

tripropylamine, n_{D}^{25} 1.4116, 0.00 atom % excess deuterium.⁶ Vapor phase chromatography of this material demonstrated that less than 1% of dipropylamine was present.

Runs 46–56 involved procedures similar to those employed previously except for the added salts. Those involving lithium bromide were carried out as follows. A flask was weighed and commercial lithium bromide was added. The flask was evacuated and heated with a flame. The solid melted, the melt bubbled, and finally a white powder was produced. The flask was re-

weighed (8.28 g. of salt) and 190 ml. of purified tetrahydrofuran was added. After the salt dissolved, Molecular Sieves were added. The 0.05 *M* solutions were obtained by appropriate dilution of aliquots of this stock solution. The amine–amine salt mixtures (runs 48, 50, 51, and 52) were obtained by measuring the appropriate amounts of amine and glacial acetic acid into the reaction tube with a syringe. In all of these runs, the recovered amide was chromatographed (83–95% recovery) and totally distilled (5–22% loss).

[CONTRIBUTION NO. 1641 FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES, CALIFORNIA]

Electrophilic Substitution at Saturated Carbon. XXI. Isoracemization Reactions Involving Ion-Pair Intermediates¹

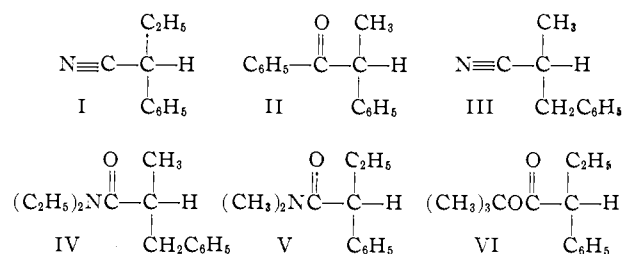
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RECEIVED JUNE 1, 1964

The stereochemical course of the base-catalyzed deuterium–hydrogen exchange reaction at carbon has been studied with (+)-2-phenylbutyronitrile-2-*d* ((+)-I-*d*) and (+)-1,2-diphenyl-1-propanone ((+)-II) in a variety of solvent–base systems. The relative rates of the exchange reaction (rate constant k_e) and of racemization (rate constant k_a) were measured, and the ratios of k_e/k_a were used as a criterion of steric course. Values of k_e/k_a greater than unity point to substitution with retention of configuration; values of unity require substitution with racemization; values of less than unity but greater than 0.5 can indicate substitution with net inversion; values of less than 0.5 require racemization without substitution (*isoracemization*). With ammonia as base in *tert*-butyl alcohol, or tetrahydrofuran as solvent, substitution proceeded with low net retention ($k_e/k_a = 1.5$ to 1.2). This result is interpreted in terms of rotation of the ammonium ion within an ammonium carbanide ion-pair intermediate. With ammonia as base in methanol or dimethyl sulfoxide, with tetramethylammonium phenoxide in 90% benzene–10% phenol, or with *n*-propylamine in tetrahydrofuran, exchange proceeded with racemization ($k_e/k_a = 1$). In these runs, the ion-pair intermediates appear to dissociate faster than they rotate. With potassium bicarbonate in ethylene glycol or tripropylamine in methanol, exchange proceeded with net inversion ($k_e/k_a \sim 0.85$). With tripropylamine as base in a variety of nondissociating solvents, values of k_e/k_a ranging from 0.72 (tetrahydrofuran 1.5 *M* in methanol and 1.5 *M* in dimethyl sulfoxide) to 0.05 (tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol) were observed. Addition of tetrabutylammonium iodide (0.1 *M*) to the last reaction mixture gave $k_e/k_a = 0.09$, whereas tripropylammonium iodide gave 0.19. In these experiments, isoracemization occurs, probably by carbanion rotation within tripropylammonium carbanide ion-pairs. Treatment of ketone (+)-II with tripropylamine in either *tert*-butyl alcohol-*O-d* or tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol-*O-d* gave $k_e/k_a = 1$. This result is interpreted in terms of ion-pair dissociation occurring faster than carbanion rotation within the ion-pair.

In a preceding paper of this series,³ the rates of base-catalyzed hydrogen–deuterium exchange and racemization of optically active nitrile III, amides IV and V, and ester VI with *tert*-butyl alcohol-*O-d* were compared and found to be equal to one another. Similarly, nitrile III and amide V underwent exchange and racemization at equal rates in ethylene glycol-*O-d*–potassium ethylene glycolate. In a much earlier study, Wilson, *et al.*,⁴ found that the rates of hydrogen–deuterium exchange and racemization of optically active 1-phenyl-2-methyl-1-butanone were equal in a basic solution of dioxane–deuterium oxide. In all of these investigations, the results were interpreted as involving a symmetrical ambident carbanion as an intermediate, which protonated largely on the more electronegative element to form a tautomer incapable of optical activity. Subsequently, this tautomer reverted to its more stable form with hydrogen attached to carbon.

In investigations of the stereochemical course of the base-catalyzed decarboxylation reaction,⁵ nitriles I



and III were produced with a maximum of 16% net retention and 12% net inversion, depending on the nature of the solvent and the cation of the basic catalyst. This low order of specificity was interpreted as reflecting asymmetric solvation of carbanions or asymmetric ion-pairs as intermediates. The competing racemization process was considered to reflect at least partial protonation on nitrogen of the nitrile anions.

Subsequently, the base-catalyzed deuterium–hydrogen exchange reactions of 2-(*N,N*-dimethylcarboxamido)-9-methylfluorene-9-*d*-(VII-*d*) with a variety of alcohols and amines were studied.⁶ The 9-fluorenyl anion is undoubtedly an intermediate in these exchange reactions. Charge is highly delocalized in this ion and, although itself symmetric, it was found capable of maintaining an asymmetric environment long enough

(1) This work was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund.

(2) U. S. Rubber Fellow at the University of California at Los Angeles, 1963–1964.

(3) D. J. Cram, C. A. Kingsbury, and P. Haberfeld, *J. Am. Chem. Soc.*, **83**, 3678 (1961).

(4) (a) C. L. Wilson, *J. Chem. Soc.*, 1550 (1936); (b) S. K. Hsu, C. K. Ingold, and C. L. Wilson, *ibid.*, 78 (1938).

(5) (a) D. J. Cram and P. Haberfeld, *J. Am. Chem. Soc.*, **83**, 2354 (1961); (b) *ibid.*, **83**, 2363 (1961).

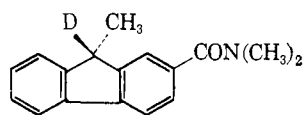
(6) D. J. Cram and L. Gosser, *ibid.*, **86**, 5445 (1964).

TABLE I
RATIOS OF VALUES OF RATE CONSTANTS FOR BASE-CATALYZED HYDROGEN-DEUTERIUM EXCHANGE (k_e) AND RACEMIZATION (k_α) OF (+)-2-PHENYL-BUTYRONITRILE-2-*d* ((+)-I-*d*)^a

Run	Subst. concn., M	Base		Solvent	T, °C.	Time, hr.	% exch. ^b	% rac. ^c	k_e/k_α
		Nature	Concn., M						
1	0.10	NH ₃	0.50	(CH ₃) ₃ COH	145	14	72	57	1.5
2	.06	NH ₃	.60	(CH ₂) ₄ O	145	6	23	20	1.2
3	.03	(CH ₃) ₄ NOC ₆ H ₅	.05	90% C ₆ H ₆ -10% C ₆ H ₅ OH	75	17	38	40	1.0
4	.06	<i>n</i> -C ₃ H ₇ NH ₂	.50	(CH ₂) ₄ O	100	18	69	69	1.0
5	.07	NH ₃	.30	CH ₃ OH	50	3	41	42	1.0
6	.06	NH ₃	.20	(CH ₃) ₂ SO	25	3	44	43	1.0
7	.20	KHCO ₃	.1	HOCH ₂ CH ₂ OH	25	5	48	53	0.87
8	.40	(<i>n</i> -C ₃ H ₇) ₃ N	.3	CH ₃ OH	50	4.5	32	37	.84
9	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M (CH ₃) ₃ COH-0.4 M LiBr	100	15	41	47	.83
10	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M (CH ₃) ₃ COH-0.1 M LiBr	150	2	37	45	.77
11	.02	KOC ₆ H ₅	.06	90% C ₆ H ₆ -10% C ₆ H ₅ OH	75	24	52	62	.76
12	.20	KOC ₆ H ₅	.15	(CH ₃) ₃ COH-0.13 M C ₆ H ₅ OH	25	3	37	46	.75
13	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M CH ₃ OH-1.5 M (CH ₃) ₂ SO	160	3.8	62	74	.72
14	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.4 M C ₆ H ₅ OH	160	5	62	76	.68
15	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-3 M CH ₃ OH	160	5	37	57	.55
16	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M CH ₃ OH	160	15	35	69	.37
17	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M H ₂ O	160	14	32	71	.31
18	.30 ^d	(<i>n</i> -C ₃ H ₇) ₃ N	.50	(CH ₃) ₃ COD ^e	145	7	12 ^f	48	.20
19	.20	(<i>n</i> -C ₃ H ₇) ₃ N	.50	(CH ₃) ₃ COH	145	14	20	70	.19
20	.10	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M C ₆ H ₅ NH ₂	160	18	8	77	.06
21	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M (CH ₃) ₃ COH	160	28	6	74	.05
22	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M (CH ₃) ₃ COH-0.10 M (<i>n</i> -C ₄ H ₉) ₄ NI	160	23	11	74	.09
23	.07	(<i>n</i> -C ₃ H ₇) ₃ N	.60	(CH ₂) ₄ O-1.5 M (CH ₃) ₃ COH-0.10 M (<i>n</i> -C ₈ H ₇) ₃ NHI	160	23	25	79	.19

^a 0.97 atom of deuterium per molecule by combustion and falling drop method. ^b Deuterium content determined by infrared spectrophotometry using standards of known isotopic composition. ^c $\alpha^{25,46}_{\text{obsd}}$ 2.88-12.30°. ^d (-)-I-*h* was employed, $\alpha^{25,46}$ -27.44°, neat, $l = 1$ dm. ^e 0.98 atom of deuterium per molecule by combustion and falling drop method. ^f Analyzed for deuterium by combustion and falling drop method.

in many media (either through ion-pairing or hydrogen bonding) to give optically active product.



VII-*d*

In connection with the last study, ammonia, amine, and phenoxide bases provided most of the stereospecific results, since the conjugate acids of these bases provided proton sources acidic enough to capture the carbanions before they passed into symmetric environments. The question arose whether or not application of the same bases to potentially ambident anion systems might not produce stereospecific results. Two systems, nitrile I and ketone II, were selected for study for the following reasons: (1) The two systems have pK_a 's near that of fluorenyl system VII (~ 21), and therefore the same solvent-base combinations could be applied to all three carbon acids. (2) The nitrile- and ketone-stabilized carbanions are representative of a family of ambident anions, and their behavior might reflect the stereochemical capabilities of a large number of other ambident anions. (3) The two systems are readily prepared in an optically active state, and deuterium could be easily introduced into the starting materials used to prepare 2-phenylbutyronitrile-2-*d*.

Results

Nitrile (+)-I-*d* was prepared from 2-phenylbutyric acid-2-*d* available from another study⁷ through the corresponding acid chloride and amide.^{5a} No exchange

(7) D. J. Cram and A. Wingrove, *J. Am. Chem. Soc.*, **86**, 5490 (1964).

occurred during these transformations as shown by a comparison of the deuterium content of the starting acid (0.965 atom of deuterium per molecule) and nitrile (+)-I-*d* (0.972 atom of deuterium per molecule).⁸ Ketone (+)-II was prepared as in a previous investigation.⁹

The exchange-racemization reactions of the nitrile were all carried out in nondeuterated solvents except run 18, in which (+)-I-*h* was exchanged with *tert*-butyl alcohol-*O-d*. Sealed tubes were usually employed and the reactions were interrupted before complete exchange and racemization had occurred. The nitrile was recovered, its rotation measured, and the amount of deuterium present was measured by an infrared analytical technique (see Experimental). The values of k_e/k_α , the ratio of the rate constant for exchange to that for racemization, were calculated with eq. 1. Table I records the results.

$$k_e/k_\alpha = \frac{\log(1 - \text{fraction of material that underwent exchange})}{\log(1 - \text{fraction of material that underwent racemization})} \quad (1)$$

Small errors are undoubtedly incorporated into these values by neglect of the isotope effect.¹⁰ When this ratio equals unity or zero, the isotope effect plays no role. Most of the values of Table I are close to unity or zero, and the errors introduced by neglect of isotope effect are probably comparable to those of ex-

(8) Combustion and falling drop technique performed by J. Nemeth, Urbana, Ill.

(9) F. A. Abd Elhafez and D. J. Cram, *J. Am. Chem. Soc.*, **74**, 5846 (1952).

(10) The magnitude of such errors is discussed elsewhere (ref. 6).

perimental origin. Comparison of the values of k_e/k_α for runs 18 and 19 provide calibration on this point. In these two runs, the position of the isotopic label was interchanged (substrate *vs.* solvent), and yet the values were 0.20 and 0.19.

Ketone (+)-II was submitted to racemization-exchange conditions with tripropylamine as base and *tert*-butyl alcohol-*O-d* as solvent in one run and tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol-*O-d* in the other. For both runs, $k_e/k_\alpha = 1$.

Discussion

The four values of k_e/k_α which correspond to the four discrete stereochemical courses for the isotopic exchange-racemization reaction are outlined. The values of this ratio were found to vary between extremes of 1.5 and 0.05 (see Table I), and thus all four stereochemical courses possibly are available to nitrile I-*d*. However, for the two runs made with ketone II-*h*, only values of unity were observed.

k_e/k_α	Steric course
∞	100% retention
1	100% racemization
0.5	100% inversion
0	100% isoracemization ¹¹

In those reactions involving neutral bases and substrates, the rates of racemization and exchange were increased by an estimated 4-6 powers of ten as the ionizing power of the solvent was increased (compare conditions for runs 1 and 6, or runs 8 and 16 of Table I). This large rate dependence on solvent leaves little doubt that carbanions are generated as intermediates in these reactions.

TABLE II
COMPARISON OF VALUES OF k_e/k_α OBTAINED FOR THREE SYSTEMS IN NONDISSOCIATING MEDIA

Solvent	Base	Fluorene VII- <i>d</i>	Nitrile I- <i>d</i>	Ketone II- <i>h</i>
(CH ₂) ₄ O	NH ₃	148	1.5	..
(CH ₃) ₂ COH(D)	NH ₃	>50	1.2	..
90% C ₆ H ₆ -10% C ₆ H ₅ OH	KOC ₆ H ₅	18	0.76	..
(CH ₃) ₂ COH(D)	NPr ₃	6	0.20	1

In the first four sections of the discussion, mechanisms associated with each of the four stereochemical courses are developed. In the fifth section, a comparison of the stereochemical fates of the 2-phenyl-2-butyronitrile anion when generated by deuterium abstraction and decarboxylation is made. In the sixth section, a comparison is made between the behavior of ion-pairs which involve carbonium ions and carbanions as one of their component parts.

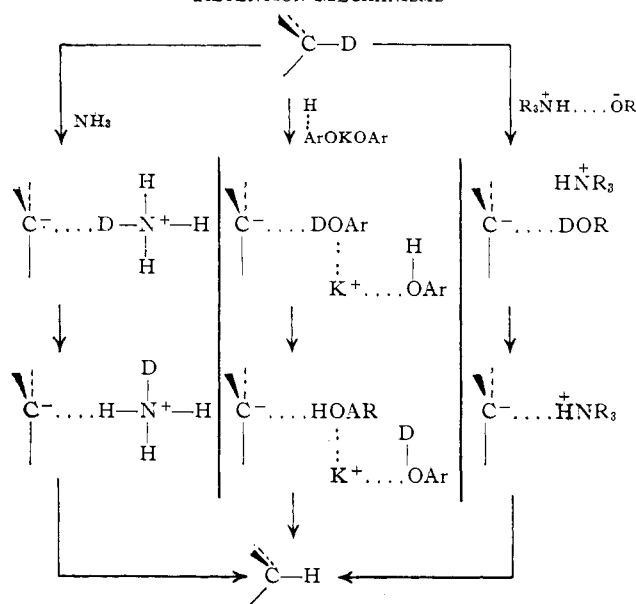
Retention Mechanisms.—Three retention mechanisms were identified in connection with the exchange reactions of fluorene system VII-*d*. The essential portion of each of these is outlined in Chart I. These mechanisms were found only in media poor at dissociating ion-pairs, and only when the basic catalyst

(11) The term "isoracemization" defines a process in which a compound with a single asymmetric center racemizes without exchanging any of the groups attached to the asymmetric center with potential external sources of such groups. The prefix "iso" means "equal." Thus the four groups attached to the optically active starting material are "equal" to those of the racemic product in an "isoracemization." This new term is operational, and can be applied equally well to carbanion, carbonium ion, or radical processes. For example, in Chart VII, an example of "isoracemization" of a benzhydryl halide through a carbonium halide ion-pair intermediate is cited.

was in some way associated with a proton donor acidic enough to capture a carbanion faster than ion-pair dissociation occurred.

Table II compares the values of k_e/k_α for the fluorene, nitrile, and ketone systems obtained with those solvents and bases which produced high retention with the fluorene system. Of the three retention mechanisms observed for the fluorene system (Chart I), only that which involves ammonia as base is visible when nitrile I-*d* is substrate. Even then, stereospecificity is very low ($k_e/k_\alpha = 1.2$ to 1.5). This net retention probably reflects rotation of an ammonium ion within an ammonium carbanide ion-pair intermediate (see Chart I). Aside from this shred of similarity between the nitrile and fluorene systems, the three kinds of substrates exhibit different stereochemical behavior in these nondissociating media. The reasons for this are discussed in subsequent sections.

CHART I
RETENTION MECHANISMS

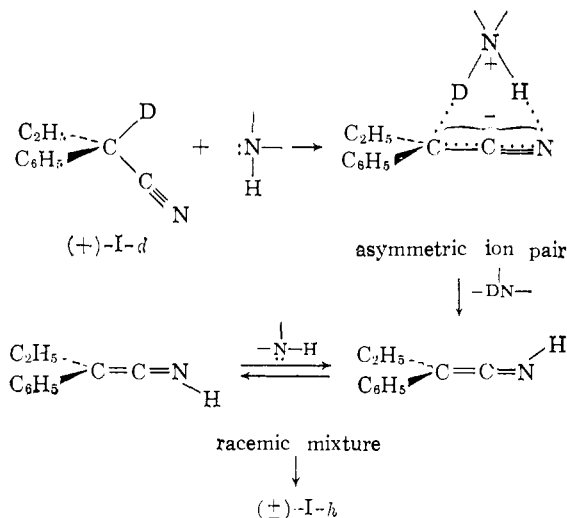


Racemization Mechanisms.—Three of the four sets of conditions that produced k_e/k_α values of unity for nitrile I-*d* (runs 3-6, Table I) also gave unity for fluorene VII-*h*. Ammonia in methanol or dimethyl sulfoxide, or tetramethylammonium phenoxide in 90% benzene-10% phenol, all gave complete racemization for both systems. The mechanism which best explains these results first involves formation of an asymmetric ion-pair, whose carbanion separates and passes into a symmetrical environment faster than proton capture occurs.⁶

The value of unity observed for nitrile I-*d* in tetrahydrofuran-propylamine (run 4, Table I) contrasts with the value of >56 obtained for the fluorene system.⁶ This difference in behavior correlates with the reduced retention observed for the nitrile system with ammonia in tetrahydrofuran. The ambident character of the nitrile anion and lack of that character in the fluorenyl anion is probably responsible for the difference in the fate of the ammonium carbanide ion-pairs. Donation of a proton to nitrogen by the ammonium ion would provide a tautomer of the nitrile

system, which, although initially optically active (allenic asymmetry), should invert and racemize rapidly much as imines are observed to invert.¹² Such a scheme is outlined in Chart II.

CHART II
RACEMIZATION MECHANISM



A simpler scheme can be used to explain the value of $k_e/k_a = 1$ when ketone II-h was treated with tripropylamine in either tetrahydrofuran-*tert*-butyl alcohol-*O-d* or *tert*-butyl alcohol-*O-d* itself. It is probable that the enol formed from ketone II-h protonates or deuterates on oxygen much faster than on carbon, and that the enol formed goes to anion faster than does the ketone. Consequently, even if an initial C to O proton transfer occurred, deuterium would enter the enol in subsequent exchanges before ketone was regenerated, and k_e/k_a would equal unity.

Inversion Mechanisms.—Runs 7–15 of Table I with nitrile (+)-I-d provide values of k_e/k_a which lie between 0.87 and 0.55. These values could reflect net inversion blended with racemization, or blends of isoracemization and ordinary racemization with exchange. Those runs made in the dissociating solvents ethylene glycol (run 7) and methanol (run 8) are compared in Table III with similar runs made with fluorene system VII-d as substrate.

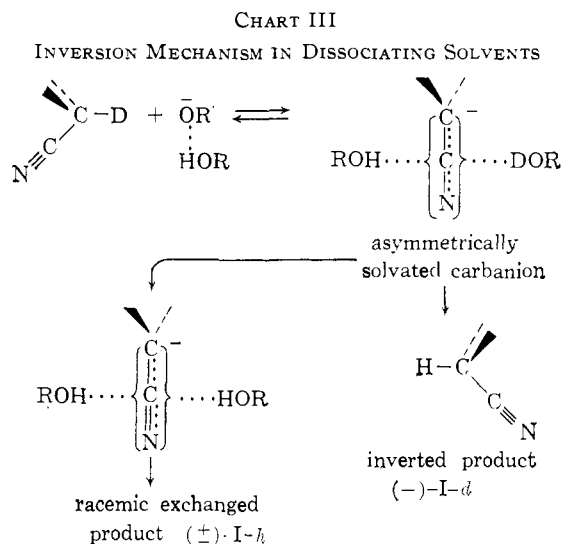
TABLE III

COMPARISON OF VALUES OF k_e/k_a OBTAINED FOR TWO SYSTEMS IN DISSOCIATING MEDIA

Solvent	Base	Fluorene VII-d	Nitrile I-d
HOCH ₂ CH ₂ OH	HOCH ₂ CH ₂ OK	1	0.87
CH ₃ OH	NPr ₃	0.67	0.84
CH ₃ OH	CH ₃ OK	0.69	...

The values of k_e/k_a for the two substrates are not far from one another, and the two reactions probably share the same mechanism. In these dissociating media, the free alkoxide anion is probably the active catalytic species,³ and a carbanion is formed which is hydrogen bonded at the front and back faces by solvent molecules bearing different isotopic labels. Front side deuterium capture by carbon produces starting material. Back side hydrogen capture by carbon gives inverted material. Both of these processes compete with exchange of solvent for the molecules hydrogen bonded to

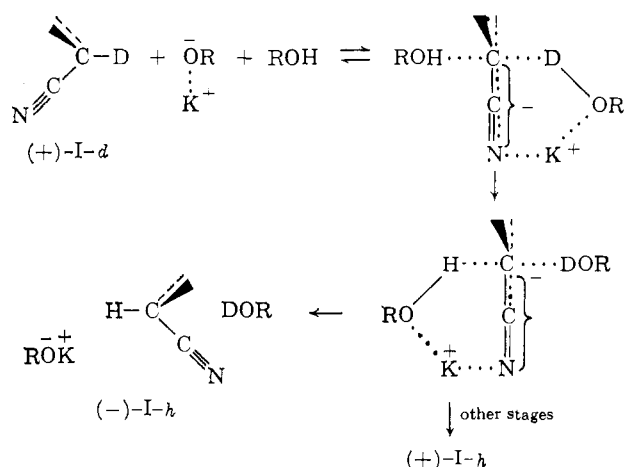
carbon, which leads to symmetrically hydrogen-bonded carbanions, and to racemic-exchanged product. Protonation on nitrogen also probably competes when nitrile is substrate, but this process also leads ultimately to racemic-exchanged product. This inversion mechanistic scheme, as applied to the nitrile (+)-I-d, is embodied in Chart III.



In runs 11 and 12 of Table I, nitrile (+)-I-d underwent reaction catalyzed by potassium phenoxide in 90% benzene-phenol or *tert*-butyl alcohol 0.13 *M* in phenol to give $k_e/k_a = 0.76$ and 0.75. When tetramethylammonium phenoxide was substituted for the potassium phenoxide in 90% benzene-phenol, k_e/k_a increased to unity (run 3). The ability of the potassium ion to coordinate with atoms carrying unshared electrons is therefore a necessary component of the stereospecific portion of the mechanism. Since under the conditions of runs 11 and 12 fluorene system VII-d gave k_e/k_a values of 18 and 6, it is clear that the nitrile group also plays some special role in providing k_e/k_a of less than unity in runs 11 and 12. The mechanistic scheme of Chart IV invokes the ability of the potassium ion and the nitrogen of the nitrile to coordinate with one another.

CHART IV

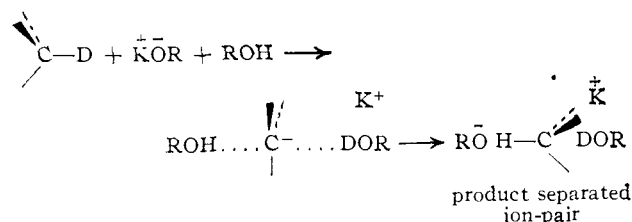
INVERSION MECHANISM IN NONDISSOCIATING SOLVENTS



In nondissociating solvents, an inversion mechanism is highly improbable, unless some special means is avail-

(12) D. Y. Curtin and J. W. Hausser, *J. Am. Chem. Soc.*, **83**, 3474 (1961).

able for the cation of an ion-pair base to get around to the rear of the carbanion formed by proton abstraction. Otherwise, proton capture from the back of a carbanion produces a product-separated ion-pair with considerable charge separation. The nitrile group provides just such a means.



Although runs 9 and 10 and 13–15 gave values of k_e/k_a between 0.83 and 0.55, discussion of these experiments is deferred to the next section.

Isoracemization Mechanisms.—The most novel results of this investigation are those obtained with tripropylamine in nondissociating solvents such as *tert*-butyl alcohol, 90% benzene–10% phenol, or tetrahydrofuran containing such proton sources as *tert*-butyl alcohol, methanol, water, or aniline (runs 9, 10, and 13–21 of Table I). In these runs, isotopic exchanges of (+)-I-*d* with proton pools occurred to give values of k_e/k_a which varied from 0.83 to 0.05.

In principle, those values between 0.5 and 1 could be attributed to blends of inversion and ordinary racemization, to blends of isoracemization and ordinary racemization-with-exchange, or to blends of all three processes. The last possibility provides the greatest over-all amount of internal consistency between the results of a large variety of runs.

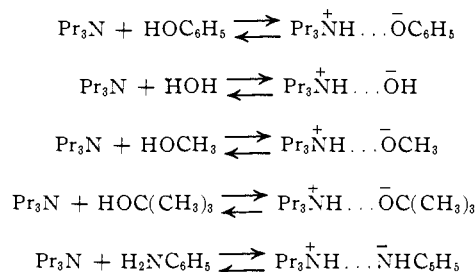
Two main sources of information provide insight into the nature of isoracemization and competing processes. The first comes from the change in values of k_e/k_a when medium and base are changed, the second from the changes in values when substrate is changed.

In Table IV are collated the results of runs made to determine the effect of the acidity and dielectric constant of the proton pool in the medium on the values of k_e/k_a in runs made with tripropylamine as catalyst, and tetrahydrofuran as solvent. No straightforward correlation with dielectric constant of the added proton pool is evident. As the pK_a of the proton pool was changed from 10 to about 28, k_e/k_a decreased from 0.68 to 0.06. Only a very rough correlation between pK_a and k_e/k_a is evident. For example, although *tert*-butyl alcohol is more acidic than aniline by about 8 pK_a units, the two proton donors provided about the same k_e/k_a values (0.05–0.06). This result is particularly interesting since the pK_a of I-*d* is probably about 21, and lies between that of *tert*-butyl alcohol (19) and aniline (27).

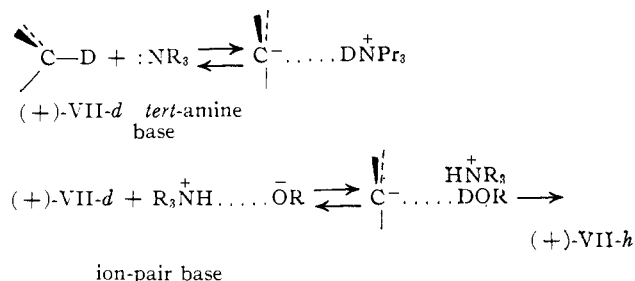
TABLE IV
EFFECT OF CHANGES IN NATURE OF A 1.5 M PROTON POOL
ON VALUES OF k_e/k_a FOR EXCHANGE-RACEMIZATION OF
(+)-I-*d* AT 160° IN TETRAHYDROFURAN WITH TRIPROPYLAMINE
AS CATALYST

Run	Nature	Proton pool		k_e/k_a
		$t, ^\circ\text{C}$	pK_a	
14	$\text{C}_6\text{H}_5\text{OH}$	9.9 ⁴⁸	10	0.68
17	H_2O	81.5 ⁰	14	.31
16	CH_3OH	34 ¹⁸	16	.37
19	$(\text{CH}_3)_3\text{COH}$	11 ¹⁹	19	.05
20	$\text{C}_6\text{H}_5\text{NH}_2$	7.3 ²⁰	27	.06

The interpretation of these results is complicated by the fact that in each of the 5 runs two bases were present, either or both of which could abstract deuterium from nitrile. That tripropylammonium *tert*-

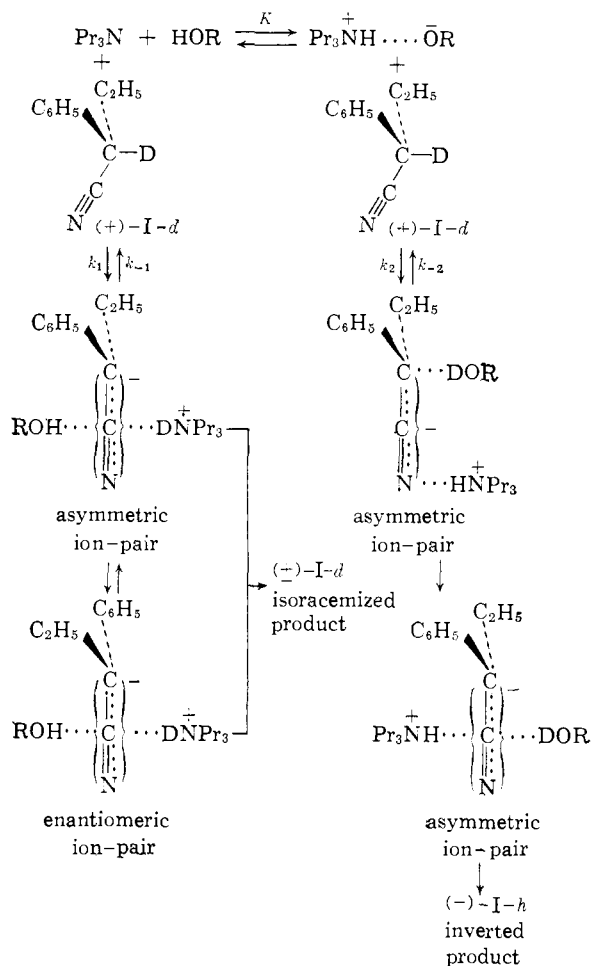


butoxide can act as the basic catalyst is indicated by operation of the retention mechanism when tripropylamine in *tert*-butyl alcohol was used as medium for exchange-racemization of fluorene system VII-*d*⁶ (see Chart I). Predominant retention was also observed for VII-*d* when tripropylamine–benzene–phenol or triethylamine–benzene–methanol were utilized.⁶ In these runs involving fluorene system VII-*d*, both the *tert*-amine and the ion-pair bases were probably operative, but the former would be expected to regenerate starting material, and only the ion-pair base to give exchange.

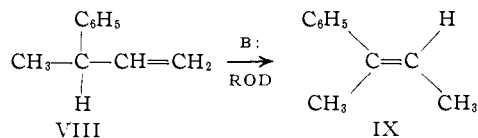


An attractive mechanistic scheme to explain the results with nitrile I-*d* involves the two forms of the base in a particular medium. With this substrate, the *tert*-amine form of the base provides an isoracemization mechanistic component, and the ion-pair form of the base a predominant inversion mechanistic component (see Chart V). A minor component (not formulated) of each is a racemization-exchange mechanism. The balance between the inversion and isoracemization components would depend on both the equilibrium constant between the two forms of the base and the relative activities of the two bases toward substrate. Both should change drastically over the range of the five bases listed, but the changes should be somewhat compensating. In other words, the more active component is expected to be present in the lower concentration.

In the mechanistic scheme of Chart V, both the isoracemization and inversion components involve (in effect) carbanion rotation with respect to the tripropylammonium ion within the ammonium carbanide ion-pair. This could occur either by simple rotation or by a "conducted tour mechanism." In the latter, the tripropylammonium ion becomes hydrogen bonded at successive molecular sites, first to carbon at the front, then to nitrogen at the front, then to nitrogen at the back, and finally to carbon at the back. In the isoracemization mechanism, covalent intermediates might

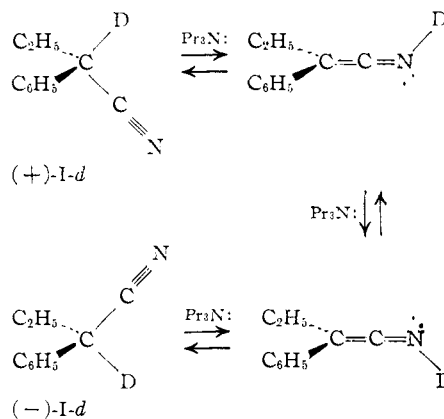
CHART V
 COMPETING ISORACEMIZATION AND INVERSION MECHANISMS


intervene. As long as the deuterium transfers from carbon to nitrogen, to inverted nitrogen, and back to inverted carbon were strictly intramolecular, the mechanism would be compatible with the data (see Chart VI). In this connection, base-catalyzed intramolecular 1,3-proton transfers have been observed for 3-phenyl-1-butene (VIII) going to *cis*-2-phenyl-2-butene (IX).¹³



In connection with the isoracemization process, the question arises as to the fate of the carbanion if the deuterated tripropylammonium carbanide dissociates. In runs 14, 16, 17, and probably 19, the proton pools ($\text{C}_6\text{H}_5\text{OH}$, H_2O , CH_3OH , and $(\text{CH}_3)_3\text{COH}$) are acidic enough to protonate the carbanion competitively with the dissociated deuterated tripropylammonium ion. Since the latter ion would be present in a concentration many orders of magnitude less than that of the proton pool, even an unfavorable balance of rate constants would be overcome by the concentration effect, and proton capture would result. In the runs with these proton pools, as well as that with aniline (run 20), isotopic exchange between the deuterated

(13) D. J. Cram and R. T. Uyeda, *J. Am. Chem. Soc.*, **86**, 5466 (1964).

 CHART VI
 RACEMIZATION-WITHOUT-EXCHANGE MECHANISM INVOLVING
 COVALENT INTERMEDIATES


tripropylammonium ion and the proton pool should be faster than recombination of the original ions, again for concentration reasons. The proton pool concentration is undoubtedly many powers of ten greater than that of carbanion concentration. On both counts, ion-pair dissociation should result in isotopic exchange.

The results of runs 22 and 23 clearly demonstrate that the tripropylammonium carbanide ion-pair racemizes and collapses faster than it dissociates. Both runs were made with 0.07 *M* (+)-*I-d* in tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol 0.6 *M* in tripropylamine. In run 22, tetrabutylammonium iodide was added (0.10 *M*), and $k_e/k_a = 0.09$. In run 23, tripropylammonium iodide was introduced (0.1 *M*), and $k_e/k_a = 0.19$. The latter value is substantially below 0.5, a fact which requires the isoracemization process. Had racemization occurred largely by a process involving dissociation of tripropylammonium-*N-D* carbanide ion-pairs, the resulting deuterated cation (extremely low concentration) would have been drowned in the pool of 0.1 *M* protonated tripropylammonium ions. As a result, k_e/k_a values would have approached unity. The fact that k_e/k_a increased from 0.09 to 0.19 when tetrabutylammonium iodide was replaced by tripropylammonium iodide indicates that at most only a small part of the racemization can be accounted for by ion-pair dissociation.

In two sets of runs with tripropylamine as base and nitrile (+)-*I-d* as substrate, an increase in concentration of the proton pool resulted in an increase in the value of k_e/k_a (Table V). This fact is consistent with the scheme of Chart V. An increase in the concentration of alcohol should shift the equilibrium to the right, favoring the ion-pair form of the base, and thus increasing the inversion mechanistic component somewhat. That an increase in dielectric constant alone alters the balance of mechanisms in the same direction is shown by the fact that addition of dimethyl sulfoxide to tetrahydrofuran 1.5 *M* in methanol gave a larger increase in k_e/k_a values than by adding an equimolar amount of methanol (compare runs 13 and 15 of Table V). The concentration of the ion-pair form of the base probably increased upon addition of dimethyl sulfoxide.

Striking increases in rate and values of k_e/k_a were observed by addition of small amounts of lithium bromide to runs carried out with (+)-*I-d* in tetrahydro-

TABLE V
EFFECT OF CHANGES IN CONCENTRATION OF PROTON POOL
ON VALUES OF k_e/k_α FOR EXCHANGE-RACEMIZATION OF
(+)-I-d WITH TRIPROPYLAMINE AS CATALYST

Run	Solvent	Proton pool		k_e/k_α
		Nature	Concn., M	
16	(CH ₂) ₄ O	CH ₃ OH	1.5	0.37
15	(CH ₂) ₄ O	CH ₃ OH	3.0	.55
13	(CH ₂) ₄ O	[CH ₃ OH·(CH ₃) ₂ SO] ^a	1.5	.72
21	(CH ₂) ₄ O	(CH ₃) ₃ COH	1.5	.05
19	(CH ₃) ₃ COH	(CH ₃) ₃ COH	~10	.19

^a 1.5 M in methanol, 1.5 M in dimethyl sulfoxide.

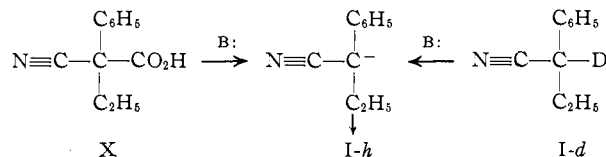
furan 1.5 M in *tert*-butyl alcohol with tripropylamine as base (Table VI). These salt effects were found to be spurious by additional experiments which demonstrated that lithium bromide in tetrahydrofuran in the presence of nitrile I generates with time a catalyst much stronger than tripropylamine.

TABLE VI
EFFECT OF LITHIUM BROMIDE ON VALUES OF k_e/k_α AND
RATE FOR EXCHANGE-RACEMIZATION OF (+)-I-d IN
TETRAHYDROFURAN 1.5 M IN *tert*-BUTYL ALCOHOL WITH
TRIPROPYLAMINE AS CATALYST

Run	LiBr concn., M	k_e/k_α	Estimated rate factor for exchange
21	0	0.05	1
10	.1	.77	10 ²
9	.4	.83	10 ³ to 10 ⁴

Values of $k_e/k_\alpha < 0.5$ could, in principle, be produced by a radical chain reaction involving deuterium transfer from (+)-I-d to optically inactive 2-phenyl-2-butyronitrile radical to give racemic deuterated I-d. This possibility was eliminated by decomposing α, α' -azobisisobutyronitrile in a solution of 1.5 M *tert*-butyl alcohol in tetrahydrofuran which was 0.6 M in tripropylamine and 0.07 M in (+)-I-h at 75° (see Experimental). The recovered substrate ((+)-I-h) exhibited an optical rotation 3% lower than a run made under identical conditions except that the radical initiator was absent. In other experiments at 140° in the same medium, the degree of racemization of (+)-I-h was demonstrated not to change with added radical chain reaction inhibitor (*p*-benzoquinone).

Comparison of the Steric Courses of Exchange for Nitrile I-d and Decarboxylation of 2-Cyano-2-phenylbutanoic Acid (X) to Nitrile I-h.—The steric course of the base-catalyzed exchange reactions of nitrile I-d correlates in general with those found under similar conditions in the production of nitrile I-h by the base-catalyzed decarboxylation of acid X.^{5a} In run 1 with



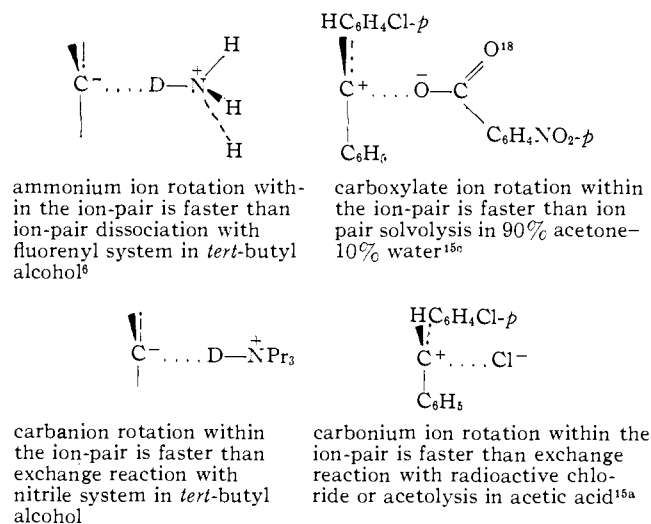
ammonia in *tert*-butyl alcohol, $k_e/k_\alpha = 1.5$, or exchange of (+)-I-d occurred with about 35% net retention. In the same solvent with the same base, decarboxylation of the acid gave the same nitrile with 10% net retention. In run 5 with ammonia and methanol, $k_e/k_\alpha = 1$, or exchange of (+)-I-d occurred with essentially complete racemization. In decarboxylation of the acid with ammonia and methanol, about 1% net retention was the result. In run 7 with potassium

bicarbonate and ethylene glycol, $k_e/k_\alpha = 0.87$, or exchange of (+)-I-d occurred with 10% net inversion. Decarboxylation of the acid to I-h with potassium carbonate in ethylene glycol gave 10% net inversion. These results indicate that in these particular cases, the general steric course of electrophilic substitution at saturated carbon is independent of leaving group.

Comparison of the Behavior of Ion-Pairs Which Involve Carbonium Ions and Carbanions as One of Their Component Parts.—In an earlier paper,¹⁴ a comparison was made between the stereochemical courses of the S_N1 and S_E1 reactions. Net retention, racemization, and net inversion are now well known for both types of substitution, and considerable mechanistic similarities were noted¹⁴ for the behavior of carbanions and carbonium ions. Other mechanistic analogies were seen between allylic rearrangements involving carbonium ions and those involving carbanions.¹³

The results of this and the previous paper⁶ coupled with recent data obtained with carbonium ions¹⁵ extend these similarities, particularly with respect to ion-pair behavior. Examples are formulated in Chart VII.

CHART VII
SIMILARITIES IN BEHAVIOR OF ION-PAIRS THAT CONTAIN
CARBANIONS WITH THOSE THAT CONTAIN CARBONIUM IONS



Experimental

(+)-2-Phenylbutyronitrile-2-d.—A mixture of 15.1 g. of 2-phenylbutyric acid-2-d (0.965 atom of deuterium per molecule, $\alpha^{27}\text{D} = -77.4^\circ$, neat, 1 dm.)¹⁶ and 30 ml. of thionyl chloride was allowed to stand at 25° for 3 hr. The solution was heated to reflux for 3 min. and cooled to 25°. The excess thionyl chloride was evaporated under vacuum at 25°, 10 ml. of benzene was added and similarly evaporated, and then 2 ml. of benzene was added and similarly evaporated. The colorless acid chloride was then dissolved in 150 ml. of methylene chloride, and this solution was cooled in an ice bath. Anhydrous ammonia (10 ml.) was collected in a cooled flask at -78° and carefully diluted with 40 ml. of methylene chloride. The chilled methylene chloride solution of ammonia (-78°) was added in three portions with swirling to the chilled acid chloride solution (very vigorous reaction). The resulting mixture was then poured into water, and an additional 50 ml. of methylene chloride was added. The basic aqueous

(14) D. J. Cram, J. L. Mateos, F. Hauck, H. Langemann, K. R. Kopecky, W. D. Nielsen, and J. Allinger, *J. Am. Chem. Soc.*, **81**, 5774 (1959).

(15) (a) S. Winstein, J. S. Gall, M. Hojo, and S. Smith, *ibid.*, **82**, 1010 (1960); (b) A. Illiceto, A. Fava, U. Muzzucato, and O. Rossetto, *ibid.*, **83**, 2729 (1961); (c) H. L. Goering, R. G. Briody, and J. F. Levy, *ibid.*, **85**, 3059 (1963).

(16) Prepared in another study (see ref. 7).

layer was acidified, and no cloudiness was visible. The organic layer was washed with water, dried, and the solvent was evaporated to give 14.3 g. of a white solid. This material was dehydrated by a procedure already recorded^{8a} to give 10.5 g. (79%) of nitrile as a colorless liquid n_D^{25} 1.5065, α_D^{25} 24.60°, neat, $l = 1$ dm., 0.97 atoms of deuterium per molecule.⁸ The substance (-)-2-phenylbutyronitrile, n_D^{25} 1.5063, α_D^{25} -23.2°, neat, $l = 1$ dm., was available from a previous investigation.^{8a}

Solvents and Bases.—Methanol, *tert*-butyl alcohol, dimethyl sulfoxide, and ethylene glycol were distilled from Molecular Sieves and stored over Molecular Sieves. The preparation of deuterated *tert*-butyl alcohol has been described earlier.¹⁷ Reagent grade benzene was dried over Molecular Sieves before use, and tetrahydrofuran was distilled from lithium aluminum hydride immediately before use.

Aniline was distilled from zinc dust, and then submitted to fractional distillation. A center cut of b.p. 182° was collected and stored over Molecular Sieves. Commercial tripropylamine (100 g.) was shaken with 40 ml. of acetic anhydride for 5 min., the layers were separated, and the amine was washed with a mixture of dilute sodium hydroxide solution and ice. The amine layer was dried and distilled from Molecular Sieves. A center cut with a constant boiling point of 155° was collected, and used within a month of the time of purification. Commercial *n*-propylamine was dried over Molecular Sieves for 24 hr. and then distilled through a 55-cm. vacuum-jacketed fractionating column. A center cut of b.p. 47.3°, n_D^{25} 1.3850, was collected and stored over Molecular Sieves.

General Procedures for Runs Involving 2-Phenylbutyronitrile (I).—The runs were mostly made in sealed tubes under nitrogen. The recovered nitrile was purified by distillation at 0.5 to 1 mm., pot temperature 90–95°. The rotations were measured neat in a jacketed 0.5-dm. polarimeter tube thermostated at 25°. Usually 10 readings for both the free path and the sample were taken, and the average deviation was about 0.01° (α_{obsd} was 2.9–12.3°). The deuterium analysis is described below. In runs 1–8, 10–12, 14, 18, and 19, the refractive indices of the distilled recovered substrate were between n_D^{25} 1.5060 and 1.5063, and each sample showed no carbonyl absorption in its infrared spectrum. In runs 9, 13, 15–17, 20, and 21, the refractive indices of the distilled recovered substrates varied from n_D^{25} 1.5055 to 1.5060, and their infrared spectra contained a peak at 6.1 μ of medium intensity for the 7 samples. In runs 13, 16, 17, 20, and 21, the substrate was further purified by preparative vapor phase chromatography to give material with n_D^{25} 1.5061 to 1.5062 which exhibited no absorption at 6.1 μ in the infrared absorption spectrum. This additional purification procedure changed the rotation by 1% or less. The appearance of the 6.1- μ absorption was associated with the amount of time between the purification and use of tripropylamine. Runs involving very freshly purified amine gave product with no 6.1- μ absorption. Most samples of nitrile showed absorptions at 2.75 and 2.85 μ in their infrared spectra which varied in intensity from sample to sample. If a solution of the nitrile in pentane was washed with a dilute, ice-cold sodium hydroxide solution, the absorption at these wave lengths vanished. The absorptions could be induced by bubbling oxygen through the neat nitrile at 25°. Either procedure resulted in changes in rotation of the nitrile of less than 1%.

Purification of 2-Phenylbutyronitrile by Vapor Phase Chromatography.—After polarimetric and deuterium analysis of nitrile recovered from runs 17 (n_D^{25} 1.5055, α_D^{25} +3.52°, neat, $l = 0.5$ dm.), 20 (n_D^{25} 1.5060, α_D^{25} +2.88°, neat $l = 0.5$ dm.), and 21 (n_D^{25} 1.5055, α_D^{25} +3.17°, neat, $l = 1$ dm.), about equal amount of each were combined to give a sample, α_D^{25} +6.30°, neat, $l = 1$ dm. This sample was chromatographed on a 6-ft. column of 20% silicone gum on 80/100 firebrick. The column was at 178°, the preheater at 210°, and the carrier gas was helium. The substrate was washed from the collector with pentane, the pentane was evaporated, and the residue was distilled at 0.5–1 mm. with a pot temperature of 90–95° to give material, α_D^{25} +6.37°, neat, $l = 1$ dm., n_D^{25} 1.5062, with no 6.1- μ absorption in the infrared spectrum. Similarly, after analysis the remainder of samples from runs 13 (n_D^{25} 1.5060, α_D^{25} +3.21°, neat, $l = 0.5$ dm.) and 16 (n_D^{25} 1.5057, α_D^{25} +3.43°, neat, $l = 1$ dm.) were combined to give material α_D^{25} +6.63°, neat, $l = 1$ dm. Chromatographic purification of this sample gave α_D^{25} +6.66°, neat, $l = 1$ dm., n_D^{25} 1.5061, with no 6.1- μ absorption in the infrared spectrum.

Sample Procedure. Run 18.—A heavy-walled Pyrex tube containing 10.0 ml. of *tert*-butyl alcohol, 0.3 ml. (290 mg.) of (+)-I-d, and 1.1 ml. of tripropylamine was closed with a drying tube and chilled to -78°. The tube was sealed under an atmosphere of pure nitrogen, and placed in a bath held at 145°. The tube was chilled to -78° and opened. The contents of the tube was shaken with 300 ml. of dilute hydrochloric acid and 50 ml. of purified pentane. The pentane layer was washed with water, dried, and the pentane was evaporated. The residue was distilled at about 0.5 mm. with a pot temperature of 90° to give 272 mg. of colorless nitrile, n_D^{25} 1.5062.

Runs 1, 2, 5, and 6.—The appropriate (known) amount of acetone was placed in a glass tube with one end sealed, and the position of the meniscus was marked. The tube was dried, fitted with a drying tube, and chilled to -78°. Anhydrous ammonia was collected in the tube until the liquid reached the mark. The top of the tube was drawn out into a fragile seal, and the tube was warmed to room temperature and dried. The ampoule, the solvent, and reagents were placed in a tube closed with a drying tube, and the reaction tube was chilled thoroughly at -78°. The tip of the sealed ampoule was broken, and the tube was sealed under an atmosphere of nitrogen. After the specified heating period, the nitrile was recovered as in run 18.

Run 3.—A solution prepared from 0.834 g. of tetramethylammonium hydroxide (0.0052 mole of hydroxide per g., about 4% trimethylamine and carbonate, and about 50% water) and 87 ml. of a 90% dry benzene–10% dry phenol was dried over Molecular Sieves under nitrogen for several hours. Titration of this solution with Karl Fisher reagent indicated the presence 0.001 g. of water per ml. . Optically active (+)-I-d (0.40 ml.) was dissolved in 78 ml. of this solution. The resulting solution was heated at 75° under nitrogen. The cooled solution was washed with excess dilute hydrochloric acid and then with water. The benzene was evaporated at 25° under reduced pressure, the residue was dissolved in 50 ml. of carbon tetrachloride, and the resulting solution was washed with four 300-ml. portions of water at 60–70°. The carbon tetrachloride solution was cooled to 0°, and washed with cold 0.5 *N* aqueous sodium hydroxide. The carbon tetrachloride solution was then washed with water, dried, and the solvent was evaporated under reduced pressure. The residue was distilled at about 1 mm. and a pot temperature of 90–95° to give 0.20 g. of colorless liquid, n_D^{25} 1.5060.

Runs 9 and 10.—An approximately 0.55 *M* solution of lithium bromide in tetrahydrofuran was prepared as follows. A flask was weighed and commercial lithium bromide was added. The flask was evacuated and heated with a flame. The solid melted, the melt bubbled, and finally a white solid was obtained. The flask was reweighed (8.30 g. net), 172 ml. of tetrahydrofuran was added, and the resulting solution was dried over Molecular Sieves. Appropriate amounts of this stock solution, tetrahydrofuran, *tert*-butyl alcohol, tripropylamine, and substrate were placed in tubes which were handled as in run 18.

Run 15.—Reagent grade phenol which had been dried over Molecular Sieves (7.44 g.) was transferred to a tube under nitrogen. Clean potassium (0.190 g.) was dissolved in the melted phenol under nitrogen, and the resulting solution was frozen at room temperature. The tube was cut just above the top of the solid, and the plug was transferred to a flask under nitrogen. Nitrile ((+)-I-d), 0.32 ml., and 75 ml. of benzene was added. The flask was flushed with nitrogen, closed with a ground glass stopper, and heated at 75° for 24 hr. The nitrile was recovered and purified as in run 3, 0.251 mg. of colorless liquid being obtained, n_D^{25} 1.5062.

Run 16.—Clean potassium (0.057 g.) was dissolved in a solution of 0.255 g. of reagent grade phenol in 10 ml. of *tert*-butyl alcohol. To this solution was added 0.30 ml. of (+)-I-d, and the new solution was allowed to stand at 25° for 3 hr. The substrate was then recovered and purified as in run 18 to give 0.233 g. of material, n_D^{25} 1.5061.

Run 14.—A solution of 21.1 g. of reagent grade phenol in 129 ml. of tetrahydrofuran was dried over Molecular Sieves for 5 days. A tube was prepared as in run 18 containing 0.30 ml. of substrate, 3.30 ml. of tripropylamine, and 27 ml. of the tetrahydrofuran–phenol solution. After heating, the substrate was recovered and purified as in run 3, except that the carbon tetrachloride was added at the beginning of the extraction procedure since the tetrahydrofuran was removed by the extractions; wt. 0.260 g., n_D^{25} 1.5063.

Run 22.—A heavy-walled Pyrex tube containing 1.11 g. of Eastman tetrabutylammonium iodide, 0.3 ml. of nitrile (+)-I-d,

(17) D. J. Cram and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 2182 (1961).

4.2 ml. of *tert*-butyl alcohol, 3.3 ml. of tripropylamine, and 22.5 ml. of tetrahydrofuran was closed with a drying tube and chilled to -79° . The tube was then evacuated to ~ 40 mm. and refilled with dry nitrogen. The tube was again evacuated and refilled and finally the tube was sealed at ~ 40 mm. The tube was then heated at 160° for 22.5 hr. The nitrile was recovered as in run 18. A colorless liquid, n_D^{25} 1.5055, was obtained. There were no spurious peaks in the infrared spectrum. The tetrahydrofuran was distilled from lithium aluminum hydride in a dry nitrogen atmosphere immediately before use. Karl Fischer titration indicated that the salt contained less than 0.2% water, and a Volhard titration of the iodide gave a result which was within 1% of that calculated from the weight of the salt taken.

Run 23.—Commercial 50% hypophosphorous acid was added to commercial concentrated hydriodic acid until the triiodide color disappeared. The system was then closed and swept out with nitrogen. The hydriodic acid–water azeotrope was then distilled under nitrogen into a receiver containing 15 ml. of tripropylamine until most of the amine was neutralized. The water and excess amine were then removed by heating at 100 – 115° under reduced pressure to give a white solid, which was not deliquescent and not noticeably hygroscopic. A Volhard titration of the iodide gave a result which was within 1% of that calculated from the weight of salt taken. The racemization–exchange experiment was carried out as in run 22, except that 0.816 g. of this tripropylammonium iodide was used instead of the tetrabutylammonium iodide. The recovered substrate, n_D^{25} 1.5063, gave an infrared spectrum which contained no spurious peaks.

Runs 1, 4, 8, 11, 13, 15–17, and 19–21 were carried out essentially in the same manner as run 18.

Kinetics of the Amine-Catalyzed Racemization of (+)-I-h.—The progress of the racemization reaction was followed roughly by quenching ampoules after various time intervals and recovering the substrate as in run 18. The results obtained at 140° with 0.6 *M* tripropylamine in tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol, 0.1 *M* in lithium bromide, and 0.13 *M* in substrate are presented in Table VII.

TABLE VII
ROUGH KINETICS OF RACEMIZATION OF 0.13 *M* SOLUTIONS
OF (+)-I-h IN TETRAHYDROFURAN, 0.6 *M* IN TRIPROPYLAMINE,
1.5 *M* IN *tert*-BUTYL ALCOHOL, AND 0.1 *M* IN LITHIUM
BROMIDE AT 140°

Time, hr.	$\alpha_{\text{obsd}}/\alpha^{\circ}_{\text{obsd}}^a$	$t_{1/2\alpha}$, hr. ^b
0.5	0.955	7.5
1	.870	5
2.8	.465	2.5
6	.000	<1

$$^a \alpha^{\circ}_{\text{obsd}} = +5.56^{\circ}. \quad ^b \text{Calculated from } t_{1/2\alpha} = \frac{(t_{\text{obsd}})(0.693)}{(-) \ln \frac{\alpha}{\alpha^{\circ}}}$$

In one ampoule the base was omitted and the rotation of the recovered substrate was low by about 3% after 2.8 hr. In another experiment, the reagent mixture above was heated at 140° for 21 hr. without the substrate. The ampoule was then opened and this pretreated reagent mixture was transferred to an ampoule containing substrate. After 1 hr. at 140° , the substrate recovered was 22.5% racemized. In all these runs, the lithium bromide solutions were freshly prepared and the concentrations calculated from the weight of lithium bromide and the volume were checked by Mohr titration.

When tetrabutylammonium iodide was substituted for the lithium bromide, no drift in $t_{1/2\alpha}$ was observed from 10 to 70% racemization (control for run 22). With 0.6 *M* tripropylamine in *tert*-butyl alcohol, there was no drift in $t_{1/2\alpha}$ from 12 to 62% racemization (control for run 23). With 0.6 *M* tripropylamine in tetrahydrofuran 1.5 *M* in *tert*-butyl alcohol no drift was observed in $t_{1/2\alpha}$ between 30 and 90% racemization.

Attempted Radical Chain Racemization of (+)-I-h.—A tube containing 12 mg. of α, α' -azobisisobutyronitrile (m.p. 100 – 103° with bubbling), 0.2 ml. of (+)-I-h, 1.4 ml. of *tert*-butyl alcohol, 2.3 ml. of tetrahydrofuran, 1.1 ml. of tripropylamine, and 5.0 ml. of a fresh 0.2 *M* solution of lithium bromide in tetrahydrofuran was sealed under a reduced pressure nitrogen atmosphere as described for run 22. After heating for 9 hr. at 75° ,¹⁸ the substrate

was recovered as in run 18 to give a colorless liquid, n_D^{25} 15.062. The rotation was about 6% low. The experiment was repeated in the absence of the initiator and the rotation of the recovered substrate was low by about 3%.

Racemization of (+)-I-h in the Presence of a Radical Trap.—An ampoule was prepared as above, except that 50 mg. of *p*-benzoquinone (m.p. 121 – 114°) was substituted for the α, α' -azobisisobutyronitrile. After heating at 140° for 3 hr., the substrate was recovered as in run 18, n_D^{25} 1.5067, 49% racemized. In the absence of the inhibitor, 53% racemization was observed in 3 hr. The agreement was adequate in light of the techniques used.

Deuterium Analyses by Infrared Spectrometry.—Five standards of known composition, varying from 0% I-d to 99% I-d, were prepared by weighing the appropriate amounts of materials into vials. A Perkin–Elmer 421 dual grating infrared spectrophotometer was used at nearly normal operating conditions: gain 4, attenuator 11.00, slits on program 10.00, suppression 0, source current 0.35, amp., scan speed 7 cm.⁻¹/min. The samples were run neat in the same 0.1-mm. cells vs. air. The peak at 986 cm.⁻¹ was used for analysis. This absorption is present in I-h but absent in I-d. The optical density at 986 cm.⁻¹ for each known was measured by scanning from 1025 to 950 cm.⁻¹. A straight line was obtained by plotting optical density vs. % I-d in the known samples, and the average scatter of points from the line was about 1%. The knowns and unknowns were always run in succession, and the calibration curve was redetermined every time the unknowns were analyzed. A protio sensitive peak at 888 cm.⁻¹ was scanned for qualitative confirmation of the numbers obtained from the 986 cm.⁻¹ peak, particularly when only a small amount of exchange occurred.

(+)-1,2-Diphenyl-1-propanone was prepared by the chromic acid oxidation of 10 g. of (–)-*threo*-1,2-diphenyl-1-propanol (m.p. 61 – 62° , $[\alpha]_D^{25}$ -46.8° , *c* 5.1 in chloroform) with sodium dichromate dihydrate in glacial acetic acid–sulfuric acid–water and benzene.⁹ Material (4.42 g.) was obtained, m.p. 31 – 32° , $[\alpha]_D^{25}$ $+196^{\circ}$, *c* 3.9 chloroform, and was used in the subsequent exchange experiments.

Exchange and Racemization of (+)-1,2-Diphenyl-1-propanone with Tripropylamine in *tert*-Butyl Alcohol-O-d.—A tube containing 0.60 ml. of optically active ketone, 1.2 ml. of tripropylamine, and 10.0 ml. of deuterated *tert*-butyl alcohol (0.976 atom of deuterium per molecule) was sealed in an atmosphere of nitrogen and heated at 145° for 6 hr. The reaction mixture was poured into 75 ml. of pentane, and the pentane solution was washed with water, with a slight excess of dilute hydrochloric acid, and again with water. The pentane solution was dried, evaporated, and the residue was distilled at 1 mm. to give 0.49 g. of ketone, $[\alpha]_D^{25}$ $+101.5^{\circ}$, *c* 3.94 in chloroform, 48% racemized. The amount of hydrogen in the 2-position of the ketone was measured using a Varian A-60 nuclear magnetic resonance spectrophotometer. The methyl group gave absorption which occurred as a doublet at about 8.4 τ and was used as an internal standard for the absorption of the benzyl hydrogen, which occurred as a quartet at about 5.3 τ . This hydrogen was $45 \pm 5\%$ exchanged and, therefore, $k_e/k_{\alpha} \sim 1$.

Exchange and Racemization of (+)-1,2-Diphenyl-1-propanone with Tripropylamine in Tetrahydrofuran 1.5 *M* in *tert*-Butyl Alcohol-O-d.—A heavy-walled Pyrex tube was cleaned with aqueous ammonia and rinsed with distilled water, acetone, and pentane. It was dried at 110° and cooled at 0.03 mm. It was then flamed out and cooled at 0.03 mm., and dry air was admitted. Tetrahydrofuran (23 ml.) was distilled from lithium aluminum hydride directly into the tube. Pipettes were dried at 115° and cooled by blowing nitrogen through them. Freshly purified tripropylamine (3.30 ml.) was placed in the tube, followed by 0.50 ml. of ketone and 4.5 ml. of *tert*-butyl alcohol-O-d (0.997 atom of deuterium per molecule). The tube was closed with a drying tube and cooled to -78° , evacuated, and sealed. It was then heated at 160° for 28 hr., cooled, and opened. The reaction mixture was shaken with 75 ml. of pentane and 300 ml. of water; the organic layer was washed with dilute hydrochloric acid and again with water. The solution was dried, evaporated, and the residue was distilled at 0.5 to 1.0 mm. with the pot at 155° to give 0.500 g. of colorless liquid, $[\alpha]_D^{25}$ $+62.8^{\circ}$, *c* 4.24 in chloroform, 68% racemized. Using the nuclear magnetic resonance method of analysis, the benzyl position contained 32% of 1 atom of hydrogen, and was therefore $68 \pm 5\%$ exchanged. Thus, $k_e/k_{\alpha} = 1$.

(18) About three-fourths of the initiator should have decomposed under these conditions; C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 469.