Electrophilic Substitution at Saturated Carbon. XLIV. Stereochemical and Isotopic Drowning Phenomena[1]

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Abstract: Optically pure (−)-3-*t*-butyl-1-methylindene-1-*h* ((−)-I-*h*), or its counterpart deuterated in the 1 position ((−)-I-*d*), was subjected to simultaneous base-catalyzed racemization, isotopic exchange, and isomerization to 1-*t*-butyl-3-methylindene (II) in various media. In all of the runs made for product analysis, after 5–45% isomerization, the reaction was interrupted, and I and II were separated by glpc and examined for optical purity and deuterium. In CH_3OD–CH_3OK (0.10 *M*) at 25°, (−)-I-*h* gave *completely racemic II which was only 87% deuterated*, and the reaction, although *nonstereospecific*, *was 13% intramolecular*. In CH_3OH–CH_3OK (0.10 *M*) at 24°, *(—)-I-d gave completely racemic II which possessed <0.5% deuterium and the reaction was <0.5% intramolecular*. Thus, drowning of CH_3OD generated in a pool of CH_3OH appears to occur at least an order of magnitude faster than drowning of CH_3OH generated in a pool of CH_3OD. At 25° with potassium methoxide as catalyst, the rate of loss of optical activity (rate constant, k_α) from a reacting solution of (−)-I-*h* in CH_3OD–CH_3OK at 25° was strictly first order over four half-lives. Over the first 20% of reaction the rate constant for isotopic exchange of I (k_e) was first order. Over the first 13% of isomerization the rate constant (k_i) was first order. Within error $k_e/k_\alpha \sim 1$. Analysis of the kinetic data established that the rate constants for isotopic exchange of (−)-I-*h* in methanol-O-*d* with retention and inversion were strictly equal to one another. Addition of 18-crown 6-ether (III, 0.20 *M*) to the CH_3OD–CH_3OK (0.10 *M*) medium had only minor effects on the three reactions of (−)-I-*h*. In 25% phenol–75% benzene by volume potassium phenoxide (0.058 *M*) at 100°, $k_e/k_\alpha = 8$ for (−)-I-*h* in the absence and $k_e/k_\alpha = 2$ in the presence of 18-crown 6-ether (0.1 *M*). The isomerization rate was depressed by almost a power of ten by the crown ether, III. In the absence of III, the 11% of (+)-II produced was 10% racemic and 87% isotopically exchanged, whereas in the presence of III, the 6% of (+)-II produced was 75% racemic and 77% isotopically exchanged. At 37° in tetrahydrofuran (0.19 *M* in n-$C_3H_7ND_2$), (−)-I-*h* after 46% isomerization gave $k_e/k_\alpha > 30$ for I, and 0% racemization and 17% isotopic exchange for II. Under the same conditions in the presence of 1.5 *M* crown ether (III) after 38% isomerization, k_e/k_α for (−)-I-*h* fell to 0.6 without much effect on the rate of isomerization. The II produced was 21% racemized and 10% isotopically exchanged. The mechanisms of these proton transfer reactions are discussed in terms of contact and separated ion pairs and dissociated ions. The stereochemical and isotopic drowning phenomena are interpreted in terms of both hydrogen-bonded carbanions and solvent cages structured by hydrogen bonds.

Previous studies in optically active and isotopically labeled indene systems demonstrated the existence of a stereospecific amine-catalyzed 1,3-hydrogen migration[3,4] into which could be designed varying amounts of isotopic exchange through the use of primary or secondary amines.[3b] The stereospecific isomerizations were limited to amines as catalysts.[4] The use of triethylenediamine in either *t*-butyl alcohol or dimethyl sulfoxide gave highly stereospecific transformations.[3b] Use of metal alkoxides in hydroxylic solvents is reported to provide rearrangement without stereospecificity.[4h]

The present study was undertaken for the following reasons. (1) Earlier work in alkoxide-catalyzed cleavage reactions of alcohols[5a] and phenoxide-catalyzed hydrogen–deuterium isotopic exchange reactions of carbon acids[5b] demonstrated that stereospecificity for the reaction depended on the ligand-organizing presence of a metal cation at the reaction site. Thus, metal (not quaternary ammonium) alkoxides or phenoxides were required for stereospecificity, as was solvent of low-ionizing power that kept the ions of the base and intermediates paired. On the other hand, the control of *intramolecularity* in 1,3- and 1,5-proton shifts catalyzed by the same bases[5c,d] seemed much less sensitive to the medium and presence or absence of metal cations than did the stereospecificity of substitution reactions. The base-catalyzed isomerization of 3-*t*-butyl-1-methylindene (I) to 1-*t*-butyl-3-methylindene (II) provides a system that allows intramolecularity and stereospecificity to be studied simultaneously as medium and cation character and positioning are varied. (2) The important discovery that 18-crown-6-cyclic polyether or 2,5,8,15,18,21-hexaoxatricyclo$[20.4.0.0^{9,14}]$hexacosane (III) possessed the ability to occupy successfully the coordination sites of potassium and even alkylammonium ions[6] suggested that this cyclic ether might be useful for purposes of mechanism differentiation. (3) In the interpretation of racemization and exchange data of carefully designed carbon acid systems, mechanisms can be envisioned as proceeding *via* highly structured but short-lived intermediates, or by random

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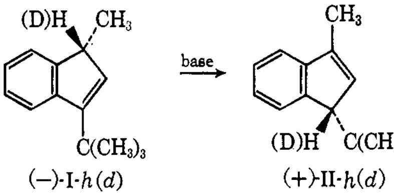
Table I. Isotopic Exchange, Racemization, and Isomerization of 0.1 M Solutions of 3-t-Butyl-1-methylindene (I) to 1-t-Butyl-3-methylindene (II)

				Base					I				II			
Run no.	Starting material	Solvent	Added III (M)	Nature	M	Temp, °C	Time, hr	$k \times 10^5$,[a] l./mol sec^{-1}	% obt	% exch[b]	% racemization[b]	$\frac{k_e{}^c}{k_\alpha{}^{\text{apparent}}}$	% yield	% exch[b]	% racemization[b]	Collapse ratio[d]
1	(−)-I-h	CH_3OD		CH_3OK	0.1	25	7.7	10.2	76.0[e]	64.1	67.3	0.92	24.0[e]	86.9[f]	>99.9[g]	2.3
2	(−)-I-d	CH_3OH		CH_3OK	0.1	25	46.2	1.8	75.1	23.2	21.0	1.12	24.9	99.7	>99.9[g]	0.7
3	(−)-I-h	CH_3OD	0.2	CH_3OK	0.1	25	3.2	15.5	88.7	47.8	44.0	1.1	11.3	83.6		4.5
4	(−)-I-d	C_6H_6–C_6H_5OH[h]		C_6H_5OK	0.057	100	29.5	1.9	88.8	15.5	2.1	7.9	11.2	87.4	9.9	1.7
5	(−)-I-d	C_6H_6–C_6H_5OH[h]	0.1	C_6H_5OK	0.058	100	120	0.22	94.5	13.1	6.0	2.3	5.5	76.5	75[g]	2.9
6	(−)-I-h	C_4H_8O		n-$C_3H_7ND_2$	0.19	37.5	40.5	2.3	54.5	28.1	0	>30	45.5	16.9	0	2.0
7	(−)-I-h[i]	C_4H_8O	1.5	n-$C_3H_7ND_2$	0.19	37.5	38	1.8	62.4	15.5	24.0	0.62	37.6	10.0	20.6	2.6

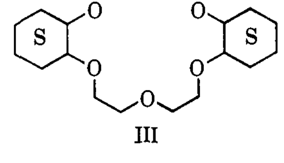
[a] One-point second-order rate constants for isomerization. [b] ±0.5%. [c] Derived from one-point rate constants. [d] Defined as (% exchange of I) (% obtained of I)/(% exchange of II) (% obtained of II); see text for the assumptions involved. If account is taken of the return of II to I and the isotope effects of exchanged I and II, these values tend to increase, particularly that of run 2, and range from 1.4 to 4 (see D. Hunter and D. J. Cram (*J. Amer. Chem. Soc.*, **86**, 5478 (1964)) for method). [e] In a parallel run to 45% isomerization, with an internal standard (tetradecane) added, 99–100% of I + II was accounted for. [f] In a duplicate run to 2% isomerization, II was 87% exchanged. [g] Determined by comparison of ORD spectrum with that for optically pure II. [h] 25% phenol, 75% benzene by volume. [i] Substrate was 0.2 M in this run.

processes in which statistical or solvent structure factors can be used to interpret the data. Thus, it seemed desirable to try to establish the threshold of stereospecificity and of intramolecularity that might arise from either statistical or solvent-structure effects. Some hints that statistical or solvent-structure effects might play minor roles in stereospecificity and intramolecularity were found in the discovery of a small isoinversion component when optically active 2-N,N-dimethylamido-9-methylfluorene was subjected to potassium methoxide catalyzed hydrogen–deuterium exchange in methanol-O-d.[7]

The reaction I → II offers special advantages for such a study. Both isomers have been prepared in an optically pure state and their configurations determined.[3] Also available was I optically pure and deuterated in the 1 position.[3] The equilibrium constant for I ⇄ II has been determined at several temperatures, and favors II at 25° by a factor of 7.5.[3] At low conversions, I → II can be studied with little interference from the reverse or any side reactions. After reaction, I and II can be separated cleanly by glpc, and each isomer examined for optical purity and deuterium.[3] Compound I is sufficiently acidic to allow the reactions of racemization, isotopic exchange, and isomerization to be studied in a variety of media with a variety of catalysts at reasonable temperatures. These reactions have been examined with amine bases, and have been demonstrated to go through highly structured ion pairs in nonpolar media.[3]



(−)-I-h(d) (+)-II-h(d)



III

Results

Products of Base-Catalyzed Isotopic Exchange, Racemization, and Isomerization of Optically Pure 3-*t*-Butyl-1-methylindene [(−)-I-*h*]. Table I reports the results of runs 1–7 in which optically pure samples of (−)-I-h or (−)-I-d were 5–45% isomerized, I and II separated by glpc,[3b] and analyzed for optical purity and deuterium (mass spectra).[3b] Under the conditions of conversion only minor amounts of II, once formed, reverted to I. In all runs the isotopic reservoir of the medium was affected little by the extent of isotopic exchange that occurred. Controls demonstrated that all of the starting material could be accounted for by the isolated products.[3b] Runs 1–3 involved a methanol–potassium methoxide medium of the opposite isotopic variety as the substrate. Runs 4 and 5 involved (−)-I-d in 25% phenol–75% benzene (by volume) with potassium phenoxide as base. Runs 6 and 7 were conducted in tetrahydrofuran with (−)-I-h and n-propylamine-N-d_2 as base and isotopic pool. Runs 1, 2, 4, and 6 conducted in the absence of crown ether III served as a basis of comparison for runs 3, 5, and 7 conducted in the presence of this material.

One-point second-order rate constants for the forward rate, k_i of isomerization, I → II, were calculated from equilibrium data previously obtained[3b] and the rate expressions for first-order approach to equilibrium.[8] The low rates of isomerization for runs 4 and 5 at 100° were comparable to the rates of thermal isomerization at 140°.[9] If one makes the reasonable assumption that $\Delta H^{\ddagger}$ for the thermal isomerization is about 30 kcal/mol, then at 100° the base-catalyzed rate exceeds the thermal rate by about two powers of ten. It is highly probable that no more than a few per cent at the most of II could have arisen in runs 4 and 5 by the thermal route.

Although the one-point rate constants for isomerization are not highly accurate, they provide semiquantitative measures of the effect of crown ether III on the reaction rates, and of the magnitude of the combined substrate–solvent isotope effects. Comparisons of the rate constants for runs 1 and 3 in methanol-O-d–potas-

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Table II. Kinetic Data for Racemization, Exchange, and Isomerization of 0.1 *M* (−)-I-*h* in Methanol-O-*d*, 0.0712 *M* Potassium Methoxide at 25.0 ± 0.1° (Run 8)

			I		II		
Aliquot	Time, min	Obsd rotation[a]	% obtained	% exchanged[b]	% obtained	% exchanged	Collapse ratio[c]
0	0	−4.684	100	0	0		
1	10	−4.640	98.3		1.7	87[d]	
2	22	−4.514	97.5		2.5		
3	35	−4.375	97.1		2.9		
4	61	−4.144	95.3		4.7		
5	90	−3.898	94.3	13.5	5.7		2.5
6	130	−3.564	92.3	18.5	7.7		2.5
7	180	−3.196	89.5	25.0	10.5		2.4
8	243	−2.785	87.0	32.8	13.0	88[e]	2.5
9	330	−2.298	84.5	42.0	15.5		2.6
10	423	−1.886	80.6	50.5	19.4		2.3
11	540	−1.460	77.7	59.2	22.3		2.3

[a] Reading at 435 mμ for total reaction mixture. In a separate experiment the observed rotation followed first-order decay through four half-lives. [b] At low deuterium incorporation the experimental error was close to the measured values for aliquots 1–4, so k_e was calculated from points 5–11. [c] Based on assumptions outlined in the Discussion and the assumption that the per cent exchange of II for aliquots 2–7 was the same as that for aliquot 1, and for aliquots 9–11 were the same as that for aliquot 8. [d] Based on a separate experiment; see footnote *f*, Table I. [e] Based on run 3, Table I.

sium methoxide, and for runs 6 and 7 in tetrahydrofuran–*n*-propylamine-N-d_2 indicate that, in these media, crown ether had only a minor effect on the rates of isomerization. In benzene–phenol–potassium phenoxide the presence of crown ether retarded the rate of isomerization by about an order of magnitude.

From the amounts of isotopic exchange and racemization of I recovered from each run, one-point rate constants for exchange (k_e) and racemization (k_α) were calculated, and the values of k_e/k_α are recorded in Table I. In methanol–potassium methoxide (runs 1–3) these values are indistinguishable from unity, both in the presence and absence of crown ether. Thus, the exchange reaction of I occurred with near racemization in these media. In benzene–phenol–potassium phenoxide, $k_e/k_\alpha \sim 8$, and isotopic exchange occurred with dominant retention of configuration. When crown ether was present (0.10 *M*), $k_e/k_\alpha \sim 2.3$. Thus, although crown ether decreased both rates, the isotopic exchange rate was decreased by a factor three times as large as that for racemization. A considerable degree of the stereospecificity of the isotopic exchange reaction was destroyed by the presence of the cyclic ether. In tetrahydrofuran–*n*-propylamine-N-d_2, $k_e/k_\alpha > 30$, and the isotopic exchange reaction occurred with high retention of configuration. However, in the presence of 1.5 *M* crown ether, k_e/k_α decreased dramatically to 0.62, which points to a small isoinversion component.

From the amounts of isotopic exchange and racemization of II recovered from each run, the effects of medium on intramolecularity and stereospecificity were determined. In methanol or methanol-O-*d*, II was more than 99.9% racemic, and the system lost its asymmetric history (runs 1 and 2). However, (−)-I-*h* in methanol-O-*d* gave II with 13% intramolecularity (run 1) in the absence of crown ether and 16% in its presence (run 3), whereas (−)-I-*d* in methanol gave only 0.3% intramolecularity. Thus, a small intramolecular component persists in the absence of any stereospecificity when hydrogen shifts in deuterated medium; but when deuterium shifts in nondeuterated medium, the amount of intramolecularity decreases by at least an order of magnitude. In run 4 with (−)-I-*d* in benzene–phenol–potassium phenoxide, isolated II was 90% optically pure, the product of a suprafacial 1,3-hydrogen shift. The presence of crown ether (0.1 *M*) in run 5 cut the optical purity of II to 25%, just as it reduced the value of k_e/k_α for I in the same run. The amount of intramolecularity in the two runs was 16 and 13%, respectively. In tetrahydrofuran–*n*-propylamine-N-d_2, II was optically pure (suprafacial 1,3-hydrogen shift) in run 6, but was 21% racemic in the presence of 1.5 *M* crown ether (run 7). Both runs exhibited high intramolecularity, 83% in 6 and 90% in 7.

Collapse ratios were calculated for all of the runs based on eq 1. These collapse ratios give a qualitative

$$\text{collapse ratio} = \frac{(\%\text{ exchange of I})(\%\text{ I recovered})}{(\%\text{ exchange of II})(\%\text{ II obtained})} \quad (1)$$

impression of the preferred direction of collapse of the allylic anion intermediates in these reactions. They have very limited value since they depend on the unconfirmed assumptions that: (1) the collapse ratio is independent of which isotope is captured; (2) proton or deuteron capture at the 1 and 3 positions are the slowest steps once ions are formed; (3) II, once formed, goes back to I to only a negligible extent; (4) exchanged I undergoes negligible further reaction.

The collapse ratios appear to favor I over II by small factors, the only exception being run 2 with (−)-I-*d* in CH_3OH (see footnote *d* of Table I).

Kinetics of Isotopic Exchange, Racemization, and Isomerization of (−)-I-*h* in Methanol-O-*d*. Table II records the data from run 8, in which (−)-I-*h* was ultimately 22% isomerized in a 0.0712 *M* solution of potassium methoxide in methanol-O-*d* at 25 ± 0.1°. Eleven aliquots were withdrawn from the isomerizing mixture, I and II were separated, and submitted to deuterium analysis. During the period of the run a portion of the original reaction mixture was held in a polarimeter tube thermostated by the same bath used for the stock solution of the run, and rotations were read at the times at which aliquots were withdrawn from the bath. The observed rotations and the per cent obtained of each isomer are recorded for each of the eleven points, and the per cent of isotopic exchange of I is recorded for the last seven points. The per cent of exchange of II was measured in three separate runs made under the same conditions (except for time), and was found to be 87–88% isotopically exchanged. In run 1, after 24% isomerization of (−)-I-*h*, the II produced was only 87% exchanged (Table I). In a duplicate run involving only 2% isomerization (footnote *f* of Table I) again II was 87% exchanged. This result demonstrates that even after as much as 24% isomerization, II-*h* once formed exchanges very little with the medium either directly or by recycling through I. The optical activity of II was found to be less than 0.1% in run 1 of Table I. Therefore, the rotations observed in the stock solution of run 8 must have been due entirely to isomer I. The fraction of optically pure I for each point was calculated from the observed and initial rotations, and the mole fraction of I obtained from each aliquot (see eq 2). A pseudo-first-order rate

$$\text{fraction of optically pure I} = (\alpha_{\text{obsd}}/\alpha_{\text{initial}})(1./\text{mol fraction I}_{\text{obtained}}) \qquad (2)$$

constant for the loss of optical activity of the total reaction mixture of run 8 was obtained by a least-squares linear regression for the eleven rotations of Table II. A plot of the data gave a good straight line,[10] and $k_\alpha{}^{\text{apparent}}$ was (3.63 ± 0.01) × 10^{-5} sec^{-1}. This rate constant reflects both the racemization of (−)-I *and* the conversion of (−)-I to racemic II. As demonstrated in the Appendix, k_α (pseudo-first-order rate constant) for racemization of (−)-I (not *via* II) was obtained from a linear least-squares treatment of the fraction of optically pure I remaining at any time (eq 2). For data points 2–11 of Table II, k_α = (2.88 ± 0.05) × 10^{-5} sec^{-1}. The fact that k_α showed good first-order behavior indicates that rate constant k_r for the reverse reaction II → I must be low valued compared to k_α.

The difference between $k_\alpha{}^{\text{apparent}}$ and k_α provides an estimate of the pseudo-first-order rate constant (k_i) for the isomerization of I → II (eq 3). This value is (0.75 ± 0.06) × 10^{-5} sec^{-1}.

$$k_\alpha{}^{\text{apparent}} = k_\alpha + k_i \qquad (3)$$

Table II lists the relative amounts of I and II obtained for each aliquot of run 8. Equation 4 expresses the rate constant ($k_i + k_r$) for approach of I to (I ⇄ II)

$$(k_i + k_r)t = -\ln\left[\frac{\%\,\text{I} - \%\,\text{I}_{\text{equilibrium}}}{100\% - \%\,\text{I}_{\text{equilibrium}}}\right] \qquad (4)$$

equilibrium. A plot of the logarithmic term of eq 4 *vs.* time shows that the first eight data points which cover the first 13% of conversion of I → II provide a good straight line. At equilibrium, I composes only 11.6% of the mixture.[3b] Curvature in the plot occurs for the later points, which undoubtedly reflects kinetic isotope effect for isomerization of I-*d* produced relative to I-*h*.[11] A least-squares treatment for the linear portion of the data gave ($k_i + k_r$) = (1.00 ± 0.04) × 10^{-5} sec^{-1}. From the equilibrium constant for isomerization at 25° ($K_{\text{equilibrium}} = k_i/k_r$ = 7.6 ± 0.1),[3b] k_i was found to be (0.88 ± 0.05) × 10^{-5} sec^{-1} and k_r about (0.12 ± 0.05) × 10^{-5} sec^{-1}. The value for k_i obtained in this manner compares favorably with the value of (0.75 ± 0.06) × 10^{-5} sec^{-1} for k_i obtained from the polarimetric data (see above). The fact that $k_\alpha/k_r \sim 25$ shows why k_α as a pseudo-first-order rate constant for the direct reaction, (−)-I-*h* → (±)-I, was not perturbed by the competing process of

$$(-)\text{-I-}h \xrightarrow{k_i} (\pm)\text{-II} \xrightarrow{k_r} (\pm)\text{-I}$$

The low value of k_r correlates with the fact that the II-*h* once formed in CH_3OD underwent negligible isotopic exchange over the time required for production of 24% total II from I. This result is understandable, since II ionizes slower than I as the following argument indicates. The product of the collapse ratio and equilibrium constant is equal to the ionization rate ratio for I relative to II (the relative kinetic acidity of I to II). The collapse ratio is close to or greater than unity depending upon isotopic composition of the substrate and solvent (Table I). Since the equilibrium constant for I ⇄ II is substantially larger than unity, II ionizes roughly an order of magnitude slower than I although the ratio does vary somewhat with substrate and solvent isotopic composition (see the Discussion).

The pseudo-first-order rate constant for isotopic exchange (k_e) of (−)-I-*h* in CH_3OD–CH_3OK for run 8 was calculated from the data of Table II. A least-squares treatment for points 5–11 gave k_e = (2.81 ± 0.03) × 10^{-5} sec^{-1}. The ratio of rate constants for exchange and racemization is k_e/k_α = (0.98 ± 0.03).

To confirm that the rate processes that contribute to the loss of optical activity of (−)-I-*h* are strictly pseudo-first-order, two additional polarimetric runs were made. In the first (run 9), the change in rotation of a solution of 90% optically pure (−)-I-*h* in a 0.0712 *M* solution of CH_3OK in CH_3OD at 25.0 ± 0.1° was followed with 10 data points through five half-lives, and a pseudo-first-order rate constant of 3.49 ± 0.01 × 10^{-5} sec^{-1} was obtained. No curvature was observed in the logarithmic plot. In a similar run (run 10, 90% optically pure (−)-I-*h* in 0.0590 *N* potassium methoxide in methanol-O-*d* at 24.95 ± 0.1°), the decrease in optical activity was followed over nearly three half-lives. The data were collected in groups of 10 points during four periods, and pseudo-first-order rate constants were calculated for each period and analyzed individually by the least-squares program. A deviation of at most 3.0% for $k_\alpha{}^{\text{apparent}}$ = 25.82 × 10^{-6} sec^{-1} for the four periods was observed and probably was due to small temperature fluctuations. The deviations are random from one period to another, and no trends are visible. Thus, it is safe to conclude that the loss of optical activity of these solutions in runs 8–10 were processes *strictly first order*.

Calculation of second-order rate constants for $k_\alpha{}^{\text{apparent}}$ for runs 8, 9, and 10 gives values of 50.7 × 10^{-5}, 49.0 × 10^{-5}, and 43.8 × 10^{-5} mol^{-1} sec^{-1}, respectively. The differences in temperature between runs 8 and 9 on the one hand and 10 on the other accounts for the small rate constant difference in these runs. The difficulty in completely excluding air (CO_2) to the same extent probably partially accounts for the small difference in rate constants for runs 8 and 9.

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[10] The correlation coefficient for the least-squares straight line was 0.99999.

[11] The data from runs 1 and 2 (Table I) indicate a substantial combined solvent–substrate isotope effect for isomerization. If corrected for an expected solvent isotope effect of about 2.3 (CH_3OD faster than CH_3OH),[3] $(k_H/k_D)_i \sim 2.5$.

Discussion

In the first section the complete lack of stereospecificity and the small amount of intramolecularity observed for I → II in methanol will be discussed. In the second section the effect of crown ether III on the stereospecificity of isotopic exchange of I and on the reaction I → II in benzene–phenol will be covered. The third section is concerned with the dramatic effect of crown ether III on the stereospecificity of isotopic exchange of I and on the reaction I → II in tetrahydrofuran–tripropylamine.

Intramolecularity *vs.* Stereospecificity in 1,3-Hydrogen Shifts in Methanol and Potassium Methoxide. The data of runs 1 and 2 demonstrate that the reaction of I → II was less than 0.1% stereospecific irrespective of the original position of the isotopic label (I or methanol). However, in run 1 with (−)-I-*h* in CH_3OD, 13% intramolecularity was observed, but with (−)-I-*d* in CH_3OH, only about 0.3% intramolecularity was found. Clearly, the drowning of the molecule of CH_3OH generated from (−)-I-*h* and CH_3O^- in the pool of CH_3OD is a far less efficient process than the drowning of the molecule of CH_3OD generated from (−)-I-*d* and CH_3O^- in the pool of CH_3OH. This very large isotope effect on intramolecularity and drowning undoubtedly reflects a complex blend of isotope effects for individual rate constants, analysis of which is beyond the scope of this paper. However, the presence of an intramolecular component for isomerization in run 1 in the absence of stereospecificity requires explanation. To facilitate discussion, the rate constants calculated for the various reactions of (−)-I-*h* in run 8 are summarized in Table III.

Table III. Pseudo-First-Order Rate Constants for Racemization, Isotopic Exchange, and Isomerization of (−)-I-*h* in CH_3OD–CH_3OK[a] at 25.0° (Run 8)

Rate constant	$k \times 10^5$ sec^{-1} [b]
$k_\alpha^{\text{apparent}}$, total polarimetric rate	3.63 ± 0.01
k_α, direct (−)-I-*h* → (±)-I-*h* or *d*	2.88 ± 0.05
k_e, direct (−)-I-*h* → (±)-I-*d*	2.81 ± 0.03
k_i, isomerization, I → II	0.75 ± 0.06[c] 0.88 ± 0.05[d]
k_r, isomerization, II → I	0.12 ± 0.05
$k_i + k_r$, rate of approach of I to equilibrium	1.00 ± 0.04
k_e/k_α	0.98 ± 0.03

[a] 0.0712 *M* potassium methoxide. [b] The error is ± two standard deviations. [c] The difference between $k_\alpha^{\text{apparent}}$ and k_α. [d] Calculated from the rate of approach of I to equilibrium and the equilibrium constant for I ⇄ II.

Two explanations are discussed. In the first of these (referred to as case I), of the 13% of II-*h* produced from (−)-I-*h* in CH_3OD, 6.5% is (−)-II-*h* and 6.5% is (+)-II-*h*, and of the 87% of II-*d* produced, 43.5% is (−)-II-*d* and 43.5% is (+)-II-*d*. Such a product distribution is expected if the solvent cage about the symmetrical indenyl carbanion intermediate became in effect symmetrical with regard to the proximity of CH_3OH and potassium ions to the two faces of the anion. This explanation invokes the reasonable hypothesis that the molecule of CH_3OH generated from one face of (−)-I-*h* becomes incorporated in the solvent enough, in effect, to symmetrize the cage, but not enough to become "drowned" in the solvent. Thus, in effect, local concentrations of CH_3OH in the vicinity of the cage, coupled with an advantageous isotope effect for proton over deuteron capture by the carbanion and a disadvantageous isotope effect for drowning of CH_3OH in CH_3OD, explain the data. The fact that the presence of crown ether III (run 3) has little effect on either the intramolecularity or stereospecificity suggests that potassium ion plays little role in any of these processes.

From the data (Table I) of runs 1 and 2, (k_α, I-*h*, CH_3OD)/(k_α, I-*d*, CH_3OH) ~ 28. If corrected for an expected solvent isotope effect of about 2.3 (CH_3OD faster than CH_3OH),[3] (k_α, I-*h*/k_α, I-*d*)$_{CH_3OD}$ ~ 12. The strictly first-order rate of disappearance of optical activity from (−)-I-*h* in CH_3OD observed in runs 8–10 coupled with this isotope effect indicates that at no time during the runs was any significant amount of *optically active* I-*d* produced.[7] Thus, the rate constants for (−)-I-*h* → (−)-I-*d* and (−)-I-*h* → (+)-I-*d* must be essentially equal. The enantiomers (−)-I-*d* and (+)-I-*d* can arise either directly by isotopic exchange of (−)-I-*h*, or *via* (+)-II-*d* and (−)-II-*d* which revert to I-*d*, particularly in the latter part of the runs. If direct isotopic exchange should proceed with either net retention or net inversion of configuration, strictly first-order kinetics should not be observed. If the concentrations of (+)-II-*d* and (−)-II-*d* produced during the run should not be equal, then unequal amounts of (−)-I-*d* and (+)-I-*d* would be generated, and deviation from first-order kinetics would be observed in the latter part of a run.

The statistics invoked in the explanation of case I require the presence of a small isoinversion component,[7] (−)-I-*h* → (+)-I-*h*, that contributes to the loss of optical activity in runs 8–10. In principle, this component should provide a decrease in k_e/k_α values below unity.[7] In practice, k_e/k_α values in run 8 were unity within probable error. However, the probable error was large enough to embrace the presence of a small amount of an isoinversion component. The process, (−)-I-*h* → (−)-II-*h*, is an *intrafacial* rearrangement that occurs with isoinversion, and contributes only 6.5% to the II produced in the explanation of case I. Thus, the isoinversion contribution to the loss of optical activity of I is also expected to be small, and k_e/k_α values were not accurate enough to reveal this otherwise invisible reaction.

In the second explanation (referred to as case II), the 13% of II-*h* produced from (−)-I-*h* in CH_3OD is assumed to be solely the product of facial retention, or (+)-II-*h*. Optically pure (−)-I-*d* possesses a rotation 1% higher than (−)-I-*h*,[3b] and it is assumed the same is true for (−)-II-*d* as compared to (−)-II-*h*. These assumptions, coupled with the maximum optical purity of 0.1% for the II produced in run 1, provide the following composition for this material: 13% (+)-II-*h*, 0% (−)-II-*h*, 37% (+)-II-*d*, 50% (−)-II-*d*. Thus, deuterium capture at the front and back faces of the indenyl anion would have to occur at unequal rates. No structural features of the system provide any explanation for this partial stereospecificity being of a magnitude that exactly compensates for the assumed complete stereospecificity of the 1,3-hydrogen shift. It is highly probable there is a kinetic isotope effect for isomerization of I → II[11] as well as for II → I. If this exists, then the above composition of II and therefore its rotation should change with time, and unequal amounts of (−)-I-*d* and (+)-I-*d* should be produced *via* II as the reaction proceeded, and the first-order loss of optical activity of the system would be perturbed. This is not observed in kinetic runs 8–10. However, the case II explanation is consistent with the observation that $k_e/k_\alpha \sim 1$.[12]

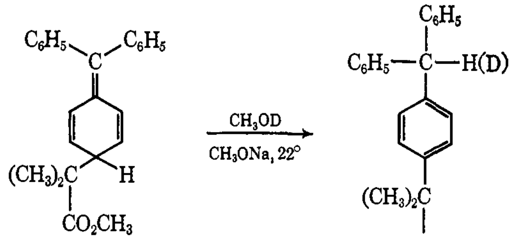
Although the preponderance of evidence strongly favors the explanation of case I, it is not completely conclusive. A desirable but difficult experiment would clearly differentiate between cases I and II. This would involve generation of II from (−)-I-*h* in CH_3OD, resolving the material into its two enantiomers, and analyzing each for deuterium. Unfortunately, no method of resolving small amounts of II is available.

The intramolecularity observed in runs 1 and 3 provides an estimate of the rate constant for drowning in the CH_3OD solvent pool of CH_3OH molecules generated by methoxide abstraction of a proton from I. In amine–methanol systems the rate constant k_H for exchange of methanol between an amine–methanol complex and the methanol solvent pool ranges between 10^8 and 10^{10} sec^{-1} at 30°.[13] Trimethylamine gave the higher and N,N-dimethyl-*m*-toluidine the lower rate constant. It is reasonable to expect[14a–c] that in methanol, indene has a pK_a of 24–25, as compared to methanol in methanol of 18.3.[14a] Thus, $K \sim 10^6$ for the equilibrium formulated is a reasonable estimate. From the correlation[15]

$$\text{ind}^- + CH_3OH \underset{k_1}{\overset{k_{-1}}{\rightleftarrows}} \text{ind-H} + CH_3O^-$$

between isotopic exchange rates and pK_a in methanol–methoxide at 45°, the isotopic exchange rate for indene (governed by k_1) is predicted to be $\sim 10^{-2}\ M^{-1}\ sec^{-1}$ at 45°, not far from $k_\alpha^{\text{apparent}}$ $5 \times 10^{-4}\ M^{-1}\ sec^{-1}$ observed for I at 25°. Thus, $k_{-1} \sim 5 \times 10^2\ M^{-1}\ sec^{-1}$ or $10^4\ sec^{-1}$. Thus, the rate of deuterium capture by the indenyl anion is about four powers of 10 slower than the rate of methanol exchange with the methanol–N,N-dimethyl-*m*-toluidine complex (a methanol drowning process). For the 13% of *stereochemically indiscriminate* but *isotopically discriminate* recapture of a proton to take place in runs 1 and 3, the rearrangement–recapture rate had to be about a power of ten slower than the isotopic drowning rate, which indicates that the drowning rate in runs 1 and 3 must have been about $10^5\ sec^{-1}$. Thus, the drowning rate for $C^- \cdots HOCH_3$ is estimated to $\sim$3 powers of 10 slower than the drowning rate for $N\colon\cdots HOCH_3$. This gross difference may be due either to the difference in charge type of the two species, or to complexities that make either isotopic exchange or racemization rates unsuitable measures of k_1 values to be used for calculation of k_{-1} from equilibrium constants.

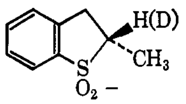
The 13% intramolecularity for isomerization of (−)-I-*h* in CH_3OD–CH_3OK is lower than that found for the 1,5-hydrogen shift observed in the same medium and temperautre in the conversion of IV to V.[5c] In this system 47% intramolecularity was observed This increase is attributed to the fact that V has a pK_a considerably higher than that of II. The expected result is that the intermediate carbanion is probably shorter lived, and the CH_3OH generated by proton abstraction has less opportunity to penetrate the $(CH_3OD)_n$ cage before its capture than in the case of the anion derived from I.



IV

47%V-*h*, 53%V-*d*

The large isotope effect for the intramolecularity in I → II observed here contrasts with the relatively small one observed for the isoinversion (intramolecular) component in the racemization of (+)-VI-*h* in CH_3OD–CH_3OK and of (+)-VI-*h* in CH_3OH–CH_3OK.[16] If k_1 is the rate constant for exchange with retention, k_2 for exchange with inversion, and k_3 for isoinversion, then $[k_3/(k_1 + k_2 + k_3)]_{CH_3OD}{}^{(+)\text{-VI-}h}/[k_3/(k_1 + k_2 + k_3)]_{CH_3OH}{}^{(+)\text{-VI-}d} = 1.9$. This difference is attributed to the presence of the sulfone group in VI which provides a conducted tour pathway for the intramolecular process which is absent in I.



(+)-VI-*h*(*d*)

The collapse ratios (Table I) favored deuteration of the methyl-bearing carbon over that of the *t*-butyl carbon of carbanion derived from I by a factor of 2.3 (run 1), but for protonation the ratio was 0.7 (run 2). This isotope effect on the collapse ratio suggests that several types of solvated indenyl anionic intermediates intervene in the isomerization reaction in any given run. The observed isotope effect on collapse ratio is probably a blend of isotope effects for discrete processes such as proton capture by carbanion, rearrangement of one hydrogen-bonded anion to another, and isotopic exchange of hydrogen-bonded anions with solvent molecules of the opposite isotopic variety.

Comparison of the values of k_α, k_e, and k_i for (−)-I-*h* in CH_3OD (Table III) provides a number of interesting conclusions. For example, k_e and k_α are both greater than k_i by a factor of about 3.5. Possibly in the indenyl anion, the carbon bearing the methyl group carries more negative charge than the carbon bearing the *t*-bu-

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[12] A kinetic model involving the eight interconverting components, (−)-I-*h*, (−)-I-*d*, (+)-I-*h*, (+)-I-*d*, (−)-II-*h*, (−)-II-*d*, (+)-II-*h*, and (+)-II-*d*, was developed with the generous help of Professor E. W. Graham. The scheme turned out to be far too elaborate for application in any other than a qualitative way to the results of this paper. The model will be useful should highly refined and much more elaborate kinetic results for the isomerization and *exchange reactions* of I and II be obtained in the future.

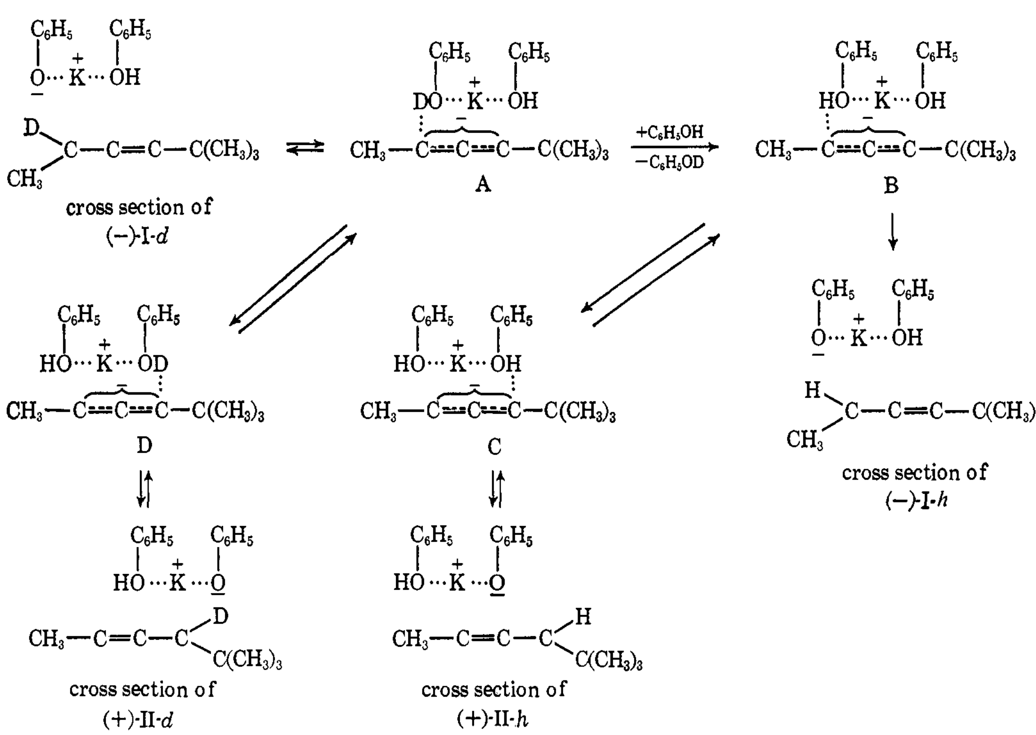
[13] (a) E. Grunwald, *J. Phys. Chem.*, 71, 1846 (1967); (b) E. Grunwald, R. L. Lipnick, and E. K. Ralph, *J. Amer. Chem. Soc.*, **91**, 4333 (1969).

[14] (a) C. D. Ritchie and R. E. Uschold, *ibid.*, 90, 2821 (1968); (b) C. D. Ritchie, *ibid.*, 91, 6749 (1969); (c) C. D. Ritchie, G. A. Skinner, and V. G. Badding, *ibid.*, **89**, 2063 (1967); (d) C. D. Ritchie and R. E. Uschold, *ibid.*, 90, 3415 (1968).

[15] A. Streitwieser, Jr., J. I. Brauman, J. H. Hammons, and A. H. Pudjaatmaka, *ibid.*, 87, 384 (1965).

[16] J. N. Roitman and D. J. Cram, unpublished work.

Chart I



tyl group due to greater steric inhibition of solvation at the latter site. Thus, a greater concentration of charge should accumulate at the less-hindered position and make this site more heavily solvated by hydroxyl groups than the more hindered (and more lypophylic) position carrying the *t*-butyl group, which acts as a hydrocarbon umbrella shielding the carbon to which it is attached.

Importance of Potassium Ion to Stereospecificity in Isotopic Exchange and Isomerization Reactions in Benzene–Phenol–Potassium Phenoxide Media. In 75% benzene–25% phenol (by volume), potassium phenoxide catalyzed the isotopic exchange, racemization, and isomerization of (−)-I-*d* at 100° (run 4). After about 11% isomerization, recovered I had undergone 15.5% isotopic exchange and 2.1% racemization, and $k_e/k_\alpha \sim 8$. Thus, isotopic exchange occurred with predominant retention. For purposes of comparison, $(k_e/k_\alpha)_{II}^{\text{pseudo}}$ was calculated by means of eq 5 to be about 20 from the 87% isotopically exchanged and 9.9% racemized II produced in run 4.

Thus, not only was the isomerization reaction highly stereospecific in the suprafacial sense (95% of II was (+)), but the isotopic exchange that accompanied the isomerization occurred with a higher stereospecificity by a factor of 2.5 (*i.e.*, 20/8) than did the simple isotopic exchange of (−)-I-*d*.

$$(k_e/k_\alpha)_{II}^{\text{pseudo}} = \frac{\ln(1 - \text{fraction of exchanged II})}{\ln(1 - \text{fraction of racemized II})} \quad (5)$$

Addition of crown ether III at 0.1 *M* level (potassium phenoxide = 0.058) to the same medium in run 5 sharply reduced the stereospecificities of the isotopic exchange reaction of (−)-I-*d*, of the isomerization reaction of (−)-I-*d* to (+)-II, and particularly of the isotopic exchange–rearrangement reaction. Thus, k_e/k_α for (−)-I-*d* in run 5 was only 2.3, only 62.5% of the II produced was (+)-II (37.5% was (−)-II), and $(k_e/k_\alpha)_{II}^{\text{pseudo}} = 1.04$. Crown ethers such as III are known to fill effectively the coordination sites of potassium ion in solvents of low dielectric constant[6,17] and convert contact ion pairs into ether-separated ion pairs. The striking reductions in the stereospecificities of the various reactions of (−)-I-*d* in run 5 indicate that their stereospecificities are dependent on the presence of potassium ion coordinated to both the molecule of phenol-O-*d* generated by deuterium abstraction from the carbon acid and the phenol-O-*h* of the medium. Removal of the potassium ion from the reaction site destroys the organizing features of the potassium ion with its ligands at the reaction site, and thereby destroys most of the stereospecificity of the reaction. The stereospecific mechanisms operative in run 4 are portrayed in Chart I in terms of the cross section of the allylic system involved. Thus, isotopic exchange of (−)-I-*d* with retention involves ionization of (−)-I-*d* by a potassium phenoxide ion pair bound to phenol to give A. Rotation of the potassium ion within the contact ion pair replaces the CH_3–$C^-\cdots$DO hydrogen bond of A with the $CH_3C^-\cdots$HO hydrogen bond of B, which collapses to (−)-I-*h*. Isomerization without exchange occurs when the CH_3–$C^-\cdots$DO hydrogen bond of A slips down the π cloud to give the OD$\cdots C^-$–$C(CH_3)_3$ hydrogen bond of D, which collapses to give (+)-II-*d*. Isomerization with exchange occurs when the CH_3–$C^-\cdots$HO hydrogen bond of B slips down the π cloud to give OH$\cdots C^-$–$C(CH_3)_3$ hydrogen bond of C, which collapses to give (+)-II-*d*. The effect of crown ether on this mechanism probably is to dissociate the potassium phenoxide contact ion pair to an ether-separated ion pair, and to occupy the ligand sites of potassium ion and exclude phenol. The fact that all of the rates (isomerization, exchange and racemization) were slower in the presence of the crown ether suggests that the contact ion pair is more reactive in the ionization process than the ether-separated ion pair, and that the

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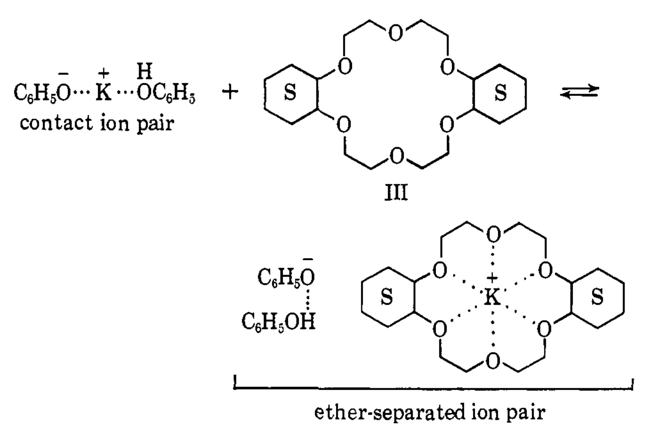
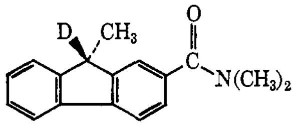
[17] D. A. Jaeger, J. N. Roitman, and D. J. Cram, unpublished work.



equilibrium constant favors the ether-separated ion pair. Apparently, the absence of potassium in the basic catalyst favors collapse to starting material over that to product since the collapse ratio value was increased in run 5 to 2.9 from a value of 1.7 in run 4.[18]

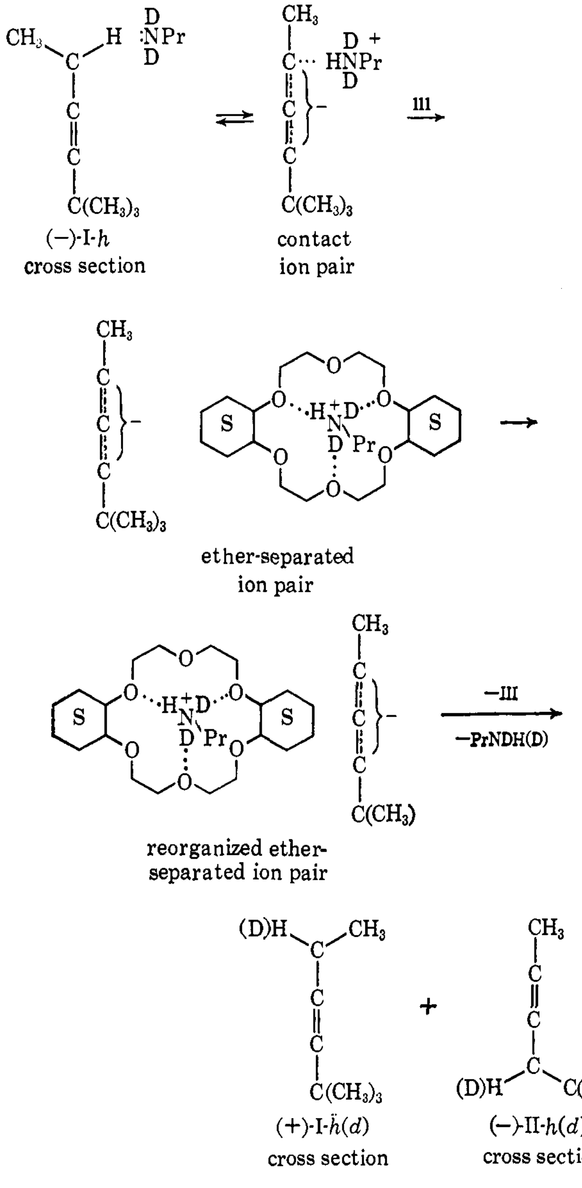
The lowering of stereospecificity of the various processes by addition of crown ether to the potassium phenoxide–phenol–benzene in run 5 recalls the effect of substituting tetramethylammonium phenoxide for potassium phenoxide as a catalyst in phenol–benzene medium for the isotopic exchange and racemization of (−)-VII-*d* at 75°.[5b] With potassium phenoxide, $k_e/k_\alpha = 18$, but with tetramethylammonium hydroxide, $k_e/k_\alpha = 1$. Clearly, in this system as well the organizing capacity of the metal cation through use of its coordinating sites played a key role in providing the stereospecific mechanistic feature of the isotopic exchange reaction.



(−)-VII-*d*

Interception of Alkylammonium Carbanide Ion Pairs by Crown Ether. In run 6, (−)-I-*h* in tetrahydrofuran (0.19 *M*) in n-$C_3H_7ND_2$ at 37.5° gave a k_e/k_α value for I of >30. The II produced was essentially optically pure and had undergone about 17% isotopic exchange. Run 7 was made under identical conditions except that the reaction medium was 1.5 *M* in crown ether, III. The isomerization and isotopic exchange rates of (−)-I-*h* were slightly lowered by the presence of the crown ether, but the racemization rate of (−)-I-*h* was increased by a factor much greater than 24, and k_e/k_α decreased from >30 to 0.62. The fact that the isomerization and isotopic exchange rates were only slightly modified by the presence of the crown ether suggests that the *n*-propylamine was no more complexed by the crown ether than by tetrahydrofuran itself. However, the fact that k_α was vastly increased in value by the crown ether suggests that the *n*-propylammonium carbanide ion pair once formed was intercepted by the crown ether and pulled apart by the established ability of crown ether to complex with alkylammonium ions.[6a] Once an ether-separated ammonium carbanide ion pair was formed, the carbanion rotated with respect to the cation and lost its stereochemical history. Apparently, the isomerization of the original *n*-propylammonium carbanide ion pair was somewhat faster than the interception reaction since the (+)-II formed was only 21% racemized, and the isotopic exchange of II was only slightly effected. Thus, only the slow reactions were increased by the crown ether present, namely, those that involved the rotation of the carbanion within the ion pair. This result is expected if the hydrogen-bonded ion pair is pulled apart by the crown ether. The value, $(k_e/k_\alpha)_{II}^{\text{pseudo}} = 0.46$, is not far from that observed for $(k_e/k_\alpha)_I = 0.62$. The similarity in these values is not surprising since both depend on the same type of ion pair reorganization reactions. A hypothetical mechanism for interception of the propylammonium carbanide ion pair and its reorganization to give (+)-I-*h*(*d*) and (−)-II-*h*(*d*) is formulated in Chart II.

Chart II



In run 6 (without crown ether III) isomerized product II contained 17% deuterium, whereas in run 7 (with

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[18] Others [T. E. Hogen-Esch and J. Smid, *J. Amer. Chem. Soc.*, **89**, 2764 (1967)] observed that addition of tetraethylene glycol dimethyl ether to fluorenyl–metal cation ion pairs moved the contact ion pair ⇌ solvent-separated ion pair equilibrium toward the right [see also L. L. Chan and J. Smid, *ibid.*, **90**, 4654 (1968)], and that the reactivity of the contact ion pair in proton abstraction reactions was greater than that of the solvent-separated ion pair.

crown ether) II contained 10% deuterium. This small increase in intramolecularity in the presence of crown ether is unexpected on the basis of the mechanism of Chart II, which assumes that crown ether and amine are not complexed and that all three hydrogen bonding sites of the ammonium ion are complexed with crown ether. Possibly in minor competing mechanisms, amine complexed with crown ether forms alkylammonium complexes in which only two rather than all three of the coordinating sites of the alkylammonium ion are involved with the crown ether. Such a scheme leaves hydrogen more available for ultimate bonding to form II-*h* than it does deuterium to form II-*d*. Clearly, these subtleties of mechanism require further work before they are understandable.

Experimental Section

General. Procedures for the purification (or preparation) of methanol,[7] methanol-O-*d*,[7] tetrahydrofuran,[19] and *n*-propylamine-N-d_2[3b] have been described previously. A stock solution of potassium phenoxide in phenol–benzene for runs 6 and 7 of Table I was prepared by adding approximately 0.100 g of freshly cut potassium to 10 ml of phenol freshly distilled from molecular sieves.[19] The mixture was warmed with stirring until all the potassium dissolved, and 40 ml of benzene distilled from lithium aluminum hydride was added. Titration of aliquots of the solution with 0.01062 *N* hydrochloric acid against a bromocresyl green–methyl red indicator gave a 0.0567 *N* base concentration. A stock solution for runs 1, 3, and 8–10 was prepared from 50 ml of methanol-O-*d* (0.99 atom of deuterium per molecule) and sufficient freshly cut potassium to achieve the desired base concentration, which was determined by titration of aliquots of the solution with a known solution of 0.0106 *N* hydrochloric acid against a bromocresyl green–methyl red indicator. Similar techniques were used for preparation of the solutions for runs 2 and 8–10. In runs 1 and 3–7, the (−)-I-*h*[3b] used possessed the following rotations: $[\alpha]^{25}_{589}$ −126°, $[\alpha]^{25}_{546}$ −159°, $[\alpha]^{25}_{436}$ −289° (*c* 0.2, $CHCl_3$). In run 2 the (−)-I-*d*[3b] used contained 0.99 of one atom of deuterium per molecule, and possessed the following rotations: $[\alpha]^{25}_{589}$ −128°, $[\alpha]^{25}_{546}$ −158°, $[\alpha]^{25}_{436}$ −292° (*c* 0.4, $CHCl_3$).

Runs Made for Product Analyses (1–7). The solutions for runs 1–7 were prepared, the runs made, and the products isolated, separated, and analyzed by procedures published previously[3b] with some exceptions. For all of these runs, analytical glpc analyses were performed on a 10 ft × 1/8 in. column containing 4% Apiezon L on 80–100 mesh Chromosorb W in a Wilkins Model 204 gas chromatograph machine. Preparative glpc separation was carried out at 110–130° on a 6 ft × 1/4 in. column packed with 10% Apiezon L on 60–80 mesh Firebrick in a Perkin-Elmer Model 154 vapor fractometer machine. In run 7 the cyclic polyether III was separated from the reaction product before analytical or preparative glpc by placing the entire reaction solution on 100 g of silica gel and eluting with freshly distilled pentane. The pentane fraction was washed with aqueous saturated potassium chloride, 0.25 *N* hydrochloric acid, and water, was dried, and concentrated. Isomer analysis was carried out by integration of the peaks for I and II during preparative glpc separation. Use of tetradecane (distilled from Matheson Coleman and Bell reagent grade) as an internal standard demonstrated that the combined amounts of I and II produced accounted for 99–100% of the starting material. For runs 3, 5, and 7, weighed amounts of cyclic polyether III[20] (mp 30–56°, mixture of diastereomers) were added to the reaction mixtures. The amounts of deuterium in I and II were determined on an MS-9 mass spectrometer by techniques already described.[3b] Rotations were taken at 436 mμ on a Perkin-Elmer Model 141 polarimeter, the cells being thermostated at 25°.

Procedure for Run 8. All glassware, except the polarimeter cell, was cleaned with hot chromic acid, rinsed with distilled water, with 0.5 *M* ammonium hydroxide, and again with distilled water before drying at 180° for 8 hr. A polarimeter cell, 1 ml capacity and 1 dm in length equipped with a thermostating jacket, was cleaned by filling the sample chamber with warm chromic acid, and rinsing successively with distilled water, dilute ammonium hydroxide, distilled water, reagent grade acetone, and reagent grade ether. The chamber was then purged thoroughly with dry nitrogen, stoppered, and placed in a Perkin-Elmer Model 141 polarimeter, thermostated at 25°, and the empty cell was calibrated at 436 mμ. To a 100-ml, round-bottomed flask was added 90 mg of (−)-I-*h*, 90% optically pure, $[\alpha]^{25}_{589}$ −112°, $[\alpha]^{25}_{546}$ −139, $[\alpha]^{25}_{436}$ −261 (*c* 0.2, $CHCl_3$). The flask was swept with nitrogen, closed with a tightly fitting syringe cap, and immersed in a constant temperature bath set at 25 ± 0.1°. The same bath was used to thermostat the polarimeter cell. To the flask was added quickly 4.84 ml of a stock solution of 0.07121 *N* potassium methoxide in methanol-O-*d* with a syringe, which was used to mix the carbon acid and base solvent by two rapid draws and ejections. A 1-ml sample of the mixture was withdrawn with the same syringe and placed in the polarimeter cell. A rapid reading of the observed rotation at zero time was facilitated by setting the analyzer near the expected rotation (∼−4°) independently with a negatively rotating sample. The first reading was made within 40 sec after the solution was mixed.

After the prescribed time period, a polarimetric reading was taken and approximately 0.35 ml of the solution in the flask was withdrawn with a clean syringe. Approximately 3 drops were placed in a centrifuge tube equipped with a ground glass stopper containing 0.2 ml of spectral grade carbon tetrachloride and 1 ml of 0.25 *N* hydrochloric acid. The tube was stoppered and shaken. The rest of the aliquot was shaken in a 60-ml separatory funnel containing 20 ml of pentane and 20 ml of 0.25 *N* hydrochloric acid. From the centrifuge tube containing the sample to be analyzed for extent of isomerization by analytical glpc, the carbon tetrachloride layer was withdrawn, shaken twice with 2% aqueous saturated sodium chloride solution, and 1-μl samples were injected onto a 10 ft × 1/8 in. column containing 4% Apiezon L on 80–100 mesh Chromosorb W. The instrument and conditions necessary for near base-line analytical separation have been described previously.[3b] For the measurement of the relative peak areas the signal for the larger peak, I (having the shorter retention time), was attenuated to fit the recorder scale, so that the uncorrected peak areas for I to II were approximately 5 to 1. A line was drawn through that part of the base of the peak for II which represented the last traces of I. The remaining area for II, and the area bound by a curve which was drawn to restore the peak for I before signal magnification were compared by a cut-and-weigh procedure.[21] The two peaks were carefully traced with a sharp, hard pencil onto uniform tracing paper, cut with a razor, and carefully weighed to 0.5 mg. In some cases the small peak was retraced several times, so that combined peaks weighed no less than 200 mg. The isomeric percentages were then determined after the appropriate attenuation and trace-duplication corrections were made. Comparison of synthetic mixtures of I and II showed that the per cent of II could be determined to ±0.5% of the mixture. Furthermore, analyses of mixtures containing more than 10% of II by both the cut-and-weigh and the disc integration procedures agreed to within 0.5%.

The part of the aliquot to be purified by preparative glpc was immediately quenched in 20 ml of 0.25 *N* hydrochloric acid and 20 ml of pentane. The pentane layer was separated, and washed twice with aqueous 2% saturated sodium chloride solution. The pentane layer was separated and concentrated under a stream of nitrogen, and then injected on a 6 ft × 1/4 in. column of 10% Apiezon L on 60–80 Firebrick. All instruments, conditions, and techniques for the purification of recovered isomer I have been reported previously.[3b] Although synthetic mixtures of I-*h* and I-*d* had previously been analyzed[3b] by mass spectral measurements within 0.5% of the actual values, a check of the synthetic mixtures during the time of run 8 showed that measured values were consistently higher in deuterium content by as much as 5% during analysis of a 50% deuterated sample. Proportionately less error was found in synthetic mixtures containing less deuterium. A calibration curve was constructed and the appropriate corrections were applied.

Procedures for Runs 9 and 10. All glassware was cleaned, and a polarimeter cell was prepared as in run 8. To a 50-ml, round-bottomed flask was added 90 mg of (−)-I-*h*, 90% optically pure, $[\alpha]^{25}_{589}$ −112°, $[\alpha]^{25}_{546}$ −139°, $[\alpha]^{25}_{436}$ −261° (*c* 0.2, $CHCl_3$). The flask was swept with nitrogen and partially immersed in a constant temperature bath set at 25.0 ± 0.1° for run 9 and 24.95 ± 0.1 for run 10. The same bath was used to thermostat the

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[19] D. J. Cram, W. T. Ford, and L. Gosser, *J. Amer. Chem. Soc.*, **90**, 2598 (1968).

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

[21] Varian-Aerograph (Walnut Creek, Calif., "Research Notes," Fall 1966) reports that although this procedure is more time consuming, it is almost as accurate as integration by a Disc Integrator.

polarimeter cell. To the flask was added quickly 4.84 ml of a stock solution of 0.0712 *N* potassium methoxide in methanol-O-*d* for run 9 (0.0590 *N* for run 10) with a syringe, which was used to rapidly mix the reagents, and transfer 1 ml of the reacting mixture to the polarimeter cell, as described in run 8. A rapid reading of the observed rotation at zero time was facilitated by presetting the analyzer near the expected rotation ($\sim -5°$) independently with a negatively rotating nonreacting solution. The first reading was made within 40 sec after the solution was mixed. Periodic readings were taken at the prescribed times. Eleven readings were taken in run 9 and forty readings were taken in run 10. The data were analyzed as described in the Results section.

Appendix. Derivation of the Kinetic Expression for k_α

The following definitions are used in the derivation of the kinetic expression for k_α: S_0 is the initial concentration of (−)-I-*h*, S is the concentration of optically pure (−)-I-*h* at any time *t*, T is the total concentration of I at any time, f is the fraction of total I which is optically pure ($f = S/T$), P is the concentration of racemic II at any time ($P = S_0 - T$), and f_{II} is the mole fraction of II at any time. Chart III shows the major reactions involved before enough isotopic exchange of I had occurred to start to effect the amount of isotopic-exchanged (±)-II formed by the reaction (±)-I-*d* → (±)-II-*d*. This chart also serves to define k_α, k_e, and k_i. The rate of loss of I by isomerization to II is given by eq 6. The rate of loss of optically active material

Chart III

$$\begin{tikzcd}
\underset{S}{(-)\text{-I-}h} \arrow[r, "k_\alpha", "k_e"'] \arrow[d, "k_i"] & (\pm)\text{-I-}d \\
\underset{P}{\begin{array}{c}(\pm)\text{-II-}d\ (87\%)\\ (\pm)\text{-II-}h\ (13\%)\end{array}} \arrow[ur, "k_r"'] &
\end{tikzcd}$$

$$\frac{\mathrm{d}T}{\mathrm{d}t} = k_r S_0 - (k_r + k_i)T \qquad (6)$$

is given by eq 7, which by use of the definition of f gives eq 8. Solution of eq 6 and 8 for df/dt and the use of the

$$\frac{\mathrm{d}S}{\mathrm{d}t} = (k_\alpha + k_i)S \qquad (7)$$

$$\frac{\mathrm{d}f}{\mathrm{d}t} = (k_\alpha + k_i)f - \frac{f\mathrm{d}T}{T\mathrm{d}t} \qquad (8)$$

definition of f_{II} ($f_{\text{II}} = P/T = (S_0/T) - 1$) gives eq 9.

$$\frac{\mathrm{d}f}{\mathrm{d}t} = -(k_\alpha + k_r f_{\text{II}})f \qquad (9)$$

For all aliquots of run 8, $f_{\text{II}} \leqq 0.25$, and $k_r \approx 10^{-6}$ sec^{-1}. Thus, for run 8, $k_r f_{\text{II}}$ can be neglected to a good approximation, and k_α calculated.

$(CH)_{10}CO_2$ Interconversions. The Electrophilic Addition of Chlorosulfonyl Isocyanate to Bullvalene[1]

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Abstract: Treatment of bullvalene with chlorosulfonyl isocyanate afforded β-lactam **3b** ⇆ **4b**, lactone **5b**, and lactam **6b**. Longer reaction times and higher temperatures gave greatly reduced yields of the β-lactam. The structure of **3b** ⇆ **4b** was deduced from its temperature-dependent nmr spectra. Spectral analysis was also employed for structural assignment to **5b** and **6b**, chemical confirmation of which was achieved by ozonolysis and esterification to dimethyl malonate in each instance. Exposure of **5b** to 30% sulfuric acid at room temperature resulted in rearrangement to lactone **10**, a mechanism for which is suggested. Double- and triple-resonance studies at 100 MHz were employed for structural assignment to this and the ensuing $(CH)_{10}CO_2$ isomers. Photorearrangement of **10** led to the formation of three isomeric γ-lactones: **14**, **20**, and **30**. In the cases of **14** and **20**, the rearrangements are believed to be initiated by Norrish type I cleavage of the carbonyl group.

Despite the innate capability of bullvalene (**1**) for degenerate Cope rearrangement to more than 1.2 million equivalent tautomeric forms,[2] little is yet known about the reactivity of this very interesting fluxional molecule.[3] For instance, only two examples of electrophilic addition to **1** have been reported, these being bromination[4a] and chlorination.[4b] Our interest in molecules which exhibit rapid and degenerate valence isomerization[5] prompted an investigation of the electrophilic addition of chlorosulfonyl isocyanate (CSI)

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[1] Unsaturated Heterocyclic Systems. LXXI. For the previous paper in this series, see L. A. Paquette, M. F. Wyvratt, and G. R. Allen, Jr., *J. Amer. Chem. Soc.*, **92**, 1763 (1970).

[2] (a) The prediction of these spectacular properties of bullvalene was initially made on theoretical grounds: W. von E. Doering and W. R. Roth, *Tetrahedron*, **19**, 715 (1963); the synthesis of bullvalene was subsequently realized; (b) G. Schröder, *Angew. Chem. Intern. Ed. Engl.*, **2**, 481 (1963); *Chem. Ber.*, **97**, 3140 (1964); (c) R. Merenyi, J. F. M. Oth, and G. Schröder, *ibid.*, **97**, 3150 (1964); (d) W. von E. Doering, B. M. Ferrier, E. T. Fossel, J. H. Hartenstein, M. Jones, Jr., G. Klumpp, R. M. Rubin, and M. Saunders, *Tetrahedron*, **23**, 2943 (1967).

[3] For recent reviews, see (a) G. Schröder, *Angew. Chem. Intern. Ed. Engl.*, **4**, 752 (1965); (b) G. Schröder and J. F. M. Oth, *ibid.*, **6**, 414 (1967).

[4] These halogenation reactions have been formulated as 1,4 cycloadditions: (a) J. F. M. Oth, R. Merenyi, J. Nielsen, and G. Schröder, *Chem. Ber.*, **98**, 3385 (1965); (b) J. F. M. Oth, R. Merenyi, H. Röttele, and G. Schröder, *Tetrahedron Lett.*, 3941 (1968).

[5] (a) L. A. Paquette, J. R. Malpass, G. R. Krow, and T. J. Barton, *J. Amer. Chem. Soc.*, **91**, 5296 (1969); (b) L. A. Paquette, G. R. Krow, and J. R. Malpass, *ibid.*, **91**, 5522 (1969); (c) L. A. Paquette and J. R. Malpass, *ibid.*, **90**, 7151 (1968); (d) L. A. Paquette and G. R. Krow, *ibid.*, **90**, 7149 (1968); (e) L. A. Paquette, G. R. Krow, J. R. Malpass, and T. J. Barton, *ibid.*, **90**, 3600 (1968); (f) L. A. Paquette, T. J. Barton, and E. B. Whipple, *ibid.*, **89**, 5481 (1967); (g) L. A. Paquette and T. J. Barton, *ibid.*, **89**, 5480 (1967); (h) L. A. Paquette, J. R. Malpass, and G. Krow, *ibid.*, **92**, 1980 (1970).