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AMMONOLYSIS OF ALKANE DIAZOTATES - THE INVERSION OF AMINES[1]

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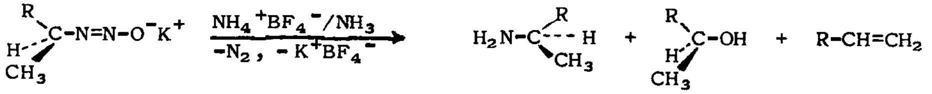
Whereas the S_N2 chemistry of alcohols is well developed, that of aminoalkanes remains primitive. To appreciate the contrast, one need only consider the relative ease of converting chiral members of these classes into their respective enantiomers. Recently, based upon labilization of the amino function as a bis-sulfonamide, S_N2 chemistry of aminoalkanes has begun to develop.[2-4]

The facile conversion of aminoalkanes to alkane diazotates,[5] coupled with the inverting hydrolytic conversion of the latter to alcohols,[6-8] led us to explore a possible S_N2 chemistry of aminoalkanes based on diazotates. Now we report that ammonolysis of chiral alkane diazotates affords inverted aminoalkanes in a new reaction of mechanistic interest

2-Aminooctane and α-phenylethyl amine were converted to their respective potassium alkane diazotates,[5] which were either dissolved in refluxing liquid NH_3 and treated with 4 equiv. of $NH_4^+BF_4^-$, or added as hexamethylphosphoric triamide (HMPA) solutions to refluxing $NH_4^+BF_4^-/NH_3$. (The method of reagent addition had little affect on the results.) After 3 hrs., NH_3 was allowed to evaporate,[9] neutral and basic products were separated, and final purifications were effected by gc. A 28% Penwalt 223, 4% KOH on 80/100 Gas Chrom R column was used for the amines. Eq. (1) summarizes typical results and absolute yields.



$$\mathrm{R(H)(CH_3)C{-}N{=}N{-}O^-K^+} \xrightarrow[-N_2,\ -K^+BF_4^-]{NH_4^+BF_4^-/NH_3} \mathrm{H_2N{-}C(R)(H)(CH_3)} + \mathrm{R(H)(CH_3)C{-}OH} + \mathrm{R{-}CH{=}CH_2} \quad (1)$$

R = C_6H_5	37%	12%	14%
R = C_6H_5[10a]	31%	24%	15%
R = $\underline{n}$-C_6H_{13}	18%	6%	32%[10b]

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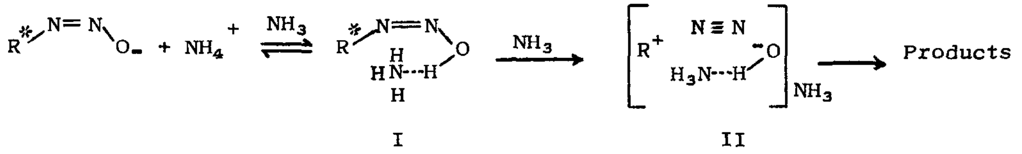
Chiral diazotates were obtained from d-α-phenylethyl amine α_D^{28} + 36.25°[*] (94.6% optically pure[11]) and from l-2-aminooctane, α_D^{23} - 4.03° (75 7% optically pure[12]) by literature procedures.[6-8,13,14] Products were isolated by gc from the ammonolyses of the chiral diazotates, and their rotations were determined with a Perkin-Elmer Model 141 Spectropolarimeter. The data is collected in Table 1. The stereochemical courses of the reactions follow from the fact that amines, alcohols, and chlorides of the 2-octyl and α-phenylethyl series display the same rotatory sign when they are of a common relative configuration.[17]

Mechanistically, the reactions can be analyzed with reference to Eq. (2).[18]



(2)

Table 1. Product Stereochemistry, Ammonolysis of $RCH(CH_3)N{=}NO^-K^+$

R	$RCH(CH_3)NH_2$			$RCH(CH_3)OH$		
	α_D	(temp., °C)	% Net Inv.	α_D	(temp., °C)	% Net Retn.[a]
n-C_6H_{13}[b]	+2 77°	(23)	69.	-1.32°	(24)	22.[c]
n-C_6H_{13}[d]	+2 92°	(25)	72.	-1.80°	(23)	30.[c]
C_6H_5[b]	-17.00°	(28)	47.	+24 84°	(22)	60[e]
C_6H_5[d]	-16.64°	(28)	46.	+24.50°	(23)	59[e]
C_6H_5[b,f]	-19.03°	(28)	52.	+31.63°	(24)	77.[e]

[a] Corrected for diazotate optical purity. [b] No HMPA present [c] α_D^{23} + 8.04° represents the maximum rotation; see ref. 12. [d] HMPA present. [e] α_D^{25} + 43.7° represents the maximum rotation.[15] [f] $NH_4^+Cl^-$ was used as the catalyst, and α-phenylethyl chloride, α_D^{25} - 32.38° (at most, 31% net inverted[16]) was isolated.

The amines arise mainly by inverting ammonolysis of I or II, although front-side participation of NH_3 (in II) precludes complete inversion. Alcoholic products form mainly by hydroxide return within assembly II Failure to obtain complete retention may reflect cation rotation-collapse within II,[19] or inverting reaction of I or II with "free" water.

Comparison of the stereochemical results with related data for deamina-

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[*] All rotations in this paper refer to neat liquids, l = 1 dm

tive processes is interesting. (1) *Overall retention*[20] *in return processes*. For R = α-phenylethyl, we find: $C_{10}H_7COO^-$ in HOAc, 81%;[21] OH^- in HOAc, 79%;[22] OH^- in C_2H_5OH, 87%;[13] $C_2H_5O^-$ in CH_2Cl_2, 82%;[13] and OH^- in NH_3, ~80% (this work). For R = 2-alkyl, we find: $C_6H_5COO^-$ in HOAc, 68%;[23] $^{16}OH^-$ in $H_2{}^{18}O$-HMPA, 73%;[6] and OH^- in NH_3-HMPA, 65% (this work). Apparently, the extent of retention in the return process depends mainly on cation identity, and less strongly on the nature of the solvent and returning group. (2) *Overall inversion*[24] *in solvolysis processes*. For R = α-phenylethyl, we find C_2H_5OH (HMPA), ~66%;[13] and NH_3 (HMPA), 73% (this work). For R = 2-octyl, we find $H_2{}^{18}O$ (HMPA), 76%;[6] and NH_3 (HMPA), 86% (this work). The limited data suggest that inversion in solvolytic deamination increases as the substrate's alkyl group is less able to support a positive charge, and as the solvent becomes more nucleophilic That is, the process takes on the stereochemical trappings of the S_N2 reaction. We are investigating related diazotate reactions, and hope to further clarify the mechanistic trends.

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References and Notes

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(9) Yields are improved if the evaporation is done through a water condenser

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(10b) Includes 1- and 2-octenes.

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(12) α_D^{19} -5.32° represents the maximum rotation: see A. Streitwieser, Jr., and W. D. Schaeffer, *J. Amer. Chem. Soc.*, **78**, 5597 (1956).

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(15) R. L. Burwell, Jr., A. D. Shields, and H. Hart, *ibid.*, **76**, 908 (1954).

(16) α_D^{25} 109° is a lower limit for the maximum rotation.[15]

(17) See J. A. Mills and W. Klyne in "Progress in Stereochemistry", Vol. I, W. Klyne, Ed., Butterworth, London, 1954, pp. 194-5

(18) The diazotate is presumed to be *syn*, see: E. H. White, T. J. Ryan, and K. W. Field, *J. Amer. Chem. Soc.*, **94**, 1360 (1972).

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