

1,3-DIPOLAR CYCLOADDITION OF NITRILE OXIDES TO CHLOROSULFONYL ISOCYANATE:

SELECTIVE FORMATION OF 3-ARYL SUBSTITUTED 1,2,4-OXADIAZOLIN-5-ONES[†]Kakulapati Rama Rao, Tiruchirapally Natesan Srinivasan, and Prahlad Balvantrao Sattur^{*}

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Abstract - Aryl substituted nitrile oxides add in a selective way to C=N of chlorosulfonyl isocyanate to afford 3-Aryl-substituted 1,2,4-oxadiazolin-5-ones after hydrolysis.

1,3-Dipolar cycloaddition reaction of diarylnitrilimines with the highly reactive heterocumulene, chlorosulfonyl isocyanate (CSI, $O=C=N-SO_2Cl$), involves both C=O and C=N of the isocyanate leading to the formation of different products depending upon the substitution and reaction conditions¹. Since the nitrile oxides as typical 1,3-dipoles undergo a wide range of cycloaddition reactions to unsaturated compounds giving a variety of heterocyclic systems^{2,3}, it is considered of interest to investigate the reaction of nitrile oxides with chlorosulfonyl isocyanate to study the dipolarophilic activity of CSI.

In the present investigation, it is observed that the reaction of various aryl substituted nitrile oxides (I) with CSI (II) is highly selective. It involves the 1,3-dipolar cycloaddition of nitrile oxide ($-C\equiv\overset{+}{N}-\overset{-}{O}$) to C=N of CSI to give unstable cycloadduct (III) which upon hydrolysis gives 3-aryl-substituted 1,2,4-oxadiazolin-5-ones (IV) in yields ranging from 60-70% (Scheme 1).

Arylnitrile oxides are prepared from the corresponding oximes⁴. The nitrile oxide is dissolved in chloroform and reacted with chlorosulfonyl isocyanate at 0-5°C. The resultant product is hydrolysed and chromatographed on silica gel to get the pure cycloadduct (IV). All the compounds are confirmed by ir, nmr, mass and accurate mass measurement data. These compounds are shown in Table 1.

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It is seen from these reactions that nitrile oxides add in a selective way at C=N of chlorosulfonyl isocyanate giving 3-aryl-1,2,4-oxadiazolin-5-ones (IV) after hydrolysis. This difference in the reactivity of nitrile oxides and nitrilimines towards CSI may be interpreted on the basis of higher electrophilicity of nitrile oxides and increased nucleophilicity of nitrilimines⁵.

Thus, this reaction opens up a new and facile way for the synthesis of potential biologically useful compounds utilising the selectivity in the dipolarophilic character of chlorosulfonyl isocyanate.

SCHEME 1

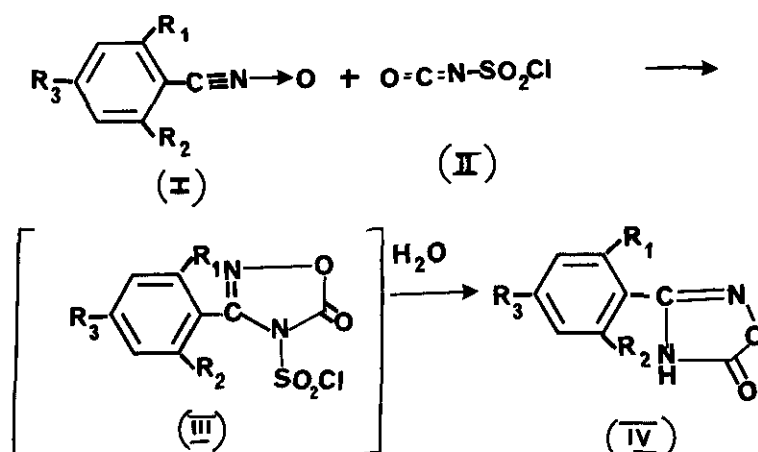


TABLE 1

No.	Product (IV)			Yield (%)	mp °C	Molecular formula (Accurate mass)
	R ₁	R ₂	R ₃			
1	Cl	Cl	H	64	172-174	C ₈ H ₄ N ₂ O ₂ Cl ₂ (230.0521)
2	OCH ₃	OCH ₃	OCH ₃	72	204-206	C ₁₁ H ₁₂ N ₂ O ₅ (252.0744)
3	CH ₃	CH ₃	CH ₃	68	185-187	C ₁₁ H ₁₂ N ₂ O ₂ (204.1054)

EXPERIMENTAL

Accurate mass measurements were carried out with VG Micromass 70-70H mass spectrometer at a resolution of 5000 with PFK as reference using the VG data system. PMR spectra were recorded on JEOL FT FX-900 spectrometer.

Aryl nitrile oxides were prepared from the corresponding oximes by sodium hypobromite oxidation as described by Grundmann and Dean⁴.

TYPICAL REACTION PROCEDURE

2,4,6-Trimethyl benzonitrile oxide (3.0 g, 18.6 mmol) was dissolved in chloroform (60 ml), cooled to 0-5°C and chlorosulfonyl isocyanate (2.64 g, 18.6 mmol) in chloroform (20 ml) was added dropwise over a period of 15 min. stirred at that temperature for 1 h and at room temperature for 10 h⁶. Then the solvent was removed under reduced pressure, ice water was added and left overnight. It was filtered and chromatographed on silica gel using chloroform followed by mixtures of chloroform and methanol as eluent. 3-(2,4,6-Trimethylphenyl)-1,2,4-oxadiazolin-5-one obtained was recrystallized from chloroform-ether.

REFERENCES AND NOTES

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- 6 Higher temperatures have no significant effect upon the yield.

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