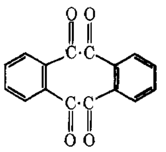

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(35) A direct conversion of **21** into **23** by attack of $(RO)_3P$ on the carbon of **21** and elimination of $(RO)_3PO$ is conceivable.

(36) In principle the carbene **15** could be trapped by PA (**5**) to give the epoxide **22** directly.

Notes

On the Catalytic Role of the Carboxyl Group in the Hydrolysis of *o*-Carboxybenzyl Bromide

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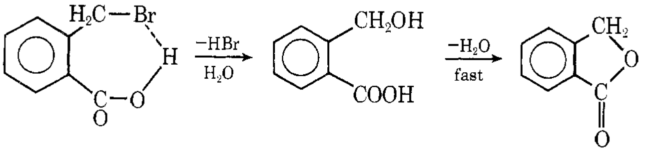
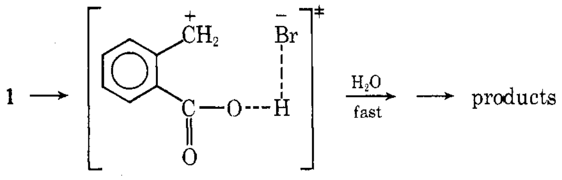
Of the isomeric carboxybenzyl bromides, *o*-carboxybenzyl bromide (1) is known to undergo solvolytic reactions many times more rapidly than *p*-carboxybenzyl bromide (2).[1] This difference—the ortho isomer (1) reacts some 84–87 times as fast as the para isomer (2)—reverses the usual order of reactivity among isomers of this type. Although differences are rarely this dramatic, the para isomer is nearly always more reactive.[2] The greater reactivity of 1 is attributed to internal participation by the un-ionized carboxyl group.[3] Such participation is not possible for **2** because of unfavorable molecular geometry. Manifestly the equation above does not show how the solvent acts.



Solvolyses of benzyl halides have been studied extensively.[4] The findings cannot be interpreted in terms of simple SN1 or simple SN2 mechanisms. It has been suggested that the mechanisms of benzyl halide solvolysis be interpreted as SN2 (1) and SN2 (2); in the former, bond ionization plays the predominant role, while the latter is more like the conventional SN2 type, nucleophilic attack being more important.[5] Two possible transition states can be postulated for the particular reaction now being discussed:



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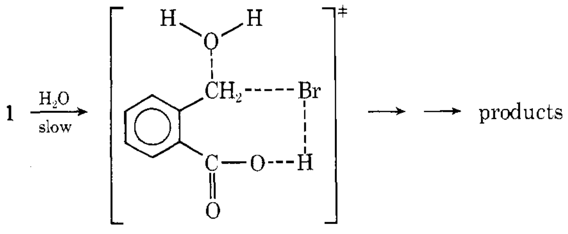

II

If the reaction proceeds through the transition state I, sufficient stretching of the reactive bond must occur to produce an ion-pair-like species. The subsequent nucleophilic attack on the ion is expected to be very fast. In this case, the carboxyl group can be said to act as an electrophilic catalyst. Reactions proceeding through this state should be little affected by nucleophiles but appreciably sensitive to the ionic strength or dielectric constant of the solvent medium. If the reaction goes through the transition state II, less bond stretching is required. The reactive bond is stretched only enough to in-

Table I. Effect of Added Nucleophiles on Solvolysis Rate Constants for Carboxybenzyl Bromides and Benzyl Bromide in 50% Aqueous Dioxane[a]

pH	[Buffer] mol/l.	$10^5\, k_s$, s^{-1} o-Carboxybenzyl bromide (1)	p-Carboxybenzyl bromide (2)	Benzyl bromide
		Hydroxylamine/Hydroxylamine Hydrochloride		
7.10	0.500	480 ± 6	335 ± 1	252 ± 9
	0.375	446 ± 6	228 ± 2	123 ± 2
	0.250	463 ± 9	125 ± 5	61.6 ± 1.9
		Morpholine/Morpholine Hydrochloride		
7.05	0.500	364 ± 6	239 ± 13	147 ± 3
	0.375	359 ± 6	87.0 ± 0.3	92.8 ± 0.4
	0.250	370 ± 14	22.9 ± 1.0	52.4 ± 2.5
		Sodium Acetate/Acetic Acid		
5.68	0.500	246 ± 5	32.8 ± 0.8	30.7 ± 0.7
	0.350	248 ± 1	30.0 ± 0.0	25.2 ± 0.2
	0.200	241 ± 1	24.0 ± 0.3	18.3 ± 0.4

[a] Temperature 40.0 °C and total ion concentration maintained at 1 M with NaCl.

Table II. Effect of Added Salt on Hydrolysis Rate Constants for Carboxybenzyl Bromides and Benzyl Bromide in Aqueous Dioxane, 60.4 °C

Aqueous dioxane, %	$[KNO_3]$, mol/l.	$10^5\, k_s^-$, s^{-1} o-Carboxybenzyl bromide (1)	p-Carboxybenzyl bromide (2)	Benzyl bromide
80	0.000	30.7 ± 0.8	0.272 ± 0.008	0.626 ± 0.010
	0.050	39.6 ± 0.6	0.328 ± 0.011	0.659 ± 0.018
	0.100	43.2 ± 0.4	0.364 ± 0.003	0.701 ± 0.015
	0.150	44.3 ± 0.6	0.405 ± 0.014	0.743 ± 0.031
	0.000[a]	68.5 ± 0.4	0.740 ± 0.005	
	0.000[b]	13.4 ± 0.1		
60	0.000	114 ± 0	1.81 ± 0.02	
	0.000[a]	217 ± 3	5.01 ± 0.05	
	0.000[b]	56.9 ± 0.5	0.722 ± 0.021	
50	0.000	183 ± 9	3.56 ± 0.12	4.50 ± 0.16
	0.100	187 ± 7	4.24 ± 0.08	10.8 ± 0.2
	0.300	195 ± 5	5.45 ± 0.19	20.9 ± 0.8
	0.500	210 ± 3	6.75 ± 0.14	32.5 ± 0.5
	0.750	210 ± 3		
	1.000		7.12 ± 0.09	
	0.000[a]	325 ± 9	8.74 ± 0.14	
	0.000[c]	86.1 ± 3.8		

[a] Temperature 70.6 °C. [b] Temperature 50.6 °C. [c] Temperature 40.0 °C.

crease the charge polarization so that nucleophilic attack in the rate-determining step is facilitated. In this case the carboxyl group can be said to act as a general acid catalyst.

We report here a series of experiments in which the nucleophilicity and ionic strength of the media have been varied and the resulting rate constants determined. From these data, we have tried to interpret the catalytic role of the carboxyl group in the solvolysis of o-carboxybenzyl bromide.

Results and Discussion

The carboxybenzyl bromides (**1** and **2**) and benzyl bromide were solvolyzed in 50% aqueous dioxane in which one of three nucleophiles was initially present. The nucleophiles used were hydroxylamine, morpholine, and acetate anion, each in the form of a buffer containing the free base and conjugate acid. Sodium chloride was added to give uniform ionic strength. In these experiments (Table I) the benzyl halides reacted at a convenient rate with all the nucleophiles used and the pseudo-first-order rate plots were linear through 3 half-lives. The rates of reaction for **2** and benzyl bromide increase linearly with the nucleophile concentration, total buffer concentration, while the rate of reaction of **1** is independent of the nucleophile concentration (Figure 1). It should be noted, also, that the behavior of the ortho isomer toward varying nucleophile concentration is not dependent on the amount of un-ionized carboxyl group present. The amount of un-ionized carboxyl group present at pH 5.68 is significantly greater than the amount present at pH 7.1.[6] This independence suggests that the reaction of **1** is proceeding predominantly by SN1 while on the other hand **2** and benzyl bromide react by SN2. Additional support for this hypothesis is obtained by comparing the ratios of the solvolysis rates of **1** and **2** in glacial acetic acid and aqueous ethanol, respectively. Jones and Thornton have suggested that the ratio, *r*, of solvolysis rates in the solvents of different nucleophilicities but the same ionizing power (i.e., the same *Y* value) measures the nucleophilic sensitivity of a substrate relative to *tert*-butyl chloride.[7] Solvolysis of this substance is used as a standard for reference because it is judged to need little nucleophilic assistance. In general, *r* values for primary substrates are considerably larger. Consequently larger ratios are expected for substrates reacting by SN2 mechanisms. The ratios calculated for **1** and

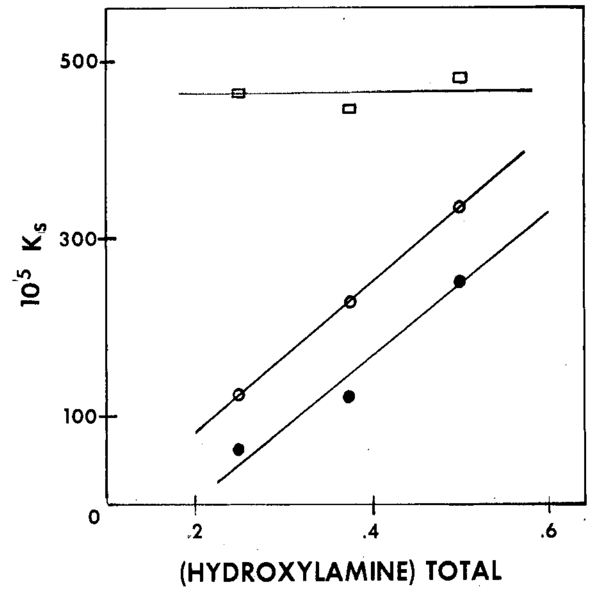

Figure 1. Solvolysis rate constants vs. total buffer concentration for 1 (□), 2 (○), and benzyl bromide (●) in hydroxylamine buffer, pH 7.1.

2 were 24 and 254, respectively.[8] The smaller *r* for 1 indicates appreciably less sensitivity to nucleophilic attack; this is consistent with the prior inference of a SN1 reaction mechanism.

Further information about the transition state of 1 was sought by determining the effect of varying ionic strength. Potassium nitrate was added to solutions of 50 and 80% aqueous dioxane and the rate constants determined (Table II). In 80% aqueous dioxane, the effect of adding 0.1 M KNO_3 initially is to increase the rate constant by 41% for **1**, by 34% for **2**, and by 12% for benzyl bromide. These values are within the range of increase expected for a SN1 reaction.[9] The magnitude of a salt effect for either SN1 or SN2 reactions is expected to be greater in a medium of low dielectric constant since charges operate more effectively in media of low dielectric constant.[10] This inverse relationship between magnitude of salt effect and dielectric constant of the medium is observed for 1; in 50% aqueous dioxane, addition of 0.1 M KNO_3 initially increases the rate constant only 2% as compared to 41% in 80% aqueous dioxane. The increases in rate constants due to salt effects for 2 and benzyl bromide in 50% aqueous dioxane are 19 and 40%, respectively, values considerably larger than for **1**. Furthermore, as the salt concentration is increased to the saturation point in 50% dioxane, the rate constants for 2 and benzyl bromide continue to increase significantly. These results are sufficiently different from those anticipated to merit further examination.

Although we cannot exclude the possibility that an ordinary salt effect is responsible for these observed differences in the rate constants, it is probable that these differences result from differences in the relative contributions of the SN1 and SN2 components in the reactions of 2 and benzyl bromide. If an increase in salt concentration can increase the ability of the medium to stabilize a SN1 transition state without significantly changing its ability to stabilize a SN2 transition state, it is probable that any change in the relative contribution of the two component reactions will favor the SN1 component with little concurrent suppression of the SN2 component. We have already inferred that the reactions of 2 and benzyl bromide proceed chiefly by SN2. Accordingly, as addition of salt increases the ionizing power of the medium, the SN1 components of these reactions should increase, too. Thus overall rate constants for these hydrolyses are expected to increase. Since 1 reacts initially chiefly via SN1, the overall rate enhancement is not so evident. The activation parameters for the hydrolyses of 1 and 2, shown in Table III, are consistent with reactions by different mechanisms for the two isomers.

Table III. Activation Parameters for Hydrolysis of *o*- and *p*-Carboxybenzyl Bromides

	o-Carboxybenzyl bromide (1)		*p*-Carboxybenzyl bromide (2)	
Solvent	$\Delta H^\ddagger$, kcal/mol	$\Delta S^\ddagger$, eu	$\Delta H^\ddagger$, kcal/mol	$\Delta S^\ddagger$, eu
80% aqueous dioxane	17.3	−22.9	21.2	−20.1
60% aqueous dioxane	14.1	−30.0	21.7	−15.3
50% aqueous dioxane	8.81	−30.8	19.4	−20.8

These data, then, support the hypothesis that *o*-carboxybenzyl bromide is hydrolyzed in aqueous dioxane by SN1 mechanism. The more rapid hydrolysis of *o*-carboxybenzyl bromide as compared with its para isomer is attributed to the action of the *o*-carboxyl group as an intramolecular electrophilic catalyst.

Experimental Section

Materials. The isomeric carboxybenzyl bromides were prepared from the corresponding toluic acid according to previously published procedures.[1] Other compounds employed were all reagent grade or were recrystallized before using.

Kinetics. All solvents used were purified according to standard procedures and distilled in all-glass apparatus. The mixed solvents (v/v) were prepared at room temperature, i.e., 80% dioxane—20 volumes of water and 80 volumes of dioxane.

In most runs, the method used in investigating the rates of hydrolysis of the various bromo compounds were essentially the same as that employed in previous investigations.[1,3] The change in reactant or product concentration was also followed spectrophotometrically. In these cases, the sample solution was placed in the thermostated cell in a Beckman DB spectrophotometer. The reactions were generally followed to about 80% of completion. At least three separate runs were made to determine all rate constants. Solvolysis rate constants were determined using the equation

$$\ln([RBr]_i/[RBr]_t) = k_s t$$

The k_s values were determined using a least-squares computer program.

Registry No.—**1**, 7115-89-1; **2**, 6232-88-8; benzyl bromide, 100-39-0.

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