[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN, MADISON 6, WIS.]

The Solvolysis and ^{18}O-Equilibration of Benzhydryl *p*-Nitrobenzoate-*carbonyl*-^{18}O in Aqueous Acetone[1]

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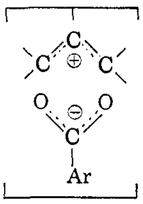
Solvolysis of *carbonyl*-^{18}O benzhydryl *p*-nitrobenzoate in 90% aqueous acetone is accompanied by equilibration of the carboxyl oxygen atoms in the unsolvolyzed ester. Both solvolysis (k_s) and oxygen-equilibration (k_{eq}) are cleanly first order and $k_{eq}/k_s = 3$. The kinetic behavior and the slow rate of exchange between ester and *p*-nitrobenzoic acid show that equilibration of the carboxyl oxygen atoms is intramolecular; *i.e.*, the *p*-nitrobenzoate moiety remains associated with the original alkyl group. Evidently, equilibration involves ion-pair return (probably internal return) from an ion-pair intermediate in which the carboxylate oxygen atoms are equivalent. The intramolecular mixing of oxygen atoms associated with solvolysis of reactive esters provides a method for measuring ion-pair return in systems in which the alkyl moiety does not rearrange or racemize.

Introduction

Solvolyses of optically active symmetrical allylic esters (alkyl–oxygen cleavage) are accompanied by internal return which results in racemization (allylic rearrangement) of the unsolvolyzed ester.[3-5] These asymmetric substrates give rise to symmetrical carbonium ions (the allylic carbon atoms are equivalent) and thus substrate, reformed by internal return, is racemic. With carbonyl-[4] or ether-oxygen-^{18}O α,γ-dimethylallyl *p*-nitrobenzoate,[6] the first-order rates of racemization (k_{rac}, eq. 1)[7] and carboxyl oxygen equilibration (k_{eq}, eq. 2) of the unsolvolyzed ester are equal for a variety of conditions. Similarly, $k_{rac} = k_{eq}$ for the *cis*-5-methyl-2-cyclohexenyl system.[5,8] This means that in the ion-pair intermediate the two allylic carbon atoms in the cation are equivalent as are the carboxyl oxygen atoms in the anion as illustrated by I.[9] The complete agreement between these two independent methods for measuring internal return indicates beyond all reasonable doubt that each measures total internal return. Or in other words, in these systems the total rate of ionization is measured by either the rate at which the carbon atoms in the allyl moiety become equivalent, k_α (polarimetric rate constant), which is equal to racemization plus solvolysis ($k_{rac} + k_s$), or the rate at which the carboxyl oxygen atoms become equivalent ($k_{eq} + k_s$).

$$(active)\text{-ROCOC}_6\text{H}_4\text{NO}_2 \xrightarrow{k_{rac}} dl\text{-ROCOC}_6\text{H}_4\text{NO}_2 \quad (1)$$

$$\text{ROC*OC}_6\text{H}_4\text{NO}_2 \xrightarrow{k_{eq}} \text{R*OC*OC}_6\text{H}_4\text{NO}_2 \quad (2)$$



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Recently it was discovered that in the *trans*-5-methyl-2-cyclohexenyl *p*-nitrobenzoate system, carboxyl oxygen equilibration in the unsolvolyzed ester is about twice as rapid as racemization.[5] Moreover, according to all criteria which were applied (*e.g.*, intramolecularity, kinetics and solvent effects), both phenomena result from ion-pair return (presumably internal return). This remarkable observation was of special interest because it has heretofore been assumed that with substrates of this type the polarimetric rate (k_α) corresponds to the total rate of ionization.[3,10] Clearly, in this system k_{rac} does not measure total internal return and thus k_α does not measure total rate of ionization. It is significant that in allylic systems of this sort there are no uncertainties concerning the time-independent equivalence of the allylic carbon atoms in the cation.

The above observations indicated that equilibration of carboxyl oxygen atoms is at least as reliable for detecting and measuring internal return as is racemization (rearrangement). Moreover, it was apparent that this method should be applicable to systems which do not rearrange. The possibility of using carboxyl oxygen equilibration for detecting internal return was investigated several years ago with negative results—*ether*-^{18}O 2,4-dimethylhex-4-yl acid phthalate remains discretely labeled during solvolysis.[11]

In work described in this paper we have examined the solvolysis of carbonyl-^{18}O benzhydryl *p*-nitrobenzoate in 90% aqueous acetone and found that the carboxyl oxygen atoms of the unsolvolyzed ester are indeed equilibrated during solvolysis.[12]

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[1] This work was reported in part in *Tetrahedron Letters*, 644 (1961), and before the Division of Organic Chemistry, A.C.S. Meeting, Chicago, Ill., Sept., 1961.

[2] National Science Foundation Predoctoral Fellow, 1959–1962.

[3] H. L. Goering, *Rec. Chem. Prog.*, **21**, 109 (1960).

[4] H. L. Goering and M. M. Pombo, *J. Am. Chem. Soc.*, **82**, 2515 (1960).

[5] H. L. Goering and J. T. Doi, *ibid.*, **82**, 5850 (1960).

[6] Unpublished work by M. M. Pombo and K. D. McMichael.

[7] The first-order rate constant for racemization of the unsolvolyzed substrate is determined from the relationship $k_{rac} = k_\alpha - k_s$ where k_α and k_s are the first-order rate constants for loss of optical activity and solvolysis, respectively.

[8] Unpublished work by K. D. McMichael and J. T. Doi.

[9] As pointed out earlier,[3-5] in this structure the carboxyl oxygen atoms and the allylic carbon atoms are presumably in a plane perpendicular to that of the allyl cation. Whether the plane of the carboxyl group relative to that of the cation is parallel *exo*, parallel *endo* or perpendicular is not known.

[10] S. Winstein and G. C. Robinson, *J. Am. Chem. Soc.*, **80**, 169 (1958), and references therein.

[11] W. E. Doering, A. Streitwieser, Jr., and L. Friedman, unpublished work cited by A. Streitwieser, Jr., *Chem. Revs.*, **56**, 663 (1956).

[12] Mr. R. Briody of these laboratories has investigated the solvolysis of *carbonyl*-^{18}O *t*-butyl *p*-nitrobenzoate in 80% aqueous acetone. In this case equilibration of oxygen atoms (internal return) is nil. Ester isolated after one solvolytic half-life is less than 1% equilibrated. The absence of internal return in this tertiary system parallels the results reported in ref. 11.

Results

First-order rate constants (k_s) for solvolysis of benzhydryl *p*-nitrobenzoate in 90% aqueous acetone[13] at 118.6° are given in Table I. These reactions were followed to about 75% completion by titration of the *p*-nitrobenzoic acid produced by the reaction. Aliquots were distributed in ampules which were flushed with nitrogen prior to sealing to prevent acid formation by oxidation of the reaction mixtures.[14]

The data show that addition of *p*-nitrobenzoic acid (expt. 2–5) or lithium *p*-nitrobenzoate (expt. 6) results in an appreciable positive salt effect. In these experiments good first-order behavior was observed. Each value of k_s is the average and average deviation of 5 to 8 integrated constants determined for various degrees of reaction. In the absence of added acid or salt (expt. 1) the integrated constants showed a small but consistent upward trend. From the effect of small amounts of added *p*-nitrobenzoic acid it is apparent that this upward trend in k_s results from increase in acid concentration (ionizing power of the medium) during solvolysis. For this experiment the initial rate constant (obtained by extrapolation to zero per cent reaction) is given as well as the average of the integrated constants.

TABLE I

FIRST-ORDER RATE CONSTANTS FOR SOLVOLYSIS OF BENZHYDRYL *p*-NITROBENZOATE IN 90% AQUEOUS ACETONE AT 118.6°

Expt.	[Ester], 10^2 M	[Solute], 10^2 M	k_s,^{a} 10^3 hr.$^{-1}$
1	4.72	None	(5.54)^b 6.37 ± 0.34^a
2	4.98	1.49 HOPNB^c	6.71 ± .12
3	4.95	2.94 HOPNB^c	7.02 ± .09
4	4.58	4.24 HOPNB^c	7.64 ± .16
5	4.10	4.26 HOPNB^c	7.50 ± .05
6	4.44	4.54 LiOPNB^c	11.6 ± .5

^{a} Average (and average deviation) of 5 to 8 values obtained for each kinetic experiment. ^{b} Initial rate constant obtained by extrapolation to zero time. ^{c} HOPNB and LiOPNB refer to *p*-nitrobenzoic acid and lithium *p*-nitrobenzoate, respectively.

The rate constant for equilibration of carboxyl oxygen atoms in the unsolvolyzed ester (k_{eq}, eq. 2) in 90% aqueous acetone at 118.6° was determined using benzhydryl *p*-nitrobenzoate-*carbonyl*-^{18}O. Unsolvolyzed ester was isolated after appropriate reaction times and the ^{18}O contents were determined.[4] This value remained constant during the solvolysis. The distribution of the label in the carboxyl group was determined as follows. The ester was reduced with lithium aluminum hydride and the resulting benzhydrol was reconverted to its *p*-nitrobenzoate derivative which was purified and analyzed for ^{18}O content.[15] The latter value corresponds to the ^{18}O abundance of the ether oxygen atom of the unsolvolyzed ester. Control experiments with discretely labeled benzhydryl *p*-nitrobenzoate showed that (a) isolation and purification (chromatography followed by recrystallization) of the *p*-nitrobenzoate does not alter the distribution of the label in the carboxyl group, and (b) reduction with lithium aluminum hydride gives benzhydrol with an ^{18}O content the same as that of the ether oxygen position in the ester.

The first-order rate constants for equilibration (eq. 2) were calculated as described previously.[5] Kinetic data, including the extent of solvolysis at the time of isolation of the unsolvolyzed ester, are presented in Table II. These data show that equilibration is cleanly first order and sufficiently more rapid than solvolysis (about 3 times faster) so that equilibration can be followed to near completion.

TABLE II

EQUILIBRATION OF CARBOXYL OXYGEN ATOMS DURING SOLVOLYSIS OF BENZHYDRYL *p*-NITROBENZOATE IN 90% AQUEOUS ACETONE AT 118.6°^{a}

Time, hr.	Solvolysis, % reacted^b	^{18}O-content, atom % excess^c	Equilibration, % reacted^d	k_{eq}, 10^3 hr.$^{-1}$
0	0	0	0	
21.0	12.5	0.54 ± 0.03	32.3	18.7
52.2	28.3	1.04 ± .01	62.3	18.7
103.0	48.1	1.43 ± .01	85.6	18.8

^{a} Initial carbonyl-^{18}O content = 3.34 ± 0.07 atom % excess. ^{b} Calculated from $k_s = 6.37 \times 10^{-3}$ hr.$^{-1}$. ^{c} Atom % excess ^{18}O and average deviation (determinations made in triplicate) of ether oxygen atom in recovered unsolvolyzed ester. ^{d} Percentage of unsolvolyzed ester which has equal amounts of label in the carbonyl and ether oxygen positions.

The first-order rates of solvolysis (followed to 75% completion) and oxygen equilibration (followed to 86% completion) show that the latter must be largely or completely intramolecular (*i.e.*, the *p*-nitrobenzoyloxy group remains associated with the same alkyl group). As shown in Table II, oxygen equilibration is relatively rapid and over 85% complete at one solvolytic half-life. Or in other words, at this point 85% of the unsolvolyzed ester has been reformed by ion-pair return. Were this extensive equilibration intermolecular (reformation of equilibrated ester by (a) reaction of the carbonium ion with *p*-nitrobenzoate ion or *p*-nitrobenzoic acid or (b) Fisher esterification of solvolysis product) neither solvolysis nor equilibration could be first-order. The only *p*-nitrobenzoic acid present is that produced by solvolysis. Thus intermolecular equilibration would be nil at the outset and increase as the reaction progressed. Similarly, equilibration by such a process would be at the expense of solvolysis and k_s would show a large downward trend.

The intramolecularity of the oxygen equilibration was established independently by determining the rate of exchange of unsolvolyzed ester with ^{14}C-labeled *p*-nitrobenzoic acid in the medium. In these experiments benzhydryl *p*-nitrobenzoate was solvolyzed in 90% acetone containing *p*-nitrobenzoic acid-7-^{14}C at 118.6° (*i.e.*, the conditions for the oxygen equilibration experiments except

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

(14) (a) H. L. Goering and W. D. Closson, *J. Am. Chem. Soc.*, **83**, 3511 (1961); (b) M. S. Silver, *ibid.*, **83**, 404 (1961).

(15) The ^{18}O-content of the *p*-nitrobenzoate derivative, rather than of benzhydrol itself, was determined so that all comparisons involved the same compound. Occasionally discrepancies have been observed between the reproducible ^{18}O-contents of alcohols and their *p*-nitrobenzoate derivatives.

for the added acid). At appropriate time intervals samples of unsolvolyzed ester were isolated and the amount of radioactivity incorporated was determined.[16]

Under the conditions investigated (initial acid concentrations of 0.0294 *M* and 0.0149 *M*) the rate of exchange is first order in both ester and *p*-nitrobenzoic acid. The second-order exchange constant (k_{exc}) was calculated using eq. 3 which is rigorous for a system of the present type.[17] In this equation $[RX]_0$ and $[HX^*]_0$ represent the initial concentrations of ester and labeled acid, respectively. The asterisk signifies material which is labeled to the same extent (same activity) as the starting labeled acid. Activities (microcuries/mmole) of the unsolvolyzed ester and of the original acid are symbolized by α_{RX} and α_{HX}. The latter value was obtained by converting a sample of labeled acid to its benzhydryl ester derivative and determining the activity of the ester. Thus all activities used to compute the exchange constant were for carefully purified samples of the same compound.

$$k_{exc} = \frac{-1}{t([HX^*]_0 + [RX]_0)} \times \ln\left\{1 - \frac{\alpha_{RX}}{\alpha_{HX}}\left[\frac{[HX^*]_0 + [RX]_0}{[HX^*]_0}\right]\right\} \quad (3)$$

Equations for calculating exchange constants for situations of the present type (*i.e.*, systems in which exchange occurs between two species and simultaneously one is converted to the other by a first-order process) have been derived by Luehr, Challenger and Masters[18] and by Koskoski, Dodson and Fowler.[19] It may be shown that their expressions are equivalent to eq. 3. This type of system has also been investigated by Swart and le Roux.[20] Their treatment leads to a differential equation (misprinted in their paper) which upon integration gives an expression (also misprinted) equivalent to eq. 3.

The results of two exchange experiments, involving different acid concentrations, are presented in Table III. Clearly the data are correlated by eq. 3 or in other words exchange is second order over the 4.5 fold variation of acid concentration; in experiment B the initial acid concentration was 0.015 *M* and in experiment A the final acid concentration (at 210 hr.) was 0.066 *M*.

The percentage of the unsolvolyzed ester which has undergone exchange can be determined for any time from the second-order exchange constant ($k_{exc} = 2.02 \times 10^{-2}$ l. mole^{-1} hr.$^{-1}$) and the average acid concentration $[HX]_{avg}$. The latter for any period from zero time to time t is $(1/t)\int_0^t [HX]dt$. Acid is produced by first-order solvolysis and, since k_s is known, $[HX]$ is a known function of t. Thus

$$[HX]_{avg} = [RX]_0\,[1 + (1/k_st)(e^{-k_st} - 1)] + [HX]_0 \quad (4)$$

The product, $k_{exc}[HX]_{avg}$, is a pseudo-first-order constant which applies for the same period as $[HX]_{avg}$, and the percentage of ester which has reacted at any time can be determined from this "constant" with eq. 5.

$$\%\ \text{exchange} = 100\,(1 - e^{-k_{exc}[HX]_{avg}t}) \quad (5)$$

TABLE III

DATA FOR SECOND-ORDER EXCHANGE BETWEEN BENZHYDRYL *p*-NITROBENZOATE AND *p*-NITROBENZOIC ACID-7-^{14}C IN 90% AQUEOUS ACETONE AT 118.6°

Time, hr.	α_{RX},[c] 10^4 μc./mmole	10^2k_{exc},[d] l. mole^{-1} hr.$^{-1}$	Ester[e] exchanged, %
(A) $10^2[\text{ester}]_0$[a] = 4.95; $10^2[HA]_0$[a] = 2.94; $10^4\alpha_{HX}$ = 580 ± 13 μc/mmole[b]			
21.00	6.77 ± 0.03	1.90	1.38
52.17	16.8 ± .1	1.96	3.87
103.00	32.4 ± .6	1.99	8.69
210.00	62.7 ± .6	2.07	20.1
	Av.	1.98 ± 0.05	
(B) $10^2[\text{ester}]_0$[a] = 4.98; $10^2[HA]_0$[a] = 1.49, $10^4\alpha_{HX}$ = 634 ± 6 μc./mmole[b]			
48.50	8.8 ± 1.9	1.98	2.15
96.00	18.4 ± 0.4	2.17	5.28
192.50	32.1 ± 1.4	2.00	13.3
	Av.	2.05 ± 0.08	

[a] Initial ester and labeled acid concentrations. [b] Activity of labeled acid (see ref. 16) counted as benzhydryl ester and average deviation of three countings. [c] Activity of unsolvolyzed ester and average deviation of three countings. [d] Second-order exchange constant calculated from eq. 3. [e] % of ester which has exchanged at time t calculated from eq. 5 using $k_s = 7.02 \times 10^{-3}$ hr.$^{-1}$ for A and 6.71×10^{-3} hr.$^{-1}$ for B.

Values for the amount of ester which has exchanged at various times are included in Table III. It is immediately apparent that even at the highest acid concentration, exchange is slow relative to oxygen equilibration (*cf.* fourth columns in Tables II and III).

The amount of exchange which occurred during the ^{18}O equilibration experiments (Table II) can be determined from eq. 5. In this case the only acid available for exchange is that produced by solvolysis (*i.e.*, $[HX]_0 = 0$). These calculations show that at 103 hours, at which time oxygen equilibration is 86% complete, only 2.6% of the unsolvolyzed ester has exchanged with the acid formed by solvolysis. Thus oxygen equilibration is almost completely intramolecular.

Discussion

From the present and related[4,5] results there is little doubt but that the intramolecular oxygen equilibration which accompanies solvolysis of benzhydryl *p*-nitrobenzoate results from ion-pair return.[21] Thus equilibration and solvolysis may be summarized

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(16) The ^{14}C contents, α (microcuries per millimole corrected for background and efficiency of counting), were determined with a Packard Tri-Carb liquid scintillation spectrometer model 314-DC (toluene–2,5-diphenyloxazole solution). We are indebted to Professor C. Heidelberger, University of Wisconsin, for making these facilities available.

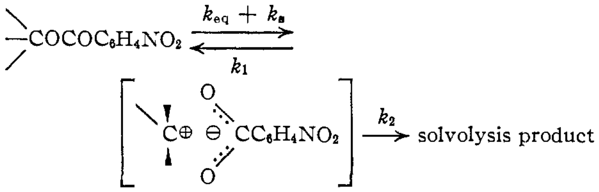
(17) We are indebted to Professor E. L. King for helpful discussions concerning treatment of the exchange data.

(18) C. P. Luehr, G. E. Challenger and B. J. Masters, *J. Am. Chem. Soc.*, **78**, 1314 (1956).

(19) W. Koskoski, R. W. Dodson and R. D. Fowler, *ibid.*, **63**, 2149 (1941).

(20) E. R. Swart and L. J. le Roux, *J. Chem. Soc.*, 21106 (195).

(21) In other work we have observed that the effect of change in structure and solvent polarity on the rates of equilibration and solvolysis with benzhydryl systems is consistent with this interpretation.



I

According to this scheme, oxygen equilibration results from internal return from an intimate ion pair I in which the carboxyl oxygen atoms are equivalent. The nature of the product-forming step (k_2) has not yet been elucidated. A solvent-separated ion pair[22] as well as the dissociated carbonium ion may be involved and external ion pair return[22] may contribute to the oxygen equilibration. In other work, we are investigating exchange reactions (with labeled common ion salts and other nucleophiles) to learn more about this part of the reaction.

If the carboxyl oxygen atoms are equivalent in the first intermediate (I), *i.e.*, if return without equilibration does not occur, k_{eq} measures total return and the rate constant for ionization is $k_{eq} + k_s$. There is evidence that this is the case. As mentioned in the introduction, three systems have been investigated in which ion pair return can be independently determined by racemization (k_{rac}) and oxygen equilibration (k_{eq}). In two of these both methods give the same result and in the third equilibration exceeds racemization. Thus it would seem that the oxygen atoms in I are equivalent. According to this interpretation the present results (Tables I and II) show that the rate of ionization ($k_{eq} + k_s$) is four times that of solvolysis and I is partitioned so that $k_1/k_2 = k_{eq}/k_s = 3$. If the oxygen atoms in I are not equivalent $k_{eq} + k_s$ does not measure total ionization but rather represents a lower limit. In any event, since return without equilibration cannot be detected, separation to a degree so that the carboxyl oxygen atoms become equivalent represents an operational criterion for ionization.

The present results show that oxygen equilibration is a useful method for detecting ion pair return in systems in which the alkyl moiety does not rearrange. Two techniques have been used earlier which are applicable in such systems. One of these involves interception of an intermediate, which would otherwise return, with an added salt (special salt effect).[22,23] The other involves comparison of rates of racemization and radio-chloride exchange of substituted benzhydryl chlorides.[24] The first of these does not detect internal return[22] and the latter does not detect that portion of the return which occurs with retention of configuration.

On the other hand, the present method is unique in that total ion pair return regardless of type or stereochemistry is measured. Moreover, optically active substrates are not required. The major limitation to this method is that reactive systems are required so that ionization involves alkyl-oxygen cleavage of the ester.

Experimental

Materials.—Benzhydryl *p*-nitrobenzoate, m.p. 133.4–134.0° (petroleum ether) (lit.[14b] 131–133°), was prepared from benzhydrol and *p*-nitrobenzoyl chloride in the usual manner.[4] *Carbonyl*-^{18}O benzhydryl *p*-nitrobenzoate was prepared in the same way using *carbonyl*-^{18}O *p*-nitrobenzoyl chloride.[4]

p-Nitrobenzoic acid-7-^{14}C was prepared by oxidation[25] of 10 g. of *p*-nitrotoluene to which had been added 28 mg. (200 μc.) of a 40:60-*ortho–para* mixture of 7-^{14}C-labeled nitrotoluenes (Nuclear Research Chemicals, Inc., Orlando, Fla.). After two recrystallizations from glacial acetic acid the labeled acid was diluted to the desired activity with *p*-nitrobenzoic acid and recrystallized twice more to ensure uniform distribution of the label and complete removal of the trace of radioactive *o*-nitrobenzoic acid.

The solvent, 90% aqueous acetone,[18] used in the kinetic experiments, was prepared from 9 volumes of purified acetone[26] and one volume of conductivity water.

Kinetic Experiments. (A) Rates of Solvolysis.—All concentrations correspond to 25°. The ampule technique was used in the solvolysis experiments and the reaction was followed by titration of 5-ml. aliquots with standard sodium hydroxide to the phenolphthalein endpoint. In these experiments ampules containing the aliquots were flushed with nitrogen prior to sealing. The results of these experiments are summarized in Table I.

(B) **Rates of Carboxyl-oxygen Equilibration.**—Three 100-ml. portions of a 0.0481 *M* solution of *carbonyl*-^{18}O benzhydryl *p*-nitrobenzoate (3.34% ^{18}O)[27] were sealed in heavy-walled glass ampules and placed in a 118.6° constant temperature bath. At appropriate intervals ampules were removed and the reaction mixtures treated as follows. The solvent was removed under reduced pressure at 30° and the residual unsolvolyzed ester was dissolved in 25 ml. of 2:1 benzene–pentane. *p*-Nitrobenzoic acid, which is only slightly soluble in this solvent pair, was separated by filtration. The ester was isolated and purified by chromatography on acid-washed alumina using 2:1 benzene-pentane as eluent. After evaporation of the solvent the ester was recrystallized three times from 90–100° petroleum ether and then reduced with lithium aluminum hydride.[4] The resulting benzhydrol was recrystallized from petroleum ether and then reconverted to its *p*-nitrobenzoate derivative. The ^{18}O-content of this derivative was determined by the method described earlier.[4] This corresponds to the ^{18}O abundance of the ether oxygen atom of the unsolvolyzed ester. The first-order rate constant for equilibration of the carboxyl oxygen atoms (k_{eq}, eq. 2) was determined as described previously.[5] The results of these experiments are summarized in Table II.

In a control experiment *carbonyl*-^{18}O benzhydryl *p*-nitrobenzoate (2.95% ^{18}O)[27] was mixed with unlabeled benzhydrol and *p*-nitrobenzoic acid. The ester was isolated (chromatography) and purified (recrystallization) as described above after which the ^{18}O content was found to be 2.95%.[27] This ester was reduced to benzhydrol which gave an ^{18}O-free *p*-nitrobenzoate derivative. These experiments demonstrate that the ^{18}O content of the unsolvolyzed ester is not altered under conditions of its isolation and purification. Moreover, lithium aluminum hydride reduction gives benzhydrol containing only the ether oxygen atom of the ester.

In another experiment *carbonyl*-^{18}O benzhydryl *p*-nitrobenzoate (2.95% ^{18}O) was solvolyzed in 90% acetone at 118.6° for 213 hr. (*ca.* 2 half-lives for solvolysis and 6 half-lives for carboxyl oxygen equilibration). The ^{18}O content of the unsolvolyzed ester was within experimental error (±0.05%) of the original amount. Thus the ester does not

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[22] S. Winstein, P. E. Klinedinst, Jr., and E. Clippinger, *J. Am. Chem. Soc.*, **83**, 4986 (1961), and references therein.

[23] S. Winstein, P. E. Klinedinst, Jr., and G. C. Robinson, *ibid.*, **83**, 885 (1961); C. G. Swain and M. M. Kreevoy, *ibid.*, **77**, 1122 (1955).

[24] S. Winstein, J. S. Gall, M. Hojo and S. Smith, *ibid.*, **82**, 1010 (1960); S. Winstein and J. S. Gall, *Tetrahedron Letters*, No. **2**, 31 (1960); S. Winstein, M. Hojo and S. Smith, *ibid.*, No. **22**, 12 (1960); Y. Pocker, *Proc. Chem. Soc.*, 140 (1961).

[25] A. Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green and Co., London, 3rd ed., 1957, p. 757.

[26] J. K. Kochi and G. S. Hammond, *J. Am. Chem. Soc.*, **75**, 3445 (1953).

[27] Atom % excess ^{18}O.

exchange oxygen with the solvent under the conditions of the solvolysis.

(C) **Exchange between Benzhydryl p-Nitrobenzoate and p-Nitrobenzoic Acid-7-^{14}C.**—Four 30-ml. portions of a 90% aqueous acetone solution 0.0495 M in benzhydryl p-nitrobenzoate and 0.0294 M in ^{14}C-labeled p-nitrobenzoic acid ($580 \pm 13 \times 10^{-4}$ μc. mmole^{-1}) were sealed (under nitrogen) in heavy walled glass ampules. The ampules were placed in a 118.6° constant temperature bath for appropriate time intervals after which the unsolvolyzed ester was isolated and purified as described in the preceding section except that silicic acid was used for the chromatographic separation. The radioactivity of the ester was determined by scintillation counting.[16] The activity of the labeled acid was determined by converting it to its benzhydryl ester derivative which after purification was counted.[16] The results of two exchange experiments are summarized in Table III.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY, TALLAHASSEE, FLA.]

Constituents of Helenium Species. X. Revised Structure of Tenulin[1,2]

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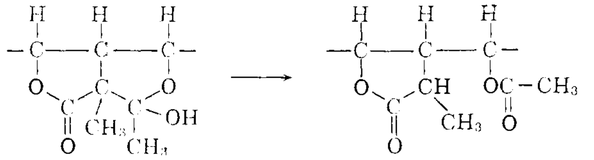
The structure of tenulin is shown to be V.

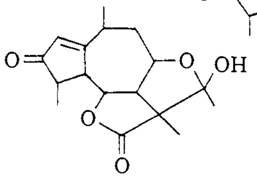
Tenulin, the bitter principle of *Helenium amarum* (Raf.)[4] and several other *Helenium* species, has been the subject of two recent investigations[6–8] which led to its formulation as a guaianolide. However, some uncertainties remained which could not be resolved satisfactorily by the generally accepted formula I or its alternative II.[9,10]

The recent demonstration[11,12] that parthenin (III) and ambrosin (IV) were not guiananolides also raised doubts about the carbon skeletons of tenulin and other sesquiterpene lactones of *Helenium* species such as helenalin,[13–16] balduilin[17] and the mexicanins.[17,18]



VI VII

In the following we show that these doubts were indeed well founded and present proof for the formulation of tenulin as V. The new formula not only accommodates all work previously published on



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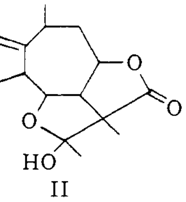

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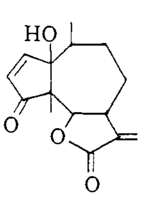

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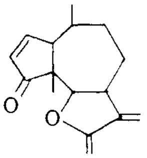

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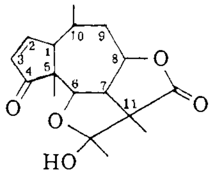

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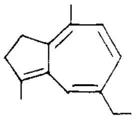

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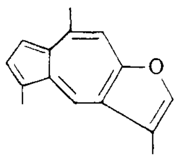

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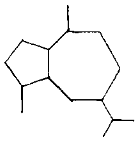

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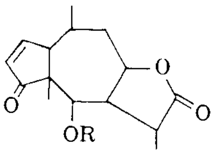
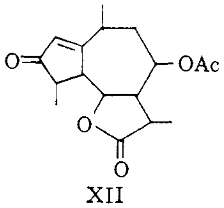


XIa, R = Ac
b, R = H



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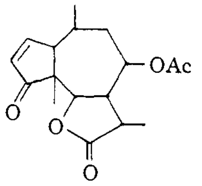

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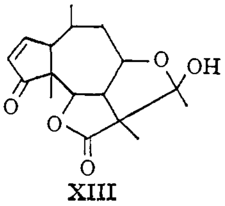

XIII

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[1] Previous paper, W. Herz, P. Jayaraman and H. Watanabe, *J. Am. Chem. Soc.*, **82**, 2276 (1960).

[2] Supported in part by grants from the National Science Foundation (NSF-G-14396), Research Corporation, and Eli Lilly and Co., Inc.

[3] Ethyl Corporation Fellow, 1957–1958; United States Public Health Fellow, 1958–1959. Abstracted in part from the Ph.D. thesis of W. A. Rohde, June, 1960.

[4] While *H. tenuifolium* Nutt. is the name by which this species is commonly known, there is a prior designation which must be used.[5]

[5] H. F. L. Rock, *Rhodora*, **59**, 128 (1957).

[6] D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 142 (1956).

[7] B. H. Braun, W. Herz and K. Rabindran, *J. Am. Chem. Soc.*, **78**, 4423 (1956).

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[9] For comments on this, see D. H. R. Barton and P. de Mayo, *Quart. Revs.*, **11**, 189 (1957).

[10] W. A. Rohde, Ph.D. Dissertation, Florida State University, June, 1960.

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[14] G. Büchi and D. Rosenthal, *ibid.*, **78**, 3860 (1956).

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[17] W. Herz, R. B. Mitra and P. Jayaraman, *ibid.*, **81**, 6061 (1959).

[18] A. Romo de Vivar and J. Romo, *Chemistry & Industry*, 882 (1959); *Ciencia* (*Mex.*), **21** (1), 33 (1961); *J. Am. Chem. Soc.*, **83**, 2326 (1961).