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Alkane Diazotates. XXI. Ethanolysis and Thioethanolysis of Octane-2-diazotate[1]

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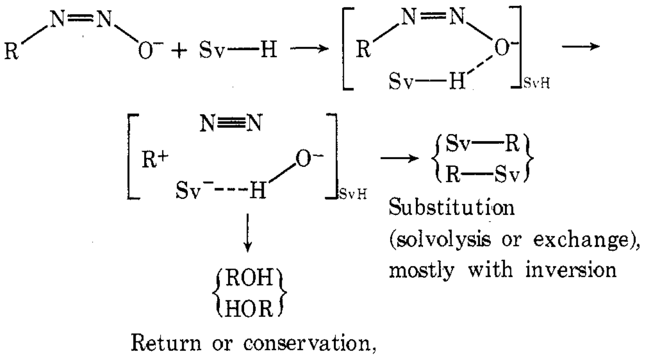
Optically active 2-aminooctane was converted to octane-2-diazotate and solvolyzed in either ethanol or thioethanol. In the ethanolysis reaction, 2-octyl ethyl ether and 2-octanol were formed with 74% overall inversion and 79% overall retention, respectively. In the thioethanolysis, 2-octyl ethyl sulfide and 2-octanol were formed with 73% overall inversion and 74% overall retention, respectively. The similarity of the results is discussed in relation to the stereochemical courses of other diazotate solvolysis reactions.

We have extensively studied the solvolysis of alkane diazotates,[3] $RN{=}NO^-$, paying particular attention to the hydrolysis,[4] ammonolysis,[5] and lithium ion catalyzed decomposition[6] of octane-2-diazotate (**1**). Scheme I has been found useful in rationalizing the results of the solvolysis reactions.[3]

Scheme I

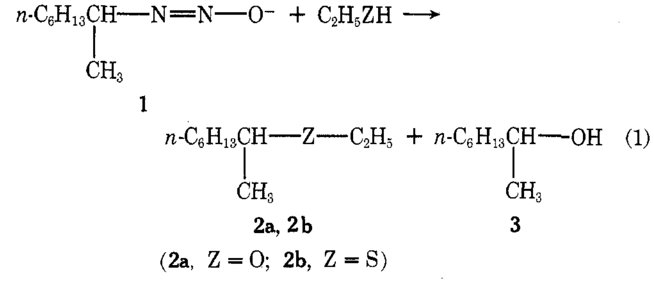


In Scheme I, Sv-H represents a protic solvent, and Sv^- represents the corresponding lyate ion. The reaction of the diazotate with a protic solvent gives the key intermediate, a nitrogen-separated ion triplet. Its collapse, by *return*, or *conservation*, affords an alcohol with net stereochemical retention, although some inverted alcohol can form if R^+ rotates within the ion triplet prior to collapse.[7] External capture of R^+ occurs mainly from the rear, affording an inverted *substitution* product, Sv-R. However, a lyate ion is hydrogen bonded to the counterion of the ion triplet, making possible a front-side collapse (*exchange*) to the stereochemically retained substitution product, R-Sv. Complete inversion in the substitution process is therefore not observed.

Upon comparison of the substitution processes in the hydrolysis[4] and ammonolysis[5] of **1**, we observed a marginally *greater overall inversion* in the formation of 2-aminooctane from **1** by ammonolysis (85%) in comparison with the formation of 2-octanol-^{18}O from **1** by hydrolysis with $H_2{}^{18}O$ (76%). Was this due to the greater nucleophilicity of the solvent ammonia, or was it merely a temperature effect? (The ammonolysis was carried out at −33 °C, the hydrolysis at 0 °C.) To obtain further information on the effect of solvent or lyate ion nucleophilicity in diazotate solvolyses, we have subjected **1** to ethanolysis and thioethanolysis, and determined the stereochemical courses of the substitution and return reactions in each case. The results follow.

Results and Discussion

Octane-2-diazotate[4] (13–18 mmol) was dissolved in HMPA[4a] and added to 200 ml of dry ethanol, or ethanethiol, at 0 °C. Nitrogen evolution was nearly quantitative (93–97%) in each reaction. After an aqueous work-up, the products of interest, 2-octyl ethyl ether (**2a**), 2-octyl ethyl sulfide (**2b**), and 2-octanol (**3**), were readily isolable by GC; cf. eq 1.



$$\underset{\mathbf{1}}{n\text{-}C_6H_{13}\underset{CH_3}{\underset{|}{C}}H{-}N{=}N{-}O^-} + C_2H_5ZH \longrightarrow \underset{\mathbf{2a},\ \mathbf{2b}}{n\text{-}C_6H_{13}\underset{CH_3}{\underset{|}{C}}H{-}Z{-}C_2H_5} + \underset{\mathbf{3}}{n\text{-}C_6H_{13}\underset{CH_3}{\underset{|}{C}}H{-}OH} \quad (1)$$

$$(\mathbf{2a},\ Z = O;\ \mathbf{2b},\ Z = S)$$

The yield of **2a** was remarkably constant over three ethanolysis reactions, 25 ± 1%, as determined by GC against a 2-hexanol standard. The yield of **3**, however, was relatively more variable, 2.8–3.8%, perhaps because of selective extractive loss during work-up. A reliable value of **2a**/**3** could therefore not be obtained. Similar problems attended the thioethanolysis experiments, in which **2b** and **3** were formed in yields comparable to those of the analogous ethanolysis products.[8] Octenes were doubtlessly formed in these reactions,[4–6] but were not examined.

Optically active 2-aminooctane was converted to **1** via its urethane and *N*-nitrosourethane derivatives,[4,9] and solvolyzed in ethanol or ethanethiol, as above. Following work-up and GC purification, the rotations of **2a**, **2b**, and **3** were polarimetrically determined. These results, and the derived *net* stereochemical courses of the reactions, are displayed

Table I. Stereochemistry of Product Formation in Solvolyses of 1

		(*S*)-(+)-n-$C_6H_{13}CH(CH_3)$-Z-C_2H_5			(*R*)-(−)-2-Octanol		
Run	Solvent	α^{25}D obsd, deg[a]	α^{25}D corr, deg[b]	Stereochem, %[c]	α^{25}D obsd, deg[a]	α^{25}D corr, deg[b]	Stereochem, %[d]
1	C_2H_5OH	+0.535	+7.38	48.9 net inv	−0.092	−4.76[e]	59.2 net retn
2	C_2H_5OH	+0.534	+7.36	48.8 net inv	−0.333	−4.59	57.1 net retn
3	C_2H_5SH	+0.473	+6.52	48.0 net inv	−0.262	−3.61	44.9 net retn
4	C_2H_5SH	+0.449	+6.19	45.6 net inv	−0.084	−3.98[f]	49.5 net retn

[a] Determined with a Perkin-Elmer Model 141 spectropolarimeter, using *neat*, GC-purified samples in a 0.1-dm cell. [b] Corrected for path length (to 1.0 dm), and for the optical purity of the *N*-2-octylurethane precursor from which **1** was derived. (*R*)-(−)-*N*-2-octylurethane had α^{25}D −3.25° (neat, 1 dm), corresponding to an optical purity of 72.5%.[10] [c] Optically pure 2-octyl ethyl ether has α^{22}D 15.08° (neat, 1 dm).[11] Optically pure 2-octyl ethyl sulfide has α^{25}D 13.59° (neat, 1 dm); see Experimental Section. The comparable literature value is α^{20}D 14.3°.[12] In the 2-octyl series, amine, alcohol, and ethyl ether belong to the same optical series when of the same rotational sign.[13] This must also be true of the ethyl sulfide derivative.[12] Initial (*R*)-(−)-2-aminooctane, the earliest precursor of **1**, had α^{24}D −3.80° (neat, 1 dm). These facts permit the assignment of inversion or retention to the stereochemical results listed in the table. [d] Optically pure 2-octanol has α^{23}D 8.04° (neat, 1 dm).[14] See also note *c*. [e] Product **3** was diluted with racemic **3** before determining the rotation. The dilution factor (3.75) is included in the correction. [f] Dilution factor 3.44; see note *e*.

Table II. Stereochemistry of Solvolyses of Octane-2-diazotate

				Substitution (2-Oct-X)		Return (2-Oct-OH)	
Solvent[a]	Ref	Rxn temp, °C	X	% inv	% retn	% retn	% inv
NH_3	*b*	−33	NH_2	85	15	65	35
$H_2{}^{18}O$	*c*	0	^{18}OH	76	24	73	27
C_2H_5OH	*d*	0	OC_2H_5	74	26	79	21
C_2H_5SH	*d*	0	SC_2H_5	73	27	74	26

[a] HMPA was present in all cases. [b] Reference 5. [c] Reference 4a. [d] This work.

in Table I. In Table II, we summarize the (average) overall stereochemical courses of product formation in various solvolytic reactions of **1**.

The most striking facet of Table II is the essential *invariance* of the stereochemistry of product formation observed in the hydrolysis, ethanolysis, and thioethanolysis of **1**. With reference to Scheme I, the substitution or solvolysis product is formed with 73–76% overall inversion, and the return product, 2-octanol, is formed with 73–79% overall retention of configuration, *irrespective of solvent or lyate ion identity*. This behavior further supports the postulated intermediate formation of an extremely unselective cationic 2-octyl moiety, probably as part of an ion triplet[3] (Scheme I, R^+ = 2-Oct^+). We have previously noted that this intermediate, when generated in a saturated aqueous solution of sodium azide, selects in a nearly statistical manner between water and azide nucleophiles,[4c,6] behavior quite at variance with that of more highly stabilized cations, which markedly prefer azide ion.[15] The sensitive stereochemical probe applied here thus affords results in agreement with the earlier observation.

Refer again to Scheme I. Ethanethiol is more acidic than ethanol,[16] so that the derived ion triplet should contain a more fully developed lyate ion in the case in which Sv^- = $C_2H_5S^-$ than in the case in which Sv^- = $C_2H_5O^-$. Moreover, the mercaptide is a stronger nucleophile than its oxygen analogue, at least when comparisons are made on scales defined by moderately reactive substrates.[19] These considerations suggest that, if the 2-octyl cation of the ion triplet were even moderately discriminating toward nucleophiles, collapse with lyate ion with front-side *exchange and stereochemical retention* would contribute to the destruction of the ion triplet more strongly when Sv = $C_2H_5S^-$ than when Sv = $C_2H_5O^-$. Accordingly, the overall stereochemistry of solvolysis product, **2**, would reflect a greater contribution from the *exchange* (retention) component in thioethanolysis than in ethanolysis; *less* overall inversion would therefore be expected in the former reaction. That this is not the case (Table II) again demonstrates the insensitivity of the ion triplet's cationic moiety to the nucleophilicity of its reaction partner.

The present results underline our previous conclusion that the nitrogen-separated ion triplet exhibits consistent and characteristic chemistry in varied reactions.[3] Small changes in the competitive blending of the pathways of Scheme I do occur, and sensibly reflect alterations of cation, nucleophile, solvent, or leaving group.[3,6] However, the hallmarks of the nitrogen-separated ion triplet's behavior appear to be its integrity and consistency, maintained despite relatively large changes in reaction parameters. This must be due to the high reactivity of its nascent cation, which ensures that subsequent reactions compete with diffusive processes, so that "selectivity" must mainly reflect the geometry of the ion triplet, particularly the relative geometry of the cation and competing nucleophiles, and that of the surrounding solvent shell.

Experimental Section

2-Aminooctane was obtained from Norse Chemical Co. and successively converted to *N*-2-octylurethane, *N*-nitroso-*N*-2-octylurethane, and octane-2-diazotate as previously described.[4] Optically active 2-aminooctane was obtained from the racemate by repeated recrystallization of its (−)-tartrate salt from methanol[20] (final mp 84–85 °C), followed by digestion of the diastereomeric salt with 6 N NaOH, extraction of the amine with ether, drying over BaO, removal of solvent, and distillation from sodium. Final purification was effected by GC, using a 5 ft × 0.25 in., 28% Pennwalt 223, 4% KOH on 80/100 Gas-Chrom R column. Samples thus purified were immediately submitted to polarimetry: α^{25}D −3.80° (neat, 1 dm). This amine was converted to (*R*)-(−)-*N*-2-octylurethane, α^{25}D −3.25° (neat, 1 dm, 72.5% optically pure[10]), with ethyl chloroformate.[4]

Solvolysis Experiments. A standard procedure is described. A slurry of 2.15 g (19.2 mmol) of potassium *tert*-butoxide in 27 ml of dry ether was prepared (under N_2) in a 250-ml three-neck flask, fitted with a low-temperature thermometer, addition funnel, gas inlet tube, and magnetic stirring bar. *N*-Nitroso-*N*-2-octylurethane (2.09 g, 9.1 mmol) in 27 ml of dry ether was slowly added, with stirring, while the reaction temperature was maintained at −30 °C. After the addition was completed, stirring was continued for 30 min at −30 °C. The reaction mixture was then allowed to warm to 20 °C, ether was removed by aspiration, and 15 ml of HMPA (Aldrich, distilled from CaH_2) was added to the residual solid to give a dark orange solution of **1**. The diazotate solution was slowly syringed into 200 ml of absolute ethanol (or ethanethiol), which was contained in a 1-l. three-neck flask, fitted with two serum caps, a gas outlet tube, and a magnetic stirring bar, and maintained at 0 °C. The solvent was vigorously stirred during the addition of 1. Evolved N_2 (97% of the theoretical quantity) was collected in a gas buret. After 1 h, the reaction mixture was poured into 600 ml of water and extracted with ether (5 × 50 ml), and the ethereal extracts were combined and dried ($MgSO_4$). After filtration, all low-boiling material was stripped on the rotary evaporator, and the products of interest were isolated by GC (Varian Aerograph, Model 90-P). From ethanolysis runs, **2a** and **3** were isolated using a 24 ft × 0.25 in., 10% tris(2-cyanoethoxy)propane (TCEP) on 45/60 Gas-Chrom R column (130 °C). From thioethanolysis runs, **2b** and **3** were isolated using a 18 ft × 0.25 in., 15% Carbowax 20M on 60/80 Gas-Chrom R column (150 °C). Product identities were established by comparison of ir and NMR spectra to those of authentic samples.[21] Product yields and ratios were determined from GC traces integrated with a Varian Model 481 electronic integrator. The GC thermal conductivity detector was calibrated with pure samples of products.

Stereochemical results were obtained from similar experiments, but using optically active *N*-nitroso-*N*-2-octylurethane; the relevant data appear in Table I.

2-Octyl Ethyl Sulfide. (*R*)-(−)-2-Octanol [Norse, $\alpha^{25}\text{D}$ −0.71° (neat, 0.1 dm), 88.3% optically pure[14]] was converted to the tosylate by adding 15.2 g (79.7 mmol) of freshly recrystallized *p*-toluenesulfonyl chloride to 5.00 g (38.4 mmol) of the alcohol in 75 ml of pyridine (distilled from BaO) maintained at 0 °C. The reaction mixture was kept in the refrigerator for 24 h, and the procedure described by Fieser and Fieser[22] was then used to isolate the oily tosylate, and to purify it (as a white glass at −75°).

A solution of 3.0 ml (40 mmol) of ethanethiol in 25 ml of tetrahydrofuran (THF) was treated with 30 ml of 2 N *n*-butyllithium in hexane, under nitrogen, at −65 °C. Then 7.0 g (25 mmol) of 2-octyl tosylate was added with stirring, as a solution in 25 ml of THF. The reaction temperature was kept below −40 °C. After the completion of addition, the reaction mixture was warmed to room temperature and then refluxed overnight. The product solution was poured into 200 ml of water and extracted with ether (5 × 50 ml). The combined ether extracts were dried ($MgSO_4$), filtered, and stripped of solvent. The residue was purified by GC on the TCEP column (see above) at 130 °C, to afford (*S*)-(+)-**2b**: $\alpha^{25}\text{D}$ +1.20° (neat, 0.1 dm); NMR (CCl_4) δ 2.47 (q, J = 7 Hz, SCH_2) superimposed on a *multiplet*, 2.90–2.4 (CHS), total 3 H, 1.65–1.08 (m) and 0.92 (crude t), alkyl protons, 19 H.

Correction of the observed rotation of the product 2-octyl ethyl sulfide for the optical purity of the precursor 2-octanol, and for path length, affords $\alpha^{25}\text{D}\,|13.59°|$ for optically pure **2b**.[12]

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Registry No.—**1,** 53475-03-9; **2a,** 36978-30-0; **2b,** 58052-40-7; **3,** 5978-70-1; (*R*)-(−)-2-aminooctane, 34566-05-7; (*R*)-(−)-*N*-2-octylurethane, 41903-73-5.

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