Electrophilic Substitution at Saturated Carbon. XLIII. Alkylammonium Carbanide Ion-Pair Reorganization Reactions in Base-Catalyzed 1,3-Proton Transfer in an Indene System[1,2]

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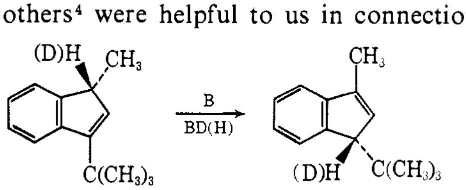
Abstract: For study of base-catalyzed proton transfer, (−)-3-*t*-butyl-1-methylindene-1-*h* ((−)-I-*h*), (−)-3-*t*-butyl-1-methylindene-1-*d* ((−)-I-*d*), and (+)-1-*t*-butyl-3-methylindene-1-*h* ((+)-II-*h*) of maximum rotations were prepared. Comparisons of their optical rotatory dispersion curves and those of their ketonic precursors, (−)-(*R*)-3-methyl-1-indanone ((−)-(*R*)-IV) and (−)-3-*t*-butyl-1-indanone ((−)-(*S*)-VI), established that (−)-I-*h* and (+)-II-*h* possess opposite configurations. Optically pure ketones (−)-VI undeuterated at the chiral center, deuterated at the chiral center, and dideuterated at the position α to the ketonic group differ in rotations by unusually large amounts up to 300% at 390 mμ. This effect is attributed mainly to the difference in steric requirements of H and D, and the consequent change in dihedral angle about the C_2–C_3 bond of the deuterated and nondeuterated indanones. Equilibrium constants for I $\rightleftarrows$ II were found to be 5.99–6.04 at 102° (*t*-butyl alcohol–triethylenediamine), 6.64–6.69 at 48° (10 mol % methanol–90 mol % dimethyl sulfoxide–triethylenediamine), and 7.50–7.60 at 25° (tetrahydrofuran, 2.0 *M* in *n*-propylamine). Under conditions that II was stable to exchange, racemization, or isomerization, I was isomerized to II; the two isomers were separated and analyzed for isotopic exchange and racemization. In all runs with amine catalysts and with transfer of either hydrogen or deuterium with solvents ranging from dimethyl sulfoxide–*t*-butyl alcohol to benzene (−)-I gave (+)-II of 97–100% optical purity, and recovered (−)-I was 98–100% optically pure. Proton transfer involved almost exclusively only one face of the allylic anion. With I-*h* in *t*-butyl alcohol-O-*d* with triethylenediamine as base and in the presence of deuterated amine salt as a primary isotope pool, the (+)-II produced had undergone only 0.35% isotopic exchange. In dimethyl sulfoxide, 1.0 *M* in *t*-butyl alcohol-O-*d* with the same base and salt, the (+)-II had undergone 1.2% isotopic exchange. In tetrahydrofuran, 0.61 *M* in *n*-propylamine, I-*d* gave II that was 95% exchanged, whereas with I-H and deuterated amine in the same solvent the II produced was 36% exchanged. Recovered I from these experiments gave k_e/k_α (rate constant for isotopic exchange over that for racemization) values >7.5. These experiments demonstrate that in the alkylammonium carbanide ion pair, alkylammonium ions reorganize enough to provide for extensive isotopic exchange, and that protium is captured by the anion more efficiently than deuterium. In benzene, 0.10 *M* in piperidine, I-*d* gave II with 27% isotopic exchange, whereas in benzene, 0.10 *M* in deuterated piperidine, I-*h* gave II with only 13% isotopic exchange. In this ion-pair intermediate, the dialkylammonium ion moved across the π cloud of the allylic anion and donated a proton or deuteron to the new site faster than the ammonium ion rotated. The anion of these contact ion-pair intermediates appears mainly to hydrogen bond no more than one hydrogen at a time.

As an extension of our investigation of the mechanism of base-catalyzed proton transfers of carbon acids,[3] we envisioned[2] 1,3-dialkylindenes as systems that with weak bases as catalysts would allow study of the stereochemical and isotopic changes that accompany 1,3-proton transfers. The key intermediate, (−)-3-methyl-1-indanone ((−)-IV), had been prepared when the first elegant kinetic results of Bergson, *et al.*,[4] appeared. After survey, we selected reaction I → II[3b,c] as most ideally suited for our investigations. This system possesses the following advantages. (1) Both I and II are readily preparable in optically pure and deuterated states, and their relative configurations are establishable by optical rotatory dispersion techniques. (2) At equilibrium, II dominates, and is much slower in its reactions than I, and at low conversions of I to II, II once formed is essentially stable under conditions of its formation. (3) Isomerization can be caused by bases as weak as amines or potassium phenoxide at convenient temperatures. (4) Isomers I and II are readily separable by vpc, possess large rotations amenable to polarimetric analysis, and can be analyzed easily for deuterium by mass spectrometry. The kinetic results of others[4] were helpful to us in connection with



(−)-I-*h*(*d*) (+)-II-*h*(*d*)

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[1] This research was supported in part by the U. S. Army Research Office, Durham, N. C., and in part by the Directorate of Chemical Sciences, Air Force Office of Scientific Research Grant No. AF-AFOSR-124-65.

[2] Some of the material of this paper appeared as a communication: J. Almy, R. T. Uyeda, and D. J. Cram, *J. Amer. Chem. Soc.*, **89**, 6768 (1967).

[3] (a) D. J. Cram and R. T. Uyeda, *ibid.*, **84**, 4358 (1962); (b) D. J. Cram and R. T. Uyeda, *ibid.*, **86**, 5466 (1964); (c) D. J. Cram, F. Willey, H. P. Fischer, and D. A. Scott, *ibid.*, **86**, 5370 (1964); (d) D. J. Cram, F. Willey, H. P. Fischer, H. M. Relles, and D. A. Scott, *ibid.*, **88**, 2759 (1966); (e) D. H. Hunter and D. J. Cram, *ibid.*, **88**, 5765 (1966); (f) D. J. Cram and L. Gosser, *ibid.*, **86**, 2950 (1964); (g) D. J. Cram and L. Gosser, *ibid.*, **86**, 5445 (1964); (h) D. J. Cram and L. Gosser, *ibid.*, **86**, 5457 (1964); (i) R. D. Guthrie, W. Meister, and D. J. Cram, *ibid.*, **89**, 5288 (1967); (j) W. T. Ford, E. W. Graham, and D. J. Cram, *ibid.*, **89**, 4661 (1967); (k) D. J. Cram, W. T. Ford, and L. Gosser, *ibid.*, **90**, 2598 (1968); (l) W. T. Ford and D. J. Cram, *ibid.*, **90**, 2606 (1968); (m) W. T. Ford and D. J. Cram, *ibid.*, **90**, 2612 (1968).

[4] (a) G. Bergson and A. Weidler, *Acta Chem. Scand.*, **17**, 1798 (1963); (b) A. Weidler, *ibid.*, 17, 2724 (1963); (c) A. Weidler and G. Bergson, *ibid.*, **18**, 1484 (1964); (d) A. Weidler and G. Bergson, *ibid.*, **18**, 1487 (1964); (e) L. Ohlsson, I. Wallmark, and G. Bergson, *ibid.*, **20**, 750 (1966); (f) G. Bergson and L. Ohlsson, *ibid.*, **21**, 1393 (1967); (g) S. Wold and G. Bergson, *Arkiv Kemi*, **28**, 245 (1968).

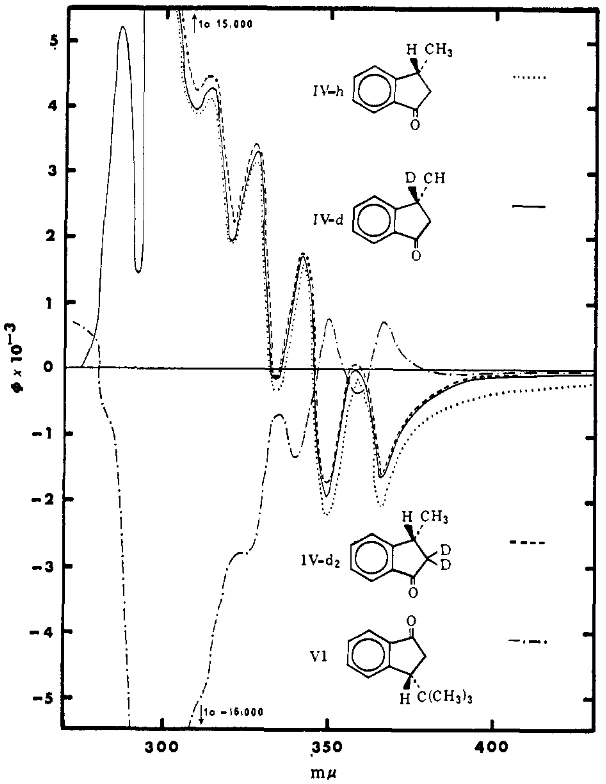


Figure 1. Optical rotatory curves of (−)-(*R*)-3-methyl-1-indanone (IV-*h*), ·····; (−)-(*R*)-3-methyl-1-indanone-1-*d* (IV-*d*), ——; (−)-(*R*)-3-methyl-1-indanone-2-d_2 (IV-d_2), - - - - -; and (−)-3-*t*-butyl-1-indanone (VI), –·–.

2 and 3, and encouraged us to anticipate high stereospecificity in our amine-catalyzed isomerizations.[3i]

Results

Starting Materials and Products. The preparations of (−)-I-*h*, (−)-I-*d*, and (+)-II-*h* are formulated. Acid (−)-III-*h* of maximum rotation and known configuration[5a,b] (*R*) exhibited a rotation close to that of (−)-III-*d*[5c] of maximum rotation which contained 99 ± 0.5% of one atom of deuterium per molecule (mass spectrometry). These acids were converted through ketones (−)-(*R*)-IV-*h* and (−)-(*R*)-IV-*d* to (−)-(*R*)-I-*h* and (−)-(*R*)-IV-*d* without modification of the asymmetric center. Acid V was brought to maximum rotation through its brucine salt, and (+)-V was converted through ketone (−)-VI to (+)-II which was separated from VII by vpc. The three compounds, (+)-V, (−)-VI, and (+)-II, exhibited sharp melting points that did not change upon recrystallization, and which were markedly different from those of the corresponding racemates. Thus, optical purity was attained, a conclusion supported (see later section) by the isomerization of optically pure (−)-I-*h* into (+)-II-*h* of the same rotation as that prepared from acid (+)-V-*h*. Although our preparations of (−)-III-*h*, (−)-IV-*h*, and (−)-I-*h* differ from those of Bergson, *et al.*,[4c] to the extent that comparisons are possible, the rotations are similar. Racemates V and VI have been reported previously,[6] but not in an optically active state.

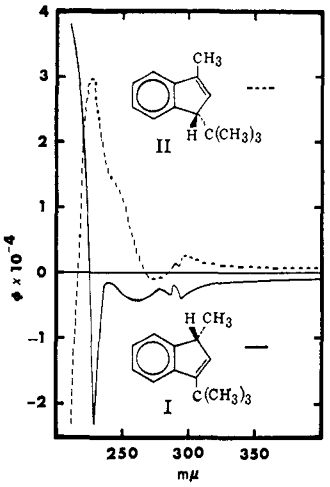
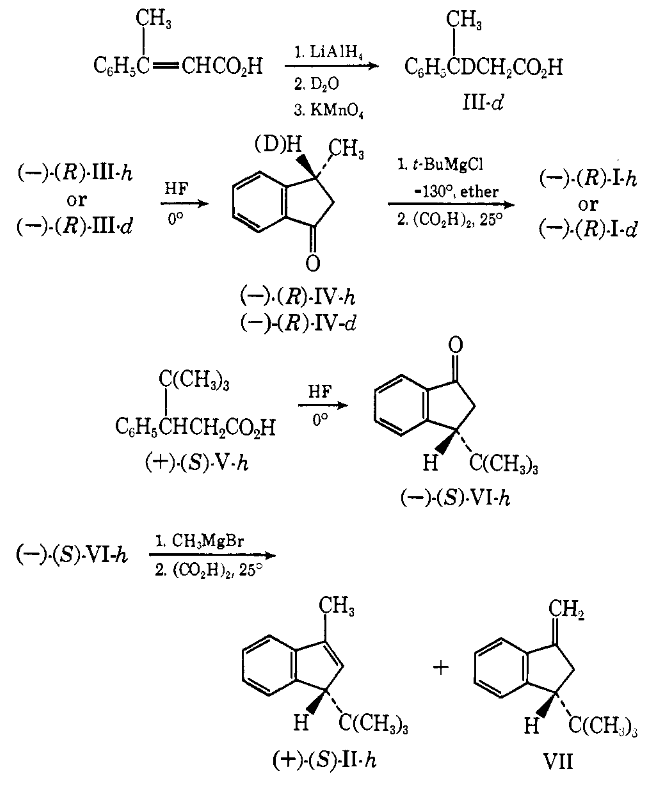


Figure 2. Optical rotatory curves of (−)-(*R*)-3-*t*-butyl-1-methylindene (I), ——, and (+)-(*S*)-1-*t*-butyl-3-methylindene (II), - - - -.

Optical Rotatory Dispersions. Figure 1 records the optical rotatory dispersion curves of ketones (−)-IV-*h* and (−)-VI-*h*, and Figure 2 of hydrocarbons (−)-I-*h* and (+)-II-*h*. The curves of the two hydrocarbons exhibit well-defined Cotton effects and are almost mirror images of one another. This fact indicates the two compounds possess configurations opposite to one another, and since the configuration of (−)-I-*h* is known, that of (+)-II-*h* can be assigned (see formulas). Ketones (−)-IV-*h* and (−)-VI-*h* also gave optical rotatory dispersion curves that are roughly mirror images of one another, although more complex, and (−)-VI-*h* and acid (+)-V-*h* are assigned the configurations formulated.



Comparisons of the maximum rotations of a variety of compounds which differ only in the substitution of hydrogen by deuterium at a single asymmetric carbon

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(5) (a) D. J. Cram, *J. Amer. Chem. Soc.*, **74**, 2137 (1952); (b) D. J. Cram, *ibid.*, **74**, 2149 (1952); (c) R. T. Uyeda and D. J. Cram, *J. Org. Chem.*, **30**, 2083 (1965).

(6) C. F. Koelsch, *J. Amer. Chem. Soc.*, **65**, 1640 (1943).

Table I. Comparison of the Maximum Rotations of Various Compounds Differing in the Substitution of Hydrogen by Deuterium at a Single Carbon Chiral Center

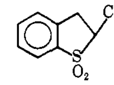
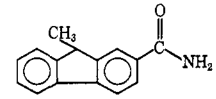
	Rotation of R–H			Rotation of R–D		
R*	Value, deg	Conditions	Ref	Value, deg	Conditions	Ref
$C_6H_5(CH_3)(C_2H_5)C$	$\alpha^{25}D$ +24.3	1 dm, neat	7a	$\alpha^{25}D$ −24.0	1 dm, neat	7b
$C_6H_5(C_2H_5)(CH_3O)C$	$\alpha^{25}D$ −120.0	1 dm, neat	7c	$\alpha^{25}D$ −120.0	1 dm, neat	7c
p-$C_6H_5C_6H_4(C_6H_5)(CH_3O)C$	$[\alpha]^{25}_{546}$ −6.3	c 2.5, $CHCl_3$	7d	$[\alpha]^{25}_{548}$ −6.3	c 2.5, $CHCl_3$	7e
$C_6H_5(CH_3)(NH_2)C$	$\alpha^{22}D$ −38.30	1 dm, neat	7f	$\alpha^{25}D$ −40.36	1 dm, neat	7g
$(CH_3)_3CCH{=}N(C_6H_5)(CH_3)C$	$\alpha^{25}D$ −21.12	0.5 dm, neat	7g	$\alpha^{25}D$ −21.92	0.5 dm, neat	7g
n-$C_6H_{13}(C_6H_5SO_2)(CH_3)C$	$[\alpha]^{26}_{546}$ −13.3	c 5.4, $CHCl_3$	7i	$[\alpha]^{31}_{546}$ −14.0	c 5.0, $CHCl_3$	7h
	$[\alpha]^{25}_{546}$ +24.1	c 4, $CHCl_3$	7h	$[\alpha]^{25}_{546}$ −24.1	c 4, $CHCl_3$	7h
	$[\alpha]^{26}_{546}$ +34.0	c 6.0, $O(CH_2CH_2)_2O$	3g	$[\alpha]^{26}_{546}$ −34.3	c 6.26, $O(CH_2CH_2)_2O$	3g

Table II. Equilibrium Constants between 3-*t*-Butyl-1-methylindene (I) and 1-*t*-Butyl-3-methylindene (II), or I ⇄ II

	Starting material			Base			Time,	
Run no.	Nature	Concn, M	Solvent	Nature	Concn, M	Temp, °C	days	K
1[a]	I-*h*	0.02	*t*-BuOH	$N(CH_2CH_2)_3N$	0.20	102	11	6.0
2	II-*h*	0.02	*t*-BuOH	$N(CH_2CH_2)_3N$	0.20	102	18	6.0
3	I-*h*	0.085	$(CH_3)_2SO$–MeOH[b]	$N(CH_2CH_2)_3N$	0.39	48	20	6.6
4	II-*h*	0.085	$(CH_3)_2SO$–MeOH[b]	$N(CH_2CH_2)_3N$	0.39	48	20	6.7
5	I-*h*	0.10	$(CH_2)_5O$	*n*-$PrNH_2$	2.0	25	18	7.6
6	II-*h*	0.10	$(CH_2)_5O$	*n*-$PrNH_2$	2.0	25	18	7.5

[a] Addition of tetradecane as an internal standard coupled with the vpc analytical data demonstrated 100% recovery of olefin. [b] 90 mol % $(CH_3)_2SO$–10 mol % CH_3OH.

(Table I) suggest that the rotations of the pairs of substances usually differ by 0 to ~4%,[3,7] with the deuterated compound more often than not exhibiting the higher rotation. The rotations of acids (−)-III-*h* and (−)-III-*d* and of hydrocarbons (−)-I-*h* and (−)-I-*d* are also within about a per cent of one another, but the maximum rotation of ketone (−)-IV-*h* exceeds that of (−)-IV-*d* by about 23% at the sodium D line.

For purposes of comparison, (−)-2,2-dideuterio-3-methyl-1-indanone (66% deuterated at the methylene position by nmr analysis) was prepared from ketone (−)-IV-*h* of maximum rotation by potassium carbonate catalyzed isotopic exchange with deuterium oxide.[8] Figure 1 compares the optical rotatory dispersion curves of (−)-IV-*h*, (−)-IV-*d*, and (−)-IV-d_2 (mainly). The curves of (−)-IV-*d* and (−)-IV-d_2 resemble one another much more than (−)-IV-*d* and (−)-IV-*h*. For example, at 390 mμ, (−)-I-*h* exhibits Φ 500°, whereas (−)-IV-*d* has Φ 200° and (−)-IV-d_2 has Φ 150°. These data suggest that the origin of the major difference in rotations of the substances lies in the larger steric requirement of H compared to D.[9] Thus, the dihedral angle about the C_2–C_3 bond should be slightly sensitive to the bulk of the attached groups, which are close to an eclipsed conformation due to the steric requirements of the five-membered ring fused to a benzene ring. The rotations of the substances are probably extremely sensitive to small changes in the dihedral angle, and therefore to substitution of hydrogen by deuterium in either the 2 or 3 position of the ketone. The large differences in rotations of the ketones indicate that in kinetic studies of optical changes of substances undergoing isotopic exchange at or near the asymmetric center, the differences in rotation of the deuterated and nondeuterated compounds should not be assumed to be identical without experimental verification.

Equilibration (I ⇄ II) of 3-*t*-Butyl-1-methylindene (I) and 1-*t*-Butyl-3-methylindene (II). The two indenes were equilibrated at 25° in tetrahydrofuran–*n*-propylamine at 48° in 90 mol % dimethyl sulfoxide–10 mol % methanol–triethylenediamine, and at 102° in *t*-butyl alcohol–triethylenediamine. Use of an internal standard in the vpc analyses of the equilibrium mixtures demonstrated the two olefins to be stable under the conditions of equilibration. With each set of experimental conditions, equilibrium was approached from both sides, and the sets of equilibrium constants obtained differed from one another by from a little under to a little over 1%. Table II (runs 1–6) records the conditions and results.

Although solvent and catalyst were different under the three sets of conditions, a three-point plot of log K (for I ⇄ II) against $1/T$ gave a good straight line, from which $\Delta H°$ and $\Delta S°$ were determined to be −0.6 kcal/mol and 2 eu. Since the two olefins are hydrocarbons of very similar rigid structures, probably their solvation energies are small and very similar to one another, which facts account for the linearity of the plot. The predominance of II at equilibrium probably

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[7] (a) D. J. Cram, *J. Amer. Chem. Soc.*, **74**, 2137 (1952); (b) D. J. Cram and B. Rickborn, *ibid.*, **83**, 2181 (1961); (c) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *ibid.*, **83**, 3688 (1961); (d) W. D. Kollmeyer and D. J. Cram, *ibid.*, **90**, 1779 (1968); (e) W. D. Kollmeyer, private communication; (f) W. Theilacker and H. S. Winkler, *Ber.*, **87**, 690 (1954); (g) R. D. Guthrie, D. A. Jaeger, and D. J. Cram, unpublished results; (h) D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967); (i) D. J. Cram, W. Nielson, and B. Rickborn, *ibid.*, **82**, 6415 (1960).

[8] A. C. Cope and D. M. Gale, *ibid.*, **85**, 3747 (1963).

[9] K. Mislow, R. Graeve, A. J. Gordon, and G. H. Wahl, Jr., *ibid.*, **86**, 1733 (1964), and references quoted therein.

Table III. 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				$k^a \times 10^5$, l./(mol sec)	I, %^{b}			II, %^{b}		
Run no.	Starting material	Solvent	Nature	Concn, *M*	Temp, °C	Time, hr		Obt	Exch^c	Rac	Obt	Exch^c	Rac
7	(−)-I-*h*^{d}	*t*-BuOD	$N(CH_2CH_2)_3N^e$	0.14	50	16	4.5	73.5	0.45	1.0 ± 2	26.5	0.35	1 ± 3
8	(−)-II-*h*	*t*-BuOD	$N(CH_2CH_2)_3N^e$	0.14	50	16	3.1	2.9			97.1	0	
9	(−)-I-*d*	*t*-BuOH	$N(CH_2CH_2)_3N$	0.17	50	26.5	1.5	81.1	2.7	0 ± 0.5	18.9	4.8	0 ± 0.5
10	(−)-I-*h*	$(CH_3)_2SO^f$	$N(CH_2CH_2)_3N^g$	0.10	25	0.83	100	76.0	2.1	2 ± 1	24.0	1.2	3 ± 1
11	(−)-I-*d*	$(CH_2)_4O$	*n*-$PrNH_2$	0.61	25	44	0.36	73.6^h	20.6	2 ± 1^i	26.4	94.9	0 ± 1
12	(±)-I-*d*	$(CH_2)_4O$	*n*-$PrNH_2$	0.61	25	13.3		96.0	4.1		4.0	89.1	
13	(−)-I-*h*	$(CH_2)_4O$	*n*-$PrND_2$	0.61	25	13.3	1.1	74.5	20.3	2 ± 1^j	25.5	35.8	1 ± 1
14	(±)-I-*h*	$(CH_2)_4O$	*n*-$PrND_2$	0.61	25	1.3		95.3	4.0		4.7	34.7	
15	(±)-II-*h*	$(CH_2)_4O$	*n*-$PrND_2$	0.61	25	13.3	0.84	2.5			97.5	0.1	
16	(±)-I-*h*	C_6H_6	$(CH_2)_5NH$	0.074	37	80	1.3	79			21		
17	(±)-I-*d*	C_6H_6	$(CH_2)_5NH$	0.10	37	7.5	0.41	99	1.9		1.0 ± 0.2	27.4	
18	(−)-I-*h*	C_6H_6	$(CH_2)_5ND$	0.10	37	115	1.1	67.1	9.1	0 ± 1	32.9	11.2	0 ± 1
19	(±)-I-*h*	C_6H_6	$(CH_2)_5ND$	0.10	37	3.0	1.1	99.0	0.76		1.0	13.4^k	
20	(±)-I-*d*	$(CH_2)_4O$	$(CH_2)_5NH$	0.10	25	7.0	1.4	96.9	6.0		3.1	56.1	

[a] k = observed one-point, second-order rate constant for isomerization ($k_i + k_{-i}$). [b] Runs (simulating runs 7 and 10) with internal standard (tetradecane) demonstrated that 99–100% could be accounted for. [c] ±0.5%. [d] 87% optically pure data corrected to 100% optical purity. [e] Solution was 0.0012 *M* in $N(CH_2CH_2)_3N^+HI^-$. [f] Solution was 1.0 *M* in *t*-BuOD. Control experiment demonstrated no isotopic exchange between two solvents. [g] Solution was 0.002 *M* in $N(CH_2CH_2)_3N^+HI^-$. [h] In a separate run with I-*h* in the same solvent–base solution, isomerization proceeded 53.2% in 20 hr. Thus, $(k_h/k_d)_i^{PrNH_2} \sim 5.7$. [i] For I-*d*, $PrNH_2$, $k_e/k_\alpha > 7.6$. [j] For I-*h*, $PrND_2$, $k_e/k_\alpha > 7.5$. [k] Calculated on analysis of a sample containing 36% of I. All other analyses carried out on separated I and II.

reflects the release of *peri*-nonbonded steric interactions in deeclipsing *t*-butyl and hydrogen *vs.* methyl and hydrogen.

Amine-Catalyzed Isomerizations of 3-*t*-Butyl-1-methylindene (I) to 1-*t*-Butyl-3-methylindene (II) and the Accompanying Isotopic Exchange and Configurational Modification Reactions. Table III records the results of runs 7–20 in which various amines were used to catalyze conversion of optically active I to II in the presence of a large isotopic reservoir of hydrogen of the type opposite to that in the 1 position of I (runs 7, 9–14, and 16–20). In runs 8 and 15, II was isomerized to I to the extent of 2–3%. The products were then isolated and quantitatively separated by vpc, and each isomer was submitted to the appropriate analysis (racemization or deuterium, neither, either, or both). Control runs established that 99–100% of the starting material could be accounted for after the runs were made. Although thermal isomerization also occurs,[10] a much higher temperature is required.

One-point, second-order rate constants for conversion of I and II to the equilibrium mixture in the various runs also are found in Table III. Although of very limited accuracy, comparisons of certain of these rate constants are useful.[11] For example, comparisons of *k*'s for runs 7 and 8 and for runs 13 and 15 indicate that I and II go to the equilibrium mixtures at somewhere near the same rates. The equilibrium constant lies well on the side of II, and in most runs the conversions of I → II were not carried past the 26% mark. Particularly in those carried only 1–5%, it is safe to assumed that within error and the generalizations derived from the data, II once formed does not further react. Furthermore, in reactions carried to 1–5% isomerization, secondary reactions of isotopically exchanged starting material are trivial.

In run 7, (−)-I-*h* in *t*-butyl alcohol-O-*d* was 26.5% isomerized by triethylenediamine in the presence of a 0.0012 *M* concentration of triethylenediamine–deuterium iodide salt. The product, (+)-II-*h*, proved to be only 0.35% isotopically exchanged and only 1 ± 3% racemized. In run 9, similar results were obtained with the deuterium label in the starting material and product rather than the medium. Isotopic exchange between the primary (amine salt) and secondary (*t*-butyl alcohol) isotopic reservoir was undoubtedly many powers of ten faster than that between the olefin and the reservoirs.[12] Thus, there was available to the alkylammonium carbanide intermediates, which must have been present at extremely low concentration, a comparatively large concentration of the alkylammonium ion of the opposite isotopic variety in the medium. In spite of this opportunity for cationic exchange, little occurred. Clearly, the product was formed with little or no racemization, and thus a suprafacial hydrogen ion migration catalyzed by amine has occurred with the near-exclusion of antarafacial processes. The same pattern of results is visible in run 10 carried out with the same amine and amine salt, but in dimethyl sulfoxide, 1.0 *M* in *t*-butyl alcohol-O-*d*. Even in this relatively polar solvent, isotopic exchange (1.2%) and racemization (3 ± 1%) in conversion of I to II were minimal. As very minor competing reactions, starting material (I) underwent isotopic exchange and racemization in runs 7, 9, and 10. No conclusions can be drawn about the stereochemical course of the exchange reaction of starting material in these runs because the analyses were insensitive at the low levels of conversion.

Use of *n*-propylamine in tetrahydrofuran in runs 11–15 produced a similar pattern of stereochemical results for the isomerization reaction (almost a completely suprafacial process), but extensive isotopic exchange occurred, both in starting material and product (runs

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(10) J. Almy and D. J. Cram, to be published.

(11) In other work, the kinetics of racemization and isotopic exchange in fluorenyl carbon acid systems catalyzed by tri-*n*-propylamine in *t*-butyl alcohol–tetrahydrofuran were found to be first order in carbon acid and first order in amine.[31] In similar reactions in tetrahydrofuran in which *n*-propylamine served as base, the isotopic exchange reactions tended to be first order in base but the racemization reactions approached second order in *n*-propylamine at 0.6 and became second order at higher concentrations.[3m]

(12) E. Grunwald, *J. Phys. Chem.*, 71, 1846 (1967), and references cited therein.

11 and 13). Thus, isotopic exchange occurred almost exclusively on the face of the intermediate allylic anion from which the protium or deuterium was abstracted by the amine. Isotopic exchange of deuterium for protium in production of II was more complete (95%) than in the reciprocal process of exchange of protium for deuterium (36%) (see runs 11 and 13). The isotopic exchange of starting material was an accompanying reaction, and $k_e/k_\alpha > 7.5$ in each run. Here k_e is the one-point rate constant for isotopic exchange, and k_α that for racemization. From a run which paralleled that of run 11, except that I-*h* was substituted for I-*d*, an isotope effect for the isomerization was estimated to be $k_H/k_D \sim 5.7$ (one-point rate constants).

In runs 17–19, piperidine served as base and benzene as solvent. In run 18 with (−)-I-*h* and $(CH_2)_5ND$ in which 33% isomerization occurred, recovered I and II were 0 ± 1% racemized, and again isotopic exchange and isomerization were exclusively suprafacial in character. Unlike the *n*-propylammonium ion which has three protons, the piperidinium has only two, and isotopic exchange in an ion pair involving the latter cation is the simpler process. In runs 17 and 19, isomerization was carried only 1%. From I-*d* and protonated piperidine was obtained II that was 27.4% protonated. From I-*h* and deuterated piperidine was obtained II that was 13.4% deuterated. Recovered I-*d* was 1.9% protonated and recovered I-*h* was 0.76% deuterated, respectively, in the two runs. Thus, replacement of deuterium at carbon by hydrogen *once the ion-pair stage is reached* seems to be a more facile process than replacement of hydrogen at carbon by deuterium. Of course, the reverse is true with respect to the nitrogen since the two processes are reciprocal. Run 20, carried out with piperidine in tetrahydrofuran, gave results that suggested that isotopic exchange was not qualitatively different in this solvent than in benzene.

Discussion

Extensive use of stereochemical and isotopic techniques has established that at least in nonpolar solvents, carbanions are ion paired with ammonium or metal cations.[3] From the changes in structural relationships between starting materials and products that occur as the nature of the cation and medium are changed, conclusions have been drawn about the structures of these ion-pair intermediates. The data of this paper provide detailed information about ion-pair structure, and particularly about ion-pair reorganization reactions.

1,3-Asymmetric Induction in Isomerization Reactions. The data of runs 7, 9, 10, 11, 13, and 18 (Table III) show that optically pure (−)-I gave 97–100% optically pure (+)-II. The relative configurations of (−)-I and (+)-II are such that the stereospecific proton transfer involved in the reaction occurred across a single face of the indenyl carbanion intermediate. This stereospecificity persisted to 97% when the isomerization took place in the most polar solvent used, dimethyl sulfoxide (run 10). Thus, in spite of extensive reorganizations of some of the alkylammonium ions (and probably of the solvent shell) in the ion-pair intermediates, recapture of protium (deuterium) by the indenyl carbanion takes place almost exclusively on one face of the carbanion. Thus, the pseudoallylic anion in effect underwent enough of a shuffle with respect to the alkylammonium ion to interchange the 1 and 3 positions, but not a rotation that would interchange the two faces of the anion.[13] Similar conclusions were drawn from the study of potassium *t*-butoxide isomerization of an open-chain azaallylic system.[3i]

Isotopic Exchange of Starting Material with Retention. In runs 7, 9, 10, 11, 13, and 18, starting material underwent extensive isotopic exchange in the 1 position with medium (0.5–21%) with little or no racemization. Minimum values for k_e/k_α (ratio of pseudo-first-order rate constants for exchange and racemization) for runs 11 and 13 with *n*-propylamine as base are 7.6 and 7.5. The isotopic labels were in different positions in the two runs, and although (−)-I-*h* isomerized about three times as fast as (−)-I-*d*, the isotopic exchange reactions of the two substrates both occurred with the same high retention of configuration within experimental error. As expected, isotopic exchange of starting material was greatest with the primary amine, next with the secondary amine, and least with the tertiary amine. This observation correlates with the fact that in the alkylammonium carbanide intermediates, the primary cations carry two, the secondary cations one, and the tertiary cations no exchangeable hydrogens. When tertiary amines are involved, exchange involves reactions with tertiary cations of the medium, and this process appears slow compared to the isomerization and collapse reactions. Prominent in the exchange data is the fact that more exchange occurs when deuterium is in the substrate and protium is in the solvent–base than when the placement of isotopes is reversed (runs 9 *vs.* 7; 11 *vs.* 13; and 17 *vs.* 19, respectively). These comparisons have been noted in a similar system[3b] and reflect the greater facility of proton (*vs.* deuteron) transfers from substrate to catalyst and from catalyst to substrate. A similar trend in the data also applies to the isomerization reaction, where intramolecular hydrogen transfer is a more efficient process than intramolecular deuterium transfer.

Isotopic Exchange that Accompanies Isomerization. The wide spread in the extent of isotopic exchange that accompanied production of II (0.35–94.9%) indicates that the mode of cation–solvent reorganization that accompanies rearrangement of the anion is sensitive to both the nature of the isotope in the medium and the structure of the amine catalyst. For example, in the reaction of I-*h* with $PrND_2$ in tetrahydrofuran (run 14) II was produced with only 35% exchange, whereas in that of I-*d* with $PrNH_2$ in the same medium (run 12) 89% exchange occurred. Although much less pronounced, a similar trend was observed when secondary and tertiary amines were employed.

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[13] Bergson, *et al.*,[4] was the first to postulate 1,3-asymmetric induction in the amine-catalyzed isomerization of optically active alkyl-substituted indene systems. Their extensive kinetic data on these systems provided strong support for this hypothesis. Our investigation differs from theirs in these respects. (1) We prepared the product of isomerization, determined its maximum rotation and configuration relative to that of starting material. (2) After partial isomerization, we isolated both starting material and product, separated them, and examined each for optical purity and isotopic content. (3) We carried out the isomerization, exchange, and stereochemical reactions with the positions of the isotopic label (substrate *vs.* medium) interchanged. (4) In most of our runs, an isotopic reservoir was available in the medium whose pK_a was the same (except for isotope effect) as the pK_a of the conjugate acid of the base used as catalyst. (5) We determined the equilibrium constant between starting material and product, and carried out many of our runs under conditions that the products once formed underwent negligible further reactions.

Collapse Ratios. The simplest mechanistic version of the isomerization and isotopic exchange reactions involves formation of a contact ion-pair intermediate that can collapse to either starting material or product without exchange, or can go to a second ion-pair intermediate of the opposite isotopic variety which collapses to isotopically exchanged starting material or product (Chart I). If the simple assumption is made that the collapse ratio of the ion-pair intermediate to starting material and to product (k_{-1}/k_{-2}) has no isotope effect ($k_{-1}/k_{-2} = k_{-4}/k_{-5}$), these collapse ratios can be calculated from the amounts of isotopic exchange of recovered starting material (I) *vs.* that of product (II). If the mechanism and assumptions are valid, the collapse ratio should be independent of whether I-*h* or I-*d* serves as starting material. When the isomerization was carried to only a few per cent as in runs 12, 14, 17, 19, and 20, no account needs to be taken of the secondary reactions of exchanged I or II in calculating the collapse ratios. When isomerization was carried to about 25% as in runs 11 and 13, collapse ratio calculations that take account of isomerization of exchanged starting material were made by a kinetic method previously reported.[14] In this calculation, isotope effects for the exchange reaction of I are required. However, collapse ratios calculated for runs 11 and 13 were shown to be relatively insensitive to assumed isotope effects for isotopic exchange of I between the values of 2 and 4, and the collapse ratios calculated for these runs agree fairly well with those calculated for runs 12 and 14 in which secondary reactions played little role. Table IV records the collapse ratios.

Chart I

$$\begin{tikzcd}
\text{I-}h + :\text{B} \arrow[r, shift left, "k_1"] & \text{carbanion}\cdots\text{HB} \arrow[l, shift left, "k_{-1}"] \arrow[r, shift left, "k_{-2}"] \arrow[d, shift right, "k_3"'] & \text{II-}h + :\text{B} \arrow[l, shift left, "k_2"] \\
\text{I-}d + :\text{B} \arrow[r, shift left, "k_4"] & \text{carbanion}\cdots\text{DB} \arrow[l, shift left, "k_{-4}"] \arrow[r, shift left, "k_{-5}"] \arrow[u, shift right, "k_{-3}"'] & \text{II-}d + :\text{B} \arrow[l, shift left, "k_5"]
\end{tikzcd}$$

Table IV. Collpase Ratios k_{-1}/k_{-2} for Ammonium Carbanide Ion Pair

Run no.	Isotope in I	Amine	% isomeriz[a]	k_{-1}/k_{-2} b	c	d
11	D	n-PrNH$_2$	26.4	0.6	1.1	0.86
12	D	n-PrNH$_2$	4.0	1.1 ± 0.06		
13	H	n-PrND$_2$	25.5	1.7	2.7	2.7
14	H	n-PrND$_2$	4.7	2.34 ± 0.10		
17	D	(CH$_2$)$_5$NH	1.0 ± 0.2	6.9 ± 2		
19	H	(CH$_2$)$_5$ND	1.0 ± 0.2	6.7 ± 2		

[a] Error ±0.2%; limits of error appearing in k_{-1}/k_{-2} are propagated from this error. [b] Collapse ratios calculated from deuterium analyses of I and II based on assumption indicated in text. [c] Calculated from exchange analysis of I + II by method of ref 14 assuming a $k_H/k_D = 4$ for ionization. [d] Calculated from exchange analysis of I + II by method of ref 14 assuming a $k_H/k_D = 2$ for ionization.

A number of generalizations emerge from the data. (1) When primary amine served as catalyst and isotopic reservoir, different collapse ratios were observed when the deuterium label was in substrate than when it was in the amine. Some of the assumptions that went into these calculations are clearly invalid. (2) When secondary amine served as catalyst and isotopic reservoir, within experimental error the collapse ratios are independent of whether the isotopic label was in the carbon acid or in the amine. (3) The collapse ratios favored starting material over product, particularly when secondary amine served as catalyst.

Mechanisms for Alkylammonium Carbanide Ion-Pair Reorganization Reactions. The above results indicate that four fast reactions of alkylammonium carbanide ion pairs occur simultaneously: (1) carbanion reorganization, but only on one of its two skeletal faces; (2) alkylammonium ion reorganization; (3) collapse to starting material; (4) collapse to product. These four reactions occur at rates much faster than ion-pair dissociation, metathesis, or reorganization that involves moving the alkylammonium ion from one to the other face of the indenyl anion.

Charge is largely concentrated at the 1 and 3 positions of the indenyl anion since distribution at the other positions involves dearomatization of the benzene ring. Hydrogen bonds of the alkylammonium ion to the carbanion are expected to be strongest at these sites. Two extreme detailed mechanisms are envisioned in Charts II and III. In the first, the alkylammonium ion hydrogen bonds at both the 1 and 3 positions at the same time. In its simplest form only one ion-pair intermediate would be generated, and this could collapse to either isotopically unexchanged starting material, or to only isotopically exchanged product when either primary or secondary amine carried an isotopic label different from that of the carbon acid. This mechanism in its simplest form does not account for the following facts. In all runs that involved primary or secondary amines, the starting material underwent partial isotopic exchange, and the product was partially formed without isotopic exchange. The mechanism of Chart II in its simplest form predicts no exchange of starting material and no nonexchanged product. Further, this mechanism cannot apply to the isomerization with tertiary amine, which has no hydrogen on nitrogen.

The mechanism of Chart III in its extreme form involves hydrogen bonding at only one site at a time, and mainly at the 1 and 3 positions (intermediates A and B). In this scheme at least two types of ion-pair intermediates are involved. When the amine is primary or secondary, alkylammonium ion reorganization without carbanide reorganization in either A or B is possible. In this reaction of the alkylammonium ion, the old hydrogen bond is broken and a new hydrogen bond is made in the same transition state, a process of lower energy than one involving complete breaking of the hydrogen bond. If the amine is wholly or partially dimerized as is likely at high concentrations in *n*-propylamine,[3m] this process might occur *via* a hydrogen transfer within the dimeric alkylammonium ion as envisioned in C → D + E.[15] If the base is monomeric as is probable with the secondary amine at low concentrations, this exchange of one hydrogen bond for

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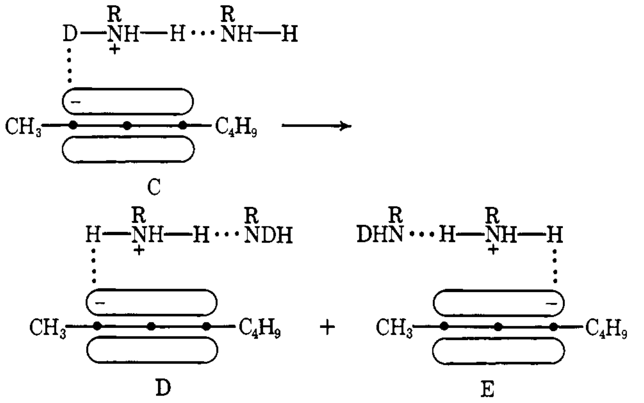
(14) D. J. Cram and D. H. Hunter, *J. Amer. Chem. Soc.*, **86**, 5478 (1964).

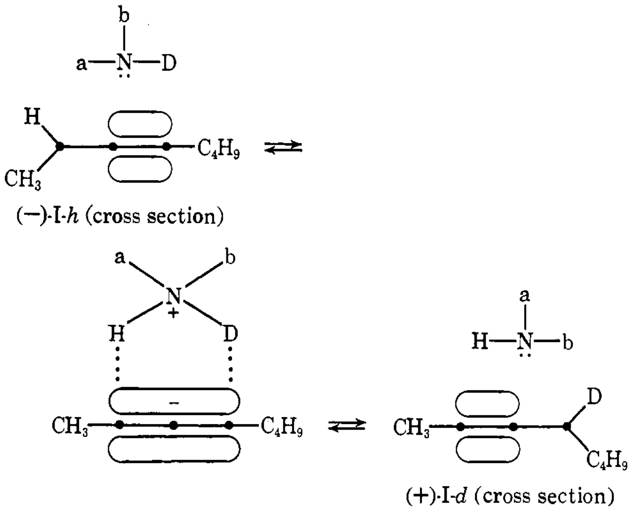
(15) Evidence for multiple or relayed proton transfer reactions has been reported: M. Cocivera, *ibid.*, **88**, 672 (1966).

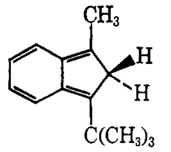
another in the same transition state probably occurs *via* a rotation of the dialkylammonium ion.[8f–h]



The carbanion reorganization involved in going from A to B (Chart III) involves a "conducted-tour mechanism" in which the hydrogen-bonded alkylammonium ion passes along the π cloud of the pseudoallylic anion from the 1 to the 3 position without rupture of the hydrogen bond, and with charge following charge. The species in which the 2 position is hydrogen bonded in an ion pair is probably an intermediate rather than a transition state, but is of much higher energy than either A or B and is not included in Chart III. Should such an intermediate containing a single isotope of hydrogen collapse to the covalent state, a tetraene with a plane of symmetry would be produced (VIII), and only racemic II could result. The fact that essentially only optically pure II was obtained from optically pure I indicates that such a path is little used.

Chart II





VIII

A possible modification of the mechanism of Chart III involves processes such as A-*d* ⇄ B-*h* and B-*d* ⇄ A-*h* by a tumbling process in which both ions of the ion pair undergo reorganization at once. Although no evidence excludes this possibility as a contributing mechanistic component, the data rule it out as a major pathway for the same reasons that the mechanism of Chart II is eliminated.

In Chart III, rate constants k_a, k_{-a}, etc. are assigned to each step of the mechanism. Initially, ionization rate constants k_a, k_d, k_f, and k_n undoubtedly are orders of magnitude lower valued than the other rate constants. The three rates that are observable experimentally are isomerization without exchange (k_x's), isomerism with exchange (k_y's), and exchange without isomerism (k_z's). Solution of this general scheme involves the expression of the steady-state concentrations of A-*h*, B-*h*, A-*d*, and B-*d* in terms of k_a, k_b, etc., and then the expression of $k_x{}^H$, $k_y{}^H$, etc. in terms of k_a, k_b, etc. Particularly desirable would be an expression for the relative rates of carbanion *vs.* alkylammonium ion reorganization (k_b/k_c) in terms of the observable rates, $k_x{}^H$, $k_y{}^H$, etc. Complete solution of this scheme is beyond the present investigation, but a simpler version is useful. If it is assumed that the isomerization rate constants (k_b, k_{-b}, etc.) are much higher valued than the collapse rate constant (k_{-a}, k_{-d}, etc.), then the equilibrium mixtures A-*h* ⇄ B-*h* and A-*d* ⇄ B-*d* in effect become a single kinetic entity. These simplifications reduce the mechanistic scheme of Chart III to that of Chart I. The fact that the collapse ratios were independent of isotope position in runs 17 and 19 (Table IV) with piperidine as base (the isomerizations were carried to only about 1%) is consistent with this simplified version of the mechanism of Chart III, and suggests that, indeed, isomerization is faster than collapse, and that the collapse ratio has no isotope effect.

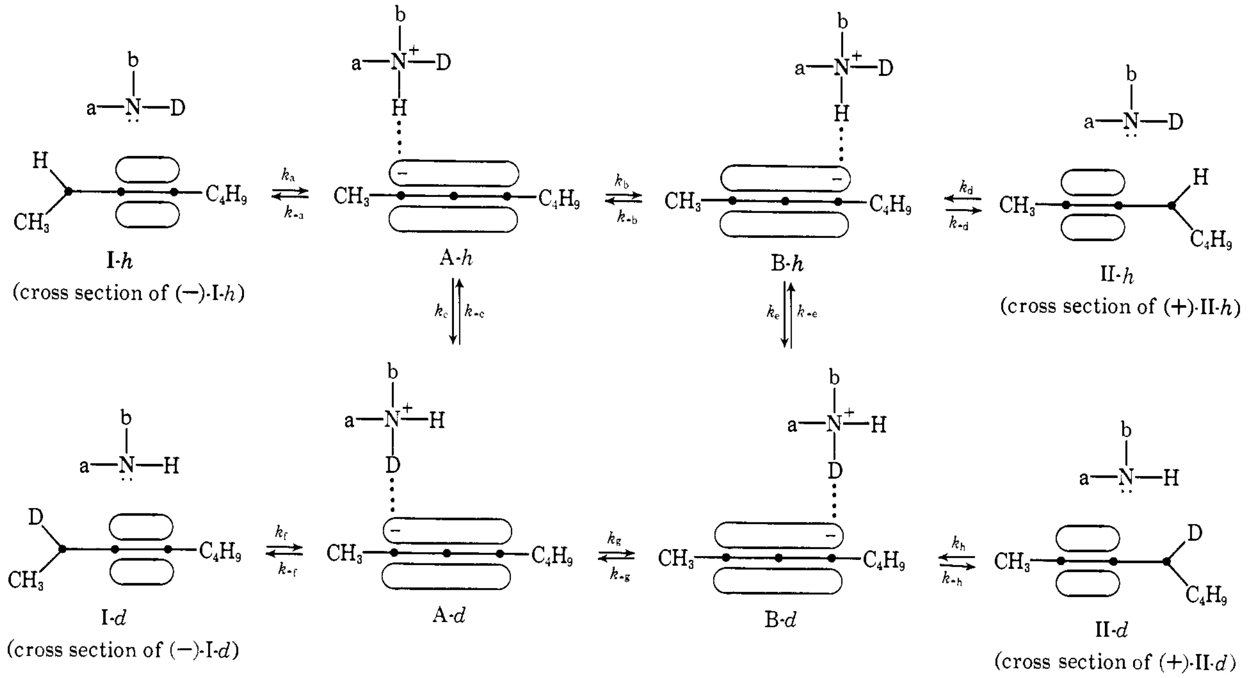
$\text{I-}h \xrightarrow{k_x{}^H} \text{II-}h$	isomerism without exchange	$\text{I-}d \xrightarrow{k_x{}^D} \text{II-}d$
$\text{I-}h \xrightarrow{k_y{}^H} \text{II-}d$	isomerism with exchange	$\text{I-}d \xrightarrow{k_y{}^D} \text{II-}h$
$\text{I-}h \xrightarrow{k_z{}^H} \text{I-}d$	exchange without isomerization	$\text{I-}d \xrightarrow{k_z{}^D} \text{I-}h$

With primary amine the collapse ratios clearly depend on the position of the isotopic label. Thus, in run 12 with I-*d* and *n*-$PrNH_2$ a collapse ratio of 1.1 was observed, whereas in run 14 with I-*h* and *n*-$PrND_2$, the value was 2.3. These results suggest that rate constants k_b, k_{-b}, k_g, and k_{-g} for proton conduction along the carbanion are not much higher valued than those for ion-pair collapse (k_{-a}, k_{-d}, k_{-f}, and k_{-h}) or alkylammonium ion reorganization (k_c, k_{-c}, k_e, or k_{-e}). This difference between behavior of primary and secondary amines is tentatively attributed to the probable difference in state of aggregation of the two amines in the reactions. Extensive kinetic studies based on the techniques reported here are required to test the hypothesis that arises from the qualitative observations of this investigation.

Experimental Section

General. All rotations were taken on a Perkin-Elmer Model 141 polarimeter. All nuclear magnetic resonance spectra were recorded with a Varian A-60 instrument. All mass spectral measurements were made on an AEI Model MS-9 mass spectrometer. Optical rotatory dispersion (ORD) curves were obtained on a Cary Model 60 spectropolarimeter in spectroquality cyclohexane; concentrations are reported in grams per 100 ml of solution. Anhydrous magnesium sulfate was uniformly used as drying agent.

Chart III



3-Phenyl-1-butanol-3-*d*.[16] All glassware was carefully cleaned, and extreme precautions were taken to dry all apparatus before use. To a 2-l., three-necked flask was added 36 g of lithium aluminum hydride under dry nitrogen, together with 500 ml of tetrahydrofuran freshly distilled from lithium aluminum hydride. The mixture was stirred under a positive pressure of nitrogen at −78°, and a solution of 100 g of *trans*-β-methylcinnamic acid, mp 98–98.5°, in 400 ml of tetrahydrofuran was added over a period of 1 hr. The reacting mixture turned a dark red. The temperature was allowed to rise to 25° over a period of 5 hr, then maintained at 25° for 12 hr, during which time the color changed from red to yellow to red. The flask was cooled to −10° and 90 ml of deuterium oxide (99.9% deuterium) was slowly added. The slurry was stirred at 25° for 7 hr, then 350 ml of cold 6 *N* sulfuric acid was added. The aqueous solution was extracted five times with ether. The combined organic layer was washed with brine, saturated sodium bicarbonate solution, and again with brine; after drying, the ether was evaporated, and the residue was distilled at 103° (4.5 mm) to give 81.4 g (87%) of 3-phenyl-1-butanol-3-*d*. Analysis of this material by vpc (5% *m*-phenyl ether on Fluoropak at 170°) indicated the compound to be 99.5% pure, and to have a retention time identical with that of authentic 3-phenyl-1-butanol.[5a] A sample of the major peak was collected and found to have 0.986 atom of D per molecule.[17] The nmr spectrum was consistent with complete loss of the proton at the benzyl position.

3-Deuterio-3-phenylbutyric Acid (III-*d*). To a stirred solution composed of 418 g of potassium diacid phosphate, 54 g of dipotassium acid phosphate, 396 g of potassium permanganate, and 2 l. of water was added 110 g of 3-phenyl-1-butanol-3-*d* in 440 ml of distilled *t*-butyl alcohol at 15° over 1.5 hr. After stirring for 48 hr at 15°, the excess permanganate was decomposed with 150 g of sodium sulfite, then enough 12 *N* sulfuric acid was added to dissolve the manganous dioxide. The oil which separated was extracted five times with ether. The extract was concentrated in order to expel sulfur dioxide. Ether was again added to 500 ml, and the solution was shaken twice with 1 l. of saturated sodium bicarbonate solution. The neutral organic layer, after washing with sodium bicarbonate solution and brine, was dried and concentrated to give 6.2 g of residue composed of 40% acetophenone and 60% of starting material as determined by vpc. The combined aqueous bicarbonate solution was extracted three times with ether, then acidified to pH 1 with 12 *N* sulfuric acid. The oil that separated was washed with brine and dried, and the ether was evaporated. The residue was distilled at 116° (0.8 mm) to give 92.4 g (77%) of 3-deuterio-3-phenylbutyric acid, 99.5% pure by vpc analysis (5% *m*-phenyl ether on Fluoropak at 200°). The retention time of the major component was identical with that of authentic 3-phenylbutyric acid.

Resolution of 3-Deuterio-3-phenylbutyric Acid [(−)-(*R*)-**III**-*d*] **and 3-Phenylbutyric Acid** [(−)-(*R*)-**III**-*h*]. Resolution of (−)-(*R*)-III-*d* and (−)-(*R*)-III-*h* was accomplished *via* their respective menthyl esters according to the method of Rupe.[18a] Maximum rotations of (−)-(*R*)-III-*d* are α^{25}_{546} −69.4°, α^{25}_{589} −57.8° (neat, 1 dm) and $[\alpha]^{25}_{546}$ −69.1°, $[\alpha]^{25}_{589}$ −57.6° (*c* 2.7, benzene). Maximum rotations of (−)-(*R*)-III-*h* are α^{25}_{546} −68.8°, α^{25}_{589} −57.3° (neat, 1 dm) and $[\alpha]^{25}_{546}$ −68.9, $[\alpha]^{25}_{589}$ −57.6° (*c* 2.7, benzene).[5] To ensure the optical purity of (−)-(*R*)-III-*h*, 3.1 g of the acid of the maximum rotation was mixed with a solution of 12 ml of water, 12 ml of ethanol, and 2.4 g of α-phenylethylamine whose rotations were: α^{25}_{546} +49.4°, α^{25}_{589} +38.0° (neat, 1 dm) and $[\alpha]^{25}_{589}$ +40.5°.[7f] The amine salt of (−)-III-*h* precipitated and weighed 5.5 g on collection. This salt was recrystallized three times from ethanol. The last crystallization yielded 1.5 g salt which was then added to 6 ml of 1.8 *N* potassium carbonate. This aqueous mixture was extracted three times with equal volumes of chloroform, and the organic layers were discarded. The aqueous layer was then acidified with 12 *N* sulfuric acid and extracted again with chloroform. The acidic organic phase was washed with brine, dried, and evaporated under 12-mm pressure to yield an oil which was flash distilled at 80° under 0.1-mm pressure to yield 0.9 g of acid (−)-III-*h* whose rotations were: $[\alpha]^{25}_{546}$ −68.9°, $[\alpha]^{25}_{589}$ −57.4° (*c* 2.7, benzene). Thus, the rotations of (−)-III-*h* are unchanged after repeated crystallizations of salts of two different resolving agents.

Optically Pure (−)-3-Deuterio-3-methylindanone ((−)-(*R*)-**IV**-*d*) **and (−)-3-Methylindanone** ((−)-(*R*)-**IV**-*h*). To a 1-l. polyethylene bottle was added 31.5 g of (−)-III-*h*, α^{25}_{589} −57.3°, α^{25}_{546} −68.8° (neat, 1 dm), and 200 ml of anhydrous liquid hydrogen fluoride at 0°. The red-brown solution was maintained at 25° for 36 hr, then the hydrogen fluoride was evaporated with a stream of dry nitrogen. To the residue was added slowly 500 ml of saturated sodium bicarbonate solution, and the oil was extracted three times with 75 ml of ether. The organic layer was, in turn, washed with 50 ml of 0.5 *N* sodium hydroxide solutions and 50 ml of brine. The solvent was dried and evaporated, and the residue was distilled at 60° (0.3 mm) to give 26.0 g (93%) of (−)-(*R*)-IV-*h*, a pale yellow oil, α^{25}_{589} −4.08°, α^{25}_{546} −7.41° (neat, 1 dm). The ring closure of (−)-III-*d*, α^{25}_{589} −57.9°, α^{25}_{546} −69.6° (neat, 1 dm), under the same conditions gave (−)-IV-*d*, α^{25}_{589} −3.33°, α^{25}_{546} −6.30° (neat, 1 dm). An ORD spectrum of (−)-IV-*h* (*c* 0.052) appears in Figure 2.

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(16) For the preparation of 3-phenyl-1-butanol-3-*d* and 3-deuterio-3-phenylbutyric acid, we thank Dr. R. T. Uyeda.

(17) Combustion and falling-drop technique performed by J. Németh, Urbana, Ill.

(18) (a) H. Rupe, *Ann.*, **369**, 323 (1909); (b) large-scale resolution of III-*h* and III-*d* was performed by Dr. R. T. Uyeda.

Optically Pure 1-Methyl-3-*t*-butylindene ((−)-(*R*)-I-*h*) and 1-Deuterio-1-methyl-3-*t*-butylindene ((−)-(*R*)-I-*d*).[19] The reagent *t*-butylmagnesium chloride was made with 23.0 g of magnesium and 100 ml of *t*-butyl chloride in 700 ml of ether.[20] The Grignard reagent was cooled to −130° using a pentane slush for 3 hr, during which time 26 g (0.178 *M*) of (−)-3-methylindanone, (−)-IV-*h*, α^{25}_{589} −4.08°, α^{25}_{546} − 7.41° (neat, 1 dm), was added with stirring. After the addition was complete, the reaction was stirred for an additional 1.5 hr while warming slowly. The pentane bath was removed, and the reaction stirred for an additional 2.5 hr. The reaction mixture was poured on a mixture of 500 g of ice and 50 g of ammonium chloride. The organic phase was separated and the basic solution was extracted three times with 200 ml of ether. The combined organic layers were washed with 500 ml of brine and dried, and the solvent was evaporated under 20-mm pressure. Without purification the residual oil (35 g) was combined with 500 ml of 1 *M* aqueous oxalic acid and stirred vigorously under nitrogen for 48 hr. The oil was extracted three times with 200 ml of ether. The combined organic phase was, in turn, washed with 250 ml of brine, 250 ml of saturated sodium bicarbonate solution, and again with 250 ml of brine. The solvent was dried and evaporated, and the residue was placed on 500 g of silica gel and eluted with pentane to give 13 g of a pale yellow oil which was distilled at 70° (0.3 mm). The distillate, 11.5 g (35% from the ketone), was a colorless oil, α^{25}_{589} −109.7° and α^{25}_{546} −132.4° (neat, 1 dm). The nmr spectrum of (−)- and racemic I-*h* closely fitted the data published for the compound.[4] The ORD curve of optically pure I-*h* appears in Figure 2; *c* 0.0013 between 210 and 280 mμ, *c* 0.030 between 280 and 550 mμ.

Under identical conditions (−)-3-deuterio-3-methylindanone, (−)-IV-*d*, α^{25}_{589} −3.33°, α^{25}_{546} −6.30° (neat, 1 dm), gave (−)-1-deuterio-1-methyl-3-*t*-butylindene, α^{25}_{589} −110.7°, α^{25}_{546} −133.8° (neat, 1 dm). Mass spectral analysis at 20-eV ionization potential showed that the peak at *m/e* 186 was 0.7% of the height of *m/e* 187. Thus, the compound was at least 99.3% deuterated. Both (−)-I-*h* and (−)-I-*d* exhibited only one peak on analytical vpc; mixtures of I and II were clearly identifiable under the same analytical conditions (see below).

Resolution of (+)- and (−)-3-*t*-Butylhydrocinnamic Acid ((+)- and (−)-V-*h*). The brucine salt of the acid was obtained by dissolving 18.5 g of racemic 3-*t*-butylhydrocinnamic acid[6] (mp 114–116°) and 42.0 g of brucine in 140 ml of hot methanol. The solution was cooled slowly to −20° for 48 hr and 17.0 g of salt was collected and recrystallized. The amounts of salt recovered at different stages of the resolution and the rotations of the corresponding acids were: first crystallization, 17 g, $[\alpha]^{25}_{546}$ +15.9°; third, 8.3 g, $[\alpha]^{25}_{546}$ +17.3°; fourth, 4.0 g, $[\alpha]^{25}_{546}$ +24.3°; fifth, 1.7 g, $[\alpha]^{25}_{546}$ +24.5° (*c* 2, $CHCl_3$, all rotations). A small amount of the fifth crop was again recrystallized from methanol, with no improvement in the rotation of the corresponding acid. The fifth crop was then hydrolyzed under the same procedure used for 3-phenylbutyric acid. The free acid was then recrystallized twice from cyclohexane to give the optically pure acid, $[\alpha]^{25}_{546}$ +26.0°, $[\alpha]^{25}_{589}$ +22.2° (*c* 2, $CHCl_3$), mp 94.5–95.0°. Further crystallization from cyclohexane failed to improve the rotation or the melting point.

The (−)-enantiomer of 3-*t*-butylhydrocinnamic acid, (−)-V-*h*, was obtained from its cinchonidine salt. Mother liquors from the brucine resolution were hydrolyzed, and the partially active (−)-acid was dissolved with an equimolar amount of cinchonidine. The progress of the resolution was followed as before. The fifth crystallization yielded a salt whose melting point (161–161.5°) was no higher than that of the fourth. The salt was then hydrolyzed, and the corresponding acid, $[\alpha]^{25}_{546}$ −24.1° (*c* 2, $CHCl_3$), was crystallized twice from cyclohexane, $[\alpha]^{25}_{546}$ −26.4° and $[\alpha]^{25}_{569}$ −22.4° (*c* 2, $CHCl_3$), mp 94.5–95.5°.

(−)-3-*t*-Butylindanone ((−)-VI-*h*). To 4.5 g of optically pure (+)-3-*t*-butylhydrocinnamic acid, $[\alpha]^{25}_{546}$ +26.0°, $[\alpha]^{25}_{589}$ +22.2° (*c* 2, $CHCl_3$), in a polyethylene bottle was added 50 ml of liquid anhydrous hydrofluoric acid at 0°. The reaction was left at room temperature for 3 days, then an additional 50 ml of acid was added, and the reaction left for 2 more days. Isolation and purification procedures were identical with those of (−)-3-methylindanone. The final product upon distillation at 70° (0.2 mm) was a pale yellow solid, 4.0 g (94%), mp 38–39°, $[\alpha]^{25}_{589}$ −34.7°, $[\alpha]^{25}_{546}$ −42.8°, $[\alpha]^{25}_{365}$ +53.1° (*c* 0.56, $CHCl_3$). An ORD spectrum of this product is shown in Figure 1; *c* 0.24, 550–300 mμ; *c* 0.019, 300–250 mμ.

Racemic 3-*t*-butylindanone, whose preparation from racemic 3-*t*-butylhydrocinnamic acid was identical with the one described above, was distilled to give a pale yellow oil, whose melting point was below room temperature.[6]

Optically Pure and Racemic 3-Methyl-1-*t*-butylindene ((+)- and (±)-II-*h*). Gaseous methyl bromide was bubbled through a stirred mixture of 2.0 g of magnesium in 40 ml of ether. After the reaction was complete, a solution of 4.0 g of 3-*t*-butylindanone, $[\alpha]^{25}_{589}$ −34.7°, in 80 ml of ether was added slowly, and the reaction mixture was stirred at room temperature for 10 hr. The isolation and dehydration procedures were identical with those used for synthesis of 1-methyl-3-*t*-butylindene, I-*h*, above. The crude product of dehydration, a yellow oil, was purified as before by elution chromatography. A vpc analysis of the pentane-soluble fraction showed the presence of a minor peak, varying in size from 3 to 8% of the reaction product, probably the exocyclic isomer, VII, of the desired product. The major fraction was obtained pure by preparative vpc on a 10 ft × $^3/_8$ in. column packed with 17% silicon nitrile on 60–80 mesh Firebrick at 192° on a Wilkins Autoprep gas chromatograph. The pure isomer was obtained as a white solid, 2.8 g (71%), mp 59–60°, $[\alpha]^{25}_{589}$ +126°, $[\alpha]^{25}_{546}$ +151° (*c* 0.7, $CHCl_3$). Crystallization from cyclohexane failed to raise the melting point. An ORD spectrum of this product is displayed in Figure 2; *c* 0.0012, 210–280 mμ; *c* 0.0012, 280–550 mμ.

Racemic 3-methyl-1-*t*-butylindene, II-*h*, was obtained in the same manner, mp 33–34°. *Anal.* Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.36; H, 9.71. The nmr spectra of (+)- and (±)-II-*h* closely fitted the data published[4b] for the unanalyzed compound.

(−)-2,2-Dideuterio-3-methylindanone ((−)-IV-*d*₂). To a mixture of 1 g of anhydrous potassium carbonate[8] (dried at 120° for 3 days) in 10 ml of deuterium oxide was added 0.50 g of 99% optically pure 3-methyl-1-indanone, $[\alpha]^{25}_{589}$ −16.6°, $[\alpha]^{25}_{546}$ −21.9° (*c* 2.0, $CHCl_3$). The mixture was refluxed under nitrogen for 2 hr, then cooled and extracted three times with chloroform. The combined organic layers were washed twice with water and dried, and the solvent was evaporated. The residue was reexchanged twice and then distilled at 60° (0.3 mm) to give 0.48 g (96%) of a colorless oil, which exhibited one peak on analytical vpc. The nmr spectrum of this product showed 66% exchange at the methylene region. No measurable deuteration occurred after the second exchange. To ascertain the effect of the exchanging conditions on the optical stability of the compound, 0.3 g of the exchanged material was reexchanged in water as before. The purified product had <1% deuterium by nmr and showed no change in rotation: $[\alpha]^{25}_{589}$ −16.6°, $[\alpha]^{25}_{546}$ −21.9° (*c* 2, $CHCl_3$).

Isomerization, Exchange, and Racemization Runs. Experiments above 37° (runs 1–4 and 7–9) were made in sealed tubes. The starting olefin was measured into clean, dry test tubes that were drawn out to facilitate sealing. Nitrogen was continually passed through while the solvent–base mixture was added. The tubes were sealed under nitrogen, warmed, shaken momentarily, and placed in the appropriate temperature bath. The experiments at 25 and 37° were run under nitrogen in clean, dry glass-stoppered flasks. For the isolation of the reacted mixture for isomeric analysis by analytical vpc (see below), 0.2 ml of the reacting mixture was quenched in 2 ml of 0.25 *N* hydrochloric acid. Spectroquality grade carbon tetrachloride (0.2 ml) was added, the mixture was shaken, and the organic layer was transferred to a test tube containing 2 ml of 2% aqueous saturated sodium chloride. The mixture was shaken again and the organic layer removed. The carbon tetrachloride solution was injected (1–2 μl) for analysis by vpc (see below).

For the isolation of the reacted mixture for preparative vpc separation of I and II, the reaction mixture was poured into a separatory funnel containing 0.25 *N* hydrochloric acid and shaken three times with pentane. The organic layers were combined and shaken twice with brine, and the pentane was evaporated.

Separation of Indenes I and II by Vapor Phase Chromatography. Analyses of indene mixtures were carried out on a Wilkins Model 204 gas chromatograph with flame ionization detectors. The column used in runs 1–8 and 10–15 was 10 ft × $^1/_8$ in. containing 4.0% of 4-methyl-4-nitropimelonitrile, 1.0% of 2,4,5,7-tetranitrofluorenone, and 0.5% of Atpet 80 on 100–120 mesh acid-washed dimethylsilanized Chromosorb G. This column had to be replaced frequently because of excessive column substrate bleeding. A

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(19) Preliminary work on this reaction was performed by Dr. R. T. Uyeda.

(20) S. V. Putnambeker and E. A. Zoellner, "Organic Synthesis," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1947, p 524. The glass equipment was dried with a flame before use. The reaction was easily started by addition of a reacting mixture of 0.5 ml of ethylene dibromide, 0.5 g of magnesium, and 3 ml of ether.

similar column packed with 4% Apiezon L on Chromosorb W was as effective in the separation of I and II, did not bleed at the temperature used, and was therefore employed in runs 9 and 16–20. The injection block, column oven, and detector oven were *ca.* 130, 100, and 130°, respectively. Nitrogen, the carrier gas, was controlled at ~25 ml/min.

Preparative separations of indenes I and II for individual analysis by polarimetry and mass spectrometry were made on a Perkin-Elmer Model 154 vapor fractometer. The column used in runs 1–8 and 10–15 was 6 ft × 0.25 in. packed with 20% of 3-methyl-3-nitropimelonitrile and 3% of 2,4,5,7-tetranitrofluorenone on 60–80 Firebrick at 110°. For runs 9 and 16–20, a column of 10% Apiezon L on 60–80 Firebrick was used. Helium was used as a carrier gas. Glass tube collectors were tightly fitted into a silicon rubber septum cut to accommodate the collector and the exit port of the chromatograph. With the exception of run 19, each isomer was rechromatographed until it was at least 99.5% pure by analytical vpc.

Optical Activity Measurements on I and II. Optical rotations of the olefins were measured on a Perkin-Elmer Model 141 automatic polarimeter. Because of the continuous liquid phase bleeding of the preparative vpc column, the olefin samples were chromatographed subsequently on silica gel columns eluted with pentane. The hydrocarbon fraction was evaporated for at least 15 min under 18-mm pressure. Further evaporation failed to change the rotation of the olefin.

Samples (7–10 mg) for the polarimetric solutions were weighed on a Cahn Model G electrobalance to three significant figures. The weighing pan was transferred to a volumetric flask and rinsed with reagent grade chloroform to the calibration mark. The solution was transferred to a clean, dry, 1-dm polarimeter cell, and readings were recorded at 589, 578, 546, and 436 mμ. The specific rotations of each wavelength were compared individually to rotations of optically pure I and II measured by the same procedure. The per cent of optical purity for each sample was the average of the percentage of optical purity over the four wavelengths.

Exchange Measurements of I and II. The extent of hydrogen–deuterium exchange of each isomer was measured by mass spectrometry on samples of about 0.5 mg. The heated inlet system was maintained at 120° and 20-eV ionization potential was used. The extent of exchange was calculated from the ratio of parent peak heights of *m/e* 187 to 186. A device (decapot) to reduce signal strength was connected to the machine output. Both peaks were displayed on a Leeds and Northrup Model G recorder; the smaller peak was adjusted to almost full scale and the larger signal reduced by a known amount to fit the chart scale. Each peak was scanned at a slow, fixed rate, and a line connecting the tops of the two small peaks was measured at the time of the large peak scan, together with the height of the large peak. The peak height comparison and the decapot adjustment produced the *m/e* 187 to 186 peak height ratio (*R*).

In the mass spectrum of an unexchanged sample of I-*h* or II-*h* naturally occurring ^{13}C and D account for $R = 0.154$;[21] the fraction of deuterated indene in a partially exchanged sample is

$$\frac{R - 0.154}{1 + (R - 0.154)}$$

The peak height of *m/e* 186 was *ca.* 0.5% of the parent peak for the fully deuterated indene. Therefore, contributions of deuterated material to *m/e* 186 were not considered. Mixtures of I-*h* and I-*d* were weighed and analyzed. Values from mass spectral analysis were consistently within 0.5% of the actual values.

Internal Standard Runs. A mixture of tetradecane (distilled from Matheson Coleman and Bell, Reagent Grade) and I was prepared and its composition determined by the analytical vpc procedure (see above). The mixture was used in runs 1 and 2 and in tubes duplicating conditions of runs 7 and 10. The composition of the indene mixture and tetradecane was again determined by analytical vpc. Comparison of the composition of indene–tetradecane mixtures showed 99–100% recovery of indenes. The reasonable assumption was made that tetradecane remains stable under the reaction conditions.

Solvents and Bases. The purification of *t*-butyl alcohol,[3k] tetrahydrofuran,[3k] benzene,[3k] and *n*-propylamine,[3g] and the preparation of triethylenediamine[3d] and *t*-butyl alcohol-O-*d*[14] have been described previously. Dimethyl sulfoxide (Baker Reagent) was distilled from sodium amide and stored over molecular sieves. Triethylenediamine was sublimed twice at 50° (0.3 mm) and stored under desiccation, mp 159–160°. Piperidine (Abbott Laboratories) was distilled from barium oxide after reflux for 2 hr. The 106–106.5° fraction was collected on molecular sieves.

Piperidine-N-*d*. To 50 ml of deuterium oxide was added 30 ml of piperidine and one drop of 18 *N* sulfuric acid. The solution was shaken and then extracted three times with ether. The ether solution was evaporated and the residue shaken again with acidic deuterium oxide. After five exchanges the ether solution was dried, the filtered solution was evaporated, and the exchanged amine distilled as before. The 106–107° fraction showed 99.5% exchange by nmr; yield: 10 g (33% over-all).

***n*-Propylamine-N-d_2.** To 95 g of *n*-propylamine was added 80 g of deuterium oxide containing a trace of deuterium chloride. The partially exchanged amine was distilled through a 12-in. column of packed helicies. The fraction distilling at 48° weighed 80 g (85%) and was reexchanged with fresh deuterium oxide. After the sixth exchange and distillation, the nmr analysis showed roughly 98% exchange. Since the signal for the N protons (τ 8.9) coincided with the complex multiplet (τ 8.1–9.2) for the ethyl protons, the exchangeable proton could not be separated and integrated individually. However, in a spectrum of 300 mg of the compound and 26 mg of 5.80 *N* deuterium acetate in deuterium oxide, the free proton signal was well separated and showed 98.5% exchange.

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[21] J. K. Beynon and A. E. Williams, "Mass and Abundance Tables for Use in Mass Spectrometry," Elsiever Publishing Co., New York, N. Y., 1963, p 54.