



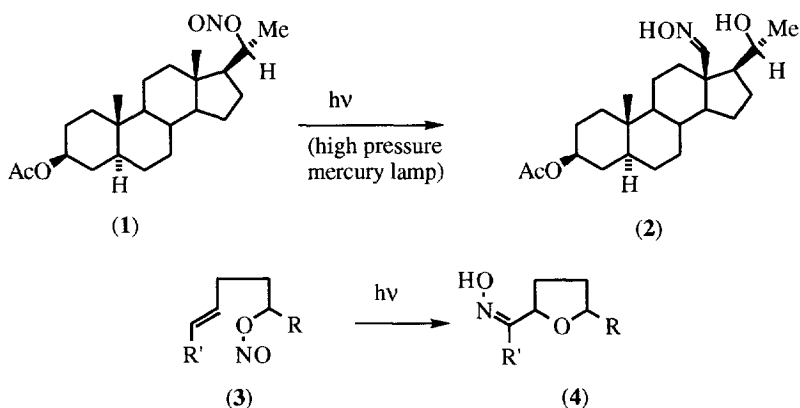
## Novel Radical-Induced C-N Bond Formation.

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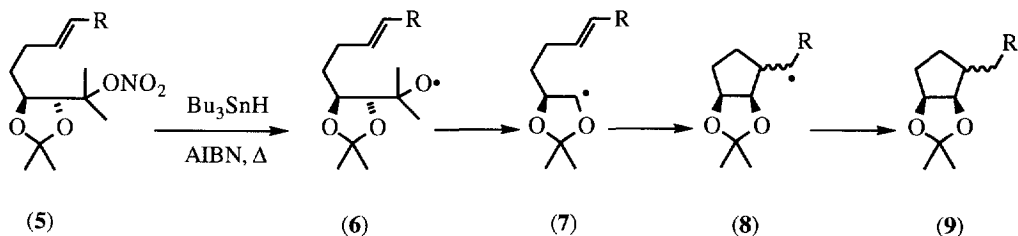
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**Abstract:** Investigation of anomalous products from nitrate ester fragmentations have led to the discovery of a new route from alkyl halides to oximes.

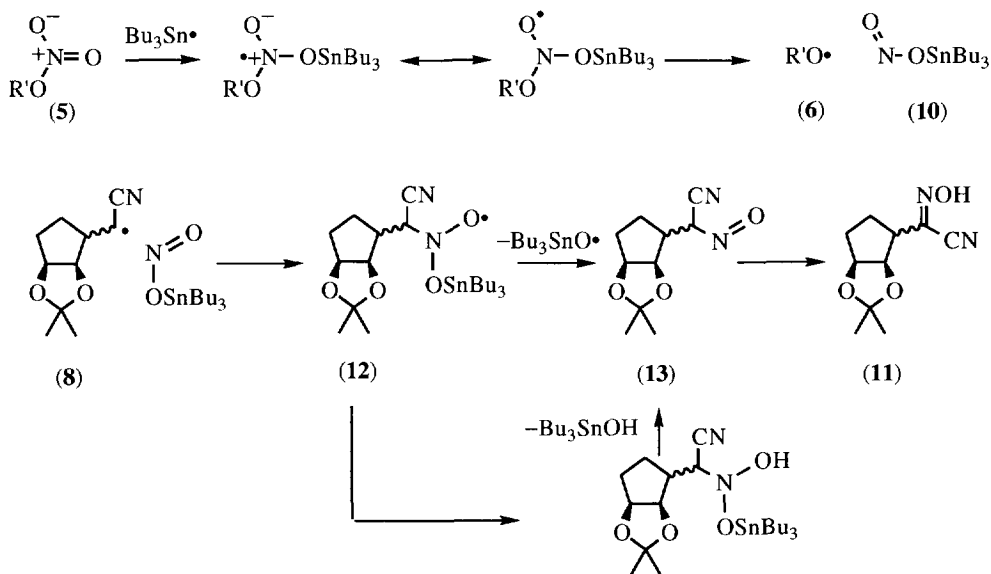
One of the most useful reactions for remote functionalisation of carbon skeletons is the Barton photolysis of nitrite esters. This reaction<sup>1,2</sup> has achieved particular fame for its success in steroid transformations e.g. (1)→(2). Nitrite esters have also been used photochemically (using a medium-pressure<sup>3</sup> or high-pressure<sup>4</sup> mercury lamp) to generate oximes following cyclisation, e.g. (3)→(4). In both cases the nitrite ester can (presumably reversibly) cleave to an alkoxyl radical. After the alkoxyl radical has either abstracted a hydrogen atom or cyclised to form a carbon-centred radical, irreversible trapping of NO occurs, followed by tautomerism to yield an oxime.



In both of the above cases, an alkoxyl radical is a necessary intermediate. This paper extends the scope of oxime functionalisation<sup>5</sup> by not requiring alkoxyl radical intermediates on the substrate but, instead, deriving the carbon radicals from the very convenient normal source, alkyl halides. The discovery arose from our studies of the stereoselective cyclisations<sup>6</sup> of dioxolanyl radicals (7), which were prepared<sup>7</sup> from fragmentation of alkyl nitrates (5). In these cases, the nitrate esters reacted to form alkoxyl radicals (6) which

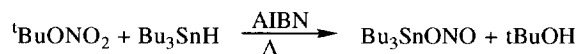


were fragmented to afford the required dioxolanyl radicals. Cyclisation to radical (8) and termination by hydrogen atom abstraction from tributyltin hydride afforded products (9). In all of the examples, reductive termination was observed; no incorporation of nitrogen from the nitrate ester was observed. This termination is in marked contrast with the behaviour of nitrite esters which, under the photochemical conditions described above, trap NO quite efficiently. However, we now report on one substrate (5,  $\text{R} = \text{CN}$ ) which behaved anomalously, giving not only the expected nitrile products (9,  $\text{R} = \text{CN}$ ) but two minor products, the oxime isomers (11) in a total of 6%. To explain this reaction, which occurred by [non-photochemical] activation with tributyltin hydride and AIBN, we propose that an expected by-product of the reaction, tributyltin nitrite (10), was implicated. Either the tributyltin nitrite underwent thermal decomposition<sup>8</sup> to NO which was acting as the trapping agent, or, more likely, (8) attacks tributyltin nitrite directly, and the resulting intermediate (12) breaks down to a nitroso product (13), and thence to the oxime (11), either by homolytic or by heterolytic means. It is reasonable that nitrite esters,  $\text{RONO}$ , should react well with carbon-centred radicals,  $\text{RNO}$ .

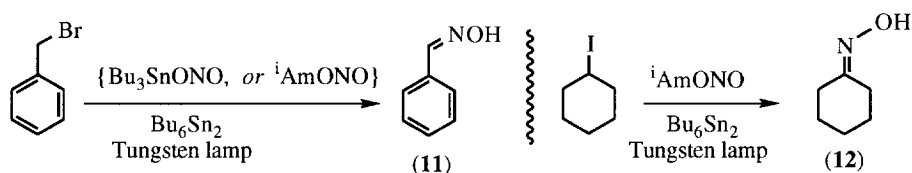


To test the proposal, *tert*-butyl nitrate was prepared and reacted with tributyltin hydride and AIBN so as to give tributyltin nitrite. This unpurified product was then reacted with benzyl bromide and hexabutylditin

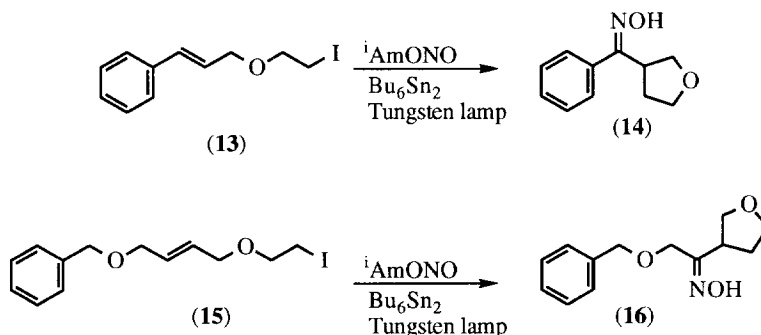
under irradiation with a tungsten lamp (300W) for three hours. Gratifyingly, a 63% yield of benzaldoxime (**11**) resulted.



To see if tributyltin nitrite were a special case, benzyl bromide was exposed to isoamyl nitrite and hexabutylditin under a tungsten lamp for 4 hours. An 84% yield of benzaldoxime (**11**) resulted, showing that simple nitrite esters can function satisfactorily. With cyclohexyl iodide, a 71% yield of cyclohexanone oxime (**12**) was isolated, but on changing the substrate to cyclohexyl bromide, no oxime was afforded, and cyclohexyl bromide was recovered. A blank experiment in which cyclohexyl iodide and isoamyl nitrite were subjected to tungsten lamp irradiation in the absence of tributyltin hydride and AIBN led to recovery of cyclohexyl iodide and no formation of oxime. This indicates that tributyltin radicals are playing an intimate part in the reaction. The failure of the cyclohexyl bromide reaction may indicate that the tributyltin radicals are reacting with the nitrite ester faster than with the bromide. The benzyl bromide would of course be expected to have a weaker C-Br bond than a secondary alkyl bromide, and hence the success of the benzyl bromide is not anomalous.

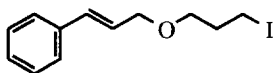


To further test the scope of this chemistry, four more complicated substrates were subjected to our conditions. The primary iodide (**13**) cyclised in 73% yield to the oxime (**14**) as the only isolated product. Oximes were isolated as mixtures of *E*- and *Z*-isomers. To show that this successful result was not due to the special nature of the styrene double bond, the iodide (**15**) was synthesised and converted to cyclised oxime (**16**) in 61% yield. Although these substrates cyclised very cleanly prior to termination, the homologues (**17**) and (**19**) which would lead to 6-membered ring formation, did not cyclise: instead, the acyclic oximes (**18**) (70%) and (**20**) (70%) were isolated. Decreasing the relative concentration of the isoamyl nitrite did not lead to isolation of cyclised products, and the yield of the oximes decreased.

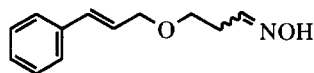


In conclusion, investigations into anomalous products from nitrate ester fragmentations have led to a

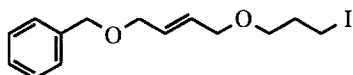
new route to oximes from alkyl iodides. The chemistry extends to reactive benzyl bromides. The simplicity of the starting materials, the ability to use a liquid nitrite ester rather than gaseous NO, and the general familiarity of synthetic chemists with trialkyltin reagents suggest that this chemistry will have useful applications. This transformation to oximes adds to the rapidly growing arsenal of radical methods for carbon-nitrogen bond formation<sup>9-13</sup>.



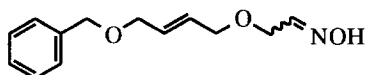
(17)



(18)



(19)



(20)

#### Acknowledgements.

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