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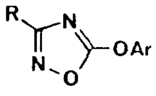
1,3-DIPOLAR CYCLOADDITIONS OF NITRILE OXIDES TO ARYL THIOCYANATES: A NEW SYNTHETIC ROUTE TO 5-ARYLTHIO-1,2,4-OXADIAZOLES

R. Michael Paton* and Douglas G. Hamilton

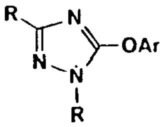
Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ

Summary: Nitrile oxides, generated *in situ* by thermal dehydrochlorination of hydroximoyl chlorides, undergo 1,3-dipolar cycloaddition to aryl thiocyanates yielding 5-arylthio-1,2,4-oxadiazoles.

Aryl cyanates react with 1,3-dipoles such as nitrile oxides[1], nitrile imines[1] and nitrones[2] to afford 5-aryloxy-1,2,4-oxadiazoles (1), 1,2,4-triazoles (2) and Δ^4-1,2,4-oxadiazolines (3), resulting from cycloadditions to the nitrile group. In these cases the C≡N of the cyanate proves to be a more reactive dipolarophile than the corresponding nitriles. In contrast cycloaddition reactions involving thiocyanates have received much less attention, the formation of the triazoloisoquinoline (4) from isoquinolinium N-imide being a rare example[3]. We now report that 5-arylthio-1,2,4-oxadiazoles may be prepared by the reaction of aryl thiocyanates with nitrile oxides.



(1)



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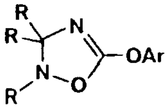

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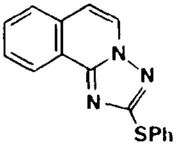
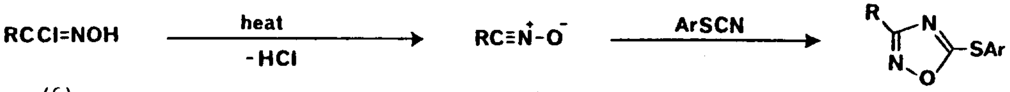


(4)

The nitrile oxides (5) were prepared *in situ* by the thermal dehydrochlorination[4] of the corresponding hydroximoyl chlorides (6). A solution of benzohydroximoyl chloride (6a) (6.0 mmol) and α-naphthyl thiocyanate (6.0 mmol) in xylene (50 ml) was heated under reflux for 16 h. Removal of the solvent and chromatography on silica of the resulting yellow oil yielded 5-(α-naphthylthio)-3-phenyl-1,2,4-oxadiazole (7a) (4.7 mmol, 79%) as a white crystalline solid[5], mp 85°C. 4-Nitrobenzonitrile oxide (5b) behaved similarly; (7b, 75%), (7c, 52%), (7d, 66%) and (7e, 51%) being formed from 6b with α-naphthyl, 4-nitrophenyl, 2,4-dinitrophenyl and 2-chloro-4,6-dinitrophenyl thiocyanates respectively. The reaction of nitrile oxides with thiocyanates thus provides a straightforward synthetic approach to 5-arylthio-1,2,4-oxadiazoles, complementing existing routes to their 5-alkylthio analogues such as the alkylation[6] of either the 5-thiol or the tautomeric Δ^2-1,2,4-oxadiazoline-5-thione.



(6) (5) (7)

(5,6a); R = C_6H_5

(5,6b); R = $4\text{-}O_2NC_6H_4$

(7a); R = C_6H_5, Ar = $\alpha\text{-}C_{10}H_7$

(7b); R = $4\text{-}O_2NC_6H_4$, Ar = $\alpha\text{-}C_{10}H_7$

(7c); R = Ar = $4\text{-}O_2NC_6H_4$

(7d); R = $4\text{-}O_2NC_6H_4$, Ar = $2,4\text{-}(O_2N)_2C_6H_3$

(7e); R = $4\text{-}O_2NC_6H_4$, Ar = $2\text{-}Cl\text{-}4,6\text{-}(O_2N)_2C_6H_2$

The behaviour of thiocyanates towards nitrile oxides closely paralles that of cyanates[1], suggesting that they may provide *via* their reactions with 1,3-dipoles easy access to a range of arylthio-substituted 5-membered heterocycles.

References and Footnotes

1. D. Martin and A. Weise, Chem. Ber., 99, 317 (1966).
2. E. Grigat, R. Pütter and E. Mühlbauer, Chem. Ber., 98, 3777 (1965).
3. R. Huisgen, R. Grashey and R. Krischke, Leibigs Ann. Chem., 1977, 506.
4. T. Sasaki and T. Yoshioka, Bull. Chem. Soc. Japan, 40, 2604 (1967).
5. Found: C, 70.8; H, 4.1; N, 9.2. $C_{18}H_{12}N_2OS$ requires C, 71.0; H, 4.0; N, 9.2%. δ_C ($CDCl_3$) 176.2 (C-5), 168.8 (C-3), 134.1, 128.5, 126.2, 122.3 (ArC), 135.7, 134.2, 131.9, 131.0, 128.5, 127.7, 127.2, 126.6, 125.5, 125.0 (12 ArCH).
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