and the extraction residues were sublimed at a bath temperature of 75° (0.1 mm.). When cis-stilbene was employed, the material from extraction was distilled at a bath temperature of 110–120° at 0.1 mm.

The oxidations of the products from the exchange runs to benzoic acid were conducted as follows. From 150 to 300 mg. of cis- or trans-III was dissolved in a mixture of 20 ml. of tert-butyl alcohol and 10 ml. of water, heated to reflux, and crystalline potassium permanganate was added until a pink color persisted. The solution was held at reflux for an additional 15 min., cooled, and sodium bisulfite was added until a colorless solution was obtained. The precipitate was removed by filtration through Celite, and the clear filtrate was evaporated to dryness on a rotatory evaporator. The residue was dissolved in a minimum of water, washed with ether, acidified with 3 N hydrochloric acid, and extracted continuously with ether. The ether layer was evaporated, and the residual benzoic acid was sublimed at 80° (0.1 mm.) and submitted for deuterium analysis by combustion and falling drop method.[14] An 80% yield of benzoic acid was obtained from trans-III, and 65% from cis-III.

Ozonolysis of trans-α-Methylstilbene from Run 19.—Ozone-enriched oxygen was bubbled into a solution of 1.06 g. of trans-α-methylstilbene (trans-I) in 25 ml. of cyclohexane at 0° until thin layer chromatography (0.25 mm. silica gel G plate with 2% methanol–pentane as developer and iodine as detector) indicated absence of olefin. The volume of cyclohexane had diminished to about 10 ml. Ether (25 ml.) was added, followed by slow addition of 1.0 g. of lithium aluminum hydride. The reaction mixture was stirred an additional 4 hr., and a saturated solution of sodium sulfate in water was added dropwise until no more hydrogen was evolved. The ether layer was decanted, and the precipitate was re-extracted with ether. The combined ether layers were washed once with water, once with 10% sodium bicarbonate, three times with water, and dried. The ether was evaporated, and the residual oil was distilled (bath temperature 125–140°) to give 0.896 g. of a clear oil. The mixture was analyzed by v.p.c. (0.25 in. × 6 ft. column of 20% 30M Carbowax on 60/80 firebrick), and found to contain 35% benzyl alcohol, 37% α-methylbenzyl alcohol, 1.3% acetophenone, 0.1% benzaldehyde, and 13% cyclohexane. The alcohols were each produced in 55% yield. This mixture was separated by preparative v.p.c. on a column of 20% 30M Carbowax on 60/80 firebrick. The samples

were immediately distilled and sealed in an ampoule to avoid air oxidation. Oxidation of a 0.203-g. sample of trans-I by the procedure given for cis- and trans-stilbene yielded 0.144 g. (57%) of benzoic acid.

Analytical Method and Error Analysis.—All v.p.c. analyses were performed on a 9-ft. × 0.25-in. column of 20% silicone nitrile gum (XE-60) on 60/80 mesh firebrick (column 200°, inlet 280°, detector 300°, helium flow rate 30 ml./min.). Sample sizes from 1–10 μl. of solution yielded about 1500 theoretical plates for the column. The peaks had little tailing and came at 21 min. (cis-I), 28 min. (II), and 42 min. (trans-I). In the analyses for cis- and trans-stilbene mixtures, the retention times were 20 and 54 min., respectively.

For the 3 peaks of the α-methylstilbene system, the absolute mean deviation was about ±0.05% in the range 0–10%, and increased to ±0.20% in the range 10–70%. These reproducibility values were obtained as the result of three v.p.c. analyses per sample in runs 3 and 4. The accuracy of the analyses was tested with a known mixture and is reported in Table XIII.

TABLE XIII

ACCURACY OF V.P.C. ANALYSES

	cis-I	trans-I	II
Weight, %	7.42	63.08	29.49
Area, %	7.38 ± 0.09	63.9 ± 0.4	28.8 ± 0.3
Deviation, %	−0.5	+1.1	−2.3

Deuterium analyses[14] run on compounds containing less than 0.20 atom/mole-% excess deuterium were run against a standard protio sample, and were reproducible to within ±0.02 atom % excess deuterium. Deuterium analyses by n.m.r. in carbon tetrachloride were run with the maximum expanded field. The integrated peak area of the methylene hydrogens of a weighed acenaphthene internal standards was compared with that of the methyl or vinyl hydrogens of a weighed, purified sample of olefin. The % mean deviation in repeated integrations was 5% of total hydrogen. By "mean deviation" is meant the average of the absolute deviations of the values from the mean. Error estimates in calculations are by the method of total differentials.[34]

(34) L. L. Smail, "Analytical Geometry and Calculations," Appleton-Century–Crofts, New York, N. Y., 1953, p. 544.

Electrophilic Substitution at Saturated Carbon. XXIV. Trifluoromethyl as a Carbanion-Stabilizing Group[1]

BY DONALD J. CRAM AND ALAN S. WINGROVE

Two systems have been prepared for study of the stereochemical course of the base-catalyzed hydrogen–deuterium exchange at carbon attached to a trifluoromethyl group. Optically active 2-methyl-3-phenyl-1,1,1-trifluoropropane (I), and the same compound deuterated in the 2-position, and optically active 2-phenyl-1,1,1-trifluorobutane (II), and its deuterated counterpart (2-position), were examined. In tert-butyl alcohol-O-d at 124°, (+)-I-h was found to undergo elimination reaction to the exclusion of isotopic exchange. The initially formed 1,1-difluoro-2-methyl-3-phenylpropene underwent a base-catalyzed allylic rearrangement to give a 6.5 to 1 mixture of trans- to cis-3,3-difluoro-2-methyl-1-phenylpropene (trans- to cis-III), which were identified by their spectral properties. The base-catalyzed elimination reaction exhibited a kinetic isotope effect of 1.2, a fact which suggests a carbanion intermediate for the reaction. The 2-phenyl-1,1,1-trifluorobutane system (II) also underwent elimination to give 1,1-difluoro-2-phenyl-1-butene (IV) and its polymers. However, hydrogen–deuterium exchange also occurred, but at a much slower rate. In tert-butyl alcohol–potassium tert-butoxide, and in ethanol–potassium ethoxide, isotopic exchange went with total racemization (k_e/k_α, the ratio of the rate constant for exchange to the rate constant for racemization, was equal to unity). In methanol–potassium methoxide, or methanol–lithium methoxide, isotopic exchange went with net inversion (k_e/k_α ranged from 0.60 to 0.84, depending on whether the substrate or the solvent was deuterium labeled). This result is interpreted in terms of an asymmetrically solvated symmetrical and dissociated carbanion.
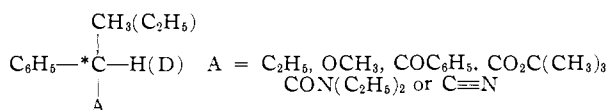
In previous investigations, the stereochemistry of the base-catalyzed hydrogen–deuterium exchange of a number of α-substituted α-phenylethyl or α-phenylpropyl systems has been examined by measuring the
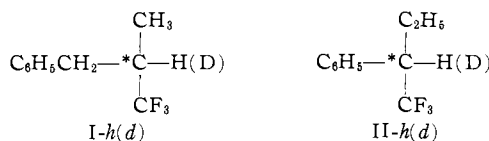
value of k_e/k_α ratios, where k_e is the rate constant for exchange and k_α the rate constant for racemization. The substituents examined were ethyl,[2a] methoxy,[2a]

(2) (a) D. J. Cram, C. A. Kingsbury, and B. Rickborn, J. Am. Chem. Soc., 83, 3688 (1961); (b) D. J. Cram, B. Rickborn, C. A. Kingsbury, and P. Haberfield, ibid., 83, 3678 (1961); (c) D. J. Cram and L. Gosser, ibid., 86, 5457 (1964).

carbo-tert-butoxy,[2b] N,N-diethylamido,[2b] benzoyl,[2c] and cyano.[2c] Those substituents which stabilized the carbanion intermediate through delocalization of charge onto oxygen (carbonyl-containing groups) gave k_e/k_α ratios of unity under all conditions examined,[2b,c] probably because of the intervention of tautomers as discrete and symmetrical intermediates. The ethyl and methoxy groups do not stabilize carbanions, and in the systems containing these substituents only the phenyl group acidified the benzyl hydrogen. These two systems underwent substitution with retention in nondissociating solvents such as tert-butyl alcohol (k_e/k_α = 5–10), with racemization in dissociating but nonhydroxylic solvents such as dimethyl sulfoxide (k_e/k_α = 1), and with inversion in dissociating and hydroxylic solvents such as diethylene glycol (k_e/k_α = 0.7 to 0.9). The retention results were attributed to asymmetric ion-pairs, the racemization to symmetrical carbanions, and the inversion to asymmetrically solvated symmetrical carbanions. The cyano substituent provided a system whose k_e/k_α values ranged from 1.5 (retention) to 1 (racemization) to 0.83 (inversion) to 0.05 (isoracemization).[2c]

$$\begin{array}{c} CH_3(C_2H_5) \\ | \\ C_6H_5-\overset{*}{C}-H(D) \quad A = C_2H_5, OCH_3, COC_6H_5, CO_2C(CH_3)_3 \\ | \qquad\qquad\qquad\qquad CON(C_2H_5)_2 \text{ or } C\equiv N \\ A \end{array}$$

The present investigation is concerned with the effect of the trifluoromethyl group on the symmetry properties of an attached carbanion. Two systems were adopted for study, I and II, both of which contain an asymmetric carbon attached to the trifluoromethyl group.

$$\begin{array}{cc} CH_3 & C_2H_5 \\ | & | \\ C_6H_5CH_2-\overset{*}{C}-H(D) & C_6H_5-\overset{*}{C}-H(D) \\ | & | \\ CF_3 & CF_3 \\ I\text{-}h(d) & II\text{-}h(d) \end{array}$$

Preparation of 2-Methyl-3-phenyl-1,1,1-trifluoropropane (I) and 2-Phenyl-1,1,1-trifluorobutane (II).—Optically active (−)-2-methyl-3-phenylpropanoic acid was prepared as previously (see Experimental). The same acid deuterated in the 2-position was prepared by decarboxylating O-deuterated benzylmethylmalonic acid. These acids were converted to (+)-I-h and I-d, respectively, by treatment with sulfur tetrafluoride. Since no deuterium was lost during the fluorination (I-d contained 0.97 atom of deuterium[3]), it seems likely that no racemization occurred when optically active starting material was used.
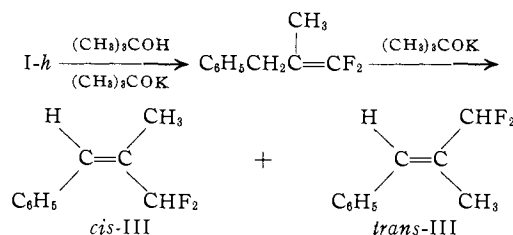
Optically active 2-phenylbutanoic acid was prepared as before (see Experimental). Deuterated material was obtained by subjecting 2-phenylbutyronitrile to sodium deuteroxide catalyzed hydrogen–deuterium exchange with deuterium oxide, and hydrolyzing the nitrile to acid in the same mixture at an elevated temperature. The acid contained 0.97 atom of deuterium per molecule.[3] Resolved (+)-acid and resolved (−)-deuterated acid were treated with sulfur tetrafluoride to produce (+)-II-h and (−)-II-d, respectively. The latter compound contained 0.98 atom of deuterium per molecule, and thus no deuterium was lost during the fluorination. This result suggests that no racemization occurred during the conversion.

(3) Combustion and falling drop method by J. Nemeth, Urbana, Ill.

The infrared spectra of I-h and I-d (neat) differed substantially from one another. The deuterated material exhibited bands at 968 (weak shoulder), 943 (strong), 776 (weak), 630 (weak shoulder), and 610 (weak) cm.$^{-1}$, which were absent in I-h. The band at 943 cm.$^{-1}$ was used to determine whether deuterium had been incorporated into I-h by treatment with base and deuterated solvent. The nuclear magnetic resonance (n.m.r.) spectrum in a 20% solution by weight in carbon tetrachloride (Varian Associates H-60 spectrophotometer) gave the following bands (tetramethylsilane as internal standard): I-h, 5 aromatic protons centered at 2.92 τ as a triplet, 3 unresolved methylene–methine protons 6.8 to 7.9 τ as a multiplet, and 3 methyl protons centered at 9.00 τ as a quintet; I-d, 5 aromatic protons centered at 2.92 τ as a doublet, 2 benzyl protons centered at 7.27 as a quartet (J_{HF} = 43 c./sec. splitting constant), and 3 methyl protons at 9.05 as a singlet.

The infrared spectrum (neat) of II-d contained the following bands which were absent in the spectrum of II-h: 1084 (weak), 980 (strong), 958 (strong), 809 (weak), 740 (weak), and 604 (weak) cm.$^{-1}$. The bands at 980 and 958 cm.$^{-1}$ were used for deuterium analysis (see Experimental).

Reaction of 2-Methyl-3-phenyl-1,1,1-trifluoropropane (I) with Base.—Attempts to conduct hydrogen–deuterium exchange reactions between I-h and tert-butyl alcohol-O-d or I-d and tert-butyl alcohol resulted only in an elimination reaction. The initial product of the base-catalyzed reaction (1,1-difluoro-2-methyl-3-phenylpropene) was not isolated, since it underwent a base-catalyzed allylic isomerization to give a mixture of cis- and trans-3,3-difluoro-2-methyl-1-phenylpropene (cis- and trans-III). Starting ma-

$$I\text{-}h \xrightarrow[\text{(CH}_3\text{)}_3\text{COK}]{\text{(CH}_3\text{)}_3\text{COH}} C_6H_5CH_2\overset{\overset{\displaystyle CH_3}{|}}{C}=CF_2 \xrightarrow{\text{(CH}_3\text{)}_3\text{COK}}$$

$$\begin{array}{cc} \underset{C_6H_5}{\overset{H}{\diagdown}}C=C\underset{\diagdown CHF_2}{\overset{CH_3}{\diagup}} \quad + \quad \underset{C_6H_5}{\overset{H}{\diagdown}}C=C\underset{\diagdown CH_3}{\overset{CHF_2}{\diagup}} \\ cis\text{-III} \qquad\qquad trans\text{-III} \end{array}$$

terial recovered after as much as half of it had been destroyed exhibited neither racemization nor exchange at the 2-position. Reaction occurred at a reasonable rate with I-h in tert-butyl alcohol-O-d–potassium tert-butoxide at 125°, but 150° was required for a reasonable rate of reaction for I-d in tert-butyl alcohol–potassium tert-butoxide (compare conditions of runs 1, 2, and 4 of Table I). Most of this isotope effect seems to be associated with the solvent–base, since in a competition experiment conducted in tert-butyl alcohol–potassium tert-butoxide at 134°, a one-to-one mixture of I-h to I-d gave a kinetic isotope effect of only k_H/k_D = 1.2 (see Experimental).

In run 3, although no isotopic exchange occurred at the 2-position (infrared analysis), total deuterium analysis[3] of recovered starting material indicated that 0.96 atom of deuterium had been introduced into the molecule. The infrared spectrum (neat) of this recovered starting material exhibited a strong C–D stretching band at 2180 cm.$^{-1}$, which was absent in the starting material. Thus, deuterium must have been introduced

TABLE I

RESULTS OF REACTIONS OF (+)-2-METHYL-3-PHENYL-1,1,1-TRIFLUOROPROPANE[a] ((+)-I-h) AND 2-METHYL-3-PHENYL-1,1,1-
TRIFLUOROPROPANE[b] (I-d) WITH POTASSIUM tert-BUTOXIDE IN tert-BUTYL ALCOHOL OR tert-BUTYL ALCOHOL-O-d[c]

| | Substrate | | Solvent | Base | | | % base | Recovered substrate, % | |
Run	Nature	Concn., M	type	concn., M	T, °C.	Time, hr.	loss	Exch.[d]	Rac.[e]
1	(+)-I-h	1.0	ROD	0.60	124	41	33	0	0
2	(+)-I-h	1.0	ROD	.60	124	97	55	0	0
3	(+)-I-h	0.77	ROD	.60	124	183	..	0[f]	0
4	I-d	1.0	ROH	.70	148	93	73	0	..
5	I-h	0.72	ROH	.69	136	187	..	..	..

[a] α^{25}D +15.0° (l = 1 dm., neat).   [b] 0.97 atom of deuterium per molecule; ref. 3.   [c] 0.99 atom of deuterium per molecule; ref. 3.
[d] Infrared analysis at 943 cm.$^{-1}$ for deuterium at the 2-position (see Experimental).   [e] Polarimetric analysis, l = 1 dm., neat.   [f] Although infrared analysis indicated no deuterium attached to the asymmetric center, combustion analysis (ref. 3) indicated 0.96 atom of deuterium per molecule, probably substituted at the benzyl position (see Experimental).

into the benzyl position of I-h at a rate comparable to that of the elimination reaction. Deuterium analysis[3] of the cis- and trans-III produced in run 3 indicated that each contained 2.98 atoms of deuterium per molecule. This result indicates that the olefins once formed undergo extensive hydrogen–deuterium exchange with solvent.

The olefins, trans- and cis-III, were obtained in a ratio of 6.5 to 1 in an experiment in which I-h was treated with a solution of potassium tert-butoxide in tert-butyl alcohol (run 5, Table I). The two olefins were separated by preparative v.p.c. (vapor phase chromatography), and identified by their analyses and spectral properties. In the ultraviolet (Cary Model 14 ultraviolet spectrophotometer), trans-III in hexane gave λ_{max} at 201 mμ (ϵ 22,200) and 242 mμ (ϵ 14,700), whereas cis-III in hexane gave λ_{max} at 200 mμ (ϵ 24,000) and 237.5 mμ (ϵ 11,650). Coplanarity of the benzene ring and the double bond should be more inhibited in the cis than the trans isomer (CF_2H > CH_3 in bulk), and the more conjugated isomer usually absorbs at longer wave lengths and higher intensities for the longer wave length band.[4]

The n.m.r. spectra (60 Mc. on a Varian Associates Model A-60 spectrophotometer, 20% carbon tetrachloride solutions by weight with tetramethylsilane as internal standard) of the two isomers also supported this assignment. The cis isomer gave the following bands: 5 aromatic protons, singlet at 2.82 τ; 1 vinyl proton, broad singlet at 3.34 τ; 1 difluoromethyl proton, triplet centered at 3.80 τ, areas 1 to 2 to 1, J_{HF} 56 c./sec.; 3 methyl protons, singlet at 8.03 τ. The spectrum of the trans isomer was: 5 aromatic protons, singlet at 2.85 τ; 1 vinyl proton, broad singlet at 3.48 τ; 1 difluoromethyl proton, triplet centered at 4.11 τ, areas 1 to 2 to 1, J_{HF} 56 c./sec.; 3 methyl protons, singlet with shoulders at 8.10 τ. In the trans isomer, the methyl and phenyl groups are cis to one another, and the small shift of the methyl group to higher field (as compared to the geometric isomer) is attributable to the shielding effect of the ring current. The methyl group probably remains partially in the field of the ring current of the benzene ring, since the size of the methyl group is small enough to allow the benzene ring to approach coplanarity with the double bond of the side chain. In the cis isomer, the difluoromethyl and phenyl groups are cis to one another, but here the difluoromethyl proton is moved to considerably lower field as compared to the geo-

(4) For example, cis-2-phenyl-2-butene (less hindered isomer) absorbs at λ_{max} 243 mμ (ϵ 12,000), whereas trans-2-phenyl-2-butene at λ_{max} 234 mμ (ϵ 8300) [D. J. Cram, J. Am. Chem. Soc., 71, 3883 (1949)].

metric isomer. The proton of the difluoromethyl group is probably acidic enough to hydrogen bond with the π-electrons of the benzene ring, and this effect tends to deshield the proton. Furthermore, the bulk of the difluoromethyl group coupled with this hydrogen bonding on the one hand, and the tendency for phenyl side-chain conjugation on the other, probably place the proton of the difluoromethyl group in the deshielding region of the benzene ring.

The fact that in run 5 trans-III predominated over cis-III is compatible with what is expected if thermodynamic control of products applied. Although the olefins once formed went to carbanions repeatedly, it is not clear whether or not cis–trans isomerization occurred as a consequence.

Exchange Reactions of 2-Phenyl-1,1,1-trifluorobutane (II).—System II also underwent a base-catalyzed elimination reaction, but hydrogen–deuterium exchange at the benzyl position of II occurred competitively, though at a much slower rate.

Three solvent systems were examined: methanol, ethanol, and tert-butyl alcohol. The competing elimination reaction prevented the isotopic exchange reaction from being carried very far, particularly in tert-butyl alcohol, in which the relative rates of elimination and exchange were highly unfavorable for study of exchange. The reactions were allowed to go until most of the starting material had gone to olefin or its polymers, at which time II was recovered, purified by v.p.c., and examined for exchange at the benzyl position by infrared analysis, and for racemization by polarimetric analysis. One-point rate constants were calculated for the exchange and racemization reactions, and values of k_e/k_α determined. The conditions and results of these experiments are presented in Table II. In run 12, 1,1-difluoro-2-phenyl-1-butene was isolated and characterized.

Discussion

In this section, the competition between the elimination and isotopic exchange reactions is first discussed, followed by an interpretation of the stereochemical course of the isotopic exchange reaction.

Competition between the Elimination and Isotopic Exchange Reactions.—Treatment of I with potassium tert-butoxide in tert-butyl alcohol resulted exclusively in an elimination reaction which exhibited a kinetic isotope effect of about $k_H/k_D \sim 1.2$ at 134°. At this temperature a maximum isotope effect of about 5 is possible.[5] In most E2 reactions, kinetic isotope effects

(5) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Co., New York, N. Y., 1960, p. 22.

Table II

Ratio of Rate Constants for Base-Catalyzed Isotopic Exchange (k_e) and for Racemization (k_α) of (+)-2-Phenyl-1,1,1-trifluorobutane ((+)-II-h)^a in ROD and of (−)-II-d^b in ROH

| | Substrate | | Base | | | | | % | % | |
Run	Nature	Concn., M	Nature	Concn., M	Solvent	T, °C.	Time, hr.	exch.^{c}	rac.^{d}	$k_e/k_\alpha{}^e$
6	(+)-II-h	0.55	CH$_3$OK	0.82	CH$_3$OD	120	89	16.5	20.2	0.80
7	(−)-II-d	.56	CH$_3$OK	.91	CH$_3$OH	120	89	12	14	.84
8	(+)-II-h	.57	CH$_3$OLi	.73	CH$_3$OD	120	214	14.5	18.5	.77
9	(−)-II-d	.54	CH$_3$OLi	.86	CH$_3$OH	120	214	8.5	12.8	.65
10	(+)-II-h	.56	C$_2$H$_5$OK	.72	C$_2$H$_5$OD	120	53	11.0	11.0	1
11	(−)-II-d	.56	C$_2$H$_5$OK	.82	C$_2$H$_5$OH	120	53	12.0	11.4	1
12	(+)-II-h	.64	(CH$_3$)$_3$COK	1.01	(CH$_3$)$_3$COD^f	64	138	7	8.0	1

^{a} $\alpha^{25}{}_{546}$ +36.2° (l = 0.5 dm., neat). ^{b} $\alpha^{25}{}_{546}$ −31.3° (l = 0.5 dm., neat); contained 0.98 atom of deuterium by combustion and falling drop method; ref. 3. ^{c} Deuterium analysis by infrared method. ^{d} Measured on neat samples, l = 1 dm. ^{e} One-point rate constants. ^{f} 0.99 atom of deuterium per molecule.

of 3–8 are observed.[6] However, in base-catalyzed reactions such as hydrogen isotope exchange, racemization, or allylic rearrangement, kinetic isotope effects which are considerably lower have been obtained (k_H/k_D = 0.5 to 3).[2b,7] The very low kinetic isotope effect observed in the elimination reaction of I suggests that this reaction also involves a carbanion intermediate, which eliminates fluoride ion much faster than it captures protons from solvent. The fact that system II undergoes isotopic exchange and elimination competitively suggests that the carbanion of this system partitions between proton capture and fluoride ion loss. The fact that elimination is more favored by potassium tert-butoxide in tert-butyl alcohol than by lithium or potassium methoxide in methanol is attributed to the presence of the metal ion in the catalytic species of the former solvent–base system, and the absence of the metal ion in the catalytic species of the latter solvent–base system.[2a] The metal ion may well serve as an electrophile which abstracts fluoride ion from the carbanion to complete the elimination reaction.
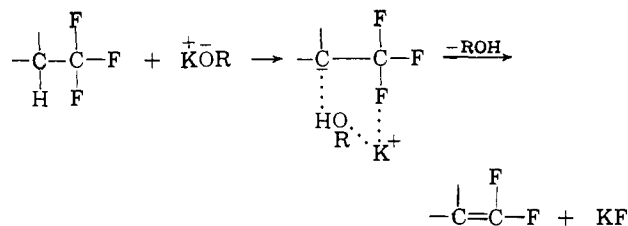
The low isotope effect for carbanion formation may be attributed either to a pre-equilibrium reaction (fast recapture by the carbanion of the hydrogen just abstracted), or to a highly unsymmetrical transition state for proton abstraction. These two possibilities have been discussed previously in other connections.[7b,c]

Stereochemical Course of the Base-Catalyzed Isotope Exchange Reaction.—Values of k_e/k_α ranged from 0.60 to 0.84 when (+)-II-h was exchanged with methanol O-d, or (−)-II-d was exchanged with methanol, and either potassium methoxide or lithium methoxide was employed as base (see runs 6–9 of Table II). No trends are visible in the data, either with respect to the direction of the isotope transfer, or the type of metal methoxide used. It is highly likely that the active catalytic species was dissolved methoxide ion.[2b]

(6) For discussions and examples see: (a) W. H. Saunders and D. H. Edison, J. Am. Chem. Soc., **82**, 138 (1960); (b) C. H. DePuy and E. A. Bishop, ibid., **82**, 2532 (1960); (c) E. Buncel and A. N. Bourns, Can. J. Chem., **38**, 2452 (1960).

(7) (a) D. J. Cram, D. A. Scott, and W. D. Nielsen, J. Am. Chem. Soc., **83**, 3696 (1961); (b) D. J. Cram and R. T. Uyeda, ibid., **86**, 5466 (1964); (c) S. Andreades, ibid., **86**, 2003 (1964).

The fact that this exchange reaction occurred with net inversion (k_e/k_α = 0.5 for 100% inversion) is attributed to formation of an asymmetrically solvated symmetrical carbanion. Hydrogen (or deuterium) recapture at the front face regenerates starting material. Deuterium (or hydrogen) capture at the back face produces inverted and exchanged product. The competing racemization reaction reflects the asymmetrically solvated carbanion passing into a symmetrical solvent shell and collapsing to exchanged racemic product. This mechanism is outlined.

As far as this stereochemical process is concerned, the trifluoromethyl as a carbanion stabilizing group is little different from the aryl or cyano groups.[2b,c,8]
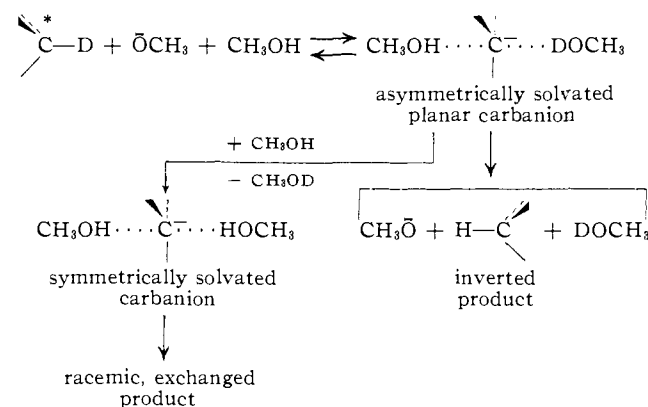

With aryl or cyano as carbanion stabilizing groups, metal alkoxides in nondissociating solvents gave k_e/k_α values greater than unity, and substitution occurred with retention.[2b,c] This result was attributed to formation of solvated and asymmetric potassium carbanide ion-pairs, the potassium ion of which rotated with its ligands to cause formation of new isotopic hydrogen bonds to the carbanion. Cation rotation and return of the carbanion to the covalent state by hydrogen capture occurred faster than ion-pair dissociation. Hydrogen capture from the rear face of the carbanion did not occur since such a process would produce a *product-separated ion-pair* in a nondissociating solvent.

Unlike the aryl or cyano group, the trifluoromethyl as a carbanion-stabilizing group in II causes exchange to occur with complete racemization in ethanol and tert-butyl alcohol (k_e/k_α = 1 for runs 10–12 (Table II)). Particularly in tert-butyl alcohol, the active catalytic species was undoubtedly a potassium alkoxide ion-pair. The observed racemization is attributed to the ability

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

of the three fluorine atoms to become ligands of the potassium ion, and cause that ion to pass into the plane of symmetry of the carbanion. Proton capture front and back with equal probability is the result.
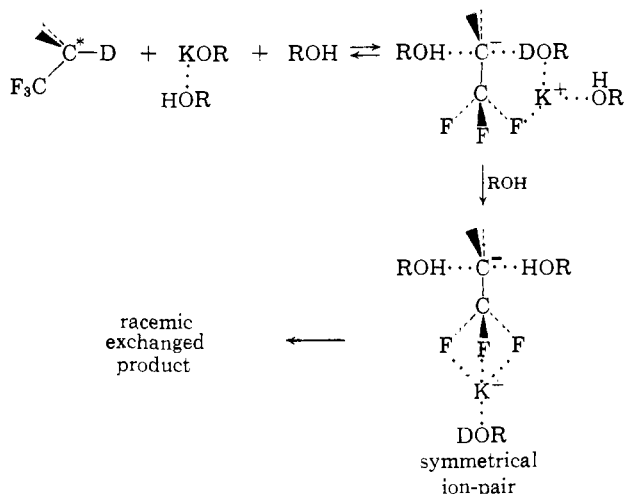
Experimental

2-Methyl-3-phenylpropanoic Acid and 3-Deuterio-2-methyl-3-phenylpropanoic Acid.—A total of 562 g. of diethyl benzylmethylmalonate was prepared,[2b,9] b.p. 85–96° (0.08 mm.). This material (200 g.) was hydrolyzed and decarboxylated to 2-methyl-3-phenylpropanoic acid,[2b,9] 154 g. (93%), b.p. 112–113° (0.12 mm.), and was resolved through the quinine salt from ethanol-water.[2b,9a] Four recrystallizations of the quinine salt and recovery of the acid gave a 13% yield of (+)-2-methyl-3-phenylpropanoic acid, b.p. 125–126° (1.5 mm.), α^{26}D + 22.92° (l = 1 dm., neat).

Deuterated acid was prepared as follows. Diethyl benzylmethylmalonate (53 g.) was held at reflux with a solution of 20 g. of sodium hydroxide and 150 ml. of water. The resulting homogeneous solution was heated until the ethanol evaporated, cooled to 0°, and acidified to congo red with concentrated hydrochloric acid. The solid diacid was extracted with dichloromethane, washed with water, and dried. The solvent was evaporated, and the solid diacid dried over phosphorus pentoxide. The resulting acid was dissolved in 100 ml. of anhydrous ether, and the solution was mixed with 3 successive 20.0-g. portions of 99.5% deuterium oxide. Each exchange involved 24 hr. of mixing. The ether layer was then evaporated, and the resulting diacid was decarboxylated with heat at 150–160° for 4–6 hr. The oily residue was distilled to give 25.0 g. of 2-deuterio-2-methyl-3-phenylpropanoic acid, b.p. 120° (1.2 mm.), n^{25}D 1.5112. Deuterium analysis was deferred to the next stage in the synthesis.

2-Methyl-3-phenyl-1,1,1-trifluoropropane (I) and 2-Deuterio-2-methyl-3-phenyl-1,1,1-trifluoropropane (I-d).—A 180-ml. capacity Monel steel bomb was charged with 16.5 g. of 2-methyl-3-phenylpropanoic acid and 25 ml. of dichloromethane. The bomb was sealed and cooled to −80°. It was then evacuated to 0.01 mm. and closed. A tank of sulfur tetrafluoride was attached to the bomb with stainless steel tubing, and 32 g. of gas was condensed in the bomb under vacuum. The bomb was shaken at 30° for 4.5 days, vented in a hood, opened, and the contents (intense purple color) were immediately poured onto 20 g. of sodium fluoride (light tan). The bomb was rinsed with two 30-ml. portions of dichloromethane, and the washes were combined with the original mixture. The mixture was filtered, and the solvent evaporated on a rotary evaporator to give 15.5 g. of a light tan residue. Distillation of this material gave 11.6 g. (62%) of produt as a sweet-smelling liquid, b.p. 88–89° (50 mm.), 80–81° (40 mm.), 63–64° (15 mm.), n^{25}D 1.4390. *Anal.* Calcd. for $C_{10}H_{11}F_3$: C, 63.82; H, 5.89. Found: C, 63.74; H, 5.87.[10]

A sample of partially optically active 2-methyl-3-phenylpropanoic acid (α^{26}D −9.42°, l = 1 dm., neat) was similarly treated

to give the trifluorinated product ((+)-II 53%), α^{27}D +15.0° (l dm., neat), n^{25}D 1.4388. Similarly, 2-deuterio-2-methyl-3-phenylpropanoic acid was converted to 2-deuterio-2-methyl-3-phenyl-1,1,1-trifluoropropane (I-d, 57%), n^{25}D 1.4383. *Anal.* Calcd. for $C_{10}H_{10}DF_3$: C, 63.48; mg. (H$_2$O + D$_2$O)/mg. sample, 0.527. Found: C, 63.39; mg. (H$_2$O + D$_2$O)/mg. sample, 0.531. Deuterium analysis[9] gave 0.974 atom of deuterium per molecule.

(−)-2-Deuterio-2-phenylbutanoic Acid.—Nondeuterated 2-phenylbutyronitrile,[11] b.p. 94° (4 mm.), n^{25}D 1.5070, 220 g., was added to 500 ml. of pure, dry (to Molecular Sieves, Linde, Type 4H) benzene. A solution was prepared by adding 0.60 g. of sodium metal to 400 g. of 99.8% deuterium oxide at 0°. A mixture of 66 g. of this solution was added to the benzene solution. The aqueous layer was acidic, so enough of a 5 M solution of sodium deuteroxide in deuterium oxide was added to give a pH of 12–13 (12 ml.). The mixture was heated at reflux (pot temperature of 125°) for 43 hr., and cooled. The aqueous layer was discarded, and the benzene layer returned to the flask with 109 g. of fresh stock solution of sodium deuteroxide-deuterium oxide. After 24 hr. of reflux, the aqueous layer was replaced with 110 g. of fresh solution, and again the mixture was heated to reflux for 24 hr. This process was repeated once more with 111 g. of fresh stock solution. The organic layer was added to 500 ml. of dichloromethane, the solution was dried and evaporated under reduced pressure. The residue was distilled to give 192 g. (87%) of deuterated nitrile, b.p. 94° (4 mm.). Analysis[3] of this material showed the presence of 0.98 atom of deuterium per molecule.

This deuterated nitrile was hydrolyzed to the deuterated acid as follows. To 300 g. of 99.8% deuterium oxide under nitrogen (reflux condenser) cooled in a bath at −20° was added with stirring 40.2 g. of freshly cut sodium metal. After the metal had dissolved, 192 g. of deuterated nitrile was added, and the mixture was heated to reflux and stirred in an atmosphere of dry nitrogen. After 24 hr. the mixture was homogeneous. It was cooled to 25°, and concentrated hydrochloric acid was added until the solution was thoroughly acidic. The acid was extracted with dichloromethane, and the resulting solution was extracted at 0° with cold 15% sodium hydroxide solution. The extracts were acidified at 0° with cold concentrated hydrochloric acid, and the mixture was extracted with cold dichloromethane. At no time did the mixture rise above 5°. The base extraction, reacidification, and extraction was repeated; the organic layer was washed with water and dried. The solvent was evaporated under reduced pressure, and the residual carboxylic acid distilled to give 175 g. (81%), b.p. 110° (0.7 mm.). Analysis[3] indicated the presence of 0.97 atom of deuterium per molecule.

This material (175 g.) was resolved through the cinchonidine salt[12] (6 recrystallizations) to give 61.8 g. (39%) of (+)-2-deuterio-2-phenylbutanoic acid, α^{25}D +93.9° (l = 1 dm., neat), α^{25}_{546} +56.45° (l = 0.5 dm., neat), n^{25}D 1.5131. Less optically pure acid was also recovered, 37 g., α^{27}D −78.0° (l = 1 dm., neat); 17.2 g., α^{27}D −6.2° (l = 0.5 dm., neat); 29 g., α^{27}D −38.7° (l = 0.5 dm., neat).

(−)-2-Deuterio-2-phenyl-1,1,1-trifluorobutane ((−)-II-d).—The procedure resembled that recorded earlier in the Experimental. The bomb was charged with 35.4 g. of (−)-2-deuterio-2-phenylbutanoic acid, α^{30}_{546} −93.0° (l = 1 dm., neat), 25 ml. of dichloromethane, and 69 g. of sulfur tetrafluoride, and was shaken at 35–40° for 9 days. The product, 23.0 g. (57%), b.p. 55–56° (10 mm.), n^{25}D 1.4400, gave α^{25}_{546} −31.32° (l = 0.5 dm., neat) after purification on a v.p.c. $^5/_8$ in. × 6 ft. column of 20% silicone gum (SE 30) on firebrick operating at 100° and a helium pressure of 5–6 lb. and microdistillation. Analysis of this material ((−)-II-d) for deuterium[3] gave 0.98 atom of deuterium per molecule.

(+)-2-Phenyl-1,1,1-trifluorobutane ((+)-II-h).—With the above procedure, 33.0 g. of (+)-2-phenylbutanoic acid, α^{25}_{546} +56.73° (l = 1 dm., neat) was converted to 20.3 g. (54%) of (+)-2-phenyl-1,1,1-trifluorobutane, b.p. 55–56° (10 mm.), α^{25}_{546} +36.16° (l = 0.5 dm., neat), n^{25}D 1.4400. *Anal.* Calcd. for $C_{10}H_{11}F_3$: C, 63.82; H, 5.89. Found: C, 63.62; H, 5.82.

Ethanol-O-d and Methanol-O-d.—Fractional distillation of 1500 g. of triethyl orthoformate through a 100-cm. column packed with glass helices was carefully conducted until the head temperature reached 144°. An additional 150 g. of the orthoformate was collected at this temperature, and the pot was cooled to 25°.

(9) (a) F. S. Kipping and A. E. Hunter, *J. Chem. Soc.*, 1005 (1903); (b) C. S. Marvel, in "Organic Syntheses," Coll. Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 705.

(10) This procedure was patterned after that of D. J. Martin and F. Kagan, *J. Org. Chem.*, **27**, 3164 (1962); see also W. R. Hasek, W. C. Smith, and V. A. Engelhardt, *J. Am. Chem. Soc.*, **82**, 543 (1960).

(11) D. J. Cram and P. Haberfield, *ibid.*, **83**, 2360 (1961).

(12) P. A. Levene, L. A. Mikeska, and K. Passoth, *J. Biol. Chem.*, **88**, 27 (1930).

To the pot was added 100 g. of 99.8% deuterium oxide, and the mixture was heated. The resulting mixture was carefully fractionally distilled, and the fraction boiling at 79–80° was collected over Molecular Sieves (which had been dried at 600°F. for 2 days) to give 400 g. of ethanol-O-d. Analysis[3] of this material showed the presence of 0.995 atom of deuterium per molecule.

The same procedure was applied to 2000 g. of trimethyl orthoformate and 203 g. of 99.8% deuterium oxide. The fractional distillations were conducted with great care, and 410 g. (62%) of methanol-O-d was collected over dried Molecular Sieves; b.p. 65–66°. Analysis[3] of this material showed the presence of 0.99 atom of deuterium per molecule.

Representative Attempt to Exchange and Racemize (+)-2-Methyl-3-phenyl-1,1,1-trifluoropropane (Run 1).—In a dry ampoule was placed 1.30 g. of (+)-2-methyl-3-phenyl-1,1,1-trifluoropropane. α^{25}D +15.0° (l = 1 dm., neat). To the ampoule was added 6.00 ml. of 0.70 M potassium tert-butoxide in tert-butyl alcohol-O-d (0.99 atom of deuterium per molecule[3]). The ampoule was flushed with pure nitrogen gas, sealed, heated at 124° for 41 hr., cooled to 25°, and its contents were added to 10.00 ml. of 0.5113 N sulfuric acid. The ampoule was rinsed with 3 10-ml. portions of water which were added to the solution, which was titrated to a phenolphthalein end point with 4.46 ml. of 0.5212 N sodium hydroxide. Thus, about 20% of the substrate reacted by neutralizing base. The mixture was extracted with pure pentane, the combined extracts were washed with water, dried, and the pentane evaporated through a 1 × 30 cm. Vigreux column, and the tan liquid remaining was subjected to preparative v.p.c. on a 5/8 in. × 6 ft. column packed with 30% polyethylene glycol on firebrick at temperatures between 83 and 85° and a helium pressure of 18 lb. The starting material was obtained with a retention time of 42 min., the sample taking 28 min. to come off the column. The material was washed from the collector with 50 ml. of pure pentane, the pentane was evaporated through a Vigreux column, and the residue distilled; α^{27}D +14.9° (l = dm., neat). The high resolution infrared spectrum of this compound (Perkin–Elmer Model 421 dual grating instrument) showed no deuterium incorporation at the methine position.

Other runs (2–4) conducted in a similar manner and carried as far as 50% destruction of starting material showed no loss of optical activity and no deuterium incorporation at the methine position (see Table I).

Formation, Separation, and Identification of cis- and trans-3,3-Difluoro-2-methyl-1-phenylpropene (Run 5).—A dry ampoule was charged with 1.54 g. of 2-methyl-3-phenyl-1,1,1-trifluoropropane (I) and 10 ml. of 0.78 M potassium tert-butoxide in tert-butyl alcohol. The tube was flushed with dry nitrogen, sealed, heated to 136° for 187 hr., cooled, opened, and the contents were shaken with water and pure pentane. The water layer was washed with pentane, and the combined extracts were washed with water, dried, and the pentane evaporated through a Vigreux column. The residue was submitted to v.p.c. as described above. The following fractions were collected: (1) 42–70 min., (2) 116 to 150 min., (3) 176 to 242 min. Each fraction was washed from the collector with pure pentane; the pentane was evaporated as before and distilled at reduced pressure. Fraction 1 was unreacted starting material I (n^{25}D 1.4390) as shown by an infrared absorption spectrum identical with that of starting material. Fraction 2 was cis-3,3-difluoro-2-methyl-1-phenylpropene, cis-III (see Results). Anal. Calcd. for $C_{10}H_{10}F_2$: C, 71.41; H, 5.99. Found: C, 71.59; H, 6.24. Fraction 3 was trans-3,3-difluoro-2-methyl-1-phenylpropene, trans-III, n^{25}D 1.5073 (see Results). Anal. Calcd. for $C_{10}H_{10}F_2$: C, 71.41; H, 5.99. Found: C, 71.39; H, 6.08.

Kinetic Isotope Effect, k_H/k_D, for Elimination Reactions of Undeuterated and Deuterated 2-Methyl-3-phenyl-1,1,1-trifluoropropane.—Substrate was prepared by adding 2.0006 g. of undeuterated and 2.1181 g. of 2-deuterio-2-methyl-3-phenyl-1,1,1-trifluoropropane containing 0.97 atom of deuterium per molecule.[3] This mixture was calculated to contain 50.1% of one atom of deuterium, and was analyzed[3] to give 49.5%. An ampoule was charged with 1.4212 g. of this material and 20.0 ml. of 0.532 M potassium tert-butoxide in tert-butyl alcohol. The tube was flushed with nitrogen, sealed, held at 134° for 143.5 hr., cooled, and the contents were mixed with standard acid and back-titrated with standard sodium hydroxide to a phenolphthalein end point. The organic material was isolated as before, submitted to v.p.c. separation, and the starting material analyzed for deuterium,[3] and found to contain 0.525 atom of deuterium per molecule. The moles of base consumed was assumed to equal the moles of

substrate consumed, and solution of eq. 1 and 2 provided the moles of deuterated and undeuterated substrate present at the end of the reaction. Equation 3 was used to calculate the isotope effect.

$$\% \text{ D in recovered substrate} = \frac{\text{moles of deuterated substrate remaining} \times 100\%}{\text{total moles of substrate remaining}} \quad (1)$$

$$\text{total moles of substrate remaining} = \text{total initial moles substrate} - \text{moles base consumed} \quad (2)$$

$$\frac{k_H}{k_D} = \frac{\log (C_0/C_t)_H}{\log (C_0/C_t)_D} = \frac{\log (3.82/2.09)}{\log (3.69/2.32)} = 1.2 \quad (3)$$

Representative Run for Exchange and Racemization of (+)-2-Phenyl-1,1,1-trifluorobutane in Methanol-O-d (Run 6).—To 50 ml. of methanol-O-d (0.99 atom of deuterium per molecule) was added at −20° with stirring under nitrogen 1.95 g. of clean potassium cut into small pieces. The basic solution obtained was shown by titration of an aliquot to be 0.90 M. To a dry 6-in. ampoule was added 1.700 g. of (+)-2-phenyl-1,1,1-trifluorobutane, α^{25}_{546} +36.2° (l = 0.5 dm., neat) and 15 ml. of the above solution. The tube was flushed with dry nitrogen, sealed, and placed in a 120° bath for 89 hr. The tube was cooled, opened, and the contents were shaken with water and pure pentane. The pentane extracts were water-washed, dried, and the pentane was evaporated through a 1 × 30 cm. Vigreux column. A small portion of the residue was subjected to analytical v.p.c. on a 3-ft. column of 20% silicone gum (SE 30) on a temperature programmed F and M dual column, Model 700. About 70 ± 10% of the material present was not starting material, but polymeric products of material which had undergone elimination (over 7 in number). These materials came off the column between 200 and 300°, and no monomeric olefin was observed. The rest of the residue was submitted to preparative v.p.c. on a 5/8 in. × 6 ft. column packed with 20% silicone gum (SE 30) on firebrick at 100° with 5–6 lb. of helium. The starting material was collected over a period of 8 min., after 26 min. had elapsed since the time of injection. The product was washed from the collector with pure pentane and, after removal of the pentane by distillation through a Vigreux column, was distilled. The material gave α^{25}_{546} +28.9° (l = 0.5 dm., neat) and was shown by infrared analysis to have undergone 16.5 ± 0.5% exchange (see below).

Exchange and Racemization of (+)-2-Phenyl-1,1,1-trifluorobutane in tert-Butyl Alcohol-O-d (Run 12).—When submitted to the action of 1.13 M potassium tert-butoxide in tert-butyl alcohol-O-d (0.99 atom of deuterium per molecule[3]) at 64° for 138 hr. and to the above isolation procedure, (+)-2-phenyl-1,1,1-trifluorobutane (α^{25}_{546} −29.42°, l = 0.5 dm., neat) gave a mixture of starting material and 1,1-difluoro-2-phenyl-1-butene. Analytical v.p.c. (see above) indicated that 90 ± 5% elimination had occurred, and that besides starting material and olefin, more than 7 high boiling components were present. Preparative v.p.c. (see above conditions) was used to separate the two substances, the starting material being collected 26–31 min. and the olefin from 31–40 min. after injection. Each fraction was rechromatographed, and analytical v.p.c. showed that separation was complete. Recovered starting material exhibited α^{25}_{546} −27.08° (l = 0.5 dm., neat), and was shown by infrared analysis to contain 0.065 atom of deuterium (8% racemization and 7% exchange, k_e/k_α = 0.90 ± 0.2).

The olefin was identified as 1,1-difluoro-2-phenyl-1-butene by spectral means. The infrared spectrum exhibited a strong band at 1730 cm.$^{-1}$ attributed to the C=CF$_2$ linkage. The nuclear magnetic resonance spectrum in carbon tetrachloride (A-60) showed a singlet (5 protons) at 2.77, a quartet (2 protons) centered at 7.59, and a triplet (3 protons) centered at 8.97 τ. The ultraviolet spectrum in hexane gave λ_{max} 233 mμ (ϵ 80,500). Anal. Calcd. for $C_{10}H_{10}F_2$: C, 71.41; H, 5.99. Found: C, 71.57; H, 6.16.

Infrared Analysis of 2-Phenyl-1,1,1-trifluorobutane (II) for Deuterium.—Two sets of synthetic mixtures of known deuterium content were prepared, one which ranged from 0 to 30% of one

atom of deuterium, and the other from 70 to 98.3% of one atom of deuterium. The standard deuterated material contained 0.983 atom of deuterium per molecule.[3] These known mixtures and the unknown mixtures were run consecutively on a Perkin–Elmer Model 421 dual grating spectrophotometer (sodium chloride optics). The samples were run neat in an 0.025-mm. sodium chloride cell at a scan rate of 7 cm.[-1] per sec., and were scanned through the region from 900 to 1025 cm.[-1]. The difference in

absorbance was determined for each standard sample, and this value was plotted against the amount of deuterium in the samples. For the 0 to 30% deuterium samples, the difference in absorbance of the 980 cm.[-1] band was used; for the 70–98.3% deuterium samples, the 958 cm.[-1] band was employed. For both the lower and upper ranges, a straight line plot was obtained, the average deviation being ±0.5%. The amounts of deuterium in the unknowns were determined with an error estimated at ±1%.

Observations Regarding the Mechanism and Steric Course of the α-Bromination of Carboxylic Acid Derivatives. An Electrophilic Substitution Reaction in Nonpolar Media

BY HAROLD KWART AND F. V. SCALZI[1]

Evidence is presented which supports a mechanism involving rate-determining electrophilic displacement by halogen on a cationic complex (II) which, in turn, is formed *via* acid-catalyzed bridging of the α-proton to the carbonyl center in a nonrate-determining step. In agreement with this proposal the following lines of argument have been cited. (1) A linear Hammett plot is obtained with *negative slope* ($\rho = -1.39$), in a hydratropic acid reaction series where the application of σ^+-values afford only a nonlinear correlation. (2) The polar substituent effect shows negligible implication of kinetic energy terms ($\Delta\Delta S^* \cong 0$). (3) A lack of stereoelectronic effects and any important degree of overlap control or resonance interaction with aromatic substituents is clearly indicated. (4) A direct parallel is demonstrated between 4-substituent effects on the rates of bromination of cyclohexanecarboxylic acid and solvolysis of cyclohexyl tosylates. (5) The magnitude of k_H/k_D is considerably less than half as great as anticipated for a rate-determining enolization mechanism. (6) There is a clear suggestion of the dependence of the rate on bromine concentration. The stereochemistry of both the brominated product and the unreacted acid chloride reagent, after extended heating in SOCl₂ in the presence of HCl, provides strong indication that long range field effects[31] (charge–dipole and dipole–dipole interactions) exert predominant control over the steric course of electrophilic displacement reactions of such protonated complex ion intermediates (II). Furthermore, the existence of such field effects on equilibrium is demonstrated to parallel the earlier observation[31] of an analogous influence on the kinetic course of various reactions.

The halogenation of carboxylic acids occurs with random orientation unless one resorts to the so-called Hell–Volhard–Zelinsky procedure,[2] or some modification thereof. Lapworth[3] was the first to recognize that the exclusive α-halogenation achieved by the H.V.Z. method was attributable to the intermediate formation of an enol, formally analogous to that which has been invoked in the acid-catalyzed halogenation of ketones and related carbonyl compounds. General confidence in this interpretation is indicated by its widespread appearance in standard texts and references.[4]

More recent experimental studies of the stereochemistry of bromination[5] and debromination[5,6] reactions in carboxylic acid–base systems have not found it necessary to assume that the product-forming step (in either case) involves the rapid attack of an electrophilic reagent (a proton or positive halogen source) on the enolic intermediate. While the kinetic approach has been applied very extensively and is regarded as the classical method for establishing the rate-determining formation of enol in both the base-[7,8]

and acid-catalyzed[9,10] halogenation of ketones,[7,8] such criteria have not been used to evaluate the indications that enolization is the slow step in the H.V.Z. mechanism as it appears to be in the reverse debromination reactions[6] (with Zn or HI). Against this background, then, we have sought to attain more detailed knowledge of the nature of the α-bromination reaction of carboxylic acids in thionyl chloride media by gathering kinetic information that could be compared with available results on bromination in ketones.

Results

The reaction medium chosen was not unfamiliar to previous investigators.[6,11] The determination of the relative rates of bromination of a variety of carboxylic acids selected for study was carried out by means of a competition technique,[12] after a series of attempts to accomplish this purpose by more direct methods encountered unsurmountable analytical difficulties. These difficulties were traceable to the nature of the reaction medium (SOCl₂) interfering with the direct determination of bromine concentration; the competition method of measuring relative rates thus held very evident attractions, since we did not wish to alter the reaction medium in which conventionally the H.V.Z. is carried out.

The members of two reaction series were subjected to competition with the unsubstituted case for a de-

(1) Part of the data discussed in this article has been taken from the Ph.D. Thesis of F. V. Scalzi presented in partial fulfillment of the requirements for this degree at the University of Delaware, June, 1963.

(2) C. Hell, *Ber.*, **14**, 891 (1881); C. Hell and J. Sadowski, *ibid.*, **24**, 2388 (1891); N. Zelinsky, *ibid.*, **20**, 2026 (1887); J. Volhard, *Ann.*, **242**, 141 (1887).

(3) A. Lapworth, *J. Chem. Soc.*, **85**, 30 (1904).

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(5) J. Klein and G. Levin, *J. Am. Chem. Soc.*, **80**, 1707 (1958).

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(7) R. P. Bell and H. C. Longuet-Higgins, *J. Chem. Soc.*, 636 (1946).

(8) P. D. Bartlett, *J. Am. Chem. Soc.*, **56**, 967 (1934).

(9) L. Zucker and L. P. Hammet, *ibid.*, **61**, 2791 (1939).

(10) P. D. Bartlett and Stauffer, *ibid.*, **57**, 2580 (1935).

(11) (a) C. K. Ingold, *J. Chem. Soc.*, **119**, 316 (1921); (b) E. Schwenk and D. Pappa, *J. Am. Chem. Soc.*, **70**, 3626 (1948).

(12) See, for a full discussion of this approach, G. A. Russell in "Technique of Organic Chemistry," Vol. VIII, Interscience Publishers, Inc., New York, N. Y., 1961.