Mechanism of a Novel Spirocyclisation Reaction; Intramolecular Oxygen Transfer to Carbon Radicals by Nitro Groups

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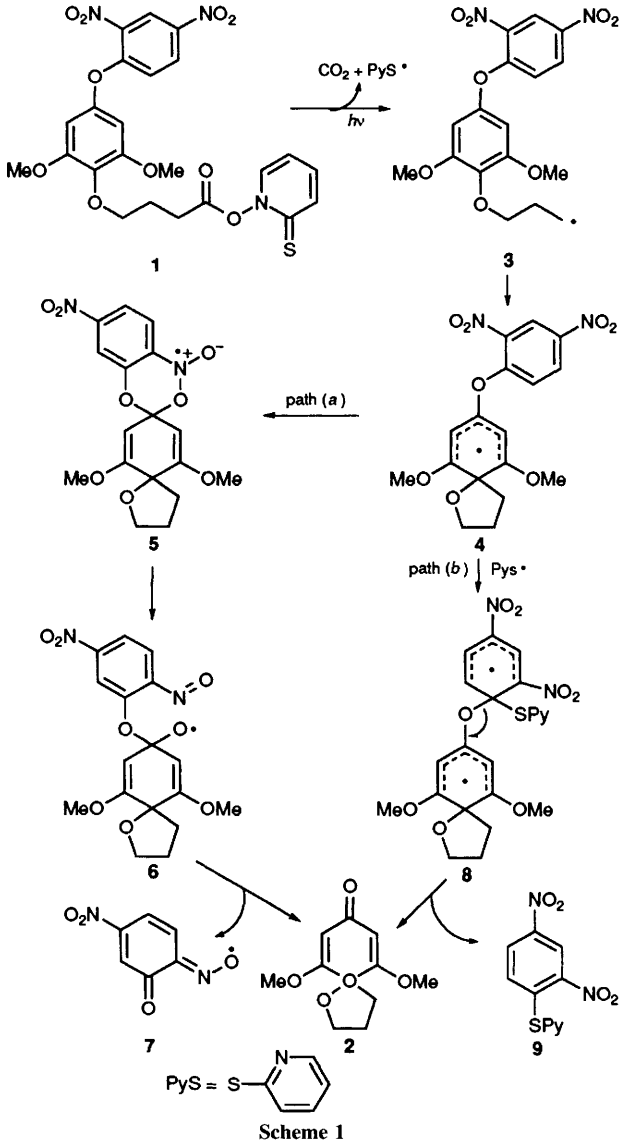
A mechanism for the novel radical spirocyclisation reaction **1** → **2** is proposed, and is shown by isotopic labelling to involve transfer of oxygen from an aromatic nitro function to carbon in a cyclohexadienyl radical.

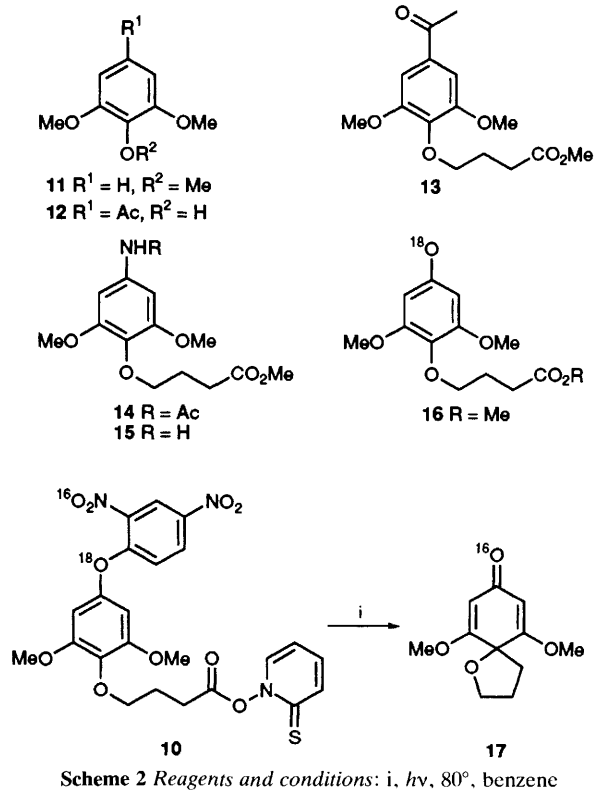
In the preceding communication[1] we postulated a mechanism for the biogenesis of spirodienone substructures found in an unusual set of *o,o*-bridged biaryl lignans, and we reported a biomimetic parallel based unambiguously on radical chemistry. This biomimetic process involved the transformation, to the best of our knowledge unprecedented, of the thiohydroxamate ester **1**, containing a 2,4-dinitrophenyl ether moiety, to the spirodienone **2** (49%), upon irradiation. This reaction could plausibly follow more than one pathway, and required further investigation. In this note we report an isotopic study of the process and indicate a preferred mechanism.

Scheme 1 shows the two mechanisms which appeared to us to be the most likely. Initial N–O homolysis and decarboxylation[2] must afford the primary radical **3**, which can cyclise to the spirocyclohexadienyl radical **4**. Trapping (6-*endo*-trig) of the carbon radical by oxygen of the *ortho*-nitro group [path(*a*)] would lead to the nitrogen centred radical **5**, which is set up to undergo N–O α-scission followed by fragmentation of the oxygen radical **6**, providing the product spirodienone **2** and the relatively stable radical **7**. In other work, a similar iminoxyl radical has been studied by ESR,[3] but its further reactions remain unknown. In the present work, we have so far not detected any products arising from the expelled 2,4-dinitrophenyl unit. Alternatively, the intermediate species **4** could react with a pyridine thiyl radical still within a solvent cage, to form the diradical **8** which undergoes swift α-cleavage to form the observed dienone **2** and 2,4-dinitro-1-(2-pyridylthio)-benzene **9**. Despite the fact that we could determine, using an authentic sample, that the thioether **9** was not among the reaction products, we sought a clear distinction between these pathways which would establish that the carbonyl oxygen of the final product **2** did not derive from the aryl ether oxygen of the biaryl ether **1** (and originally from a phenolic oxygen), but from the *ortho*-nitro group. To this end we synthesised the ^{18}O-labelled biaryl ether **10**.

3,4,5-Trimethoxyacetophenone **11** was reacted with aluminium chloride to form the *para*-demethylated ketone **12** (60%), which was reacted with methyl 4-bromobutanoate to afford ester **13** (60%). Beckmann rearrangement to amide **14** (45%) was followed by selective amide cleavage in dry acidic methanol to yield the amine **15** (85%). Diazotisation in 10% ^{18}O-water gave the ^{18}O-labelled phenol **16** (50%), with parallel incorporation of the isotope very clearly shown by mass spectrometry. Formation of the 2,4-dinitrophenyl ether using Sanger's reagent, ester hydrolysis, and formation of the



Scheme 1



Scheme 2 *Reagents and conditions*: i, *hν*, 80°, benzene

thiohydroxamate under standard conditions gave the required radical precursor **10**, ^{18}O-labelled. Irradiation of this compound under the conditions used previously (see preceding communication) gave the spirodienone product **17**, the mass spectrum of which showed complete loss of the ^{18}O-label, within experimental error.†

Thus, we conclude that the carbonyl oxygen is derived from the *ortho*-nitro group as in Scheme 1, path (*a*). Limited precedent for nitro-group oxidation of carbon radicals was found in the literature. Thus, aromatic nitro groups were postulated by Jackson and Waters[4] to be oxygen donors in the oxidation of benzyl radicals to benzaldehyde, although the nitroso products were not isolated. Hey, Perkins and coworkers[5] explained the role of added nitrobenzene on homolytic aromatic phenylation reactions in terms of reduction of nitrobenzene to nitrosobenzene by phenylcyclohexadienyl radicals. The relatively stable diphenylnitroxide was then formed, the concentration of which determined product ratios.

Investigations of the scope of this new reaction are in progress.

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Footnote

† All new compounds gave satisfactory spectroscopic and analytical data

References

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