

With five of the mercaptans the reactions with ethylene oxide were studied at three temperatures: 20, 30 and 40°. From the slopes of the strictly linear plots of $\log k_2$ vs. reciprocal of the absolute temperature the activation energies for each of these reactions were determined (Table IV). While the differences are small, they are considered to be significant, and they raise a rather interesting question, for the activation energies are in completely reversed order from what might have been expected from the observed rates of reaction. The thioglycolate ion, which reacts the most rapidly, has the highest activation energy, while the mercaptoethylammonium ion, which reacts least rapidly, has the lowest activation energy. However, when values for entropy of activation and frequency factors are calculated from the data it is seen that for both terms the order of the values favors the order of reaction rates actually observed. A consideration of the two extreme cases gives us some basis for accounting for the fact that the rates of reaction are so highly dependent on entropy effects.

Over the whole *pH* range in which thioglycolate was studied the carboxyl group is completely dissociated so that the mercaptide which attacks the ethylene oxide is a doubly charged anion with the two negative charges separated only by a short distance. This should be a highly solvated species with water dipoles attracted to the negative charges. The product of reaction, however, is a singly charged anion and should be much less solvated.

TABLE IV
ACTIVATION ENERGIES, ENTROPIES OF ACTIVATION AND FREQUENCY FACTORS FOR THE REACTIONS OF FIVE MERCAPTANS WITH ETHYLENE OXIDE

Mercaptan	ΔE_a , kcal./mole	ΔS_a^* , u.u.	A , l. m. ⁻¹ sec. ⁻¹
Thioglycolic acid	11.65	-25.32	5.0×10^7
β -Mercaptopropionic acid	11.53	-26.53	2.7×10^7
2-Mercaptoethanol	11.48	-27.74	1.4×10^7
1-Thio-D-sorbitol	10.87	-31.62	0.2×10^7
2-Mercaptoethylamine	10.78	-32.57	0.13×10^7

The reaction can be considered then as consuming a highly solvated species to form a less solvated species with the release of a considerable number of solvent molecules.

Over the *pH* range in which the mercaptoethyl ammonium ion was studied the substituted ammonium group is unassociated so that the species which attacks the ethylene oxide is a dipolar ion with electrostatic attraction holding the two charged groups relatively close together. Because of the partial neutralization of the opposing charges this species is probably not too highly solvated. The product of reaction, however, is singly charged cation which should be appreciably more solvated. In this reaction, then, the consumption of a slightly solvated species to form a more highly solvated species brings about the restriction of position of a large number of solvent molecules.

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Stereochemistry of Allylic Rearrangements. X. The Isomeric Rearrangement and Solvolysis of *trans*- α,γ -Dimethylallyl *p*-Nitrobenzoate in Aqueous Acetone¹

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The first-order solvolysis of optically active *trans*- α,γ -dimethylallyl *p*-nitrobenzoate (I) in 90% aqueous acetone is accompanied by a first-order intramolecular (S_N1') rearrangement of the ester—in this system rearrangement results in the interconversion of enantiomers, *i.e.*, racemization. The first-order rate constant for racemization (k_{rac}) is over four times larger than that for solvolysis (k_t). Thus during solvolysis the remaining ester becomes progressively racemic and at 50% reaction is about 95% racemic. The racemization of carbonyl-¹⁸O labeled I in the presence of unlabeled *p*-nitrobenzoic acid and lithium *p*-nitrobenzoate does not result in exchange. From this and from the kinetic behavior it is clear that the rearrangement (racemization) is completely intramolecular. The relative positions of the oxygen atoms in the reactant (*d*-ester) and product (*dl*-ester) have been determined using carbonyl-¹⁸O labeled optically pure *d*-ester. Isolation of the unsolvolyzed but racemized (rearranged) ester followed by resolution showed the label to be distributed between the two positions in each enantiomer. The rate of ¹⁸O equilibration in the two enantiomers is 1/2.9 times that of racemization. The kinetic and ¹⁸O experiments are consistent with the idea that the intramolecular rearrangement involves internal return from an internal ion-pair intermediate. According to this interpretation, the data show that in the present case there is one chance in 2.9 that the oxygen atoms will become equivalent on passing through the intermediate.

Introduction

Evidence was presented in earlier papers in this series³⁻⁵ that an internal ion-pair⁶ intermediate is

involved in carbonium-ion reactions of allylic esters and chlorides. This intermediate can (a) return to the original allylic compound or its allylic isomer (internal return⁶)—this is an intramolecular isomeric (S_N1') rearrangement—or (b) dissociate to the carbonium ion and the accompanying anion. As was pointed out in the previous paper in this series⁵ in hydroxylic solvents the carbonium ion formed by dissociation of the intermediate is completely intercepted by the solvent

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(3) H. L. Goering and E. F. Silversmith, *THIS JOURNAL*, **77**, 1129 (1955); **77**, 6249 (1955); **79**, 348 (1957).

(4) H. L. Goering, T. D. Nevitt and E. F. Silversmith, *ibid.*, **77**, 5026 (1955).

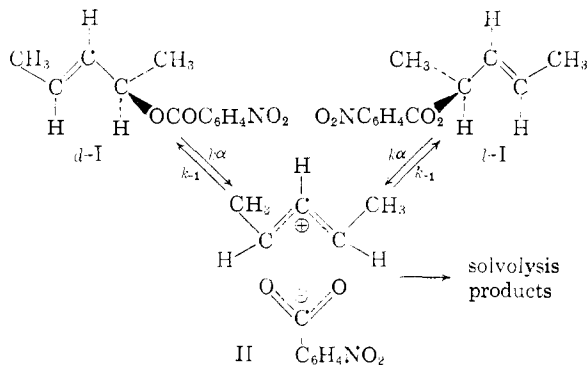
(5) H. L. Goering and R. W. Greiner, *ibid.*, **79**, 3464 (1957).

(6) S. Winstein, E. Clippinger, A. Fainberg, R. Heck and G. Robinson, *ibid.*, **78**, 328 (1956).

(*i.e.*, there is no external return⁶) and the isomeric rearrangement which accompanies solvolysis is intramolecular. In the present work we have used this technique to isolate and study the intramolecular isomeric rearrangement of *trans*- α , γ -dimethylallyl *p*-nitrobenzoate (I).

In this system the intramolecular rearrangement (internal return) results in the interconversion of enantiomers.⁵ Thus the rearrangement is a simple first-order equilibration; *d*-ester \rightleftharpoons *l*-ester. The accompanying solvolysis, which precludes intermolecular isomeric rearrangement, is incidental to the intramolecular rearrangement and has no effect on the kinetics or thermodynamics of the equilibration. Solvolysis does, however, introduce a practical problem in that the ester is slowly consumed and thus the equilibration can only be investigated for a limited period of time. To obtain more information about the intramolecular isomeric rearrangement we have investigated the relative positions of the oxygen atoms in the reactant (*d*-ester) and product (*dl*-ester) for the rearrangement in 90% aqueous acetone.⁷

The rearrangement and solvolysis of I is illustrated below. Details of the conversion of the internal ion-pair intermediate to solvolysis products, which are incidental in the present work, are not considered in this illustration. It was shown in earlier papers that complete stereochemical integrity is maintained in such processes in the sense that the migrating group remains on its original side of the plane of the allyl moiety.³⁻⁵



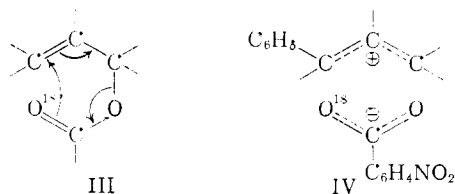
The rate of racemization (rearrangement), *i.e.*, *d* \rightarrow *dl*, can be obtained from the rates of (a) solvolysis (titrimetric rate) and (b) loss of optical activity (polarimetric rate). It is apparent that the constant for racemization (k_{rac}) is the difference between that for loss of optical activity ($k\alpha$) and solvolysis (k_t), *i.e.*, $k_{rac} = k\alpha - k_t$.⁵ The latter constants can be measured directly and the extent of racemization of the unsolvolyzed ester at any time can be determined from k_{rac} . The rate constant, k_{rac} , corresponds to the rate of production of that fraction of the intermediate which returns to I; the rate constant for the interconversion of the enantiomers is $(1/2)k_{rac}$.

Clearly the relationship between the locations of the oxygen atoms in the reactant and product is dependent upon the structure and bonding in the intermediate II. The three possibilities starting

with carbonyl- O^{18} labeled *d*-ester (*d*- $ROCO^{18}Ar$) are

- (1) $d-ROCO^{18}Ar \rightleftharpoons l-RO^{18}COAr$
- (2) $d-ROCO^{18}Ar \rightleftharpoons l-ROCO^{18}Ar$
- (3) $d-ROCO^{18}Ar \rightarrow dl-RO^{18}CO^{18}Ar$

The first case corresponds to a process summarized by III. This apparently is the situation in the intramolecular rearrangement of α -phenyl- γ -methylallyl⁸ and α -phenylallyl *p*-nitrobenzoate,⁹ *i.e.*, the carbonyl oxygen in the reactant becomes the alkyl oxygen atom in the product. This indicates that the intermediate in these cases has the geometry shown by IV.



The present system offers a very important advantage over the phenylallyl systems for a detailed study of the rearrangement. In the phenylallyl systems the rearrangement is irreversible. Thus the product is examined after a single conversion or pass through the intermediate. A slight tendency for oxygen scrambling in the intermediate could not readily be detected in systems of this type. In the one case⁹ where information is available, the rearrangement was carried out in a non-hydroxylic solvent and was complicated by an intermolecular component as might be expected.^{3-5,10} Because of this complication, which results in scrambling and must be corrected for, and uncertainties in the analytical method it is not clear if the process proceeds entirely as illustrated by III.

In the present system the rearrangement is an equilibrium and the rearranged (unsolvolyzed) ester can be examined after several interconversions or passes through the intermediate. The only limitation on the number of interconversions is imposed by the relatively slow destruction of material by solvolysis.

The second possible O^{18} result corresponds to the process summarized by V. In this event the intermediate would have the structure shown by VI. This process would be similar to that observed by Denney and Denney¹¹ for the rearrangement of *trans*-9-decalyl perbenzoate to 1-benzoyl-1,6-epoxycyclodecane—a process which presumably involves an internal ion-pair intermediate^{12,13,14} in that the carbonyl oxygen would retain its identity. However, such a process would be expected to be less likely for the 1,3-migration in the allylic system than for the 1,2-migration in the decalyl perbenzoate system.

(8) W. von E. Doering, private communication, 1955.

(9) E. A. Braude and D. W. Turner, *J. Chem. Soc.*, 2404 (1958).

(10) H. L. Goering, J. P. Blanchard and E. F. Silversmith, *This Journal*, **76**, 5409 (1954).

(11) D. B. Denney and D. G. Denney, *ibid.*, **79**, 4806 (1957).

(12) P. D. Bartlett and J. L. Kice, *ibid.*, **75**, 5591 (1953).

(13) H. L. Goering and A. C. Olson, *ibid.*, **75**, 5853 (1953).

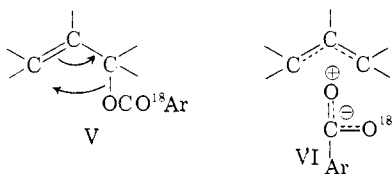
(14) S. Winstein and G. C. Robinson, *ibid.*, **80**, 169 (1958).

(7) The solvent composition is based on the volumes of the pure components at 25° prior to mixing.

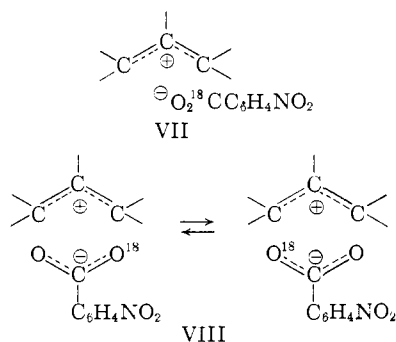
TABLE I
POLARIMETRIC (k_α) AND TITRIMETRIC (k_t) FIRST-ORDER RATE CONSTANTS FOR THE SOLVOLYSIS OF *trans*- α,γ -DIMETHYLALLYL *p*-NITROBENZOATE IN 90% AQUEOUS ACETONE

Temp., °C.	Ester, 10 ² M	Solute, 10 ² M	10 ² k_α , ^a hr. ⁻¹	10 ² k_t , ^a hr. ⁻¹	k_α/k_t ^b
99.61	4.896	None		4.22 ± 0.07	5.4 ± 0.1
99.61	4.903	None		4.23 ± .04	
99.61	6.218	None	22.5 ± 0.6		
99.61	5.605	None	23.1 ± .8		
99.70	4.925	2.6 LiPNB ^c		4.87 ± .02	5.03 ± .1
99.70	5.814	2.6 LiPNB	24.5 ± .3		
99.70	4.771	2.6 PNBA ^c		4.58 ± .06	5.04 ± .1
99.70	5.617	2.6 PNBA	23.1 ± .3		

^a The indicated uncertainty is the average deviation from the mean of the 8 to 12 values for each experiment. ^b The uncertainty was determined from the limiting values for k_α and k_t . ^c LiPNB and PNBA indicate lithium *p*-nitrobenzoate and *p*-nitrobenzoic acid, respectively.



The third possibility represents a case in which the oxygen atoms are equilibrated at some intermediate stage and thus the label is distributed between both positions in each enantiomer. The extent of equilibration could vary from 100% to partial equilibration for each pass through the intermediate. Complete equilibration would result if the oxygen atoms in the ion-pair intermediate were equivalent as illustrated by VII. On the other hand, if the most stable orientation in the intermediate is that shown by VIII and if the barrier separating the two equivalent structures (minima) is low enough so that the interconversion competes with internal return, partial equilibration would result. In this illustration the plane of the carboxyl group is considered to be nearly or completely perpendicular to the plane of the allylic cation. From VIII it is apparent that there can be a gradual transition from the first possibility (high barrier) to the third possibility (no barrier) in which case VIII degenerates to VII.



The second possibility can obviously be distinguished from the other two because in this case the label would remain in the carbonyl position. An optically active reactant would not be required to make this distinction provided that k_{rac} were known.

The difference between the first and third possibilities is more subtle because, as mentioned

above, there is no sharp distinction between them but rather they are limiting situations which merge. Moreover, in either case or for any intermediate situation, scrambling would occur at the same rate as racemization, *i.e.*, in any event carbonyl labeled *d*-ester would give racemic material with the label equally distributed between the two positions. However, one can distinguish between these limiting cases (or determine the contribution of each) by using an optically active labeled reactant, reresolving the racemized (rearranged) unsolvolyzed ester and determining the O¹⁸ content of each position in the enantiomers. In one limiting case (first possibility) the enantiomers would be discretely labeled: the *d*-isomer in the carbonyl position and the *l*-isomer in the ether-oxygen position. The other extreme (third possibility) would result in product (*dl*-ester) with the label equally divided between the two positions in both enantiomers during all stages of the reaction. An intermediate situation would result in equilibration of the oxygen atoms in each enantiomer but at a slower rate than that of racemization.

Results

Kinetic Experiments.—The necessary kinetic data for determining the rate constant for racemization (k_{rac}), *i.e.*, $k_\alpha - k_t$, for the rearrangement in 90% aqueous acetone⁷ are presented in Table I. These data show that $k_\alpha > k_t$ and also demonstrate that the discrepancy between these rates is due to internal return rather than external return.

The titrimetric rate constants (k_t) were determined in the usual manner^{3,5} by measuring the rate of formation of *p*-nitrobenzoic acid. In all cases these constants were steady and the reactions were followed to *ca.* 80% completion. The observed infinity values were within 1% of the calculated values.

Polarimetric constants (k_α) were determined by measuring the rate of loss of optical activity.³⁻⁵ These constants were steady for the complete reaction. The infinity rotations measured at ten half-lives were about 1% of the original value. This residual activity was lost completely at a slower rate. In one experiment the reaction was carefully followed to over 98% reaction (6.5 half-periods). The constants for the final stages of the reaction—the observed infinity value was used in the calculations—showed no significant

trends. Thus it is clear that all of the optical activity (except the trace of residual activity) is lost by a clean first-order process. The cause of the slight residual activity remains obscure. It seems unlikely that it is due to formation of active alcohol because α,γ -dimethylallyl alcohol even when optically pure has a rather low rotation.⁵ More likely this trace of activity is due to contamination by a small amount of an active isomeric non-allylic *p*-nitrobenzoate, e.g., 4-pentene-2-yl *p*-nitrobenzoate. In any event it is clear that this minor disturbance in no way affects the kinetic or O¹⁸ experiments.

The data in Table I show that in the absence of added solutes $k_\alpha/k_t = 5.40 \pm 0.3$. Thus $k_{rac}/k_t = 4.4$ and the absolute value of k_{rac} under these conditions is $18.6 \pm 0.3 \times 10^{-3} \text{ hr.}^{-1}$. From k_{rac}/k_t it is apparent that during solvolysis the unsolvolyzed ester becomes progressively racemic at a relatively fast rate—the half-period for racemization is 1/4.4 times that for destruction of the ester by solvolysis.

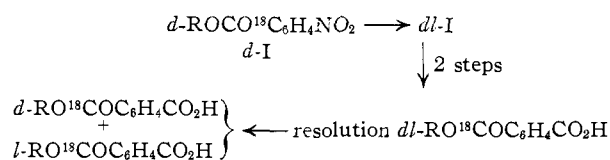
Internal return is substantially more important in the present system than in the 5-methyl-2-cyclohexenyl system. The values for k_α/k_t for the solvolysis of *cis*- and *trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoate in 80% acetone at 100° are 1.74 and 1.53, respectively.^{3b} Presumably these values would be about 30% higher in 90% acetone than in 80% acetone.¹⁵

The experiments in the lower part of the table show the effect of lithium *p*-nitrobenzoate and *p*-nitrobenzoic acid on k_α and k_t . These solutes cause a small increase in rate (salt effect) and have a somewhat greater effect on k_t than k_α . i.e., k_α/k_t is decreased. It is clear from these experiments that the discrepancy between k_α and k_t is due to internal return and that external return is not involved. If this were not the case k_{rac} would not be cleanly first order and would be increased considerably (at the expense of solvolysis) by the addition of the solutes (common-ion sources). It is significant that unsolvolyzed ester isolated after two half-lives for solvolysis (over eight half-lives for racemization) has an infrared spectrum indistinguishable from that of the original pure *trans*- α,γ -dimethylallyl *p*-nitrobenzoate. This provides additional evidence that the reactive conformation is the one indicated in the illustrations because the other conformation would result in the formation of *cis*-I.⁵ Thus internal return results only in the interconversion of the two *trans* optical antipodes. Similar behavior has been observed previously in this system⁵ and in the 5-methyl-2-cyclohexenyl system.^{3b} In the latter case, internal return results in the racemization of the isomeric *p*-nitrobenzoates without geometric isomerization.

We have used the same method as that used earlier to demonstrate that alkyl-oxygen cleavage is involved exclusively in the solvolysis.^{3b} The difference in reactivity between I and its saturated analog, 2-pentyl *p*-nitrobenzoate, is considerable. The latter compound is solvolyzed (probably by acyl-oxygen cleavage) only to the extent of about 0.6% in a period of time corresponding to 9.08

half-periods for the solvolysis of I. The difference in reactivity is at least a factor of 10³. Since both compounds would be expected to solvolyze by acyl-oxygen cleavage at about the same rate, clearly the allylic ester is reacting by a much more favorable process, i.e., alkyl-oxygen cleavage.

Oxygen-18 Experiments.—Carbonyl-O¹⁸ (+)-*trans*- α,γ -dimethylallyl *p*-nitrobenzoate (*d*-ROCO¹⁸C₆H₄NO₂) was partially solvolyzed in 90% acetone. The location of the label in the racemized unsolvolyzed *p*-nitrobenzoate was determined by the sequence summarized below. The *p*-nitrobenzoate was reduced with lithium aluminum hydride and the resulting *trans*- α,γ -dimethylallyl alcohol was converted to the acid phthalate (ROCO₂C₆H₄CO₂H) which was resolved. The O¹⁸ contents of the enantiomeric acid phthalates were determined. These values correspond to the O¹⁸ contents of the ether-oxygen atoms in the corresponding enantiomeric *p*-nitrobenzoates; the O¹⁸ contents of the carbonyl-oxygen atoms in the enantiomeric *p*-nitrobenzoates can be obtained by difference.



Optically pure *d*-ROCO¹⁸C₆H₄NO₂ was prepared from optically pure (+)-*trans*- α,γ -dimethylallyl alcohol (derived from (+)-acid phthalate) and carbonyl-O¹⁸ *p*-nitrobenzoyl chloride. In one experiment a 0.0485 molar solution of *d*-ROCO¹⁸-C₆H₄NO₂ (3.07 atom % excess O¹⁸)¹⁶ in 90% aqueous acetone was heated at 99.62° for 113.73 hr. From k_t and k_{rac} it can be calculated that 38% of the ester solvolyzed and the remaining ester was 88% racemic (i.e., 56% *d*-isomer and 44% *l*-isomer). In a control experiment using *dl*-ROCO¹⁸C₆H₄NO₂ it was found that unsolvolyzed ester isolated after 288 hr. contained the same amount of O¹⁸ as the original material. Thus there is no loss of O¹⁸ from the carboxyl group during racemization.

The unsolvolyzed *p*-nitrobenzoate was converted to the acid phthalate which was resolved. The (+)-acid phthalate (87.6% optically pure) contained 0.80 atom % excess O¹⁸ (calculated for one position labeled). The (−)-acid phthalate (43.6% optically pure) contained 1.76 atom % excess O¹⁸. These data provide two linear equations, the solution of which shows that the pure *d*-enantiomer contained 0.71 atom % excess O¹⁸ and the pure *l*-enantiomer contained 2.17 atom % excess O¹⁸. These values correspond to the O¹⁸ contents of the ether-oxygen atoms in the enantiomeric acid phthalates (and *p*-nitrobenzoates). The recovered *p*-nitrobenzoate contained 12% excess *d*-isomer which had not yet reacted and thus was labeled in the carbonyl position. Correcting for this contamination by unreacted starting material [(56/44) × 0.71] gives a value of 0.90 atom % excess O¹⁸ for *d*-isomer derived from the completely racemic *p*-nitrobenzoate, i.e., material which had reacted

(15) Cf. the values of k_α/k_t for solvolysis of *trans*- α,γ -dimethylallyl acid phthalate in 80% and 90% aqueous acetone; ref. 5.

(16) The O¹⁸ contents were determined in triplicate. The deviations from the mean were less than 1% of the average value.

(racemized). It is noteworthy that the sum of the O¹⁸ contents of the ether-oxygen atoms in the enantiomers (0.90 + 2.17) agrees with the total O¹⁸ content of the carboxyl group of the reactant. This clearly shows that rearrangement does not involve the process illustrated by V.¹⁷

The results of the experiment outlined above are presented in Table II together with the results of a similar experiment. In the latter case optically pure *d*-ROCO¹⁸C₆H₄NO₂ (3.07 atom % excess O¹⁸) was heated in 90% acetone at 99.62° for 206.33 hr. From k_t and k_{rac} it can be shown that under these conditions 58% of the ester is solvolyzed and the remaining ester is 98% racemic, *i.e.*, 51% *d*-isomer, 49% *l*-isomer. For this experiment the sum of the O¹⁸ contents of the enantiomers derived from completely racemic product [1.92 + 1.10 (51/49)]—the isolated material was contaminated with 2% of unreacted *d*-isomer—is 3.07 which agrees with the known O¹⁸ content of the carboxyl group.

TABLE II

OXYGEN-18 DATA FOR REARRANGEMENT (RACEMIZATION) OF CARBONYL-O¹⁸ *trans*- α,γ -DIMETHYLALLYL *p*-NITROBENZOATE IN 90% AQUEOUS ACETONE⁷ AT 99.6^{oa,16}

Compound	Optical purity, %	Atom % excess O ¹⁸ Obsd.	Corrected ^b
A. Product isolated after 113.7 hr.			
<i>d</i> -ROCO ¹⁸ C ₆ H ₄ NO ₂	100	3.07 ^c	3.07
<i>d</i> -RO ¹⁸ COC ₆ H ₄ CO ₂ H	87.6	0.80	0.71 ^d
<i>l</i> -RO ¹⁸ COC ₆ H ₄ CO ₂ H	43.6	1.76	2.17 ^d
B. Product isolated after 206.3 hr.			
<i>d</i> -ROCO ¹⁸ C ₆ H ₄ NO ₂	100	3.07 ^c	3.07
<i>d</i> -RO ¹⁸ COC ₆ H ₄ CO ₂ H	97.6	1.11	1.10 ^d
<i>l</i> -RO ¹⁸ COC ₆ H ₄ CO ₂ H	64.8	1.78	1.92 ^d

^a In each case the O¹⁸ was located in only one position; the values given are for the O¹⁸ content of this one position. ^b These values (calculated from observed values) correspond to the O¹⁸ content of the pure enantiomers. ^c This is the value for the original reactant. ^d Determined by solution of linear equations (see text).

It can be shown in another way that V does not contribute to the rearrangement (racemization). If there was a contribution of this type the rate of equilibration of the label between the two positions would be less than that of racemization. However, the data show these rates are the same. After 113.7 hr. (88% racemization) 44% of the label is in the ether-oxygen position [56 (0.71/3.07) + 44 (2.17/3.07)] and after 206.3 hr. (98% racemization) 48.9% of the label has shifted to the ether-oxygen position [51 (1.10/3.07) + 49 (1.92/3.07)].

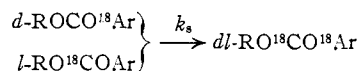
That the reactant, ROCO¹⁸C₆H₄NO₂, was discretely labeled in the carbonyl position and the method used to locate the label does not result in mixing of the oxygen atoms was shown by the following experiment. Carbonyl labeled *dl*-I (3.07 atom % excess O¹⁸) was converted to the acid phthalate by the series of reactions described above. The acid phthalate did not contain excess O¹⁸.

(17) Except for rearrangement by the process illustrated by V, the O¹⁸ content of carbonyl-oxygen in the *d*-enantiomer should be the same as that of the ether-oxygen in the *l*-enantiomer and *vice versa*. Thus if V is not involved, the sum should equal the O¹⁸ content of the carboxyl group.

In a series of 3 control experiments *dl*-ROCO¹⁸-C₆H₄NO₂ (3.86 atom % excess O¹⁸) was heated for 288 hr. at 99.64° in (a) 90% aqueous acetone, (b) 90% acetone containing 0.027 *M* *p*-nitrobenzoic acid and (c) 90% acetone containing 0.025 *M* lithium *p*-nitrobenzoate. This corresponds to over 7 half-periods for racemization of the unsolvolyzed ester. In each case the initial concentration of ester was 0.048 *M*. The unsolvolyzed ester isolated in these three experiments contained 3.85, 3.81 and 3.79 atom % excess O¹⁸. In each case the observed O¹⁸ content is well within the combined experimental uncertainties of the value of the original ester. These experiments clearly demonstrate that the rearrangement (racemization) is indeed completely intramolecular.

The O¹⁸ results (Table II) show that the oxygen atoms are scrambled in each enantiomer of the unsolvolyzed but rearranged ester. In each experiment the *d*-enantiomer, derived from that fraction of the ester which had racemized, had over half of the label in the carbonyl position. The *l*-enantiomer had over half of the label in the ether-oxygen position. From this it is apparent that in each interconversion there is a somewhat more than 50% chance that the carbonyl-oxygen atom in the reactant will become the ether-oxygen atom in the product, *i.e.*, the reaction shows a tendency to follow the course summarized by III. However, it is clear that there is a rather large probability that the oxygen atoms will become scrambled during the rearrangement. Thus, qualitatively, the results correspond to a situation somewhere between the first and third possibilities discussed in the introduction. It is significant in this connection that rearrangement (and scrambling) by the process illustrated by V definitely can be ruled out.

The first-order rate constant for scrambling of the oxygen atoms (k_s) during the rearrangement can be determined from the data in Table II and the composition of the ester at the time of isolation. This constant is given by $k_s = (1/t) \ln 100/Z$, where Z is the percentage of the ester in which the oxygen atoms have not been equilibrated. This constant is for the process



The symbol *dl*-RO¹⁸CO¹⁸Ar represents ester in which the label is equally divided between the two positions in each enantiomer. If there were no scrambling both enantiomers would be discretely labeled, the *d*-isomer in the carbonyl position and the *l*-isomer in the ether-oxygen position. The percentage of the *d*-enantiomer in which the oxygen atoms are scrambled (equilibrated) is two times the percentage labeled in the ether-oxygen position and the percentage of *l*-enantiomer which is equilibrated is two times the percentage labeled in the carbonyl position. The remaining *d* and *l* material is unreacted (discretely labeled). The values of Z for 113.7 and 206.3 hr. are given by

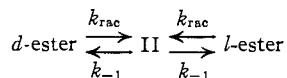
$$Z_{113.7 \text{ hr.}} = 100 - 2[56(0.71/3.07) + 44(0.90/3.07)] = 48.30$$

$$Z_{206.3 \text{ hr.}} = 100 - 2[51(1.10/3.07) + 49(1.15/3.07)] = 26.74$$

The constant (k_s) calculated for the data at 113.7 hr. is 6.40×10^{-3} hr.⁻¹. That for the data at 206.3 hr. is 6.39×10^{-3} hr. This agreement shows that oxygen scrambling is a first-order process. The average value for k_s is 6.4×10^{-3} hr.⁻¹ and $k_{rac}/k_s = 18.6/6.4 = 2.9$. Thus the oxygen atoms become equilibrated 1/2.9 times as fast as the ester racemizes.

Discussion

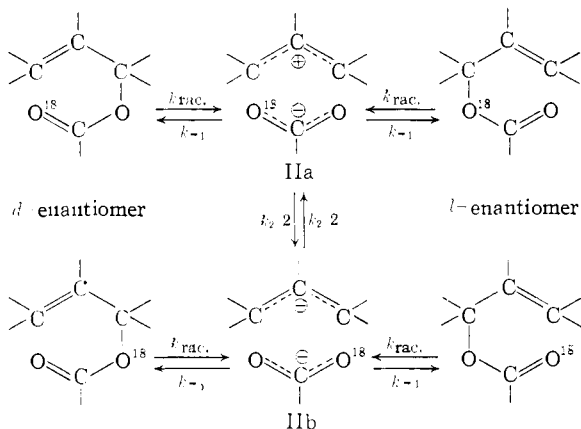
The present data are consistent with the idea³⁻⁵ that the intramolecular rearrangement (racemization) involves an intermediate which can best be described as an internal ion pair.⁶ If this interpretation is correct the racemization can be summarized as



In this scheme k_{rac} is the rate constant for the production of that fraction of the intermediate (II) involved in the racemization, *i.e.*, the fraction of the intermediate that is converted to solvolysis product in no way disturbs the first-order equilibration.

The O¹⁸ experiments provide pertinent information concerning structural details of the intermediate (II). From the present and earlier work^{3b,5} it is clear that the bonding in II is such that the rearrangement is completely intramolecular and stereospecific. It is also apparent from the sensitivity of the rate of production of the intermediate (k_a) toward variation of the ionizing power of the solvent that this type of intermediate has considerable polar character.³⁻⁵ Now it is shown that the bonding between the allyl moiety and the migrating ester group in II is such that the oxygen atoms become equivalent at a rate somewhat slower than that of rearrangement.

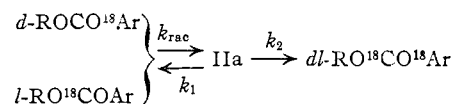
To include the O¹⁸ results it is necessary to expand the earlier mechanism^{3,5} (summarized above) as shown in the accompanying scheme. Evidently



in the ion-pair intermediate II, the configuration corresponding to an energy minimum is that in which the plane of the carboxylate ion is perpendicular to and intersects the plane of the allyl cation at the terminal carbon atoms. This minimum is separated by a rather low energy barrier from the equivalent structure derived by rotating the car-

boxyl group 180°. In fact the barrier for the interconversion of IIa and IIb is not much greater than that for return to *dl*-ester. Presumably the bonding in II is largely or completely electrostatic as indicated in the illustrations. However, as was pointed out during the early development of the theory with which we are herein concerned, the cation-anion interaction in species of this type may have some covalent character.¹⁸ An excellent discussion concerning the nature of the bonding in internal ion-pair intermediates has appeared recently.¹⁴

The significance of the relative rates of racemization and oxygen scrambling can perhaps best be discussed using the abbreviated scheme shown below. In this scheme k_{rac} is the constant for the production of the internal ion-pair intermediate IIa. The constant k_2 is the rate constant for equilibration of IIa and IIb, *i.e.*, two times the constant for conversion of IIa to IIb, and k_1 corresponds to $2k_{-1}$.



From this scheme it can be seen that

$$k_s = k_{rac}([k_2/(k_1 + k_2)])$$

thus

$$k_{rac}/k_s = 1 + k_1/k_2$$

Since $k_{rac}/k_s = 2.9$, $k_1/k_2 = 1.9$. Thus the intermediate IIa returns to racemic ester without scrambling 3.8 times faster than it is converted to IIb. From the above ratios it can be shown that II gives unscrambled product 4.8 times faster than it gives product with inverse labeling. In other words, II is partitioned so that 17.2% of the product has inverse labeling (34.4% of the product is scrambled).

The present results are similar to those reported by Denney and Goldstein¹⁹ for the isomerization of 2-phenyl-1-propyl bromobenzenesulfonate to 1-phenyl-2-propyl bromobenzenesulfonate in acetic acid. In this case it was found that the oxygen atoms undergo partial equilibration during the rearrangement.

According to the present interpretation one might expect an inverse relationship between k_{rac}/k_s and the ionizing power of the solvent and there is evidence that this is the case. The rearrangements of α -phenylallyl *p*-nitrobenzoate in chlorobenzene⁸ and α -phenyl- γ -methylallyl *p*-nitrobenzoate in benzene, acetone, acetic anhydride and acetonitrile⁹ to the γ -phenylallyl esters apparently do not result in any scrambling. On the other hand, in the present system 34.4% of the material is scrambled on each pass through the intermediate. In other problems we are investigating the effect of varying structure and solvent on k_{rac}/k_s for the racemization of symmetrical allylic esters.

(18) S. Winstein and K. C. Schreiber, *THIS JOURNAL*, **74**, 2171 (1952).

(19) D. B. Denney and B. Goldstein, *ibid.*, **79**, 4948 (1957).

Experimental²⁰

Materials.—(+)-*trans*- α,γ -Dimethylallyl acid phthalate, m.p. 80.7–83.5°, $[\alpha]_D^{25}$ 38.0° (lit.⁵ m.p. 78–83.6°, $[\alpha]_D^{25}$ 35.4°), was prepared as described in an earlier paper.⁵ The specific rotations of this material was not increased by additional recrystallizations of (a) the acid phthalate or (b) the brucine salt of the acid phthalate. The acid phthalate was reduced with LiAlH₄ to the alcohol⁵ which was converted to (+)-*trans*- α,γ -dimethylallyl *p*-nitrobenzoate, m.p. 45.7–46.7° (pentane), $[\alpha]_D^{25}$ 42.5° (*l* 4, *c* 2, CHCl₃) (lit.²¹ m.p. 48°, $[\alpha]_D$ 45.0°), by the general method described earlier.²²

Anal. Calcd. for C₁₂H₁₃NO₄: C, 61.27; H, 5.57. Found: C, 61.22; H, 5.36.

Optically active *trans*- α,γ -dimethylallyl *p*-nitrobenzoate has a different crystal form from racemic material and optically pure material can be obtained readily by recrystallization (pentane) of the *p*-nitrobenzoate which is nearly optically pure.

2-Pentyl *p*-nitrobenzoate, m.p. 28.5–29.0° (pentane), was prepared from pure (gas chromatography) 2-pentanol.²³

Anal. Calcd. for C₁₂H₁₅NO₂: C, 60.75; H, 6.37. Found: C, 61.00; H, 6.71.

Lithium *p*-nitrobenzoate was prepared by titrating reagent grade *p*-nitrobenzoic acid with lithium methoxide in absolute methanol to the equivalence point (Beckman pH meter). After removal of the solvent the residual salt was purified by recrystallization from aqueous ethanol.

p-Nitrobenzoyl Chloride-carbonyl-O¹⁸.—To a solution of 10 g. (0.555 mole) of H₂O¹⁸ (6–7 atom % oxygen-18)²⁴ in 175 ml. of dry tetrahydrofuran was added 74 g. (0.40 mole) of *p*-nitrobenzoyl chloride. The solution was stirred for 24 hr. at room temperature after which the solvent and excess water were removed under high vacuum. The crude acid was treated with 94.5 g. (0.80 mole) of thionyl chloride in 150 ml. of toluene. After refluxing for 18 hr., the solvent and excess thionyl chloride were removed under vacuum. The *p*-nitrobenzoyl chloride-carbonyl-O¹⁸ was vacuum distilled at 0.2 mm. (125°) and recrystallized from dry CCl₄. The over-all yield was 56 g., 75.5%, m.p. 72–73°.

Kinetic Experiments.—All standard solutions were prepared at 25°. The polarimetric and titrimetric rates were determined by the previously described methods.^{3,4} In the polarimetric experiments the total change in rotation was > 2° and individual measurements were reproducible to within 0.01°. The ampule technique was used in the titrimetric experiments³ and the reaction was followed by titrating 5 ml. aliquots (measured at 25°) to the brom thymol blue endpoint with 0.04845 *N* NaOH. The results of the kinetic experiments are summarized in Table I.

Determination of O¹⁸ Content.—An Unterzucker apparatus^{25,26} was used to convert the oxygen-containing substances

to carbon dioxide.²⁷ The temperature of the carbon-packed tube was maintained at 1120–1150°. There was little if any memory effect. The O¹⁸ determinations were done in triplicate and the scatter was usually less than 1% of the observed value.

The O¹⁸ content of the carbon dioxide was determined with a Consolidated model 21–260 recording mass spectrometer. The atom fraction O¹⁸, X in the compound was determined from the equation,²⁸ $X = R'/(1 + R')$, where $R' = (R_s/R_t) 0.00409 - 0.00204$. In the latter equation R_s and R_t are the mass ratios of 46/44 peaks for the CO₂ from the sample (R_s) and for CO₂ containing the normal abundance of O¹⁸ (R_t). The atom % excess O¹⁸ for the one oxygen atom in the CO₂ that is derived from the sample is $100(X - 0.00204)$. If all of the oxygen atoms in the sample are not labeled this value must be multiplied by the appropriate factor to give the O¹⁸ content (as atom % excess) for the labeled positions.

Isolation and Reresolution of Unsolvolyzed Partially Racemic *trans*- α,γ -Dimethylallyl *p*-Nitrobenzoate-carbonyl-O¹⁸.—One liter of a 0.049 *M* solution of (+)-*trans*- α,γ -dimethylallyl *p*-nitrobenzoate-carbonyl O¹⁸ (3.07 atom % excess) in 90% aqueous acetone⁷ was solvolyzed in each of two experiments. The material was sealed in glass bombs and heated at 99.63 ± 0.03° for 3 and 5.5 half-lives, respectively, for racemization of the ester as measured by ($k\alpha - k_t$). After the reaction period the solvent was removed at room temperature under reduced pressure. The dry residue was extracted several times with pentane to separate the soluble α,γ -dimethylallyl *p*-nitrobenzoate from the insoluble *p*-nitrobenzoic acid. The pentane was removed under vacuum and the crude residual *trans*- α,γ -dimethylallyl *p*-nitrobenzoate²⁹ was reduced to *trans*- α,γ -dimethylallyl alcohol with LiAlH₄. In a typical experiment 4.70 g. (0.02 mole) of recovered crude *p*-nitrobenzoate in 50 ml. of ether was added to a solution of 2.3 g. (0.06 mole) of LiAlH₄ in ether at 0° with vigorous stirring. The solution was stirred for 8 hr. at room temperature after which 20 ml. of a saturated aqueous ammonium chloride solution was added. The ether layer was separated, dried over MgSO₄, concentrated, dried again, and finally concentrated to less than 5 ml. In order to remove non-volatile impurities (*e.g.*, azo compounds formed in the reduction) the material was distilled under high vacuum at room temperature. Most of the ether was removed and the residual alcohol was converted to its acid phthalate derivative and resolved.⁵ The O¹⁸ content of the pure resolved acid phthalates were determined. The (+)-isomer was nearly optically pure and the (–)-isomer was about 85% optically pure. In all cases samples for O¹⁸ determinations were shown to be pure by physical properties including infrared spectra. The results of these experiments are presented in Table II.

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(20) S. J. Clark, "Qualitative Methods of Organic Microanalysis," Butterworths Scientific Publications, London, 1956.

(21) See W. E. Doering and E. Dorfman, *THIS JOURNAL*, **75**, 5595 (1953); M. L. Bender and K. C. Kemp, *ibid.*, **79**, 118 (1957); D. B. Denney and M. A. Greenbaum, *ibid.*, **79**, 979 (1957).

(22) W. G. Miller and L. Anderson, *Anal. Chem.*, **31**, 1669 (1959).

(23) The infrared spectra of the samples of unsolvolyzed *p*-nitrobenzoate isolated in this manner were indistinguishable from that of pure *trans*- α,γ -dimethylallyl *p*-nitrobenzoate.

(20) All melting points are corrected.

(21) H. W. J. Hill, J. Kenyon and H. Phillips, *J. Chem. Soc.*, 576 (1936).

(22) H. L. Goering and J. P. Blanchard, *THIS JOURNAL*, **76**, 5405 (1954).

(23) H. C. Brown and O. H. Wheeler, *ibid.*, **78**, 2199 (1956).

(24) Oxygen-18 enriched water was obtained from the Weizmann Institute of Science.

(25) A. Steyermark, "Qualitative Organic Microanalysis," Blakiston and Co., Philadelphia, Pa., 1951.