The Autoxidation of a 1,4-Dihydronicotinamide catalyzed by 4-Amino-2,6-di-iodophenol

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THE mononegative *o*-diphenol ion, the monoprotonated *p*-phenylenediamines, and the iodide ion increase the rate of the autoxidation of one-electron donors by preferential stabilization of the oxygen molecule in the transition state.[1]

We have found that protonated 4-amino-2,6-di-iodophenol[2] (ADIP) catalyzes the autoxidation of 1-benzyl-1,4-dihydronicotinamide[3] (I) to the pyridinium cation (II), but has no effect upon the autoxidation of *p*-hydroquinone (pH 5·5—8·8), of *p*-phenylenediamine (pH 7·0—8·5), or of benzenethiol (pH 7·6). Since the last three substrates are oxidized by one-electron or H• atom-transfer, whereas H^- ion is removed in the oxidation of (I), the reaction was studied at 25° in 0·1M-methanolic Tris-buffer [tris(hydroxymethyl)aminomethane] (1 : 1; v/v) (Figure 1).

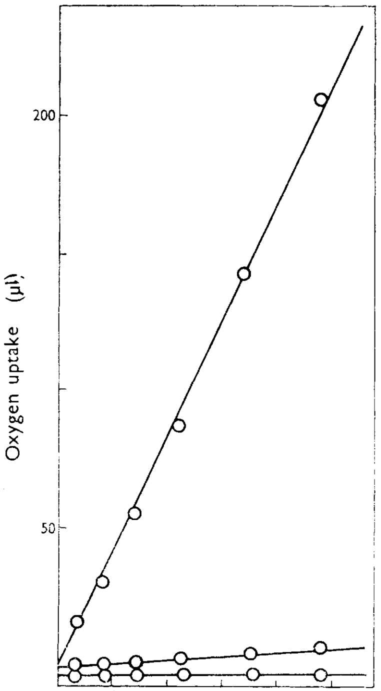
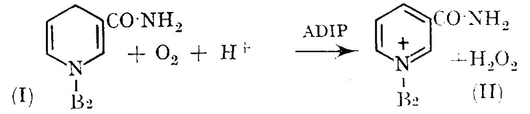


FIGURE 1. *Oxygen uptake in the system of* 4×10^{-2}M (I) *and* 2×10^{-3}M *4-amino-2,6-di-iodophenol at* pH 6·8. *Middle line,* (I) *alone; lower line, 4-amino-2,6-di-iodophenyl alone.*

The theoretical amount of O_2 for water formation is taken up and compound (I) completely disappears; some increase in pH is always observed. Starch–iodide tests for H_2O_2 were positive. Therefore the following scheme is proposed:



$$H_2O_2 \longrightarrow H_2O + \tfrac{1}{2}O_2$$

The yield of (II), as isolated with the cation-exchange resin Dowex 50X-4, was substoicheiometric (62% at pH 7·4). The reason is that the 4-amino-2,6-di-iodophenol or any 2,6-dihalogenophenol,[4] promotes solvent addition to the 5,6-double bond of (I), a reaction followed spectrometrically in evacuated cells; the resulting product is soon catalytically oxidized. At higher pH values this secondary reaction becomes less serious and at pH 8·3, 80% of (I) is directly autoxidized.

The effect of the pH upon the rate indicates that both the *N*-protonated ion and the zwitterion are active species, which are unlikely to undergo chemical changes. In fact the manometric and spectrophotometric stability of the catalyst at neutral pH values rules out the possibility that the catalyst is an oxidation product of 4-amino 2,6-di-iodophenol; moreover, 2,6-di-iodo-*p*-benzoquinone itself was inactive at neutral pH values. Neither does the catalyst undergo cyclic reduction–oxidation changes as confirmed by the kinetics. The reaction is first order in dihydronicotinamide (5×10^{-3}—4×10^{-2}M) and, at pH 8·3, first order in oxygen (air–pure O_2).

The effect of the catalyst concentration (Figure 2) indicates two concomitant processes; one extremely efficient and reaching saturation at very low concentrations of the active forms.

Radical mechanisms in the oxidation of dihydronicotinamides are likely[5] but not in the present case as the reaction is light-insensitive and is only slightly inhibited by 9,10-dihydroanthracene, a good radical scavenger; moreover the catalyst does not promote the autoxidation of one-electron donors.

The most probable mechanism involves stabilization of the O_2 molecule in the transition state by charge-transfer forces and proton donation. However, since the non-halogenated *p*-hydroxyanilinium cation is inactive as a catalyst, even in much larger concentrations than those of 4-amino-2,6-di-iodophenol, a fundamental role for the iodine substituents is indicated. The H^- ion transfer to oxygen is forbidden by the spin-conservation rule; the reverse process from the peroxide ion to a suitable acceptor leads to singlet oxygen.[6] It is, therefore, possible that the heavy iodine substituents partially remove the prohibition through the spin–orbital coupling effect.[7]

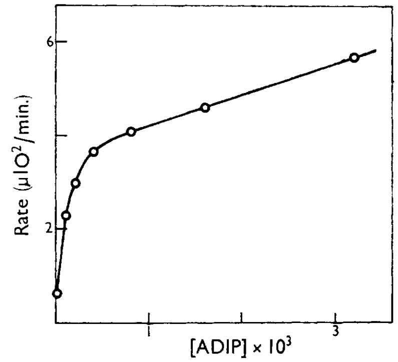


FIGURE 2. *The effect of* 4-*amino*-2,6-*di-iodophenol concentration upon the autoxidation of* 4×10^{-2}M (I) *at* pH 6·8.

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