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The reactivity characterization of azanone (HNO) and its selected donors

Abstract

Azanone (**HNO**), the protonated one-electron reduction product of nitric oxide (**$^{\bullet}$NO**), remains one of the most elusive compound in the "reactive nitrogen species" family. In recent years, interest in this molecule has increased significantly due to the unique pharmacological effects observed after the use of its donors. It is believed that some of them are caused by high reactivity of azanone towards biologically important thiol compounds and metalloproteins.

For a long time one of the most mysterious reaction of azanone was its reaction with molecular oxygen, which led to the formation of oxidant of unknown nature. Recent work of Adam Sikora *et al.* allowed unambiguous identification of that oxidant and showed that it is peroxynitrite **$ONOO^-$** (reaction 1).

$$HNO + O_2 \rightarrow ONOO^- \qquad \text{(reaction 1)}$$

Thanks to the development of the kinetic method, that is based on application of boronic probes selective towards **$ONOO^-$**, I have determined the value of the rate constant of the reaction between **HNO** and molecular oxygen to be equal to $(1.8 \pm 0.3) \times 10^4\ M^{-1}s^{-1}$. My further research allowed me also to evaluate a number of values of **HNO** reaction rate constants with its selected scavengers, important from the perspective of biological chemistry, detection and effective generation of azanone.

Instability of azanone in aqueous solutions, due to fast dimerization reaction (reaction 2), causes the necessity of application in reactivity studies appropriate donor compounds, that decompose with the release of **HNO**.

$$2HNO \rightarrow [HONNOH] \rightarrow N_2O + H_2O \qquad \text{(reaction 2)}$$

To date, the only donor useful in biological studies was Angeli's salt ($Na_2N_2O_3$) since another well-known azanone donor, Piloty's acid (N-hydroxybenzenesulfonamide), releases **HNO** only in alkaline solutions. Recently, a modification of Piloty's acid structure has been proposed. It has been established that introduction of appropriate substituent's at *orto*-position at Piloty's acid ring provides an improvement of physicochemical properties and as a consequence such donors release **HNO** at a lower pH than the parent compound. In my doctoral dissertation, I have performed the kinetic studies on the mechanism of **HNO** release from three *ortho*-substituted Piloty's acid derivatives: 2-bromo-, 2-chloro- and 2-trifluoromethyl-N-hydroxybenzenesulfonamide. Among them, the bromine derivative exhibited a kinetic profile that was closest to the most commonly used **HNO** donor – Angeli's salt.

The main disadvantage of Piloty's acid derivatives is their low solubility in water. To improve the solubility of the donor in aqueous solutions **β-cyclodextrin** derivative can be used as solubilizing agent. To check whether such complexation of this group of donors with **β-cyclodextrin** sulfobutyl ethers-ethyl ethers, sodium salt may affect significantly **HNO** release, I have studied the kinetics of 2-bromo-N-hydroxybenzenesulfonamide, decomposition in the presence and absence of **β-cyclodextrin** sulfobutyl ethers-ethyl ethers, sodium salt. Obtained results indicate that the 2-bromo-N-hydroxybenzenesulfonamide:**β-cyclodextrin** complex is well soluble in water and exhibits very similar **HNO** donating properties as 2-bromo-N-hydroxybenzenesulfonamide itself.

In conclusion, gathered results of my research are a valuable complement to the current state of knowledge on the reactivity of azanone and its selected donors.

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