A Facile 1,3-Dipolar Cycloaddition of Nitrile Oxides to Chlorocarbonyl Isocyanate: Synthesis of 4-Chlorocarbonyl-5-oxo-4,5-dihydro-1,2,4-oxadiazoles[1]

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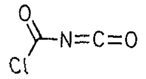
The 1,3-dipolar cycloaddition of substituted benzonitrile oxides to the C=N group of chlorocarbonyl isocyanate in chloroform gives potentially useful 3-aryl-4-chlorocarbonyl-5-oxo-4,5-dihydro-1,2,4-oxadiazoles in 75–80% yields.

Chlorocarbonyl isocyanate (**1**) has been extensively employed in the synthesis of heterocycles by a variety of cyclization reactions.[2–5] However, only few cycloaddition reactions[6,7] have been documented. The ability of the related chlorosulfonyl isocyanate (**2**) to undergo cycloadditions even with poorly polar double bonds has not been observed with chlorocarbonyl isocyanate. This contrasting behavior of chlorocarbonyl isocyanate led us to study its dipolarophilic activity in various cycloaddition reactions.

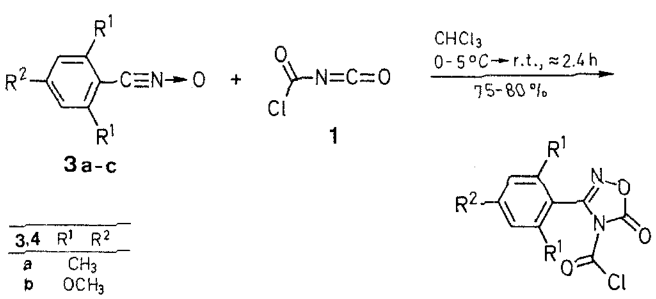


1

$ClSO_2-N=C=O$

2

In continuation of our work on dipolar cycloaddition reactions of nitrile oxides[8] and on new synthetic applications of chlorocarbonyl isocyanate,[9] we investigated the use of the latter compound as a dipolarophile in 1,3-dipolar cycloaddition reactions with nitrile oxides **3**. We have found that this cycloaddition is highly selective, involving only the C=N group of chlorocarbonyl isocyanate (**1**) and affording exclusively the potentially biologically active 3-substituted 4-chlorocarbonyl-5-oxo-4,5-dihydro-1,2,4-oxadiazoles **4** in good yields.



3a-c **1** **4a-c**

3,4	R^1	R^2
a	CH_3	
b	OCH_3	
c	Cl	H

This is the first report on the synthesis of a 1,2,4-oxadiazole derivative with a chlorocarbonyl function on nitrogen which can be further utilized for the synthesis of functionalized oxadiazoles.

The benzonitrile oxides **3** are prepared from the corresponding oximes.[10] They are submitted to the reaction with chlorocarbonyl isocyanate (**1**) in chloroform at 0-5°C. The structure of the resultant products **4** was confirmed by microanalysis, mass spectral data, and the presence of two C=O absorption bands at ν = 1810 and 1720 cm^{-1} in the IR spectra (Table).

Table. 3-Aryl-4-chlorocarbonyl-5-oxo-4,5-dihydro-1,2,4-oxadiazoles **4** Prepared

Product	Yield (%)	mp (°C)[a]	Molecular Formula[b]	IR (KBr)[c] $\nu_{C=O}$ (cm^{-1})	^{1}H-NMR[d] (DMSO-d_6/TMS) δ
4a	75	232-233	$C_{12}H_{11}ClN_2O_3$ (266.7)	1810, 1720	6.92 (s, 2H); 2.25 (s, 3H); 2.14 (s, 6H)
4b	80	112-113	$C_{12}H_{11}ClN_2O_6$ (314.7)	1820, 1730	6.32 (s, 2H); 3.81 (s, 3H); 3.74 (s, 6H)
4c	78	250-251	$C_9H_3Cl_3N_2O_3$ (293.5)	1805, 1720	7.30-7.41 (m, 3H)

[a] Uncorrected, measured with a Buchi-510 apparatus.
[b] Satisfactory microanalyses: C ±0.25, H ±0.14, N ±0.12.
[c] Recorded on a Perkin-Elmer Model 283B Infrared spectrophotometer.
[d] Obtained on a JEOL FT FX-900 spectrometer.

4-Chlorocarbonyl-3-(2,4,6-trimethylphenyl)-5-oxo-4,5-dihydro-1,2,4-oxadiazole (4a); Typical Procedure:

2,4,6Trimethylbenzonitrile oxide (**3a**; 3.0 g, 18.6 mmol) is dissolved in $CHCl_3$ (60 mL), this solution is cooled to 0-5°C, and a solution of chlorocarbonyl isocyanate (**1**; 1.96 g, 18.6 mmol) in $CHCl_3$ (20 mL) is added dropwise, with stirring, over a period of 20 min. The mixture is stirred at 0-5°C for 2 h and at room temperature for 10 h. The solvent is then removed under reduced pressure and the residual product is stirred with hexane (30 mL), isolated by suction, dried over Na_2SO_4 in a desiccator, recrystallized from $CHCl_3/Et_2O$ (7:3).

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