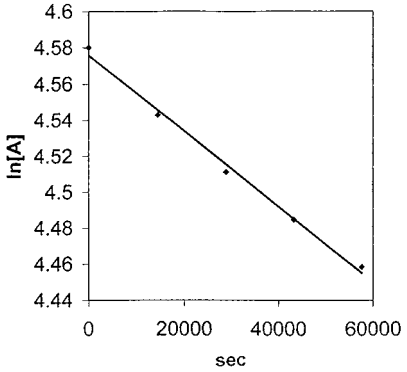

Figure 1. Least-squares plot of rate data for **9** at −30 °C.

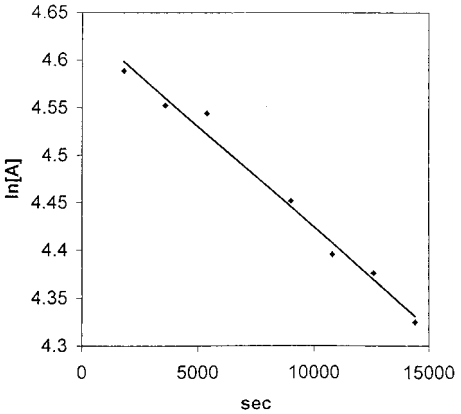

Figure 2. Least-squares plot of rate data for **12** at −30 °C.

because no exception to the adoption of this reaction trajectory by related compounds is currently known.[26]

Determination of Rearrangement Rates. The thermodynamic driving force underlying the oxy-Cope rearrangements of **9**−**13** is sufficiently elevated that no need existed to introduce 18-crown-6 in order to sequester the potassium ions. At the experimental level, 5% solutions of each carbinol in rigorously dried and deoxygenated THF were thermostated at the appropriate temperature and treated via a precooled syringe or an insulated cannula with comparably cooled solutions of potassium hexamethyldisilazide in toluene (0.5 M). Three equivalents of this base served to achieve conditions that were first-order in potassium alkoxide.

The progress of each reaction was followed by the removal of aliquots after specific periods of elapsed time with immediate quenching in cold NH_4Cl solution. Following ether extraction, drying, and solvent evaporation, the individual samples were analyzed by ^{1}H NMR at 300 MHz. In each case, only a single product was formed (see below). The extent to which the carbinol was consumed and its oxy-Cope-derived ketone formed was convenient to monitor because at least one proton signal from each appeared in an isolated region of the spectrum. Processing of the data by means of a weighted least-squares analysis showed that good first-order behavior was being observed. Exemplary plots for **9** and **12** at −30 °C are given in Figures 1 and 2.

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Table 1. Rate Profiles for the Charge-Accelerated Oxy-Cope Rearrangements of **9**−**13**

reactant	k, s^{-1} (t)	relative rate
9$^-$ K$^+$	2.25 (±0.18) × 10^{-5} (−30 °C)	1
10$^-$ K$^+$	3.20 (±0.25) × 10^{-5} (−30 °C)	1.4
	1.13 (±0.25) × 10^{-4} (−10 °C)	
	7.66 (±0.42) × 10^{-4} (+10 °C)	
	1.16 × 10^{-7} (−78 °C)[a,b]	0.52[a]
12$^-$ K$^+$	1.68 (±0.41) × 10^{-6} (−30 °C)	0.075
	3.58 (±0.42) × 10^{-6} (−10 °C)	
	2.15 (±0.16) × 10^{-5} (+10 °C)	
	1.66 × 10^{-8} (−78 °C)[a,c]	0.075[a]
11$^-$ K$^+$	7.68 (±0.24) × 10^{-4} (−78 °C)	3450
13$^-$ K$^+$	2.61 (±0.42) × 10^{-4} (−78 °C)	1175

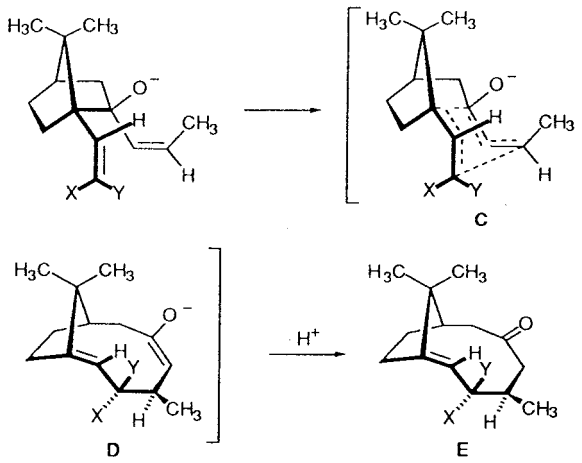
[a] Extrapolated values. [b] An Eyring plot gives $\Delta H^{\ddagger} = 10.2$ kcal/mol and $\Delta S^{\ddagger} = -36$ cal/(mol K). [c] An Eyring plot gives $\Delta H^{\ddagger} = 8.1$ kcal/mol and $\Delta S^{\ddagger} = -51$ cal/(mol K).

The rate constants determined for all five potassium alkoxides are compiled in Table 1. The rate difference that was observed between the ionized forms of **9** and **10** is very small, thus indicating that a trans aryloxy substituent has little observable impact on the overall reaction velocity. When the same OPMP group is fixed cis at C6, as in **12**, rearrangement occurs at a relative rate of 0.07, as compared to **9**. The deceleration conforms to previous observations recorded for **5**.[16]

In contrast, the rate data for the rearrangement of the potassium alkoxides of the sulfur-containing systems **11** and **13** proved to be so accelerated as to require measurements at −78 °C. Although the *trans*-S/*cis*-S rate difference (k_{11}/k_{13} = 2.9 at −78 °C) reasonably closely parallels that seen for the oxygen series ($k_{10}/k_{12} = 20$ at −30 °C), the speed of reaction is markedly enhanced for both **11** and **13**. A direct comparison of the k values experimentally determined for the sulfides versus the extrapolated rate constants for the OPMP derivatives is especially telling: $k_{11}/k_{10} = 6620$ and $k_{13}/k_{12} = 15\,700$. These findings support the concept of a more dissociative transition state when the C6 substituent is constituted of a divalent sulfur atom. The increased stability of these transition states could arise by substantial contribution on the part of sulfur to delocalization, thereby causing a lowering in activation enthalpy. An alternative explanation is that complete sigma-bond homolysis occurs in the direction of a less energy-demanding nonconcerted reaction trajectory. The most recent calculations available favor the latter option.[18] The consequences are clearly very dramatic.

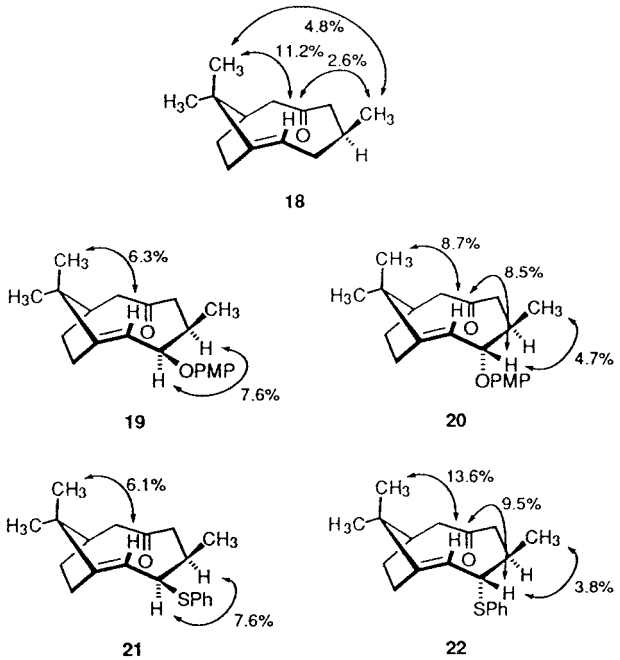
Product Characterization. A compelling feature of the [3,3] sigmatropic behavior of *exo*-2-norbornanols related to **9**−**13** is the wholesale extent to which the so-called "endo-chair" topography (as in **C**) is adopted by these substances. The particular spatial orientation of both the bridgehead double bond and its counterpart at C2 eventuates in stereospecific transfer of chirality during the conversion to enolate anion **D**, which is formed in strikingly regiocontrolled fashion as well. Finally, proton transfer to **D** delivers **E**, whose olefinic geometry and combination of stereogenic centers are uniformly generated with high fidelity.[26]

In each of the five examples selected for kinetic analysis, only a single product was formed. Two options were exercised for preparative-scale purposes. In the first, the accumulated aliquots from the rate studies were combined, dissolved in THF, and resubjected to the action of potassium hexamethyldisilazide until such time that no carbinol remained (TLC analysis). Alternatively, the analogous experiment originated with pure carbinols. The charge-accelerated rearrangement of **9** gives **18**, a ketone that adopts a conformation particularly well-suited to NOE analysis. Thus, the syn-apical methyl group is in suf-

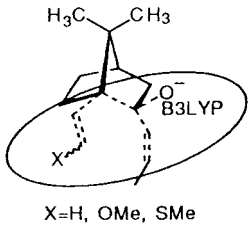


ficiently close spatial proximity to the vinylic proton and to the secondary methyl to elicit the significant interactions that are noted on the formula.

When the heteroatomic substituent eventuates as the β isomer (see **19** and **21**), some flattening of the medium ring is encountered because of the driving force underlying their adoption of quasi-equatorial status. In these examples, the stereochemistry of the double bond is again easily deduced. The cis relationship of the vicinal X and CH_3 substituents was made possible by the unique chemical shifts of the associated methine protons for which an interaction level of 7.6% was measured. That the OPMP and SPh substituents are α-oriented in **20** and **22** was confirmed in comparable fashion. Particular attention is called to the triple relay that proved feasible in this pair of examples.



Theoretical Methods. The rearrangement of **9** was studied with B3LYP/6-31+G* calculations and the PCM solvation model. The parent, **9**, and alkoxy- and thioalkoxy-substituted cases were investigated with the ONIOM method,[27] using B3LYP/6-31+G* for the core and PM3 for the peripheral sections of the molecule. For computational simplicity, the OPMP and SPh substituents of **10**−**13** were replaced with OMe and SMe substituents. Solvation calculations were performed on gas-phase optimized geometries. All transition structures were proved by frequency calculations. All calculations were performed using GAUSSIAN 98.[28]



Dissection of the model to core (B3LYP) and peripheral (PM3) layers. The core layer is drawn in dashed lines.

Results and Discussion. Acyclic molecules of the generic type **A** are recognized to rearrange in one step through a concerted highly asynchronous transition state. The ring strain for compound **9**, however, alters the mechanism. Now, cleavage to an allyl anion and enone occurs (Figure 3). The combined effects of the oxido substituent[14] and ring strain weaken the breaking bond so that even in the ground state (GS1), its length is 1.69 Å. The activation energy for bond cleavage drops from 8.3 kcal/mol in 3-oxido-1,5-hexadiene to 2.5 kcal/mol in **9** (see Table 2). The intermediate is slightly below the reactant in energy. Solvation energies change the picture. Solvation increases the energy of both transition states and the intermediate relative to reactant. This raises the barrier of the reaction from 2.5 to 6.6 kcal/mol and moves the intermediate above the transition states. The mechanism now resembles that of the gas-phase rearrangement of the parent system.

The substituent influence was studied utilizing ONIOM and B3LYP//ONIOM methods. The geometries obtained by the ONIOM method for **9** are nearly the same as for the full B3LYP calculation, but the ONIOM energies are not consistent with experimental trends. The major geometrical deviation is a slightly earlier transition state (TS1) from ONIOM geometries. The breaking CC bond is 2.03 and 2.10 Å in ONIOM- and B3LYP-calculated TS1 of **9**, respectively.

Intermediates are formed in the gas phase for methoxy- and thiomethoxy-substituted derivatives of **9**. Solvation increases the energies of the intermediates and, in the case of methoxy derivatives, the intermediates become the highest-energy structures (see Table 3). For the thiomethoxy derivative, the rearrangement is predicted to proceed without a barrier through cleavage to an allyl anion that is stabilized by the thioalkyl group, even in solution.

In conclusion, heteroatomic and structural effects on the rate and mechanism of electronic reorganization operate with

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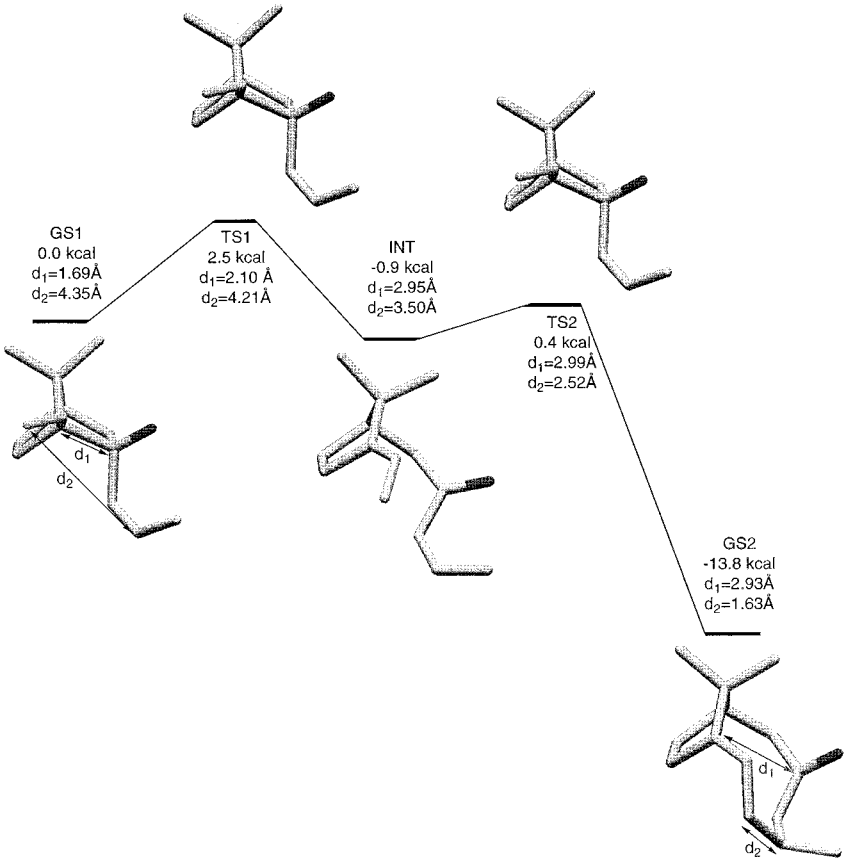

Figure 3. B3LYP/6-31+G* energies and structures for the Cope rearrangement of **9**.

Table 2. Relative Energies (kcal/mol) of TS and Intermediates for Rearrangement of **9** to **18**

	9	TS1	intermediate	TS2	18
gas (B3LYP/6-31+G*)	0.00	2.5	−0.9	0.4	−13.8
THF (B3LYP/6-31+G*)	0.00	6.6	5.0	3.5	−14.8
gas (ONIOM)	0.00	1.7	−10.0	−3.2	−14.8

Table 3. B3LYP//ONIOM Relative Energies (kcal/mol) of TS and Intermediates for Rearrangements of **9** and Its Methoxy and Thiomethoxy Derivatives in THF Utilizing the PCM Solvation Model

reactant	GS1	TS1	intermediate	TS2
9	0.00	4.4	7.3	−1.6
cis-methoxy	0.00	4.1	8.2	1.3
trans-methoxy	0.00	4.8	7.6	2.5
trans-thiomethoxy	0.00	−2.5	−3.1	−5.6

impressive consequences. On the basis of the present findings, it is highly likely that the consequences of heteroatoms other than O and S on the course of anionically accelerated sigmatropic processes will be uncovered and additionally enrich these reaction manifolds.

Experimental Section

General Considerations. Melting points are uncorrected. The column chromatographic separations were performed using Woelm silica gel (230−400 mesh). Solvents were reagent grade and, in most cases, dried prior to use. The purity of all compounds was shown to be >95% by TLC and high-field ^{1}H NMR. The high-resolution electron-impact mass spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA.

(1*S*,2*S*,4*R*)-7,7-Dimethyl-2-[(*Z*)-1-propenyl]-1-vinylbicyclo[2.2.1]-heptan-2-ol (9). Anhydrous cerium trichloride[29] (5.44 g, 14.6 mmol) was stirred at 20 °C with dry THF (200 mL) for 4 h, and the resulting slurry was cooled to −78 °C and titrated with *tert*-butyllithium until an orange color developed. A solution of *cis*-1-propenylmagnesium bromide (14.6 mmol) in dry THF (50 mL) was slowly introduced and stirred at this temperature for 1 h in advance of the addition of **14**[20] (1.6 g, 9.8 mmol) in the same solvent (50 mL) via syringe. The reaction mixture was stirred at −78 °C for 2.5 h, quenched with saturated NH_4-Cl solution, and extracted with ether. The combined organic phases were washed with water and brine, dried, and concentrated. The residue was purified by chromatography on silica gel (elution with 5% ethyl acetate in petroleum ether) to furnish 1.12 g (56%) of **9** as a colorless oil; IR (neat, cm^{-1}) 3495, 1634, 1489, 1455; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.18 (dd, J = 17.7, 11.0 Hz, 1H), 5.78 (dd, J = 11.3, 1.7 Hz, 1H), 5.56−5.45 (m, 1H), 5.28 (dd, J = 11.0, 2.1 Hz, 1H), 5.11 (dd, J = 17.7, 2.1 Hz, 1H), 2.39−2.32 (m, 1H), 1.84−1.47 (m, 9H), 1.23 (s, 3H), 0.80 (s, 3H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 136.4, 127.4, 117.1, 81.9, 59.4, 49.4, 47.8, 46.3, 26.6, 25.9, 21.6, 21.1, 15.2; HRMS (EI) m/z (M^+) calcd 206.1671, obsd 206.1679; $[\alpha]_D^{22}$ −79.4 (*c* 5.3, $CHCl_3$). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.57; H, 10.66.

(1*S*,2*S*,4*R*)-1-[(*E*)-2-(*p*-Methoxyphenoxy)vinyl]-7,7-dimethyl-2-[(*Z*)-1-propenyl]bicyclo[2.2.1]heptan-2-ol (10). Reaction of dry cerium trichloride (634 mg, 1.7 mmol) and *cis*-1-propenylmagnesium bromide (1.7 mmol) in anhydrous THF (45 mL) with (1*S*,4*R*)-1-[(*E*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanone[22] (326 mg, 1.1 mmol) in the predescribed manner afforded 117 mg (31%) of **10** after chromatographic purification (silica gel, elution with 4% ethyl acetate in petroleum ether); white solid, mp 64−66 °C; IR (CH_2Cl_2, cm^{-1}) 3528, 1662, 1504, 1463, 1226; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95−6.83 (m, 4H), 6.31 (d, J = 12.5 Hz, 1H), 5.75 (dd, J = 12.9, 1.6 Hz, 1H), 5.60−5.52 (m, 2H), 3.77 (s, 3H), 2.38−2.32 (m, 1H), 1.84−1.49 (m, 9H), 1.23 (s, 3H), 0.86 (s, 3H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.2, 151.3, 144.7, 136.3, 127.6, 117.6, 114.6, 109.5,

(29) Paquette, L. A. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley and Sons: Chichester, 1995; Vol. 2, p 1031.

81.6, 56.6, 55.6, 49.6, 47.6, 45.7, 26.8, 26.7, 21.5, 21.1, 15.2; HRMS (EI) *m/z* (M^+) calcd 328.2038, obsd 328.2030; $[\alpha]_D^{22}$ −62.1 (*c* 0.73, $CHCl_3$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.89; H, 8.62.

(1*S*,2*S*,4*R*)-1-[(*Z*)-2-(*p*-Methoxyphenoxy)vinyl]-7,7-dimethyl-2-[(*Z*)-1-propenyl]bicyclo[2.2.1]heptan-2-ol (12). Reaction of dry cerium trichloride (303 mg, 0.81 mmol) and *cis*-1-propenylmagnesium bromide (0.74 mmol) in anhydrous THF (40 mL) with (1*S*,4*R*)-1-[(*Z*)-2-(*p*-methoxyphenoxy)vinyl]-7,7-dimethyl-2-norbornanone[22] (156 mg, 0.54 mmol) dissolved in THF (20 mL) in the manner described above led to the isolation (SiO_2, elution with 3% ethyl acetate in petroleum ether) of pure **12** (52 mg, 29%) as a colorless oil; IR (neat, cm^{-1}) 3553, 1584, 1478, 1455, 1438; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23−6.75 (m, 4H), 6.43 (d, J = 10.6 Hz, 1H), 6.12 (dd, J = 14.7, 1.6 Hz, 1H), 5.54−5.45 (m, 1H), 4.70 (d, J = 10.6 Hz, 1H), 3.75 (s, 3H), 2.38−2.31 (m, 1H), 2.03−1.59 (m, 9H), 1.21 (s, 3), 0.89 (s, 3H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 151.4, 143.3, 137.3, 127.3, 117.3, 114.6, 108.3, 82.3, 57.1, 55.6, 49.9, 47.4, 45.2, 28.2, 27.1, 21.6, 21.5, 15.1; HRMS (EI) *m/z* (M^+) calcd 328.2038, obsd 328.2036; $[\alpha]_D^{22}$ −105.8 (*c* 1.23, $CHCl_3$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 77.00; H, 8.64.

***(E* and *Z*)-(1*S*,4*R*)-7,7-Dimethyl-1-[2-(phenylthio)vinyl]-2-norbornanone.** Commercial [(phenylthio)methyl]triphenylphosphonium chloride (4.2 g, 10 mmol) was dissolved in dry THF (50 mL) under N_2, cooled to 0 °C, and treated dropwise with a solution of potassium hexamethyldisilazide in toluene (23 mL of 0.5 M, 10 mmol). After the reaction mixture had been stirred at this temperature for 45 min, a solution of keto aldehyde **15**[22] (1.5 g, 9.0 mmol) in dry THF (25 mL) was introduced, the cooling bath was removed, and stirring was continued for 2 h. Following a quench with saturated NH_4Cl solution, the products were extracted into ether, washed with brine, dried, and freed of solvent. Chromatography of the residue on silica gel (elution with 7% ethyl acetate in petroleum ether) gave 1.29 g (54%) of a 65:35 mixture of the *Z* and *E* isomers (GC analysis). Separation was effected by MPLC (SiO_2, elution with 5% ethyl acetate in hexanes). For the *Z*-isomer: white crystals, mp 71−72 °C; IR (CH_2Cl_2, cm^{-1}) 1738, 1570, 1472, 1413, 1260; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.20 (m, 5H), 6.55 (d, J = 10.6 Hz, 1H), 5.61 (d, J = 10.6 Hz, 1H), 2.50−2.31 (m, 2H), 2.16−1.92 (m, 3H), 1.51−1.42 (m, 2H), 1.05 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.9, 136.7, 129.5, 129.2, 128.9, 126.4, 124.6, 63.8, 49.4, 45.1, 43.4, 42.5, 27.4, 26.4, 20.3, 19.9; HRMS (EI) *m/z* (M^+) calcd 272.1235, obsd 272.1241; $[\alpha]_D^{22}$ −80.2 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{17}H_{20}OS$: C, 74.95; H, 7.40. Found: C, 74.71; H, 7.43. For the *E*-isomer: colorless oil; IR (neat, cm^{-1}) 1741, 1582, 1479, 1452, 1439; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37−7.21 (m, 5H), 6.39 (d, J = 15.5 Hz, 1H), 5.84 (d, J = 15.5 Hz, 1H), 2.49−2.40 (m, 1H), 2.15−1.87 (m, 4H), 1.69−1.42 (m, 2H), 0.97 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.1, 135.6, 129.0, 128.9, 128.1, 126.6, 126.3, 63.9, 49.0, 43.5, 43.0, 27.2, 27.0, 20.1, 19.4; HRMS (EI) *m/z* (M^+) calcd 272.1235, obsd 272.1234; $[\alpha]_D^{22}$ −59.2 (*c* 0.5, $CHCl_3$). Anal. Calcd for $C_{17}H_{20}OS$: C, 74.95; H, 7.40. Found: C, 74.93; H, 7.50.

(1*S*,2*S*,4*R*)-7,7-Dimethyl-1-[(*E*)-2-(phenylthio)vinyl]-2-[(*Z*)-1-propenyl] bicyclo[2.2.1]heptan-2-ol (11). Reaction of dry cerium trichloride (279 mg, 0.75 mmol) and *cis*-1-propenylmagnesium bromide (0.75 mmol) in anhydrous THF (40 mL) with (1*S*,4*R*)-7,7-dimethyl-1-[(*E*)-2-(phenylthio)vinyl]-2-norbornanone (136 mg, 0.50 mmol) dissolved in THF (20 mL) in the manner described above gave, following chromatographic purification on silica gel (elution with 3% ethyl acetate in petroleum ether), 48 mg (32%) of **11** as a colorless oil; IR (neat, cm^{-1}) 3518, 1584, 1478, 1437; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.19 (m, 5H), 6.35 (d, J = 15.5 Hz, 1H), 6.21 (d, J = 15.5 Hz, 1H), 5.74 (dd, J = 11.0, 1.7 Hz, 1H), 5.54−5.50 (m, 1H), 2.37−2.30 (m, 1H), 1.81−1.55 (m, 9H), 1.28 (s, 3H), 0.90 (s, 3H) (OH not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 136.4, 134.1, 128.9, 128.6, 127.8, 126.1, 123.8, 82.2, 60.1, 50.2, 48.2, 46.2, 26.7, 26.5, 21.6, 21.2, 15.2; HRMS (EI) *m/z* (M^+) calcd 314.1704, obsd 314.1693; $[\alpha]_D^{22}$ −62.2 (*c* 1.22, $CHCl_3$). Anal. Calcd for $C_{20}H_{26}OS$: C, 76.38; H, 8.33. Found: C, 76.22; H, 8.43.

(1*S*,2*S*,4*R*)-7,7-Dimethyl-1-[(*Z*)-2-(phenylthio)vinyl]-2-[(*Z*)-1-propenyl] bicyclo[2.2.1]heptan-2-ol (13). Reaction of dry cerium trichloride (558 mg, 1.5 mmol) and *cis*-1-propenylmagnesium bromide (1.5 mmol) in anhydrous THF (40 mL) with (1*S*,4*R*)-7,7-dimethyl-1-[(*Z*)-2-(phenylthio)vinyl]-2-norbornanone (272 mg, 1.0 mmol) dissolved in dry THF (10 mL) in the manner described above gave, following chromatographic purification on silica gel (elution with 2% ethyl acetate in petroleum ether), 112 mg (32%) of **12** as a colorless oil; IR (neat, cm^{-1}) 3553, 1584, 1479, 1457; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39−7.21 (m, 5H), 6.47 (d, J = 10.9 Hz, 1H), 6.16 (dd, J = 1.5, 11.3 Hz, 1H), 5.90 (d, J = 10.8 Hz, 1H), 5.60−5.54 (m, 1H), 2.40−2.36 (m, 1H), 2.18−2.10 (m, 2H), 1.87−1.64 (m, 7H), 1.27 (s, 3H), 1.14−1.11 (m, 1H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 137.2, 129.6, 129.1, 128.9, 128.0, 126.8, 126.3, 83.2, 60.2, 50.9, 48.0, 45.3, 27.4, 27.2, 21.6, 21.5, 15.1; HRMS (EI) *m/z* (M^+) calcd 314.1704, obsd 314.1696; $[\alpha]_D^{22}$ −58.7 (*c* 1.13, $CHCl_3$). Anal. Calcd for $C_{20}H_{26}OS$: C, 76.38; H, 8.33. Found: C, 76.00; H, 8.38.

(1*R*,5*S*,7*E*)-5,11,11-Trimethylbicyclo[6.2.1]undec-7-en-3-one (18). A solution of **9** (412 mg, 2.0 mmol) in dry THF (10 mL) containing 18-crown-6 (1.58 g, 6.0 mmol) was cooled to 0 °C, deoxygenated with N_2 for 30 min, treated with potassium hexamethyldisilazide (11.9 mL of 0.5 M in toluene, 6.0 mmol), stirred at 0 °C for 25 min, and warmed to room temperature. After another 30 min, saturated NH_4Cl solution was introduced, and the product was extracted into ether. The combined organic layers were washed with water and brine, dried, and concentrated. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) afforded 290 mg (70%) of **18** as a colorless oil; IR (neat, cm^{-1}) 1730, 1687, 1452, 1383; ^1H NMR (300 MHz, $CDCl_3$) δ 5.25 (dd, J = 14.2, 2.2 Hz, 1H), 2.55−2.28 (m, 4H), 2.14−1.77 (series of m, 7H), 1.66 (dd, J = 12.7, 4.4 Hz, 1H), 1.24 (s, 3H), 1.07 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.1, 147.4, 120.7, 51.7, 49.4, 45.12, 45.09, 31.8, 30.4, 24.9, 23.9, 22.9, 22.1, 21.8; HRMS (EI) *m/z* (M^+) calcd 206.1671, obsd 206.1674; $[\alpha]_D^{22}$ −69.3 (*c* 2.3, $CHCl_3$). Anal. Calcd for $C_{14}H_{22}O$: C, 81.49; H, 10.74. Found: C, 81.44; H, 10.65.

Oxyanionic Rearrangements of 10−13. These experiments were performed as described above but without added 18-crown-6 at the highest temperature given in Table 1. In several examples, the concentrated aliquots from the kinetic runs were combined and used to deliver the product ketones.

(1*R*,5*R*,6*R*,7*E*)-6-(*p*-Methoxyphenoxy)-5,11,11-trimethylbicyclo-[6.2.1] undec-7-en-3-one (19): white crystals, mp 77−79 °C; IR (CH_2Cl_2, cm^{-1}) 1730, 1686, 1506, 1421; ^1H NMR (300 MHz, $CDCl_3$) δ 6.85−6.77 (m, 4H), 5.34 (d, J = 1.8 Hz, 1H), 4.94 (dd, J = 10.7, 7.5 Hz, 1H), 3.75 (s, 3H), 3.03−2.96 (m, 1H), 2.63−1.87 (series of m, 9H), 1.29 (s, 3H), 1.13 (s, 3H), 1.09 (d, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.5, 171.9, 155.2, 137.3, 135.3, 129.0, 128.9, 127.1, 116.2, 116.1, 115.3, 66.9, 66.2, 56.9, 38.3, 32.6, 28.1, 26.9, 24.9; HRMS (EI) *m/z* (M^+) calcd 328.2038, obsd 328.2056; $[\alpha]_D^{22}$ −82.6 (*c* 0.78, $CHCl_3$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.38; H, 8.93.

(1*R*,5*R*,6*S*,7*E*)-6-(*p*-Methoxyphenoxy)-5,11,11-trimethylbicyclo-[6.2.1] undec-7-en-3-one (20): colorless oil; IR (neat, cm^{-1}) 1728, 1686, 1505, 1465; ^1H NMR (300 MHz, $CDCl_3$) δ 6.81−6.78 (m, 4H), 5.39 (d, J = 4.8 Hz, 1H), 4.35 (dd, J = 4.9, 4.9 Hz, 1H), 3.74 (s, 3H), 2.89−2.86 (m, 1H), 2.66−2.59 (m, 2H), 2.48−2.47 (m, 1H), 2.12−1.94 (m, 6H), 1.26 (d, J = 7.2 Hz, 3H), 1.25 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.8, 184.5, 153.5, 152.3, 150.0, 121.1, 116.2, 114.2, 81.2, 55.6, 49.7, 45.6, 45.1, 41.8, 25.6, 25.2, 23.6, 22.1, 21.9; HRMS (EI) *m/z* (M^+) calcd 328.2038, obsd 328.2047; $[\alpha]_D^{22}$ −121.9 (*c* 0.52, $CHCl_3$). Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 77.08; H, 8.74.

(1*R*,5*R*,6*R*,7*E*)-5,11,11-Trimethyl-6-(phenylthio)bicyclo[6.2.1]undec-7-en-3-one (21): IR (neat, cm^{-1}) 1728, 1687, 1582, 1498; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60−7.38 (m, 3H), 7.25−7.15 (m, 2H), 5.24 (d, J = 12.0 Hz, 1H), 4.12 (dd, J = 11.9, 12.0 Hz, 1H), 2.82−2.76 (m, 1H), 2.58−2.45 (m, 2H), 2.26−2.07 (m, 2H), 1.94−1.80 (m, 5H), 1.28 (s, 3H), 1.20 (d, J = 7.0 Hz, 3H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.9, 149.5, 151.1, 130.8, 128.6, 126.3, 121.1, 51.8, 50.6, 48.2, 45.7, 45.4, 35.2, 28.9, 24.9, 24.8, 22.9, 21.8; HRMS (EI) *m/z* (M^+) calcd 314.1704, obsd 314.1701; $[\alpha]_D^{22}$ −248.9 (*c* 0.19, $CHCl_3$). Anal. Calcd for $C_{20}H_{26}OS$: C, 76.38; H, 8.33. Found: C, 76.00; H, 8.73.

(1*R*,5*R*,6*S*,7*E*)-5,11,11-Trimethyl-6-(phenylthio)bicyclo[6.2.1]undec-7-en-3-one (22): colorless oil; IR (neat, cm^{-1}) 1731, 1686, 1468, 1264; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35−7.31 (m, 2H), 7.27−7.18 (m, 3H), 5.73 (d, J = 10.1 Hz, 1H), 3.34−3.32 (m, 1H), 2.68−2.59 (m, 3H), 2.33−2.24 (m, 2H), 1.98−1.85 (m, 5H), 1.24 (s, 3H), 1.22 (d, J = 6.5 Hz, 3H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.1, 151.3, 138.0, 129.8, 128.6, 125.9, 123.0, 51.3, 51.1, 50.8, 45.4, 44.1, 41.5, 26.8, 25.1, 23.5, 22.5, 22.4; HRMS (EI) m/z (M^+) calcd 314.1704, obsd 314.1694 $[\alpha]_D^{22}$ −215.1 (c 1.27, $CHCl_3$). Anal. Calcd for $C_{20}H_{26}OS$: C, 76.38; H, 8.33. Found: C, 76.09; H, 8.36.

Kinetic Experiments. All flasks were base-washed (20% ethanolic KOH) and flame-dried under argon immediately prior to use. A 5% THF solution of the carbinol (ca 30 mg) was introduced, deoxygenated with bubbling N_2 for 15 min, and cooled to the desired temperature in a thermostated cooling bath. In another flask was placed a THF solution of potassium hexamethyldisilazide (0.5 M in toluene, 3.0 molar equiv), and this vessel was cooled to the same temperature. After 15 min of temperature equilibration, the base solution was transferred via a precooled syringe or insulated cannula into the reaction mixture. A first aliquot was immediately removed at time zero. Following this, additional aliquots were removed at 15−60 min intervals, quenched with cold (0 °C) saturated NH_4Cl solution, and extracted with ether. The combined organic layers were washed with water and brine prior to drying and solvent evaporation. ^1H NMR analysis at 300 MHz followed, and the percent conversion versus time (s) data were subjected to least-squares analysis. All experiments were performed in triplicate. Good first-order behavior was observed in all cases.

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