

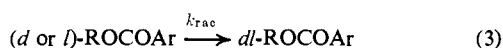
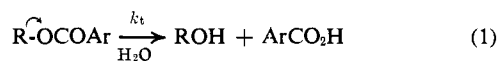
Ion-Pair Return Associated with Solvolysis of α -*p*-Anisylethyl and α -Phenylethyl *p*-Nitrobenzoates¹

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Abstract: Solvolysis of α -*p*-anisylethyl and α -phenylethyl *p*-nitrobenzoates in aqueous acetone involves alkyl oxygen cleavage (eq 1) and is accompanied by ion-pair return that results in randomization of the carboxyl oxygen atoms in the unsolvolyzed ester (eq 2). At 60° the anisylethyl ester solvolyzes $>3 \times 10^4$ times faster than the phenylethyl ester; however, the k_{eq}/k_t ratios are remarkably similar. The stereochemistry of return is strikingly different for the two esters. For the anisylethyl ester, return results in substantial racemization of the unsolvolyzed ester (eq 3). On the other hand, return associated with solvolysis of the phenylethyl ester does not result in detectable racemization. Thus the *p*-methoxyl substituent has a much larger effect on stereochemistry than on the amount of return. Unlike with the less reactive *p*-chlorobenzhydryl system, that fraction of return that results in racemization of the anisylethyl ester is not eliminated by addition of azide ion.

In several nonrearranging systems that have been investigated including benzhydryl,² para-substituted benzhydryl,^{3,4} 2-phenyl-2-butyl,^{5a} cyclopropylmethyl-carbinyl,^{5b} and *trans*- α -methyl- γ -phenylallyl⁶ *p*-nitrobenzoates, ion-pair return associated with solvolysis results in randomization of the carboxyl oxygen atoms of ¹⁸O-labeled substrates (eq 2) and partial racemization of optically active substrates (eq 3). In these systems solvolysis in aqueous acetone involves alkyl oxygen cleavage (eq 1) and the two transformations of the unsolvolyzed ester (eq 2 and 3) are intramolecular; solvolysis in the presence of labeled *p*-nitrobenzoate salts or *p*-nitrobenzoic acid does not result in significant exchange.²⁻⁶



The amount of oxygen equilibration associated with return without rearrangement (*i.e.*, rebonding of the anion to the original carbon atom) has been investigated in several systems in which total return can be determined by an independent method. These systems include *trans*- α , γ -dimethylallyl,⁷ *cis*- and *trans*-5-methyl-2-cyclohexenyl,^{8a} *exo*-bicyclo[3.2.1]oct-3-en-2-yl,^{8b} and *trans*- α -methyl- γ -phenylallyl⁶ *p*-nitrobenzoates.

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(1) This work was supported by the Air Force Office of Scientific Research (AFOSR-847-67) and the National Science Foundation (GP6555X).

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In the *trans*- α , γ -dimethylallyl system, return to the original carbon atom results in incomplete equilibration (42% in 60% acetone and 34% in 90% acetone).⁷ On the other hand, return without rearrangement results in substantial (>90%), if not complete, equilibration in the *trans*- α -methyl- γ -phenylallyl system.⁶ This suggests that the amount of equilibration increases with the stability of the carbonium ion. In the other systems return results in complete equilibration.

Providing return results in complete oxygen equilibration. $k_{eq} + k_t$ is the rate constant for total ionization. In this case k_{eq}/k_t is the return to solvolysis ratio and k_{rac}/k_{eq} is the fraction of return that results in loss of optical configuration. In several nonrearranging systems that have been examined²⁻⁵ $k_{eq} > k_{rac}$ which means that return involves predominating retention of configuration. In such systems any return that does not result in oxygen equilibration would not be detected; thus k_{eq} is a lower limit for return. From the behavior of systems mentioned above, we tend to feel that in systems which give resonance-stabilized carbonium ions such as the benzhydryl system, return results in substantial or complete equilibration.

This paper reports an investigation of oxygen equilibration (eq 2) and racemization (eq 3) associated with solvolysis of α -*p*-anisylethyl and α -phenylethyl *p*-nitrobenzoates in aqueous acetone. It was of interest to determine the effect of the methoxyl group on the relative rates of reactions 1-3 and to compare the amount (k_{eq}/k_t) and stereochemistry (k_{rac}/k_{eq}) of ion pair return with that observed in other secondary systems.³⁻⁵

Results

First-order rate constants for solvolysis (k_t), and for oxygen equilibration (k_{eq}) and racemization (k_{rac}) of the unsolvolyzed ester, are presented in Table I for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 70 and 90% acetone⁹ and solvolysis of α -phenylethyl *p*-nitrobenzoate in 70% acetone. The rate constants for racemization of the unsolvolyzed ester (k_{rac}) were determined from the constants for loss of optical activity (k_a) and solvolysis (k_t), *i.e.*, $k_{rac} = k_a - k_t$.^{7,8} In one case k_{rac} was determined directly from the specific rotations of isolated

(9) Solvent composition based on volumes of pure components at 25° prior to mixing.

Table I. Rate Constants for Solvolysis (k_t), Equilibration of Carboxyl Oxygen Atoms (k_{eq}), and Racemization (k_{rac}) for Solvolysis of α -*p*-Anisylethyl and α -Phenylethyl *p*-Nitrobenzoates in Aqueous Acetone

Ester ^a	Temp, °C	$10^3 k_t$, ^b hr ⁻¹	$10^3 k_{eq}$, ^b hr ⁻¹	$10^3 k_{rac}$, ^c hr ⁻¹	
A. 90% acetone ⁱ Anisylethyl	60.0 (3.62) ^d	3.76 ± 0.06	9.75 ± 0.1 ^e	4.41 ± 0.01	
	78.6 (26.6) ^d	27.4 ± 0.3	60.5 ± 1.4 ^f	32.9 ± 0.7 32.1 ± 1.5 ^g	
B. 70% acetone ⁱ Anisylethyl	48.0	48.0 ± 0.2			
	60.0	170.0 ± 0.4	97.5 ± 4.8 ^f	69.1 ± 3.4	
	Phenylethyl	120.04	6.88 ± 0.13	5.21 ± 0.05 ^f	0.21 ± 0.21
		99.38	0.77 ± 0.01		
	60.0	0.0056 ^h			

^a Initial concentrations were about 0.04 M. ^b Uncertainties are average deviations from the mean. ^c Unless otherwise noted determined from the titrimetric and polarimetric rate constants, i.e., $k_{rac} = k_\alpha - k_t$. ^d Initial value obtained by least squares extrapolation to zero time; integrated constants showed slight upward drift. ^e Determined with carbonyl-¹⁸O-labeled ester. ^f Determined with ether-¹⁸O-labeled ester. ^g Determined directly from rotations of isolated unsolvolyzed ester. ^h Value obtained by extrapolation of data for other temperatures. ⁱ See ref 9.

samples of unsolvolyzed ester. As shown in Table I, the constants determined by the two methods are in excellent agreement.

The titrimetric (k_t) and polarimetric (k_α) rate constants were determined as described earlier.^{4,7,8} Reactions were followed to about 70% completion and good first-order behavior was observed except for a small, but consistent, upward trend in the titrimetric rate; the upward drift in k_t was ~3% for the periods that reactions were followed. Independent experiments with added *p*-nitrobenzoic acid showed that this upward drift is due to the acid produced by solvolysis. At ten half-lives the infinity titers were within 1% of the calculated values.

Solvolysis of optically active esters resulted in complete loss of optical activity except for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 70% acetone at 60°. In this case there was residual activity which was lost at a slower rate. This results from the formation of partially active α -*p*-anisylethyl alcohol. From the average optical purity of the ester (original optical purity times k_t/k_α),¹⁰ the magnitude of the residual rotation (~8% retention of the original activity), and the rate at which optically active α -*p*-anisylethyl alcohol racemizes under these conditions, it was determined that solvolysis proceeds with about 12% retention of optical configuration. It should be noted that from the relative reactivities of the two esters it is clear that solvolysis involves exclusive alkyl oxygen cleavage. This stereochemical result is similar to that observed for solvolysis of optically active *p*-chlorobenzhydryl^{4a} and 2-phenyl-2-butyl *p*-nitrobenzoates in aqueous acetone.^{5a}

First-order rate constants for oxygen equilibration (k_{eq} , eq 2) were determined by a method described earlier.²⁻⁶ Both ether-¹⁸O- and carbonyl-¹⁸O-labeled esters were used in these experiments and reactions were followed to at least 50% completion.

As shown in Table I, solvolysis of the anisylethyl *p*-nitrobenzoate is accompanied by oxygen equilibration (eq 2) and racemization (eq 3) of the unsolvolyzed ester. Oxygen equilibrium is also involved during solvolysis of the phenylethyl ester. However, in this case racemization is not detectable; k_α and k_t are within the combined experimental uncertainties.

That oxygen equilibration and racemization are intramolecular processes is apparent from the first-order

(10) S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, **74**, 1154 (1952).

behavior of these transformations.² This was also confirmed by exchange experiments. The second-order rate constant for exchange between α -*p*-anisylethyl *p*-nitrobenzoate and added *p*-nitrobenzoic acid-¹⁴C in 90% acetone at 60° is 8.14×10^{-3} l. mol⁻¹ hr⁻¹. From this constant it can be determined² that after 97 hr (31% solvolysis; 61% equilibration; 35% racemization) less than 0.5% of the remaining ester has undergone exchange with the acid produced by solvolysis.

The data in Table I for α -*p*-anisylethyl *p*-nitrobenzoate show that the three rates have about the same temperature dependence; the k_{rac}/k_t ratios are the same (within experimental error) and the k_{eq}/k_t ratios are similar for the two temperatures. The three reactions are faster in 70% than in 90% acetone by factors of 45 for k_t , 10 for k_{eq} and 16 for k_{rac} .

Table II shows the relative solvolytic reactivities (k_t), the ion-pair return to solvolysis ratios (k_{eq}/k_t), and the racemization to return ratios (k_{rac}/k_{eq}) for the two esters. The k_{eq}/k_t ratio for the anisylethyl ester decreases from 2.2 for 90% acetone to 0.57 for 70% acetone. A simi-

Table II. Relative Rates, Return to Capture Ratios (k_{eq}/k_t), and Stereochemistry of Return (k_{rac}/k_{eq}) for Solvolysis of α -*p*-Anisylethyl and α -Phenylethyl *p*-Nitrobenzoates in Aqueous Acetone

Ester	Solvent, % ace- tone ^b	Temp, °C	Rel k_t	k_{eq}/k_t ^a	k_{rac}/k_{eq} ^a
Anisylethyl	70	60	30,500	0.57 ± 0.3	0.71 ± 0.07
	90	60	670	2.59 ± 0.04	0.45 ± 0.01
	90	78.6	4,893	2.21 ± 0.07	0.54 ± 0.03
Phenylethyl	70	60	1		
	70	120		0.76 ± 0.02	0.03 ± 0.03

^a Uncertainties estimated from limiting values of rate constants.

^b See ref 9.

lar decrease in return with increase in water content has been observed for solvolysis of benzhydryl⁴ and allylic⁷ *p*-nitrobenzoates in aqueous acetone. The larger solvolytic rate in 70% acetone than in 90% acetone is primarily due to a less favorable entropy of activation in the latter solvent. Activation parameters for the two solvents (60°) are $\Delta H^\ddagger = 23.6 \pm 0.2$ kcal and $\Delta S^\ddagger = -7.48 \pm 0.54$ cal deg⁻¹ mol⁻¹ for 70% acetone and $\Delta H^\ddagger = 24.2 \pm 0.2$ kcal and $\Delta S^\ddagger = -12.70 \pm 0.60$ cal deg⁻¹ mol⁻¹ for 90% acetone.

The anisylethyl ester solvolyzes $>3 \times 10^4$ times faster than the phenylethyl ester in 70% acetone at 60°. This results from a lower enthalpy of activation for the former. Activation parameters for k_t in 70% acetone at 60° are $\Delta H^\ddagger = 30.1 \pm 0.4$ kcal and $\Delta S^\ddagger = -8.46 \pm 1.10$ cal deg⁻¹ mol⁻¹ for α -phenylethyl *p*-nitrobenzoate and $\Delta H^\ddagger = 23.6 \pm 0.2$ kcal and $\Delta S^\ddagger = -7.48 \pm 0.54$ cal deg⁻¹ mol⁻¹ for the anisylethyl ester.

It is of interest to note that although the rates are very different, the amounts of ion-pair return (k_{eq}/k_t) are remarkably similar for the two esters. There is, however, a striking difference in the stereochemistry of return. In the α -phenylethyl ester return proceeds with preservation of optical configuration whereas substantial racemization is observed with the anisyl analog—as for several other nonrearranging systems,³⁻⁵ the k_{rac}/k_{eq} ratio is less than one which means return involves predominating retention of configuration. These results suggest that the stereochemistry of return depends on the stability (or lifetime) of the intermediate(s) *i.e.*, the more stable the intermediate(s) the more racemization. A more specific interpretation is that only internal return,¹¹ with complete retention of configuration, is involved in the α -phenylethyl ester and racemization in the anisyl analog results from external ion-pair return.¹¹

Similar behavior has been observed for substituted benzhydryl *p*-nitrobenzoates.³ The rate of solvolysis in 90% acetone increases about 2500-fold as the substituent is varied from *p*-chloro to *p*-methoxyl. The k_{eq}/k_t ratios remain constant (except for random scatter) over this range and k_{rac}/k_{eq} ratios increase with increasing reactivity.

In some ways the present results parallel those reported for acetolysis of 3-phenyl-2-butyl and 2-phenyl-1-propyl *p*-toluenesulfonate and their anisyl analogs.¹² In these systems the *p*-methoxyl substituent also increases ionization rates, has little effect on the amount of return, but changes the behavior of return. The latter is revealed by a special salt effect¹¹ for the anisyl analogs instead of by a difference in stereochemistry as in the present work.

The data in Tables I and II provide impressive evidence that reactions 1-3 are indeed mechanistically related instead of being independent parallel processes. The large similar effect of the methoxyl group on k_t and k_{eq} , the similar temperature dependence of the three reactions, and the solvent effects on the rates and relative rates, are consistent with the interpretation²⁻⁸ that oxygen equilibration and racemization result from ion-pair return. Or to put it another way, changes in structure, temperature, and solvent change the rate of ionization which is the first step for each of the three transformations.

The effect of azide ion on the amount and stereochemistry of return for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% acetone was also investigated. In an earlier investigation⁴ it was found that solvolysis of *p*-chlorobenzhydryl *p*-nitrobenzoate in 80% acetone involves ion-pair return that results in oxygen equilibration and partial racemization of the unsolvolyzed ester. In the absence of azide ion $k_{rac}/k_{eq} = 0.42$ which means

that return results in 42% racemization. In the presence of 0.14 *M* sodium azide ion-pair return (oxygen equilibration) also occurs; however, racemization is suppressed from 42% to an undetectable level.^{4b} This result was interpreted^{4b,11} in terms of return from two distinct ion-pair species: one which returns with partial or complete racemization and is captured by azide ion and another which returns with retention of configuration and is less capturable by azide ion. In the present work we have examined the α -*p*-anisylethyl system in a similar manner.

The effect of sodium and tetrabutylammonium azide on k_t , k_{eq} , and k_{rac} for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% aqueous acetone at 78.6° is shown in Table III. In the presence of azide ion sol-

Table III. Rate Constants for Solvolysis (k_t), Carboxyl Oxygen Equilibration (k_{eq}), and Racemization (k_{rac}) for Solvolysis of α -*p*-Anisylethyl *p*-Nitrobenzoate in 90% Acetone at 78.6° in the Presence of Sodium and Tetrabutylammonium Azide^a

Expt	Solute, <i>M</i>	$10^3 k_t$, hr ⁻¹	$10^3 k_{eq}$, ^b hr ⁻¹	$10^3 k_{rac}$, ^b hr ⁻¹
1	None	27.4 ± 0.3	60.5 ± 1.4	32.5 ± 1.6
2	0.120 NaN ₃	126.9 ± 0.3	53.2 ± 0.4	23.1 ± 1.5 ^c
3	0.180 Bu ₄ NN ₃	81.2 ± 1.6	44.9 ± 0.5	23.5 ± 0.9
4	0.202 Bu ₄ NN ₃	84.7 ± 1.5		22.5 ± 0.3

^a Initial ester concentration 0.03 *M* except for experiment 1 for which it was 0.04 *M*. ^b Average of two or three independent determinations. ^c Average (and average deviation) of six independent experiments.

volysis gives a mixture of alkyl azide and alcohol. Solvent capture to give alcohol results in formation of an equivalent of acid. However, capture by azide ion to give azide does not produce acid. Thus, less than 1 equiv of acid is produced. The observed infinity titers were used to calculate the rate constant for disappearance of ester (k_t). The ratio of alkyl azide to alcohol in the product can be determined from the infinity titer. The difference between the observed and calculated infinity titer corresponds to alkyl azide and the observed titer corresponds to alcohol.

Because of the enhanced rate of disappearance of ester in the presence of azide salts, oxygen equilibration was only followed to 32% (expt 2) and 41% (expt 3) completion. The racemization constants (k_{rac}) in Table III were determined from optical rotations of isolated samples of unsolvolyzed ester. Control experiments showed that isolation and purification of the unreacted ester do not result in optical fractionation. Because of the low k_{rac}/k_t ratios, racemization was only followed to 17% (expt 2) and 25% (expt 3) completion. As indicated in the table, k_{rac} was reproducible to within about 6% in independent experiments.

Under the conditions of the experiments in Table III oxygen equilibration and racemization are intramolecular. This was established by exchange experiments with ¹⁴C-labeled *p*-nitrobenzoic acid; in the presence of azide salts *p*-nitrobenzoic acid is converted to *p*-nitrobenzoate ion.^{4b} Under the conditions of experiment 2 the second-order rate constant for exchange between ester and sodium *p*-nitrobenzoate is 0.075 ± 0.002 l. mol⁻¹ hr⁻¹. For the conditions of experiment 3 the exchange constant is 0.071 ± 0.008 l. mol⁻¹ hr⁻¹. From these constants it can be determined² that in experiment 2 when equilibration is 32% complete and

(11) S. Winstein, B. Appel, R. Baker, and A. Diaz, Special Publication No. 19, The Chemical Society, London, 1965, p 109, and references therein.

(12) S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.*, **80**, 169 (1958); S. Winstein and A. H. Fainberg, *ibid.*, **80**, 459 (1958).

racemization is 17% complete <1% of the unsolvolyzed ester has undergone exchange with *p*-nitrobenzoate ion produced by solvolysis. The corresponding data for experiment 3 are ~1% exchange at a point corresponding to 41% equilibration and 24% racemization of the unsolvolyzed ester.

The effect of azide ion on the amount and stereochemistry of return for solvolysis of the anisylethyl ester is shown in Table IV. These data show that

Table IV. Relative Rates, Return to Capture Ratios (k_{eq}/k_t), and Stereochemistry of Return (k_{rac}/k_{eq}) for Solvolysis of α -*p*-Anisylethyl *p*-Nitrobenzoate in 90% Acetone^b at 78.6° in the Presence of Sodium and Tetrabutylammonium Azide

Solute, <i>M</i>	Rel k_t	k_{eq}/k_t^a	k_{rac}/k_{eq}^a
None	1	2.21 ± 0.07	0.54 ± 0.03
0.120 NaN ₃	4.6	0.42 ± 0.05	0.43 ± 0.04
0.180 Bu ₄ NN ₃	3	0.55 ± 0.02	0.52 ± 0.03

^a Uncertainties estimated from limiting values of rate constants.
^b See ref 9.

sodium and tetrabutylammonium azide increase the rate of solvolysis (k_t), decrease the amount of return (k_{eq}/k_t), and have little effect on the stereochemistry of return (k_{rac}/k_{eq}). Sodium azide is more effective than tetrabutylammonium azide for increasing k_t and decreasing the return to solvolysis ratio. The small effect of azide ion on the stereochemistry of ion-pair return is in sharp contrast to the report^{1b} that 0.14 *M* sodium azide eliminates racemization associated with return for solvolysis of *p*-chlorobenzhydryl *p*-nitrobenzoate in 80% acetone.

Because of the different results for the two systems the effect of sodium azide on the amount and stereochemistry of ion-pair return associated with solvolysis of *p*-chlorobenzhydryl *p*-nitrobenzoate was reinvestigated. The results of the present investigation of this system are presented in Table V. These data are in good agree-

Table V. Rate Constants for Solvolysis (k_t), Carboxyl Oxygen Equilibration (k_{eq}), and Racemization (k_{rac}) for Solvolysis of *p*-Chlorobenzhydryl *p*-Nitrobenzoate in 80% Acetone^b at 99.38° in the Presence of Sodium Azide

Solute, <i>M</i>	10 ³ k_t , ^a hr ⁻¹	10 ³ k_{eq} , ^a hr ⁻¹	10 ³ k_{rac} , ^a hr ⁻¹
None	4.17 ± 0.05	6.0 ± 0.3	2.45 ± 0.03
0.141	26.3 ± 0.3	7.3 ± 0.3	0.0 ± 0.1

^a Initial ester concentration was 0.02 *M*. ^b See ref 9.

ment with those reported earlier^{4b} and confirm the earlier observation that 0.14 *M* sodium azide eliminates detectable racemization associated with ion-pair return. In a crucial experiment ester having $[\alpha]_{435}^{25} - 28.8^\circ$ (CHCl₃) was solvolyzed for 26 hr in the presence of 0.14 *M* sodium azide. The isolated unsolvolyzed ester had $[\alpha]_{435}^{25} - 28.8^\circ$. In the absence of sodium azide the unsolvolyzed ester undergoes 7% racemization during this period.¹³ In another experiment ester having $[\alpha]_{435}^{25} - 26.8^\circ$ was solvolyzed for 53 hr in 80% acetone containing 0.14 *M* sodium azide. The recovered ester had $[\alpha]_{435}^{25} - 26.7^\circ$. In the ab-

(13) Because of the positive salt effect of sodium azide, more than this amount of racemization would be expected if the salt were not suppressing racemization.

sence of sodium azide over 12% racemization would occur during this period.¹³

The reason why racemization associated with ion-pair return is eliminated by 0.14 *M* sodium azide in the *p*-chlorobenzhydryl system but not in the α -*p*-anisylethyl system is not clear. The latter system is more reactive (by a factor of 370 for solvolysis in 90% acetone at 100°) and as a result different solvents (90 and 80% acetone) and temperatures (78.6 and 100°) were used. It is not clear if the different behavior results from a change in temperature or solvent or if other factors are involved. A possible explanation is that attractive forces are weaker in the ion-pair intermediates in the more reactive α -*p*-anisylethyl system and that in this case internal return, as well as external ion-pair return, results in partial racemization.

The data in Tables III and IV show that sodium or tetrabutylammonium azide causes a large increase in the rate of solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% acetone. This results from a positive salt effect on the S_N1 solvolytic reaction instead of from azide ion promoted acyl oxygen cleavage of the type observed in the *p*-chlorobenzhydryl system.^{4b} In this connection it is important that the present system is about 400 times more reactive than *p*-chlorobenzhydryl *p*-nitrobenzoate in 90% acetone and thus the azide ion promoted acyl oxygen cleavage would not be expected to compete with alkyl oxygen cleavage. Also, control experiments showed that under these conditions *p*-nitrobenzoyl azide (the expected product of the acyl oxygen cleavage process) undergoes a Curtius rearrangement to give *p*-nitroaniline. Careful analysis showed that the latter was not present in the solvolysis products. It should also be noted that sodium azide results in positive salt effects for solvolysis of benzhydryl and *p*-*tert*-butylbenzhydryl chloride in 90% acetone¹⁴ and *p*-methoxybenzyl chloride in 70% acetone^{15,16} of magnitudes similar to that observed in the present work.

The effect of tetrabutylammonium azide on the rate of solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% acetone⁹ at 78.6° was investigated for a range of salt concentrations up to 0.2 *M*. These results are summarized in Table VI, which shows the rate constants (k_t) and alkyl azide to alcohol ratios (RN₃/ROH) for the various salt concentrations. The [RN₃]/[ROH] ratios were determined from the calculated and observed infinity titers. Formation of alkyl azide consumes azide ion. Solvent capture also consumes azide ion indirectly because the stronger *p*-nitrobenzoic acid ($K_A \sim 4 \times 10^{-4}$) produced by solvolysis liberates undissociated hydrazoic acid ($K_A \sim 2 \times 10^{-5}$) from the salt. Thus 1 equiv of azide ion is consumed for each equivalent of reaction. In these experiments the ester concentration was 0.03 *M*. Except at the lower salt concentrations, the change in azide ion during solvolysis was small. For example, at an initial salt concentration of 0.1 *M* the azide ion concentration decreases 15% at 50% solvolysis.

As has been pointed out,¹⁶ for a mechanism that involves competitive capture of reactive intermediates

(14) L. C. Bateman, M. G. Church, E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 979 (1940).

(15) G. Kohnstam, A. Queen, and B. Shillaker, *Proc. Chem. Soc.*, 157 (1959).

(16) R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 362, 6031 (1969).

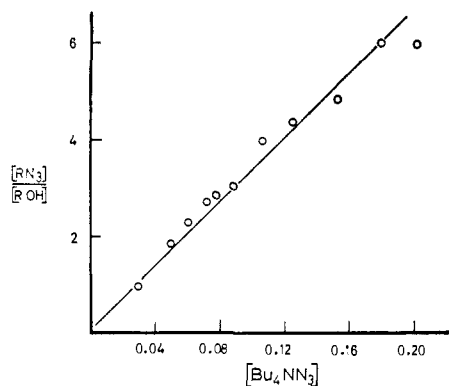


Figure 1. Plot of $[RN_3]/[ROH]$ vs. $[Bu_4NN_3]$ for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% acetone at 78.6°.

by azide ion and solvent (eq 4) there is a linear relationship between the $[RN_3]/[ROH]$ ratio and salt concentration. As shown by Figure 1 there is a reasonably good linear relationship between $[RN_3]/[ROH]$ and salt con-

Table VI. Rates and Alkyl Azide to Alcohol Product Ratios $[RN_3]/[ROH]$ for Solvolysis of 0.03 *M* α -*p*-Anisylethyl *p*-Nitrobenzoate in 90% Acetone^a at 78.6° in the Presence of Tetrabutylammonium Azide^b

$[Bu_4NN_3]$, <i>M</i>	$10^3 k_t$, hr ⁻¹	$[RN_3]/[ROH]^c$
None	27.4 ± 0.3	
0.030	28.9 ± 0.9	0.95
0.050	41.7 ± 0.1	1.85
0.061	47.2 ± 1.0	2.29
0.072	55.9 ± 0.6	2.70
0.078	58.9 ± 1.2	2.85
0.089	64.9 ± 1.3	3.03
0.106	70.7 ± 0.5	4.00
0.125	73.7 ± 1.6	4.38
0.153	77.1 ± 0.6	4.85
0.180	81.2 ± 1.6	6.04
0.202	84.7 ± 1.5	6.00

^a See ref 9. ^b Solvent from the same batch was used for all of the experiments. Initial ester concentrations were 0.03 *M* except for experiment 1 where it was 0.04 *M*. ^c Azide to alcohol product ratio determined from concentration of ester and observed infinity titer.

centrations—the salt concentrations are initial values and have not been corrected for consumption of azide ion during the reaction. The slope of this plot corresponds to the selectivity ratio (k_N/k_S)¹⁶ and has a value of 35.

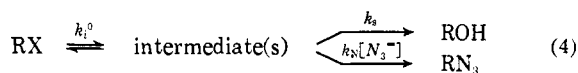


Figure 2 shows a plot of k_t vs. tetrabutylammonium azide concentration. This plot reveals a striking salt effect. The salt effect is small at low salt concentrations (<0.03 *M*). This is followed by a very steep rise in k_t for the range of 0.03–0.1 *M* and a subsequent small increase that is linear in salt concentration.

We believe that this behavior results from a special salt effect of the type reported for acetolysis of certain alkyl arenesulfonates in the presence of lithium perchlorate.¹¹ Except for the level portion at very low concentrations this plot is remarkably similar to those reported by Winstein and coworkers for systems that

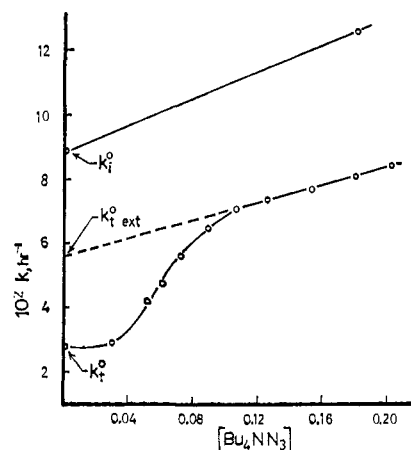


Figure 2. Plots of titrimetric (k_t) and ionization ($k_i = k_t + k_{eq}$) rate constants vs. $[Bu_4NN_3]$ for solvolysis of α -*p*-anisylethyl *p*-nitrobenzoate in 90% acetone at 78.6°.

show “special” salt effects.^{11,17} Presumably the small effect at low salt concentrations result from consumption of much of the azide ion (to give hydrazoic acid and alkyl azide) during solvolysis. The initial steep rise in k_t is evidently due to capture by azide ion of an intermediate that otherwise would return to substrate. The subsequent gradual linear increase in k_t is thought to be a normal salt effect with little, if any, alteration of ion-pair return over this range of concentrations.

The linear increase in k_t at salt concentrations >0.1 *M* is correlated by eq 5^{11,18} in which $k_{t(\text{ext})}^0$ is the intercept

$$k_t = k_{t(\text{ext})}^0(1 + b_t[Bu_4NN_3]) \quad (5)$$

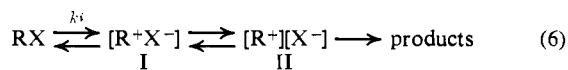
obtained by extrapolation to zero salt concentration. The slope of the linear plot is proportional to b_t , a parameter that is a measure of the sensitivity of k_t to salt concentration. The value of b_t for the linear plot is 2.6. The slope of the linear plot is about six times smaller than the maximum slope in the special-salt-effect region. It is significant that in the region of the normal salt effect, *i.e.*, $[Bu_4NN_3] > 0.1$ *M*, ion-pair return (oxygen equilibration) is still occurring. This is shown by experiment 3 in Table III. This means that the special salt effect (steep portion of the plot) results from elimination of part, but not all, of the ion-pair return. Thus, evidently return occurs from two distinct species, one which is completely captured by 0.1 *M* azide ion and another which is not, or only partially, captured by azide ion over the range of concentrations investigated.

The present results are correlated by the Winstein mechanism for solvolysis shown in eq 6.^{11,18} According to this interpretation the solvent-separated ion-pair intermediate (II) is intercepted by azide ion and external ion-pair return from II is thus eliminated by >0.1 *M* tetrabutylammonium azide. It is not clear if there is partial capture of the intimate ion-pair intermediate (I)—from the high selectivity ratio (k_N/k_S) and the fact that internal return (oxygen equilibration) is observed at the highest salt concentrations (Table III), it seems that solvent capture of I is unimportant.

(17) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *J. Amer. Chem. Soc.*, **78**, 328 (1956).

(18) S. Winstein, E. Clippinger, A. H. Fainberg, and G. C. Robinson, *ibid.*, **76**, 2597 (1954).

Presumably, in the absence of azide ion the product-forming step involves dissociation of II to give the dissociated carbonium ion which is captured by solvent. The absence of exchange with *p*-nitrobenzoate ion shows that external return is not important.



The value of $k_{t(\text{ext})}^0$ in eq 5 and Figure 2 is $55.5 \times 10^{-3} \text{ hr}^{-1}$. This is the rate constant for formation of the capturable solvent-separated ion pair at zero salt concentration. The rate constants for ionization, $k_i = k_t + k_{\text{eq}}$, in the absence and presence of 0.18 *M* salt are included in Figure 2. As mentioned above, if return results in complete equilibration k_i is the constant for total ionization. As shown by Figure 2, $k_{t(\text{ext})}^0$ falls short of the observed ionization constant k_i^0 . This gap, which is 37% of k_i^0 (54% of total return), results from return that is not eliminated by azide ion (*i.e.*, internal return). The gap between $k_{t(\text{ext})}^0$ and k_t^0 (32% of ionization and 46% of return) is due to return that is eliminated by $>0.1 \text{ M}$ tetrabutylammonium azide. It is interesting to note that the observed k_i/k_t ratio for 0.18 *M* salt and the $k_i^0/k_{t(\text{ext})}^0$ are nearly identical. This is consistent with the view that the difference between k_i^0 and k_t^0 is due to two kinds of return, internal and external ion-pair return and azide ion is effective in eliminating the latter and has little, if any, effect on the former.

The stereochemical results reported in Table III show that the attractive forces in the intimate ion pair (the one not captured by azide ion) are weak enough so that optical configuration is not fully preserved. In fact, in this system there seems to be little difference in the amount of racemization associated with internal (experiments 2 and 3, Table III) and external ion-pair return. Other noteworthy points are that the solvent-separated ion pair, which is readily captured by azide ion, does not undergo detectable exchange with labeled *p*-nitrobenzoate ion and the intimate ion-pair intermediate seems to be remarkably unreactive toward nucleophilic attack by azide ion.

Experimental Section

Compounds. α -Phenylethyl alcohol [bp 89–90° (16 mm), n_{D}^{25} 1.5257 (lit.¹⁹ bp 92.5–93.5° (16 mm), n_{D}^{25} 1.5253²⁰)] was prepared in 68% yield by addition of methyl Grignard to benzaldehyde and in 86% yield by reduction of acetophenone with sodium borohydride. Resolution²¹ by recrystallization of the brucine salt of the acid phthalate derivative gave (–)- α -phenylethyl alcohol, $\alpha_{\text{D}}^{25,435} -39.37^\circ$, $\alpha_{\text{D}}^{25,365} -63.74^\circ$ (rotations for neat liquids in 0.5-dm tube).²²

dl- α -Phenylethyl *p*-nitrobenzoate, mp 42.4–43.7° (lit.²³ mp 42.5–43.5°), was prepared from pure racemic α -phenylethyl alcohol in the usual way.²⁴ (+)- α -Phenylethyl *p*-nitrobenzoate,²² $[\alpha]_{\text{D}}^{25}$ 122.5° (CHCl₃), was prepared²⁴ from the (–)- α -phenylethyl alcohol described above. α -Phenylethyl *p*-nitrobenzoate-*carbonyl*-¹⁸O (2.68% ¹⁸O)²⁵ was prepared in the same way using *p*-nitrobenzoyl-*carbonyl*-¹⁸O chloride.⁷

(19) E. L. Eliel, *J. Amer. Chem. Soc.*, **71**, 3970 (1949).

(20) R. R. Dreisbach and R. A. Martin, *Ind. Eng. Chem.*, **41**, 2875 (1949).

(21) E. Downer and J. Kenyon, *J. Chem. Soc.*, 1156 (1939).

(22) Infrared spectra of liquid films or solutions of optically active samples were indistinguishable from those of corresponding authentic racemic samples.

(23) L. F. King, *J. Amer. Chem. Soc.*, **61**, 2383 (1939).

(24) H. L. Goering and J. P. Blanchard, *ibid.*, **76**, 5405 (1954).

(25) Oxygen-18 contents are atom per cent excess ¹⁸O.

α -*p*-Anisylethyl alcohol, bp 95° (1.5 mm), was prepared in 84% yield by reduction of commercial *p*-methoxyacetophenone with lithium aluminum hydride. The alcohol was resolved as described earlier²⁶ (recrystallization of the cinchonidine salt of the acid phthalate derivative) with the modification that active acid phthalate was converted to alcohol by reduction with lithium aluminum hydride.²⁷ Different resolutions gave (–)- α -*p*-anisylethyl alcohol having $[\alpha]_{\text{D}}^{25}$ ranging from –30 to –44.4° (CHCl₃).²²

dl- α -*p*-Anisylethyl *p*-nitrobenzoate, mp 64–65°, was prepared²⁴ from racemic alcohol and in a typical case (+)- α -*p*-anisylethyl *p*-nitrobenzoate,²² $[\alpha]_{\text{D}}^{25}$, 23.2° (CHCl₃), was obtained from (–)- α -anisylethyl alcohol, $[\alpha]_{\text{D}}^{25}$, –33.1° (CHCl₃). The active ester purified by chromatography on silicic acid (CHCl₃ eluent) was a light yellow oil which solidified slowly to an amorphous mass. To avoid optical fractionation the optically active ester was not purified by recrystallization. α -*p*-Anisylethyl *p*-nitrobenzoate-*carbonyl*-¹⁸O (2.65% ¹⁸O),²⁵ mp 62.64°, was prepared in the same way using *p*-nitrobenzoyl-*carbonyl*-¹⁸O chloride.⁷ α -*p*-Anisylethyl *p*-nitrobenzoate-*ether*-¹⁸O (3.86% ¹⁸O)²⁵ was prepared from ¹⁸O-labeled alcohol prepared by lithium aluminum hydride reduction of ¹⁸O-labeled *p*-methoxyacetophenone. The latter was prepared by stirring a mixture of 30 g of *p*-methoxyacetophenone and 12 g of ¹⁸O-enriched water (~5% ¹⁸O) containing a trace of *p*-toluenesulfonic acid for 37 hr at 40°. After cooling to room temperature the solid ketone was collected, dried, and recrystallized from pentane. This ketone was converted to the above ether-¹⁸O-labeled *p*-nitrobenzoate derivative.

The *p*-chlorobenzhydryl system was resolved by a modification of a method reported earlier²⁸ which involves recrystallization of the brucine salt of the acid phthalate derivative. A solution of 106.7 g of *p*-chlorobenzhydryl acid phthalate, mp 148–149.4° (lit.²⁸ mp 152°), and 115 g of anhydrous brucine in 535 ml of dry ethyl acetate was allowed to stand at room temperature for 3 days. The precipitate (55 g) was placed in 650 ml of ethyl acetate which was refluxed for 45 min and the insoluble material was removed by filtration. The filtrate was concentrated to 200 ml and allowed to stand at room temperature for 3 days. Recrystallization of the precipitate twice from ethyl acetate gave 31 g of the brucine salt of the acid phthalate, mp 114–116° (lit.²⁸ mp 113°). The brucine salt gave²⁸ (–)-*p*-chlorobenzhydryl acid phthalate²² in 76% yield which had mp 134–135°, $[\alpha]_{\text{D}}^{25}$ –5.23° (benzene) (lit.²² mp 135°, $[\alpha]_{\text{D}}^{25}$ –3.5°). The (–)-acid phthalate was converted to (–)-*p*-chlorobenzhydryl,²² mp 54–55°, $[\alpha]_{\text{D}}^{25}$ –16.0° (CHCl₃) in 75% yield by reduction with lithium aluminum hydride.²⁷

dl-*p*-Chlorobenzhydryl *p*-nitrobenzoate, mp 120.5–122.3° (lit.²⁹ mp 120–123°), was prepared in the usual manner. *p*-Chlorobenzhydryl *p*-nitrobenzoate-*carbonyl*-¹⁸O (2.68% ¹⁸O)²⁵ was prepared²⁴ using ¹⁸O-labeled *p*-nitrobenzoyl chloride.

(–)-*p*-Chlorobenzhydryl *p*-nitrobenzoate,²² $[\alpha]_{\text{D}}^{25,435} -26.8^\circ$, was obtained from the above (–)-*p*-chlorobenzhydryl. The active ester was purified by chromatography on silicic acid using a 2:1 benzene-hexane mixture as eluent.

Anal. Calcd for C₂₀H₁₄ClNO₄: C, 65.31; H, 3.84. Found: C, 65.12; H, 4.07.

Tetrabutylammonium azide was prepared by neutralizing 400 ml of 25% tetrabutylammonium hydroxide in methanol with excess hydrazoic acid in ether (prepared by stirring 20 g of sodium azide in a mixture of 400 ml of ether and 8 ml of sulfuric acid and removal of sodium sulfate by filtration). After evaporation of the ether, the oily residue was dried under high vacuum and recrystallized from benzene. After several recrystallizations and drying under high vacuum the pure hygroscopic tetrabutylammonium azide, mp 83–85°, was obtained in 64% yield (68.8 g). The infrared spectrum (CHCl₃) showed intense azide absorption at 4.98–5.00 μ and there was no evidence of NH absorption. The nmr spectrum (CCl₄) had three groups of peaks at 70, 104, and 214 cps with relative areas of 3:4:2 as expected for the *n*-butyl group. Titration of azide ion³⁰ gave a molecular weight of 283.5 (theory 284.4).

p-Nitrobenzoyl azide, mp 71–72°, was prepared in 71% yield by slow addition of 3.9 g of sodium azide (20% molar excess) in 30 ml of water to a solution of 9.3 g of *p*-nitrobenzoyl chloride in 125

(26) M. P. Balfe, J. Kenyon, A. Ecans, and K. N. Nandi, *J. Chem. Soc.*, 803 (1946).

(27) W. E. Doering and H. H. Zeiss, *J. Amer. Chem. Soc.*, **72**, 149 (1950).

(28) G. H. Green and J. Kenyon, *J. Chem. Soc.*, 751 (1950).

(29) M. S. Silver, *J. Amer. Chem. Soc.*, **83**, 404 (1961).

(30) E. Krejzova, V. Simm, and J. Zyka, *Chem. Listy*, **51**, 1764 (1957).

ml of acetone at 0°. The product was purified by recrystallization from benzene.

Anal. Calcd for $C_7H_4O_3N_4$: C, 43.76; H, 2.10; N, 29.19. Found: C, 43.71; H, 2.18; N, 29.24.

Kinetic Experiments.³¹ (A) **Titrimetric Rates.** The ampoule technique was used and ampoules containing reaction mixtures were flushed with nitrogen prior to sealing. For experiments without added azide salts reactions were followed as described earlier.^{7,8}

For solvolysis in the presence of azide salts, a pH meter (Beckman Model H2), instead of bromothymol blue, was used to determine end points—visual indicators did not give sharp color changes at the equivalence point. Equivalence points were determined from plots of the slope of the titration curve *vs.* amount of base. Titration of synthetic solutions of *p*-nitrobenzoic acid of known concentrations in aqueous acetone containing 0.12 *M* sodium azide showed that equivalence points can be determined accurately by this method. Observed infinity titers and corrected zero point titers were used to calculate the first-order rate constants. Corrected zero point titers were obtained by extrapolation of plots of the log of the ester concentration (*i.e.*, the difference between the infinity titer and titers at various times) *vs.* time to zero time.³² Reactions were followed to about 70% reaction and in all cases, good first-order behavior was observed.

(B) **Rates of Carboxyl Oxygen Equilibration.** In a typical experiment three heavy-wall ampoules containing a 0.0436 *M* solution of α -*p*-anisylethyl *p*-nitrobenzoate-*ether*-¹⁸O (4.13% ¹⁸O)²⁶ in 90% acetone were placed in a 78.60° constant-temperature bath. At time intervals corresponding to 22, 31, and 43% solvolysis, ampoules were removed and chilled to quench the reaction. In each case the solvent was removed under reduced pressure at room temperature after which the residue was taken up in ether. The ether solution was extracted several times with saturated aqueous sodium carbonate and then washed with water and dried over sodium sulfate. After evaporation, the residual neutral mixture of unsolvolyzed ester and alcohol (solvolysis product) was heated to 50° under high vacuum to separate the alcohol from the ester. The residual ester was purified by recrystallization from a benzene-hexane mixture. About 1 g of unsolvolyzed ester was recovered from each ampoule. In all cases the ¹⁸O content of the recovered ester was the same as that of the starting ester. Lithium aluminum hydride reduction of the recovered ester gave α -*p*-anisylethyl alcohol which was purified by vacuum transfer. The purified alcohol was reconverted to the *p*-nitrobenzoate derivative which was purified by chromatography on silicic acid (CHCl₃) followed by two recrystallizations (benzene-hexane). The ¹⁸O content of this *p*-nitrobenzoate corresponds to the ¹⁸O content of the ether oxygen atom of the unsolvolyzed ester.

(31) Concentrations are for 25° and aliquots were measured at 25°.

(32) In the absence of azide salts these plots are linear from the outset. In the presence of azide ion the initial experimental points (for times corresponding to <5% reaction) fall above the straight line that fits the rest of the points. This means that the corrected titers for zero time are a little larger than the observed values.

In the presence of azide salts, alkyl azide is a component of the neutral mixture obtained by concentration of the ether extract. In the α -*p*-anisylethyl system this is separated with the alcohol by distillation at 50° under high vacuum. In the *p*-chlorobenzhydryl system the mixture of the unsolvolyzed ester, *p*-chlorobenzhydryl, and *p*-chlorobenzhydryl azide was separated by chromatography on silicic acid with benzene-hexane as eluent. The alkyl azide is eluted first followed by the unsolvolyzed ester.

The purity of the samples of ester prepared for ¹⁸O analysis was checked by thin layer chromatography with a 15% ethyl acetate in benzene system on silica gel plates. Control experiments showed that trace amounts of alkyl azide or alcohol in the unsolvolyzed ester can be detected by this method.

Control experiments demonstrated that starting esters were discretely labeled and methods involved in isolation and purification do not result in loss or equilibration of label. Oxygen-18 contents were determined as described earlier.⁶⁻⁸ Good first-order behavior was observed in all of these experiments.

(C) **Rates of Racemization.** In the polarimetric experiments the ampoule technique was used. Reactions were followed as described earlier^{7,8} and first-order rate constants for loss of optical activity (k_α) were determined from the rate of loss of optical activity. Initial observed rotations ranged from 1.4° to almost 3° and good first-order behavior was observed. The rate constant for racemization (k_{rac}) was determined from k_α and k_t ; *i.e.*, $k_{rac} = k_\alpha - k_t$.^{7,8}

The rate of racemization was also determined directly from rotations of isolated samples of unsolvolyzed ester. In these experiments four portions of a solution of active ester were sealed in heavy-walled glass ampoules and placed in a constant-temperature bath. After appropriate time intervals the unsolvolyzed ester was isolated as described in the preceding section with the exception that the residual unsolvolyzed ester was purified by chromatography (silicic acid with CHCl₃ as eluent) instead of by recrystallization. The purity of the recovered ester was determined by thin layer chromatography as described above.

In control experiments solutions of (+)- α -*p*-anisylethyl *p*-nitrobenzoate, $[\alpha]^{25}_D$ 20.13° (CHCl₃) in 90% acetone and 90% acetone containing tetrabutylammonium azide, were prepared and the ester was isolated as outlined above. The samples recovered from the two solutions had $[\alpha]^{25}_D$ 20.52° and 20.19°. In another experiment (–)-*p*-chlorobenzhydryl *p*-nitrobenzoate, $[\alpha]^{25}_{435} -13.24^\circ$, was dissolved in 80% acetone containing sodium azide. The recovered ester had $[\alpha]^{25}_{435} -13.48^\circ$.

(D) **Rates of Exchange.** Second-order rate constants for exchange between ester and *p*-nitrobenzoic acid- α -¹⁴C³ were determined as described earlier.^{2,6} The activity of the labeled acid was determined as the corresponding ester derivative and thus, for each experiment, all radioactivities were determined for the same derivative. The activity of the α -*p*-anisylethyl derivative of the added labeled *p*-nitrobenzoic acid was 502×10^{-3} μ Ci/mmol and the activity of the *p*-chlorobenzhydryl derivative was 448×10^{-3} μ Ci/mmol. All activities were determined in triplicate. Reactions were followed until most of the ester was consumed by solvolysis and second-order rate constants² for these periods were steady.