

TABLE I
SAPONIFICATION RATE OF ETHYL CYCLOHEXANECARBOXYLATE IN 70% ETHANOL AT 25.2°

Base, 30 ml. of 0.2206 *N* NaOH; ester equivalent, 1.0341 g. quench acid, 10 ml. of 0.05043 *N* HCl, indicator, phenolphthalein; back titration alkali, 0.05651 *N* NaOH; $a = 0.03308$ mole/l.

Time, sec.	Titer, ml. of NaOH 0.05651 <i>N</i>	x , mole/l.	$a - x$, mole/l.	Reaction, %	$k \times 10^4$, l./mole/sec.
Zero	3.07	0	0.03308	0	..
10175	4.21	0.00644	.02664	19.5	7.19
13892	4.56	.00842	.02466	25.5	7.39
17474	4.79	.00970	.02336	29.3	7.21
20673	5.03	.01107	.02201	33.5	7.34
22701	5.14	.01170	.02138	35.4	7.26
25624	5.27	.01243	.02065	37.6	7.13
27779	5.44	.01339	.01969	40.5	7.42
35455	7.01	.02226	.01082	67.3	7.24
98900	7.22	.02345	.00963	70.9	7.41
Mean $k = 7.29$					

TABLE II
SUMMARY OF SAPONIFICATION RUNS

Ethyl ester of acid	a , mole/l.	$k \times 10^4$, l. mole ⁻¹ sec. ⁻¹	Reacn., %
Cyclohexanecarboxylic	0.03414	7.31 ± 0.14 ^b	68
	.03408	7.16 ± .07	67
	.03395	7.17 ± .11	67
	.03308	7.29 ± .09	71
	.02746 ^a	7.31 ^a ± .13	63 ^a
<i>cis</i> -4- <i>t</i> -Butylcyclohexanecarboxylic	.03410	0.428 ± .016	28
	.03308	0.427 ± .012	26
<i>trans</i> -4- <i>t</i> -Butylcyclohexanecarboxylic	.03414	8.52 ± .13	51
	.03442	8.48 ± .12	47
	.03297	8.49 ± .18	45
<i>cis</i> -4-Methylcyclohexanecarboxylic	.02788 ^a	2.82 ^a ± .19	42 ^a
	.02758 ^a	2.47 ^a ± .03	53 ^a

^a These runs were carried out using 15 ml. of 0.2 *N* NaOH and an equivalent amount of ester, each diluted to 50 ml. of 70% ethanolic solution. ^b This figure and all corresponding ones indicate mean deviations.

The basic aqueous layer was acidified with concentrated hydrochloric acid and the acid liberated was extracted with petroleum ether. The crude acid recovered from the petroleum ether layer in the usual manner melted at 107–112°, raised to 115–117° by one recrystallization from petroleum ether (b.p. 30–60°). Its infrared spectrum was identical with that of the pure *cis*-acid (lit.⁶ m.p. 117–118°), indicating that little if any epimerization had occurred in the saponification.

Kinetic Saponification Runs.—The alkali solution for the kinetic runs was prepared by diluting exactly 30 ml. of standardized 0.2 *N* carbonate-free aqueous sodium hydroxide to 100 ml. by means of absolute ethanol in a volumetric flask. An amount of ester exactly equivalent to 30 ml. of the alkali was weighed out in a small weighing bottle, transferred to a 100-ml. volumetric flask and made up to the mark with absolute ethanol after prior addition of exactly 30 ml. of boiled distilled water. Both solutions then were placed in a thermostat at 25.2° for at least 60 minutes and then mixed by pouring them through a wide-necked funnel into a 250-ml. glass-stoppered round-bottom flask in the thermostat. A 10-ml. aliquot was withdrawn immediately and the clock started. This sample and all aliquots subsequently withdrawn were quenched in a mixture of 10 ml. of standardized hydrochloric acid and 25 ml. of absolute ethanol (in some cases 15 ml. of absolute ethanol) and back-titrated with 0.05 *N* sodium hydroxide using phenolphthalein as an indicator. A blank was run at the start of each saponification run.

Specific rates were calculated from the equation $k = x/a \times t(a-x)$ where t is the time in seconds, a is the initial concentration of ester or base in moles/l. and x is the amount of ester or base, expressed in moles/l. consumed in time t .

A typical saponification run is detailed in Table I. Table II summarizes the specific rates determined in this investigation.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, LOS ANGELES 24, CALIF.]

Electrophilic Substitution at Saturated Carbon. XI. Steric Course of the Base-catalyzed Decarboxylation Reaction¹

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The steric course of the base-catalyzed decarboxylation of optically pure 2-cyano-2-phenylbutanoic acid to 1-cyano-1-phenylpropane has been studied. The reaction was found to occur with 16% net retention to 11% net inversion. The steric course was controlled by the dissociating power and acidity of the solvent and, in some media, by the character of the cation. In *t*-butyl alcohol, the ammonium salt gave 10% retention, whereas metal salts provided almost completely racemic product. In ethylene glycol, the extreme inversion solvent, the stereospecificity of the reaction was independent of the concentration and nature of the cation for five different cations. In phenol, ammonium and potassium salts gave 16% and 8% net retention, respectively, whereas lithium and tetramethylammonium salts gave 5% and 6% net inversion, respectively. The results are interpreted in terms of a mechanistic scheme in which intimate ion pairs cleave to give retention, and solvent-separated or dissociated anions to give inversion of configuration. Both processes involve carbanion intermediates, which collapse to optically active product because of the asymmetric character of their environment. The more acidic the proton donor, the shorter the life of the carbanion, and the more stereospecific the reaction.

The decarboxylation of carboxylic acids has long been considered one of the most ubiquitous ex-

amples of an electrophilic substitution reaction. Suggestions have been made² that this reaction

(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 donors of this fund.

(2) (a) H. Schenkel and M. Schenkel-Rudin, *Helv. Chim. Acta*, **31**, 514 (1948); (b) B. R. Brown, D. L. Hammick and A. J. B. Scholefield, *J. Chem. Soc.*, 778 (1950).

TABLE I
EFFECT OF SOLVENT ON STERIC COURSE OF DECARBOXYLATION OF AMMONIUM (-)-2-CYANO-2-PHENYLBUTYRATE^a

Run	Base concn., <i>M</i>	Temp., °C.	Time, hr.	Yld., %	Product ^b		Steric direction ^d	Solvent Nature	ε ^c , °
					α ²⁵ _D ^e	% opt. purity			
1	0.025	68	86	21	-3.39°	14.7	Ret.	C ₆ H ₅ OH	9.9 ¹⁸
2	.10	25	39	89	-2.23	9.7	Ret.	(CH ₃) ₃ COH	6.6 ¹⁹
3	.10	100	122	50	-1.18	5.1	Ret.	CH ₃ CO ₂ H	6.4 ²⁰
4	.10 ^f	25	70	90	-0.90	3.9	Ret.	O(CH ₂ CH ₂) ₂ O	2.2
5	.025 ^g	25	39	81	-.45	2.0	Ret.	C ₂ H ₅ OH	22 ²⁰
6	.025 ^g	25	63	84	-.16	0.7	Ret.	CH ₃ OH	33 ²⁰
7	.025 ^g	25	75	71	+2.57	11.1	Inv.	HOCH ₂ CH ₂ OH	35 ²⁰

^a Unless otherwise indicated, 0.10 *M* solutions of optically pure salt were employed. ^b Optically pure 1-cyano-1-phenylpropane has α_D + or -23.1° (1 dm., neat). ^c *l* = 1 dm., neat. ^d See Discussion for assignment of steric direction. ^e Value for dioxane from D. W. Thomas and A. E. Martell, *J. Am. Chem. Soc.*, **78**, 1337 (1956). All others are taken from the "International Critical Tables of Numerical Data of Physics, Chemistry and Technology," Vol. 6, (1929). ^f Solution was heterogeneous throughout due to insolubility of salt in dioxane. All other solutions were homogeneous. ^g Solutions were 0.025 *M* in optically pure ammonium (-)-2-cyano-2-phenylbutyrate, and 0.075 *M* in optically pure (-)-2-cyano-2-phenylbutyric acid.

may proceed by either an S_E1 or an S_E2 mechanism, and a large amount of kinetic data has been gathered in support of one or the other mechanism.³

Evidence for the intervention of carbanions (and hence for an S_E1 mechanism) in the decarboxylation of trihaloacetic acids^{3b,3c,4} is found in the correlation of the rates of this process and that of proton abstractions of the corresponding haloform products.⁵ The decarboxylation of quinaldinic and isoquinaldinic acids in the presence of aldehydes and ketones is known to yield the carbinols expected from the addition of the 2-quinolyl or 2-isoquinolyl carbanion to the carbonyl group of the aldehyde or ketone.⁶ No difference in rate was observed in the decarboxylation of trinitrobenzoic acid in ordinary and heavy water,⁷ a fact consistent with a carbanionic mechanism for the reaction.

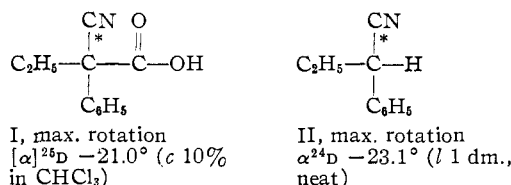
The stereochemical course of the decarboxylation reaction in systems containing several asymmetric centers has been studied,⁸ as has the decarboxylation of optically active acids catalyzed by optically active bases.⁹

The stereochemical capabilities of carbanions formed by decarboxylation of systems containing a single asymmetric center have been examined in a few systems. The decarboxylation of optically active 2-methyl-2-(1-pyridyl)-butyric acid in water gave racemic 1-*sec*-butylpyridine.¹⁰

A number of optically active α-cyano and α-carbomethoxy acids were observed to decarboxylate without solvent to give racemic products.¹¹ In

contrast, the amine-catalyzed decarboxylation (no solvent) of optically active 2-methyl-2-benzenesulfonylbutyric acid has been reported to give optically active 2-benzenesulfonylbutane.¹² The stereospecificity was considered to be evidence against a carbanionic mechanism. Decarboxylation of optically active 2-methyl-2-phenylbutanoic acid could be carried out only under conditions which completely racemized the product, although base-catalyzed deamidations and decyanations in aromatic amine solvents were found to occur with low retention of configuration.¹³

This paper describes the decarboxylation of various metal and ammonium salts of (-)-2-cyano-2-phenylbutanoic acid (I) to give optically active 1-cyano-1-phenylpropane (II). The widely recognized carbanion-stabilizing effect of phenyl and cyano groups activated this system enough to allow the reaction to be carried out at 25° in most solvents.¹⁴



Relative Configurations of I and II.—Optically pure (-)-I and (-)-II were prepared. The ammonium salt of (-)-I was found to decarboxylate in a variety of solvents to give product II whose sign and optical purity depended on the character of the medium. Table I summarizes the results. Appropriate control reactions demonstrated that the product once formed maintained its configurational integrity.

The pattern of results obtained in the four alcohols as solvents resembles that obtained when sys-

(3) (a) K. J. Pedersen, *J. Phys. Chem.*, **38**, 559 (1934); (b) R. A. Fairclough, *J. Chem. Soc.*, 1186 (1938); (c) F. H. Verhoek, *J. Am. Chem. Soc.*, **56**, 571 (1934), and subsequent papers; (d) B. R. Brown and D. L. Hammick, *J. Chem. Soc.*, 659 (1949), and subsequent papers; (e) W. M. Schubert, *J. Am. Chem. Soc.*, **71**, 6639 (1949); (f) W. S. Johnson and W. E. Heinz, *ibid.*, **71**, 2913 (1949).

(4) (a) L. M. Sutherland and J. G. Aston, *ibid.*, **61**, 241 (1939); (b) I. Auerbach, F. H. Verhoek and A. L. Henne, *ibid.*, **72**, 299 (1950).

(5) J. Hine, N. W. Burske, M. Hine and P. B. Langford, *ibid.*, **79**, 1406 (1957).

(6) P. Dyson and D. L. Hammick, *J. Chem. Soc.*, 1724 (1937).

(7) R. E. Glick, *Chemistry & Industry*, 716 (1955).

(8) (a) T. L. Jacobs and W. M. Florsheim, *J. Am. Chem. Soc.*, **72**, 256 (1950); (b) H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956), and subsequent papers.

(9) (a) P. Pratesi, L. Arpesella and A. LaManná, *ibid.*, **75**, 5476 (1953); (b) P. Pratesi, A. LaManná and L. Arpesella, *Il Farmaco (Pavia)*, *Ed. Sci.*, **11**, 27 (1956); *C. A.*, **50**, 13800 (1956).

(10) W. E. Doering and V. Z. Pasternak, *J. Am. Chem. Soc.*, **72**, 143 (1950).

(11) J. Kenyon and W. A. Ross, *J. Chem. Soc.*, 3407 (1951).

(12) J. E. Taylor and F. H. Verhoek, *J. Am. Chem. Soc.*, **81**, 4537 (1959).

(13) D. J. Cram, A. Langemann, J. Allinger and K. R. Kopecky, *ibid.*, **81**, 5740 (1959).

(14) Interesting examples of the anion-stabilizing effects of the nitrile group are found in the facile cleavage of malononitriles with Grignard reagents [T. L. E. Erickson and M. M. Barnett, *ibid.*, **57**, 560 (1935)], and the cyanide ion-catalyzed decarboxylation of α-ketoacids followed by benzoin condensation of the products [V. Franzen and L. Fikentscher, *Ann.*, **613**, 1 (1952)].

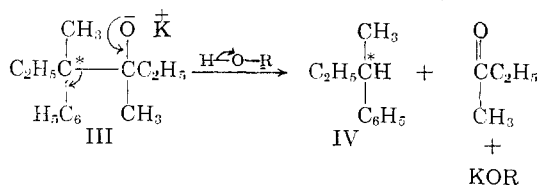
TABLE II

EFFECT OF CATION VARIATION ON STERIC COURSE OF DECARBOXYLATION OF (-)-2-CYANO-2-PHENYLBUTYRATE ANION^a IN *t*-BUTYL ALCOHOL AT 25°

Run	Base		Time, hr.	Yld., %	Product ^b		Steric direction	Cation
	Nature ^d	Concn., M			α^{25} -D ^e	% opt. purity		
2	NH ₃ ^d	0.10	39	89	-2.23°	9.7	Ret.	NH ₄ ⁺
8	K ₂ CO ₃ ^{d,f}	.025	68	71	0.00	0.0	Rac.	K ⁺
9	KOC(CH ₃) ₃ ^{d,g}	.025	46	69	-.07	.3	Rac.	K ⁺
10	KO ₂ CC(CH ₃) ₃ ^h	1.10	120	55	+.08	.3	Rac.	K ⁺
11	Li ₂ CO ₃ ^d	0.05	91	28	.00	.0	Rac.	Li ⁺
12	None ⁱ	..	110	90	-.47	2.1	Ret.	H ⁺

^a Optically pure materials were used throughout. ^b Optically pure 1-cyano-1-phenylpropane has $\alpha_D^{25} +$ or -23.1° (*l* 1 dm., neat). ^c *l* = 1 dm., neat. ^d Solution 0.10 M in ammonium salt of acid. ^e Solution was 0.10 M in acid. ^f Much of the potassium carbonate remained undissolved. ^g Solution was homogeneous for first 35 hours of reaction, after which metal carbonate precipitated. ^h Voluminous precipitate appeared when the reagents were mixed. ⁱ Much of the lithium carbonate remained undissolved. ^j Reaction was carried out at 125°.

tems such as III were cleaved to give IV in the same solvents.¹⁵ The relative configurations of



III and IV were demonstrated by independent experiments,¹⁶ and the steric course and specificities of the reactions are tabulated. Attempts to relate the configurations of I and II by independent means failed. However, the behavior patterns of I and III in the four solvents are similar enough to one another to allow the relative configurations of I and II to be assigned with considerable confidence. Thus III gives IV with decreasing retention as the solvent is changed from *t*-butyl to ethyl to methyl alcohol, whereas ethylene glycol provides inverted product. The ammonium salt of (-)-I gives (-)-II of decreasing optical purity as the solvent is changed from *t*-butyl to ethyl to methyl alcohol, and (+)-II is produced in ethylene glycol. Clearly in the three alcohols the decarboxylation occurs with retention and in ethylene glycol with inversion of configuration. Further support for this conclusion is found in the fact that the steric course of electrophilic substitution of a large variety of systems depends in a similar way on the character of the solvent.¹⁷ The above correlation not only allows the relative configurations of I and II to be assigned, but also permits the steric courses

Solvent	Net steric course for cleavage of III	
	NH ₄ ⁺ salt of I (run no., Table I)	(run no., ref. 15)
(CH ₃) ₂ COH	(-)-II, 10% opt. pure (2)	89% ret. (18)
C ₂ H ₅ OH	(-)-II, 2% opt. pure (5)	60% ret. (21)
CH ₃ OH	(-)-II, 0.7% opt. pure (6)	11% ret. (24)
HOCH ₂ CH ₂ OH	(+)-II, 11% opt. pure (7)	48% inv. (29)

(15) D. J. Cram, A. Langemann and F. Hauck, *J. Am. Chem. Soc.*, **81**, 5750 (1959).

(16) D. J. Cram, K. R. Kopecky, F. Hauck and A. Langemann, *ibid.*, **81**, 5754 (1959).

(17) (a) D. J. Cram, A. Langemann, W. Lwowski and K. R. Kopecky, *ibid.*, **81**, 5760 (1959); (b) D. J. Cram, F. Hauck, K. R. Kopecky, and W. D. Nielsen, *ibid.*, **81**, 5767 (1959); (c) D. J. Cram, J. L. Mateos, F. Hauck, A. Langemann, K. R. Kopecky, W. D. Nielsen and J. Allinger, *ibid.*, **81**, 5774 (1959); (d) D. J. Cram and W. D. Nielsen, *ibid.*, **83**, 2174 (1961); (e) D. J. Cram and B. Rickborn, *ibid.*, **83**, 2178 (1961); (f) D. J. Cram, L. Gaston and H. Jäger, *ibid.*, **83**, 2183 (1961).

of the decarboxylation reaction to be determined under conditions unattainable with other systems.

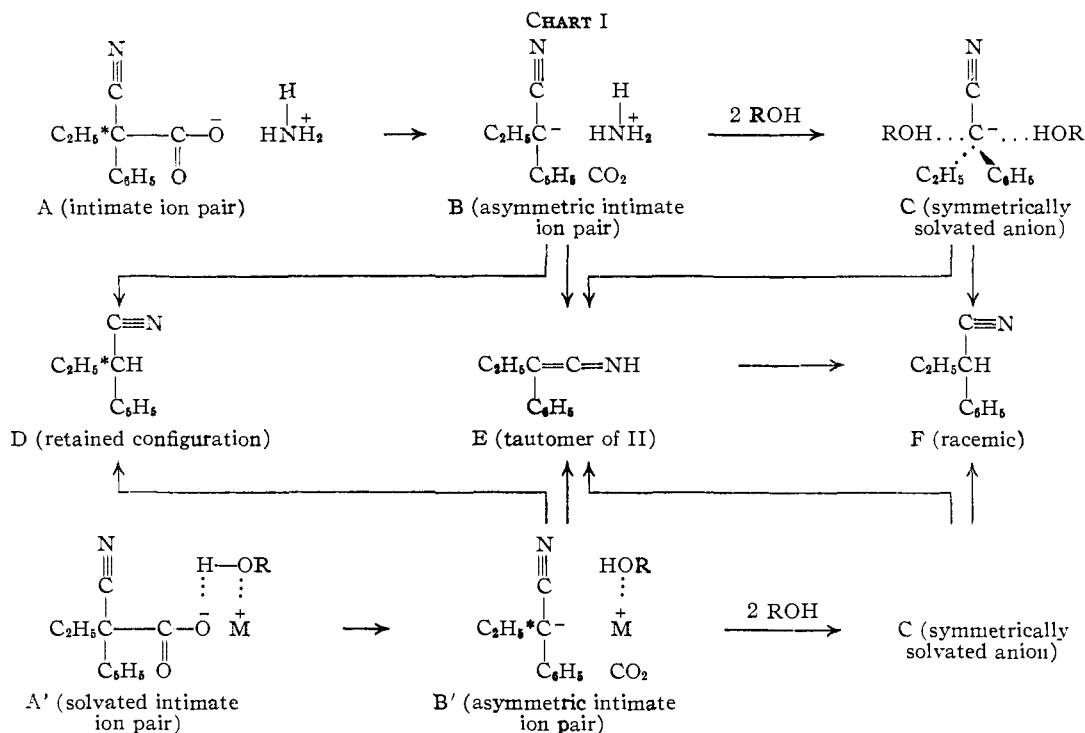
Decarboxylations in *t*-Butyl Alcohol.—Table II reports the results of decarboxylations in *t*-butyl alcohol as solvent. The steric course in this solvent depends on the nature of the cation of the salt which undergoes the cleavage reaction. The ammonium salt gives II with about 10% net retention of configuration (run 2), whereas the potassium and lithium salts give essentially racemic product (runs 9–11). These reactions were carried out under conditions which preserved the optical integrity of the product once formed. The free acid was also stable under these conditions. At 100° higher temperature, the acid did cleave to give II with 2% net retention of configuration (run 12).

The low dissociating power of *t*-butyl alcohol coupled with the sensitivity of the steric course to the cation suggests that intimate ion pairs are the species which cleave in this medium. The mechanisms considered most likely to apply are outlined in Chart I. The sequence, A → B → D, describes the retention mechanism for the ammonium salt, while sequences A → B → E → F and A → B → C → F account for the racemic product. The stereospecific mechanism results from the ammonium ion donating a proton to the carbanion of the asymmetric intimate ion pair. The non-stereospecific mechanism results from either the formation of the tautomer E or from relatively long-lived carbanions becoming symmetrically solvated (C) and giving racemic product.

When metal cations are substituted for the ammonium ion, mechanisms A → B' → C → E → F and A' → B' → C → F dominate. Mechanism A' → B' → D is relatively unimportant because unlike the ammonium ion, *t*-butyl alcohol is not sufficiently acidic to capture this rather stable carbanion before it passes into a symmetrical environment.¹⁸

Decarboxylations in Ethylene Glycol.—Table III records the results of decarboxylations conducted in ethylene glycol as solvent. The ammonium, tetramethylammonium, potassium, lithium and magnesium salts gave product with 10.9 to 11.6% net inversion of configuration (runs 13–16). The

(18) The stability of the 1-cyano-1-phenylpropyl anion is indicated by the fact that optically active 1-cyano-1-phenylpropane racemizes in a 0.005 M solution of sodium bicarbonate in methanol at 25° with a half-life of 14 hours.



rates of these reactions were not widely dissimilar, and the reactions were conducted under conditions in which both the free acid I and optically active product II were stable.

the value of the equilibrium constant between ion pairs and dissociated ions K was high enough to provide dissociated anions as the main reactive species, even in the presence of added common

TABLE III

EFFECT OF CATION VARIATION ON STERIC COURSE OF DECARBOXYLATION OF (-)-2-CYANO-2-PHENYLBUTYRATE ANION^a AT 25° IN ETHYLENE GLYCOL

Run	Base		Time, hr.	Yld., %	Product ^b		Steric direction	Cation
	Nature	Concn., M			α_D^{25}	% opt. purity		
7	NH ₃	0.025	75	71	+2.57°	11.1	Inv.	NH ₄ ⁺
13	(CH ₃) ₄ NOH	.025	94	73	+2.66	11.6	Inv.	(CH ₃) ₄ N ⁺
14	K ₂ CO ₃	.025	65	85	+2.58	11.2	Inv.	K ⁺
15	Li ₂ CO ₃	.025	65	69	+2.61	11.3	Inv.	Li ⁺
16	MgO ^d	.025	140	78	+2.53	10.9	Inv.	Mg ⁺⁺
17	K ₂ CO ₃	.010	75	59	+2.64	11.4	Inv.	K ⁺
18	K ₂ CO ₃ ^e	.025	66	83	+2.08	9.0	Inv.	K ⁺ + (CH ₃) ₄ N ⁺
19	NH ₃ ^f	.025	75	65	+2.28	9.9	Inv.	NH ₄ ⁺
20 ^g	None	...	127	82	0.00	0.00	Rac.	H ⁺

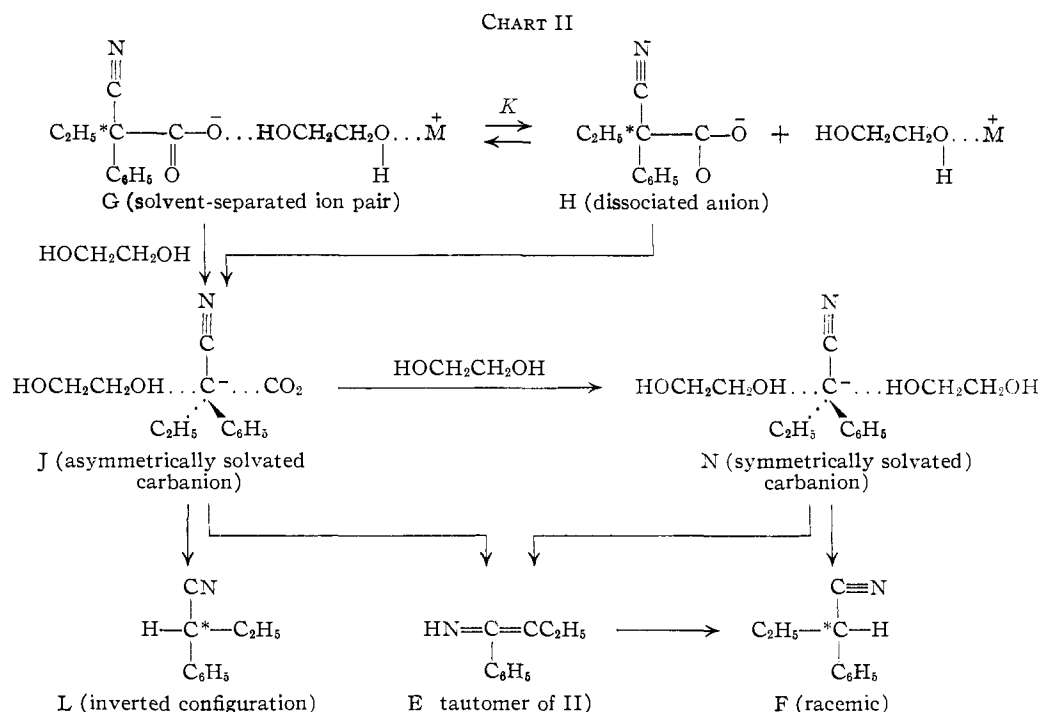
^a Solutions 0.10 M in optically pure acid were used. ^b Optically pure 1-cyano-1-phenylpropane has α_D^{25} + or -23.1° (l 1 dm., neat). ^c l = 1 dm., neat. ^d Much of this oxide remained as a second phase throughout the reaction; all other runs were homogeneous. ^e Solution was 0.50 M in (CH₃)₄NBr. ^f Solution was 0.50 M in NH₄Br. ^g Run at 125°, unlike the other runs which were conducted at 25°.

The similarity of the results indicates that the nature of the cation plays little or no role in determining the steric course of the reaction. This fact points to either a solvent-separated ion pair or a dissociated anion as the reacting species. In runs 14, 17, 18 and 19, efforts were made to determine if the stereochemical results and gross rates were subject to common ion mass law effects. Whatever effects exist appear to be extremely small.

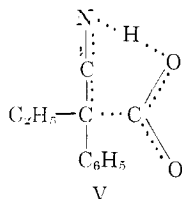
The mechanism considered most likely to apply is outlined in Chart II. Probably the dissociated anion H and solvent-separated ion pairs G cleave at similar rates, and provide a similar steric result. The absence of any mass law effect suggests that

the cleavage of either G or H is aided by solvation of the incipient anion by hydrogen bonding both at nitrogen and carbon. The species produced (J) is solvated on one side by solvent and on the other by carbon dioxide, and is therefore asymmetric. Immediate protonation of carbon provides inverted product L. Protonation of nitrogen gives tautomer E which ultimately gives racemic product. Another route to racemic product involves the symmetrically solvated anion N as an intermediate.

The free acid I decarboxylated only at a temperature 100° higher than any of the salts. The production of racemic product suggests that the reaction occurred by a mechanism different from



that operative with any of the salts (see run 20). The reaction might involve a single transition state (V) similar to that proposed for the decarboxylation of acetoacetic acid.¹⁹



Decarboxylation in Phenol.—Phenol as a solvent differs from *t*-butyl alcohol and ethylene glycol in the sense that although its dielectric constant is similar to that of *t*-butyl alcohol, its acidity and therefore its strength as an electrophile is greater than either of the two alcohols. Because phenol is a solid at room temperature, the decarboxylation reactions had to be conducted at 48° or above. Table IV records the results.

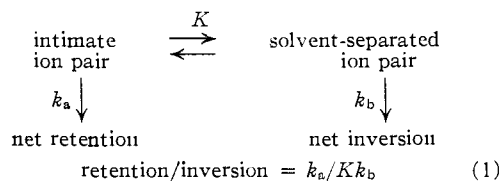
Over the temperature range of 48 to 100°, the steric results for cleavage of the ammonium salt varied only between 13.5 and 16% net retention of configuration (runs 21 to 24). Decarboxylation of the free acid I occurred at a much slower rate and with much lower stereospecificity (2.7% net retention). A temperature of 125° was needed to produce the reaction (run 31), and therefore the other runs are essentially free of product that arose from the free acid.

In this solvent, changes in cation affected both the steric direction and stereospecificity of the reaction. This result is interpreted as reflecting

NH ₄ ⁺	K ⁺	Mg ⁺⁺	Li ⁺	(CH ₃) ₄ N ⁺
16% ret.	8% ret.	0.4% inv.	5% inv.	6% inv.

(19) F. H. Westheimer and W. A. Jones, *J. Am. Chem. Soc.*, **63**, 3283 (1941).

cleavage of both intimate and solvent-separated ion pairs. The relative amounts of each which reacts is controlled by the interplay of the values of the equilibrium constant (K) between the two kinds of ion pairs, as well as the values for the rate of cleavage (k_a and k_b) of each species.^{17b} With the ammonium and potassium salts, the intimate ion pair accounts for more of the product. The ammonium salt gave the highest retention because of the advantageous orientation of the proton-donating ammonium ion on the side of the leaving group (mechanism A → B → D of Chart I). Potassium salt gives lower retention by the route A' → B' → D (Chart I). Unlike *t*-butyl alcohol, the acidity of phenol is high enough to dispose of the carbanion of B' before it becomes symmetrically solvated. Solvation on the side of the leaving group in B' is more important than on the remote side because the hydroxyl group coordinates with potassium ion in the starting intimate ion pair. With the lithium salts, the solvent-separated ion pair is considered to account for more of the product by the route G → J → L (Chart II). With the magnesium salt both species cleave. The relative values of K , k_a and k_b would be expected to vary with changes in solvation of the cation and anion of each ion pair, and relatively



subtle changes in solvation energies with changes in the cation would be enough to provide a change from net retention to net inversion.

The observed steric course (inversion) for reaction of the quaternary ammonium salt may involve

TABLE IV
EFFECT OF CATION VARIATION AND TEMPERATURE ON STERIC COURSE OF DECARBOXYLATION OF (-)-2-CYANO-2-PHENYLBUTYRATE ANION^a IN PHENOL

Run	Base		Temp., °C	Time, hr.	Yld., %	Product ^b		Steric direction	Cation
	Nature	Concn., M				α^{23-21D^c}	% opt. purity		
21	NH ₃ ^d	0.10	48	192	22	-3.10°	13.6	Ret.	NH ₄ ⁺
22	NH ₃ ^d	.10	68	85	70	-3.62	15.7	Ret.	NH ₄ ⁺
23	NH ₃ ^d	.10	85	88	76	-3.31	14.3	Ret.	NH ₄ ⁺
24	NH ₃ ^d	.10	100	43	76	-3.12	13.5	Ret.	NH ₄ ⁺
25	K ₂ CO ₃ ^e	.025	48	88	10	-1.51	6.5	Ret.	K ⁺
26	KOC ₆ H ₅ ^e	.10	68	90	52	-1.82	7.9	Ret.	K ⁺
27	MgO ^f	.05	68	255	2	+0.10	0.4	Inv.	Mg ⁺⁺
28	LiOC ₆ H ₅ ^{e,g}	.10	68	233	63	+1.13	4.9	Inv.	Li ⁺
29	LiOC ₆ H ₅ ⁺	.10 ^h	68	288	24	+0.96	4.2	Inv.	Li ⁺
30	(CH ₃) ₄ NOH ^e	.10	68	93	76	+1.36	5.9	Inv.	(CH ₃) ₄ N ⁺
31	None ^e	..	125	110	78	-0.62	2.7	Ret.	H ⁺

^a Optically pure ammonium salt or acid was used throughout. ^b Optically pure 1-cyano-1-phenylpropane has $\alpha_D^{20} +$ or -23.1° (*l* 1 dm., neat.) ^c *l* = 1 dm., neat. ^d Solution 0.10 M in ammonium salt of the acid was used. ^e Solution 0.10 M in acid used. ^f Only a fraction of this oxide dissolved. ^g A gelatinous precipitate was present throughout the reaction; all other runs were homogeneous. ^h Solution was 0.80 M in LiClO₄.

TABLE V
EFFECT OF CATION CONCENTRATION AND NATURE ON STERIC COURSE OF DECARBOXYLATION OF (-)-2-CYANO-2-PHENYLBUTYRATE ANION^a AT 25° IN ETHANOL AND METHANOL

Run	Solvent	Base		Added salt		Time, hr.	Yld., %	Product ^b		Steric direction
		Nature	Concn., M	Nature	Concn., M			α^{23-21D^c}	% opt. purity	
5	C ₂ H ₅ OH	NH ₃	0.025	39	81	-0.45°	2.0	Ret.
32	C ₂ H ₅ OH	NH ₃	.77	20	66	-1.03	4.5	Ret.
6	CH ₃ OH	NH ₃	.025	63	84	-0.16	0.7	Ret.
33	CH ₃ OH	NH ₃	.48	40	70	-0.40	1.7	Ret.
34	CH ₃ OH	NH ₃	.025	NH ₄ Br	0.50	49	59	-1.07	4.6	Ret.
35	CH ₃ OH	K ₂ CO ₃	.025	48	90	+0.066	0.3	Inv.
36	CH ₃ OH	K ₂ CO ₃	.025	7	41	+ .022	.1	Inv.
37	CH ₃ OH	K ₂ CO ₃	.025	KI	0.50	72	90	+ .024	.1	Inv.
38	CH ₃ OH	K ₂ CO ₃	.025	KI	0.50	13	38	+ .29	1.7	Inv.
39	CH ₃ OH	Na ₂ CO ₃	.025	48	83	+ .17	0.7	Inv.
40	CH ₃ OH	Na ₂ CO ₃	.025	18	69	+ .13	0.6	Inv.
41	CH ₃ OH	Na ₂ CO ₃	.025	NaClO ₄	2.0	88	62	+ .65	2.8	Inv.
42	CH ₃ OH	Na ₂ CO ₃	.025	NaClO ₄	2.0	51	24	+ .59	2.6	Inv.
43	CH ₃ OH	Li ₂ CO ₃	.025	55	79	- .03	0.1	Ret.
44	CH ₃ OH	Li ₂ CO ₃	.025	LiClO ₄	2.0	384	76	+ .16	.7	Inv.
45	CH ₃ OH	MgO	^d	50	83	+ .08	.4	Inv.

^a Solutions were 0.10 M in (-)-2-cyano-2-phenylbutyric acid except run 32 which was 0.77 M in acid and run 33 which was 0.48 M in acid. ^b Optically pure 2-phenylbutyronitrile has $\alpha_D^{20} +$ or -23.1° (*l* 1 dm., neat.) ^c *l* = 1 dm., neat. ^d MgO did not dissolve perceptibly.

a mechanism in which intimate ion pair cleaves to give a new intimate ion-pair clump, which does not involve a proton donor. The side of the anion remote from the leaving group is more exposed to electrophiles, and net inversion results.

Decarboxylations in Other Solvents.—A number of decarboxylations were carried out in ethanol and methanol, which are intermediate between *t*-butyl alcohol and ethylene glycol in their ability to dissociate ion pairs. Table V records the results. In these solvents, probably both intimate and solvent-separated ion pairs cleave. As anticipated, the stereochemical results are between those in *t*-butyl alcohol and in ethylene glycol. The results can be interpreted in terms of competition between the two stereospecific mechanisms and the non-stereospecific mechanisms of Charts I and II. A number of special features deserve mention.

In both ethanol and methanol, a small mass law effect is visible. Thus, an increase in ammonium ion concentration in the medium raises the re-

tained product from 2 to 4.5% in ethanol (runs 5 and 32), and from 0.7 to 4.6% in methanol (runs 6-34). This result suggests that a small amount of free anion undergoes decarboxylation to give inversion of configuration, and that this reaction is suppressed by addition of ammonium ion by shifting the equilibrium toward the ion pairs.

A salt effect which operates in the opposite direction is apparent particularly in runs 39-42. Addition of enough sodium perchlorate to make the solution 2 M increased the amount of inversion from 0.7 to 2.7%. The absence of a visible mass law effect suggests that only ion pairs undergo cleavage, and that the large increase of polarity of the medium with added salt increased the concentration of the solvent-separated ion pairs.

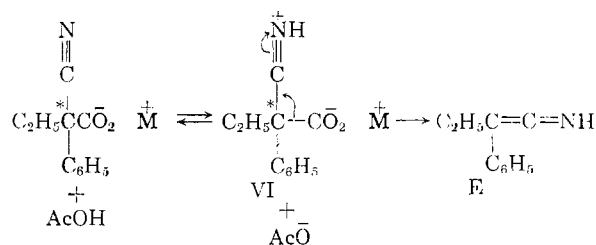
Table VI records the results of decarboxylations carried out in glacial acetic acid, and in mixtures of glacial acetic acid-dioxane and glacial acetic acid-*t*-butyl alcohol mixtures. The very low stereospecificities observed are attributed to the predomi-

TABLE VI
EFFECT OF CATION ON STERIC COURSE OF DECARBOXYLATION OF (-)-2-CYANO-2-PHENYLBUTYRATE ANION^a AT 25° IN ACETIC ACID AND ACETIC ACID-SOLVENT MIXTURES

Run	Solvent	Base		Temp., °C.	Time, hr.	Yld., %	Product ^b		Steric direction	Cation
		Nature	Concn., M				α^D_{25} ^c	% opt. purity		
3	CH ₃ CO ₂ H	NH ₄ ^d	0.10	100	122	50	-1.18°	5.1	Ret.	NH ₄ ⁺
46	CH ₃ CO ₂ H	KO ₂ CCH ₃	.10	68	120	83	-0.09	0.4	Ret.	K ⁺
47	CH ₃ CO ₂ H	KO ₂ CCH ₃ ^e	.10	25	1218	23	-.08	0.4	Rac.	K ⁺
48	CH ₃ CO ₂ H	None	.	100	210	50	-.36	1.6	Ret.	..
49	CH ₃ CO ₂ H	LiO ₂ CCH ₃ ^e	0.10	68	220	72	+.01	0.0	Rac.	Li ⁺
50	10% CH ₃ CO ₂ H-90% O(CH ₂ CH ₂) ₂ O	KO ₂ CCH ₃ ^e	.10	25	73	69	-.06	0.3	Ret.	K ⁺
51	20% CH ₃ CO ₂ H-80% O(CH ₂ CH ₂) ₂ O	KO ₂ CCH ₃ ^e	.10	25	70	69	-.27	1.2	Ret.	K ⁺
52	40% CH ₃ CO ₂ H-60% O(CH ₂ CH ₂) ₂ O	KO ₂ CCH ₃ ^e	.10	25	124	70	-.26	1.1	Ret.	K ⁺
53	5% CH ₃ CO ₂ H-95% (CH ₃) ₃ COH	KO ₂ CCH ₃ ^e	.10	25	160	86	-.01	0.0	Rac.	K ⁺

^a Optically pure acid or ammonium salt used in all cases. ^b Optically pure 1-cyano-1-phenylpropane has α^D_{25} + or -23.1° (l 1 dm., neat). ^c l = 1 dm., neat. ^d Solutions were 0.10 M in ammonium salt of acid. ^e Solutions were 0.10 M in (-)-2-cyano-2-phenylbutyric acid.

nance of mechanisms which involve tautomer E as an intermediate in the sequence. Unlike phenol, acetic acid is probably a strong enough acid to donate a proton reversibly to the nitrile group, and the conjugate acid of the salt VI is possibly the species which cleaves. In the absence of basic



salts, the decarboxylation occurred at a rate less than one-third the rate of decarboxylation of the ammonium salt (run 48).

Another possible reason why acetic acid does not give retention in the decarboxylation of metal salts is because of its low basicity. Orientation of acetic acid by metal cation of an intimate ion pair is probably less than with more basic solvents such as phenol.

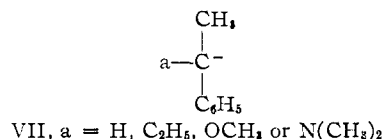
Comparison of Electrophilic Substitutions at Saturated Carbon in Different Systems.—Papers I-VI and VIII-X of this series reported the stereochemical course of electrophilic substitution at saturated carbon in a variety of systems and solvents.^{13,15-17} The stereochemical results ranged from 99% net retention¹⁷ to complete racemization^{17c,17e} to 65% net inversion.^{17e} The striking feature of the results taken as a whole is the similarity in behavior of the various systems studied. The reactions involve such diverse types as base-catalyzed cleavages of alcohols, ketones, nitriles, amides, hydrocarbons, ethers²⁰ and carboxylic acids, and base-catalyzed hydrogen-deuterium exchange reactions.²¹ Similar mechanistic schemes have been devised to correlate and explain the various effects observed.^{17c,17d,17e,20,21}

A notable difference between the decarboxylations of this paper and the reactions described in the previous investigations deserves mention. The

(20) D. J. Cram, C. A. Kingsbury and A. Langemann, *J. Am. Chem. Soc.*, **81**, 5785 (1959).

(21) D. J. Cram, C. A. Kingsbury and B. Rickborn, *ibid.*, **81**, 5835 (1959).

carbanions formed in the previous studies were stabilized by only a phenyl group, whereas the carbanion involved in the decarboxylations was stabilized by both phenyl and cyano groups. The consequences of this difference are clearly evident in the facts: (1) The decarboxylations of salts of I occurred at temperatures as much as 235° lower than that required for the other cleavage reactions. (2) The stereospecificity of the decarboxylations was lower due to the greater stability and lifetime of the anion, to the inferior shielding ability of carbon dioxide as a leaving group, and to the formation of tautomer of the nitrile. (3) The stereospecificity and even the steric direction of the reaction was subject to the acidity of the solvent. In the other cleavages, the carbanion was so unstable that it was unable to discriminate between solvents whose acidity ranged over many powers of 10.



Experimental

2-Phenylbutyronitrile was prepared in 87% yield from 2-phenylbutyramide by dehydration with phosphorus oxychloride.²² The substance was a colorless liquid, b.p. 132-135° (24 mm.),²³ n^{25}_D 1.5060.

Anal. Calcd. for C₁₀H₁₁N: C, 82.71; H, 7.64. Found: C, 82.77; H, 7.57.

(-)-2-Cyano-2-phenylbutanoic Acid.—To 300 ml. of liquid ammonia was added with stirring the minimum amount of sodium necessary to produce a permanent blue color. A small amount of ferric chloride was added to the solution, and when the blue color vanished, 13.8 g. (0.6 mole) of sodium was added. To this solution was added 43.4 g. (0.30 mole) of 2-phenylbutyronitrile in 50 ml. of dry ether. The reaction was exothermic, and a color change from brown to green was observed. The reaction flask was warmed and the ammonia allowed to evaporate, during the course of which 300 ml. of dry ether was added. After the ammonia had evaporated, 66 g. (1.5 moles) of Dry Ice was added with stirring. The reaction mixture was allowed to come to room temperature, and was shaken with 200 ml. of water and 350 ml. of ether. The aqueous phase was washed with ether, and was acidified with a mixture of 100 ml. of concentrated hydrochloric acid and 50 g. of ice. The white oil that separated was extracted with four 200-ml. portions of ether, and the combined ether layers were dried and evapo-

(22) D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954).

(23) F. Bodroux and F. Taboury [*Bull. soc. chim.*, [4] **7**, 666 (1910)] reported a b.p. 114-115° (15 mm.) for the substance.

rated. The residue, a yellow oil, wt. 43.5 g. (73%), n_D^{25} 1.5173, could not be induced to crystallize, nor could the material be distilled without decomposition.

A solution of 250 g. of this crude acid and 250 g. of quinine in 500 ml. of methanol was cooled, and the salt that separated was collected. This material was recrystallized three times from methanol, care being taken never to heat any solutions over 25°. Hydrolysis of samples of salt from these three recrystallizations yielded 2-cyano-2-phenylbutanoic acid of the rotations: $[\alpha]_D^{25-27}$ -18.85, -21.0 and -21.0° (*c* 10% in CHCl_3), respectively. The main batch of salt after the third recrystallization was shaken with a mixture of 200 ml. of dilute sulfuric acid and 400 ml. of ether. The ether solution was washed with water, dried, and evaporated under reduced pressure below 25°. Solvent was removed from the residual oil at 1 mm. and 25°, and the residue crystallized when cooled (white needles), m.p. 41-43° (sealed tube), wt. 37 g., $[\alpha]_D^{25}$ -21.0° (*c* 10% in CHCl_3). After standing at 0° for about one year, this acid lost its hygroscopic character, and its melting point changed to 86-87° (sealed tube). At 0° the compound is optically stable for long periods of time.

Anal. Calcd. for $\text{C}_{11}\text{H}_{11}\text{NO}_2$: C, 69.82; H, 5.85; N, 7.40. Found: C, 69.58; H, 6.03; N, 7.24.

An additional 26 g. of optically pure acid was obtained from recrystallizations of second crops of the quinine salt.

(+)-Ammonium 2-Cyano-2-phenylbutanoate.—Into a solution of 6.5 g. of (-)-2-cyano-2-phenylbutanoic acid in 50 ml. of dry ether was passed ammonia gas. The resulting precipitate of ammonium salt amounted to 6.7 g., m.p. 111° dec., $[\alpha]_D^{25}$ +29.7° (*c* 10% in CH_2OH).

Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_2$: C, 64.06, H, 6.84. Found: C, 63.83; H, 6.83.

(+)-2-Phenylbutyramide.—Resolution of 34 g. of racemic 2-phenylbutyric acid²⁴ through its cinchonidine salt gave 8.45 g. of optically pure (+)-2-phenylbutanoic acid, n_D^{25} 1.5130, α_D^{25} +96.5° (neat, *l* 1 dm.), which compares with material previously resolved,²⁵ n_D^{25} 1.5128, α_D^{25} +96.2° (*l* 1 dm., neat). A mixture of 5.0 g. of this acid and 8.4 g. of PCl_5 was heated at 90° for 1 hour. The mixture was cooled and poured into 40 ml. of concentrated ammonium hydroxide and 40 g. of ice. The resulting mixture was extracted with benzene, the benzene was evaporated and the residue was recrystallized from aqueous ethanol to give 3.6 g. of white needles of amide, m.p. 79-80°, $[\alpha]_D^{27}$ +73.7° (*c* 3% in CHCl_3).

The optical purity of this amide is demonstrated by its sharp melting point, and by the fact that its rotation did not change with five recrystallizations from ethanol: 1st. recryst., $[\alpha]_D^{27}$ +75.4° (*c* 3% in CHCl_3); 3rd. recrystn., $[\alpha]_D^{27}$ +74.7° (*c* 3% in CHCl_3); 5th recrystn., $[\alpha]_D^{27}$ +75.4° (*c* 3% in CHCl_3).

Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{NO}$: C, 73.59; H, 8.03. Found: C, 73.76; H, 8.05.

(-)-2-Phenylbutyronitrile.—A mixture of 0.90 g. of optically pure amide (see above) and 2.0 g. of P_2O_5 was heated to 120°. The product was distilled at 2 mm. from this reaction mixture in three portions, and the rotations of the distillate were determined. The first fraction was collected after 15 minutes, α_D^{24} -23.1° (*l* 1 dm., neat); the second fraction after 1 hour, α_D^{24} -23.0° (*l* 1 dm., neat); the third fraction after 3 hours, α_D^{24} -22.8° (*l* 1 dm., neat). The constancy of these rotations indicated that nitrile did not racemize under the conditions of its formation. All fractions possessed n_D^{25} 1.5061.

Anal. Calcd. for $\text{C}_{10}\text{H}_{11}\text{N}$: C, 82.71; H, 7.64. Found: C, 82.71; H, 7.82.

Representative Decarboxylations of (-)-2-Cyano-2-phenylbutanoic Acid: Run 5.—Optically pure (-)-2-cyano-2-phenylbutanoic acid, 0.283 g. or 0.0015 mole, and 0.103 g. or 0.00050 mole of optically pure (+)-ammonium 2-cyano-2-phenylbutanoate were dissolved in 20 ml. of absolute ethanol. After the solution stood for 39 hours at 25°, it was added to 50 ml. of water, made basic with a saturated aqueous solution of potassium carbonate, and the

resulting solution was extracted with two 15 ml. portions of pure pentane. The organic layers were washed with two 50-ml. portions of water and dried. The pentane was evaporated under reduced pressure, and the residue was distilled at 2 mm. (pot temperature 120°) to give 0.24 g. of 2-phenylbutyronitrile, n_D^{25} 1.5060, α_D^{25} -0.45° (neat, *l* 1 dm.).

Run 13.—Optically pure acid (0.19 g., 0.0010 mole) and 0.0278 g. (0.00025 mole) of tetramethylammonium hydroxide dihydrate were dissolved in 10 ml. of purified ethylene glycol. The solution was allowed to stand at 25° for 94 hours, was made basic with a solution of sodium carbonate, and was extracted with two 20-ml. portions of pentane. The extracts were washed with water, and dried. The solvent was evaporated and the residue distilled at 2 mm. (pot temperature 120°) to give 0.11 g. of product, n_D^{25} 1.5063, α_D^{25} +2.66° (*l* 1 dm., neat).

Run 25.—Potassium metal (0.078 g., 0.0020 g. atom) was dissolved in 10 ml. of phenol at 40°. After the metal had dissolved, 0.378 g. (0.0020 mole) of optically pure (-)-2-cyano-2-phenylbutanoic acid was added and the resulting solution was sealed in a glass tube under nitrogen. After standing for 90 hours at 68°, the solution was dissolved in 300 ml. of refluxing pentane, and the resulting mixture was cooled to 0°. The phenol that separated was recrystallized from 150 ml. of pentane. The two filtrates were combined, evaporated to 100 ml., and cooled to 0°. The phenol that separated was collected and recrystallized from 100 ml. of pentane. The combined filtrates were evaporated to 50 ml., cooled to 0° and washed with 10 ml. of ice-cold aqueous 1 *N* sodium hydroxide solution (contact time of 1 minute). The pentane layer was washed with water, dried, evaporated, and the residue on distillation at 2 mm. gave 0.15 g. of 2-phenylbutyronitrile, n_D^{25} 1.5057, α_D^{25} -1.82° (*l* 1 dm., neat).

In a control experiment for the above isolation procedure, a 69% recovery of a 0.145-g. sample of optically active nitrile was obtained whose rotation was unchanged by the treatment.

Run 8.—Optically pure (-)-2-cyano-2-phenylbutanoic acid, 0.458 g. or 0.00242 mole, was dissolved in 25 ml. of purified *t*-butyl alcohol. To this solution was added 0.0862 g. (0.000625 mole) of potassium carbonate, and the resulting mixture was allowed to stand at 25° for 68 hours. At the end of this time, much of the original potassium carbonate remained undissolved, and was covered with an additional precipitate. The mixture was shaken with a mixture of 20 ml. of pentane and 75 ml. of water, and the aqueous layer was washed with an additional 20 ml. of pentane. The pentane extracts were washed with three 75-ml. portions of water and dried. The pentane was evaporated, and the residue was distilled at 2 mm. to yield 0.25 g. of 2-phenylbutyronitrile, n_D^{25} 1.5058, α_D^{25} 0.00° (*l* 1 dm., neat).

Run 49.—Optically pure (-)-2-cyano-2-phenylbutanoic acid (0.378 g. or 0.0020 mole) and 0.074 g. (0.0010 mole) of lithium carbonate were dissolved in 20 ml. of acetic acid. The optical rotation of this solution remained unchanged for 3 days at room temperature. The temperature of the solution was raised to 68°, whereupon the rotation of the solution diminished by one-half in 40 hours. After 220 hours, an ice-cold, saturated aqueous solution of potassium carbonate was added to the reaction mixture with stirring until a pH of 6 was reached. The resulting solution was twice extracted with 20-ml. portions of pentane. The pentane extracts were washed with water, dried, and the solvent was evaporated. The residue was distilled to give 0.21 g. of 2-phenylbutyronitrile, n_D^{25} 1.5058, α_D^{25} +0.01 ± 0.01° (*l* 1 dm., neat).

The other runs were made with procedures similar to those reported above. The infrared spectra of the 1-cyano-1-phenylpropane product (runs 2, 8 and 37) were determined in representative cases and were identical with that of authentic material.

Stability of (-)-2-Cyano-2-phenylbutanoic Acid in Various Solvents in Absence of Base.—A solution of 0.312 g. of the optically pure acid in 18 ml. of purified ethylene glycol was allowed to stand at 25° for 45 hours. The solution was poured into 50 ml. of water made basic with potassium carbonate solution, and extracted with two 20-ml. portions of pentane. The pentane extracts were found to contain no 1-cyano-1-phenylpropane. The aqueous phase was acidified with hydrochloric acid and extracted with two 50-ml. portions of ether. The ether phases were washed with water, dried and evaporated at room temperature to a

(24) P. A. Levene, L. A. Mikeska and K. Passoth, *J. Biol. Chem.*, **83**, 27 (1930).

(25) D. J. Cram and J. Allinger, *J. Am. Chem. Soc.*, **79**, 2864 (1957). A typographical error was made in this article in the rotation of (+)-2-phenylbutanoic acid α_D^{25} +96.2° (*l* 1 dm., neat).

TABLE VII
 OPTICAL STABILITY OF 0.10 M SOLUTIONS OF (+)-2-PHENYLBUTYRONITRILE IN VARIOUS BASIC SOLUTIONS

Run	Solvent	Nature	Base	Concn., M	pH meter reading (m.v.)	Time, hr.	% racem.	T_{D_2} , hr.
54	HOCH ₂ CH ₂ OH	NH ₃		Satd.	-220	48	100	..
55	HOCH ₂ CH ₂ OH	(NH ₄) ₂ CO ₃ ·H ₂ O		0.10	-80	160	75	79
56	HOCH ₂ CH ₂ OH	KHCO ₃		.10	-174	72	93	13
57	HOCH ₂ CH ₂ OH	KHCO ₃		.005	-25	30	0.0	..
58	CH ₃ OH	(NH ₄) ₂ CO ₃ ·H ₂ O		.10	-120	64	14	292
59	CH ₃ OH	NaHCO ₃		<.005 ^b	-200	92	99	14
60	CH ₃ OH	CH ₃ CO ₂ Na		.10	-90 to -80	114	5.93	1350
61	C ₂ H ₅ OH	(NH ₄) ₂ CO ₃ ·H ₂ O		.10	-183	116	30	224
62	O(CH ₂ CH ₂) ₂ O	NH ₃		Satd.	.. ^a	72	0.0	..
63	(CH ₃) ₃ COH	NH ₃		Satd.	-215	41	2	1430
64	(CH ₃) ₃ COH	KHCO ₃		<0.01 ^b	+110 to +90	47	0	..
65	(CH ₃) ₃ COH	(CH ₃) ₃ CCO ₂ K		1.0 ^c	-205	3900	5.0	5530
66 ^d	C ₆ H ₅ OH	CH ₃ CO ₂ NH ₄		0.10	...	120	1.72	4370
67 ^d	C ₆ H ₅ OH	K ₂ CO ₃		.05	...	408	19.0	1340
68 ^d	CH ₃ CO ₂ H	(NH ₄) ₂ CO ₃ ·H ₂ O		.10	...	100	0.0	..

^a Solution was too basic to measure pH. ^b Insoluble NaHCO₃ and KHCO₃ were present, respectively. ^c Carbon dioxide gas was passed into this solution for about 1 minute whereupon a cloudy precipitate appeared and remained throughout. ^d Runs 66 and 68 were conducted at 100°, and run 67 at 68°; all other runs were made at 25°.

volume of 10 ml. Ammonia gas was passed through this solution, and the resulting precipitate was collected; wt. 0.255 g., m.p. 90° dec., $[\alpha]^{25}_D +28.4^\circ$ (*c* 9% in CH₃OH). The ammonium salt prepared from optically pure acid was $[\alpha]^{25}_D +29.7^\circ$ (*c* 10% in CH₃OH), and had a half-life for loss of its optical activity of about 6 hours.

A solution of 0.100 g. of optically pure (-)-2-cyano-2-phenylbutanoic acid in 5.3 ml. of purified *t*-butyl alcohol was allowed to stand at 25° for 144 hours. The resulting solution was treated as in the procedure for run 25. Only a trace of 2-phenylbutyronitrile was present in the pentane extracts.

A solution of 0.190 g. of optically pure (-)-2-cyano-2-phenylbutanoic acid was dissolved in 10 ml. of glacial acetic acid, and this solution had a rotation, $\alpha^{25}_D -0.50^\circ$ (*l* 1 dm.). The solution was held at 68° for 6 days without a detectable change in rotation, the final reading being $\alpha^{25}_D -0.51^\circ$ (*l* 1 dm.).

Optical Stability of (-)-1-Cyano-1-phenylbutanoic Acid in Ethylene Glycol under Conditions of Decarboxylation.—A solution of 0.15 g. of optically pure (-)-acid and 0.055 g. of potassium carbonate in 1.5 ml. of ethylene glycol was allowed to stand at room temperature for 5 hours. The solution was shaken with a mixture of water and pentane and the water layer was washed with pentane. The water layer was acidified with 2 *N* hydrochloric acid and extracted three times with ether. The combined ether extracts were washed several times with water, dried and evaporated. The residual oil was dried for 12 hours at 2 mm. and 25° to give 0.055 g. of starting acid, $[\alpha]^{25}_D -22.3^\circ$ (*c* 1.9 in CHCl₃).

Optical Stability of (-)-2-Phenylbutyronitrile under Conditions of Its Formation.—To ascertain that optically active 2-phenylbutyronitrile was not racemized under the conditions of its formation, (+)-2-phenylbutyronitrile was subjected to the conditions of the decarboxylation reactions in representative cases. The basicity of the medium in the control runs was measured with a glass electrode pH meter, and was compared in each case with the basicity of the reaction mixtures just before product was isolated. The results are recorded in Table VII.

Runs 1 to 7 of Table I are controlled by the results of runs 66, 63, 68, 62, 61, 58 and 55 of Table VII, respectively. The basicities of the solutions at the end of runs 2, 5, 6 and 7 were lower than those measured in the corresponding

control runs. The basicities were not measured for runs 1, 3 and 4, but they are clearly less basic than the control runs 66, 68 and 62. Although appreciable racemization took place in control run 55, this is not serious as the solution in this run was 2 pH units more basic than that in run 7. Further evidence that no racemization of product took place in run 7 is the fact that no more stereospecificity was observed in run 14 than in run 7 even though run 18 had a distinctly acid pH throughout, due to the buffering effect of the large quantity of NH₄Br.

Runs 8–11 of Table II are controlled by run 64 of Table VII. The basicity of the solution in run 64 was higher than that for the solutions at the end of runs 8–12.

Runs 13–19 of Table III are controlled by the results of runs 55 and 57 of Table VII. The basicities of the solutions at the end of runs 13–19 were less than those in control runs 55 and 57. Further evidence that no racemization of the product once formed occurs in runs 13–19 is the fact that the stereochemical results of runs 14 and 17 were essentially identical even though the basicity of the solution at the end of the run was much greater in 14 than in 17.

Runs 21–30 of Table IV are controlled by the results of runs 66 and 67 of Table VII. Both the base concentrations and temperatures of the control runs were equal to or greater than those of any of runs 21–30.

Runs 5 and 32 of Table V are controlled by the results of run 61 of Table VII. Runs 6, 33 and 34 of Table V are controlled by run 58 of Table VII. Run 36 (Table V) was stopped before the solution became basic. Thus no racemization of product took place in either run 36 or 35 (Table V), which gave identical steric results. Run 38 (Table V) was stopped before it became basic. Some racemization of product probably occurred in run 37. Runs 39–42 of Table V involved no racemization since the optical purity of the product was independent of the duration of the run. Runs 43–45 of Table V probably involved no racemization of product once formed because of the similarity of condition of those and previous runs which involved no racemization.

Runs 46–49 of Table VI are controlled by the results of run 68 of Table VII. Runs 50–53 of Table VI were not controlled, but probably no racemization occurred in these runs since similar base strengths in other solvents provided no racemization of product once formed.