CATION-RADICAL OXIDATION STEP IN THE NITRATION OF PHENOTHIAZINE WITH NITRIC ACID

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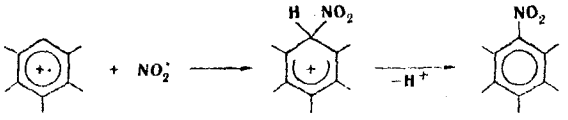
A phenothiazine cation radical, which was isolated preparatively in the form of the perchlorate in the reaction of phenothiazine with the minimum amount of nitric acid in aqueous perchloric acid, is formed initially in the nitration of phenothiazine with nitric acid to give 3-nitrophenothiazine S-oxide. The perchlorate is also converted to the nitro compound by nitration. During nitration the phenothiazine cation radical is oxidized to the phenazthionium cation, the perchlorate of which was also isolated preparatively in the reaction of phenothiazine with HNO_3 in amounts that were twice the amount required for the formation of the phenothiazine cation radical. This is followed by the formation of the nitro derivative, which involves the reaction of the phenazthionium cation with the nitrite anion of nitrous acid. The resulting 3-nitrophenothiazine is then converted to the final product.

The formation of cation radicals of aromatic and heteroaromatic compounds is possible during their nitration; these cation radicals may, in principle, lie on the reaction coordinate for nitration [1-6]. In processes of this sort the most important pathway for the transformation of cation radicals to nitro compounds is evidently recombination of the cation radical with the $NO_2^{\cdot}$ molecule as two free radicals:



However, other pathways for the conversion of cation radicals to nitro compounds may also exist. In the present research in the case of the nitration of phenothiazine (I) we demonstrated that the formation of the nitro compound may be preceded by one-electron oxidation of the cation radical (see also a previous brief communication [4]).

In the reaction of I with nitric acid (at an HNO_3:I molar ratio of 4.7) in aqueous perchloric acid we obtained a nitration product, viz., 3-nitrophenothiazine S-oxide (II), in 81% yield. However, the initial product is a cation radical ($I^{+\cdot}$), which can be isolated preparatively in the form of the perchlorate in 78% yield when the minimum amount of nitric acid (an HNO_3:I molar ratio of 0.32) is used.

When we carried out the reaction of I with nitric acid in acetonitrile we recorded the electronic absorption spectrum of $I^{+\cdot}$, which coincides with the spectrum of a genuine solution of the perchlorate of the cation radical of I [7].

If cation radical salt $I^{+\cdot}ClO_4^-$ rather than azine I is subjected to the reaction with nitric acid, nitro compound II is also formed in 85% yield, and this confirms the intermediate formation of the cation radical of I.

Under the conditions of our experiments cation radical $I^{+\cdot}$ is not a direct precursor of the nitro derivative: Under the influence of excess nitric acid it undergoes subsequent one-electron oxidation to the phenazthionium ion (III^+), which was isolated in 68% yield in the form of the perchlorate at an HNO_3:I molar ratio of 0.64 (i.e., at a ratio that is twice the ratio required for the formation of the phenothiazine cation radical).

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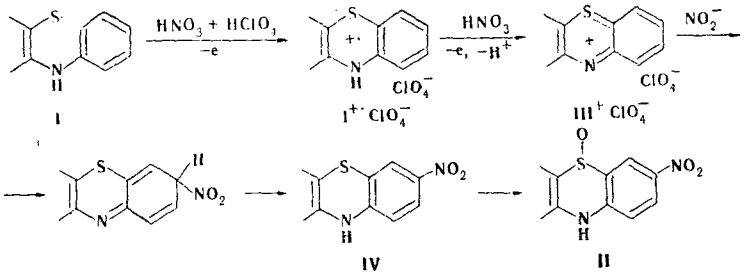
The subsequent conversion of cation III^+ to nitro compound II evidently takes place under the influence of the nitrite ion of nitrous acid, which exists in equilibrium with nitrogen oxides and is formed in the reduction of nitric acid in the steps involving oxidation of I to $I^{+\cdot}$ and subsequently to cation III^+.



In fact, treatment of a solution of perchlorate III^+ in acetonitrile with sodium nitrite leads to the formation of 3-nitrophenothiazine (IV). In addition, phenazthionium perchlorate ($III^+ClO_4^-$) does not react in aqueous perchloric acid with nitric acid that does not contain nitrogen oxides but, on the other hand, is converted rapidly to nitro compound II on treatment with a mixture of nitric acid with nitrogen dioxide or only with nitrogen oxide.

Thus it may be assumed that two successive steps involving one-electron oxidation of the starting substrate are realized in the initial phase of the nitration of I, whereas nucleophilic attack on the III^+ cation by the nitrite anion can be regarded as the final step.

EXPERIMENTAL

The electronic spectra were recorded with a Specord UV-vis spectrophotometer. The IR spectra were recorded with a Specord IR-71 spectrometer. Chemically pure-grade nitric acid was used for the reactions. Pure-grade phenothiazine was recrystallized from acetic acid for use in the spectroscopic studies.

Phenothiazine Cation-Radical Perchlorate ($I^{+\cdot}ClO_4^-$). A 1-ml sample of a solution of HNO_3 in 57% perchloric acid containing 0.045 g (0.4 mmole) of 55% HNO_3 was added with stirring in the course of 10 min to a mixture of 0.25 g (1.3 mmole) of phenothiazine and 3 ml of 57% perchloric acid. After 10 min, the dark-green precipitate of the cation-radical salt was removed by filtration and washed with dry ether to give 0.29 g (78%) of product. IR spectrum, cm^{-1} (mineral oil): 1560 m, 1297 s, 1266 s, 1180 s, 1100 s, 966 m, 936 s, 853 s, 765 s, and 720 s. The IR spectra of the product obtained by this method and a genuine sample [8] coincided. The electronic absorption spectrum contained bands with λ_{max} at 271, 438, 480 (shoulder), and 515 nm (acetonitrile).

Phenazthionium Perchlorate ($III^+ClO_4^-$). This compound was similarly obtained in 68% yield as a dark-red finely crystalline powder, except that the amount of nitric acid was doubled. The IR spectrum coincided with the spectrum of a genuine sample [8] (1580 m, 1498 m, 1326 s, 1252 m, 1166 m, 1090 s, 877 m, 775 s, 730 s, and 710 m cm^{-1}).

3-Nitrophenothiazine S-Oxide (II). A) A solution of 0.54 g (4.7 mmole) of 55% HNO_3 in 2 ml of 42% perchloric acid was added to 0.20 g (1 mmole) of phenothiazine in 6 ml of 42% perchloric acid. After 30 min, the precipitated II was removed by filtration and washed with small amounts of ethanol and ether to give 0.21 g (81%) of a product with mp 277-280°C (from propanol). No melting-point depression was observed for a mixture with a genuine sample [9].

B) The reaction was carried out similarly, except that phenothiazine was replaced by an equivalent amount of phenothiazine cation-radical perchlorate. Nitro derivative II was obtained in 85% yield.

C) A 0.1-g (0.3 mmole) sample of $III^+ClO_4^-$ was suspended in 3 ml of 42% perchloric acid, and 3 ml of a solution of HNO_3 and nitrogen dioxide in 42% perchloric acid containing 0.16 g (1.4 mmole) of 55% HNO_3 and 0.044 g (1 mmole) of nitrogen dioxide were added to the suspension. After 30 min, the precipitate of nitro compound II was removed by filtration to give 0.06 g (66%) of a product with mp 275-277°C. Only the starting perchlorate was

isolated in 81% yield from the reaction mixture in a similar experiment by the action of HNO_3 that did not contain nitrogen oxides on 0.1 g of $III^+ClO_4^-$ in 42% perchloric acid.

3-Nitrophenothiazine (IV). A 0.70-g (10.1 mmole) sample of sodium nitrite was added to a solution of 0.15 g (0.5 mmole) of phenazthionium perchlorate in 12 ml of acetonitrile, and the reaction mixture was stirred for 30 min. The excess sodium nitrite was removed by filtration, and the filtrate was diluted with water (30 ml). The precipitate was removed by filtration, washed with 20 ml of water, dried, and treated with boiling benzene (three 10-ml portions). The insoluble material was identified as 3,7-dinitrophenothiazine. The yield of the dinitro derivative was 0.02 g (13%). The IR spectrum of a genuine sample of 3,7-dinitrophenothiazine prepared by the method in [10]. Evaporation of the benzene filtrate gave 0.05 g (42%) of 3-nitrophenothiazine with mp 209-210°C (from benzene) (mp 210-211°C [11]).

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RING-CHAIN TAUTOMERISM OF SUBSTITUTED HYDRAZONES.

17.* ALKYL-SUBSTITUTED PERHYDRO-1,3,4-THIADIAZINES

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It was demonstrated by PMR spectroscopy that alkylidene derivatives of vic-(N-alkylhydrazino)thiols in solutions exist exclusively in the cyclic form, i.e., as perhydro-1,3,4-thiadiazines. Only pinacolone derivatives undergo reversible isomerization to the corresponding hydrazones. The thermodynamic parameters of the ring-chain equilibria were determined. The static stereochemistry and the dynamics of the conformational transitions of perhydro-1,3,4-thiadiazines are discussed.

To ascertain the general principles that govern reversible additive isomerization processes it is important to evaluate both the role of the heteroatom in the added grouping and the common character of the effect of substituents in different but similar series. Up until now, one of the most extensively studied systems has been the perhydro-1,3,4-oxadiazine—(β-hydroxyalkyl)hydrazone tautomeric system [4]; however, virtually no study has been devoted to similar transformations in series of analogs of hydroxyalkylhydrazones.

*See [1] for Communication 16; see [2, 3] for preliminary communications.

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