molecule. Run 6 was modeled after run 5. The (±)-I isolated from run 6 contained 53.5 ± 0.5% excess deuterium per molecule; the (+)-I contained 16.3 ± 0.5% deuterium.

Run 8. The procedure for the reaction resembled that of run 5 except 350 mg of (−)-II-*d* was employed and temperature was 150.5 ± 0.1°. After being cooled the ampoule's content was washed into 100 ml of dilute hydrochloric acid. The product separated as a white solid, was collected, washed with water, dried, and totally sublimed, wt 336 mg, $[\alpha]^{25}_{546}$ −3.01° (*c* 4.7, chloroform). This material was fractionally crystallized from pentane, and Table V records the results. Crops 1, 2, and 3 were combined and recrystallized from 5 ml of pentane by cooling slowly to 6°. The product (65 mg) of long, fine needles was sublimed, mp 102.5–103.1°, $[\alpha]^{25}_{546}$ −6.2° (*c* 5.5, chloroform), 61.4% atom excess deuterium (mass spectrometry). Crops 9 and 10 were combined and sublimed, mp 76.3–77.7°, $[\alpha]^{25}_{546}$ 0.0° (*c* 3.3, chloroform), 30.6% atom excess deuterium.

Limits of Error. The limits of error given in Table II were obtained by recalculation of the rate constants k_1, k_2, and k_3 using reasonable error values for deuterium content (±0.5%), time (1% of total), rotation (0.2% of observed), and k_4 (standard deviation of $k_\alpha/2$).

Deuterium Analyses. Deuterium analyses of II were performed by mass spectrometry as previously described.[11] Analyses of I were similar except that 20 eV and the direct heated inlet system were used.

Electrophilic Substitution at Saturated Carbon. XLVI. Crown Ethers' Ability to Alter Role of Metal Cations in Control of Stereochemical Fate of Carbanions[1]

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Abstract: The effect of dicyclohexyl-18-crown-6 cyclic polyether (V) on rates and the stereochemical course of potassium alkoxide catalyzed carbanion-generating reactions in alcoholic solvents have been studied. When treated at 70° with 0.17 *M* potassium *tert*-butoxide in *tert*-butyl alcohol, 0.17 *M* in crown ether, (−)-4-biphenylylphenylmethoxydeuteriomethane ((−)-I-*d*) underwent deuterium–hydrogen exchange (k_e) and racemization (k_α) at essentially the same rates ($k_e/k_\alpha \sim 1$). In the absence of crown ether, $k_e/k_\alpha = 46$. The presence of crown ether increased dramatically the rates of both isotopic exchange and racemization, the former by a factor estimated to be between 30 and 1000, and the latter between 500 and 17,000. When treated at 101° with a solution of 0.13 *M* potassium *tert*-butoxide in *tert*-butyl alcohol, 0.13 *M* in crown ether V, (+)-4-phenyl-3,4-dimethyl-3-hexanol ((+)-II) cleaved to 2-phenylbutane ((+)-III) with 15% net *inversion* of configuration. In the absence of crown ether, the reaction occurred with 89–93% net *retention* of configuration. These results are interpreted in terms of the ability of crown ether to occupy the coordination sites of potassium ion, and forbid these sites to the leaving and entering groups on the front face of the carbanion intermediates in these electrophilic substitution reactions. Clearly the retention mechanism is dependent on the metal ions' organizing capacity. The rate constants for isotopic exchange and racemization of (+)-2-methyl-2,3-dihydro-2-deuteriobenzo[*b*]thiophene 1,1-dioxide ((+)-IV) in 0.148 *M* potassium methoxide–methanol that was 0.148 *M* in crown ether were found to be close to those obtained in the absence of crown ether. The k_e/k_α value of 0.66 was the same as that obtained without crown ether. In this more polar medium, the metal cation or the crown ether appears to play no role in determining the stereochemical course of exchange.

Earlier studies established that potassium *tert*-butoxide catalyzed hydrogen–deuterium exchange of carbon acid I[3a] and cleavage of tertiary alcohol II[3b,c] to 2-phenylbutane III in the same medium proceeded with high retention of configuration. Explanation of these results involved formation of potassium carbanide ion pairs in which the leaving and entering electrophile occupied coordination sites on the potassium ion, which played an organizing role on the front face of the carbanion.[3a,4] The preceding paper[5] reported that carbon acid III underwent isotopic exchange catalyzed by potassium methoxide in methanol in which racemization, inversion-with-exchange, and isoinversion components were blended. The explanation did not assign any role to the potassium ion in any of the mechanistic components.

Pedersen[6] reported that dicyclohexyl-18-crown-6 cyclic polyether V and many other cyclic ethers exhibited the ability to complex potassium ion in a variety of solvents that ranged from hexane to methanol. Smid and coworkers[7] have demonstrated that crown ethers and glyme ethers in ethereal solvents complex the metal ion

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[3] (a) W. D. Kollmeyer and D. J. Cram, *J. Amer. Chem. Soc.*, **90**, 1779 (1968); (b) D. J. Cram, A. Langemann, and F. Hauck, *ibid.*, **81**, 5750 (1959); (c) D. J. Cram, F. Hauck, K. R. Kopecky, and W. D. Nielsen, *ibid.*, **81**, 5767 (1959).

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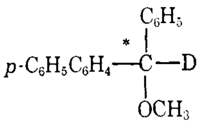
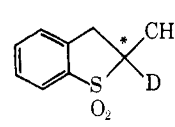


(−)-I-*d*



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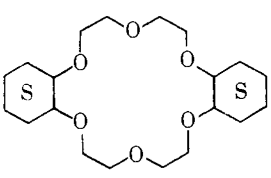

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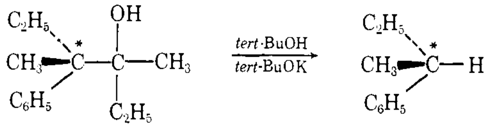

(+)-II (−)-III

of fluorenyl alkali metal salts to give spectra similar to that of solvent-separated ion pairs. These facts suggested that the presence of crown ethers in the reaction media in the reactions of I, II, and IV would have a good chance of complexing the potassium ion of the potassium alkoxide catalyst. If this should happen, the ion pair postulated as necessary to the observed stereochemical course of reactions of systems I and II should be seriously altered, but that of IV should remain unchanged. In addition, complexation of the metal alkoxides if they are ion paired might seriously affect their activity, and the reaction rates would be altered. These expectations were realized.

Results

Isotopic Exchange and Racemization of (−)-4-Biphenylylphenylmethoxydeuteriomethane ((−)-I-*d*). In run 1, (−)-I-*d*[3a] (98% of one atom of D) essentially optically pure as a 0.05 *M* solution in *tert*-butyl alcohol, 0.14 *M* in potassium *tert*-butoxide, and 0.14 *M* in crown ether[8] V was heated to 116° for 0.17 hr, cooled, and found to be totally racemic. In run 2, a 0.05 *M* solution of (−)-I-*d* in *tert*-butyl alcohol, 0.17 *M* in potassium *tert*-butoxide, and 0.17 *M* in crown ether V was heated at 70° for 6.9 hr, isolated, and found to have undergone 67% racemization and 64% isotopic exchange (mass spectrometry). Calculation of pseudo-first-order rate constants for k_e and k_α gave $k_e/k_\alpha \sim 0.9$. At 116°, $k_e/k_\alpha = 46$ for (−)-I-*h* in *tert*-butyl alcohol-*O-d*,[3a] and both rates were much slower. If one assumes an activation energy of 20–40 kcal mol^{-1} for racemization and exchange,[9] and makes corrections for differences in isotope,[3a] the effect of crown ether on the rates of exchange and racemization can be estimated at 70°. Thus crown ether enhances the rate of exchange by a factor between 30 and 1000 and of racemization by a factor between 500 and 17,000.

Cleavage of (+)-4-Phenyl-3,4-dimethyl-3-hexanol ((+)-II). A sample of (+)-II configurationally homogeneous at the benzyl carbon (mixture of diastereomers of maximum rotation) was available from previous studies,[10a] and the relative configurations and maximum rotations of the starting materials ((+)-II) and 2-phenylbutane (III) had been determined.[10b] Either set of diastereomers of II with the same configuration at benzyl carbon exhibited the same sign of rotation at the sodium D line, and the material used here was that produced by addition of ethyllithium to optically pure (+)-3-methyl-3-phenyl-2-butanone.[10a] This material was the same as that used in previous studies[3c] where it was demonstrated that the stereochemical outcome was independent of the configuration of the leaving group.[3c] In run 3, (+)-II was heated at 101° for 4.5 days in a solution of *tert*-butyl alcohol, 0.131 *M* in potassium *tert*-butoxide and 0.131 *M* in crown ether V. The 2-phenylbutane produced (86%) was of 15% optical purity, the product of electrophilic substitution with net inversion of configuration at benzyl carbon. A control experiment demonstrated the 2-phenylbutane produced was optically stable under the conditions of the experiment. Runs made previously on II in *tert*-butyl alcohol–potassium *tert*-butoxide gave product with 89% net retention (83°), 93% net retention (150°), and in *tert*-butyl alcohol–lithium *tert*-butoxide, 98% net retention (150°).[3a]

Isotopic Exchange and Racemization of (+)-2-Deuterio-2-methyl-2,3-dihydrobenzo[*b*]thiophene 1,1-Dioxide ((+)-IV-*d*). The rates of isotopic exchange and of racemization of (+)-IV-*d* were followed as before[5] in methanol, 0.148 *M* in potassium methoxide and 0.148 *M* in crown ether V at 75.00 ± 0.05° (run 4). The second-order rate constants were calculated from six points in each case, gathered over 64% of the reaction for exchange and 75% of the reaction for racemization. The constants are of a least-squares variety with a one standard deviation probable error. For exchange, $k_e = 5.90 \pm 0.11 \times 10^{-5}$ l. mol^{-1} sec^{-1}, and $k_\alpha = 8.75 \pm 0.02 \times 10^{-5}$ l. mol^{-1} sec^{-1}, and $k_e/k_\alpha = 0.66$. A racemization run made previously[5] under the same conditions except potassium methoxide was 0.172 *M* and crown ether V was absent, gave $k_\alpha = 12.0 \pm 0.08 \times 10^{-5}$ l. mol^{-1} sec^{-1}. Values for k_e/k_α in methanol–potassium methoxide at 75° ranged from 0.63 to 0.66.[5]

Discussion

In *tert*-butyl alcohol–potassium *tert*-butoxide, the effect of the presence of crown ether V on the isotopic exchange and racemization reactions of diarylmethoxymethane, carbon acid I, was twofold. Both rates increased by several powers of 10. However, that of racemization increased over that of exchange by a factor of about 50, enough to drop the k_e/k_α value from 46 to about 0.9. These results point to two conclusions. (1) At least some potassium *tert*-butoxide was complexed by crown ether, and the complexed material possessed much greater kinetic basicity than the noncomplexed potassium *tert*-butoxide. As a result, all of the reaction was caused by complexed metal alkoxide. (2) The complexed alkoxide base was incapable of

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[8] The authors warmly thank Dr. E. K. Gladding of the Elastomers Department of E. I. du Pont for a supply of this material.

[9] The nearest model for which data are available is the isotopic exchange of diphenylmethane in methanol-*O-d*–dimethyl-d_6 sulfoxide containing potassium methoxide, which gave $\Delta H^{\ddagger}$ of 34–38 kcal mol^{-1} [see D. J. Cram and W. D. Kollmeyer, *J. Amer. Chem. Soc.*, **90**, 1791 (1968)].

[10] (a) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5853 (1952); (b) D. J. Cram, K. R. Kopecky, F. Hauck, and A. Langemann, *ibid.*, **81**, 5754 (1959).

providing the high retention stereochemical pathway for isotopic exchange characteristic of the uncomplexed base. Since crown ether complexes the potassium ion,[6] that ion complexed with *tert*-butyl alcohol appears to be a necessary condition for the retention mechanism.

This result supports the mechanistic suggestion made earlier[4b] that retention occurs as follows. (1) Metal-alkoxide contact ion pair complexed through coordination with alcohol abstracts deuterium from the carbon acid to form a metal carbanide contact ion pair. (2) The metal cation with its ligands of alcohol rotates while remaining on the front face of the near-planar carbanion. During rotation, ROD and ROH exchange places of proximity to the negative charge of the carbanion. (3) After rotation, the contact ion pair collapses by proton transfer to the carbanion to regenerate the carbon acid of the same configuration, but of the opposite isotopic type. The latter two reactions compete successfully with carbanion rotation, or ion pair dissociation. In the presence of crown ether, the coordination sites of the potassium being occupied are denied to the *tert*-butyl alcohol, and the potassium ion loses its organizing ability at the front face of the carbanion.

A similar effect of crown ether on the stereochemical course of the cleavage of *tert*-alcohol II to 2-phenylbutane (III) was observed in *tert*-butyl alcohol–potassium *tert*-butoxide. In the absence of crown ether, the cleavage went with about 90% net retention; in the presence with 15% net inversion. This result supports the mechanism developed earlier,[3b,c,4] which envisioned the cleaving species as potassium alkoxides coordinated with at least one molecule of alcohol solvent. In the contact ion pair formed, the potassium ion with ketone and alcohol ligands rotated on the front face of the near planar carbanion. Finally the advantageously positioned alcohol molecule donated its proton to the carbanion to give product. All of these steps were envisioned as happening within a contact ion pair.

In the presence of crown ether, the species that cleaves might be the crown ether-separated ion pair, in which the coordination sites of potassium are occupied neither by the alkoxide nor solvent molecules. This species resembles in properties the more ordinary solvent-separated ion pair.[7a] Cleavage occurs to form an ether-separated potassium carbanide ion pair, the front face of which is more shielded by the cation than the back. Competitive with *carbanion rotation* within this ion pair, proton capture from bulk solvent occurs on the face remote from the leaving group of the starting material. Small net inversion is the result. Net inversion ranging from 25 to 50% was observed when the cleavage was conducted in either methanol or ethylene glycol–potassium alkoxide.[3c] The inversion was attributed in these media to cleavage of solvent-separated ion pairs or dissociated ions. Again shielding by the leaving carbonyl group at the front face allowed capture of a proton from bulk solvent at the remote face of the carbanion intermediate.[3c] The lower inversion observed by cleavage of II as a crown ether-separated ion pair in *tert*-butyl alcohol as compared to cleavage of II as solvent-separated ion pairs in methanol or ethylene glycol is attributed to a combination of solvent acidity and proton donor concentration effects. On both counts, *tert*-butyl alcohol's proton should be captured more slowly, and competing stereochemically nondiscriminating reactions should be more important as a result in this solvent. These new results lend considerable support to the mechanisms set forth previously.[4b] A similar mechanistic picture based on complete ion pair dissociation caused by crown ether in *tert*-butyl alcohol equally well explains the results.

Unlike the results observed with systems I and II obtained in *tert*-butyl alcohol, the reactions of cyclic sulfone IV in methanol were very little affected by the presence of crown ether. The stereochemical course of the potassium methoxide-catalyzed isotopic exchange was unaltered by addition of the crown ether ($k_e/k_\alpha = 0.66$), and the rate of racemization was only depressed by an amount consistent with a small medium effect. This result is compatible with the mechanism developed elsewhere[5] for isotopic exchange of IV in methanol in which methoxide anion (either dissociated or as solvent-separated ion pairs) was the active catalytic species. Potassium ion was assigned no role in the observed net inversion and isoinversion components present.[5] Although crown ether was probably at least partially complexed with the potassium ion in methanol,[6a] the activity of the methoxide anion was little affected.

The results of this study suggest that both the rate and stereochemical course of many metal-alkoxide catalyzed reactions carried out in nonpolar solvents might be drastically modified by addition of catalytic amounts of crown ethers to the medium.

Experimental Section

General. Solvents used were all carefully purified as before[3a,5] and stored in sealed flasks over molecular seives. Nitrogen was purified by passing it through hot (>300°) copper wool, followed by a train containing Ascarite, potassium hydroxide pellets, and Drierite. Melting points were corrected. Mass spectrometric data were obtained on an AEI MS-9 spectrometer. Analyses of I for deuterium were obtained by direct insertion because of low volatility.

Ionizing voltages were employed which produced less than 0.5% of $M^+ - 1$ for pure proteo substrates. Peak height ratios were measured with a Leeds and Northrup recorder connected to a potentiometric attenuator which allowed display of both peaks in question to approximately full scale. Since the instrument has a single collector, peaks were scanned sequentially and always in groups of three (*i.e.*, small, large, small) in order that the peak heights of the outside peaks could be averaged. Sample size continually increased or decreased during measurements necessitating the bracketing procedure described. The average of at least four scans was used to compute the per cent deuterium. Equation 1 was used, in which k_2 is the ratio of peak height for the molecular ion of monodeuterated substrate over that for the molecular ion of proteo substrate, and k_1 is the ratio of $(M^+ + 1)/M^+$ for pure proteo substrate (determined by a separate measurement). This equation is valid only for molecules containing from 0 to 1 atom of deuterium. All analyses were accurate to better than 0.5% of 1 atom of D.

$$\%\,\mathrm{D} = (100)\frac{k_2 - k_1}{1 + k_2 - k_1} \qquad (1)$$

Polarimetric measurements were obtained in jacketed 1 dm cells at 25.0° with a Perkin-Elmer 141 digital readout polarimeter, and are accurate to ±0.002° observed or ±2%, whichever is larger.

Glassware used for all runs (kinetic and otherwise) was washed with warm chromic acid, rinsed well, washed with dilute ammonia, rinsed at least five times with distilled water, and oven dried at 120°. All kinetic runs were carried out in heavy-walled ampoules which were degassed and sealed *in vacuo*. Ampoules were prepared for a kinetic run by addition of a measured amount of stock base–solvent solution to a weighed sample of substrate in a small flask in a drybox. Then *ca.* 1.2-ml aliquots were transferred to the ampoules. Ampoules were withdrawn at various time intervals and quenched in ice–water. All rates were measured at elevated temperatures, and rates at room temperatures were negligible. Polarimetric rates were obtained by direct examination of the samples from the ampoules.

Base concentrations were determined by titration with aqueous standardized hydrochloric acid to the phenolphthalein end point. Thermostated oil baths which varied less than ±0.1° were used for the kinetics.

Starting Materials. Compounds I–IV were all available from previous studies, or were prepared as described previously. Essentially, optically pure (−)-4-biphenylylphenylmethoxydeuteriomethane ((−)-I-*d*) was prepared as before,[3a] mp 102.4–103.3°, $[\alpha]^{25}{}_{546}$ $-6.2°$ (*c* 4.2, chloroform), 0.98 atom excess deuterium. A mixture of optically pure diasteromers of (+)-4-phenyl-3,4-dimethyl-3-hexanol ((+)-II) configurationally homogeneous at the benzyl carbon was available from other studies,[10a] $n^{25}\mathrm{D}$ 1.5203, $\alpha^{25}\mathrm{D}$ +7.28° (*l*, 1 dm, neat). A sample of partially optically active (+)-2-phenylbutane ((+)-II) was available from other work,[3c,d] $n^{25}\mathrm{D}$ 1.4882, $\alpha^{25}\mathrm{D}$ 1.62° (*l*, 0.5 dm, neat). A sample of optically pure (+)-2-deuterio-2-methyl-2,3-dihydrobenzo[*b*]thiophene 1,1-dioxide ((+)-IV-*d*) was also available,[5] mp 73–74°, $[\alpha]^{25}{}_{546}$ +24.2° (*c* 4.16, chloroform), 0.99 atom excess deuterium. Crown ether V (2,5,8,15,18,21-hexaoxatricyclo[20.4.0.0^{9,14}]hexacosane) was kindly given to us.[8]

Runs 1, 2, and 4. Base solutions were prepared from freshly cut potassium metal and the appropriate alcohol, which had been degassed with pure nitrogen. Concentration of base was determined by titration with standardized aqueous hydrochloric acid to the phenolphthalein end point. Pipeted quantities of base solutions were added to accurately weighed amounts of crown ether V to ensure equimolar concentration. Base concentration was then redetermined by titration to avoid any error caused by dilution by crown ether.

Kinetic run 4 was determined by the sealed ampoule technique employing six ampoules. After direct polarimetric examination of the kinetic solutions at the end of each time period, the samples were shaken with aqueous hydrochloric acid and dichloromethane. The extracts were dried, chromatographed on silica gel to remove crown ether, and totally sublimed. Each sublimate was examined for deuterium content by mass spectrometry. Runs 1 and 2 were conducted similarly.

Run 3. To a heavy-walled ampoule containing 1.71 g of cyclic ether V and 0.750 g of (+)-II was added 35 ml of a solution of 0.131 *M* potassium *tert*-butoxide in *tert*-butyl alcohol. The ampoule was degassed three times, sealed *in vacuo*, and heated at 101° for 108 hr. The contents were shaken with pentane and water; the pentane layer was washed with water, dried, and evaporated through a 2-ft Vigreux column to yield an oil. This material was chromatographed on 100 g of alumina (activity I) and eluted with pentane. The pentane was evaporated through the same column, and the residue was distilled to give 0.413 g (85%) of 2-phenylbutane. This material was redistilled to give 0.373 g of III, $\alpha^{25}\mathrm{D}$ 1.81° (*l*, 0.5 dm, neat). Optically pure material has $\alpha^{25}\mathrm{D}$ ±24.2 (*l*, 1 dm, neat).[3b,c]

Control Experiment for Run 3. An ampoule was prepared as in run 3 except that it contained 0.198 g of crown ether V, 0.357 g of (+)-III, and 5.00 ml of 0.106 *M* potassium *tert*-butoxide in *tert*-butyl alcohol. The sealed ampoule was heated for 49 hr at 100°, and the 2-phenylbutane isolated as in run 3 to give 0.230 g. Before this treatment, (+)-III gave $n^{25}\mathrm{D}$ 1.4882, $\alpha^{25}\mathrm{D}$ 1.62° (*l*, 0.5 dm, neat). After the treatment it gave $n^{25}\mathrm{D}$ 1.4876, $\alpha^{25}\mathrm{D}$ 1.61° (*l*, 0.5 dm, neat).