at 1098 cm$^{-1}$, which appeared in IV-$h$ but was absent in IV-$d$, and base line at 1028 cm$^{-1}$ was measured on a Perkin-Elmer Model 421 dual-grating spectrophotometer with the following adjustments: slit program, 2 × 1000; amplifier gain, 5; attenuator speed, 700; scan speed, 30 cm$^{-1}$/min; suppression, 0; scale, IX; source current, 0.36 A. Under these conditions $\Delta$abs was reproducible to ±0.004 absorbance unit for 100% IV-$h$ and ±0.001 unit for 90.8% IV-$d$.

The standards which had not been chromatographed gave a linear plot of 100 × abs/weight of sample in milligrams against per cent H in which no point was located more than 1% H from the line. The chromatographed standards gave a similar plot in which all points but one were located within 3% H of a straight line. The two plots had the same slope but different intercepts; the values of 100 × $\Delta$abs/mg for chromatographed material averaged about 0.11 unit higher than those for unchromatographed material. This shift in base line for chromatographed material was probably due to residue from evaporation of 30–50 ml of ether.

Unknown samples from runs 5–13 were analyzed by the procedure used for chromatographed standards. Deuterium contents were determined by interpolation from a calibration plot of chromatographed standards made immediately before unknown samples were analyzed. The per cent exchange results for runs 8, 9, and 11 were obtained from one analysis, while those for runs 5, 7, 10, 12, and 13 are average values for analysis of two independently chromatographed samples. Results of pairs of independent determinations differed by 1–4% except for run 12 where they differed by 10% H.

**Relative Reactivities of Fluorene Compounds.** The relative racemization rates of (+)-I-$h$ and (+)-IV-$h$ in methanol-O-$d$ with potas-

Table V. Racemization Rates of Fluorene Compounds in Tetrahydrofuran with $n$-Propylamine at 24.9°

| Compound | | Amine | | $k_3$, l.$^2$ |
| Nature | Concn, $M$ | concn, $M$ | $k_1$, sec$^{-1}$ | mol$^{-2}$ sec$^{-1}$ |
|---|---|---|---|---|
| (−)-IV-$d$ | 0.032 | 0.801 | 2.09 × 10$^{-5}$ | 3.25 × 10$^{-5}$ |
| (−)-II-$d$ | 0.033 | 0.780 | 7.44 × 10$^{-4}$ | 1.22 × 10$^{-3}$ |
| (−)-III-$d$ | 0.034 | 0.819 | 1.97 × 10$^{-3}$ | 2.94 × 10$^{-3}$ |
| (−)-V-$d$ | 0.036 | 0.797 | 1.14 × 10$^{-2}$ | 1.79 × 10$^{-2}$ |

sium methoxide were calculated from second-order rate constants in Table IV and from those reported previously.[3] Only the relative racemization rates of (−)-II-$d$, (−)-III-$d$, and (−)-V-$d$ were determined specially for the comparisons in Table II. Data for these racemization rates are reported in Table V for $n$-propylamine catalysis in tetrahydrofuran. The procedure used was identical with that reported elsewhere[6b] for racemization of (+)-IV-$h$. Solutions were prepared at 25° and quickly transferred to a thermostated polarimeter cell. Because the half-life of racemization of (−)-V-$d$ was about 1 min, for its rate the temperature was probably 25.0 ± 1.0°. Even an error of 5° in temperature would not qualitatively affect the relative rate of (−)-V-$d$ because of the very low enthalpy of activation.[6b] At least eight points over one to three half-lives were taken in each run. If racemizations of V, II, and III were not third order, the results in Table II would not be greatly affected because of the narrow range of $n$-propylamine concentrations used.

<br>

## Electrophilic Substitution at Saturated Carbon. XXXIX. Kinetics of Isoracemization of a Fluorenyl Carbon Acid[1]

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**Abstract:** The kinetics of tri-$n$-propylamine-catalyzed isotopic exchange and of racemization of (−)-2-(N,N-dimethylcarboxamido)-7-nitro-9-methylfluorene-9-$d$ ((−)-V-$d$) in $t$-butyl alcohol–tetrahydrofuran 20:80 by volume were studied. The racemization reaction was first order in carbon acid over a concentration range of 0.0084 to 0.101 $M$. The changes in second-order rate constant for racemization as the amine concentration varied from 0.0168 to 1.08 $M$ and from 0.0729 to 1.07 $M$ for exchange were small enough that both reactions are properly considered first order in amine. The rate constant for exchange ($k_e$) decreased by a factor of 3 as the amine concentration was increased by a factor of 16. The rate constant for racemization decreased by 30% as the amine concentration was increased by a factor of 16. These trends are attributed to the change of dielectric constant of the medium as the amine concentration increased. The activation parameters for isotopic exchange were $\Delta H^{\pm} = 7.1 \pm 0.9$ kcal/mol and $\Delta S^{\pm} = -54 \pm 4$ eu, and for racemization were $\Delta H^{\pm} = 10.5 \pm 0.5$ kcal/mol and $\Delta S^{\pm} = -39 \pm 2$ eu. Values of $k_e/k_\alpha$ ranged from a low of 0.10 at 10 mol % amine to a high of 0.22 at 0.6 mol % amine concentration. Concentrations of tri-$n$-propylammonium iodide or tetra-$n$-butylammonium iodide of 0.0001 $M$ had no effect on $k_e/k_\alpha$ values (~0.1), but concentrations of 0.03 $M$ of either salt produced values of unity. The observed isoracemization (intramolecular) is interpreted as occurring through a series of contact ion pairs by a conducted tour mechanism. The slower isotopic exchange is interpreted as involving reaction of solvent-separated ion pairs with solvent. The increase in the isotopic exchange rate relative to racemization when salts are added is interpreted in terms of salt catalyzing the formation of solvent separated from contact ion pairs.

T he previous paper of this series reported the results of a survey of the stereochemistry of base-catalyzed hydrogen–deuterium exchange of five carbon acids derived from 9-methylfluorene (I–V). The technique involved determination of $k_e/k_\alpha$ values (ratios of one-point rate constants for isotopic exchange of carbon acids with medium to those for racemization).[2] In $t$-butyl

alcohol–tri-$n$-propylamine, (−)-I-$d$ gave $k_e/k_\alpha = 5.7$, whereas in the same medium II–IV gave $k_e/k_\alpha$ values of about 0.1. In 4:1 by volume $t$-butyl alcohol–tetrahydrofuran with tri-$n$-propylamine, (+)-V-$d$ also gave $k_e/k_\alpha \sim 0.1$.[2] The difference in behavior of the systems was interpreted in terms of charge distribution effects of the substituent and its position on the carbanion. Greater localization of negative charge at C-9 led to exchange with retention of configuration ($k_e/k_\alpha > 1$) as was observed with I. Greater delocalization of nega-

(1) This research was sponsored by the U. S. Army Research Office, Durham, N. C. The authors extend their thanks.

(2) D. J. Cram, W. T. Ford, and L. Gosser, *J. Am. Chem. Soc.*, **90**, 2598 (1968).

Table I. Rate Constants for Racemization and Isotopic Exchange of $(-)$-V-$d$ in Tetrahydrofuran–$t$-Butyl Alcohol[a] with Tri-$n$-propylamine

| Run | Concn of V, $M$ | Concn of $Pr_3N$, $M$ | $T$, °C[b] | % reacn followed | No. of pts | $10^6 k_1$, sec$^{-1}$ | $10^5 k_2$, l. mol$^{-1}$ sec$^{-1}$ |
|---|---|---|---|---|---|---|---|
| | | | Racemization | | | | |
| 1[c,d] | 0.101 | 0.0168 | 24.81 | 45 | 16 | 5.01 ± 0.04 | 29.8 ± 1.0 |
| 2 | 0.0333 | 0.0745 | 24.81 | 60 | 26 | 22.1 ± 0.1 | 29.7 ± 0.5 |
| 3 | 0.0329 | 0.0774 | 24.80 | 60 | 24 | 22.2 ± 0.1 | 28.7 ± 0.5 |
| 4 | 0.101 | 0.261 | 24.83 | 65 | 23 | 72.5 ± 0.1 | 27.8 ± 0.8 |
| 5 | 0.0333 | 0.273 | 24.78 | 65 | 26 | 73.1 ± 0.2 | 26.8 ± 0.9 |
| 6 | 0.0084 | 0.261 | 24.82 | 77 | 27 | 64.1 ± 0.2 | 24.5 ± 0.3 |
| 7[d] | 0.0342 | 1.07 | 24.81 | 85 | 27 | 228 ± 2 | 21.3 ± 0.6 |
| 8[c,d] | 0.101 | 1.08 | 24.81 | 93 | 27 | 237 ± 1 | 22.0 ± 0.7 |
| 9 | 0.0358 | 0.0529 | 50.10 | 80 | 7 | 66.8 ± 1.2 | 126 ± 4 |
| 10 | 0.0516 | 0.103 | 50.15 | 60 | 8 | 128 ± 8 | 125 ± 9 |
| 11 | 0.0484 | 0.120 | 75.86 | 81 | 7 | 541 ± 14 | 451 ± 16 |
| | | | Hydrogen–Deuterium Exchange | | | | |
| 12 | 0.0341 | 0.0729 | 24.88 | 87 | 7 | 4.77 ± 0.19 | 6.55 ± 0.27 |
| 13 | 0.0348 | 0.268 | 24.87 | 87 | 8 | 15.2 ± 0.6 | 5.68 ± 0.34 |
| 14 | 0.0855 | 1.06 | 24.82 | 63 | 7 | 20.2 ± 0.8 | 1.90 ± 0.10 |
| 15 | 0.101 | 1.07 | 24.81 | 87 | 7 | 23.6 ± 0.5 | 2.19 ± 0.12 |
| 16 | 0.0358 | 0.0529 | 50.10 | 75 | 7 | 9.7 ± 0.8 | 18.3 ± 1.6 |

[a] Tetrahydrofuran, four volumes, $t$-butyl alcohol, one volume before mixing at 25°. No corrections were made for volume changes at 50 and 75°. [b] ±0.05°. [c] These runs were followed on a Zeiss polarimeter. All others were followed on a Perkin-Elmer Model 141 polarimeter. [d] Base concentrations in these runs were determined by one titration. In all others, at least three were used.

tive charge onto the heteroatom of the functional group led to intramolecular racemization or *isoracemization* ($k_e/k_\alpha < 0.5$). A conducted-tour mechanism for proton conduction from the front to the back face of the fluo-



I, X = CON(CH₃)₂
II, X = CN
III, X = NO₂

IV

V
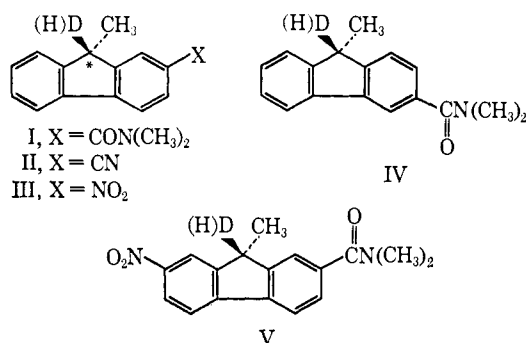
renyl anion around the hydrogen-bonding sites of the heteroatom was proposed to explain this result. Systems I, IV, and V were chosen for detailed kinetic examination, V because its acidity makes it particularly amenable to kinetic measurements, and I and IV because of their isomeric relationship. This paper reports the results obtained for V, and the next for I and IV.[3]

## Kinetics

**Kinetic Order.** First- and second-order rate constants for racemization and exchange of $(-)$-V-$d$ in tetrahydrofuran–$t$-butyl alcohol 80:20 by volume with tri-$n$-propylamine are reported in Table I. First-order rate constants with their standard deviations were calculated by a least-squares computer program. Second-order rate constants were calculated by dividing first-order constants by base concentrations. Errors reported in the second-order rate constants were calculated by the method of total differentials using the reported errors in first-order constants, an estimated error of ±1% for base concentrations determined by three titrations, and an estimated error of ±3% for base concentrations determined by one titration.

(3) W. T. Ford and D. J. Cram, *J. Am. Chem. Soc.*, **90**, 2612 (1968).

The changes in second-order rate constants as the amine concentration varied from 0.0168 to 1.08 $M$ for racemization, and from 0.0729 to 1.07 $M$ for exchange, were small enough that both reactions are properly considered first order in amine. Racemization was first order in substrate concentration over a 0.0084 to 0.010 $M$ range. It is assumed that exchange was also first order in substrate. This appears reasonable because the second-order exchange rate constants decreased with increased base and substrate concentration. Any significant contribution from higher order dependence on substrate concentration would cause the opposite trend in the data.

**Activation Parameters.** Activation parameters for the racemization and exchange reactions are reported in Table II. These values are averages of several calculations. The 25° rate constants used in the calculations were obtained from plots of second-order rate constants against base concentrations. Limits of error were calculated by the method of total differentials from relative errors in the second-order rate constants of Table I.

Table II. Activation Parameters for Racemization and Exchange of $(-)$-V-$d$ in Tetrahydrofuran and $t$-Butyl Alcohol with Tri-$n$-propylamine

| Reaction | $\Delta H^\ddagger$, kcal/mol | $\Delta S^\ddagger$, cal/deg mol |
|---|---|---|
| Exchange | 7.1 ± 0.9 | −54 ± 4 |
| Racemization | 10.5 ± 0.5 | −39 ± 2 |

**Medium Effects on Rates.** Variations of $k_e/k_\alpha$ values for $(-)$-V-$d$ with medium composition and temperature are listed in Table III. Stereospecificity increased as the tri-$n$-propylamine content of the medium increased. This effect might be predicted, because the dielectric constant of tri-$n$-propylamine ($D^{20} = 2.277$) is considerably lower than those of tetrahydrofuran ($D^{25} = 7.39$) and $t$-butyl alcohol ($D^{26} = 12.27$).[4] Since dielectric constants usually decrease

(4) "Landolt-Börnstein Tabellen," Vol. 6, Springer-Verlag, Berlin, 1959, pp 634, 635, 652.

Table III. Temperature and Medium Effects on Isoracemization of (−)-V-d

| Runs | T, °C | Pr₃N, mol % | t-BuOH, mol % | $k_e/k_\alpha$ |
|---|---|---|---|---|
| 2, 3, 12 | 25 | 0.6 | 17.6 | 0.22 |
| 4, 5, 13 | 25 | 2.3 | 17.3 | 0.21 |
| 7, 8, 14, 15 | 25 | 10.0 | 16.0 | 0.10 |
| 9, 16 | 50 | 0.4 | 17.7 | 0.15 |

Table IV. Effect of Added Salts on Isoracemization of 2-(N,N-Dimethylamido)-9-methyl-7-nitrofluorene (V)[a]

| Run | Carbon acid Nature | Concn, M | Salt Nature | Concn, M | Time, hr | % exch | % rac | $k_e/k_\alpha$ |
|---|---|---|---|---|---|---|---|---|
| 17 | (+)-V-d | 0.014 | Pr₃NHI | 0.0001 | 2.0 | 11 | 72 | 0.1 |
| 18[b] | (+)-V-h | 0.014 | Pr₃NDI | 0.030 | 0.3 | 44 | 40 | 1 |
| 19 | (+)-V-d | 0.014 | Bu₄NI | 0.0001 | 2.0 | 25 | 93 | 0.1 |
| 20 | (+)-V-d | 0.014 | Bu₄NI | 0.0010 | 1.0 | 25 | 51 | 0.4 |
| 21 | (−)-V-d | 0.026 | Bu₄NI | 0.0050 | 1.0 | 49 | 63 | 0.7 |
| 22 | (−)-V-d | 0.026 | Bu₄NI | 0.010 | 0.5 | 32 | 43 | 0.7 |
| 23 | (−)-V-d | 0.026 | Bu₄NI | 0.020 | 0.3 | 24 | 31 | 0.7 |
| 24 | (−)-V-d | 0.026 | Bu₄NI | 0.030 | 0.2 | 13 | 13 | 1 |
| 25 | (+)-V-d | 0.014 | Bu₄NI | 0.030 | 0.2 | 52 | 51 | 1 |

[a] All runs were made with 0.30 M n-Pr₃N in tetrahydrofuran, 1.5 M in t-butyl alcohol at 40°. [b] t-Butyl alcohol-O-d, 0.99 atom of deuterium per molecule was used in place of t-butyl alcohol-O-h.

with increasing temperature, the lower $k_e/k_\alpha$ value at 50° than at 25° in the same medium might also be anticipated. The data of Table III indicate that second-order rate constants for both racemization and exchange decreased as the amine concentration increased. Isotopic exchange was more sensitive than racemization to medium changes at 25°. Thus, a decrease in isotopic exchange rate by a factor of about 3 accompanied an increase by a factor of 16 in the amine concentration (runs 12 and 14). The decrease in racemization rate was only about 33% when the amine concentration was increased by a factor of 16 (runs 1 and 8).

Changes in the relative amounts of t-butyl alcohol and amine in the medium could also be responsible for the variation in second-order rate constants. In a low dielectric medium where t-butyl alcohol molecules outnumber amine molecules by 7:1 or more, as they did in all runs containing 0.27 M or less amine, each amine molecule may have been hydrogen bonded to a t-butyl alcohol molecule. Consequently, whenever an amine abstracted a deuteron from the substrate, an alcohol most likely was located near the newly formed ion pair. If an amine–alcohol pair were the active base, the racemization and exchange rates would also be first order in t-butyl alcohol, a possibility that is compatible with but not proven by the available data. Decreased medium polarity, or specific involvement of an alcohol molecule, or both, can explain the decreases in second-order racemization and exchange rates with increased amine concentration.

**Effect of Added Salts on Isoracemization.** Prior to this investigation isoracemization of carbon acids had been reported with three compounds: nitroamide V,[2,5a,6] 2-phenylbutyronitrile,[5b,6] and 3,3,3-triphenyl-2-methyl-propionitrile.[6] Racemization without exchange also was observed when carbon acid IV was treated with triethylamine in tetrahydrofuran at 145°,[7] but it was not defined as isoracemization because no source of exchangeable hydrogen was present in the medium to ensure that intramolecular rather than intermolecular racemization had occurred.

Results that qualitatively show the effect of added tri-n-propylammonium iodide and tetra-n-butylammonium iodide on $k_e/k_\alpha$ values (determined from one-point rate constants) for tri-n-propylamine-catalyzed isoracemization of V appear in Table IV. Comparison of runs 17 and 18 with runs 19, 24, and 25 demonstrates that the effects of the two salts are identical. Runs 19–25 indicate that $10^{-4}$ M noncommon ion salt had little effect on $k_e/k_\alpha$, and that gradual increases in salt concentration to 0.03 M eliminated the stereospecificity.

Run 17 carried out in the presence of $10^{-4}$ M tri-n-propylammonium iodide provided an isotopic reservoir of essentially the same p$K_a$ as the ion formed by amine abstraction of deuterium from the carbon acid. However, since (+)-V-d was 0.014 M, the reservoir would be quickly flooded with deuterium unless isotopic exchange between the tri-n-propylammonium iodide and the t-butyl alcohol (1.5 M) were very fast compared to the rate of accumulation of isotope from the carbon acid in the salt. Others[8] have found that the rate of proton exchange between trimethylammonium bromide and trimethylamine in t-butyl alcohol at 35° was first order in both amine and salt with a second-order rate constant of 5.3 × $10^5$ l./mol⁻¹ sec⁻¹. After temperature and concentration corrections were made, their rate of exchange was $10^6$ times faster than the rate of exchange of (+)-V-d in run 17. A one-point isotopic exchange rate for carbon acid I with tri-n-propylamine as catalyst indicates that the change in solvent from tetrahydrofuran–t-butyl alcohol to pure t-butyl alcohol would decrease the rate by a factor of about 20.[7] Very likely, the steric difference between trimethylamine and tri-n-propylamine and a hydrogen isotope effect should provide rate changes small compared to the ~$10^7$ difference in rates between carbon acid isotopic exchange and t-butyl alcohol–trimethylamine isotopic exchange. Clearly, any depletion in the isotopic reservoir of tri-n-propylammonium iodide of run 17 would be essentially instantaneously replenished from the much larger t-butyl alcohol isotopic reservoir.

The use of tri-n-propylammonium iodide as a proton reservoir in run 17 also depends on the concentration of the salt ($10^{-4}$ M) exceeding or being comparable to a possible equilibrium concentration of tri-n-propylammonium-N-d ions formed from carbon acid and the amine. An estimate of a possible equilibrium concentration is made as follows.

The p$K_a$ of carbon acid V was estimated to be not far from 15 by the following rough experiment. A 0.02 M solution of V in methanol, which was 0.6 M in potassium methoxide, gave a deep purple color that was immediately discharged upon addition of acid. Thus, a substantial amount of carbanion was present. Carbon acids I–IV gave no such color under these conditions. The basic medium has an H₋ function of 13.67.[9] If it is

(5) (a) D. J. Cram and L. Gosser, J. Am. Chem. Soc., 86, 2950 (1964); (b) D. J. Cram and L. Gosser, ibid., 86, 5457 (1964).
(6) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 98–103.
(7) D. J. Cram and L. Gosser, J. Am. Chem. Soc., 86, 5445 (1964).
(8) (a) M. Cocivera, ibid., 88, 672 (1966); (b) M. Cocivera and E. Grunwald, ibid., 87, 2070 (1965).
(9) K. Bowden, Chem. Rev., 66, 119 (1966).

assumed that a $2 \times 10^{-4}$ $M$ solution of the fluorenyl carbanion is visibly colored, then eq 1 indicates that a compound with a $pK_a$ of less than 15.7 would be visible in this medium. Therefore, V has a $pK_a$ of less than 15.7 and I–IV of more than 15.7.

$$H_- = pK_a - \log([HA]/[A^-]) \qquad (1)$$

If $t$-butyl alcohol has a $pK_a$ of about 19,[10] carbon acid V about 15, and tri-$n$-propylammonium ion about 10.8,[11] and if the ammonium carbanide ion pairs were completely dissociated, the equilibrium concentration of tri-$n$-propylammonium-N-$d$ would be $10^{-4}$ $M$, or comparable to the added salt. Thus, there seems little doubt the $k_e/k_\alpha$ values reflect an *intramolecular* rather than *intermolecular* racemization process. This conclusion is greatly strengthened by the facts that tri-$n$-propylammonium iodide and tetra-$n$-butylammonium iodide have essentially the same effects on $k_e/k_\alpha$.

## Discussion

Isoracemization, the intramolecular transfer of hydrogen or deuterium from the front to the back face of the fluorene system, cannot be a concerted reaction. The acidic nature of V coupled with the facts that the reaction is first order in carbon acid and in amine indicate that the reaction must involve fluorenide anions as intermediates. These anions are intrinsically planar, and any departure of $k_e/k_\alpha$ values from unity require that at least partially the anions be produced and consumed in an asymmetric environment. Asymmetric ion pairing and solvation are structural features that can provide such an asymmetric environment.

**General Ion Pair Mechanism for Racemization and Isotopic Exchange.** By its very nature, isoracemization must occur through ion-pair intermediates. Isotopic exchange could in principle occur either exclusively through ion-pair intermediates, exclusively through dissociated ions, or by blends of these extremes. If exchange occurred *via* dissociated ions, the addition of tri-$n$-propylammonium iodide should lower the $k_e/k_\alpha$ value by common ion depression of the exchange rate. The increase of $k_e/k_\alpha$ to 1.0 at 0.3 $M$ salt concentration indicates that if common ion rate depression ever existed, it was hidden by a large positive salt effect. The fact that the response of $k_e/k_\alpha$ values to the common ion and noncommon ion salt were the same also points to the same conclusion.

Treatment of (−)-2-(N,N-dimethylcarboxamido)-9-methylfluorene-9-$d$ ((−)-I-$d$) with tri-$n$-propylamine in $t$-butyl alcohol gave isotopic exchange with retention of configuration ($k_e/k_\alpha$ = 5.8).[7] This value decreased to 3.1 when the reaction was carried out in the presence of 0.4$M$ tri-$n$-propylammonium acetate. Isotopic exchange of (−)-I-$d$ with retention must have occurred *via* ion pairs, which to some extent added salt intercepted. All of these facts strongly support the conclusion that isotopic exchange of nitro amide V also occurs through ion-pair reactions, not through dissociated ions.
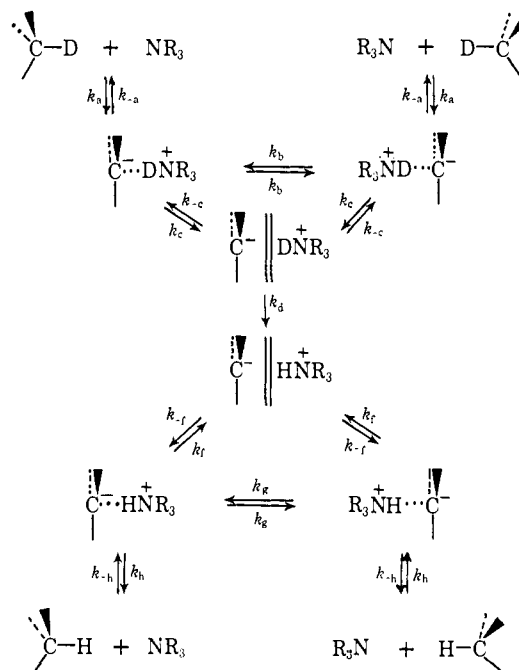
Spectroscopic and conductometric measurements of ether solutions of fluorenyllithium, -sodium, and -cesium provided good evidence for the existence of two types of fluorenide ion pairs, which are referred to as contact and

solvent-separated ion pairs.[12,13] The concentration of solvent-separated ion pairs decreased and the concentration of contact ion pairs increased when the dielectric constant of the solvent was lowered either by increasing temperature in a single solvent or by changing solvents. The data of Table III with nitro amide V demonstrate that $k_e/k_\alpha$ values decreased when the dielectric constant of the medium was decreased by the same two methods. This analogy coupled with the other results on both I and V suggest that isoracemization occurs through contact ion pairs and isotopic exchange through solvent-separated ion pairs.

Other comparisons are relevant. Further work by others[14] demonstrated that solvent-separated ion pairs were much more reactive than contact ion pairs in abstraction of protons from 1,2- and 3,4-benzofluorene. With fluorenylsodium they calculated an enthalpy of −7 kcal/mol and an entropy of −33 eu for conversion of the contact ion pair to the solvent-separated ion pair.[12b] In the present investigation, $\Delta H_e^{\ddagger} - \Delta H_\alpha^{\ddagger} = -3.4$ kcal/mol and $\Delta S_e^{\ddagger} - \Delta S_\alpha^{\ddagger} = -15$ eu (Table II). The similarity between our $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ values and those obtained for conversion of contact to solvent-separated ion pairs suggests that our transition state for racemization resembles a contact ion pair, and that for exchange, a solvent-separated ion pair.

A mechanistic scheme involving the two types of ion pairs is depicted in Chart I. The exchange step (rate constant $k_d$) is considered irreversible because, once deuterium reaches the solvent, it rapidly becomes randomized in a 20- to 50-fold excess of exchangeable protons. In Chart I the ion pairs that exchange are

Chart I. Mechanism for Net Isoracemization of (−)-V-$d$

(10) Reference 6, p 4.

(11) R. G. Pearson and D. A. Vogelsong, *J. Am. Chem. Soc.*, **80**, 1038, 1048 (1958).

(12) (a) T. E. Hogen-Esch and J. Smid, *ibid.*, **88**, 307 (1966); (b) T. E. Hogen-Esch and J. Smid, *ibid.*, **88**, 318 (1966).

(13) Ion pairs that contain carbonium ions had previously been found to exist in two possible states, *intimate* and *solvent separated*. This work has been reviewed: S. Winstein, B. Appel, R. Baker, and A. Diaz, Special Publication No. 19, The Chemical Society, London, 1965, pp 109–130.

(14) T. E. Hogen-Esch and J. Smid, *J. Am. Chem. Soc.*, **89**, 2764 (1967).

formulated as symmetric. While that may not be correct, its adoption simplifies the mechanism and does not qualitatively alter its explanation. If hydrogen-deuterium exchange of a solvent-separated ion pair is much faster than its collapse to a contact ion pair ($k_d \gg k_{-c}$), application of the steady-state approximation to the scheme gives eq 2 and 3 which relate $k_e$

$$k_e = \frac{k_a k_c}{k_{-a} + k_c} \qquad (2)$$

$$k_\alpha = k_e + \frac{2k_a k_{-a} k_b}{(k_{-a} + k_c)(k_{-a} + k_c + 2k_b)} \qquad (3)$$

and $k_\alpha$ to the rate constants of Chart I. Equation 3 contains terms for exchange with total racemization and isoracemization. Because of the observed isoracemization, the interconversion of asymmetric ion pairs (rate constant $k_b$) must be substantially faster than formation of solvent-separated ion pairs (rate constant $k_c$). The difference in p$K_a$ values of (−)-V-$d$ and tri-$n$-propylammonium ion (∼4) requires that $k_{-a} \gg k_a$. Two extreme approximations can be made to simplify eq 2 and 3. The assumption $k_{-a} \ll k_c < k_b$ leads to the erroneous conclusion that $k_e \sim k_\alpha \sim k_a$. On the other hand, the assumption $k_{-a} \gg k_b > k_c$ leads to eq 4. A $k_e/k_\alpha$ value of 0.1 would then correspond to

$$k_e/k_\alpha = k_c/(k_c + 2k_b) \qquad (4)$$

$k_b = 4.5k_c$. The rate of hydrogen transfer from ammonium ion to carbanion must be at least of the same order of magnitude as the rate of conversion of a contact to a solvent-separated ion pair, and is probably much greater.

**Participation of $t$-Butyl Alcohol in Isotopic Exchange.** The kinetic data for isoracemization of (−)-V-$d$ are compatible with a mechanism in which one $t$-butyl alcohol molecule remains associated with the tri-$n$-propylamine catalyst throughout the racemization and exchange processes, making both third-order reactions, monomolecular in alcohol as well as in (−)-V-$d$ and in amine. Alternatively, the alcohol might not participate until the exchange step (rate constant $k_d$), in which case both reactions would be independent of alcohol concentration. If solvent participated in formation of the exchange ion pair, the participant was probably the most polar solvent component, $t$-butyl alcohol. A mechanism for participation of its hydroxyl group in the exchange process is shown in Chart II. Comparable intermolecular proton transfers involving a molecule each of amine, alcohol, and ammonium ion are reported to occur at rates slightly slower than diffusion controlled.[15] In Chart II the mechanism for alcohol
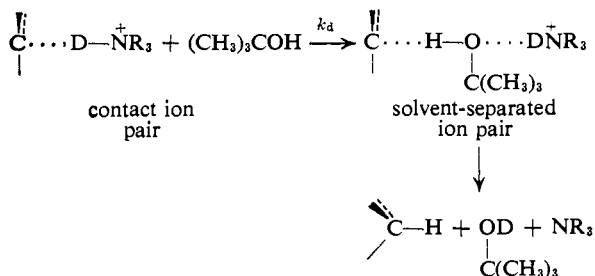
participation is drawn to give exchange with retention irreversibly. The only effect this specific explanation for exchange would have on the more general mechanism in Chart II would be to require that $k_b \gg k_c$ to account for the net isoracemization that was observed.

**Salt Effects on Relative Rates of Racemization and Exchange.** The data of Table IV indicate that concentrations of 0.03 $M$ tri-$n$-propylammonium iodide or tetra-$n$-butylammonium iodide are enough to increase $k_e/k_\alpha$ values from ∼0.1 to 1.0. In terms of the mechanism of Chart I, at zero or $10^{-4}$ $M$ salt concentration, $k_b$(isoracemization) > $k_c$(exchange), whereas at 0.03 $M$ salt concentration, $k_c \gg k_b$. In other words, the salt increased the value of $k_c$ (and probably $k_a$) much more than that of $k_b$. In the study of (+)-2-phenyl-butyronitrile-2-$d$ in tetrahydrofuran, 1.5 $M$ in $t$-butyl alcohol and 0.60 $M$ in tri-$n$-propylamine, $k_e/k_\alpha$ values of 0.05 were observed.[5b] Addition of 0.10 $M$ tetra-$n$-butylammonium iodide increased $k_e/k_\alpha$ to only 0.09, whereas addition of 0.10 $M$ tri-$n$-propylammonium iodide to only 0.19.[5b] Apparently, the sensitivity of $k_e/k_\alpha$ values to salt depends on carbanion structure. Addition of salts in the reaction of (−)-2-(N,N-dimethylcarboxamido)-9-methylfluorene-9-$d$[7] ((−)-IV-$d$) with $n$-propylamine reduced the amount of retention observed, but the effect was small compared to the salt effects observed in this study.

**Conducted-Tour Mechanism.** A special ion-pair mechanism for isoracemization of (−)-V-$d$ with tri-$n$-propylamine in tetrahydrofuran and $t$-butyl alcohol is the *conducted-tour mechanism*. In this mechanism, the amine rapidly conducts the proton to many sites in the carbanion by shifts of the C$^-\cdots$H–N$^+$ hydrogen bond. When the ammonium ion becomes associated with a heteroatom on a substituent, as in structure A, the ion pair in effect possesses a plane of symmetry and racemization results. The conducted-tour mechanism



A
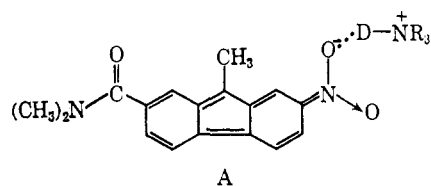
involves a whole spectrum of contact ion pairs in which charge follows charge. The one where the cation is hydrogen bonded to the 9 position would be most stable. Exchange would still occur *via* solvent-separated ion pairs in this special mechanism. All of the evidence supporting the more general ion pair mechanism of Chart I also applies to the structurally oriented conducted-tour mechanism.

**Chart II.** Mechanism for $t$-Butyl Alcohol Participation in Isotopic Exchange



### Experimental Section

**Racemization Kinetics at 25°.** Run 3 will serve as a typical example. In a 5-ml volumetric flask were placed 0.075 ml of tri-$n$-propylamine, 0.98 ml of $t$-butyl alcohol, and sufficient tetrahydrofuran to reach the 5.00-ml line. Carbon acid[2] (−)-V-$d$, 9.8 mg, was weighed into a 1-ml volumetric flask. After equilibrating 1 hr at 25°, 1 ml of the basic solution was transferred to the flask containing the substrate. As soon as the substrate dissolved, the solution was transferred to a thermostated 1-dm polarimeter cell.

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

The change in rotation was observed with a Perkin-Elmer Model 141 polarimeter at 436 mμ. The resulting data, shown in Table V, gave a computed least-squares rate constant of $2.22 \pm 0.01 \times 10^{-5}$ sec$^{-1}$.

Table V. Racemization at 24.80° of 0.0329 $M$ $(-)$-V-$d$ with 0.774 $M$ Tri-$n$-propylamine in Tetrahydrofuran-$t$-Butyl Alcohol 80:20 by Volume (Run 3)

| Time, min | $\alpha_{436}$, deg | Time, min | $\alpha_{436}$, deg |
|---|---|---|---|
| 6.2 | −1.155 | 294.0 | −0.796 |
| 29.0 | −1.125 | 309.4 | −0.779 |
| 51.0 | −1.095 | 343.4 | −0.746 |
| 73.0 | −1.065 | 381.4 | −0.709 |
| 95.8 | −1.035 | 423.4 | −0.670 |
| 117.8 | −1.005 | 458.0 | −0.639 |
| 137.8 | −0.979 | 491.0 | −0.611 |
| 157.8 | −0.953 | 523.5 | −0.585 |
| 179.0 | −0.928 | 563.9 | −0.556 |
| 206.0 | −0.895 | 599.9 | −0.528 |
| 230.9 | −0.864 | 643.9 | −0.498 |
| 260.9 | −0.837 | 687.9 | −0.467 |

All glassware used in this work, except the polarimeter cell, was cleaned with chromic acid, rinsed with water and dilute ammonium hydroxide solution, and dried in an oven at 110° for at least 12 hr. The polarimeter cell was thoroughly rinsed with solvent and purged with dry nitrogen before use. In a control experiment addition of 0.001 $M$ water to the basic solution caused the rate of racemization to increase noticeably with time. Base concentration was determined by titration of three 1-ml aliquots of the remaining basic solution to the brom cresol green end point with standard hydrochloric acid. In representative cases aliquots recovered from the polarimeter cell were found to have the same titer as the solvent containing no substrate. Runs 1 and 8 were followed on a Zeiss polarimeter at 546 mμ.

**Racemization Kinetics at 50 and 75°.** Run 9 was made concurrently with run 16. The solvent was prepared by adding 0.25 ml of tri-$n$-propylamine, 4.95 ml of $t$-butyl alcohol, and tetrahydrofuran to the mark of a 25-ml volumetric flask. No corrections were made for concentration changes due to solvent expansion at 50 and 75°. Substrate $(-)$-V-$d$, 212 mg, was weighed into a 25-ml flask, and 20.0 ml of the basic solution were added. After mixing, aliquots of 0.6 ml were pipetted into each of five constricted test tubes, and aliquots of 2.2 ml were pipetted into each of seven constricted test tubes. The tubes were cooled to −78°, sealed at less than 5 mm, and placed in a 50° bath. Three of the tubes were used as exchange points in run 16 as well as rotation points in this run. At appropriate times they were quenched at −78° and opened. After melting, 0.50 ml of homogeneous solution was transferred with a 500-μl Hamilton syringe fitted with Chaney adapter to a 1-ml volumetric flask containing 0.4 ml of a solution of 1 $N$ hydrochloric acid in 90% ethanol. The resulting acidic solution was diluted to the mark with more ethanolic hydrochloric acid. Rotations were taken in a 1-dm polarimeter cell at 436 mμ and

25°. Base concentration was determined by the method described for 25° runs.

**Run 11.** In a 10-ml volumetric flask were placed 1.96 ml of $t$-butyl alcohol, 0.15 ml of tri-$n$-propylamine, and sufficient tetrahydrofuran to reach the 10-ml mark. Into a 5-ml volumetric flask was weighed 72.1 mg of $(-)$-V-$h$. After mixing, 5 ml of the solvent was added to the substrate. The substrate solution was mixed and transferred in 0.6-ml aliquots to each of seven constricted test tubes. After they were cooled to −78° and sealed at less than 1 mm, the tubes were transferred to a 75° bath. Tubes were withdrawn at appropriate times and quenched at −78°. The remainder of the procedure was identical with run 9.

**Exchange Kinetics at 25°.** Run 14 serves as a typical example. In a 10-ml volumetric flask were placed 254 mg of carbon acid[2] $(-)$-V-$d$ and less than 8 ml of solvent. The solution of substrate, 2.0 ml of tri-$n$-propylamine, and more solvent were added to the 10-ml mark. Aliquots of 1 ml were withdrawn with a syringe from the septum-capped flask and quenched in 4 ml of 2 $N$ hydrochloric acid. The recovery, chromatographic purification, and deuterium analysis of V by infrared spectrophotometry were carried out by the method described in the previous paper[2] for one-point runs. The resulting data appear in Table VI. A least-squares rate constant of $2.02 \pm 0.08 \times 10^{-5}$ sec$^{-1}$ was computed. Base concentration was determined by titration of 1-ml aliquots of each of the last three points. The substrate in each titrated aliquot was recovered and purified for deuterium analysis.

Table VI. Exchange at 24.82° of 0.0855 $M$ $(-)$-V-$d$ with 1.07 $M$ Tri-$n$-propylamine in Tetrahydrofuran-$t$-Butyl Alcohol 80:20 by Volume (Run 14)

| Time, min | % D | Time, min | % D |
|---|---|---|---|
| 83 | 92 | 564 | 53 |
| 163 | 88 | 696 | 47 |
| 260 | 80 | 823 | 38 |
| 409 | 67 | | |

**Exchange Kinetics at 50°.** Run 16 was made concurrently with run 9. Each of the tubes containing 2.2 ml of solution was quenched and opened at −78°. As soon as the contents melted, they were added to 4 ml of 2 $N$ hydrochloric acid. The substrate was recovered, purified, and analyzed as described for run 14. Recovered V had no extraneous peaks in its infrared spectrum.

**One-Point Kinetic Runs Used for Salt Effect Studies on $k_e/k_\alpha$ Values (Runs 17–25).** Tetra-$n$-butylammonium iodide (Eastman White Label) was used without further purification. It contained within 0.4% of the theoretical amount of iodide by Volhard titration.[16] Tri-$n$-propylammonium iodide prepared by conventional methods contained within 1.5% of the theoretical amount of iodide.[14] The runs were made by the methods described for runs 14–20 in ref 2, except that appropriate amounts of the above salts were added. Values of $k_e/k_\alpha$ were calculated as previously described.[2]

(16) W. C. Pierce, E. L. Haenisch, and D. T. Sawyer, "Quantitative Analysis," 4th ed, John Wiley and Sons, Inc., New York N. Y. 1958 pp 325–327.