The Journal of
Organic
Chemistry

VOLUME 56, NUMBER 3 FEBRUARY 1, 1991

# *Communications*

## Stereochemistry of Nucleophilic Displacement on 1-Alkanediazonium Ions

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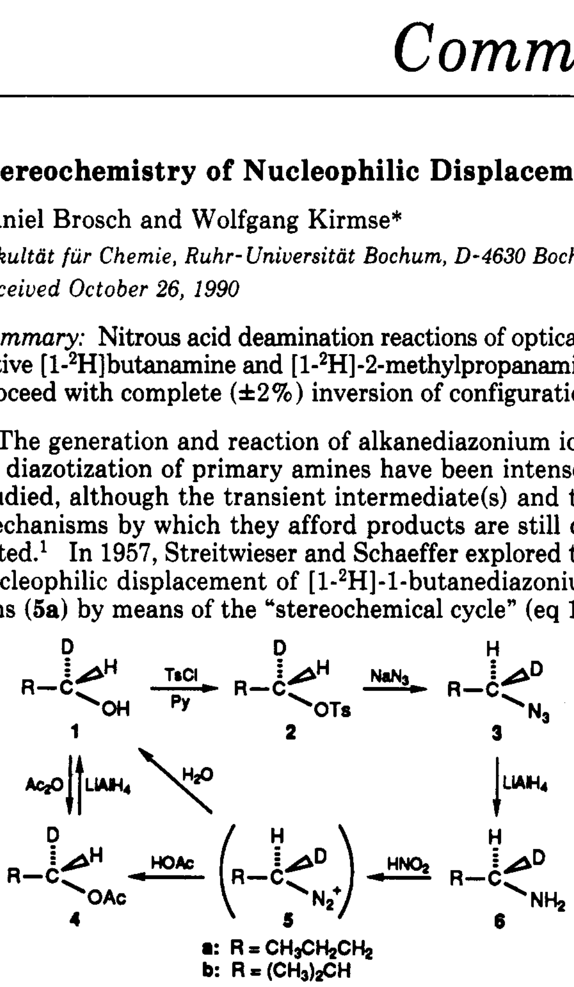
*Received October 26, 1990*

*Summary:* Nitrous acid deamination reactions of optically active [1-$^2$H]butanamine and [1-$^2$H]-2-methylpropanamine proceed with complete (±2%) inversion of configuration.

The generation and reaction of alkanediazonium ions by diazotization of primary amines have been intensely studied, although the transient intermediate(s) and the mechanisms by which they afford products are still debated.[1] In 1957, Streitwieser and Schaeffer explored the nucleophilic displacement of [1-$^2$H]-1-butanediazonium ions (**5a**) by means of the "stereochemical cycle" (eq 1).[2]



(1)

The [1-$^2$H]-1-butyl acetate (**4a**) obtained from optically active [1-$^2$H]-1-butanamine (**6a**) was found to be 69 ± 7% inverted (31 ± 7% racemized). This result was attributed to a combination of backside displacement on **5a**, yielding inverted product, and formation of 1-butyl cations, leading to racemization. The notion that 1-alkanediazonium ions give rise to primary carbocations (ion pairs) has endured[1,3] although experiment and theory indicate that the dediazoniation of 1-alkanediazonium ions in the gas phase is endothermic.[4] These inconsistencies induced us to reinvestigate the reaction sequence, eq 1, with modern techniques.

**Table I. Enantiomeric Composition (±1%) of 1 and 6**

| | a | | b | |
|---|---|---|---|---|
| | *R* | *S* | *R* | *S* |
| **1**, from fermenting yeast reduction of RCD=O | ≤1 | ≥99 | 4 | 96 |
| **6**, obtained from **1** by way of **2** and **3** | 98 | 2 | 96 | 4 |
| **1**, obtained from nitrous acid deamination of **6** in water, pH 3.5 | 4 | 96 | 4 | 96 |
| in acetic acid (followed by $LiAlH_4$ reduction of **4a**) | 3 | 97 | | |

The conclusions of Streitwieser and Schaeffer were based on polarimetry, the only tool available in 1957. In the present study, compounds **1** and **6** were treated with camphanoyl chloride to give the analogous esters and amides, 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, as exemplified in Figure 1.[5]

When we reacted the crude tosylate **2a** with sodium azide, according to the original procedure,[2] the amine **6a** was obtained with 86 ± 2% ee. The apparent racemization

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[1] For reviews, see: (a) White, E. H.; Woodcock, D. J. in *The Chemistry of the Amino Group*; Patai, S., Ed.; Wiley-Insterscience: 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.

[2] Streitwieser, A., Jr.; Schaeffer, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 2888.

[3] For recent applications, see: Gold, B.; Deshpande, A.; Linder, W.; Hines, L. *J. Am. Chem. Soc.* **1984**, *106*, 2072.

[4] Ford, G. P.; Scribner, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 349 and references cited therein.

[5] For previous applications of this technique, see: (a) Shapiro, S.; Arunachalam, T.; Caspi, E. *J. Am. Chem. Soc.* **1983**, *105*, 1642. (b) Parker, D. *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.

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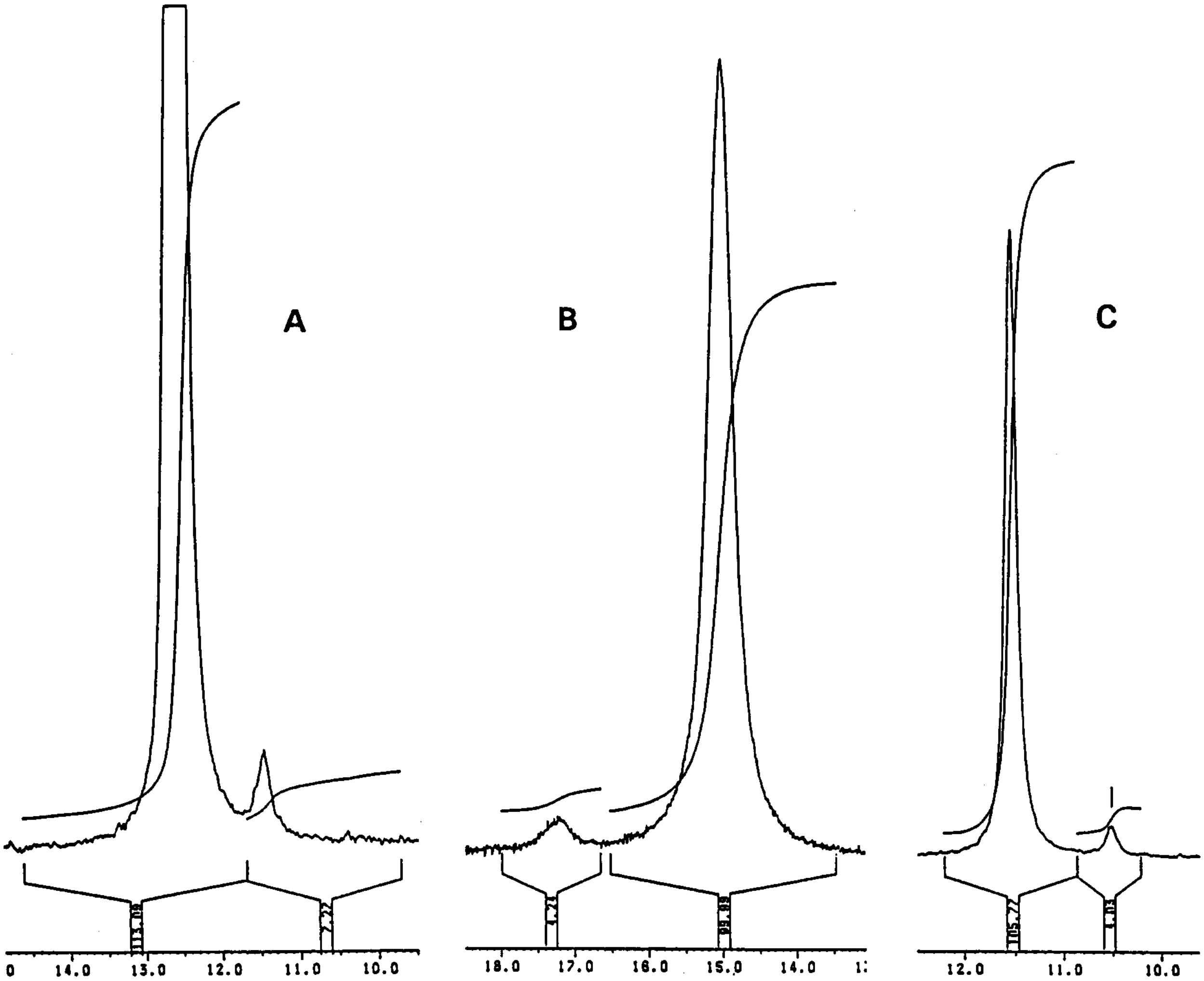

**Figure 1.** $^2$H NMR spectra ($CCl_4$, 0.9 equiv of $Eu(dpm)_3$) of camphanic acid derivatives of **1b** from yeast reduction of i-PrCDO (A), **6b** (B), and **1b** from nitrous acid deamination of **6b** (C). Assignment of the minor peaks to *ent*-**1b** and *ent*-**6b** is confirmed by the $^2$H NMR spectra (not shown) of the camphanic acid derivatives of *rac*-**1b** and *rac*-**6b**, respectively.

was traced to the formation of [1-$^2$H]-1-chlorobutane as a byproduct in the reaction of **1a** with tosyl chloride, presumably via inverting displacement of tosylate from **2a** by chloride ion. (*R*)-[1-$^2$H]-1-chlorobutane will subsequently lead to (*S*)-**6a**, thus accounting for the decrease in enantiomeric purity. The intervention of 1-chlorobutane may have contributed to the partial racemization observed by Streitwieser and Schaeffer. These authors were not able to determine the ee of **6a** since the specific rotation of the optically pure compound was not known.

Purification of **2a** by LC avoided the complications mentioned above. The amine **6a** was thus obtained with 96 ± 2% ee. Nitrous acid deamination of **6a**, performed in water and in acetic acid, produced **1a** with virtually complete inversion of configuration (Table I).[6] Since there is no evidence for a primary carbocation in this reaction, the hydride shift leading to 2-butyl products[7] is likely to proceed in concert with the expulsion of nitrogen.

The effect of $\beta$-branching on the stereochemistry of *sec*-alkanediazonium ions[8] prompted us to include [1-$^2$H]-2-methylpropanamine (**6b**) in the present study. The nitrous acid deamination of **6b** was found to give **1b** with complete inversion of configuration (Table I). This result does not exclude methyl participation in the decomposition of **5b** (12% of 2-butanol is obtained in addition to 67% of 2-methyl-2-propanol and 8% of **1b**). However, the methyl-bridged structure intervening between **5b** and the 2-butyl cation should be viewed as a transition state rather than a capturable intermediate.

In conclusion, we reiterate Streitwieser's proposal[2] that the ease of nitrogen expulsion from 1-alkanediazonium ions leads to small differences in activation energy for the various pathways, *with the exception of the $k_c$ process*. Inverting displacement ($k_S$) is recognized as the exclusive mechanism by which 1-alkanediazonium ions are converted into 1-alkanols. Primary carbocations (ion pairs) are not involved.

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(6) Deprotonation of **5a** to the analogous diazo compound, followed by regeneration of (*R*,*S*)-**5a**, would also be a source of racemization. Nitrous acid deamination of 1-butanamine in $D_2O$ (pH 3.5) led to incorporation of 0.03–0.05 D into the 1-butanol thus obtained.

(7) Product distributions in water [1-butanol (51%), 2-butanol (30%)] and in acetic acid [1-butyl acetate (52%), 1-butanol (3%), 2-butyl acetate (27%), 2-butanol (1%)] were in agreement with previous reports.[1b]

(8) Banert, K.; Bunse, M.; Engbert, T.; Gassen, K.-R.; Kurnianto, A. W.; Kirmse, W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 272 and references cited therein.