Nitrous Acid Oxidation of *N,N*-Dialkylanilines

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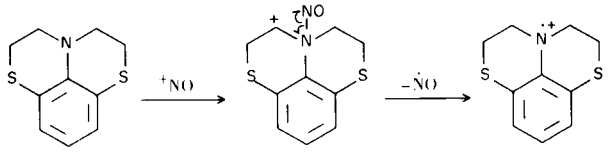
Sir:

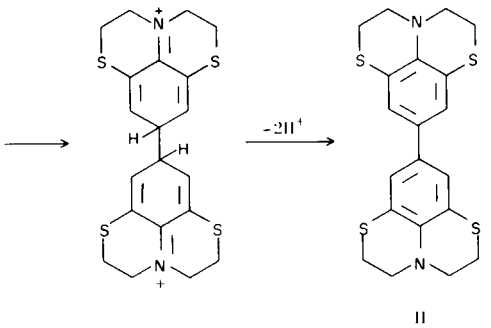
The oxidation of *N,N*-dialkylanilines by nitrous acid to give benzidine derivatives has rarely been reported and appears to be poorly understood. We wish to report our results with the nitrous acid oxidation of 2,3,5,6-tetrahydro[1,4]thiazino[4,3,2-*de*][1,4]benzothiazine (I) (2) and to discuss the properties of the molecule which cause the oxidation reaction to be favored over the anticipated aromatic nitrosation reaction.

Following a standard nitrosation procedure (3), an aqueous solution of sodium nitrite was added slowly at 5° to a solution of the benzothiazine I in aqueous hydrochloric acid. Nitric oxide was evolved immediately. After ten minutes the solution was diluted with water, the product collected by filtration and purified by vacuum sublimation to give a 50 percent yield of 2,2′,3,3′,5,5′,6,6′-octahydro-9,9′-bi-[1,4]thiazino[4,3,2-*de*][1,4]benzothiazine (II).

The reaction was found to be independent of temperature, light, acid concentration or oxygen. The following mechanism is consistent with the data and with mechanisms proposed for oxidation of aminobenzenes (4,5).

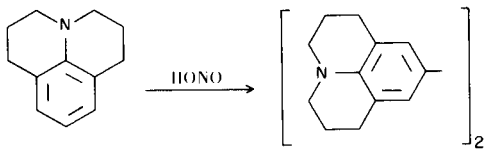


I



II

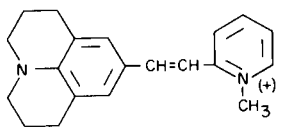
A similar dimerization has been observed upon reaction of nitrous acid with julolidine (III); bijulolidine (IV) was isolated in 14% yield (6). Therefore the oxidation reaction is characteristic of the tricyclic ring system and is not caused by the sulfur atoms.



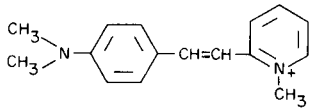
III IV

Nitrous acid oxidation of *N,N*-dimethylaniline to tetramethylbenzidine normally occurs during aromatic nitrosation but at a relatively slow rate (7). Therefore the results with the benzothiazine I or with julolidine III can be explained if one assumes that the rate of nitrosation for these compounds is extremely slow; then oxidation would be the major reaction.

Evidence exists to support this assumption. Examination of the ultraviolet spectra of the stilbazole dyes of julolidine V (478 mμ, ε, 26,100) and of dimethylaniline VI (437 mμ, ε, 25,300) reveals a strong bathochromic shift upon closing to the tricyclic ring system (6); this is consistent with a destabilization of the ground state resonance of the positive charge rather than stabilization of the excited state. Thus, delocalization of the positive charge onto the julolidine nitrogen must be reduced probably because of the increasing strain generated as the bonding about the nitrogen becomes trigonal. Similarly, because strain increases in the transition state, the unshared electrons on nitrogen do not sufficiently activate the benzene ring for attack by the weakly electrophilic nitrosonium ion and nitrosation does not occur. These results suggest that other *N,N*-dialkylanilines which have sterically hindering *ortho*-substituents will be readily oxidized by nitrous acid.



V



VI

EXPERIMENTAL (8)

2,2′,3,3′,5,5′,6,6′-Octahydro-9,9′-bi-[1,4]thiazino[4,3,2-*de*][1,4]-benzothiazine (II).

A solution of sodium nitrite (0.70 g., 11 mmoles) in water (10 ml.) was added over 10 minutes to an ice cold solution of the benzothiazine I (2.0 g., 10 mmoles) in concentrated hydrochloric acid (150 ml.). The solution turned green immediately evolving nitric oxide (identified by its infrared spectrum). After 30 minutes, the reaction mixture was poured into ice water and the precipitate was collected. The solid was washed with acetone, hot dimethylformamide and acetone, then dried to give 1.0 g. (50%) of the dimer II: m.p. 265-295° dec. Sublimation at 270° (3 microns Hg) gave 0.7 g. (35%) of the pure dimer II: m.p. 305° dec.; nmr (trifluoroacetic acid), δ 3.48 (m, 8, SCH_2CH_2N:, 4.14 (m, 8, SCH_2CH_2N), and 7.32 (singlet, 4, equivalent aromatic protons); mass spectrum, P^+ 416.0505 (calcd. 416.0509).

Anal. Calcd. for $C_{20}H_{20}N_2S_4$: C, 57.65; H, 4.84; N, 6.73. S, 30.78. Found: C, 57.90; H, 4.92; N, 6.70; S, 30.75.

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(8) Melting points are uncorrected. The nuclear magnetic resonance spectrum was taken in the solvent indicated with a Varian A60 instrument. The nmr spectra were compared with TMS as an internal standard.

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