

New Features of Isoxazole Chemistry. The Reaction of Ethyl 4-Nitro-3-phenylisoxazole-5-carboxylate with 2,3-Dimethylbuta-1,3-diene

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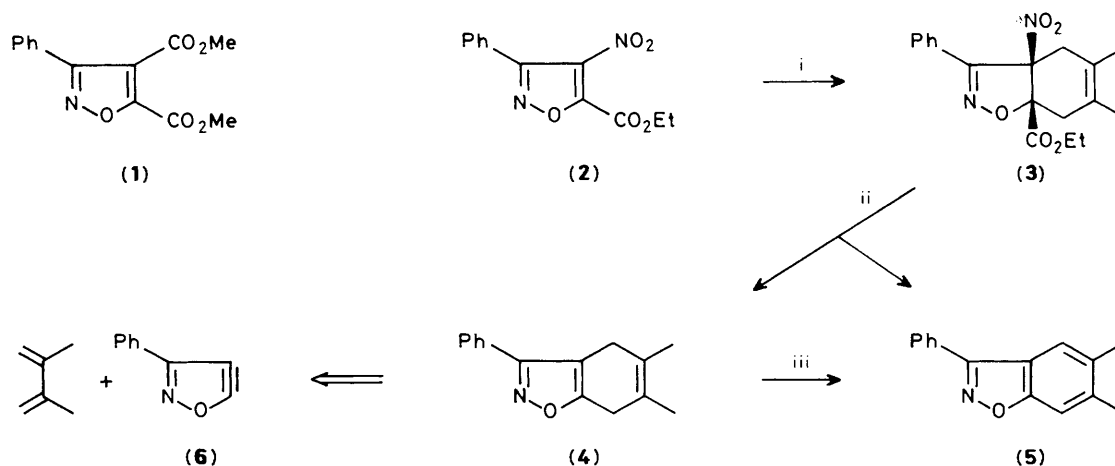
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The title compound (2) was found to undergo a (2 + 4) cycloaddition with 2,3-dimethylbuta-1,3-diene affording the tetrahydro-1,2-benzisoxazole (3), which could be easily converted into the corresponding dihydro derivative (4) by elimination of the NO₂ and CO₂Et groups.

Although cycloadditions of 2-,¹ 3-,² and 4-isoxazolines³ have been known for several years, only recently have two examples involving, in different ways, the C(4)–C(5) double bond of 'aromatic' isoxazoles been reported; namely, the [Mo(CO)₆]-induced reaction of variously substituted derivatives with acetylenic esters,⁴ and the (4 + 2) cycloaddition of 3-methyl-5-vinylisoxazole with activated dienophiles.⁵ However, the possibility of employing the above double bond

as a dienophile in Diels–Alder reactions remained, to our knowledge, unexplored.

In this context and with the aim of determining if the presence of two electron-withdrawing groups at the 4- and 5-positions could provide a sufficient activation, we investigated the behaviour of compounds (1) and (2) with 2,3-dimethylbuta-1,3-diene (DMB). No reactivity was observed with (1) which appeared unchanged after prolonged heating



Scheme 1. Reagents and conditions: i, DMB, toluene, 110 °C; ii, DMB, xylene, 150 °C; iii, xylene 110–120 °C.

with DMB in xylene at 150 °C in a sealed tube; by contrast, the nitroester (2), easily available from α -nitroacetophenone oxime,⁶ reacted with the same diene (molar ratio 1:5) under milder conditions (toluene, 110 °C, 48 h) to afford in good yield (87%, based on the recovered starting material) the derivative (3) through a (2 + 4) cycloaddition (Scheme 1). From the reaction we also isolated by flash-column chromatography a very small amount of compound (4) which represents the elimination product of (3) with loss of the nitro and ester groups. Attempts to achieve this elimination merely by thermolysis failed; the cycloadduct (3) was stable at 110 °C, but it completely decomposed in xylene at 150 °C, yielding a complex reaction mixture which did not contain (4) (¹H n.m.r. spectrum). Nevertheless, surprisingly, when the reaction was carried out under similar conditions in the presence of DMB (molar ratio 1:5, 7 h), the desired dihydro derivative (4) was obtained in 55–60% yields together with a minor amount of the known 1,2-benzisoxazole (5),⁷ which, in turn, could be prepared from (4) by prolonged heating in the same solvent.

The peculiar role of DMB in promoting the clean loss of NO₂ and CO₂Et might be connected with a group transfer reaction, and mechanistic investigations will start from this assumption.

Since the nitroester (2) can be easily converted into (4) via the nitro derivative (3), it can be regarded as an attractive synthetic equivalent of the 4,5-didehydroisoxazole (6) for similar cycloaddition processes.

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