

Formation of Singlet Oxygen in the Deoxygenation of Heteroarene *N*-Oxides by Dimethyldioxirane

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4-Dimethylaminopyridine-*N*-oxide **2** and 2',3',5'-triacetyladenosine-*N*'-oxide **4** are partially deoxygenated by dimethyldioxirane (DMD) to the corresponding amines **1** and **3**; the formation of singlet oxygen suggests a polar rather than a radical mechanism, in which we propose S_N2 attack of the *N*-oxide on the dioxirane peroxide bond.

The mechanism of *N*-oxidation of heteroarenes of the pyridine type has been recently established¹ to be an S_N2 attack of the nitrogen lone pair on the peroxide bond, to afford usually high yields of *N*-oxides. However, here we provide cogent experimental evidence that at least in some cases the resulting *N*-oxide efficiently decomposes the dioxirane with liberation of oxygen gas and regeneration of the heteroarene.

An optimal case concerns the DMD oxidation of 4-dimethylaminopyridine **1** to its *N*-1-oxide **2**. While 1.0 equiv. of DMD led to 57% conversion, 3.0 or 5.0 equiv. reached maximally 84% *N*-oxide. Nevertheless, the DMD was consumed within a few minutes at 0 °C with gas evolution. By means of a gas burette, the expected amount (ca. 4.3 equiv.) of oxygen gas evolution was established. The suspicion that the *N*-oxide **2** decomposed the dioxirane was confirmed by the reaction of the authentic *N*-oxide with DMD; thus, the use of 1, 2 and 5 equiv. of DMD led to the same mixture of 84:16 (*N*-oxide-amine) under oxygen gas liberation. These experiments are summarized in Fig. 1.

If the deoxygenation of *N*-oxides by dioxirane proceeds also by an S_N2 attack of the nucleophilic *N*-oxide oxygen atom on the dioxirane peroxide bond, the mechanism in Scheme 1 should apply. The proposed dipolar intermediate should lead to singlet oxygen in this novel deoxygenation, as is observed in other heterolytic dioxygen-producing processes, most prominently the chemiluminescent decomposition of hydrogen peroxide by hypochlorite ion² and triphenyl phosphite ozonide.³ Thus, as a crucial test for the postulated singlet oxygen generation (Scheme 1), we searched and, indeed, observed the expected dimol visible [eqn. (1)] and monomol IR [eqn. (2)] chemiluminescence⁴ in the *N*-oxide-promoted decomposition of dimethyldioxirane.

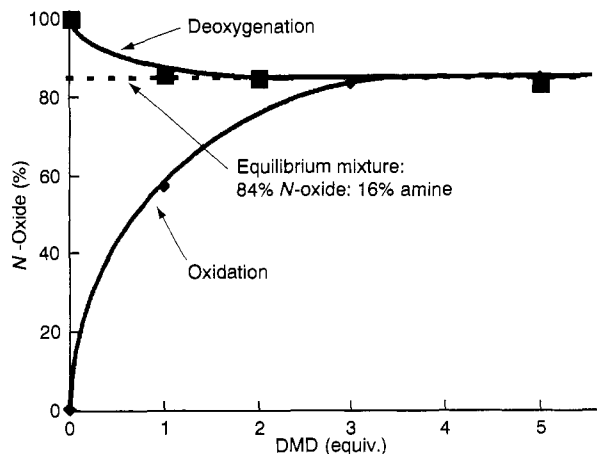
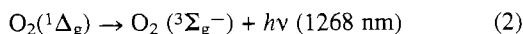
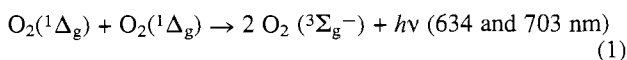
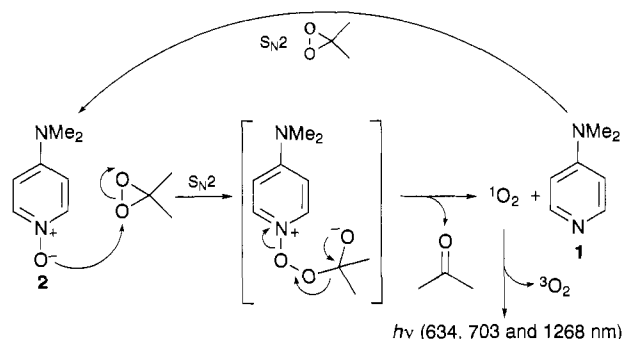


Fig. 1 Oxidation of 4-dimethylaminopyridine **1** and deoxygenation of its *N*-oxide **2** by DMD

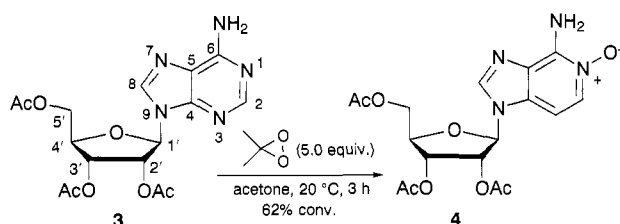
The monomol emission of ¹O₂ in the DMD-*N*-oxide reaction was measured by means of a liquid nitrogen-cooled germanium photodiode detector⁵ (800–1800 nm) with a bandpass filter for 1270 ± 10 nm.† The intensity of the IR chemiluminescence was solvent dependent, *i.e.* the relative intensities were 1.0:0.38:0.088 in acetone, acetone-methanol (33.8:66.2) and acetone-water (33.8:66.2), which is in agreement (*r*² = 0.967) with the singlet oxygen lifetimes in these solvent mixtures.⁶ Since the *N*-oxide **2** concentration remains constant (it is also continuously reformed by oxidation of the amine until all DMD is consumed), pseudo-first-order kinetics of the infrared chemiluminescence emission applies, as manifested by a plot of log (*I*/*I*₀) against time (*r*² = 0.999).

2',3',5'-Triacetyladenosine **3** was oxidized at the *N*-1 position, which is known to be the most nucleophilic site in adenosine.^{7a} However, analogously to 4-dimethylaminopyridine **1**, the *N*-oxide **4** was incompletely formed. Even with a five-fold excess of DMD only 62% conversion was observed, but the dioxirane was consumed with oxygen gas evolution (Scheme 2). Indeed, when the adenosine *N*-oxide **4** was treated with 5.0 equiv. of DMD at 20 °C in CH₂Cl₂, the same 62:38 *N*-oxide-adenosine mixture was observed as had been found in the oxidation of the adenosine **3** to the *N*-oxide **4** (Scheme 2). Presumably also in this case singlet oxygen is produced, a novel pathway for ¹O₂ generation with interesting implications in biochemical systems.^{7b}

In summary, we suspect that the deoxygenation of *N*-oxides by dimethyldioxirane with ¹O₂ evolution may be a more general phenomenon that previously recognized. In this context,



Scheme 1



Scheme 2

Murray⁸ already in 1989 and recently Messeguer and coworkers⁹ brought attention to the fact that DMD is decomposed by *N*-oxides, but the formation of singlet oxygen was not demonstrated.

We are grateful for generous financial support from the Deutsche Forschungsgemeinschaft (Schwerpunktprogramm 'Peroxidchemie: Mechanistische und präparative Aspekte des Sauerstofftransfers') and the Fonds der Chemischen Industrie.

Received, 11th April 1995; Com. 5/02338F

Footnote

† The ¹O₂ production was calibrated by the thermolysis of the disodium 3,3'-(1,4-naphthylidene)dipropionate endoperoxide (NDPO₂).⁵ Thus, in the reaction of *N*-oxide **2** (0.24 mmol dm⁻³) with DMD (7.0 mmol dm⁻³) in methanol-acetone (11 : 1) at 37 °C, ca. 5% of the total oxygen gas evolved

was produced as ¹O₂ when compared with the NDPO₂ standard (7.5 mmol dm⁻³ produced 62 μmol dm⁻³ ¹O₂ min⁻¹).

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