181. Diazotisations in Highly Concentrated Mineral Acids: The Nitrosation Mechanism of Anilinium and Hydroxylammonium Ions through Proton Loss from the Ammonio Group

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It is shown that the acidity dependence of the rate of nitrosation of aromatic amines and of hydroxylamine in strongly acidic aqueous solutions does not necessarily involve the rearrangement of a charge transfer complex (consisting of the NO^+ ion and the substrate with an NH_3^+ group) in concert with a proton loss at the NH_3^+ group. More likely, proton loss of the charge complex preceeds the $\pi \rightarrow N$ rearrangement of the NO^+ ion.

Introduction. – The influence of the acidity of the aqueous medium on diazotisations has been an object of investigation since the pioneering work of *Ridd* and coworkers in 1958 [1]: in the low acidity region (normally in the pH range of 1 to 3), the rate of diazotisation decreases with increasing concentration of hydrogen ions. In an intermediate region, corresponding to h_0 of *ca.* 10^{-1} to 10^3, the rate increases linearly with acidity, and finally, in high acidity media ($h_0 > 10^4$), the rate decreases again with acidity.

For all three regions, *Ridd* [2] [3] proposed mechanisms which are consistent with the kinetic results. In this paper, we discuss only the mechanisms in the intermediate and high-acidity regions.

The marked acid catalysis in the intermediate region indicates that the new nitrosating reagent is the (solvated) nitrosyl cation (NO^+) formed in the overall *Equilibrium 1.*

$$H_2SO_4 + HNO_2 \rightleftarrows NO^+ + HSO_4^- + H_2O \qquad (1)$$

The linear correlation between the concentration of the effective nitrosating reagent and the rate of diazotisation implies, however, as postulated by *Challis* and *Ridd* [4], that the anilinium ion and not aniline must enter the substitution proper, forming a dicationic charge-transfer complex of NO^+ with the anilinium ion. For the rate-limiting step, a $\pi \rightarrow N$ rearrangement, concerted with *N*-deprotonation, forming the *N*-nitrosoanilinium monocation was postulated [5]. This conclusion is supported by some other unusual features, notably in the pattern of substituent effects in the aniline ring; the influence of *p*-substituents is the reverse of that observed in the low-acidity range.

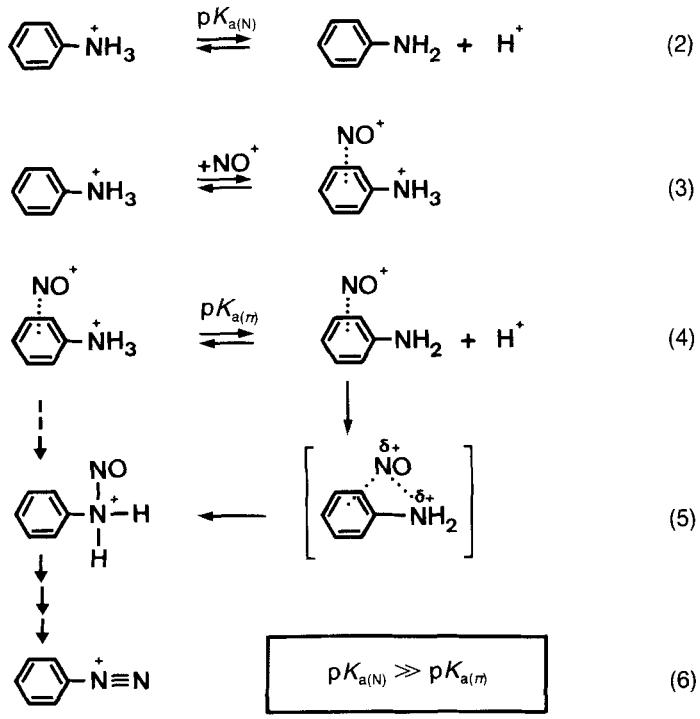
Ridd [2] explained the anewed rate decrease at high acidities by assuming that the rate-limiting step at high acidities is the deprotonation of the *N*-nitrosoanilinium ion.

In the present communication, we intend to present a mechanism which involves also the anilinium ion, but which offers a reasonable explanation for the reactivity of this relatively weak nucleophile.

Discussion. – Since the 1960's, a large amount of data with several completely different probes indicate that the Me_3N^+ group, along with the unsubstituted ammonio group NH_3^+, is a modest π donor with a resonance effect similar to that of the isoelectronic Me_3C group. The donor activity of the NH_3^+ substituent, however, is much smaller than that of the NH_2 group.

It is, therefore, not trivial to ask, if the NH_3^+ group of the anilinium ion is really not changed in the course of the formation of the covalent N–N bond yielding the *N*-nitroso-anilinium ion.

The fundamental issue of our present communication is based on the postulate that the pK_a value of the dicationic charge-transfer complex must be significantly lower than that of the anilinium ion: electrophilic complexation of any benzene derivative bearing a *Brönsted*-acid group such as NH_3^+ will increase the acidity constant of that group. Incorporating this consideration into the reaction mechanism of diazotisation, the *Ridd* mechanism is modified as shown in *Eqns. 2–6*.



(2) (3) (4) (5) (6)

The essential basis of this mechanism, therefore, is the deprotonation of the charge-transfer complex *(Eqn. 4)*. That equilibrium is situated more on the right side than that of the uncomplexed anilinium ion *(Eqn. 2)*: $pK_{a(N)} \gg pK_{a(\pi)}$. This facilitates the rearrangement of the NO^+ group from the charge-transfer position to an NH_2 group and not anymore to an NH_3^+ group. Comparing our mechanism *(Eqns. 2–6)* with the original *Ridd* mechanism, one realizes that *Ridd* combined the steps of *Eqns. 4* and *5* in a concerted

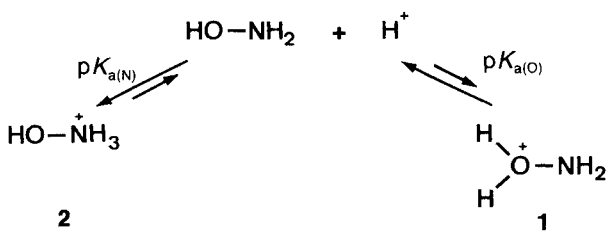
rearrangement-deprotonation step. This is indicated in *Eqns. 4* and *5* by the dashed-arrow 'short-cut' between the charge-transfer complex and the *N*-nitrosoanilinium ion.

Our mechanism *(Eqns. 2–6)* is of course also applicable to strongly acidic conditions. The only difference is the deprotonation of *N*-nitrosoanilinium ion, *i.e.* the first step of the steps summarized in *Eqn. 6* becoming rate-limiting.

In that context the diazotisation of heteroaromatic amines in highly acidic media is interesting. Recently *Diener* [6] demonstrated that the rates of diazotisation of 2-aminothiazole in 65 to 75% H_2SO_4 solution show a dependence on acidity and a kinetic deuterium isotope effect which is significantly lower than the corresponding figures for the diazotisation of aniline [7] in the same medium (2-aminothiazole: rate proportional to $h_o^{-0.69}$, $k_H/k_D = 5.8$; aniline: $h_o^{-2.4}$, $k_H/k_D = 10$). This comparison shows clearly that the rate-determining part of the diazotisation of 2-aminothiazole contains only one deprotonation, whereas that of aniline contains two.

2-Aminothiazole is protonated first at the heterocyclic N-atom ($pK_a = 5.28$, [6]), but does not add a second proton up to solutions in 90% H_2SO_4 (see [8]). It is, therefore, possible, but less likely that, in nitrosations of 2-aminothiazole, a π-complex of NO^+ with the heteroaromatic thiazolium system is formed first. Direct *N*-nitrosation is easier, however, for that heterocyclic amine than for the anilinium ion, because it contains an NH_2 and not an NH_3^+ group.

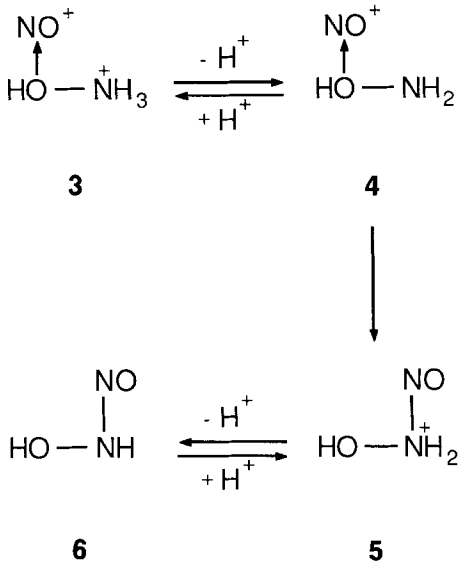
In the nitrosation of an inorganic amino compound, namely hydroxylamine, dinitrogenoxide (N_2O) is the final reaction product. As shown by *Hughes* and *Stedman* [9], the kinetics of that reaction in acidic solution are very similar to the diazotisation of aniline. They showed that the overall reaction rate is too great to involve the *O*-protonated hydroxylamine (**1**) which is present only in an extremely small concentration in the acidic media used by *Hughes* and *Stedman* (aqueous $HClO_4$). The equilibrium between the two protonated isomers of hydroxylamine *(Eqn. 7)* is very much in favour of the *N*-protonated isomer **2**. Therefore, *Hughes* and *Stedman* suggested that the nitrosating agent replaces a proton of the hydroxylammonium ion **2**.



(7)

$pK_{a(N)} \gg pK_{a(O)}$

In analogy to *Ridd*'s work with aromatic amines, it is possible that the O-atom of the hydroxylammonium ion **2** provides electrons for the formation of a charge-transfer complex **3** with the NO^+ ion *(Eqn. 8)*. For obvious reasons, the NH_3^+ group of complex **3** is much more acidic than the NH_3^+ group in non-complexed hydroxylammonium ion **2**: $pK_{a(3)} \gg pK_{a(N)}$. Complex **3** will, therefore, loose a proton of the NH_2 group relatively



(8)

easily[1]). *Afterwards,* the NO^+ group of the complex **4** can rearrange to the hydroxy-nitroso-ammonium ion **5** which, in turn, will loose another proton yielding *N*-nitroso-hydroxylamine **6**.

The essence of the mechanism which we postulate is a separation of the *concerted* rearrangement and the deprotonation into *two* steps, namely *de*protonation of the NH_3^+ ion complex *followed* by rearrangement of NO^+ to the NH_2 group. In a review of nitrosation published more than 10 years after his original work on diazotisations in relatively strong acid asolutions, *Ridd* [10] points out in a footnote that in such reactions 'the interaction of NO^+ with the protonated amine appears to facilitate the proton loss'. This statement is almost in agreement with our mechanism *(Eqns. 2–6)* !

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[1]) *O*-Deprotonation of **3** is, of course, possible too. It is even more dominant than *N*-deprotonation for obvious reasons. It can be neglected, however, in this context, because *O*-deprotonation is a side-equilibrium which does not lead to the reaction product N_2O.