Effect of the Leaving Group on Relative Reactivity and Products in Solvolysis[1]

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Phenyldimethylcarbinyl chloride, *p*-nitrobenzoate, and thionbenzoate have been found to be more reactive than the corresponding benzhydryl compounds by factors of 5.5, 23, and 4700, respectively, in ethanolysis at 50°. For the cumyl derivatives, kinetic isotope effects and solvolysis products are consistent with an ionization-type reaction for the three leaving groups. The results are interpreted in terms of an observed kinetic isotope effect containing contributions from the isotope effect on elimination from the carbonium ion because of ion-pair return. The high reactivity of cumyl thionbenzoate is attributed to a decrease in the importance of ion-pair return in this system relative to the model compounds.

The nature of the anion formed in limiting solvolysis reactions is known[3,4] to affect the partitioning of carbonium ions among possible reaction products because of the intervention of ion-pair intermediates. For example, the ratio of elimination[3] to substitution is markedly dependent on the nature of the counter ion under conditions where significant fractions of the products arise from the ion pairs. Of related interest[5] is an understanding of the factors affecting limiting solvolytic reactivity as the nature of the anionic leaving group is changed. Relative reactivities have been found to depend markedly on the leaving group when different types of reactions are compared.[5-7] For example, DePuy[6] noted that some alkyl bromides undergo bimolecular elimination at a faster rate than the corresponding *p*-toluenesulfonate although toluenesulfonate esters are often more reactive than bromides in limiting solvolysis. In addition, Hoffmann[7] has reported that the ratio $k_{\mathrm{OTs}}/k_{\mathrm{Br}}$ varies from 0.36 to 5000 with changes in the character of the reactions.

In this work the solvolytic reactivities of phenyldimethylcarbinyl chloride, *p*-nitrobenzoate, and thionbenzoate are compared with the behaviors of the corresponding benzhydryl derivatives. For the cumyl derivatives, the effect of deuteration of one or both methyl groups on solvolysis rates[8] and products[9] as a function of leaving group is reported and discussed in terms of the importance of ion-pair intermediates and ion-pair return.

Results

The kinetics and products in the ethanolysis of phenyldimethylcarbinyl chloride, *p*-nitrobenzoate, and thionbenzoate have been reported.[3] To facilitate comparisons with the d_3 and d_6 derivatives, new measurements of the kinetics and products from undeuterated cumyl derivatives were made in parallel runs with the deuterated analogs. Comparison of the present data with earlier results[3] is satisfactory.

Kinetics.—The ethanolysis of cumyl chloride at 25.0° was followed by electrical conductance. Standardized hydrochloric acid solutions were used for calibration of the conductance over the concentration region used in the kinetics. At 50°, the automatic titration procedure described for thion esters was used. Calculated first-order rate constants are summarized in Table I.

TABLE I

SUMMARY OF REACTION RATE CONSTANTS FOR THE SOLVOLYSIS OF CUMYL DERIVATIVES IN ETHANOL

Leaving group	Deuteration, °C	Temp, °C	Number of runs	10^4k,[a] sec^{-1}	k_H/k_D
Chloride[b-d]	d_0	25.0	10	3.44 ± 0.04	
	d_3	25.0	5	2.83 ± 0.06	1.22
	d_6	25.0	4	2.36 ± 0.01	1.46
p-Nitrobenzoate[e]	d_0	100.0	9	1.77 ± 0.06	
	d_3	100.0	5	1.40 ± 0.05	1.27
	d_6	100.0	3	1.06 ± 0.02	1.63
	d_0	50.0		0.0058[f]	
Thionbenzoate[c,g]	d_0	50.2	14	1.46 ± 0.03	
	d_3	50.2	10	1.09 ± 0.02	1.34
	d_6	50.2	7	0.75 ± 0.02	1.94

[a] Average of indicated number of measurements. Error is average derivation. [b] Concentration: (6–10) × 10^{-3} *M*. [c] Thymol blue indicator concentration: 2.1 × 10^{-5} *M*. [d] 1% (v/v) in pentane. [e] Concentration: 1 × 10^{-2} *M*. [f] Calculated from data of R. L. Buckson and S. G. Smith.[3] [g] Concentration: (0.8–20) × 10^{-3} *M*.

The solvolysis of cumyl thionbenzoate was monitored by plotting on a strip chart recorder the volume of standardized sodium ethoxide required to maintain a thermostated sample containing thymol blue at the indicator end point. The addition of titrant from a piston buret was controlled by a servo system so that the light intensity from a filtered tungsten source passing through the stirred reaction mixture and falling on a phototransistor was constant.[10,11] Aliquots from *p*-nitrobenzoate ester solvolysis were titrated in the usual way,[3] a deuterated and undeuterated compound being solvolyzed concurrently. The derived rate constants are summarized in Table I. The observed kinetic secondary deuterium isotope effects for six

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(1) Research supported by the National Science Foundation.

(2) D. J. W. Goon, Ph.D. Thesis, University of Illinois, Urbana, Ill., 1968.

(3) R. L. Buckson and S. G. Smith, *J. Org. Chem.*, **32**, 634 (1967).

(4) (a) D. J. Cram and M. R. Sahyun, *J. Amer. Chem. Soc.*, **85**, 1257 (1963); (b) M. Cocivera and S. Winstein, *ibid.*, **85**, 1702 (1963); (c) P. S. Skell and W. L. Hall, *ibid.*, **85**, 2851 (1963); (d) T. Cohen and J. Lipowitz, *Tetrahedron Lett.*, No. 49, 3721 (1964).

(5) (a) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963); (b) R. G. Pearson and J. Songstad, *J. Org. Chem.*, **32**, 2899 (1967); (c) W. S. Trahanovsky and M. P. Doyle, *J. Amer. Chem. Soc.*, **89**, 4867 (1967).

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(7) H. M. R. Hoffmann, *J. Chem. Soc.*, 6753 (1965).

(8) For reviews, see, *e.g.*, (a) W. H. Saunders, Jr., *Surv. Progr. Chem.*, **3**, 109 (1966); (b) E. A. Halevi, *Progr. Phys. Org. Chem.*, **1**, 109 (1963); (c) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).

(9) For representative examples of deuterium isotope effects on solvolytic products, see (a) V. J. Shiner, Jr., *J. Amer. Chem. Soc.*, **75**, 2925 (1953); (b) V. J. Shiner, Jr., *ibid.*, **76**, 1603 (1953); (c) M. S. Silver, *ibid.*, **83**, 3487 (1961); (d) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958); (e) A. C. Cope R. B. Kinnel, *J. Amer. Chem. Soc.*, **88**, 752 (1966); (f) C. E. Boozer and E. S. Lewis, *ibid.*, **76**, 794 (1954); (g) V. J. Shiner, Jr., and J. S. Jewett, *ibid.*, **87**, 1382 (1965); (h) G. J. Frisone and E. R. Thornton, *ibid.*, **90**, 1211 (1968).

(10) The design of this instrument will be described elsewhere.[11]

(11) R. Anderson and S. Smith, unpublished work.

deuterium atoms range from k_H/k_D of 1.46 for the chloride to 1.94 for the thionbenzoate.

The reaction rates of cumyl derivatives may be compared with the rates of corresponding benzhydryl compounds. The data reported by Winstein, Fainberg, and Grunwald[12] for the benzhydryl chloride were used in this comparison. The reaction rates of the *p*-nitrobenzoate, summarized in Table II, were obtained by titration of aliquots, and the solvolysis of the thion esters was followed by the disappearance of absorption at 436 mμ.

Table II

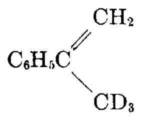
Summary of Solvolysis Rates for Benzhydryl Derivatives[a] in Ethanol

Derivative	Temp, °C	10^5k, sec^{-1}
Chloride	50	89.0[b]
p-Nitrobenzoate	100.0	0.36 ± 0.02
	125.0	2.70 ± 0.01
	50	0.0026[c]
Thionbenzoate	75.0	0.84 ± 0.02
	100.0	14.4 ± 0.1[d]
	50	0.031[c]

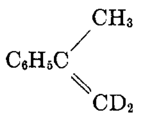
[a] *Ca.* 1 × 10^{-2} *M*. [b] Data from ref 12. [c] Calculated from data at higher temperatures. [d] Previously reported as 13.6 × 10^{-4} sec^{-1} [S. G. Smith, *Tetrahedron Lett.*, No. 21, 979 (1962)].

Products.—Product analyses were carried out by glpc with internal standards as previously described.[3] An excess of 2,6-lutidine was present in product runs involving the chloride or *p*-nitrobenzoate. With thion esters, an automatic photometric titrator[10,11] was used to neutralize continuously developed acid. The results, summarized in Table III, indicate that, as found before,[3] the fraction elimination increases in the order chloride < *p*-nitrobenzoate < thionbenzoate, with the chloride giving only 12% elimination while the thionbenzoate gives 91% elimination. Successive deuteration of the methyl groups decreases the fraction elimination and increases substitution. With the chloride, for example, elimination drops from 12 to 4% and substitution increases from 89 to 96% with six deuteriums per molecule. Similar large changes in product composition upon deuteration are noted with the other leaving groups (Table III).

The deuteration pattern of the olefin formed from the d_3 derivative is of considerable interest since elimination of a proton would form 2-phenylpropene-3,3,3-d_3 (compound I) and elimination toward the deuterated methyl group would give 2-phenylpropene-1,1-d_2 (II). The ratio of these products, which reflects the isotope effect on the elimination step in the solvolysis, was obtained by proton nmr analysis of olefin fractions isolated by preparative glpc. The aromatic protons were used as an internal standard for the repeated integrations. Subject to the reservation of the limitation of the accuracy of the experimental method, the results summarized in Table IV indicate that with a chloride leaving group elimination discriminates between hydrogen and deuterium more than with the other leaving groups. The present data indicate that the thionbenzoate ester displays the smallest isotope effect in this competition, the observed ratio of the two products being only 1.7.


$C_6H_5C(=CH_2)CD_3$

I


$C_6H_5C(CH_3)=CD_2$

II

Discussion

Measured solvolytic characteristics of the cumyl derivatives studied in this work are summarized in Table V. These data indicate that changing the leaving group from chloride to *p*-nitrobenzoate to thionbenzoate results in a steady increase in the measured kinetic isotope effect and fraction elimination, and a decrease in ρ, *m*, and the discrimination between CH_3 and CD_3 in elimination. These trends suggest changes in the detailed nature of the reaction but do not seem to dictate invoking fundamentally different types of reactions for each leaving group. The large effect of the leaving group[3] on the fraction elimination in this and other similar reactions[4] suggests[3,4,13] that elimination occurs from some variety of ion pair. Substitution could also occur within the ion pair or from further stages of dissociation.[3,4] Since return from dissociated ions has not been observed in these cumyl systems,[3] the reaction may be approximated by the scheme given in eq 1, although it is clear that more than one variety[14,15] of ion pair may be involved and a significant portion of product may come from more dissociated species. The rate constants in eq 1 could each represent more than one kinetically important step. With these limitations, the observed rate constant is given by eq 2.

$$\begin{tikzcd} RX \arrow[r, shift left, "k_1"] & R^+X^- \arrow[l, shift left, "k_{-1}"] \arrow[r, "k_S"] \arrow[d, "k_E"] & \text{substitution} \\ & \text{elimination} & \end{tikzcd} \tag{1}$$

$$k^{\text{obsd}} = \frac{k_1(k_E + k_S)}{k_{-1} + k_E + k_S} \tag{2}$$

The decrease in fraction elimination and corresponding increase in ether formation and, in the case of the thionbenzoate, thiol ester formation with deuteration of the methyl groups may be correlated[16] with the observed ratio of 2-phenylpropene-3,3,3-d_3 to 2-phenylpropene-1,1-d_2, Table IV. For example, the product from the d_3 chloride may be considered as the result of a k_S for substitution essentially the same as that for the undeuterated material and an elimination toward the CH_3 group with a rate constant of $^1/_2k_E$ and a rate constant for elimination toward the CD_3 of $^1/_2k_E$ multiplied by the measured isotope effect for this process. Such a calculation is necessarily an approximation since isotope effects on all product-forming steps but one have been neglected. However, as summarized in Table VI, this scheme predicts all of the observed products for the d_3 and d_6 compounds with considerable accuracy.

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[12] S. Winstein, A. H. Fainberg and E. Grunwald, *J. Amer. Chem. Soc.*, **79**, 4146 (1957).

[13] H. L. Goering and K. Humski, *ibid.*, **90**, 6213 (1968).

[14] S. Winstein, P. E. Klinedinst, Jr., and G. C. Robinson, *ibid.*, **83**, 885 (1961).

[15] H. L. Goering and J. F. Levy, *ibid.*, **86**, 120 (1964).

[16] D. S. Noyce and C. A. Lane, *ibid.*, **84**, 1641 (1962).

TABLE III

PRODUCTS OF THE SOLVOLYSIS OF CUMYL DERIVATIVES IN ETHANOL

Derivative	% olefin[a]	% ether[b]	% ester[c]	Total % yield
Chloride[d,e]				
d_0	11.8 ± 2.4	89.0 ± 1.7		100.8 ± 1.6
d_3	8.6 ± 0.7	92.4 ± 2.2		101.0 ± 2.2
d_6	3.9 ± 0.3	98.1 ± 1.4		102.0 ± 2.3
p-Nitrobenzoate[e,f]				
d_0	49.6 ± 0.5	49.6 ± 0.3		99.2 ± 0.1
d_3	41.7 ± 0.1	56.9 ± 0.2		98.6 ± 0.3
d_6	31.7 ± 1.1	67.1 ± 0.4		98.8 ± 0.7
Thionbenzoate[g]				
d_0	90.6 ± 0.8	5.8 ± 0.3	2.3 ± 0.7	98.7 ± 0.9
d_3	85.6 ± 2.2	7.6 ± 0.3	3.4 ± 0.2	96.6 ± 2.3
d_6	81.6 ± 0.4	10.8 ± 0.4	6.4 ± 0.3	98.8 ± 0.6

[a] 2-Phenylpropene. [b] Ethyl cumyl ether. [c] Cumyl thiolbenzoate. [d] At 25.0°. [e] 2×10^{-2} *M*. [f] At 100.0°. [g] At 50.2°.

TABLE IV

DEUTERATION OF THE OLEFIN FROM THE ETHANOLYSIS OF d_3-CUMYL DERIVATIVES

Derivative	Temp, °C	2-Phenylpropene ratio, 3,3,3-d_3/1,1-d_2
Chloride	25	3.15 ± 0.06
	50	2.9[a]
p-Nitrobenzoate	100	2.10 ± 0.06
	50	2.4[a]
Thionbenzoate	50	1.68 ± 0.02

[a] Calculated by assuming $\Delta F^{\ddagger}_{H} - \Delta F^{\ddagger}_{D}$ is independent of temperature.

TABLE V

SUMMARY OF RESULTS FROM THE ETHANOLYSIS OF CUMYL DERIVATIVES

	Derivative		
	Chloride	*p*-Nitrobenzoate	Thionbenzoate
ρ^a	−4.67		−2.9
$m^{a,b}$	1.3	0.8	0.54
$k_H/k_{D(d_3)}$	1.2[c]	1.32[c]	1.34[c]
$k_H/k_{D(d_6)}$	1.42[c]	1.76[c]	1.94[c]
% substitution	89[d]	50[e]	6[c]
% elimination	12[d]	50[e]	91[c]
I/II[f]	2.9	2.4	1.7

[a] Reference 3. [b] Aqueous ethanol. [c] At 50°. [d] At 25°. [e] At 100°. [f] Product ratio: 2-phenylpropene-3,3,3-d_3 (I)/2-phenylpropene-1,1-d_2 (II).

The observed kinetic isotope effect, k_H^{obsd}/k_D^{obsd}, does not necessarily represent the isotope effect on the ionization step of these reactions. To the extent that k_{-1} is important, the isotope effect on the product forming steps such as elimination are reflected in the observed rate constant because of the competitive nature of k_{-1}, k_E, and k_S. That k_{-1} might not be negligible has been demonstrated by Goering and Chang[17] in the structurally similar system, 2-phenyl-2-butyl *p*-nitrobenzoate, where acyl–alkyl oxygen equilibration was found to occur in competition with solvolysis, and it is not clear how much return escapes detection by this method.[18-20] In the absence of ion-pair return to covalent starting material, the observed isotope effects would be expected to be cumulative,[21] with k_H/k_D being equal to the square of k_H/k_{D_3}. However, if k_{-1} is not negligible relative to k_E and k_S and a significant isotope effect exists on k_E, then, to the extent that elimination contributes to the reaction, deviation from cumulative behavior would be expected. The present data are not sufficiently accurate to provide an adequate test, although k_H/k_{D_6} tends to be larger than $(k_H/k_{D_3})^2$; *e.g.*, the thion ester gives 1.8 calculated *vs.* 1.9 observed.

If this treatment is extended further with the assumption that k_{-1} is large relative to k_E and k_S and that, as a first approximation, a cumulative isotope effect exists on k_1, then, with the observed kinetic isotope effects and the observed product isotope effects, the deuterium isotope effect of one CD_3 group on ionization, k_1, is found to be 1.15 for the chloride and *p*-nitrobenzoate and 1.10 for the thionbenzoate. These values may be closer to the actual β-deuterium isotope effects on ionization than the measured kinetic isotope effects of 1.2, 1.32, and 1.34, respectively. By this analysis, the isotope effect on proton loss from the carbonium ion makes a substantial contribution to the measured overall kinetic isotope effect.

Further understanding of the course of these reactions comes from a comparison of the reactivities of the cumyl derivatives with those of the corresponding benzhydryl compounds. The rate constants either observed at or corrected to 50° are summarized in Table VII. These data indicate that the ratios of the rate constants for cumyl chloride, *p*-nitrobenzoate, and thionbenzoate to those of the corresponding benzhydryl derivatives are 5.5, 23, and 4700. Cumyl thionbenzoate is substantially more reactive than expected on the basis of the benzhydryl system as a model. The change in the products from 50% elimination with the *p*-nitrobenzoate to 91% elimination with the thion ester does not adequately account for the observed rate increase. If the concept of approximate group additivity in linear free-energy relationships[22] is preserved, it follows that the measured rate constants do not reflect, to the same extent, the free energy of activation associated with ionization. Although a large number of other factors may be involved, a preliminary understanding of these relative rates may be obtained from

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(20) C. D. Ritchie in "Solute–Solvent Interaction," J. F. Coetzee and C. D. Ritchie, Ed., Maycel-Dekker, New York, N. Y., 1969, in press.

(21) V. J. Shiner, Jr., B. L. Murr, and G. Heinemann, *J. Amer. Chem. Soc.*, **85**, 2413 (1963).

(22) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963, p 135 ff.

Table VI

Comparison of Observed and Calculated Products in the Ethanolysis of Cumyl-d_3 and -d_6 Derivatives

Derivative	Deuteration	Observed products[a] Olefin[b]	Observed products[a] Ether[c]	Observed products[a] Ester[d]	Calculated products, % Olefin[b]	Calculated products, % Ether[c]	Calculated products, % Ester[d]
Chloride (25°)	d_3	8.6	91.4		8.0	92.0	
	d_6	3.8	96.2		4.1	95.9	
p-Nitrobenzoate (100°)	d_3	42.4	57.6		42.5	57.5	
	d_6	32.1	67.9		32.2	67.8	
Thionbenzoate (50°)	d_3	88.6	7.9	3.5	90	7.2	2.8
	d_6	82.6	10.9	6.5	86.8	9.5	3.8

[a] Observed product yields normalized to 100%. [b] 2-phenylpropene. [c] Ethyl phenyldimethylcarbinyl ether. [d] Phenyldimethylcarbinyl thiolbenzoate.

Table VII

Comparison of Cumyl and Benzhydryl Ethanolysis Rate Constants at 50°

	10^4k, sec^{-1} Chloride	10^4k, sec^{-1} *p*-Nitrobenzoate	10^4k, sec^{-1} Thionbenzoate
Cumyl	49	0.0058	14.6
Benzhydryl	8.9	0.00026	0.0031
Cumyl/benzhydryl	5.5	23	4700

the following considerations. The observed rate constant is clearly dependent on the magnitude of the rate constant for ionization, k_1, and, if ion-pair return is fast relative to product formation, on the value of k_{-1}, the rate constant for re-formation of starting material. Since the process corresponding to k_{-1} involves the reaction of a relatively unstable carbonium ion with a nucleophilic anion which, at least initially, is within the same solvent cage, k_{-1} might well be quite large.[20] The activation energy associated with the recombination of the ions is likely to include contributions from changes in solvation,[23,24] nonbonded repulsions,[23] and the energy required to reorganize[25,26] the structure of the cation and anion to begin to re-form a covalent bond. The importance of these effects will depend on the structures of the cation and anion as well as the nature of the solvent. Since the comparison cited above involves two cations and three anions, each with its specific reactivity modified by the proximity of the counter ion, it would not be surprising if large changes in the magnitude of k_{-1} were found. On this basis, the present results are compatible with the cumyl thionbenzoate ion pair giving substantially less return to covalent material than the other systems. Since inductive stabilization of the transition state between a covalent molecule and an ion pair is less sensitive to geometry (noncoplanarity) than is resonance stabilization,[26] the cumyl cation may contribute less to the barrier to return than the benzhydryl cation. This would increase the sensitivity of k_{-1} for the cumyl system, to the nature of the anion. Among these anions, the thionbenzoate should be relatively poor at ion-pair return, since, in the absence of the perturbing effect of the carbonium ion, it tends to be more nucleophilic at sulfur than oxygen;[27] as first formed, the sulfur is not properly positioned for covalent bonding to carbon.

The marked dependence of relative reactivity on leaving groups noted here indicates that rate comparisons involving corrections for different leaving groups may contain unknown but substantial effects resulting from the nature of the specific groups involved.

Experimental Section

Cumyl Chloride, *p*-Nitrobenzoate, and Thionbenzoate.—These materials were prepared as previously described.[3]

Acetophenone-d_3.—This compound was prepared from acetophenone by base-catalyzed exchange with D_2O (99.5% deuterated). Acetophenone (10 ml) was added to a mixture of anhydrous potassium carbonate (0.1 g) and D_2O (5 ml). After the mixture had been refluxed for 16 hr, the acetophenone was removed and placed into a fresh D_2O–base mixture. The initial D_2O mixture was refluxed with another portion of acetophenone. Ten portions of acetophenone were subjected to this procedure. The first portion was exchanged four times with fresh D_2O mixtures. The final exchanges of the other nine samples were each performed in a fresh D_2O mixture. The combined fractions were dried over magnesium sulfate and distilled to give 74.7 g (71%) of acetophenone-d_3, bp 93–95° (10 mm). Analysis by nmr indicated deuteration of the acetophenone-d_3 was *ca.* 98%.

Cumyl Alcohols.—Cumyl alcohol was commercially available from Aldrich Chemical Co. and was distilled before use. It was also prepared by the Grignard reaction between acetone and phenylmagnesium bromide. d_3-Cumyl alcohol was prepared in 86% yield after distillation from the reaction of acetophenone-d_3 and methylmagnesium iodide. The mass spectrum indicated that the product d_3-cumyl alcohol prepared was 95% d_3 and 5% d_2.

Cumyl-β-d_6 alcohol was prepared in 93% yield from acetone-d_6 (1.6 g, Merck Sharp and Dohme of Canada, Ltd.) and phenylmagnesium bromide. The mass spectrum indicated that the alcohol consisted of the following deuterated species: d_6, 92.8%; d_5, 4.4%; d_4, 0.4%; d_3, 2.4% (corresponding to 98% deuteration of the methyl groups).

Product Analysis.—Quantitative product analyses were done by glpc as previously described[3] except that the thionbenzoate product analyses were done on the same solutions used in the kinetic studies.

Isolation and Analyses of Olefin Fraction.—The products of solvolysis in ethanol of the three d_3-cumyl derivatives were concentrated as previously described.[3] The olefin was separated from the other products by preparative glpc with a $^1/_4$-in.-diameter XF-1150 (silicone nitrile) on Chromosorb P column, 3 ft long, at 100° in an F & M Scientific 200 vapor phase chromatograph. The olefin fraction was collected, reinjected, and collected again. Carbon tetrachloride was used to rinse the olefin fractions into tubes. The ratio of 2-phenylpropene-3,3,3-d_3 to 2-phenylpropene-2,2-d_2 was determined by proton nmr analysis (Varian HA-100, unlocked for maximum sensitivity). The relative areas of the aromatic, olefinic, and methyl absorptions were determined by averaging several integrations of each peak. The area of the aromatic absorption was used as a standard of comparison. Each experiment was run two times and the results were averaged.

Product Stability.—2-Phenylpropene and ethyl cumyl ether have been shown to be stable to the conditions of ethanolysis of cumyl chloride and *p*-nitrobenzoate previously.[3] The stability of the products of ethanolysis of cumyl thionbenzoate was determined by addition of the appropriate acid (*ca.* 0.01 *M*) to ethanol containing thymol blue indicator (*ca.* 2×10^{-5} *M*), titration to a green end point with sodium ethoxide or methoxide, addition of one of the products (*ca.* 0.01 *M*), and allowing the

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[23] E. F. Caldin, *J. Chem. Soc.*, 3345 (1965).

[24] C. D. Ritchie, G. A. Skinner, and V. G. Badding, *J. Amer. Chem. Soc.*, **89**, 2063 (1967).

[25] We are indebted to Professor C. D. Ritchie for substantial contributions to the development of these ideas.

[26] J. Hine, *J. Org. Chem.*, **31**, 1236 (1966).

[27] S. G. Smith, *Tetrahedron Lett.*, **21**, 979 (1962).

solution to stand at the reaction temperature for a time corresponding to 10 half-lives of the undeuterated derivative. By this method an average of 100% of the olefin, 97% of the ethyl ether, and 99% of the thiol ester were recovered.

Kinetic Procedures.—The reaction rates of d_0-, d_3-, and d_6-cumyl chloride in ethanol were determined conductometrically at 25.0°. The reactions were run in a 2.5 × 15 cm test tube into which a Radiometer electode, type CDC 140, was placed. In each run, 25 ml of ethanol was added to the test tube and equilibrated in a water bath maintained at 25.00 ± 0.01°. Then a 0.245-ml aliquot of the chloride in pentane was added and the solution was briefly agitated. Usually 90–100 resistance measurements were taken at intervals varying from 15 sec to 3 min with an Industrial Instruments, Inc., conductivity bridge, Model RC-15. The reactions were followed to at least 62%, and infinity readings were taken after 10 half-lives. At least 20 measurements selected at appropriate times were used to calculate the rate constant. A weighted, least-squares FORTRAN program for the IBM-7094 computer took the measured resistance and time data for the run, converted the resistance into concentration, and applied the first-order equation. A calibration of resistance *vs.* concentration of hydrochloric acid in ethanol was determined, and a third-order polynomial was fitted to the data. The hydrochloric acid–ethanol solutions used in the calibration were *ca.* 1% in pentane, as were the solutions used in the kinetic and product runs.

The usual sealed-ampoule technique was used for the determination of the rates of solvolysis of the cumyl *p*-nitrobenzoates.[3] For all determinations a deuterated ester and an undeuterated ester were run concurrently in the same constant-temperature bath maintained at 100.00 ± 0.02°. In an additional method, a specially constructed titration apparatus was used which electronically detected a bromthymol blue end point. This method was also used to determine the rates of solvolyses of the benzhydryl *p*-nitrobenzoates.

The rates of ethanolysis of cumyl chloride and of cumyl thionbenzoate at 50° were determined by the use of a photometric titrator.[10,11] The apparatus consisted of a light source and an optical system which collimated the light on a band pass filter (λ_{max} 600 mμ) before it passed through a stirred and thermostated reaction cell to a phototransistor.

A servo-system controlled the addition of titrant from a piston buret so that the energy falling on the sensor was constant. The reaction cell had two cavities sealed by screw-caps containing silicone rubber plugs. Syringe needles were used for the introduction of titrant, substrate, and nitrogen gas. In a kinetic run, *ca.* 20 ml of solvent containing thymol blue indicator (*ca.* 2×10^{-5} *M*) was thermostated at the reaction temperature. Dry nitrogen was bubbled through the solution very briefly and the indicator was brought to the appropriate end point. The introduction of the chlorides into the reaction cell was by injection of pentane solutions. Thionbenzoates were added as solids. The apparatus added titrant (maximum volume was *ca.* 2 ml) as necessary to maintain the selected indicator end point. Readings at appropriate times were selected from the resulting titration volume *vs.* time curve and used directly to calculate the integrated first-order rate constant.

The solvolysis of benzhydryl thionbenzoates was studied in sealed, degassed ampoules thermostated in Carbowax-400 baths maintained at 75.00 ± 0.02 and 100.00 ± 0.02°. At appropriate times the ampoules were removed from bath, cooled to room temperature, and analyzed for absorption at 436 mμ with a Beckman DU spectrophotometer.

Calculations.—First-order rate constants were calculated with a FORTRAN program and IBM-7094 and -1800 computers. The program calculated the best fit, least-square line through the points of a plot of ln *Y* *vs.* time. The points were weighted in proportion to the relative magnitude of the *Y* values.

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Effect of Solvent on the Photolysis of α-Lipoic Acid[1]

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The photolysis of α-lipoic acid in different solvents was followed by tlc and uv. It was found that a number of products are formed in each solution and the number and kind of product are dependent on the solvent. The chain length is determined by the kind of solvent; the length of the polymer chain decreased with increased availability of hydrogen atoms in the solvent. The amounts of products as well as the rate of formation of products are also solvent dependent. A mechanism is postulated in which the disulfide bond is broken homolytically in the first step. It is postulated that the reaction proceeds by chain transfer of hydrogen atoms from the solvent, causing short chains; by attack of the radicals on the other lipoic acid molecules, forming chains of longer length; or by the hydrolysis of the thio ketone formed by intramolecular abstraction of the tertiary hydrogen.

Because α-lipoic acid (1,2-dithiolane-3-valeric acid) has been found to be important biologically in the oxidative decarboxylation of α-keto acids,[3] and because it is thought to participate in photosynthesis,[4–7] several studies have been made of the photolysis of α-lipoic acid and the related compound, 1,2-dithiolane.[4,8,9]

In 1954, Barltrop, *et al.*,[4] reported that the photolysis of 1,2-dithiolane in neutral solution resulted in polymerization. They found that in acidified ethanol, the dithiolane ring was destroyed but no polymerization occurred. They suggested that the dithiyl radicals, produced by photolysis, reacted with the solvent. When Whitney and Calvin[8] photolyzed α-lipoic acid, the uv spectra indicated that a definite set of products was formed. These products were not identified. They also conducted a number of exploratory experiments on the relations between water concentration, pH, and polymerization, and concluded that polymer formation is not a simple consequence of the fission of the S–S bond. They postulated that the ultraviolet light causes slight polymerization and then inhibits it. They also felt that the failure of the biradicals to polymerize in ethanol solution was consistent with the views of Zimm and Bragg[10] that it is improbable for biradicals to form long chains. In 1956, while studying

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(2) Union Carbide Fellow, 1966–1967. National Institute of Health Special Research Fellow, 1967–1968, Grant 1-F1-GM-35,937-01.

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