Photolysis of *o*-Nitrophenoxyacetic Acids: a New Synthesis of *o*-Nitroso-phenols

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Summary Photolysis of *o*-nitrophenoxyacetic acids gives the corresponding *o*-nitroso-phenols.

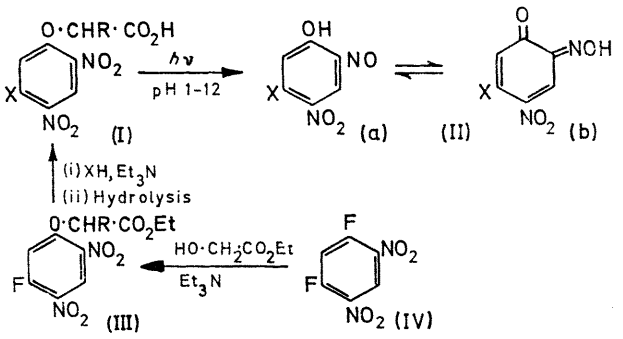
THE uncoupling of oxidative phosphorylation in mitochondria by 2,4-dinitrophenol is well known, but the biological properties of the analogous 4-nitro-2-nitrosophenol (II; X = H) have not been described. This compound and several of its 5-substituted derivatives (II; X = alkoxy) have now been prepared with a view to examining their biological activities. The synthesis employed a new reaction which offers an alternative to that of Baudisch,[1] hitherto the only general method for preparing *o*-nitroso-phenols.

A solution of α-(2,4-dinitrophenoxy)propionic acid[2] (I; X = H, R = Me) at pH 7 was irradiated with u.v. light in a standard "Hanovia" photochemical reactor. Carbon dioxide and acetaldehyde were evolved. The reaction mixture after acidification yielded green 4-nitro-2-nitrosophenol, $C_6H_4N_2O_4$, (II; X = H) obtained in 65% yield after one recrystallization. The structure was supported by the following evidence. The compound formed a deep red copper complex, a general property of *o*-nitrosophenols;[1b] it was readily oxidized to 2,4-dinitrophenol; and it condensed with aniline in acetic acid to give 4-nitro-2-phenylazophenol. It sublimed unchanged *in vacuo* but was converted into the brown, tautomeric, quinonoid form[1b,3] (IIb; X = H) by recrystallization from aqueous ethanol. The green, benzenoid form (IIa; X = H) had no detectable O–H stretching band in the i.r. spectrum, a phenomenon also observed with 1-nitroso-2-naphthol[4] and attributable to strong intramolecular hydrogen bonding. The brown quinonoid form had a moderately strong O–H band, λ_{max} (paraffin mull) 2·86 μm.

The effect of pH on the reaction was studied by measuring the changes produced in the u.v. spectra of dilute (10^{-4}M) solutions by illumination. Throughout the pH range 1—12, 4-nitro-2-nitrosophenol was formed almost exclusively. In its pH-independence the reaction differs from the photolysis of 2,4-dinitrophenylamino acids in aqueous solution.[5]

For comparison, synthesis of 4-nitro-2-nitrosophenol by the Baudisch reaction was attempted. Under the conditions described for the *o*-nitrosation of *p*-chlorophenol,[1b] *p*-nitrophenol gave none of the required product after 3 days.

A series of 5-substituted derivatives (II; X = alkoxy) was prepared from ethyl 5-fluoro-2,4-dinitrophenoxyacetate (III; R = H). This intermediate, obtained from ethyl glycollate and 1,5-difluoro-2,4-dinitrobenzene (IV) as shown



in the accompanying scheme, reacted readily with primary and secondary alcohols in the presence of tertiary base. Hydrolysis of the resulting esters gave the required phenoxyacetic acids (I; R = H; X = OMe, OEt, OPr, OPr^{i}, OBu, OBu^{t}, or cyclohexyloxy). These on photolysis yielded the corresponding *o*-nitroso-phenols, which were isolated in the green benzenoid form.

o-Nitroso-phenols have occasionally been prepared by partial reduction of *o*-nitro-phenols with zinc and acetic acid.[1c,6] The reaction is difficult to control, and in our hands it failed with 2,4-dinitrophenol. Conversion of an *o*-nitrophenol into the corresponding *o*-nitrophenoxyacetic acid,[7] followed by photolysis of the latter, offers an indirect method for accomplishing such a reduction.

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