# Micellar Effects in the Nitrous Acid Deamination Reaction of (*R*)-[1-$^2$H]-1-Octanamine

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The nitrous acid deamination of 1-octanamine (1) afforded mixtures of isomeric octenes, octanols, and octyl nitrites. The aggregation of 1·$HClO_4$ in micelles induced the formation of dioctyl ethers and of 1-nitrooctane as additional products. In homogeneous solution (submicellar aqueous conditions or HOAc), [1-$^2$H]-1-octanol was obtained from [1-$^2$H]-1 with ca. 95% inversion of configuration. Above the critical micelle concentration, the enantiomeric purity of [1-$^2$H]-1-octanol decreased while [1-$^2$H]-1-nitrooctane was formed with ca. 90% retention of configuration. 1-Octyl··$NO_2$ radical pairs, rather than ion pairs, are likely to intervene on the retentive route to 1-nitrooctane and 1-octyl nitrite. Equilibration, via NO exchange, of (*R*)-[1-$^2$H]-1-octyl nitrite with the more abundant (*S*)-[1-$^2$H]-1-octanol is thought to account for the diminished ee of both products.

## Introduction

Some 20 years ago, Moss discovered micellar effects in nitrous acid deamination reactions of long-chain amines.[1] The stereochemistry of the 2-aminobutane to 2-octanol conversion could be changed from 24% net inversion, in homogeneous aqueous solution, to 6% net retention, under certain miceller deamination conditions. The dediazoniation reactions of *sec*-alkanediazonium ions are known to proceed by reaction mechanisms that range from inverting nucleophilic displacement ($k_s$) to the intervention of solvated carbocations ($k_c$).[2] Micellation can influence the relative contributions of the competing pathways through a local solvent effect.[3] Moreover, the orientation of counterions and solvent molecules at the micellar surface is thought to differ from homogeneous solution in such a way as to favor retention of configuration.[1]

We have recently shown that the nitrous acid deamination reactions of optically active [1-$^2$H]-butanamine and [1-$^2$H]-2-methylpropanamine afford the corresponding primary alcohols with complete (±2%) inversion of configuration.[4,5] It appears that the extrusion of nitrogen from 1-alkanedizaonium ions proceeds entirely by way of $S_N2$-type displacement, bypassing the highly energetic primary alkyl cations. Would these mechanistically simple reactions be subject to micellar control of stereochemistry? In response to this question, we initiated a study of (*R*)-[1-$^2$H]-octanamine. To our surprise, we observed micellar effects similar to those reported by Moss.[1] The underlying cause, however, is probably not the same. Our data, including the analysis of byproducts, suggest different interpretations for primary and secondary alkanediazonium ions.

## Results

**Product Distribution.** Nitrous acid deamination reactions were performed by addition of sodium nitrite to 1-octanamine (1) in dilute perchloric acid at pH 3.5. The critical micelle concentration (cmc) of 1·$HClO_4$ at pH 3.5 is 0.105 M; in the presence of 3 equiv of NaCl, the cmc drops to 0.018 M. The latter conditions were recommended to account for the formation of inorganic salts in the course of deamination reactions.[1] Thus, the onset of micellation is not precisely defined but should occur within the range of 0.02–0.1 M.

The product mixtures were routinely analyzed (GC) for the isomeric octanols **2–5**, 1- and 2-octyl nitrite (**6**, **7**), 1-octyl nitrate (**8**), 1-nitrooctane (**9**), di-1-octyl ether (**10**), and 1-octyl 2-octyl ether (**11**).[6] Very minor amounts of additional nitrites, nitrates and ethers may have been present but were not reliably detected. The presence of 2-nitrooctane (>0.1%) was definitely excluded. Although reproducibility of the analyses suffered somewhat from the instability of the nitrites, the data collected in Table I reveal the following trends:

(i) Rearrangements, proceeding predominantly by way of consecutive 1,2-hydride shifts, are not significantly affected by micellation. If the products of nucleophilic substitution in Table I (alcohols, nitrites, nitrates, and ethers) are analyzed for the distribution of isomers, fairly constant fractions of 1-octyl (64.7 ± 1.5%), 2-octyl (30.6 ± 1.2%), 3-octyl (4.4 ± 1.1%), and 4-octyl derivatives (0.3 ± 0.2%) are observed.

(ii) With increasing concentration of 1·$HClO_4$, the yield of octyl nitrites passes through a maximum. Acid-catalyzed reaction of the octanols with $HNO_2$ is thought to be the major source of octyl nitrites (for alternative pathways, see below). In terms of the equilibrium, R–OH + $HNO_2$ ⇄ R–ONO + $H_2O$, the yield of octyl nitrites would be expected to increase steadily with [ROH], which

(1) Moss, R. A.; Talkowski, C. J.; Reger, D. W.; Powell, C. E. *J. Am. Chem. Soc.* **1973**, *95*, 5215.

(2) For reviews, see: (a) White, E. H.; Woodcock, D. J. In *The Chemistry of the Amino Group*; Patai, S. Ed.; Wiley-Interscience: New York, 1968; pp 440–483. (b) Keating, J. T.; Skell, P. S. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1970; Vol. 2, pp 573–653. (c) Friedman, L. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1970; Vol. 2, pp 655–713. (d) Collins, C. J. *Acc. Chem. Res.* **1971**, *4*, 315. (e) Kirmse, W. *Angew. Chem.* **1976**, *88*, 273; *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 251. (f) Whittaker, D. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley-Interscience: Chichester, 1978; pp 617–639. (g) Laali, K.; Olah, G. A. *Rev. Chem. Intermed.* **1985**, *6*, 237.

(3) For solvent effects in deamination reactions, see: Banert, K.; Bunse, M.; Engbert, T.; Gassen, K.-R.; Kurnianto, A. P.; Kirmse, W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 272.

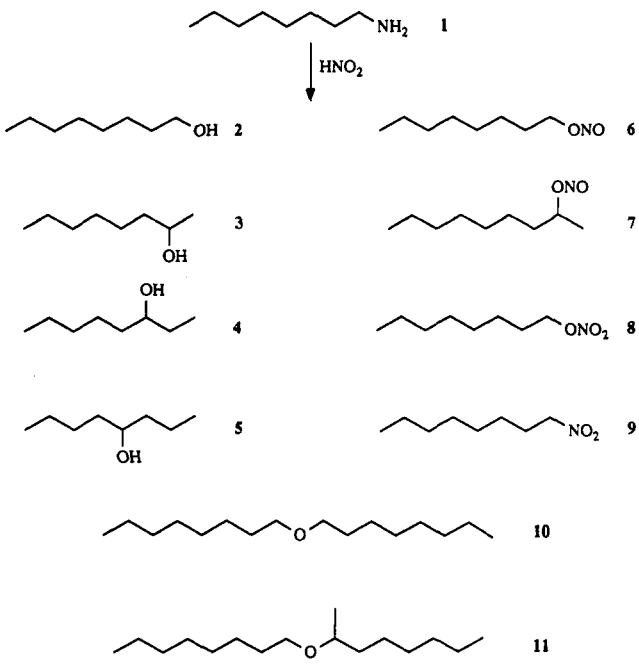
(4) Brosch, D.; Kirmse, W. *J. Org. Chem.* **1991**, *56*, 907.

(5) For a previous report of partial inversion, see: Streitwieser, A., Jr.; Schaeffer, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 2888.

(6) Octenes are also formed but were disregarded in the present study. The substitution/elimination ratio in deamination reactions of 1-octanamine has been scrutinized in a recent paper: Monera, O. D.; Chang, M.-K.; Means, G. E. *J. Org. Chem.* **1989**, *54*, 5424.

0022-3263/93/1958-1118$04.00/0 

**Scheme I**




is directly related to the concentration of the amine precursor. As a rationale for our deviating results, we suggest that incorporation of the octanols into micelles inhibits the esterification by $HNO_2$.

(iii) 1-Nitrooctane (**9**) and the octyl ethers (**10, 11**) arise predominantly or exclusively from reactions in the micellar phase, as indicated by sharp increases in yield above the cmc. The formation of **10** and **11** can be attributed to high local concentrations of the octanols in the micellar phase, as compared to bulk solution. Nitro compounds have rarely, if ever, been obtained from nitrous acid deamination reactions of 1-alkanamines. In order to exclude oxidation of **1** by nitrous gases as a trivial route to **9**, the deamination of **1** was performed with $Na^{15}NO_2$. The incorporation of $^{15}N$ into **9** was found to be virtually complete (100 ± 2%, IR). Clearly, the nitro group of **9** derives from the nitrosating agent rather than from the amino group of **1**. The origin of **9** will be considered more explicitly in the light of stereochemical evidence, to be presented in the following section.

**Stereochemistry.** In analogy to established procedures,[4,5] (*S*)-[1-$^2$H]-1-octanol was obtained by fermenting yeast reduction of [1-$^2$H]-octanal (**12**). Conversion of (*S*)-[1-$^2$H]-**2** into (*R*)-[1-$^2$H]-octanamine was achieved by way of the tosylate **13** and the azide **14** (Scheme II). For the estimation of enantiomeric purity, [1-$^2$H]-**1** and [1-$^2$H]-**2** were treated with camphanoyl chloride to give the corresponding amide and ester, respectively. In the presence of the shift reagent $Eu(dpm)_3$, the $^2$H NMR spectra of these derivatives exhibited nicely resolved peaks for the diastereotopic deuterons.[7] Some deamination products were converted into **1** or **2** for stereochemical analysis. Thus, reduction of [1-$^2$H]-1-octyl acetate (**15**) with $LiAlH_4$ and hydrolysis of [1-$^2$H]-1-octyl nitrite[8] afforded [1-$^2$H]-**2** while [1-$^2$H]-1-nitrooctane was hydrogenated (Pd–C) to give [1-$^2$H]-**1**.

By application of these techniques, nitrous acid deamination reactions of (*R*)-[1-$^2$H]-**1** in acetic acid[9] and in dilute aqueous solution ($c$ = 0.048 M) were found to proceed with ca. 95% inversion of configuration (Table II). The data obtaind with **1** in homogeneous phases approach those reported for 1-butanamine and 2-methyl-1-propanamine.[4] Above the cmc, however, a decrease in stereoselectivity to ca. 80% inversion ($c$ = 0.80 M) was observed. Not surprisingly, the enantiomeric purities of [1-$^2$H]-**2** and of the corresponding nitrite agree within experimental error. Even if the alcohol and the nitrite should originate by stereochemically distinct routes, the acid-catalyzed exchange reaction R–ONO + R'OH ⇄ R–OH + R'ONO[8] will blur these distinctions. [1-$^2$H]-1-nitrooctane, on the other hand, is formed with ca. 90% retention of configuration. The divergent stereochemistry indicates that the nitro compound does not arise via nucleophilic displacement on 1-octanediazonium ions.

## Discussion

Stereochemical data are now available for the 1-aminooctane to 1-octanol and 2-aminooctane to 2-octanol[1] conversions. Micellar effects of the same sign and of similar magnitude are found, although at widely different levels of stereoselectivity. These effects might be explained by enhanced unimolecular decay ($k_c$) of 1-octanediazonium ions in the micellar phase, owing to inhibition of the nucleophilic displacement reaction ($k_s$) that predominates in aqueous solution. The intervention of primary alkyl cations (ion pairs) in deamination reactions has occasionally been postulated[2,10] but is not generally accepted.[2,11] Moreover, the $k_c$ mechanism is difficult to reconcile with the increase in chemoselectivity ($k_{x^-}/k_{H_2O}$) that is induced by micellation.[12] The chemoselectivity of alkyl cations is notoriously low, even for tertiary species.[13]

An alternative mechanism was suggested to us by the unexpected formation of 1-nitrooctane (**9**) from **1** in the micellar phase. Nitro compounds were recently reported to be major products in nitrous acid deamination reactions of α-amino nitriles.[14] Free radicals, rarely encountered in the chemistry of aliphatic diazonium ions, were identified as precursors of the α-nitro nitriles. Destabilization of the electron-deficient α-cyanocarbocations[15] is thought to favor homolysis of diazo nitrites (**16**) over the conventional heterolytic ($k_c$) pathway (Scheme III). We were intrigued by the idea that 1-nitrooctane should be formed analogously. Some implications of this hypothesis will now be considered.

The reluctance to generate highly energetic carbocations is clearly a common feature of α-cyanoalkyl and primary alkyl systems. Aside from that, there are substantial

(7) For previous applications of this technique, see: (a) Shapiro, S.; Arunachalam, R.; Caspi, E. *J. Am. Chem. Soc.* **1983**, *105*, 1642. (b) Parker, D. J. *J. Chem. Soc., Perkin Trans. 2* **1983**, 83. (c) Caspi, E.; Eck, C. R. *J. Org. Chem.* **1977**, *42*, 767. (d) Gerlach, H.; Zagalak, B. *J. Chem. Soc., Chem. Commun.* **1973**, 274.

(8) The acid-catalyzed hydrolysis of alkyl nitrites is known to involve the O–NO bond, rather than the R–O bond: Allen, A. D. *J. Chem. Soc.* **1954**, 1968.

(9) For product distributions obtained from **1**, see: Southam, R. M.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 2* **1982**, 597.

(10) Gold, B.; Deshpande, A.; Linder, W.; Hines, L. *J. Am. Chem. Soc.* **1984**, *106*, 2072.

(11) Computational studies indicate that the dediazonation of 1-alkanediazonium ions in the gas phase is endothermic: (a) Ford, G. P.; Scribner, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 349. (b) Glaser, R.; Choy, G. S.-C.; Hall, M. K. *J. Am. Chem. Soc.* **1991**, *113*, 1109.

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(14) Bunse, M.; Jödicke, D.; Kirmse, W. *J. Chem. Soc., Chem. Commun.* **1992**, 47.

(15) For reviews, see: (a) Gassman, P. G.; Tidwell, T. T. *Acc. Chem. Res.* **1983**, *16*, 279. (b) Creary, X. *Chem. Rev.* **1991**, *91*, 1625.

**Table I. Product Distributions from Nitrous Acid Deamination Reactions of 1-Octanamine (1)**

| [1], M | $1.99 \times 10^{-2}$ | $3.98 \times 10^{-2}$ | $7.81 \times 10^{-2}$ | $1.44 \times 10^{-1}$ | $2.78 \times 10^{-1}$ | | | $4.56 \times 10^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| $NaNO_2$, equiv | 2 | 1 | 1 | 1 | 0.5 | 1 | 2 | 1 |
| 1-octanol (2) | 64.1 | 59.4 | 52.0 | 47.8 | 53.6 | 46.7 | 49.0 | 44.6 |
| 2-octanol (3) | 28.9 | 30.1 | 22.6 | 21.1 | 26.5 | 23.2 | 21.1 | 23.7 |
| 3-octanol (4) | 4.7 | 6.4 | 4.2 | 2.9 | 4.5 | 3.4 | 3.1 | 3.6 |
| 4-octanol (5) | 0.5 | 0.5 | 0.2 | 0.1 | 0.4 | 0.1 | 0.1 | 0.2 |
| 1-octyl nitrite (6) | 1.0 | 2.1 | 11.2 | 4.0 | 2.0 | 3.2 | 2.1 | 4.2 |
| 2-octyl nitrite (7) | 0.5 | 0.7 | 6.4 | 3.5 | 1.0 | 2.7 | 3.2 | 3.6 |
| 1-octyl nitrate (8) | | 0.2 | 0.5 | 0.5 | 1.2 | 0.7 | 0.6 | 0.6 |
| 1-nitrooctane (9) | 0.3 | 0.6 | 0.5 | 9.5 | 4.6 | 10.3 | 8.5 | 8.9 |
| di-1-octylether (10) | | | 1.6 | 5.6 | 4.0 | 5.1 | 6.6 | 6.1 |
| 1-octyl-2-octyl ether (11) | | | 0.8 | 5.0 | 2.2 | 4.6 | 5.7 | 4.5 |

**Scheme II**

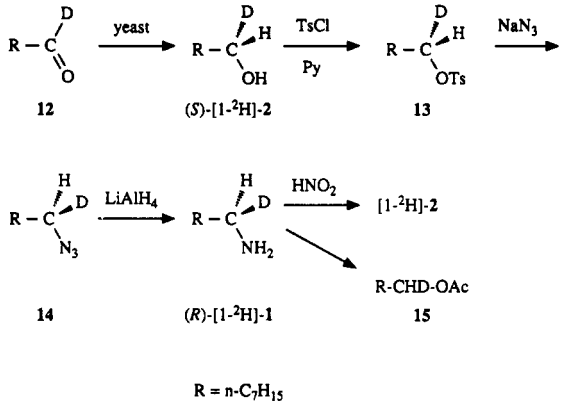
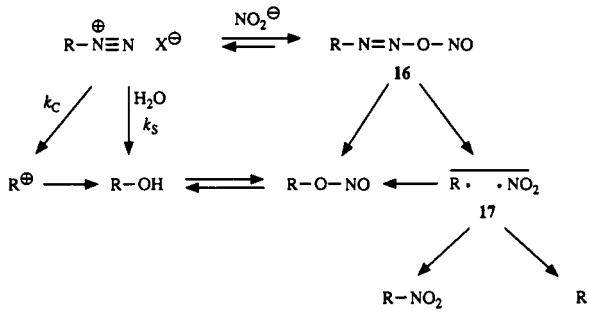



**Table II. Enantiomeric Composition (±1%) of [1-$^2$H]-Octyl Derivatives**

| | *R* | *S* |
|---|---|---|
| [1-$^2$H]-2, from fermenting yeast reduction of 12 | ≥1 | ≤99 |
| [1-$^2$H]-1, obtained from [1-$^2$H]-2 by way of 13 and 14 | 98.2 | 1.8 |
| [1-$^2$H]-2, obtained from nitrous acid deamination of [1-$^2$H]-1 in water, pH 3.5, $c$ = 0.048 M | 5.8 | 94.2 |
| $c$ = 0.146 M | 11.7 | 88.3 |
| $c$ = 0.80 M | 20.0 | 80.0 |
| [1-$^2$H]-6, obtained as before, $c$ = 0.146 M | 12.7 | 87.3 |
| [1-$^2$H]-9, obtained as before, $c$ = 0.80 M | 89.6 | 10.4 |
| 15, obtained from nitrous acid deamination of [1-$^2$H]-1 in acetic acid | 5.4 | 94.6 |

**Scheme III**




differences: (i) Inverting solvolytic displacement ($k_s$) proceeds readily with 1-alkanediazonium ions, in contrast to secondary and tertiary diazonium species. Therefore, 1 gives rise to 1-nitrooctane only in the micellar phase where inverting nucleophilic displacement is slowed down. The $k_s$ process is not available to (tertiary) α-cyanoalkanediazonium ions which consequently produce nitro compounds in homogeneous solution. (ii) Radicals originating from diazo(nium) nitrites are paired with $NO_2$ (17). Being sufficiently stable to escape in part from the solvent cage, α-cyanoalkyl radicals can be intercepted by added scavengers, such as TEMPO, and show little stereoselectivity in their recombination with $NO_2$. 1-Octyl radical pairs, on the other hand, collapse rapidly to give 1-nitrooctane with predominant retention of configuration.

How does the intervention of 1-octyl radicals in micellar deamination reactions of 1 affect the enantiomeric purity of 1-octanol? $NO_2$ is known to associate with alkyl radicals at oxygen as well as nitrogen.[16] Therefore, recombination of the radical pair (17) is expected to yield 1-octyl nitrite with predominant retention of configuration, as was observed for 1-nitrooctane. While the nitro compound persists, (*R*)-[1-$^2$H]-1-octyl nitrite undergoes exchange of the nitroso group with (*S*)-1-$^2$H]-1-octanol, leading eventually to the same ee for both products. Since 1-butanol is formed in 5–10-fold excess, the configuration of the equilibrium mixture will be (*S*) and the ee of 60–80% is compatible with product distribution.

Our reasoning, based on precedent and analogy, accounts for micellar effects that are otherwise difficult to explain. For long-chain 1-alkanamines, a radical component of the micellar deamination reaction should be considered as a viable alternative to the unlikely intervention of primary alkyl cations.

## Experimental Section

**General.** $^1$H NMR and $^2$H NMR spectra were obtained at ambient temperature at 80 and 400 MHz for $^1$H and 61.42 MHz for $^2$H (Bruker AM-400). Chemical shifts are reported in δ relative to tetramethylsilane as as internal standard, unless otherwise indicated. IR spectra were recorded on a Perkin-Elmer 257 instrument. GC analyses were run on a Siemens Sichromat equipped with glass capillary columns. Preparative gas chromatography (PGC) utilized Varian Aerograph 920 instruments equipped with packed glass columns. HPLC was performed with LDC (Milton Roy) chromatographs and refractometric detection. The cmc's were determined from graphs of observed surface tension vs log (concentration) of 1 in dilute perchloric acid (pH 3.5).[1]

**(*S*)-[1-$^2$H]-1-Octanol.** Reduction of methyl octanoate with $LiAlD_4$ (97%) yield) and oxidation of [1-$^2$H$_2$]-1-octanol with pyridinium chlorochromate (PCC)[17] (47% yield) were achieved by standard procedures. Baker's yeast (21 g) was added to a solution of glucose·$H_2O$ (200 g) in water (1 L). Fermentation was initiated at 30 °C, and a solution of [1-$^2$H]-octanol (5.28 g, 41 mmol) in ethanol (10 mL) was added dropwise. Fermentation was continued with vigorous stirring for ca. 48 h, until the gas evolution subsided. The mixture was subjected to steam distillation until ca. 1 L of distillate had been collected in the receiver. The distillate was extracted continuously with ether (500 mL) for 24 h. The extract was dried ($MgSO_4$) and concentrated by distillation (30-cm Vigreux column). The residue was purified by PGC (2 m carbowax, 140 °C) to give 2.43 g (47%) of (*S*)-[1-$^2$H]-1-octanol.

To a solution of (−)-camphanoyl chloride (325 mg, 1.5 mmol) in pyridine (2.5 mL) was added a solution of (*S*)-[1-$^2$H]-1-octanol (175 mg, 1.3 mmol) in pyridine (2.5 mL). The mixture was stirred

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at room temperature for 2.5 h, diluted with water (10 mL), and extracted with chloroform (4 × 5 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. HPLC (silica gel, ether:pentane = 3:1) of the residue afforded 275 mg (66%) of [1-$^2$H]-1-octyl camphanoate as a viscous oil: $^1$H NMR ($CDCl_3$) δ 0.7–1.0 (6 H, m), 1.04 (3 H, s), 1.10 (3 H, s), 1.15–1.45 (10 H, m), 1.5–2.6 (6 H, m), 4.17 (1 H, t, $J$ = 6.4 Hz). A solution of the ester (40 mg, 0.13 mmol) and of the shift reagent $Eu(dpm)_3$ (79 mg, 0.88 equiv) in $CCl_4$ (0.7 mL) was prepared in order to estimate the diastereomeric purity (≥99%) by $^2$H NMR.[7] Complete resolution of the diastereotopic deuterons (Δδ = 0.95 ppm) was demonstrated with the camphanoate of racemic [1-$^2$H]-1-octanol. The (*S*) configuration was assigned to the optically active sample by analogy with (*S*)-[1-$^2$H]-1-butanol.[4,5] In both cases the deuteron of the (*S*) enantiomer is shifted further downfield than the deuteron of the (*R*) enantiomer.

**(*R*)-[1-$^2$H]-1-Octanamine.** To a solution of (*S*)-[1-$^2$H]-1-octanol (6.0 g, 46 mmol) and pyridine (7.4 mL, 91 mmol) in chloroform (50 mL) was added at 0 °C *p*-toluenesulfonyl chloride (13.1 g, 69 mmol) in small portions. The mixture was stirred at 0 °C for 1 h, followed by 2 h at room temperature. The reaction solution was poured into water (35 mL) and extracted with ether (140 mL). The organic phase was washed with 2 M HCl (10 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), and water (2 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo. Purification on silica, eluent hexane:ether = 93:7, afforded 12.1 g (93%) of the tosylate 13: $^1$H NMR ($CDCl_3$) δ 0.85 (3 H, t, $J$ = 6 Hz), 1.0–1.8 (12 H, m), 2.43 (3 H, s), 3.98 (1 H, t, $J$ = 6 Hz), 7.2–7.9 (4 H, m).

A solution of 13 (12.0 g, 42 mmol), lithium azide (4.1 g, 82 mmol), and 12 crown-4 (0.74 g, 4.2 mmol) in 1,2-dimethoxyethane (180 mL) was stirred at 80 °C for 24 h. The solution was filtered and concentrated in vacuo (20 mm). Short-path distillation of the residue (30 °C, 0.05 mm) yielded 5.0 g (68%) of the azide 14: IR (film) 2090 $cm^{-1}$ ($\nu_{N_3}$); $^1$H NMR ($CDCl_3$) δ 0.87 (3 H, t, $J$ = 6 Hz), 1.05–1.80 (12 H, m), 3.20 (1 H, t, $J$ = 6 Hz). The azide 13 (5.0 g, 32 mmol), dissolved in ether (100 mL), was added dropwise to $LiAlH_4$ (1.52 g, 40 mmol) in ether (100 mL). The mixture was heated at reflux for 3 h, cooled, and hydrolyzed by dropwise addition of 5 M NaOH, followed by water. The flaky precipitate was filtered and washed repeatedly with ether. The combined ether solutions were dried ($K_2CO_3$) and concentrated by distillation. Fractional distillation of the residue afforded 3.14 g (75%) of (*R*)-[1-$^2$H]-1-octanamine: bp 71 °C/20 mm; $^1$H NMR ($C_6D_6$) δ 0.70 (2 H, s), 0.88 (3 H, t, $J$ = 6 Hz), 1.0–1.5 (12 H, m), 2.48 (1 H, m).

To a solution of (*R*)-[1-$^2$H]-1 (65 mg, 0.5 mmol) and triethylamine (0.9 mL) in dichloromethane (3 mL) was added (−)-camphanoyl chloride (108 mg, 0.5 mmol). The mixture was stirred at room temperature for 3 h, diluted with 0.5 M NaOH (1 mL), and extracted with dichloromethane (2 × 5 mL). The combined extracts were washed with water (2 × 4 mL), dried ($K_2CO_3$), and concentrated in vacuo. HPLC (silica, hexane:ether = 1:1) of the residue afforded 73 mg (47%) of *N*-[1-$^2$H]-1-octylcamphanamide: $^1$H NMR ($CDCl_3$) δ 0.7–1.0 (6 H, m), 1.08 (6 H, s), 1.15–1.6 (12 H, m), 1.7–2.1 (3 H, m), 2.2–2.7 (1 H, m), 3.1–3.45 (1 H, m), 6.40 (1 H, s). For analysis of the de by $^2$H NMR (Table II), 28 mg of the amide and 63 mg (1 equiv) of $Eu(dpm)_3$ were dissolved in 0.6 mL of $CCl_4$. Complete resolution of the diastereotopic deuterons (Δδ = 2.4 ppm) was confirmed with the corresponding racemate.

**Nitrous Acid Deamination Reactions.** (a) Product Distribution (Table I). 1-Octanamine (0.50 g, 3.87 mmol) was mixed with the appropriate amount of water (e.g., 193 mL for the 0.02 M solution). The pH was adjusted to 3.5 by dropwise addition of 5 M $HClO_4$ (glass electrode). A solution of $NaNO_2$ (0.53 g, 7.74 mmol) in water (4 mL) was then added with vigorous stirring while pH = 3.5 ± 0.2 was maintained with additional $HClO_4$. After stirring at room temperature for 18 h, the mixture was neutralized with $NaHCO_3$, saturated with NaCl, and extracted with ether (4 × 10 mL). The combined extracts were dried ($MgSO_4$), concentrated, and analyzed by GC (60-m Marlophen and 120-m Edenol). Product peaks were assigned by comparison with authentic samples.

(b) Stereochemical Studies (Table II). Analogous treatment of (*R*)-[1-$^2$H]-1 afforded product mixtures that were separated by HPLC (reversed-phase RP 18, methanol:water = 4:1) into fractions containing the octanols (14–16 min), 1-nitrooctane (18 min), and 1-octyl nitrite (35 min). The eluate containing the octanols was concentrated by distillation (30-cm Vigreux column) and extracted with *n*-pentane (4 × 10 mL). The combined extracts were dried ($MgSO_4$) and concentrated in vacuo. [1-$^2$H]-1-Octanol was isolated from the residue by HPLC (silica, ether) and derivatized with camphanoyl chloride as described above.

After adding Pd–C (10%, 20 mg) to the 1-nitrooctane fraction, hydrogenation was performed at 1.1 atm $H_2$ and room temperature. The solution was filtered and concentrated by distillation. The residue was treated with (−)-camphanoyl chloride, as described above for 1. The desired camphanamide was isolated by HPLC (silica, ether:pentane = 1:1) and analyzed by $^2$H NMR in the presence of $Eu(dpm)_3$.

The fraction containing 1-octyl nitrite was stirred with 0.5 mL of 5 M $HClO_4$ for 16 h. The mixture was neutralized with $NaHCO_3$, the methanol was distilled off (30 cm Vigreux column), and the aqueous phase was extracted with *n*-pentane (4 × 10 mL). The combined extracts were concentrated and purified by HPLC to provide [1-$^2$H]-1-octanol for camphanoylation.

An analogous deamination reaction was performed with $Na^{15}NO_2$ (labeled 96.4% $^{15}$N by the supplier). 1-Nitrooctane was isolated from the second HPLC fraction of this run and analyzed by IR ($CCl_4$): 1552 ($\nu_{as}$ $^{14}NO_2$, 3.5%) and 1520 $cm^{-1}$ ($\nu_{as}$ $^{15}NO_2$, 96.5%). For comparison, [$^{15}$N]-1-nitrooctane was prepared from 1-bromooctane and $Na^{15}NO_2$ in DMF (25 °C, 3 h, 76%). The IR spectrum of this sample matched that of the deamination product perfectly.

A solution of (*R*)-[1-$^2$H]-1 (0.40 g, 3.1 mmol) in anhydrous acetic acid (6.2 mL) was purged with nitrogen. Sodium nitrite (0.41 g, 6 mmol) was added in small portions within 1 h. After being stirred at room temperature for 18 h, the mixture was poured into a cold (0 °C) solution of potassium hydroxide (6.2 g) in water (15.4 mL) and extracted with *n*-pentane (5 × 3 mL). GC (120-m Edenol, 120 °C) of the extracts indicated the presence of 1-octyl acetate (62.3%), 1-octanol (4.3%), 2-octyl acetate (23.6%), 2-octanol (1.0%), 3-octyl acetate (3.7%), 3-octanol (0.1%), 4-octyl acetate (0.3%), and 1-octyl nitrate (4.7%). 1-Octyl acetate (90 mg) was isolated by HPLC (silica, hexane:ether = 96:4) and treated with $LiAlH_4$ (50 mg) in ether (5 mL) at reflux for 1 h. Standard workup, followed by HPLC (silica, pentane:ether = 55:45), afforded 32 mg of [1-$^2$H]-1-octanol which was converted into the camphanoate for $^2$H NMR analysis (Table II).