The Solvolysis of Alkyl Diazotates. VI. Stereochemical Dissection of Return and Exchange Pathways[1]

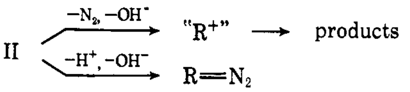
Robert A. Moss, David W. Reger,[2] and Edgar M. Emery[3]

*Contribution from the Wright Laboratory, School of Chemistry,
Rutgers University, The State University of New Jersey,
New Brunswick, New Jersey 08903, and from The Colgate-Palmolive
Research Center, Piscataway, New Jersey.* *Received July 9, 1969*

Abstract: Optically active octane 2-diazotate (^{16}O) was hydrolyzed with $H_2{}^{18}O$. Product 2-octanol was converted to the L-acetyl lactate diastereomers, which were separated by glpc and analyzed for ^{18}O content by mass spectroscopy. From the (glpc) stereochemical data and the ^{18}O analyses, 2-octanol formation could be partitioned into four pathways: ^{16}O conservation-retention, ^{16}O conservation–inversion, ^{16}O exchange-retention, and ^{18}O exchange–inversion. The percentages corresponding to the above pathways, for the $H_2{}^{18}O$ hydrolysis of dry octane 2-diazotate (^{16}O) were 26.6, 16.7, 13.8, and 43.1%, respectively. The results are discussed in terms of an intermediate cationic 2-octyl moiety which largely fails to become symmetrically hydrated before collapse to 2-octanol. Consequences for the study of deamination reactions are highlighted.

The cleavage of N-alkyl-N-nitrosourethans by ethereal potassium *t*-butoxide provides a direct route to alkyl diazotate salts, I.[4] Hydrolysis of the salt, I,

$$\underset{\text{I}}{RN{=}NO^-K^+} + H_2O \rightleftharpoons \underset{\text{II}}{RN{=}NOH} + K^+OH^- \quad (1)$$



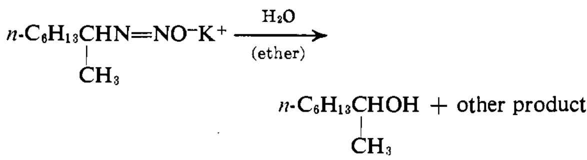
$$\text{II} \xrightarrow{-N_2,\,-OH^-} \text{"}R^+\text{"} \longrightarrow \text{products}; \qquad \text{II} \xrightarrow{-H^+,\,-OH^-} R{=}N_2 \quad (2)$$

yields an alkyl diazotic acid, II, which partitions, in the strongly basic aqueous medium, to diazoalkane and/or products commonly associated with alkyl cations (eq 1 and 2). The partition of II is dependent on the structure of R.[4] When R readily supports a positive charge, diazoalkane is bypassed (*e.g.*, R = cyclopropylcarbinyl[5]). When R is somewhat less capable of supporting a positive charge (*e.g.*, R = 2-octyl[6]), diazoalkane assumes a minor (*ca.* 20%) importance in partition (2). With R a primary alkyl group, finally, the formation of diazoalkane becomes as important as nitrogen-loss, "carbonium ion" pathways.[4]

The diazotate method of "deamination" is of general mechanistic interest because it is the only way of generating alkyl diazotic acids in a strongly basic (nucleophilic) medium. There is thus the opportunity to compare the behavior of II, so generated, with that of II as generated by the more common aqueous nitrous acid deamination of an alkyl amine. Important aspects of this comparison stress the stereochemistry of ROH formation from optically active II[6] and the extent of rearrangement within R as II passes to products.[7]

An important advantage of the diazotate method is that there is already present an oxygen atom in I (and hence in II) which can be easily differentiated from the oxygen atoms of the water solvent (*i.e.*, by supplying the latter as $H_2{}^{18}O$). It is thus possible to examine the alcohols formed in the diazotate hydrolyses, so as to determine the origin of their hydroxyl residues.[6,7] Such labeling experiments are not easily carried out with amine–aqueous nitrous acid reactions, and reported attempts led to somewhat equivocal results.[8]

The stereochemical comparison has been studied in some detail for the 2-octyl system.[6] The basic hydrolysis of optically active octane 2-diazotate (eq 3)



$$n\text{-}C_6H_{13}\underset{\displaystyle CH_3}{CH}N{=}NO^-K^+ \xrightarrow[\text{(ether)}]{H_2O} n\text{-}C_6H_{13}\underset{\displaystyle CH_3}{CH}OH + \text{other products} \quad (3)$$

afforded 2-octanol with 16% net inversion. *With ether present, inversion increased to 46%.*[6] Hydrolysis of the racemic diazotate with $H_2{}^{18}O$ (ether present or absent) demonstrated that *ca.* 40% of the total 2-octanol had formed with conservation of the diazotate ^{16}O.[6] Since (ether–water conditions) 46% net inversion required 73% total inversion, it was clear that some part of the 40% hydroxide conservation must have occurred with *inversion*. Moreover, the high degree of inversion *and* gegenion conservation made it seem unlikely that "free," hydrated cations were importantly involved in this deaminative process. Ion pairs or even II itself seemed more suitable as key intermediates.[6]

The major obstacle to a more complete understanding of the foregoing studies has been a lack of knowledge of the stereochemistry of the hydroxide conservation pathway. We assumed[6] *ca.* 60% net retention[9] for this process and gave a tentative role to free 2-octyl cations (*ca.* 20% of 2-octanol formation) in the ether-free hydrolysis of octane 2-diazotate. We have now removed this obstacle and here present *direct* evidence for return of diazotate oxygen with inversion; dissect return and exchange (solvent OH incorporation) path-

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(1) Part V: R. A. Moss and G. H. Temme, III, *Tetrahedron Lett.*, 3219 (1968).

(2) Allied Chemical Fellow, 1968–1969.

(3) Colgate-Palmolive Research Center.

(4) R. A. Moss, *J. Org. Chem.*, 31, 1082 (1966), and references therein.

(5) R. A. Moss and F. C. Shulman, *Tetrahedron*, 24, 2881 (1968).

(6) R. A. Moss and S. M. Lane, *J. Amer. Chem. Soc.*, **89**, 5655 (1967). A bibliography of alkyl diazotate studies appears in this paper.

(7) R. A. Moss, F. C. Shulman, and E. Emery, *ibid.*, **90**, 2731 (1968).

(8) D. L. Boutle and C. A. Bunton, *J. Chem. Soc.*, 761 (1961).

(9) This assumption was based upon related deaminations in which, however, the gegenion was not identical with the lyate ion, and in which it was possible to observe directly the stereochemistry of the return process: E. H. White and F. W. Bachelor, *Tetrahedron Lett.*, 77 (1965); E. H. White and C. A. Aufdermarsh, Jr., *J. Amer. Chem. Soc.*, **83**, 1179 (1961); H. Felkin, *Compt. Rend.*, **236**, 298 (1953).

Table I. 2-Octanol from Hydrolysis of Optically Active Octane 2-Diazotate with $H_2{}^{18}O$[a]

	$\Sigma\,^{18}O$ in ROH, atom %		Stereochemistry (glpc)		Atom % ^{18}O in resolved ROH	
Run	Found	Calcd	% retention	% inversion	*l*-ROH (retained)	*d*-ROH (inverted)
1[b]	12.80	12.54	41	59	8.38	15.43[c]
	12.16[d]		40.3[d]	59.7[d]	7.11[d]	15.02[d]
2[e]	12.85	13.06	28	72	10.06	14.33
3[e]	13.19	13.25	28	72	9.28	14.76

[a] 20.82% ^{18}O, Miles Laboratories, D-normalized. Dilution of ^{18}O solvent pool by diazotate ^{16}O is calculated to be less than 0.5 atom %. [b] Ether absent. [c] Repetition of the hydrolysis and analysis gave 15.28%. In this experiment inversion was also 59%, and *l*-ROH was *ca.* 7.8% ^{18}O. (An impurity rendered this analysis less accurate than the others.) [d] Data corrected for incursion of 7.6% of a diazotate → 2-diazooctane → 2-octanol pathway, detected by a D_2O experiment and mass spectral analysis. 2-Octanol formed from 2-diazooctane should be racemic and contain 20.82 atom % ^{18}O. Diazooctane does not appreciably intrude in the ethereal hydrolyses.[2] [e] Ether present.

ways into their stereochemical components; and determine where the "ether effect" operates so as to enhance inversion. This is the first time that such an experimental analysis has been carried out for an aqueous deamination (*i.e.*, for the decomposition of II in water). The results have important significance for deamination theory.[10] Insofar as they relate to the substantial absence of free 2-octyl cations in the process represented by (3), the present results have consequences for carbonium ion chemistry, and the centrality of ion pair and related phenomena therein,[11] because they extend such mechanisms to cationic precursors with *nitrogen* leaving groups in water.

Results

Optically active (97+ % optically pure) *l*-2-aminooctane was converted to active octane 2-diazotate (potassium) as previously described.[6] The diazotate was hydrolyzed with $H_2{}^{18}O$. Isolated[6] 2-octanol was analyzed for $^{18}O/^{16}O$ by mass spectroscopy, then esterified with optically pure L-lactic acid. After acetylation of the lactate hydroxyl group, the 2-octyl L-acetyllactate diastereomers were separated by glpc.[12] The glpc peak areas afforded stereochemical data for the 2-octanol product (see below) which was in good agreement with previous data[6] obtained by polarimetric analysis. With the glpc-purified diastereomers in hand, the $^{18}O/^{16}O$ content of *l*-2-octanol (retention) and *d*-2-octanol (inversion) was determined by mass spectral analysis of the corresponding acetyllactate.[13] These data, and the glpc stereochemical data permitted back-calculation of $^{18}O/^{16}O$ for the initial *unresolved* product 2-octanol. These calculations agreed with the direct mass spectral analyses of the unresolved 2-octanol (above), and both sets of data agreed with previous data for product 2-octanol obtained from the reaction of racemic octane 2-diazotate and $H_2{}^{18}O$.[6] The data appear in Table I. Multiplication of the data in the last two columns of Table I by 100/20.82 affords percentages of *d*- or *l*-2-octanol formed with incorporation of solvent ^{18}O; the difference from 100%, in each case, represents conservation of the diazotate's ^{16}O. These new data, weighted by the glpc stereochemical data, permit construction of Table II, in which a percentage is assigned to each of the four alcohol-forming pathways: ^{18}O retention, ^{18}O inversion, ^{16}O retention, and ^{16}O inversion.

Control experiments have demonstrated the optical stability of 2-octanol under reaction and isolation conditions.[6] Control experiments with polarimetrically determined, optically active 2-octanol showed that the L-lactic acid–glpc resolution method gave accurate (within 2%) enantiomeric compositions. Finally, several internal checks are built into Table I; they are satisfactory.

Table II. Stereochemistry of Exchange and Return Pathways in Octane 2-Diazotate → 2-Octanol Reactions

		Stereochemistry[a,c]			Stereochemistry[a,c]	
Run	$\Sigma\,^{18}O$ exchange[a,b]	Retn	Inv	$\Sigma\,^{16}O$ conservation[a,b]	Retn	Inv
1[d,e]	58.4	13.8	43.1	41.6	26.6	16.7
2[f]	61.8	13.5	49.6	38.2	14.5	22.4
3[f]	63.5	12.5	51.1	36.5	15.5	20.9

[a] Per cent of total 2-octanol product. [b] Calculated from atom % ^{18}O (^{16}O) in 2-octanol. [c] Calculated from atom % ^{18}O (^{16}O) in octyl acetyllactate. That, *e.g.* $(13.8 + 43.1) \neq 58.4$, indicates the "give" in the data, since the two sides of the inequality were derived from independent experimental measurements. Data in the table are considered reliable to about ±1%. [d] Ether absent. [e] Based on corrected values, *cf.*, Table I. [f] Ether present.

Discussion

For the sake of the present discussion, we define "deamination" reactions as reactions proceeding through such species as $RN{=}NX$ or $RN{\equiv}N^+X^-$. It now seems certain that, in solvents of *low dielectric constant*, such reactions generally bypass free carbonium ion intermediates. In some cases, it has been suggested, products arise, at least partly, by SN2-type attack of solvent, gegenion, or external nucleophile on the alkyl diazonium ion. Examples include the deaminative alkylation of benzene by primary carbinylamines with minimal alkyl group rearrangement[14] and the formation, with net inversion, of *sec*-butyl benzoate upon the thermolysis of optically active N-(*sec*-butyl)-N-nitrosobenzamide in pentane.[15]

In other cases, where there is no evidence for nucleophilic attack on alkyl diazonium ions, nitrogen loss leads to alkyl cations as components of ion pairs. Much

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(10) For an excellent review of aliphatic deamination reactions, see E. H. White and D. J. Woodcock in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience Publishers, New York, N. Y., 1968 pp 440–483.

(11) See, in this regard, R. A. Sneen and J. W. Larsen, *J. Amer. Chem. Soc.*, **91**, 362 (1969).

(12) E. Gil-Av, R. Charles-Sigler, G. Fischer, and D. Nurok, *J. Gas Chromatogr.*, **4**, 51 (1966); H. C. Rose, R. L. Stern, and B. L. Karger, *Anal. Chem.*, **38**, 469 (1966).

(13) Based on *m/e* 133, 135, protonated acetyllactic acid: F. W. McLafferty, "Interpretation of Mass Spectra," W. A. Benjamin, Inc., New York, N. Y., 1967, p 137.

(14) L. Friedman and A. T. Jurewicz, *J. Amer. Chem. Soc.*, **91**, 1808 (1969).

(15) E. H. White, *ibid.*, **77**, 6014 (1955).

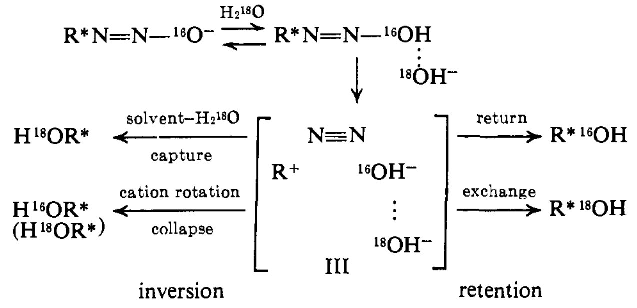
evidence exists to show that these cations rarely escape from the ion pairs in such a way as finally to become symmetrically solvated cations. Thus, the nitrous acid deamination of 2-decalylamines in water–acetic acid gave stereochemical and product distribution data consistent with a specifically solvated diazonium acetate ion pair intermediate.[16] In related work, it has been shown that the gegenion of *cis*- and *trans*-2-decalyldiazonium ethylcarbonate ion pairs is instrumental in a subsequent, stereoselective proton removal step leading to 2-octalin.[17]

Stereochemical studies of alkyl diazonium carboxylate ion pair decompositions, in solvents such as ether, acetic acid, and ether–methanol, have also demonstrated the relative unimportance of free alkyl cations as ultimate intermediates.[18,19] There are, also, numerous examples of aminocyclane deamination reactions, in various solvents in which free, solvent-equilibrated cations are at least partly excluded.[20] It should be noted that the above discussion is not intended to refer to alkyl groups which are *especially* good at bearing a positive charge (*e.g.*, cyclopropylcarbinyl) in solvents such as water. We refer primarily to the deamination of simple secondary and primary carbinamines in less ionizing solvents.

Our results help to bridge the gap between the relatively nonpolar solvents, previously considered, and water. They augment the generality of the ion pair hypothesis by demonstrating its ability, with slight modification, to include alkyl diazonium hydroxide (diazotic acid) systems in water.

Consider Table II. Run 1 demonstrates that (at least) 16.7% of the 2-octanol (eq 3) is formed with *return of original* $^{16}OH^-$ *gegenion and stereochemical inversion*. Since we have already shown that 2-octanol yield and stereochemistry in (3) are essentially unaltered upon the addition of hydroxide or azide ions,[6] we believe that ^{16}O appears in the inverted 2-octanol by a true return process. An abbreviated mechanism appears in Scheme I.

Scheme I



The principal intermediate, III, is rendered as an octyl cation, hydroxide (^{16}O) "ion pair." Extensive hydration of the gegenions in III (with $H_2{}^{18}O$) is omitted for simplicity. It should be remembered that such hydration must be important. However, as the results will demonstrate, ^{16}OH maintains intimate association with the octyl moiety. To the extent that it bears a negative charge, which is probably shared by reciprocal proton transfer with the hydrating water molecules, it can be regarded as the gegenion of an ion pair. Likewise, neighboring ^{18}O units can also be considered as potential gegenions. The fate of R^+ and ^{16}O in III could also be rationalized with water molecules as the sole oxygen-bearing units. Since this would entail attempting to describe the detailed geometry of the solvent shell, and since the reaction under consideration occurs in strong aqueous base, it seems preferable to us at this time to use the hydroxide gegenion rationale. Other authors have used similar schemes.[16,18]

In III, the separation between the partners is probably greater than that of a corresponding solvolytic ion pair, because there is a "hole" left by the departing nitrogen molecule. Such a species has been called a "vibrationally excited ion pair."[21] Inversion with ^{16}O return can occur within III by rotation of the cation before collapse to alcohol. Examples of this "intramolecular inversion" process for carbonium carboxylate ion pairs, in nonaqueous solvents, have been reviewed.[10] In White's elegant work, we find that the extent of such inversion depends on alkyl group bulk, heavier cations affording less inversion with return. On this basis, the closest literature analogy to the present work deals with the 1-phenylethyl cation. The finding of about 12.4% (overall) "intramolecular inversion" in the decomposition of N-(1-phenylethyl)-N-nitroso-2-naphthamide in acetic acid[22] is remarkably similar to the 16.7% "intramolecular inversion" found here for octane 2-diazotate hydrolysis. Further similarities of the aqueous and nonaqueous reactions are seen. In run 1 (Table II) return occurs with *more retention than inversion*. Here retention is 61% of the return process. This value may be compared with 80% retention for 2-naphthoate return in the 1-phenylethyldiazonium 2-naphthoate system (acetic acid solvent)[22] and 68% retention for benzoate ion return in the thermolysis of N-(*sec*-butyl)-N-nitrosobenzamide in acetic acid.[15]

Differences between the aqueous and nonaqueous reactions show up most strongly on comparison of the exchange pathways. For the 1-phenylethyl and *sec*-butyl acetolytic deaminations, the stereochemistry of exchange (acetate) product formation is 12% *net* retention and 14% *net* inversion, respectively.[10] In contrast, most ^{18}O incorporation in the diazotate hydrolyses occurs with marked inversion (Table II) and appears to represent collapse of III (Scheme I) with rear-side solvent capture.[23] The greater nucleophilicity of water, as compared to acetic acid, may be partly responsible for these differences.

^{18}O incorporation with retention must at least partly arise from front-side exchange of ^{18}O for ^{16}O within III, followed by collapse (Scheme I). There is ample precedent for such phenomena in deaminative processes in other solvents,[10] and with the strong hydrogen bonds

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[16] T. Cohen and E. Jankowski, *J. Amer. Chem. Soc.*, **86**, 4217 (1964).

[17] T. Cohen and A. R. Daniewski, *ibid.*, **91**, 533 (1969).

[18] E. H. White, H. Maskill, D. J. Woodcock, and M. A. Schroeder, *Tetrahedron Lett.*, 1713 (1969); E. H. White and J. E. Stuber, *J. Amer. Chem. Soc.*, **85**, 2168 (1963).

[19] A good review of these phenomena can be found in ref 10. See also H. Maskill, R. M. Southam, and M. C. Whiting, *Chem. Commun.*, 496 (1965); M. C. Whiting, *Chem. Brit.*, **2**, 482 (1966).

[20] J. A. Mills, *J. Chem. Soc.*, 260 (1953); A. Streitwieser, Jr., and C. E. Coverdale, *J. Amer. Chem. Soc.*, **81**, 4275 (1959); I. Lillien and R. A. Doughty, *J. Org. Chem.*, **33**, 3841 (1968); C. W. Shoppee, J. G. Feher, R. M. Hall, R. E. Lack, and L. Tarasoff, Jr., *J. Chem. Soc., C*, 2211 (1968); and H. Feltkamp, F. Koch, and T. N. Thanh, *Ann.*, 707, 95 (1967).

[21] E. H. White and C. A. Elliger, *J. Amer. Chem. Soc.*, **89**, 165 (1967).

[22] Reference 9, White and Aufdermarsh.

[23] For related solvolytic mechanisms, see R. A. Sneen, J. V. Carter, and P. S. Kay, *J. Amer. Chem. Soc.*, **88**, 2594 (1966).

available in water, it is hard to believe that such processes do not also occur. If only half of the 2-octanol formed with ^{18}O incorporation *and* retention (Table II, run 1) arose by front-side exchange within III, only 13.8% of the total 2-octanol could then have arisen from 2-octyl cations which had escaped into solvent.[24]

We conclude that ion pair or related phenomena are central to deaminative processes, even in water, and that they display a surprising degree of similarity in such disparate solvents as acetic acid and water.

Comparison of run 1 with runs 2 and 3 reveals that the principal source of the enhancement of inversion in the presence of ether is a change in the ^{16}O conservation process stereochemistry from *retention to inversion*. The origin of this reversal is still unclear. Perhaps, explanations should highlight a decreased importance of ion pairs such as III, and increased importance of bimolecular displacement reactions occurring with inversion (and ^{16}O conservation); possibly between $RN{=}N{-}{}^{16}OH$ molecules extracted into the organic phase. Such a mechanism would find analogy in the observation of an inverting displacement reaction on alkyl diazoesters by carboxylic acids in nonpolar solvents.[15]

Experimental Section

Optically active (97+% optically pure) octane 2-diazotate was prepared and hydrolyzed in a manner similar to that previously described.[6]

Optically active N-nitroso-N-2-octylurethan[6] (1.28 g, 5.52 mmol) in 18 ml of dry ether was injected through a septum into a magnetically stirred, nitrogen blanketed slurry of potassium *t*-butoxide (MSA Research Corp., 1.24 g, 11.1 mmol) in 18 ml of dry ether at −30°. No gas evolution was observed over 30 min. The slurry was warmed to −15° and 2.4 ml of $H_2{}^{18}O$ was rapidly injected.[25] Nitrogen evolution was very rapid and *quantitative* (gas buret).

The ethereal phase of the product mixture was separated and combined with a second ether extract of the aqueous phase. The ethereal phase was dried ($MgSO_4$). Filtration and concentration gave a yellow oil (2.13 g) from which 2-octanol was isolated by glpc.[26] A portion of the collected 2-octanol was sealed for mass spectral ^{18}O analysis, the remainder (*ca.* 180 μl, 1.13 mmol) was added to a mixture of a 40% aqueous solution of optically pure L-lactic acid (K & K, *ca.* 6.3 mmol) and 5 ml of pure benzene. The mixture was magnetically stirred and heated to 80°. A benzene–water azeotrope was removed by a Dean–Stark trap. Finally, a few A-4 molecular sieves were added and the mixture was heated to 110° for 1 hr. After cooling, 5.4 mmol of acetic anhydride in 5 ml of di-*n*-butyl ether was added, and the resulting mixture was refluxed for 7 hr. Concentration of the product mixture (rotary evaporator) gave a crude product which was directly analyzed for the 2-octyl acetyllactate diastereomers by glpc.[12,27,28]

Glpc peak areas were integrated by the cut-and-weigh method. Two analyses of the above run gave the *l*-2-octanol to *d*-2-octanol distribution of the original mixture as 28/72% (44% net inversion).

Not only does the above stereochemical result (as well as other results in Table I) agree with previous hydrolyses ($H_2{}^{16}O$) of active octane 2-diazotate,[6] but control experiments also verified the accuracy of the glpc stereochemical analysis. For example, 2-octanol, $\alpha^{21}D$ +7.18 (89.5% optically pure[29]), was analyzed to be 91.2% optically pure by the glpc method.

The hydrolytic procedure was somewhat different when carried out in the absence of ether, Table I, run 1. After generation of the diazotate as above, ether was removed under vacuum at −30°. After further "drying" at room temperature (30 min, 3 mm), the diazotate mixture was cooled to −20° and hydrolyzed with $H_2{}^{18}O$[25] as above. Nitrogen evolution was only 74% of the theoretical yield, though immediate. The resulting reaction product was red in color, suggestive of the presence of 2-diazooctane. A small portion of dry ether was added to the reaction product and the resulting solution was quickly pipetted into a separatory funnel. The ethereal phase was separated, combined with an ether extract of the aqueous phase, and the whole was allowed to dry over $MgSO_4$. After about 1 hr, the red color had faded. Drying agent was filtered and solvent was stripped to afford a crude product, which was purified and analyzed as described for Table I, run 2.

The ether-free hydrolysis was also carried out with 99.8% D_2O. The work-up was similar to that of the $H_2{}^{18}O$ run, except that the ethereal product solution from the D_2O run was washed twice with 10% aqueous $NaHCO_3$ solution, in order to free the 2-octanol of O-D. This procedure was carried out *after* the original ethereal reaction product had dried for 1 hr over $MgSO_4$ and the red diazooctane color had faded. The purified 2-octanol[26] from the D_2O run was shown by mass spectroscopy to be 7.57% d_1, presumably as 2-octanol-2-*d*.[30] Since 2-octanol arising from a reaction of 2-diazooctane and $H_2{}^{18}O$ would have to be racemic and would have to have the same ^{18}O content as the water, corrections were applied to the results of run 1, so as to have them reflect only the alcohol *not* derived from the diazoalkane.[31] As can be seen in Table I, the corrections were not large.

Mass spectral analyses were carried out on glpc[26,27] purified 2-octanol and 2-octyl acetyllactate diastereomers. A Consolidated 21-103-C mass spectrometer was employed. 2-Octanol (base peak, *m/e* 45) was analyzed for $^{16}O/^{18}O$ using (principally) *m/e* 45 and 47, and for deuterium using *m/e* 45 and 46. The 2-octyl acetyllactates were analyzed for $^{16}O/^{18}O$ using (principally) *m/e* 133 and 135.[13] In the racemic diastereomers (^{16}O), *m/e* 133 was 3.154% of the base peak (*m/e* 43) and *m/e* 135 was 0.036%. In all isotopic analyses, corrections for natural heavy isotope abundances were made, based on the fragmentation pattern of the normal compounds.

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[24] Such cations would have to afford racemic 2-octanol with full ^{18}O incorporation.

[25] The $H_2{}^{18}O$ was obtained from Miles Laboratories. It was certified as 20.82 atom % ^{18}O and was normalized for deuterium content. The water was used either immediately upon opening the sealed ampoule or after storage for no longer than 4 hr, with a temporary seal, in a freshly prepared desiccator. Calculations indicate that, in use, dilution of the ^{18}O pool by ^{16}O released from the octane 2-diazotate could amount to no more than about 0.6 atom %, under the conditions described above.

[26] An Aerograph A90-P3 instrument was used for all glpc work; injector 210°, detector 200°, column 89°, flow 120 ml/min. The column was 5 ft, 0.25 in., 5% Carbowax 20M on 60/80 Chromosorb P.

[27] Injector 260°, detector 240°, column 160°, flow 86 ml/min. The column was 20 ft, 0.25 in., 10% 1,2,3-tris(2-cyanoethoxy)propane on 45/60 Gaschrom R. The reaction product showed many components with short (0.5–10 min) retention times. The diastereomers had retention times of about 70 min. The *d*-2-octanol diastereomeric derivative had the longer retention time.

[28] Although the diastereomers are known compounds,[12] we present the following apparently unreported spectral data for the *l*-2-octyl L-acetyllactate (the *d* ester gave indistinguishable data): ir 1749 (carbonyl), 1280, 1240, 1215, 1140, 1107, and 1055 cm^{-1}; nmr a quartet centered at δ 4.86 (CCl_4, from internal TMS) assigned to *both* carbinyl protons, a singlet at 2.1 assigned to acetyl methyl, and a complex multiplet from 1.6 to 0.7 assigned to all remaining protons. The approximate area ratios were 2:3:19, respectively. The mass spectrum did not show a parent ion; the base peak was *m/e* 43.

[29] A. Streitwieser, Jr., and W. D. Schaeffer, *J. Amer. Chem. Soc.*, **78,** 5597 (1956).

[30] This represents a somewhat higher participation of 2-diazooctane as an octanol precursor than we previously reported (3% maximum).[8] We cannot account for the discrepancy.

[31] Corrections were not made for an isotope effect which could render the D_2O solvolysis of 2-diazooctane more or less efficient than the $H_2{}^{18}O$ solvolysis (as a 2-octanol source).