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# Improved Generation Method for Functionalized Nitrile Oxide

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## Abstract

Gentle generation of nitrile oxide bearing a carbamoyl group was performed. 4-Nitro-3-isoxazolin-5-one was treated with dipolarophiles in the mixed solvent (MeCN / $H_2O$) at room temperature to afford cycloadducts in good yields. © 1998 Elsevier Science Ltd. All rights reserved.

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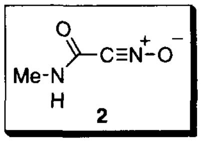
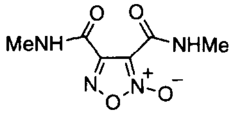
Functionalized nitrile oxides are useful for syntheses of polyfunctionalized compounds, but only several preparative methods are known [1-7]. We have previously revealed that 2-methyl-4-nitro-3-isoxazolin-5-one (**1**) [8,9] behaves as the precursor of nitrile oxide **2** bearing a carbamoyl group [10]. This reaction, however, did not satisfy us because of the requiring somewhat severe conditions which prevented the facile application of it to organic syntheses.

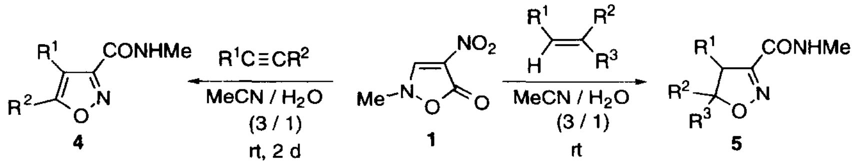
Isoxazolone **1** remained intact even though it was heated under reflux in MeCN, but furoxan **3**, the dimer of **2**, was isolated from the aqueous solution of **1** in 80 % yield at room temperature. These facts prompted us to design a convenient method for generation of nitrile oxide **2** initiated by $H_2O$ under milder conditions.



**2**



**3**



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To a solution of isoxazolone (**1**, 144 mg, 1 mmol) in MeCN (7.5 mL), phenylacetylene (202 mg, 2 mmol) and $H_2O$ (2.5 mL) were added. The reaction mixture was stirred at room temperature with monitoring by the thin layer chromatography. The solution gradually turned to yellow, and the reaction almost finished after 1 day. The solvent was evaporated under reduced pressure, and the residue was recrystallized from PhH to afford 3-carbamoyl-5-phenylisoxazole (**4a**, 171 mg, 85 %).

Table 1

| $R^1$ | $R^2$ | **4** | Yield / % |
|---|---|---|---|
| H | Ph | **a** | 85 |
| H | $CH_2OH$ | **b** | 94 |
| H | $CH_2Br$ | **c** | 61 |
| COOEt | COOEt | **d** | 29 |

Table 2

| $R^1$ | $R^2$ | $R^3$ | **5** | Time / d | Yield / % |
|---|---|---|---|---|---|
| Me | H | Et | **a** | 3 | 50 [a)] |
| H | $CH_2OH$ | H | **b** | 2 | 74 |
| H | OEt | H | **c** | 4 | 86 |
| —$(CH_2)_3$— | | H | **d** | 2 | 86 |
| —$(CH_2)_2O$— | | H | **e** | 4 | 96 |
| H | Me | COOEt | **f** | 2 | 88 |
| COOMe | COOMe | H | **g** | 2 | 81 |

a) a mixture of regioisomers

Propargyl derivatives and diethyl acetylenedicarboxylate were similarly transformed to isoxazole **4b-d** (Table 1). Versatile alkenes were investigated. Isoxazolone **1** effectively reacted with both electron-rich and electron-deficient alkenes to furnish corresponding isoxazoline derivatives **5a-g** in good yields (Table 2).

Commonly used procedures for preparation of nitrile oxides need particular conditions or reagents such as halogenating agents, dehydrating ones and strong bases [5-7]. As compared with these conventional methods, only the presence of $H_2O$ is necessary for our method. The very simple experimental procedure in cooperation with readily available **1** offers an excellent method for preparing functionalized nitrile oxide **2** although the definitive mechanism has not been evident. Since this reaction proceeds under mild conditions and **2** is formed gently, it also may be possible to control the regioselectivity or the stereoselectivity in the cycloaddition of nitrile oxides more easily.

## References

[1] Pasinszki T, Westwood NPC. J. Chem. Soc., Chem. Commun. 1995;1901-1902.
[2] Maier VG, Teles J H. Angew. Chem. 1987;99:152-153.
[3] Kozikowski AP, Adamczyk M. J. Org. Chem. 1983;48:366-372.
[4] Kaji E, Harada K, Zen S. Chem. Pharm. Bull. 1978;26:3254-3256.
[5] Basel Y, Hassner A. Synthesis 1997;309-312.
[6] Easton CJ, Hughes CMM, Savage GP, Simpson GW. Adv. Heterocycl. Chem. 1996;60:261-327.
[7] Torssell KBG. Nitrile oxides, nitrones, and nitronates in organic synthesis. New York: VCH Publishers, 1988:55-74.
[8] Ariga M, Tohda Y, Nakashima H, Tani K, Mori Y, Matsumura E. Bull. Chem. Soc. Jpn. 1991;64:3544-3547.
[9] Nishiwaki N, Takada Y, Inoue Y, Tohda Y, Ariga M. J. Heterocycl. Chem. 1995;32:473-475.
[10] Higashida S, Nakashima H, Tohda Y, Tani K, Nishiwaki N, Ariga M. Heterocycles 1992;34:1511-1514.