

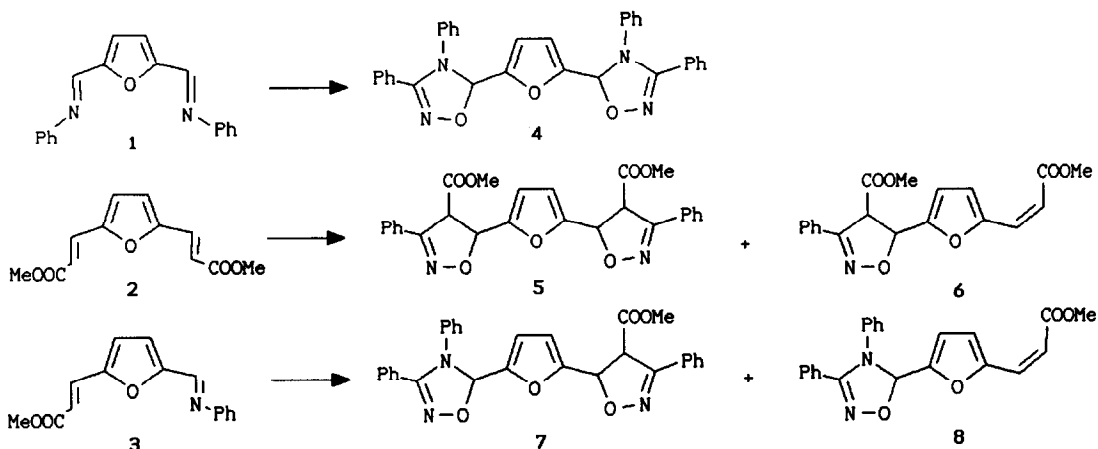
1,3-DIPOLAR CYCLOADDITIONS OF BENZONITRILE OXIDE TO VINYL AND AZAVINYL FURAN DERIVATIVES

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Dedicated to Prof. R. Huisgen on his 70th birthday

Abstract : The regiospecific and site-selective 1,3-dipolar cycloaddition reactions of benzonitrile oxide (BNO) to the C=C and the C=N double bonds of some furyl-substituted dipolarophiles is reported.

Although 1,3-dipolar cycloaddition reactions of nitrile oxides to C=C and C=N double bonds has been widely studied¹, rather little work has been devoted to furan derivatives in this concern²; and on the other hand, the competition between two dipolarophiles in the same substrate has received scant attention³. In this context we report our results on the cycloaddition of BNO as a model of nitrile oxides to furan derivatives **1**, **2**, and **3**, which gives rise to furylisoxazolines and furyl-1,2,4-oxadiazolines which may be interesting from a synthetic point of view⁴ (Scheme 1).









Scheme 1

Azomethine **1** reacts with two equivalents of BNO⁵ (CH₂Cl₂, RT, 12 h) to give **4** in 90% isolated yield⁶. Detailed conditions for the synthesis of compounds **5**, **6**⁷, **7** and **8**³ are given in Table 1. The possibility of functionalizing only one of the two α,β -unsaturated ester moieties present in **2** (entries 1 and 3, Table 1) provides a striking feature with no precedent in the literature; whereas cycloaddition of BNO to **3** can be directed at ease to the C=N or to both C=N and

Table 1

Regioselectivity in the 1,3-dipolar cycloadditions of BNO to furan derivatives **2** and **3**

Entry	Dipolarophile	Molar ratio BNO : Dipolarophile	Time (h)	Concentration of dipolarophile (g/l) ^a	Yields of cycloadducts ^b
1		2.2 : 1	13	8.0	54% ^c 5 ; 34% ^c 6
2		2.2 : 1	24	40.0	74% ^d 5
3		1.1 : 1	48	2.0	7% ^c 5 ; 43% ^c 6
4		1.1 : 1	13	6.0	92% ^d 8
5		2.2 : 1	20	12.0	62% ^c 7 ; 26% ^c 8
6		2.2 : 1	48	20.0	90% ^c 7 ; 5% ^c 8

a) In CH₂Cl₂; b) Pure, isolated yield after column chromatography of the reaction crude; c) as a 1:1 mixture of diastereomers, evaluated by integration of the ¹H-NMR 300 MHz spectra; d) only this cycloadduct was observed

C=C linkages depending on the reaction conditions (entries 4, 5 and 6, Table 1). In conclusion, an easy synthesis of highly functionalised 2,5-furyl-derivatives is described via 1,3-dipolar cycloaddition of nitrile oxides to appropriate vinyl and azavinyl furan derivatives.

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