Tetrahedron Letters No.28, pp. 3219-3222, 1968. Pergamon Press. Printed in Great Britain.

AN EXTRAORDINARY CASE OF CONFIGURATIONAL INVERSION IN A DEAMINATIVE PROCESS: THE PHENOLYSIS OF BUTANE-2-DIAZOTATE (1)

Robert A. Moss and George H. Temme III (2)

Wright Laboratory, School of Chemistry
Rutgers-The State University
New Brunswick, New Jersey

(Received in USA 18 March 1968; received in UK for publication 19 April 1968)

The basic hydrolysis of sec-alkyl diazotate salts, $R\text{-}N{=}N\text{-}\overset{-}{O}\,\overset{+}{M}$, largely bypasses the intermediacy of free carbonium ions (3). We were prompted to study the phenolysis of optically active butane-2-diazotate (potassium) in diethyl ether, hoping that unusual stereochemical consequences would attend the decomposition of the initially formed butane-2-diazotic acid-potassium phenoxide aggregate. 2-Aminobutane was converted to N-sec-butylurethan (4). The urethan was nitrosated (5), and the identity and purity of the N-nitroso-N-sec-butylurethan were established by NMR (6). The nitrosourethan was converted to potassium butane-2-diazotate by the action of 2 equivalents of potassium t-butoxide in diethyl ether (3,5). Addition (at -18°) of 2-6 equivalents of ethereal phenol led to immediate evolution of up to 90% of the theoretical nitrogen content (based on the nitrosourethan).

Simple work-up and gas chromotographic (7) procedures, coupled with IR and NMR comparisons with authentic materials, allowed the isolation and identification of sec-butylphenyl ether, o-sec-butylphenol, and p-sec-butylphenol (8). The yields of these products, based on the nitrosourethan were 9%, 10%, and 1% respectively.

(+)-2-Aminobutane, α_D^{24} + 4.99°, 93% optically pure (9), was converted to the urethan with preservation of optical purity (4). The active urethan was nitrosated and converted to the diazotate. The latter was reacted with phenol as described above.

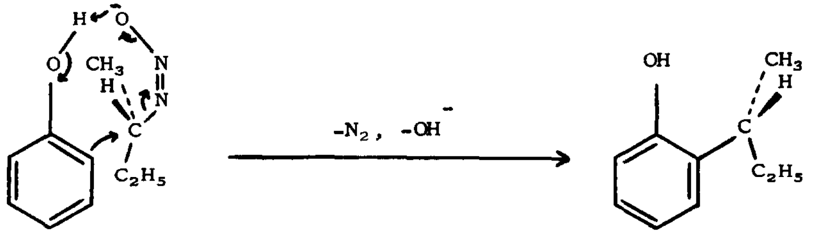
(+)-sec-Butylphenyl ether and (-)-o-sec-butylphenol were isolated from the reaction mixture. The stereochemical consequences of three experiments (based on

(+)-2-aminobutane) were: sec-Butylphenyl ether, formed with 0.14, 7.0 and 5.2% net retention (11), and o-sec-Butylphenol, formed with 80, 75, and 76% net inversion (12). Both products were shown to be optically stable to the reaction and isolation conditions. It was also shown that doubling the available phenol during the diazotate phenolysis changed neither the stereochemistry of formation of the products, nor their relative yields.

Consideration of the known absolute configurations of (+)-2-aminobutane (13), (+)-2-butanol (14), (+)-sec-butylphenyl ether (11,15) and (+)-o-sec-butylphenol (12), shows that all four compounds belong to the same optical series, when of the same rotational sign. Since (+)-2-aminobutane was converted to butane-2-diazotate by a series of reactions not involving the assymetric carbon atom, and since phenolysis of the diazotate afforded (+)-sec-butylphenyl ether and (-)-o-sec-butylphenol, we conclude that the former was produced with retention while the latter was produced with inversion of configuration.

To our knowledge, the 75-80% net inversion in the formation of sec-butylphenol from butane-2-diazotate represents the most stereospecific deaminative inversion yet described for an acylic amine derivative (16). The extent of inversion is probably greater than that reported for the bona fide S_N2 reaction of phenoxide ion and α-phenylethyl chloride, which led to o-α-phenylethylphenol with about 65% net inversion (17).

The high inversion attending conversion of the diazotate to the phenol suggests mechanism [1].



[1]

The concept of extensive concertedness in the breaking of the O-N and C-N bonds as the diazotate is protonated is in agreement with recent descriptions of related reactions (3,18). The *syn* stereochemistry shown for the N=N linkage would seem to be a logical requirement for the concertedness (19).

Attempts to account for the extensively racemized *sec*-butylphenyl ether are more speculative. The possible intermediacy of 2-diazobutane is greatly limited by our observation that the reaction of butane-2-diazotate and excess phenol-O-*d* afforded the ether with no more than 7.2% deuterium content (mass spectral analysis). The *sec*-butylphenol formed in this experiment contained 3.2% deuterium.

We tentatively suggest that the ether is derived mainly from *anti*-butane-2-diazotate. Cyclic, concerted phenolysis would here be impossible, and a resulting, spatially separated phenoxide-2-butyl ion pair might undergo cation racemization before collapsing, mainly at the most electronegative center of the anion, to *sec*-butylphenyl ether. Similar mechanistic considerations involving stereochemistry at the N=N linkage have recently been discussed by Miller (20).

Acknowledgements. Support by the National Science Foundation (GY-2745) and by the donors of the Petroleum Research Fund (PRF 2745-A4)is gratefully acknowledged. We also wish to thank Mr. Edgar Emery of the Colgate-Palmolive Co., who determined the mass spectra.

References

1. Part V in the series: "The Solvolysis of Alkyl Diazotates." Part IV, R. A. Moss and F. C. Shulman, *J. Am. Chem. Soc.*, in press.
2. National Science Foundation Undergraduate Research Participant, 1967-8.
3. R. A. Moss and S. M. Lane, *J. Am. Chem. Soc.*, **89**, 5655 (1967).
4. P. Bruck, I. N. Denton, and A. H. Lamberton, *J. Chem. Soc.*, 921 (1956).
5. See, for example, R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966).
6. R. A. Moss, *Tetrahedron Letters*, 711 (1966).
7. A 7 ft., 0.25 inch, 5% Carbowax 20M on 60-80 mesh Chromsorb G column was employed, at operating temperatures of 170-180°.
8. The expected side products, ethyl-*t*-butyl carbonate and di-*t*-butyl carbonate, as well as a 17% yield of 2-butanol, were also found in the product mixture.
9. Based upon α_D^{20} + 5.38° (1 dm, neat), L. G. Thomé, *Ber.*, **36**, 582 (1903).
10. Details of observed and corrected rotations will be found in the Henry Rutgers Thesis of G. H. Temme, Rutgers University Library, 1968.

11. Rotations of the ether were compared to α_D^{18} 33.7° (1 dm, neat). This value may not be the maximum, and the net retention given above represents a maximum for the reaction. See: M. P. Balfe, M. K. Hargreaves, and J. Kenyon, *J. Chem. Soc.*, 1861 (1950).

12. Rotations of the phenol were compared to α_D^{23} 18.6° for the optically pure compound. See: F. Hawthorne and D. J. Cram, *J. Am. Chem. Soc.*, **74**, 5859 (1952).

13. A. Kjaer and S. E. Hansen, *Acta Chem. Scand.*, **11**, 898 (1957)

14. See J. A. Mills and W. Klyne in "Progress in Stereochemistry," W. Klyne, Ed., Academic Press, Inc., New York, 1954, V. 1, p. 195.

15. M. M. Sprung and E. S. Wallis, *J. Am. Chem. Soc.*, **56**, 1715 (1934).

16. Streitwieser reported that acetolytic deamination of active 1-aminobutane-1-*d* afforded the corresponding acetate with 69 ± 7% net inversion. A. Streitwieser, Jr. and W. D. Schaeffer, *ibid.*, **79**, 2888 (1957).

17. H. Hart and H. S. Eleuterio, *ibid.*, **76**, 516 (1954).

18. M. C. Whiting, *Chem. Brit.*, **2**, 482 (1966).

19. The hypothesis that the highly inverted *o*-*sec*-butylphenol arises *via* an S_N2 attack of phenoxide on butane-2-diazotic acid, while racemic *sec*-butylphenyl ether arises *via* an S_N1 phenolysis of the diazotic acid does not account for the invariance of product stereochemistry and relative yield over several reactant concentrations. Furthermore *bona fide* examples of S_N2 displacements on *secondary* alkyl diazotic acids or their derivatives are essentially nonexistant (3,18).

20. E. R. Stedronsky, J. Gal, R. A. More O'Ferrall, and S. I. Miller, *J. Am. Chem. Soc.*, **90**, 993 (1968).