

4-Nitro-2-phenyloxazole: an Electrophilic Dienophile for Normal Diels–Alder Reactions in the Oxazole Series

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The title compound **2**, obtained by thermal isomerization of the corresponding nitroisoxazole **1**, is found to undergo [2 + 4] cycloaddition processes with 2,3-dimethylbuta-1,3-diene and cyclohexa-1,3-diene, respectively.

Since the pioneering work of Kondrat'eva on the reactivity of alkyloxazoles with maleic anhydride,¹ many derivatives of this system have been employed over the past three decades as 2-azadiene components in inter- and intra-molecular Diels–Alder reactions with olefinic and acetylenic dienophiles for the synthesis of pyridine and furan products, respectively;² more recently, the reactivity of oxazoles with different hetero-dienophiles was also examined.³

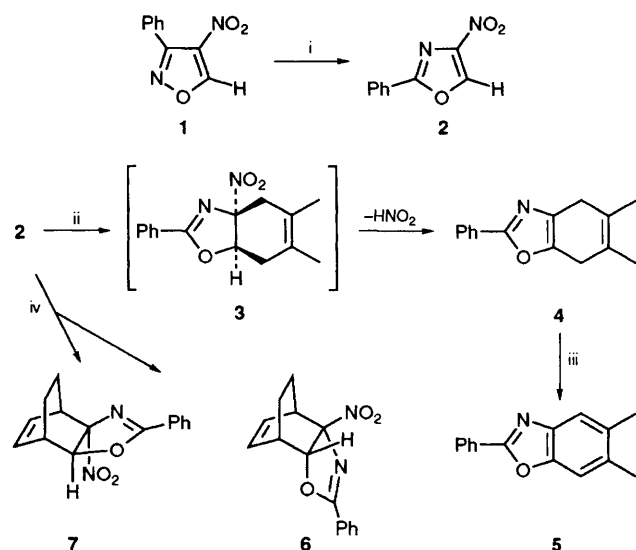
It has also been shown that the same system can enter as a nucleophilic counterpart in inverse electron demand Diels–Alder reactions with electron-deficient carbo-⁴ and heterodiene^{4,5} partners. However, the possibility of carrying out normal [2 + 4] cycloadditions on the C(4)–C(5) double bond of suitably substituted derivatives still remained, to our knowledge, unexplored.

4-Nitrooxazoles could represent good candidates for this purpose but, unfortunately, only two derivatives have been

obtained so far in very modest yields.⁶ In this context, a recent report clearly indicated that the flash vacuum pyrolysis of 5-methyl- and 5-ethyl-4-nitroisoxazoles cannot be exploited for the synthesis of the corresponding oxazoles, since this gave rise to 1-nitro-1-cyanoacetone as the only product;⁷ nevertheless, since these results were certainly due, according to the invoked mechanistic rationale, to the presence of the above alkyl groups at position 5, we decided to investigate the thermal behaviour of the 5-unsubstituted 4-nitroisoxazole **1**.

Thus, when the latter compound was gently refluxed under nitrogen in anisole, the hitherto unknown 4-nitro-2-phenyloxazole **2** was obtained as a pure product† in reasonable yield (35–40%, based on the recovered starting material), probably through a 1-azirine intermediate.

† All new compounds gave satisfactory analytical and spectral data.



Scheme 1 Reagents and conditions: i, anisole, ca. 170 °C external bath, 48 h; ii, DMB, CHCl₃, sealed tube, 110 °C, 16 h; iii, DDQ, anhydrous benzene, reflux, 30 min; iv, cyclohexa-1,3-diene, CHCl₃, sealed tube, 110 °C, 24 h

Treatment of **2** with an excess of 2,3-dimethylbuta-1,3-diene (DMB) (molar ratio 1:5) in chloroform at 110 °C afforded a mixture of the dihydrobenzoxazole **4** and the corresponding aromatic derivative **5**, which were separated by flash-column chromatography in 71 and 13% yields, respectively. The formation of these compounds could be accounted for by a Diels–Alder reaction on the starting nitrooxazole, leading to the primary cycloadduct **3** from which nitrous acid is lost; the resulting derivative **4** was, in turn, partially oxidized into **5** which could also be obtained quantitatively from the same precursor with 2,3-dichloro-5,6-dicyano-1,4-benzoquin-

one (DDQ) in boiling anhydrous benzene. Attempts to isolate or detect the labile intermediate **3** under milder conditions were unsuccessful.

In contrast, heating of **2** with cyclohexa-1,3-diene under the former conditions allowed us to isolate the tricyclic dihydrooxazoles **6** and **7** in 33 and 30% yields, respectively; their relative stereochemistry was established by comparative ¹H NMR experiments.

Whereas the increased resistance of these diastereoisomers to the elimination of HNO₂ is certainly due to the remarkable strain from the aromatization of the five-membered ring, the nearly statistical distribution of the above adducts probably arises from comparable secondary orbital interactions involving the N=C(Ph)–O moiety and the nitro group, respectively.

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