

# Intramolecular Nucleophilic Participation. X. The Solvolysis of *o*-Nitrobenzhydryl Bromide in Media of Low Nucleophilicity

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**Abstract:** A comparison of the relative rates of solvolysis of *o*- and *p*-nitrobenzhydryl bromide and of *o*- and *p*-bromobenzhydryl bromide in trifluoroethanol and trifluoroethanol-benzene mixtures has been made. The  $k_o/k_p$  ratio for the nitro compounds is 30 (25°) for reaction in pure trifluoroethanol and increases significantly as the medium is diluted with benzene. The corresponding ratios for the bromobenzhydryl bromides are less than unity. The Grunwald-Winstein  $m$  values for reaction of the *p*-nitro- and *o*- and *p*-bromobenzhydryl bromides in trifluoroethanol-benzene mixtures are all significantly larger than unity while that for *o*-nitrobenzhydryl bromide is less than unity. The increase in  $k_o/k_p$  values for the nitro compounds with increasing benzene content of the medium is, therefore, ascribed to increasing ion pair return in the reaction of the para isomer. The absence of the complication of ion pair return in the reaction of the ortho isomer is associated with participation of the *o*-nitro group as an internal nucleophile. The  $k_o/k_p$  ratio for solvolysis of the nitrobenzhydryl bromides increases significantly as the medium is changed from acetic to trifluoroacetic acid. This again is ascribed to a corresponding increase in the extent of ion pair return in the reaction of the para isomer.

When the ortho substituent is functionally incapable of serving as an internal nucleophile, an ortho-substituted benzhydryl halide solvolyzes more slowly than its para isomer.<sup>1-3</sup> Presumably the involvement of the medium in solvation processes critical to the rate-determining phases of reaction of the ortho isomer is subject to steric retardation. When the substituent is appropriately structured geometrically as well as electronically to provide anchimeric assistance, e.g., -COOR and -NO<sub>2</sub>, the ortho isomer is more reactive than the para.<sup>2-4</sup>

In 90% aqueous acetone, *o*-nitrobenzhydryl bromide solvolyzes to yield *o*-nitrosobenzophenone (I), and at 45° the halide is 83 times more reactive in this medium than *p*-nitrobenzhydryl bromide.<sup>4</sup> In acetic acid the *o*-nitro isomer reacts in the presence of hydrogen bromide to form 5-bromo-3-phenyl-2,1-benzisoxazole (II), while in the presence of sodium acetate reaction occurs at the same rate<sup>3</sup> to yield *o*-nitrosobenzophenone. At 45° the acetolysis rate ratio of *o*- and *p*-nitrobenzhydryl bromide is 1450:1. The alternate formation of nitroso ketone and isoxazole is accounted for in terms of a reaction process in which they derive from the *o*-nitro compound by way of a common precursor (III), an ion pair formed in the rate-determining step. The ion pair either can lose a proton to a base (water or sodium acetate) to produce nitroso ketone or in an acidic medium can collapse to reincorporate Br<sup>-</sup>, not at the exocyclic carbon but rather in the substituted ring, to yield irreversibly the precursor of the isoxazole.<sup>5</sup> This latter reaction is in effect ion pair return which leads to formation of product rather than starting material.<sup>6</sup>

(1) (a) J. F. Norris and C. F. Banta, *J. Amer. Chem. Soc.*, **50**, 1084 (1928); (b) J. F. Norris and J. T. Blake, *ibid.*, **50**, 1808 (1928).

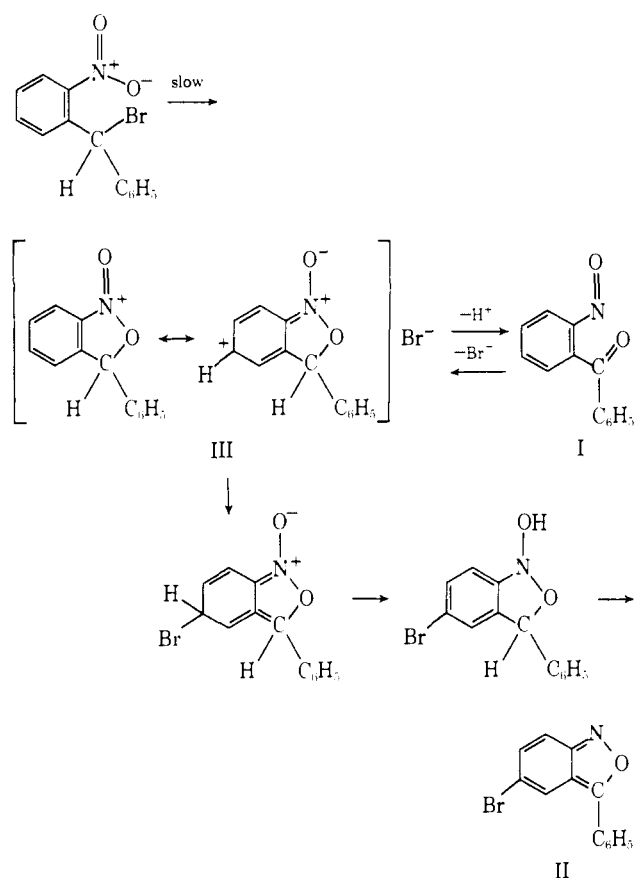
(2) A. Singh, L. J. Andrews, and R. M. Keefer, *J. Amer. Chem. Soc.*, **84**, 1179 (1962).

(3) S. Kim, S. Friedrich, L. J. Andrews, and R. M. Keefer, *J. Amer. Chem. Soc.*, **92**, 5452 (1970).

(4) A. D. Mease, M. J. Strauss, I. Horman, L. J. Andrews, and R. M. Keefer, *J. Amer. Chem. Soc.*, **90**, 1797 (1968).

(5) Cf. W. B. Dickinson, *J. Amer. Chem. Soc.*, **86**, 3580 (1964).

(6) The acid-catalyzed ring opening of *o*-nitrophenylethylene oxides appears to be closely related mechanistically to the solvolysis of *o*-nitrobenzhydryl bromide; see (a) T. W. M. Spence and G. Tennant, *J. Chem. Soc. C*, 3712 (1971); (b) I. P. Sword, *ibid.*, 820 (1971).



In accounting for the increase in the *o*-*p* reactivity ratio for nitrobenzhydryl bromide solvolysis as the solvent is changed from 90% aqueous acetone to acetic acid, it has been suggested that the ortho substituent becomes increasingly involved as an internal nucleophile, with corresponding influence on reactivity of the bromide, as the medium becomes less favorably constituted to provide for electrostatic stabilization of positive charge.<sup>3</sup> The same explanation has been applied in discussing the observation that the solvolysis rate ratio for *o*- and *p*-carbophenoxybenzhydryl bromide

drops by a factor of over 4 at 30° as the solvent is changed from 95 to 80% aqueous acetone.<sup>7</sup>

An alternate or additional explanation of the relative increase in rate influence of the *o*-nitro group as the medium is changed from aqueous acetone to acetic acid is based on the premise that, unlike the reaction of *p*-nitrobenzhydriyl bromide, the solvolysis of the ortho isomer is not subject to the complication of ion pair return to form *starting material*. With this in mind the investigation of medium influences on the solvolysis rates of the nitrobenzhydriyl bromides has been extended to solvents of low nucleophilicity, including 2,2,2-trifluoroethanol, trifluoroethanol-benzene mixtures, and trifluoroacetic acid.

## Experimental Section

**Materials.** *o*-Nitrobenzhydriyl bromide was synthesized as described previously.<sup>4</sup> In preparing *p*-nitrobenzhydriyl bromide, a slurry of 10.0 g (0.0441 mol) of *p*-nitrobenzophenone (Aldrich Chemical Co.) in 250 ml of 95% ethanol was treated dropwise with an alkaline aqueous solution of 2.0 g (0.0529 mol) of sodium borohydride. When gas evolution ceased, ether was added and the resultant mixture was extracted with dilute hydrochloric acid and then with saturated sodium bisulfite. The dried ether solution was evaporated to dryness, and the solid residue was recrystallized from 95% ethanol to yield 6.5 g (64%) of *p*-nitrobenzhydriyl, mp 75–77° (lit.<sup>4</sup> mp 76–78°). The carbinol was converted to the bromide (mp 32–35°) through gassing of its solution in benzene with hydrogen bromide.<sup>7</sup>

In preparing *p*-bromobenzhydriyl bromide, *p*-bromobenzophenone (Aldrich Chemical Co.) was reduced by the procedure described above for the preparation of *p*-nitrobenzhydriyl. The product was obtained in 90% yield, mp 55–60° (lit.<sup>8</sup> mp 62–63°), and it was converted to the corresponding bromide, bp 158–159° (2.0 Torr), by treatment with gaseous hydrogen bromide as in the preparation of *p*-nitrobenzhydriyl bromide from the corresponding carbinol.

*Anal.* Calcd for C<sub>11</sub>H<sub>10</sub>Br: C, 47.89; H, 3.09. Found: C, 48.11; H, 3.05.

*o*-Bromobenzhydriyl was prepared in 94% yield by reduction of *o*-bromobenzophenone as described above for the reduction of its para isomer. The crude carbinol, a colorless oil, was converted to the corresponding bromide, bp 144–146° (2 Torr) (lit.<sup>9</sup> bp 169° (1.2 Torr)), by treatment with gaseous hydrogen bromide (see above). The *p*-bromobenzophenone, bp 135–140° (1 Torr) (lit.<sup>10</sup> bp 151–153° (0.05 Torr)), was prepared by the Friedel-Crafts reaction of *p*-bromobenzoyl chloride (obtained by reaction of *o*-bromobenzoic acid with thionyl chloride) and benzene.

To prepare *o*-nitrosobenzophenone, 0.59 g (0.0020 mol) of *o*-nitrobenzhydriyl bromide was dissolved in 60 ml of 0.05 *M* sodium acetate in acetic acid. The mixture was allowed to stand for 48 hr, and then 100 ml of water was added to it. The resultant precipitate was recrystallized from ethyl acetate to provide 0.35 g (82% yield) of nitroso ketone, mp 127.5–128.0° (lit.<sup>4</sup> mp 127–128°).

Samples of Eastman Organic Chemicals *tert*-butyl chloride (bp 50–51°) and of 2,6-lutidine were distilled before use in rate studies. Matheson Gas Co. anhydrous hydrogen bromide was used to prepare the required solutions of hydrogen bromide. These were analyzed for bromide concentration either gravimetrically or by the Volhard method. Reagent grade samples of benzene, carbon tetrachloride, sodium trifluoroacetate, lithium perchlorate, and lithium bromide were used without further treatment.

2,2,2-Trifluoroethanol (Halocarbon Products, Inc.) was dried overnight over Linde 2A molecular sieves. It was then decanted and distilled using a Widmer column. A constant boiling middle fraction was collected for use in kinetic studies.

Reagent grade trifluoroacetic acid (Matheson Coleman and Bell) was distilled using a Widmer column. The middle fraction of the

distillate, which was shown by Karl Fischer analysis to contain no more than 0.01% water, was stored in small batches in brown bottles which in turn were stored in a desiccator.

Binary mixtures of solvents were used in a number of experiments. Their compositions are later reported in terms of the relative volumes at 25.0° of the pure solvents in the mixtures, as for example in the case of 48.6:50.0 v/v trifluoroethanol-benzene, which was prepared by adding 48.6 ml of trifluoroethanol to 50.0 ml of benzene to provide a total volume of 100 ml.

**Rates of Solvolysis of *o*-Nitrobenzhydriyl Bromide.** All runs were conducted spectrophotometrically using a Beckman DU-2 spectrophotometer equipped with a temperature-controlled sample compartment. Rate samples were contained in 1-cm absorption cells which were stored in that compartment during the course of reaction. The blank cells contained only the solvent. Formation of product, either *o*-nitrosobenzophenone or 5-bromo-3-phenyl-2,1-benzisoxazole, was monitored by observing the change in absorption of the reaction mixtures at the appropriate wavelengths. In those cases in which isoxazole was the product, measurements were made at a wavelength in the region of 350–360 nm, in which a characteristic absorption maximum of that compound in the various solvents used is located ( $\epsilon \sim 15,000$ ). In those runs with 1:6 v/v trifluoroacetic acid-carbon tetrachloride as the medium, in which nitroso ketone was the product, its formation was monitored at the wavelength of its visible absorption maximum, 745 nm ( $\epsilon$  40). The starting bromide does not absorb significantly in the 350–360 nm region as compared to the isoxazole, nor does it display absorption in the visible region, where the nitroso ketone absorbs.

Solvolysis rate constants,  $k$ , for reactions in which isoxazole was the product (see eq 1) were calculated from the slopes of the straight

$$-d[\text{RBr}]/dt = d[\text{isoxazole}]/dt = k[\text{RBr}] \quad (1)$$

lines obtained by plotting  $\log(A_t - A_\infty)$  values *vs.* time where  $A_t$  and  $A_\infty$  are the absorptions of the rate samples at times  $t$  and infinity, respectively.

Kinetic studies of the solvolysis of *o*-nitrobenzhydriyl bromide were complicated by solubility problems. The halide, even when finely ground, dissolved slowly in all of the solvents which were used, while at the same time the half-lives for reactions in these media were relatively short. Accordingly, a stock solution of the halide in carbon tetrachloride was used in preparing rate samples. Reactions were initiated by diluting 0.5 ml of this stock solution to 25 ml with the appropriate solvent (previously equilibrated to the temperature of the rate run), and a sample of this mixture was transferred to the absorption cell for spectrophotometric study.

**Volumetric Methods for Studying Solvolysis Rates.** In investigating the rates of solvolysis of *p*-nitro- and *o*- and *p*-bromobenzhydriyl bromides and of *tert*-butyl chloride in trifluoroethanol and trifluoroethanol-benzene, samples of the reaction mixtures were analyzed by titration of liberated hydrogen bromide with standard sodium hydroxide solution. Rate mixtures were prepared by diluting 1 ml of a stock solution of the halide in carbon tetrachloride to 50 ml with the appropriate solvent (at the temperature of the run). Aliquots (5 ml) removed from time to time were added to 50 ml of ice-cold reagent grade acetone. Water (2 ml) and Bromothymol Blue indicator were added and the rate samples were titrated to the green end point. The concentration of hydrogen bromide at the end of reaction was established through analysis after completion of at least 10 half-lives. Solvolysis rate constants  $k$  (eq 2)

$$-d[\text{RBr}]/dt = d[\text{HBr}]/dt = k[\text{RBr}] \quad (2)$$

were calculated from the slopes of the straight lines obtained by plotting values of  $\log[\text{RBr}]$  *vs.*  $t$ .

In the investigation of the reaction of *p*-nitrobenzhydriyl bromide, in trifluoroacetic acid, rate samples were analyzed by the Volhard method. The procedure was closely similar to that used in earlier kinetic studies<sup>2</sup> of the hydrolysis of substituted benzyl and benzhydriyl bromides.

**The Product of Trifluoroacetolysis of *o*-Nitrobenzhydriyl Bromide in the Presence of Hydrogen Bromide.** A 0.9-g sample of the bromide was stirred with a 0.02 *M* solution of hydrogen bromide in 1:6 v/v trifluoroacetic acid-carbon tetrachloride for 1 hr. The mixture was then extracted several times with water and sodium bicarbonate solution. The organic phase was dried and concentrated to provide a red oil. The oil was dissolved in boiling methanol and the solution was treated with activated charcoal. The precipitate obtained on cooling the solution was recrystallized from methanol to provide needle-like crystals; mp and mmp with an authentic sample<sup>4</sup> of 5-bromo-3-phenyl-2,1-benzisoxazole, 114–115°.

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(8) R. F. Tietz and W. E. McEwen, *J. Amer. Chem. Soc.*, **77**, 4007 (1955).

(9) H. Morren, S. Troilin, R. Denayer, E. Grivsky, and J. Marica, *Bull. Soc. Chim. Belg.*, **60**, 282 (1951).

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The Product of Trifluoroethanolysis of *o*-Nitrobenzhydryl Bromide in the Presence of Hydrogen Bromide. A 0.5-g sample of *o*-nitrobenzhydryl bromide was stirred for 2 days in 70 ml of a solution of hydrogen bromide (0.04 M) in trifluoroethanol. The solvent was then evaporated, and the residual red oil was dissolved in ether. The solution was washed with water and dried. The residue remaining after evaporation of the solvent was dissolved in boiling methanol and the solution treated with activated charcoal. The orange solid obtained on cooling the solution was recrystallized from ethanol to provide 5-bromo-3-phenyl-2,1-benzisoxazole; mp and mmp with an authentic sample, 114–115°.

## Results

**Reactions in 2,2,2-Trifluoroethanol–Benzene Mixtures.** In this investigation as in earlier work<sup>3</sup> the *o*- and *p*-bromobenzhydryl bromides have been used to monitor the changes in the relative rates of solvolysis of the ortho and para isomers with changes in the solvent assuming that the ortho substituent is nonparticipating. A summary of the solvolysis rate runs on *o*- and *p*-bromo- and *o*- and *p*-nitrobenzhydryl bromides in 2,2,2-trifluoroethanol and in its mixtures with benzene is presented in Table I. For the *p*-nitro- and the bromo-

Table I. Solvolysis Rate Constants for  $C_6H_5CH(Br)C_6H_4X$  in 2,2,2-Trifluoroethanol–Benzene (TFE–B) Mixtures at 25.0°

Solvent, <sup>a</sup> v/v (TFE–B)	$10^2[RBr]_i$ , <sup>b</sup> M	$10^2[2,6-$ Lut] <sub>i</sub> , <sup>c</sup> M	$10^6k$ , sec <sup>-1</sup>
X = <i>o</i> -Br			
73.7:25	0.95–2.0	2.7–5.7	$159 \pm 9^d$
48.6:50	0.95–2.0	3.0–6.0	$13.8 \pm 1.1$
X = <i>p</i> -Br			
73.7:25	0.95–1.9	1.3–5.7	$885 \pm 46^d$
48.6:50	0.95–1.9	3.0–6.2	$117 \pm 8$
X = <i>p</i> -NO <sub>2</sub>			
100:0	0.95–1.9	3.0–6.2	$19.4 \pm 1.6$
73.7:25	0.99–2.0	3.0–6.0	$2.42 \pm 0.12$
48.6:50	0.95–1.9	3.0–6.0	$0.323 \pm 0.006$
X = <i>o</i> -NO <sub>2</sub>			
[HBr] <sub>i</sub> , <sup>e</sup> M			
100:0	2.0–3.9	0.3	$589 \pm 9$
73.7:25	2.0–3.9	0.4	$475 \pm 20$
48.6:50	2.0–3.9	0.3	$313 \pm 10$

<sup>a</sup> In all runs the medium contained carbon tetrachloride in 2 vol % (see Experimental Section). <sup>b</sup> Several runs in which  $[RBr]_i$  was varied over the indicated range were made for each solvent mixture. <sup>c</sup> The range of initial concentrations of 2,6-lutidine in the reaction mixtures. The individual  $k$  values were not significantly affected by changes in  $[2,6-Lut]_i$ . <sup>d</sup> The reaction was so fast that rate measurements were made only during the last 50% of the reaction. <sup>e</sup> Hydrogen bromide was incorporated in the reaction mixtures at or near saturation levels (0.3–0.4 M). Some rate measurements, made using solutions of significantly lower hydrogen bromide concentrations, led to the conclusion that the solvolysis rates of *o*-nitrobenzhydryl bromide in the media in question are not greatly dependent on  $[HBr]$ .

benzhydryl bromides the rate samples were analyzed using volumetric methods (see Experimental Section). Spectrophotometric methods were used to analyze the rate samples for *o*-nitrobenzhydryl bromide. In dilute solution in trifluoroethanol this halide appears to react to form nitroso ketone (I), which gradually is converted to isoxazole (II) through reaction with hydrogen bromide in the medium. Rate constants reported for *o*-nitrobenzhydryl bromide are based on runs in which the reaction mixture was nearly saturated with hydrogen bromide, under which circumstances the isoxazole is the

immediate reaction product. The reactions of the bromobenzhydryl bromides in 100% trifluoroethanol proved to be too fast to permit rate study by conventional methods.

In Table II a summary is presented of the influence of

Table II. Rate Constant Ratios for Solvolysis ( $k_o/k_p$ ) of  $C_6H_5CH(Br)C_6H_4X$

Medium	$k_o/k_p$	
	X = NO <sub>2</sub>	X = Br
Acetic acid	3000 (25°) <sup>a</sup>	0.055 (45°) <sup>a</sup>
90% aqueous acetone	83 (45°) <sup>b</sup>	
100% TFE	30 (25°)	
73.7:25 TFE–B	196 (25°)	0.18 (25°)
48.6:50 TFE–B	969 (25°)	0.12 (25°)

<sup>a</sup> From ref 3. <sup>b</sup> From ref 4.

changes in medium on the relative reactivities of the *o*- and *p*-nitrobenzhydryl bromides and also of their *o*- and *p*-bromo analogs. The influence of the *o*-nitro group in promoting solvolysis in trifluoroethanol–benzene mixtures is clearly reflected in the relative magnitudes of  $k_o/k_p$  ratios of the bromo- and nitrobenzhydryl halides. As for reaction in acetic acid, the ratios for the bromo compounds are significantly less than unity while those for the nitro compound are much larger than unity.

It has been suggested in the introductory section that the decrease in the  $k_o/k_p$  ratio for the nitro compounds as the medium is changed from acetic acid to aqueous acetone is associated with ion pair return in the reaction of the para isomer. This suggestion is based on the observations that ion pair return becomes more important (with a resultant unfavorable effect on reaction rate) as the medium becomes a poorer nucleophile and also as its dielectric constant decreases.<sup>11</sup> It is particularly interesting in this connection that as the medium is changed from acetic acid to trifluoroethanol, the  $k_o/k_p$  ratio (25°) for the nitro compound drops (by a factor of about 100) to a value of 30. Although trifluoroethanol is a poor nucleophile (it approximates formic acid in nucleophilicity<sup>12</sup>), it has a moderately high dielectric constant (26.14 at 25°)<sup>13</sup> and presumably does not promote ion pair return nearly to the degree that acetic acid does. The  $k_o/k_p$  ratio for reaction of the nitro compounds in trifluoroethanol increases significantly as benzene is added to the medium. This can be accounted for on the assumption that the accompanying decrease in medium dielectric constant promotes ion pair return in the reaction of the para isomer.

By way of pursuing this argument further,  $Y$  values<sup>14,15</sup> for the trifluoroethanol–benzene mixtures used in this investigation have been evaluated through measurement of the solvolysis rate constants for *tert*-butyl chloride in the media in question (see Table III). In

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(12) M. D. Bentley and J. H. Lacadie, *Tetrahedron Lett.*, 741 (1971).

(13) L. M. Mukherjee and E. Grunwald, *J. Phys. Chem.*, **62**, 1311 (1958).

(14) (a) E. Grunwald and S. Winstein, *J. Amer. Chem. Soc.*, **70**, 846 (1948); (b) S. Winstein, E. Grunwald, and H. W. Jones, *ibid.*, **73**, 2700 (1951).

(15) The Grunwald–Winstein equation is most correctly applied under the condition that the nucleophilicities of the media do not vary widely with composition. Inasmuch as trifluoroethanol is a poor nucleophile, this may in fact be the case for trifluoroethanol–benzene mixtures.

Table III. Solvolysis of *tert*-Butyl Chloride in Trifluoroethanol–Benzene Mixtures (25.0°)

$10^2[t\text{-BuCl}]_i$ , <i>M</i>	$10^2[2,6\text{-Lut}]_i$ , <i>M</i>	$10^3k$ , $\text{sec}^{-1}$	$Y^a$ value of medium
Medium: 48.6:50 Trifluoroethanol–Benzene			
0.95	4.0	1.14	
1.90	4.0	1.16	
1.90	6.0	1.20	
		Av $1.17 \pm 0.02$	0.096
Medium: 73.7:25 Trifluoroethanol–Benzene			
1.90	2.9	3.70	
0.95	2.9	3.80	
1.90	4.3	3.83	
		Av $3.78 \pm 0.05$	0.605
Medium: 100% Trifluoroethanol			
		10.4	1.045 <sup>b</sup>

<sup>a</sup> The tabulated values of  $Y$  are the logarithms of the ratios of the reported rate constants and that ( $9.38 \times 10^{-6} \text{ sec}^{-1}$  at 25°) for solvolysis of *tert*-butyl chloride in 80% aqueous ethanol. The constant for reaction in 80% aqueous ethanol is taken from the reference cited in footnote *b*. <sup>b</sup> V. J. Shiner, Jr., W. Dowd, R. D. Fischer, S. R. Hartshorn, M. A. Kessick, L. Milakofsky, and M. W. Rapp, *J. Amer. Chem. Soc.*, **91**, 4838 (1969).

Figure 1 plots are shown of  $\log k$  vs.  $Y$  for solvolyses of the nitro- and bromobenzhydryl bromides in trifluoroethanol–benzene mixtures. The slopes of the plots, the so-called  $m$  values<sup>14</sup> of the reacting halides, are, in the case of the *o*- and *p*-bromo- and the *p*-nitrobenzhydryl bromides, significantly greater than unity and range from 1.65–2.08. The  $m$  value for *o*-nitrobenzhydryl bromide, on the other hand, is substantially less than unity (0.39); that is, reactivity of this halide responds much less to changes in medium than do the other three.

Some time ago it was observed that the  $m$  values for solvolysis of benzhydryl halides in acetic acid–water and formic acid–water mixtures are considerably larger than unity.<sup>16</sup> In other words their reactivities drop more sharply with decreases in medium ionizing power ( $Y$ ) than does that of *tert*-butyl chloride. This was taken as an indication that the reactions of the benzhydryl halides, in contrast to those of *tert*-butyl chloride, are strongly subject to ion pair return, the more so as the solvent becomes less favorably constituted to support ionization. The same reasoning can be applied in explaining the large difference in the  $m$  value of *o*-nitrobenzhydryl bromide and those of the other halides under investigation (Figure 1). The evidence seems rather good that in contrast to the reactions of the *p*-nitro- and bromobenzhydryl halides return does not have an important influence, if any influence, on the reactivity of *o*-nitrobenzhydryl bromide. Once the *o*-nitro group becomes affiliated as a nucleophile with exocyclic carbon (in forming intermediate III), it apparently is not dislodged through displacement by bromide ion.

It can be concluded that changes in values of  $k_o/k_p$  solvolysis rate ratios for the nitrobenzhydryl halides with changes in medium do not serve reliably to measure changes in the degree to which the *o*-nitro group provides anchimeric assistance. Certainly in a medium such as acetic acid the very low reactivity of the para isomer as compared to the ortho isomer is to a large

(16) S. Winstein, A. J. Fainberg, and E. Grunwald, *J. Amer. Chem. Soc.*, **79**, 4146 (1957).

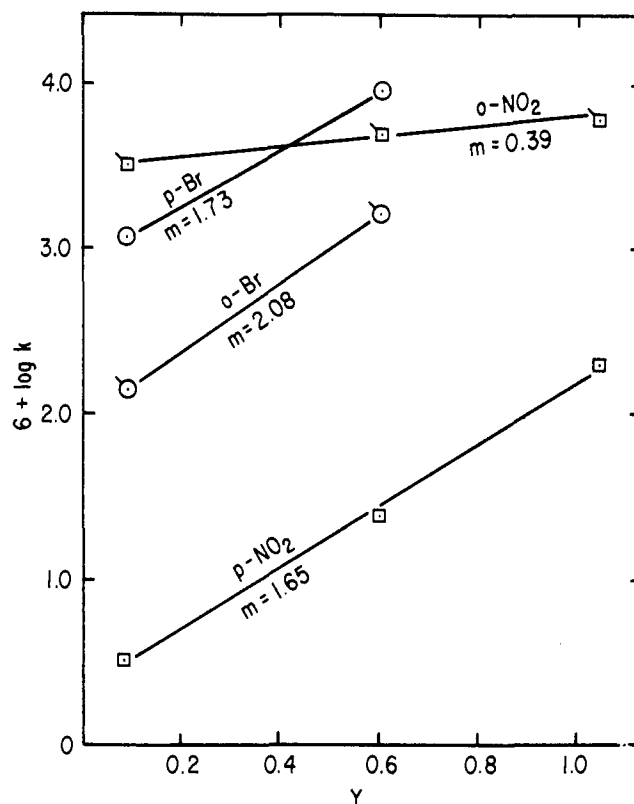


Figure 1. Plots of  $\log k$  vs.  $Y$  for solvolysis of nitro- and bromobenzhydryl bromides in trifluoroethanol (TFE)–benzene mixtures at 25.0°.

degree a reflection of the capacity of the *o*-nitro group to block ion pair return.

**Reactions in Trifluoroacetic Acid.** Though trifluoroacetic acid was a solvent of great potential interest in connection with the rate studies of nitrobenzhydryl bromide solvolysis in media of low nucleophilicity, it proved not to be particularly useful in a quantitative sense. In the pure solvent the *o*-nitro compound is so highly reactive (half-life of the order of 2 min at room temperature) and its para isomer sufficiently unreactive that an accurate comparison of their solvolysis rates could not be made. A few rate runs were conducted spectrophotometrically at 25.0° on the trifluoroacetolysis of the *o*-nitro isomer ( $[\text{RBr}]_i = 1\text{--}3 \times 10^{-4} \text{ M}$  and  $[\text{HBr}]_i = 1\text{--}2 \times 10^{-2} \text{ M}$ ). On the basis of measurements made during later phases of the reaction (in which isoxazole was the exclusive product at these hydrogen bromide concentrations) it was estimated that the solvolysis rate constant is about  $5 \times 10^{-3} \text{ sec}^{-1}$ . From data collected in studying very early phases of reaction it was estimated that the trifluoroacetolysis rate constant of the *p*-nitro isomer is of the order of  $1\text{--}2 \times 10^{-7} \text{ sec}^{-1}$ . Clearly, the  $k_o/k_p$  reactivity ratio of the two bromides is considerably greater for trifluoroacetolysis than for acetolysis (*cf.* Table II). This is regarded as reflecting primarily increased ion pair return in the reaction of the *p*-nitro isomer when the solvent is changed from acetic acid to the poorer nucleophile, trifluoroacetic acid.

A few facts concerning the influence of changes in reaction conditions on the nature of products obtained in trifluoroacetolysis of the *o*-nitro compound are worth reporting for comparison with corresponding information already available<sup>3</sup> concerning the acetolysis

products. For purposes of following spectrophotometrically the changes in product structure occurring during the course of reaction, 1:6 v/v trifluoroacetic acid-carbon tetrachloride was used as the medium in this phase of the investigation. In solutions in this mixture in which the original concentrations of *o*-nitrobenzhydryl bromide were  $2-4 \times 10^{-2} M$ , isoxazole (II) and nitroso ketone (I) were observed to form simultaneously, the latter forming rapidly during early phases of reaction and then much more slowly as hydrogen bromide in the medium increased. After at least 10 half-lives elapsed, the yields of isoxazole and nitroso ketone were of the order of 70–80% and 15–20%. In 0.1 *M* concentration in acetic acid the *o*-nitro compound solvolyzed in the initial phases of reaction to produce a small amount of nitroso ketone (6–7%), which decreased in quantity as reaction proceeded due to formation of isoxazole as the exclusive final organic product. The conversion of nitroso ketone to isoxazole by hydrogen bromide, which is very rapid in acetic acid solutions of 0.01–0.1 *M* hydrogen bromide concentration, is apparently somewhat slower in trifluoroacetic acid.

In acetic acid in the presence of sodium acetate, *o*-nitrobenzhydryl bromide solvolyzes to produce exclusively *o*-nitrosobenzophenone. The sodium salt in

this case prevents accumulation of hydrogen bromide in the medium. In 1:6 v/v trifluoroacetic acid in the presence of sodium trifluoroacetate the formation of nitroso ketone from the halide is not blocked, and in fact the nitroso ketone and isoxazole are formed in about the same proportions as when salt is omitted from the reaction mixture. It appears that trifluoroacetate ion is a weaker base than bromide ion in trifluoroacetic acid.<sup>17</sup>

In this same context it is interesting to note that nitroso ketone formation in the reaction of the *o*-nitro compound in trifluoroacetic acid-carbon tetrachloride can be eliminated completely by adding either hydrogen bromide or lithium bromide. Rate constants, based on the measurement of formation of isoxazole as the reaction product in solutions initially  $2-4 \times 10^{-4} M$  in *o*-nitrobenzhydryl bromide and  $6-10 \times 10^{-3} M$  either in hydrogen bromide or lithium bromide, were found to be in good agreement ( $k_{25^\circ} \sim 9 \times 10^{-4} \text{ sec}^{-1}$ ). Eaborn, Jackson, and Taylor have observed previously that hydrogen bromide is evolved from a solution of sodium bromide in trifluoroacetic acid.<sup>18</sup>

(17) Cf. J. Bessiere, *Bull. Soc. Chim. Fr.*, **9**, 3353 (1969).

(18) C. Eaborn, P. M. Jackson, and R. Taylor, *J. Chem. Soc. B*, 613 (1966).

## Aminolysis Reactions. II. Catalysis of Ester Aminolysis in Chlorobenzene. Correlation with Hydrogen-Bonding Ability of Catalysts

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**Abstract:** The *n*-butylaminolysis of *p*-nitrophenyl acetate in chlorobenzene at 25° follows the rate equation  $k_{1, \text{obsd}} = k_3(\text{BA})^2 + k_3'(\text{BA})(\text{cat.})$ . Dipolar oxygen bases are very effective catalysts of the reaction; *N,N*-dimethylacetamide is more than twice as effective in catalyzing the reaction as *n*-butylamine although it is a  $10^{10}$  times weaker aqueous base. The catalytic abilities of several classes of oxygen and nitrogen compounds correlate with their hydrogen-bonding ability to *p*-fluorophenol in chlorobenzene by the equation  $\log k_3' = 1.2 \log K_f - 3.3$ . This correlation indicates that there is 10–30% proton transfer to the catalyst in the transition state. The results suggest that amides could serve as general base catalysts in enzymes with hydrophobic active sites.

In 1969 we<sup>1</sup> presented evidence and arguments against the bifunctional or cyclic nonpolar mechanisms for the aminolysis and amidinolysis of *p*-nitrophenyl acetate, *p*-NPA, in chlorobenzene solvent.<sup>2</sup> We proposed that the reactions were general base catalyzed and heterolytic in mechanism and suggested the use of unhindered tertiary amines, such as 1,4-diazabicyclo-[2.2.2]octane (DABCO), and intramolecular tertiary amine catalysts as mechanistic probes to differentiate between cyclic and stepwise general base catalysis.<sup>1</sup>

(1) H. Anderson, C. Su, and J. W. Watson, *J. Amer. Chem. Soc.*, **91**, 482 (1969).

(2) (a) F. M. Menger, *J. Amer. Chem. Soc.*, **88**, 3081 (1966); (b) P. L. Lillford and D. P. N. Satchell, *Chem. Ind. (London)*, 1750 (1967); *J. Chem. Soc. B*, 360 (1967); (c) S. T. McDowell and C. J. M. Stirling, *ibid.*, 343 (1967); (d) A. Shawali and S. S. Biechler, *J. Amer. Chem. Soc.*, **89**, 3020 (1967).

Subsequent work by Pietra, *et al.*, has presented additional evidence in favor of the bifunctional catalysis mechanism for benzamidinolysis reactions.<sup>3a</sup> Although additional arguments have also been presented on behalf of the bifunctional catalysis mechanism for ester aminolysis,<sup>3b,c</sup> the most recent work of Menger, *et al.*, provides compelling evidence that the aminolysis of aryl esters in aprotic solvents proceeds by a general base-catalyzed mechanism of the general form given in eq 1.<sup>4</sup> It is surmised that the base catalyst, which may be a second molecule of the nucleophilic amine, func-

(3) (a) G. Biggi, F. Del Cima, and F. Pietra, *J. Chem. Soc., Perkin Trans 2*, 188 (1972); (b) F. M. Menger and J. H. Smith, *J. Amer. Chem. Soc.*, **91**, 5346 (1969); (c) D. P. N. Satchell and I. I. Secemski, *J. Chem. Soc. B*, 1013 (1970).

(4) (a) F. M. Menger and J. H. Smith, *J. Amer. Chem. Soc.*, **94**, 3824 (1972); (b) F. M. Menger and A. C. Vitale, *ibid.*, **95**, 4931 (1973).