Tetrahedron Letters Vol. 22, pp 803 - 806
©Pergamon Press Ltd. 1981. Printed in Great Britain

0040-4039/81/0222-0803$02.00/0

STEREOCHEMISTRY OF PHOTOSOLVOLYSIS OF A CHIRAL, ^{18}O-LABELED 1-ARYLETHYL ACETATE

David A. Jaeger* and George H. Angelos

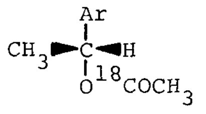
Department of Chemistry, University of Wyoming, Laramie, Wyoming 82071

Abstract: The stereochemistry of photosolvolysis of (R)-(+)-1-(3,5-dimethoxyphenyl)ethyl acetate-ether-^{18}O in methanol-water and 2,2,2-trifluoroethanol has been determined. An ion pair intermediate was detected in the latter solvent.

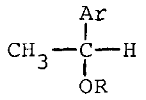
Photoinduced solvolysis has been observed[1] with numerous substituted and unsubstituted benzyl systems; structure-reactivity correlations and mechanism have been the subjects of recent reports.[1,2] This communication describes the stereochemical course of the photosolvolysis of a chiral, ^{18}O-labeled 1-arylethyl acetate, (R)-(+)-1-(3,5-dimethoxyphenyl)ethyl acetate-ether-^{18}O (1).

Acetate 1 was prepared as follows. The p-toluenesulfonic acid-catalyzed exchange of 3',5'-dimethoxyacetophenone (2) (Aldrich) with normalized $H_2{}^{18}O$ (10.2% ^{18}O) yielded 2-carbonyl-^{18}O, 5.9% excess ^{18}O,[3] which was reduced with a chiral reagent[4] derived from $LiAlH_4$ and (-)-trans-2-ethyl-4-hydroxymethyl-5-phenyloxazoline to give (R)-(+)-1-(3,5-dimethoxyphenyl)ethanol-hydroxy-^{18}O [(+)-3].[5] Integration of the benzyl proton quartets at δ 15.4 and 15.9 (larger) in the ^1H NMR spectrum (100 MHz, $CDCl_3$) of this material in the presence of tris-[(3-heptafluoropropylhydroxymethylene)-d-camphorato]europium (III) [$Eu(HFC)_3$] indicated that the enantiomeric excess (ee) was 44%,[6] and it was converted with acetic anhydride-pyridine to (+)-1, $[\alpha]_D^{25}$ +33.0 ± 0.8° (c 0.876, $CHCl_3$), 6.1% excess ^{18}O.[3]

Acetate (+)-1 was irradiated in both 50% (v/v) methanol-water and 2,2,2-trifluoroethanol (TFE) under conditions which yielded no thermal reaction. Products[7] 3, 4, 6, 7, and 8 resulted in the former solvent, and 5, 6, and 7 in the latter. Uniformly, 50 ml of a 0.02 M solution of (+)-1 was added to a quartz tube (2.5 cm i.d.) equipped with a fritted glass inlet tube and an outlet. The tube was placed 7 cm (center to center) from a quartz well fitted with a 450-W medium pressure Hanovia lamp and a 2 mm Corex sleeve. The solution was degassed with purified nitrogen for 45 min prior to and during irradiation at room temperature: 150 and 200 min for aqueous methanol and TFE, respectively. After irradiation, the aqueous methanol reaction mix-



(R)-(+)-1

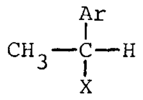


$CH_3-CH(OR)-Ar$

3, R = H

4, R = CH_3

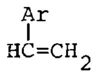
5, R = CH_2CF_3



$CH_3-CH(X)-Ar$

6, X = H

7, X = CH_3



$ArHC=CH_2$

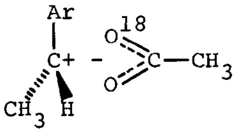
8

Ar = 3,5-$(CH_3O)_2C_6H_3$-

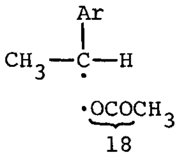
ture was worked up by addition to saturated aqueous NaCl followed by extraction with ether, and the TFE reaction mixture by distillation at 25°C (40 mm Hg). In each case, an internal standard (*n*-octadecane) and hexane were added to the resultant product mixture, and analysis was performed by GLC (15 ft x ¼ in; 8% SE-30 on 60-80 mesh Chromosorb W; helium) with correction for differences in thermal response ratios. The results are summarized in Table I.

After GLC analysis, the product mixture was column-chromatographed on silica gel with ether-hexane elution, and recovered 1 and products 3 and 4 (in aqueous methanol) and 5 (in TFE) were purified by GLC. The optical properties of these materials are summarized in Table II.[8a] Recovered 1 was analyzed[3] for total ^{18}O-content and then saponified with KOH in aqueous methanol. Resultant 3 was then re-converted to 1, which was analyzed[3] to give the ^{18}O-content at the ether position of recovered 1 and hence ^{18}O-equilibration.[8b] These results are summarized in Table II also. The *ee* of (-)-4 from run 1 was < 5% by ^{1}H NMR analysis (100 MHz, $CDCl_3$) with $Eu(HFC)_3$ based on the *α*-CH_3O singlets at δ 6.44 and 6.28 (larger). If (-)-4 is assigned the (*S*)-configuration,[9] then 4 was produced from (+)-1 with a slight net inversion of configuration. Controls using acetic acid-*d*$_4$ in both aqueous methanol and TFE demonstrated the intramolecular character of the ^{18}O-equilibration and racemization processes.

A mechanistic explanation of the above results involves partitioning of photoexcited 1[10] between (1), an allowed [1,3]-sigmatropic shift of the benzyl carbon with retention of configuration from ether to carbonyl oxygen, and (2), heterolytic and homolytic cleavages of the benzyl carbon-oxygen bond to give ion pair 9 and radical pair 10, respectively. The 1-arylethyl radical of 10 can abstract a hydrogen atom to give 6 or couple with methyl radical formed by decarboxylation of the acetoxy radical to give 7.[11] It is unlikely that 10 collapses to 1 to a significant degree since the acetoxy radical readily decarboxylates.[12] Chiral ion pair 9 can undergo (a) collapse with retention to give ^{18}O-scrambled (+)-1, (b) reorganization to give the enantiomeric ion pair, (c) capture by solvent to give inverted solvolysis product, (d) reduction by hydride abstraction[13] to give 6, (e) elimination to give 8, and (f) dissociation.



9



10

In both TFE and aqueous methanol, ^{18}O-scrambling of 1 occurred but with and without racemization, respectively. Thus in both solvents concerted pathway (1) and/or process (a) contributed to ^{18}O-scrambling, and in TFE process (b) followed by collapse to (-)-1 did also. The optical properties of the solvolysis products in both solvents are consistent with their predominant formation by capture of dissociated carbonium ion. However, the low net inversion for 4 suggests a minor contribution by process (c) with methanol.[14] McKenna *et al.*[2a] observed low net inversion also in the photosolvolysis of (-)-1-phenylethyltrimethylammonium iodide in methanol.

Table I. Product Composition and Percent Yields for Photolysis of 0.2 M Solutions of (+)-1.

Run	Solvent	1	3	4	5	6	7	8
1	CH_3OH-H_2O	25	31	27		2.1	2.4	0.4
2	CH_3OH-H_2O	20	33	32		2.3	2.3	0.4
3	CF_3CH_2OH	14			47	6.7	6.7	
4	CF_3CH_2OH	15			50	6.4	6.2	

Table II. Optical Rotations of Recovered 1 and Products, and Percent Excess ^{18}O and ^{18}O-Equilibration of Recovered 1.

	$[\alpha]^{25}_{D}$ (c 0.758 to 0.854, $CHCl_3$) unless noted otherwise				% Excess ^{18}O in Recovered 1		% ^{18}O-Equili-
Run	1[a]	3[b]	4[b]	5	Total[e,f]	Ether Postiion[e]	bration[g]
1	32.4°	0.5°	-2.9°		6.5	4.4	64
2	31.9°	0.5°	-2.8°		6.4[h]	4.4	64
3	26.2°			0[c]	6.8	3.4	101
4	26.2°			0.6°[d]		3.4	102[i]

[a] ±0.9°. [b] ±0.6°. [c] $[\alpha]^{25}_{D}$ (c 0.476, $CHCl_3$). [d] ±0.6°. [e] ±0.1 unless noted otherwise. [f] Recovered 1 was slightly enriched in ^{18}O-content relative to starting material, presumably due to an ^{18}O-isotope effect on benzyl carbon-oxygen bond cleavage. [g] Percent of 1 with equal amounts of ^{18}O at ether and carbonyl positions. [h] ±0.3. [i] Calculated with an assumed value of 6.8% for the total ^{18}O-content (not determined in run 4).

The combination of intramolecular racemization and ^{18}O-equilibration for (+)-1 in TFE is consistent with the intermediacy of ion pair 9. Thus, reorganization of ion pair 9 and its collapse to 1 apparently compete with its dissociation. In methanol-water, if 9 is an intermediate, it either does not return to 1 at all, or does so before reorganization resulting in racemization can occur.[15]

Acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

References and Notes

1. For examples, see S. J. Cristol and T. H. Bindel, J. Org. Chem., 45, 951 (1980), and references therein.
2. (a) V. Lillis, J. McKenna, J. M. McKenna, M. J. Smith, P. S. Taylor, and I. H. Williams, J. Chem. Soc., Perk. Trans. 2, 83 (1980); (b) J. R. Larson, N. D. Epiotis, and L. E. McMurchie, J. Org. Chem., 45, 1388 (1980), and references therein.
3. Analysis was made by mass spectrometry based on the molecular ion group.
4. A. I. Meyers and P. M. Kendall, Tetrahedron Lett., 1337 (1974).
5. The tentative (R) assignment is based on analogy; reduction[4] of acetophenone with the same reagent gave (R)-(+)-1-phenylethanol.

6. In a separate experiment, reduction[4] of unlabeled 2 gave (+)-3, $[\alpha]^{20}_{D}$+19.1 ±0.6° (c 11.4, $CHCl_3$), 62% ee.
7. All new compounds gave satisfactory carbon and hydrogen combustion or high resolution mass spectral analyses.
8. Controls demonstrated that (a) (+)-1 is optically stable to the GLC conditions, and (b) all of the excess ^{18}O of starting material (+)-1 is in the ether position and is undiminished by the saponification-esterification procedure.
9. Both (R)-1-phenylethanol and its ethyl ether are dextrorotatory [K. Mislow, J. Am. Chem. Soc., 73, 4043 (1951)].
10. More than one excited state may be involved.
11. With the GLC analysis used, 2,3-di-(3,5-dimethoxyphenyl)butane, if formed, would not have been detected.
12. (a) The half-lifetime of the acetoxy radical at 60°C is 4.3 x 10^{-10} sec [W. Braun, L. Rajbenbach, and F. R. Eirich, J. Phys. Chem., 66, 1591 (1962)]; (b) In a study of the photolysis of acetyl peroxide, Edge and Kochi [D. J. Edge and J. K. Kochi, J. Am. Chem. Soc., 95, 2635 (1973)] were unable to detect either the acetoxy radical or its adduct with ethylene by esr spectroscopy. They attributed the absence of an adduct to rapid decarboxylation of the acetoxy radical rather than to inefficiency in trapping of the acetoxy radical; (c) Goldstein and Haiby [M. J. Goldstein and W. A. Haiby, ibid., 96 7358 (1974)] have demonstrated that ^{18}O-scrambling of acetyl peroxide both in solution and in the gas phase results from competing [1,3]- and [3,3]-sigmatropic shifts without a contribution from geminate radical pair recombination; (d) If a fraction of 10 does collapse to 1 with ^{18}O-equilibration, it must do so with retention of configuration in aqueous methanol since recovered 1 in runs 1 and 2 was not racemized. The same is assumed for any collapse of 10 to 1 in TFE.
13. D. A. Jaeger, J. Am. Chem. Soc., 98, 6401 (1976).
14. (a) The fact that methanol was able to capture ion pair 9 to a slight degree whereas water was not is consistent with the greater nucleophilicity of methanol. For example, photosolvolysis of 1-(p-methoxyphenyl)ethyltrimethylammonium iodide in 33% (v/v) methanol-water (0.31 mole fraction CH_3OH) yielded only 1-(p-methoxyphenyl)ethyl methyl ether and none of the corresponding alcohol;[2a] (b) In a control, a 0.022 M solution of (-)-3 in 50% aqueous methanol containing 0.017 M acetic acid was irradiated with the procedure for 1. The recovered product mixture by GLC analysis was composed of 92% 3, which was 6% racemized, 6.4% 4, 1.3% 6, and minor unknowns (0.4% total). Thus in runs 1 and 2, 3 would not have been completely racemized if formed optically active; the same is assumed for 5 in runs 3 and 4.
15. In a related report [D. A. Jaeger, J. Am. Chem. Soc., 97, 902 (1975)], the ^{18}O-scrambling of 3,5-dimethoxybenzyl acetate-ether-^{18}O accompanying its photosolvolysis in aqueous methanol was interpreted in terms of internal return of an ion pair intermediate. However, later work (D. A. Jaeger, to be published) with 3,5-dimethoxybenzyl-1-d acetate-ether-^{18}O has demonstrated that ^{18}O-scrambling occurs without racemization. Thus, definitive evidence for an ion pair intermediate in this system has not been obtained. Givens and coworkers [R. S. Givens, B. Matuszewski, N. Levi, and D. Leung, ibid., 99, 1896 (1977)] have reported the photoinduced ^{18}O-equilibration of several carboxylic esters under nonsolvolytic conditions; (-)-1-phenylethyl phenylacetate does so without racemization in dioxane.

(Received in USA 18 September 1980)