The Mechanism of Nitrosation of Protonated Amino-compounds

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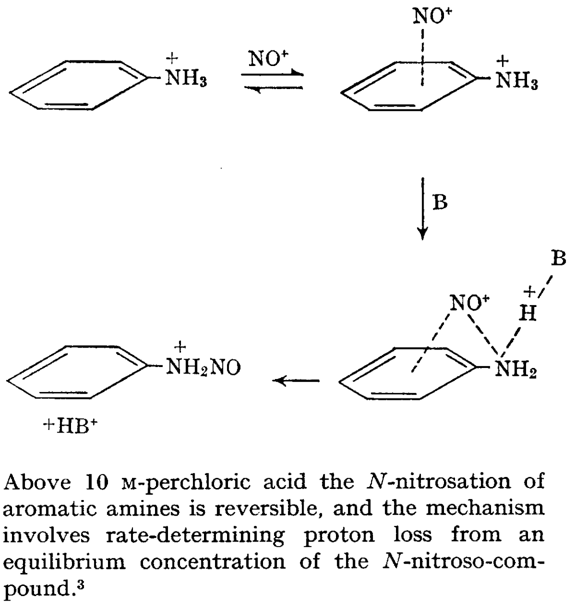
MOST *N*-nitrosation reactions occur by electrophilic attack upon the nitrogen of the free amino-compound.[1] Ridd and Challis have reported[2] a mechanism for diazotisation involving attack upon the conjugate acid of the amine, with a rate law $v = k_1[H^+][HNO_2][RNH_3^+]$. They suggest the following unusual mechanism



Above 10 M-perchloric acid the *N*-nitrosation of aromatic amines is reversible, and the mechanism involves rate-determining proton loss from an equilibrium concentration of the *N*-nitroso-compound.[3]

A similar rate law describes the reactions

$$HNO_2 + NH_2OH \rightarrow N_2O + H_2O$$
$$HNO_2 + NH{\cdot}Me{\cdot}OH \rightarrow ON{\cdot}NH{\cdot}Me{\cdot}OH + H_2O$$

in the range 0·01—2 M-[H⁺], with k_1-values of 0·90 and 0·92 mole⁻¹ sec.⁻¹ l. at 0° (1·2 M-perchloric acid). The *O*-methyl-, the *O,N*-dimethyl-, and the *O*-isopentyl-hydroxylamines show no sign of this acid-catalysed mechanism, but react through the free amino-compound with a rate law $v = k_2[HNO_2][RNH_3^+] = k_3[H^+][NHO_2][RNH_2]$ with k_3-values of 380, 660, and 200 mole⁻² sec.⁻¹ l.[2] respectively at 0°, ionic strength 0·3 M. These are reasonable values for the reaction of the nitrous-acidium ion, $H_2NO_2^+$, with the free alkylhydroxylamines, and are slightly higher than the values for aromatic amines.[1] It seems that for nitrosation of the protonated hydroxylamine it is necessary for there to be a hydroxyl group present. If the mechanism is analogous to that proposed for diazotisation, the first product for hydroxylamine would be $NH_3^+{\cdot}OH^+{\cdot}NO$ which would be unstable because of the positive charges on adjacent atoms. For hydroxylamine and *N*-methylhydroxylamine, this can be relieved by ionisation of the relatively acidic hydroxyl proton. When there is an *O*-alkyl substituent this cannot occur and presumably NO^+ is lost before ionisation of the much less acidic N–H protons would allow the nitrosonium ion to migrate to the nitrogen atom. It may be that proton loss from the hydroxyl is synchronous with the addition of NO^+ in the hydroxylamine and *N*-methylhydroxylamine systems. The other factor influencing the mechanism of nitrosation is the pK_a of the protonated hydroxylamine. For hydroxylamine and its *N*-methyl derivative it is 5·9, while for the *O*-alkyl derivatives the pK_a-values lie between 4·6 and 4·7 Under our conditions the concentration of the free base is about twenty times lower for the first two cases than the last three, and it is known that in this type of nitrosation reactivity does not vary much with basicity.[1]

At higher acid concentrations, [H⁺] > 2 M, the rate equation for the hydroxylamine–nitrous acid reaction changes to the form $v = k_4\ [HNO_2]\ [NH_3^+OH]$ with $k_4 = 2{\cdot}5$ mole⁻¹ sec.⁻¹ l. at 3M-ionic strength and 0°. As the transition to this rate equation occurs at high acidities and not low acidities it cannot be interpreted as a rate-determining attack by the nitrous-acidium ion on free hydroxylamine. This is confirmed by the fact that k_3 calculated from k_4 is about 10⁴ times greater than the normal limiting rate for the reaction of the nitrous-acidium ion with free amines, a process that is thought[1] to be encounter-controlled. We interpret this as a reversal of the initial nitrosation.

$$H^+ + HNO_2 + NH_3^+OH \underset{\text{fast}}{\rightleftharpoons}$$
$$NH_3^+O{\cdot}NO + H^+ \xrightarrow[\text{slow}]{} ON{\cdot}NHOH$$

It seems reasonable that the first stage should be reversible as it involves the acid-catalysed hydrolysis of a nitrito-structure which usually occurs readily. The details of the rearrangement of $NH_3^+O{\cdot}NO$ are not known with certainty; the intermediate $ON{\cdot}NH{\cdot}OH$ has been suggested[5] on isotopic evidence. Further evidence comes from the thiocyanate- and bromide-catalysed reactions of nitrous acid with hydroxylamine. These occur by the rate-determining reaction[4,6]

$$X{\cdot}NO + NH_2{\cdot}OH \rightarrow ON{\cdot}NH{\cdot}OH + H^+ + X^-$$

These reactions show no sign of any change in the rate equation with acidity up to at least $[H^+] = 4$ M, so the denitrosation step must occur at a stage in the mechanism before the formation of $ON{\cdot}NH{\cdot}OH$.

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