was prepared by LiAlH$_4$ reduction of the corresponding methyl ester (Aldrich). The remaining substrates were purchased from Aldrich, except *trans*-(CH$_3$)CH=CHCH$_2$OH (Fluka, contained ~5% of the cis isomer). All substrates were distilled from 3-Å molecular sieves under either argon or vacuum (0.1 mmHg) and stored under argon. The *N*,*O*-bis(trimethylsilyl)acetamide, *p*-toluenesulfonyl isocyanate, and tetracyanoethylene (TCNE) were used as supplied (Aldrich), except that TCNE was recrystallized from hot chlorobenzene before use.

Preparation of CH$_2$=CHCH$_2$OD. A solution of allyl alcohol (18.4 mL, 270 mmol) in dry Et$_2$O (50 mL) was added dropwise over 2.25 h to EtMgBr (1.5 M in Et$_2$O, 200 mL, 300 mmol) under argon. The slightly cloudy mixture was then quenched by the addition of D$_2$O (16.2 mL), and the resultant mixture was refluxed for 0.5 h. The clear supernatant was removed by cannula and the white residue extracted with Et$_2$O (2 × 75 mL, Et$_2$O extract removed by cannula). The Et$_2$O was removed by careful distillation and the residue distilled through a vacuum-jacketed Vigreux column, yielding allyl alcohol-*d* (1.98 g, 11% yield, bp 98-99 °C). A ^{1}H NMR (acetone-d_6; 200-MHz) spectrum showed the residual OH to be ~6%.

Catalytic Runs. Typically, [Rh(diphos)]$_2$(ClO$_4$)$_2$ (0.6 mg, 9.987 × 10^{-4} mmol) was dissolved in acetone-d_6 (0.6 mL) under argon. The substrate (9.987 × 10^{-2} mmol, 100 equiv) was then added via syringe. The reactions were monitored by NMR spectroscopy. The [Rh(diphosphine)(NBD)]$^+$ was hydrogenated to the [Rh(diphosphine)(sol)$_2$]$^+$ species as follows: the [Rh(diphosphine)(NBD)]$^+$ complex was suspended in the solvent, and H$_2$ was bubbled into the solvent for 3 min. The gas flow was stopped, and the NMR tube was shaken for 3 min. This procedure was repeated twice to give clear solutions of the solvento complexes. The solutions were then purged with argon, the substrate was added, and the catalysis was monitored by NMR. The results are summarized in Tables I and II. The ^{1}H and ^{2}H NMR spectra are presented in Table V. The ^{1}H NMR assignments are based on comparison with published spectra (where available), on analogies with the corresponding trimethylsilyl ethers, and on the usual principles of NMR spectroscopy. The relevant literature references are given in Table V. The enantiomeric excess from the [Rh((*S*)-binap)(S)$_2$]$^+$ catalyzed ketonization of the enol **11** was determined by the method outlined previously.[27]

[Rh(cyphos)(CH$_2$=CHCH$_2$CH$_2$OH)](ClO$_4$)·3. [Rh(cyphos)(NBD)]ClO$_4$ (8.29 mg, 1.157 × 10^{-2} mmol) was partially dissolved in acetone-d_6 (0.6 mL) under argon. A cycle of bubbling hydrogen gas through the mixture for 3 min followed by shaking for 3 min was repeated three times to dissolve and hydrogenate the catalyst precursor. Argon gas was then bubbled through the solution for 5 min to remove the excess of hydrogen gas. The solution was cooled to -40 °C, and CH$_2$=CHCH$_2$CH$_2$OH (0.77 mg, 1.068 × 10^{-2} mmol, 0.93 equiv) was added to the mixture via syringe. Integration of the ^{31}P NMR signals indicated that 85% of the Rh was in the form of the adduct **3**; the remainder was an unidentified species, believed to be bridging hydride complexes observed when an excess of hydrogen gas is used to hydrogenate the NBD complex at high [Rh].[15] This ratio is reflected in the ^{1}H NMR spectrum as well. The NMR data are presented in Table V. ^{1}H NMR assignments are based on decoupling experiments and the usual principles of NMR spectroscopy. The compound was relatively stable, decomposing ~13% after 22 min at 20 °C.

Chemical Reactions. The catalysis to generate the enol was performed as described above. Carbon monoxide was bubbled through the solution for 2 min to deactivate the catalyst at the point when all of the allylic alcohol was consumed (see Table I). The reagent (9.987 × 10^{-2} mmol, 1 equiv) was then either injected (*N*,*O*-bis(trimethylsilyl)acetamide, *p*-toluenesulfonyl isocyanate) or added as a solid. The yields based on the amount of enol originally present in solution are summarized in Table VI. The NMR data are summarized in Table V. The assignments are based on decoupling experiments, deuterium labeling, the usual principles of NMR spectroscopy, and, where possible, comparison to published data. The relevant references are given in Table V.

Acknowledgment. This work was supported by grants from the National Institutes of Health.

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Solvent, Counterion, and Secondary Deuterium Kinetic Isotope Effects in the Anionic Oxy-Cope Rearrangement

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Abstract: The potassium and sodium alkoxides of 3-methyl-1,5-hexadien-3-ol follow first-order kinetics in the process of undergoing the anionic oxy-Cope rearrangement in tetrahydrofuran (THF) and dimethyl sulfoxide (DMSO). The first-order rate constant for the rearrangement of the potassium alkoxide in DMSO is ca. 1000 times faster than that in THF, as is the first-order rate constant in THF in the presence of 1 equiv or excess 18-crown-6. The rate constants in THF are independent of initial alkoxide concentration; in contrast, the first-order rate constants in DMSO are inversely proportional to the initial alkoxide concentration, and addition of potassium salts to the DMSO solution results in a retardation of rearrangement rate. Addition of $^1/_4$ and $^1/_2$ equiv of 18-crown-6 in THF gave first-order behavior only over the first 25% of reaction with an initial rate constant linearly related to that with 1 equiv of crown ether. Secondary deuterium kinetic isotope effects have been determined at the bond-breaking and bond-making sites in the Cope rearrangement of the potassium alkoxide in THF, in THF in the presence of 18-crown-6, and in DMSO. The isotope effects indicate a highly dissociative transition state with substantial bond breaking of the C3-C4 bond and little bond making between the allylic termini (C1 and C6). The effects of aggregation and ionic dissociation are discussed in the context of mechanistic pathways proposed for the rearrangement in THF and in DMSO.

In 1975, Evans and Golob reported the remarkable rate acceleration for the Cope rearrangement of the potassium alkoxide of alcohol **1** of 10^{10}-10^{17} relative to that for the alcohol itself.[1] In general, hydroxy and alkoxy substitution at C3 of 1,5-dienes affect the rate of thermal sigmatropic 3,3 rearrangements only minimally,[2-4] while a simple change of the hydroxyl substituent

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[†] Taken from the Ph.D. Thesis of K.R.G., Indiana University, May 1990.

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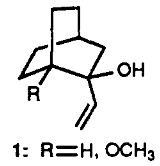


1: R═H, OCH_3

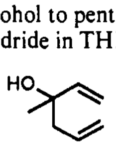
to an alkoxide results in enormous rate enhancements.[5] Sigmatropic 1,3 shifts are similarly affected.[6-8]

Considerable effort[9,10] has been devoted to understanding this singular rate acceleration effect. In view of the substantially decreased dissociation energy of bonds β to the oxyanionic moiety,[10] it seems reasonable that the transition state for these shifts would have substantial weakening of the allylic bond and little formation of the final σ bond, i.e., bond breaking proceeding far beyond bond making in these transition states.[11] The increased stability of the transition state has therefore been attributed to a result of increased distortion in the direction of a more stable nonconcerted alternative. An alternative explanation is that the oxyanion at C3 contributes substantially to delocalization in the transition state, thereby lowering the activation enthalpy.[12]

The usual method to probe concerted reaction transition-state structure is the determination of secondary deuterium kinetic isotope effects (KIE's) and comparison of these to the effects expected if the allylic bond were totally broken or if bond formation between the allylic termini were completely made in the transition state.[13] In the case of the anionic oxy-Cope rearrangement, there are further complications since counterion complexation and alkoxide aggregation play a significant role in the reaction. In the original 2-vinylnorborn-5-en-2-ol system (**1**), Evans and Golob provided the important information that the reaction of the potassium salt is first order and that it is 180 times faster in hexamethylphosphorous triamide (HMPA) than in THF. This suggests that either the more polar solvent increases the rate of rearrangement or a more activated anion is formed followed by rearrangement. There are many variations on the latter pathway: rate-determining dissociation or preequilibrium dissociation followed by rate-determining 3,3 shift or intermediate possibilities. In THF, the reaction is 180 times faster upon addition of 1 equiv of 18-crown-6; additional crown ether has little rate effect. This suggests that a more activated oxyanion is formed when the potassium is sequestered and that the rate-determining step is the 3,3 shift or, alternatively, that the transition state is more stable when the counterion is sequestered. The secondary KIE's reported here support a more dissociative transition state. However, the response to solvent and added counterion reveals more complexities than have been previously considered.

Results

3-Methyl-3-oxyanion-1,5-hexadiene Rearrangement Rates. The conjugate base of 3-methyl-1,5-hexadien-3-ol (**2**) was generated by addition of sufficient alcohol to pentane-washed 1.5–3.0 equiv of potassium (or sodium) hydride in THF to give a 0.1 M solution.



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Rates were followed by capillary gas chromatography (GC) of the neutral fraction resulting from a water quench of aliquots of the reaction mixture. Good first-order behavior was observed over at least 2 half-lives in all reactions reported ($r > 0.99$) as determined from a weighted least-squares analysis.[14]

The rate of rearrangement in THF is relatively unaffected by filtration through glass wool and is independent of the concentration of the alkoxide (Table I). Indeed, most of the solvent could be removed, and the rate in the resulting semisolid is about the same as that at 0.1 M. Attempts to look for a common ion effect were frustrated by the insolubility of most potassium salts in THF, but addition of 3 equiv of potassium *tert*-butoxide increases the rate but only by 30% at reflux (Table I).

Further, the rearrangement in THF with 1–4.5 equiv of 18-crown-6 is also ~1000 times faster than in THF alone (Table I). The rate constants determined in the presence of only 0.25 and 0.5 equiv of 18-crown-6 are the initial rate constants, since after only 25% reaction the rates fell off dramatically. Thus, the crown ether is not simply a catalyst or exchanging rapidly between product and reactant. The sodium alkoxide of **2** rearranges 40.4 times slower than the potassium alkoxide in refluxing THF, while the lithium alkoxide does not rearrange even after lengthy reaction times. Finally, attempted rearrangement of the potassium salt of **2** in refluxing THF with excess lithium bromide gives no rearrangement under conditions where the potassium salt would have undergone 60 half-lives of rearrangement.

Table I. Rate Data for the Cope Rearrangement of the Potassium Alkoxide of 3-Methyl-1,5-hexadiene in THF

k ($\times 10^6$ s^{-1})	added compds, amt (equiv)	conc (M)	T (°C)
3.2 ± 0.1[a]		neat	24
2.73 ± 0.5		0.10	24[b]
227 ± 2.0		0.10	66[b]
203 ± 3.0		0.50	66
244 ± 2.4		0.033	66
263 ± 2.0	KO-*t*-Bu, 1.0	0.10	66
313 ± 3.2	KO-*t*-Bu, 3.0	0.10	66
464 ± 11[c]	18-crown-6, 0.25	0.10	27
1670 ± 70[c]	18-crown-6, 0.50	0.10	27
3350 ± 44	18-crown-6, 1.0	0.10	29[d]
8960 ± 281	18-crown-6, 2.0	0.10	29
7060 ± 354	18-crown-6, 3.0	0.10	29
5860 ± 69	18-crown-6, 4.5	0.10	29
391 ± 1.8	18-crown-6, 1.0	0.10	2[d]
507 ± 2.1	18-crown-6, 1.5	0.10	2

[a] Solvent removed by evaporation at reduced pressure. [b] A two-point Arrhenius plot gives $\log k = 9.9 - 21\,100/2.3RT$, which corresponds to $\Delta H^{\ddagger} = 20.5$ kcal/mol and $\Delta S^{\ddagger} = -15.2$ cal/(mol K). [c] Initial rate constants since rate fall off occurs after 25% reaction. [d] A two-point Arrhenius plot gives $\log k = 7.0 - 13\,100/2.3RT$, which corresponds to $\Delta H^{\ddagger} = 12.6$ kcal/mol and $\Delta S^{\ddagger} = -28.3$ cal/(mol K).

Table II. Rate Data for the Cope Rearrangement of the Potassium Alkoxide of 3-Methyl-1,5-hexadien-3-ol in DMSO

k ($\times 10^3$ s^{-1})	added compd, amt (equiv)	conc (M)	T (°C)
25.4 ± 0.2		0.033	27
4.68 ± 0.07		0.10	27
0.903 ± 0.030		0.50	27
3.33 ± 0.05	KBF_4, 1.0	0.10	27
2.18 ± 0.03	KBF_4, 2.1	0.10	28
1.39 ± 0.05	KBF_4, 4.0	0.10	27
1.15 ± 0.05	KBF_4, 8.0	0.10	28

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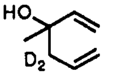
Table III. Secondary Deuterium Kinetic Isotope Effects for the Cope Rearrangement of the Potassium Alkoxides 2–4

solvent; added 18-crown-6 (equiv)	T (°C)	compd, labeling	k ($\times 10^6$ s^{-1})	k^H/k^{D_2}
THF	24	**2**, H_2	2.730 ± 0.050	
THF	24	**3**, α-D_2	2.140 ± 0.066	1.276 ± 0.04
THF	24	**4**, γ-D_2	2.850 ± 0.138	0.958 ± 0.05
THF	66	**2**, H_2	227 ± 2.0	
THF	66	**3**, α-D_2	183.8 ± 5.1	1.235 ± 0.03
THF	66	**4**, γ-D_2	238.3 ± 4.2	0.953 ± 0.02
THF; 2.0	29	**2**, H_2	8957 ± 281	
THF; 2.0	29	**3**, α-D_2	5763 ± 128	1.544 ± 0.04
THF; 2.0	29	**4**, γ-D_2	8181 ± 250	1.095 ± 0.05
THF; 1.5	2	**2**, H_2	424.2 ± 15.5	
THF; 1.5	2	**3**, α-D_2	354.3 ± 7.4	1.197 ± 0.04
THF; 1.5	2	**4**, γ-D_2	501.1 ± 9.0	0.847 ± 0.05
THF; 1.5	2	**2**, H_2	502.6 ± 2.1	
THF; 1.5	2	**3**, α-D_2	320.7 ± 11.0	1.567 ± 0.04
THF; 1.5	2	**4**, γ-D_2	463.2 ± 4.9	1.085 ± 0.01
DMSO	25	**2**, H_2	7427 ± 251	
DMSO	25	**3**, α-D_2	4437 ± 177	1.674 ± 0.05
DMSO	25	**4**, γ-D_2	7612 ± 375	0.976 ± 0.06

The rate data for the rearrangement of the potassium alkoxide of 3-methyl-1,5-hexadien-3-ol (**2**) in THF and dimethyl sulfoxide (DMSO) have been previously reported.[15] In the present study, the rearrangement takes place ~1000 times faster than in DMSO (Table II) than in THF at room temperature. Although rate data in DMSO followed good first-order kinetics (errors reported are the standard deviation in a weighted least-squares plot of ln (A/A_0) versus time), reproducibility of rate constants upon switching from one batch of DMSO to another was difficult to attain; the usual variation was ±30%. Other workers have experienced similar difficulties, and the lack of reproducibility is generally attributed to varying amounts of adventitious water.[16,17] This problem is overcome by using the same batch of DMSO throughout a set of related experiments; i.e., the same batch of DMSO was used for the runs in Table II and another batch was used for the DMSO entries in Table III. The first-order rate constant in DMSO is dependent on initial concentration, decreasing by a factor of 28 over a concentration change from 0.033 to 0.5 M with a 5-fold rate decrease between 0.033 and 0.1 M. A similar concentration dependence of potassium alkoxides in DMSO has been observed in an intramolecular (and thus unimolecular) hydride-transfer system.[18] This apparent contradiction can be resolved by a reaction mechanism involving dissociation of potassium ion from both reactant and product with compensating rate and equilibrium constants from the various reactive species and product. In an attempt to probe this hypothesis, potassium tetrafluoroborate was added to the DMSO solutions. The rate decreased by a factor of 2 with 2 equiv of added salt, by a factor of 3 with 4 equiv of added salt, and by a factor of 4 with 8 equiv of added salt (Table II). Fragmentation rates of arylpotassium alkoxides in DMSO are even more strongly dependent on addition of external potassium.[16] Four equivalents of added tetrabutylammonium iodide had a slight accelerating effect on the rate in DMSO (1.2×), and potassium bromide and potassium iodide retarded the rate but not as effectively as KBF_4.

Secondary Deuterium Kinetic Isotope Effects. Rather than preparing 4,4-dideuterio-3-methyl-3-hexa-1,5-dienol (**3**) and 6,6-dideuterio-3-methyl-3-hexa-1,5-dienol (**4**) separately and examining their kinetics separately, a 0.520:0.480 mixture of the two, respectively, was prepared from 3,3-dideuterio-3-chloropropene via Grignard formation and addition to methyl vinyl ketone. Addition of the alcohol to a stirred mixture of potassium hydride in THF followed by water quenching at intervals and GC analysis revealed first-order behavior over 3 half-lives with a half-life of 71 h at 24 °C (Table III). Comparison of the rate to that of the protio alcohol gave k^H/k^{D_2}(overall) = 1.13 (0.03). Simulation (not deconvolution) of the deuterio experiment as two decreasing exponentials given the known starting fractions of each compound verified the expection that **4** had to react more than twice as fast as **3** *relative to the protio material*. The best fit gave relative secondary KIE's at the α (**3**) and γ (**4**) positions of 1:1.33 (0.06).



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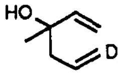

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Since the upfield deuterium resonances from **3** were separated from those of the product from **4** by 0.2 ppm in the deuterium magnetic resonance (^2H NMR) spectrum, the rates of the deuterated materials could be followed separately, which allowed determination of the absolute kinetic isotope effects. The absolute rate constants for the two deuterated materials were determined from the data obtained from the mixture of the two as follows. The ^2H NMR spectrum of the mixture before rearrangement showed two signals, one at 5.3 ppm and the other at 2.5 ppm, in a 0.480:0.520 ratio, respectively. As the rearrangement proceeded, a signal corresponding to the product from **4** began to grow at 2.3 ppm while the signal at 5.3 ppm became more complex and broad, corresponding to both **4** and the product from **3**. At each point of analysis, the mixture was analyzed by GC for total dienol relative to total heptenone and by ^2H NMR for the mole fractions of **3** and the resulting heptenone from **4** relative to the mixture of all four components. The value for the mole fraction of **3** thus determined by ^2H NMR was subtracted from the mole fraction of total **3** + **4** determined by GC, providing the value for the mole fraction of **4**. Thus, at each point of analysis the mole fraction of each deuterated dienol was divided by the starting mole fraction as determined by ^2H NMR to give $(A/A_0)_t$ separately for **3** and **4**, which allowed determination of the rate constants for each material in the same vessel. The relative kinetic isotope effects at the α and γ positions are consistent with the simulation of the deuterated compound by two exponentials as indicated previously.

Experiments in THF with added 18-crown-6 at room temperature and in an ice–water bath resulted in a ratio of $k_4{:}k_3$ that is ~1.42 in all three cases, but the absolute kinetic isotope effect, which is determined from GC analysis of side by side but separate experiments, varied substantially; see Table III. If an average were to be determined, the KIE at the γ position is negligible and that at the bond-breaking, α site is 1.44. The irreproducibility between runs is disconcerting, but the relative bond-breaking and bond-making isotope effects are reproducible as expected for two reactions being run in the same vessel. However, the large magnitude of the bond-breaking isotope effect is of concern, especially since the magnitude of the bond-breaking KIE in DMSO is even larger.

Experimental Section

1,1-Dideuterioallyl alcohol was prepared according to the method of Shuetz and Millard[19] and converted to 3,3-dideuterioallyl chloride with use of phosphorus oxychloride and DMF.[20] The corresponding Grignard reagent was added to methyl vinyl ketone by use of the Barbier modification,[21] yielding a nearly equimolar mixture of 4,4-dideuterio-3-methyl-1,5-hexadien-3-ol (**3**) and 6,6-dideuterio-3-methyl-1,5-hexadien-3-ol (**4**) in 25% yield. The protio dienol (**2**) was prepared in the same manner.

Proton NMR for the dideuterio mixture of **3** and **4** (300 MHz, $CDCl_3$): δ 5.93, dd (J = 17.4, 10.7 Hz), 1 H; 5.78, dd (J =16.4, 10.4 Hz), 1 H; 5.21, dd (J = 17.4, 1.4 Hz), 1 H; 5.13, m, 1 H; 5.06, dd (J = 10.7, 1.8 Hz), 1 H; 2.30, m, 1 H; 1.69, s, 1 H; 1.28, s, 3 H.

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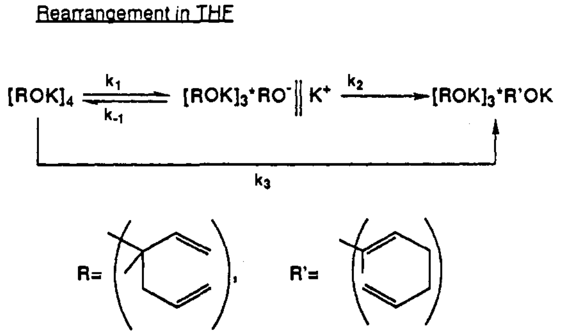
Scheme I



Deuterium NMR for the dideuterio mixture of **3** and **4** (55.4 MHz, THF, external $CDCl_3$ reference): δ 5.31, s, 1.92 D; 2.48, s, 2.08 D.

Proton NMR for the protio dienol (300 MHz, $CDCl_3$): δ 5.93, dd (J = 17.4, 10.7 Hz), 1 H; 5.78, m, 1 H; 5.21, dd (J = 17.4, 1.4 Hz), 1 H; 5.13, m, 2 H; 5.06, dd (J = 10.7, 1.8 Hz), 1 H; 2.30, m, 2 H; 1.69, s, 1 H; 1.28, s, 3 H.

Kinetics. A potassium hydride dispersion was washed three times with pentane under a nitrogen atmosphere in oven-dried glassware, weighed, and suspended in anhydrous THF (freshly distilled from sodium benzophenone ketyl). The alcohol was rapidly added from a syringe and timing for kinetics begun immediately. In a typical run, 5.8 mmol of potassium hydride was suspended in 19 mL THF and 1.9 mmol of the alcohol was added to begin the experiment. Five to six aliquots (0.5 mL) were withdrawn periodically and quenched with water, followed by extraction with pentane, drying, and analysis of the solution by capillary GC (50-m DB-5 column, Varian 3700 gas chromatograph equipped with a HP-3390 electronic integrator) and ^2H NMR (Nicolet 360 instrument) as well in the isotope effect study. The sodium and lithium alkoxides were formed from sodium hydride and lithium diisopropylamide, respectively. When 18-crown-6 was used, it was added simultaneously with the alcohol as a solution in THF. For the lithium–potassium exchange reaction, potassium hydride was suspended in a solution of dry lithium bromide in THF, the solution brought to reflux, and the alcohol added. When DMSO (freshly distilled from calcium hydride) was used, it was allowed to react with potassium hydride for 15 min to form the dimsyl anion, and the alcohol was then added. In all cases the alkoxide was soluble.

The product ketone, 6-hepten-2-one, was the only product observed in all cases. It was independently synthesized[22] and its NMR spectrum and GC behavior were compared with those of the products of the rearrangements. Proton NMR of the mixture of deuterated heptenones (300 MHz, $CDCl_3$): δ 5.76, br dd, 1 H; 4.96, m, 1 H; 2.42, t (J = 7.3 Hz), 2 H; 2.13, s, 3 H; 2.05, q (J = 7.0 Hz), 1 H; 1.67, m, 2 H.

The data from each run with the addition of a zero time point assuming no reaction were subjected to a weighted least-squares analysis.[14]

Discussion

Rearrangement in THF. The fact that the kinetics for rearrangement of the alkoxides of 3-methyl-1,5-hexadien-3-ol (**2**) are first-order requires that rearrangement occurs from the dominant species present in solution. Since potassium *tert*-butoxide is known to exist as a tetramer in THF solution, it is likely that **2** is also tetrameric in THF solution.[23] so rearrangement would appear to occur in the tetramer or in an ion pair derived from tetramer (cf. Scheme I). If rearrangement occurred by preequilibrium formation of monomer from a more stable tetramer in THF, the kinetics should be one-fourth order in tetramer or one-fourth *order in any measure of tetramer that includes that of monomeric starting alcohol after an aqueous quench.* This point requires emphasis since a reviewer argued that the reaction "is still first order in starting material, which is what he is measuring, i.e., rate = k_2[ROK] = k_2K[tetramer]$^{1/4}$ if K is an equilibrium constant between tetramer and monomer and k_2 is rate determining". This statement would be true if tetramer were less stable than monomer in the concentration regimes used and the rearrangement were unimolecular and rate determining. Since the rate of rearrangement in THF is relatively independent of concentration from 0.1 M to nearly neat alkoxide (neat potassium *tert*-butoxide is also tetrameric[24]), it is unlikely that the tetramer is in equilibrium with any other alkoxide species including a dissociated species and kinetically free potassium ion. The lack of concentration dependence does not rule out rate-determining dissociation of potassium ion or rate-determining generation of the ion pair of scheme I (i.e., $k_{exp} = k_1$); however, if either of these possibilities were correct, then no secondary deuterium KIE's at the bond-breaking site (C4) should be observed.

The rate retardation by lithium cation can occur by ion exchange in the starting material or in the tetrameric anion to give kinetically inert lithium alkoxide n-mers, although a reviewer suggested that metathesis could occur between lithium bromide and potassium hydride prior to addition either completely or coating the KH surface with KBr.

The response of the system to crown ether suggests that potassium ion is being scavenged so as to produce a more reactive alkoxide that undergoes the rearrangement as the rate-determining step. However, the saturation response of the rates to added crown ether indicate that 1–2 equiv of crown ether is sufficient to convert all of the reactants to the reactive species so that the crown ether is not a catalyst. The simpler system examined here behaves almost identically with the system studied by Evans. Of importance is the observation that <1 equiv of crown ether gives curved first-order kinetic plots, which also indicates that the crown ether is not a catalyst. It further indicates that the crown ether does not exchange from product complex to reactant complex at a rate that is fast relative to rearrangement within the complex. Finally, the initial first-order rate constants with ≤2 equiv of crown ether are linearly related to the concentration of crown ether. Thus, whatever species is generated with <1 equiv of crown ether from starting tetramer is the same as that present with excess crown ether. It is unclear what the state of aggregation of the fully "crowned" reactant is, especially since molecular weight measurements of crowned potassium *tert*-butoxide apparently have not been reported.

The fact that secondary deuterium kinetic isotope effects occur in the rearrangement of **2** in THF suggests that k_2 or k_3 is the rate-determining step (Scheme I), and their magnitudes are indicative of a transition state that is highly dissociative. The secondary isotope effect observed for two deuteriums at the bond-breaking site is nearly the maximum value, which is 1.35 for two deuteriums at room temperature where the fractionation factor for the allylic species is assumed to be the same as in the neutral Cope rearrangements.[13] The larger bond-breaking isotope effect with added crown ether suggests that the fractionation factor (relative to acetylene C–H) for allylic anionic-like moieties may be smaller (i.e., C–H bonds are looser) than for normal sp^2 C–H bonds (which themselves are looser relative to sp^3 C–H bonds, which is why k^H/k^D is greater than unity for sp^3 to sp^2 conversions). If this is the case, discussion of the extent of bond breaking in these cases sould be deferred until a maximum value can be determined. It is significant that there is but a small inverse kinetic isotope effect at C6, indicating little if any bond making between the terminal carbons in the transition state.

Rearrangement in DMSO. It is surprising that the kinetics for rearrangement of **2** in DMSO are first-order since potassium *tert*-butoxide is dimeric in DMSO and trimeric at concentrations slightly higher than those used in this study.[25] The first-order dependence over 2–4 half-lives requires that rearrangement occurs within the dimeric species in solution and not via monomers formed via preequilibrium dissociation (see discussion on rearrangement in THF). However, the strong inverse dependence on the initial concentration of starting material from 0.033 to 0.5 M and the rate retarding effect of added potassium ion suggest that dissociation of potassium ion from the dimer occurs prior to the rate-determining step, which would be k_2 in Scheme II. Thus, k_3 could only be a minor pathway at low alkoxide concentrations

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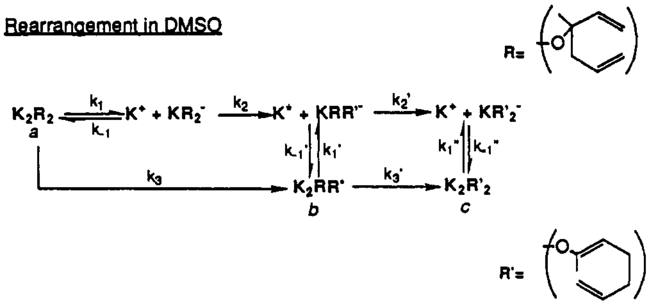
Scheme II



and in the absence of external potassium ion.

However, the rate retardation effect saturates at high concentrations of added potassium salt. This could be due to either accretion of potassium tetrafluoroborate or retardation of the rate via free ions ($k_{-1}[K^+] \gg k_2$) to the extent that a direct pathway within the dimer via k_3 becomes dominant. At higher concentrations of starting material, the rate dependence on initial concentrations in the absence of added salt also appears to be less than a square root dependence. This could also be due to greater incursion of the direct pathway via k_3.

It is not clear that the dissociation constants for the mixed reactant–product dimer (b), reactant dimer (a), and product dimer (c) are the same so that a constant concentration of potassium ion will be present to ensure first-order kinetics over 2–3 half-lives (Scheme II). Indeed, it is known that K_{as} for KO-*t*-Bu is 270/M in DMSO for 0.1 M solutions[26] and K_{as} for potassium enolates of acetophenone and cyclohexanone is <20/M in DMSO up to concentrations of 0.02 M.[27] The dissociation constant ratio would suggest that at the end of the reaction the potassium ion concentration should have increased by a factor of 3, which is well beyond the demands of first-order behavior. However, the reactant–product dimer should have a higher dissociation constant than the starting dimer so its overall rate of reaction may compenstate for the increase in potassium ion concentration to allow the kinetics to appear first order with a given concentration of starting material.

The secondary deuterium kinetic isotope effects in the rearrangement of **2** in DMSO suggest that the transition state is highly dissociative. The secondary isotope effect observed for two deuteriums at the bond-breaking site is nearly twice as large as the maximum value, which is 1.35 for two deuteriums at room temperature.[13] The origin of this anomolously high bond-breaking KIE is under investigation. Again, it is significant that there is but a small inverse kinetic isotope effect at C6, indicating little if any bond making between the terminal carbons in the transition state.

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Lactones. 1. X-ray Crystallographic Studies of Nonanolactone and Tridecanolactone: Nature of CH···O Nonbonded Interactions

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Abstract: The structures of nonanolactone and tridecanolactone have been studied via X-ray crystallography. Nonanolactone adopts an interesting conformation in which a methylene chain and the *Z* ester group are parallel, with nonbonded H···O distances of only 2.76 and 2.34 Å. The conformation is compared with those of cyclodecane, cyclodecanone, and nonanolactam. Tridecanolactone has a regular structure of all trans edges joined by gauche corners. The conformational flexibility of both size rings is discussed. The question of CH···O nonbonded interactions was studied via MP2/6-31G calculations and charge density analysis. The negative charge at oxygen reverses the normal C^+–H^- polarization in alkanes, leading to an attractive interaction. The experimental structural data have been compared with the results of MM3 calculations, and the set of lower energy conformers has been determined. The entropy changes on melting and the changes in ^{13}C NMR spectra with temperature are discussed.

Introduction

The lactone group is contained in a large number of important naturally occurring substances.[1] Despite its importance, this group has received relatively little study with regard to energies or conformations.[2] We have initiated a detailed study of simple lactones that should provide information useful in modeling compounds having this group using molecular mechanics. This includes studies of enthalpies of hydrolysis of lactones, enthalpies of reduction of lactones to diols, theoretical calculations of conformations and energies, and structural studies. This report will be concerned with the conformation of the 10-membered-ring lactone, nonanolactone, and of the 14-membered-ring tridecanolactone. The 10-membered ring appeared to be interesting for an initial study since cyclodecane,[3] cyclodecanone,[4] and nonanolactam hemihydrochloride[5] have been studied, allowing a

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