Ozonation of pyridine and other *N*-heterocyclic aromatic compounds: Kinetics, stoichiometry, identification of products and elucidation of pathways

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ABSTRACT

Pyridine, pyridazine, pyrimidine and pyrazine were investigated in their reaction with ozone. These compounds are archetypes for heterocyclic aromatic amines, a structural unit that is often present in pharmaceuticals, pesticides and dyestuffs (e.g., enoxacin, pyrazineamide or pyrimethamine). The investigated target compounds react with ozone with rate constants ranging from 0.37 to 57 M^{-1} s^{-1}, hampering their degradation during ozonation. In OH radical scavenged systems the reaction of ozone with pyridine and pyridazine is characterized by high transformation (per ozone consumed) of 55 and 54%, respectively. In non scavenged system the transformation drops to 52 and 12%, respectively. However, in the reaction of pyrimidine and pyrazine with ozone this is reversed. Here, in an OH radical scavenged system the compound transformation is much lower (2.1 and 14%, respectively) than in non scavenged one (22 and 25%, respectively). This is confirmed by corresponding high *N*-oxide formation in the ozonation of pyridine and pyridazine, but probably low formation in the reaction of pyrimidine and pyrazine with ozone. With respect to reaction mechanisms, it is suggested that ozone adduct formation at nitrogen is the primary step in the ozonation of pyridine and pyridazine. On the contrary, ozone adduct formation to the aromatic ring seems to occur especially in the ozonation of pyrimidine as inferred from hydrogen peroxide yield. However, also OH radical reactions are supposed processes in the case of pyrimidine and in particular for pyrazine, albeit negligible OH radical yields are obtained. The low compound transformation in OH radical scavenged system can prove this. As a result of negligible OH radical yields in all cases (less than 6%) electron transfer as primary reaction pathway plays a subordinate role.

1. Introduction

Nitrogen is frequently present in micropollutants, since many biologically active compounds, e.g., pharmaceuticals or pesticides, contain aromatic and aliphatic amino groups. The micropollutants can reach the environment through several input pathways according to their manifold uses. However, pharmaceuticals in particular are mainly emitted via municipal wastewater treatment plant (WWTP) effluents (Huber et al., 2005; Gabet-Giraud et al., 2010). Hence, there is a major concern about the occurrence of micropollutants in surface water and groundwater that are used as source waters for drinking water supply (Nöthe et al., 2007; Ternes et al., 2015). In surface water micropollutants can be harmful to aquatic life, even at low concentrations (Huggett et al., 2002; Küster et al., 2010). Therefore, a polishing treatment of WWTP effluents by

ozonation or activated carbon is currently discussed to minimize the discharge of micropollutants to receiving waters (Ternes et al., 2002; Huber et al., 2003; Snyder et al., 2006; Schwarzenbach et al., 2006; Benner et al., 2008; Hollender et al., 2009; Benitez et al., 2011; Zimmermann et al., 2012). However, during ozonation the oxidation of micropollutants is in competition with ozone reactions of the water matrix. Only micropollutants which react fast with ozone (t_{O3} < 100 s, Hoigné and Bader, 1983a) are easily eliminated in wastewater treatment (Lee and von Gunten, 2010). For this reason, the determination of ozone rate constants of micropollutants is essential. OH radicals ('OH), being an important oxidant in ozonation, have gained attention as a tool to transform micropollutants during treatment of not only drinking water but also wastewater (von Gunten, 2003; Snyder et al., 2006). Hence, 'OH yield is a relevant reaction parameter. In addition, the knowledge of the quantity of ozone used for full compound degradation (reaction stoichiometry) will allow the assessment of the treatment e.g., the dosage rate (Nöthe et al., 2009). Oxidative treatment does not typically result in full mineralization, but rather leads to transformation products (TPs). For a comprehensive environmental assessment it is crucial to elucidate the transformation pathways, since it cannot be ruled out, that TPs may be more toxic to aquatic life than their precursors (Shang and Yu, 2002; Huber et al., 2004; Schmidt and Brauch, 2008; Boxall et al., 2014).

In this study, the reactions of ozone with pyridine, pyridazine, pyrimidine and pyrazine were investigated in aqueous solution. Those investigations can help to elucidate the chemical mechanisms involved in the oxidation of micropollutants by ozone, in particular for aromatic heterocyclic amines (e.g. the antibacterial agent enoxacin or pyrazineamide and the antimalarial drug pyrimethamine, Ternes and Joss, 2006). Quite a lot of papers already deal with reactions of ozone with aromatic compounds (Tyupalo et al., 1974, 1980, Gilbert and Zinecker, 1980, Hoigné and Bader, 1979, 1983a, b, Gilbert and Hoffmann-Glewe, 1992, Pan et al., 1993, Mvula and von Sonntag, 2003, Naumov and von Sonntag, 2010), amines (Elmghari-Tabib et al., 1982; Cocheci et al., 1989; Andreozzi et al., 1990, 1991; Muñoz and von Sonntag, 2000b; Sein et al., 2008) and nucleobases (Flyunt et al., 2002). For ozone reactions with aromatic heterocyclic amines several principles are already known. Relating to the amine moiety, ozone reacts predominantly with activated amines. Since the free electron pair has to be available for reaction with ozone, the amines show pH-dependent kinetics (von Sonntag and von Gunten, 2012). Compounds that contain two amino groups (such as EDTA), show a high rate constant, when both amino groups are deprotonated, but reaction rates drop up to three orders of magnitude when one of them is protonated. Protonation of one of the nitrogens, apparently, also influences the electron density of the other, thereby reducing its reactivity towards ozone (Muñoz and von Sonntag, 2000b; von Sonntag and von Gunten, 2012). Considering ozone reactions of aromatic compounds the ozone-reactive site is the electron-rich aromatic ring (von Sonntag and von Gunten, 2012). In addition, ozone is a highly selective reactant and its rate constants with aromatic compounds (Neta et al., 1988), nitrogen-containing compounds (von Sonntag and von Gunten, 2012), electron-rich and electron-deficient olefins (Dowideit and von Sonntag, 1998) vary by ten orders of magnitude.

In the reactions of the investigated N-heterocyclic aromatic compounds with ozone the ozone-reactive site of the amines could be the lone electron pair at nitrogen and the electron-rich aromatic ring as mentioned above. Since, for the investigated compounds the lack of hydrogen at nitrogen disables H-abstraction and ozone insertion, the ozone is forced to addition (see pathway 1 in Scheme 1) and electron transfer (pathway 2). The addition reaction at nitrogen can lead to N-oxides (reaction (1)–(2)) and singlet oxygen
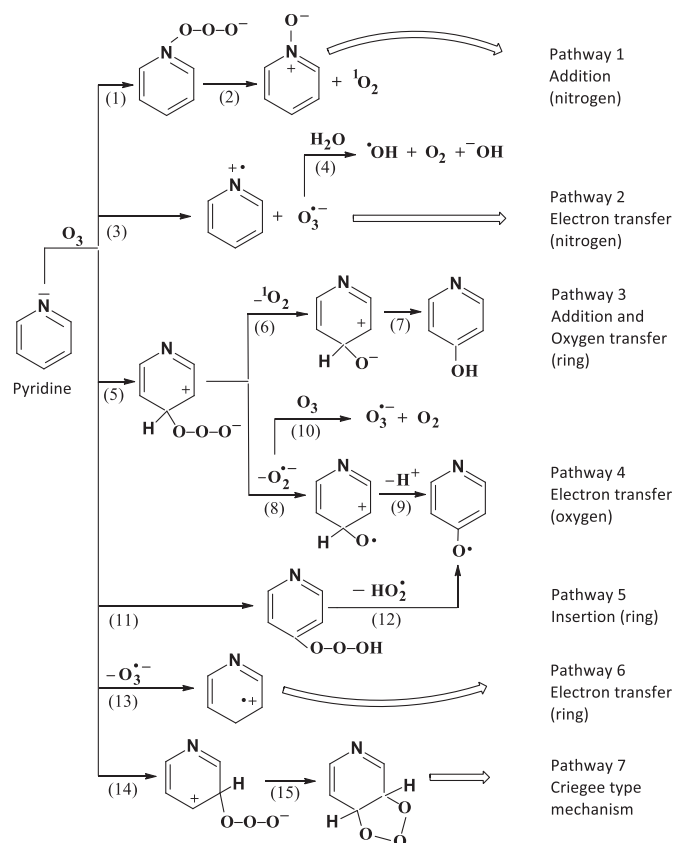
Scheme 1. Primary reaction pathways of pyridine in the reaction with ozone (all pathways are just as effectual for pyridazine, pyrimidine and pyrazine).

($^1O_2$, see Supporting Information Text S8) as final products (Tyupalo and Bernashevskii, 1980; Andreozzi et al., 1991; Muñoz et al., 2001). In competition, the ozone adduct may undergo electron transfer by dissociating into an amine radical cation and an ozonide radical anion (O_3^-). This reaction may also occur immediately via an outer sphere electron transfer, without adduct formation (reaction (3)). However, the outer sphere electron transfer and electron transfer after adduct formation cannot be distinguished experimentally. The O_3^- reacts with water giving rise to 'OH (reaction (4), Bühler et al., 1984). Furthermore, ozone addition can also take place at the slightly activated aromatic ring (reaction (5)). From the subsequent ozone adduct formation a hydroxylation can occur (reaction (6)–(7)). The formed adduct can release a singlet oxygen ($^1O_2$). The decay of ozone adduct into a phenoxyl radical and a superoxide radical anion (O_2^-) is feasible as well (reaction (8)–(9), Ragnar et al., 1999a, b). The O_2^- reacts with ozone to the O_3^- (reaction (10), Sehested et al., 1983), a precursor of 'OH (see above). From the ozone attack an insertion process can still proceed (reaction (11)). One further radical pathway after insertion is the subsequent formation of a phenoxyl radical by releasing a hydroperoxyl radical (HO_2^*) (reaction (12)). The latter is in equilibrium with its conjugate base, the super oxide radical anion, O_2^- (pK_a (HO_2^*) = 4.8, Bielski et al., 1985, Ragnar et al., 1999a, b). An electron transfer process at the aromatic ring into a radical cation and O_3^- is feasible as well (reaction (13)). A further process that can occur from ozone attack at the aromatic ring is the formation of an ozonide that is well-documented in the reaction of olefins with ozone (reaction (14)–(15), Criegee, 1975). Which of the above mentioned primary reactions take place preferentially, may be inferred from products that are formed in the ozone-compound reactions.