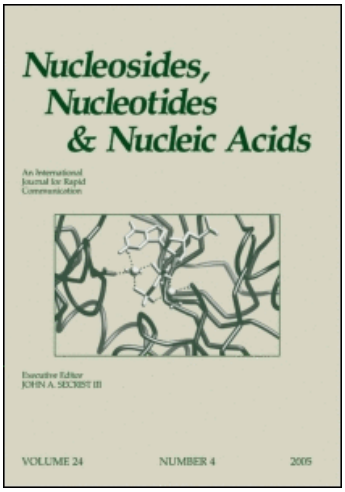

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SELECTIVE OXIDATION of 2'-DEOXYGUANOSINE to IMIDAZOLONE by the CHEMICAL NUCLEASE MnTMPyP ASSOCIATED to $KHSO_5$ or SULFITE / O_2.

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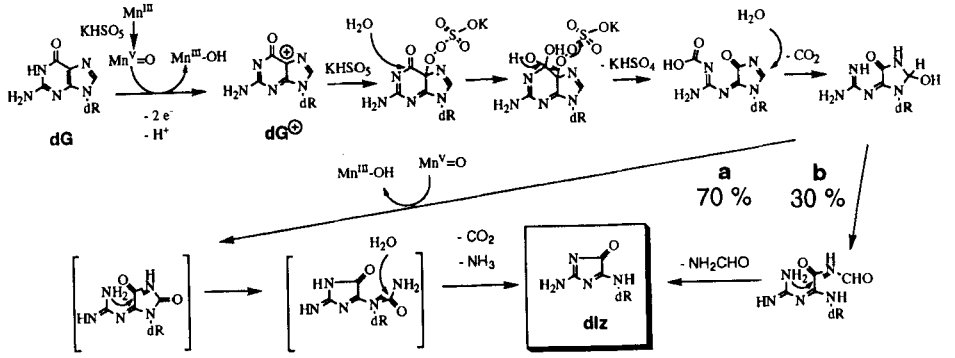
ABSTRACT: MnTMPyP in the presence of sulfite/O_2 catalyses the oxidation of **dG** into **dIz** as selectively but slower and less efficiently than in the presence of $KHSO_5$.

The manganese complex of *meso*-tetrakis(4-*N*-methylpyridiniumyl)porphyrin (MnTMPyP), associated to $KHSO_5$, was shown to mediate DNA alkali-labile lesions located at G residues.[1] We previously reported the mechanism of the highly efficient catalytic oxidation of 2'-deoxyguanosine (**dG**) by the MnTMPyP/$KHSO_5$ system.[2] **dG** was converted to 2-amino-5-[(2-deoxy-β-D-*erythro*-pentofuranosyl)amino]-4*H*-imidazol-4-one (**dIz** or imidazolone) in a nearly quantitative yield (90%), within min at room temperature. This reaction represents a convenient way to prepare **dIz**. We showed that O_2 did not participate in the formation of **dIz** contrarily to the case of photosensitized 1 e^- oxidation of **dG**.[3] We postulated that a first electron abstraction from **dG**, leading to the radical cation $\mathbf{dG}^{\bullet+}$, would be followed, after one fast deprotonation step, by a fast second electron abstraction from the neutral radical $\mathbf{dG}^{\bullet}$ by the high-valent Mn^V=O species of the metalloporphyrin, to give the $\mathbf{dG}^+$ cation. The relatively slow reaction of $\mathbf{dG}^{\bullet}$ with O_2 allows the oxidation of this neutral radical by the manganese-oxo species.

The proposed mechanism of oxidation of **dG** by MnTMPyP/$KHSO_5$ is shown on the Scheme. One key point is the fate of $\mathbf{dG}^+$ in this system. Since we found no

incorporation of ^{18}O into **dIz** when the reaction was done either in $H_2{}^{18}O$ or under $^{18}O_2$, we concluded to a nucleophilic attack of $KHSO_5$ on the C5 of **dG**$^+$. It has recently been shown that sulfite/O_2 could substitute to $KHSO_5$ in oxidation reactions catalyzed by metal complexes.[4] In the presence of MnTMPyP as catalyst, Mn^V=O species can be formed



with HSO_3^- and O_2.[5] We thus reacted MnTMPyP associated to sulfite under O_2 with **dG**. In a final volume of 250 µL of 60 mM phosphate buffer pH 6.5 and at ambient temperature, **dG** was incubated at 50 µM concentration with MnTMPyP (2 µM) and $KHSO_5$ (1 mM) for 1 min or at 500 µM concentration with MnTMPyP (10 µM) and Na_2SO_3 (added in five aliquots every 2 min to final 2 mM concentration after 10 min). As reported below, the reaction in the presence of HSO_3^- under air led to the same selective transformation of **dG** into **dIz** but the yield was only 50 %. This is due to the reductive inactivation of the metal-oxo intermediate at too high sulfite concentration. To maintain a

	time of reaction	dG	dIz
$KHSO_5$	1 min	-	100 %
HSO_3^-/O_2	10 min	50 %	50 %

concentration suitable to activate MnTMPyP but low enough to avoid the reduction of the activated metalloporphyrin, sulfite was added by fractions. However, the relatively long reaction time (10 min) may allow the **dG**$^\bullet$ radical intermediate to be trapped by O_2 instead of being further oxidized to the corresponding cation by the activated metalloporphyrin. Consequently, it would be probably impossible to check in this case the exact nature of the species (persulfate anion or persulfate radical formed *in situ*, dioxygen,...) involved in the attack on the C5 of **dG**.

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