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ALTERNATIVE MODES OF 1,3-DIPOLAR CYCLOADDITION OF NITRONES TO ARYLISOTHIOCYANATES

D. St.C. Black and K. G. Watson

Department of Chemistry, Monash University, Clayton, Victoria 3168, Australia

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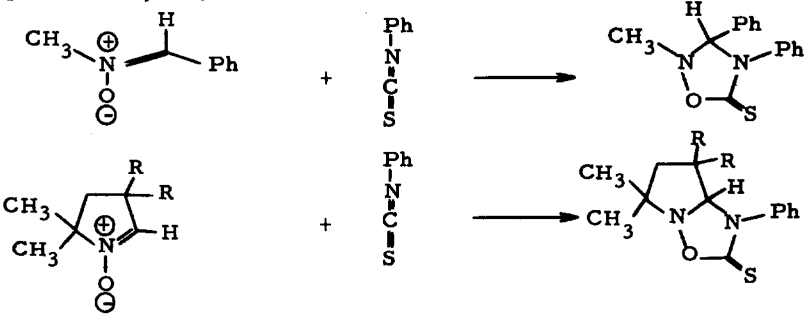
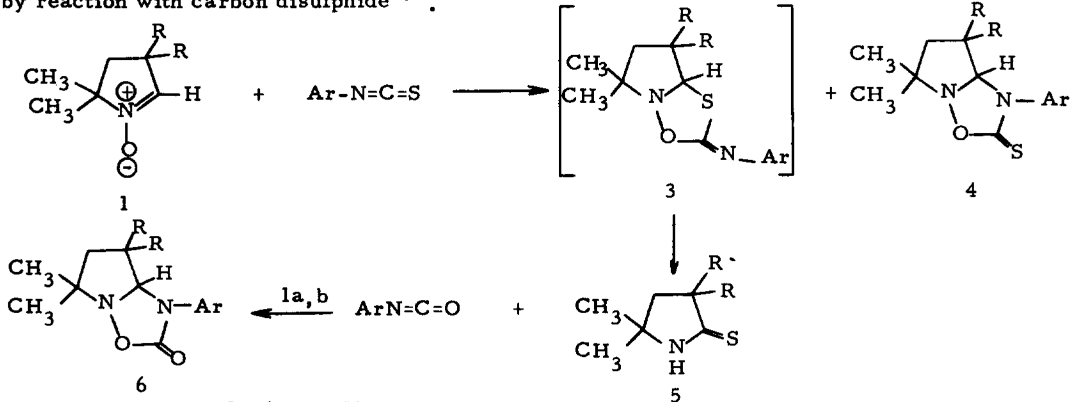
Isothiocyanates readily undergo cycloaddition to several 1,3-dipoles[1], and the reaction is known to occur exclusively across either of the heterocumulene double bonds depending upon the particular 1,3-dipole under consideration[2]. From the reaction of N-methyl-C-phenylnitrone with phenylisothiocyanate, Huisgen and co-workers[3] isolated only the adduct arising from addition to the C=N bond. Similarly our experiments show that the cyclic nitrones[4] (1a,b) also add exclusively across the C=N bond of phenylisothiocyanate to yield the adducts (2a,b) in virtually quantitative yield.



(1a) : R=H
(1b) : R=CH_3

(2a) : R=H
(2b) : R=CH_3

However, in reactions with substituted phenylisothiocyanates, the dimethylnitrone (1a) displays almost equal reactivity towards the two heterocumulene double bonds while the tetramethylnitrone (1b) undergoes addition only to the C=S bond. When the nitrones (1a,b) were treated with a range of substituted phenylisothiocyanates, the proton magnetic resonance (p.m.r.) and infrared spectra of the reaction mixtures and products all showed the formation of considerable amounts of the thiolactams (5a, b)[5]. These thiolactams (5a, b) presumably arise from addition of the nitrones to the C=S bond of the isothiocyanates, followed by the rearrangement of the resulting adducts (3a, b). This process is related to the conversion of nitrones to thioamides by reaction with carbon disulphide[5,6].



1a-6a : R=H
1b-6b : R=CH_3

The rearrangement of the adducts (3a, b) would also result in the formation of arylisocyanates, which are generally more reactive than the corresponding isothiocyanates. Consequently, the thiolactams (5a, b) are accompanied by the isocyanate adducts (6a, b), resulting from almost exclusive addition to the isocyanate C=N bond[2].

When the p.m.r. spectra of reaction mixtures showed no remaining nitrone (2 to 24hr) the percentages of thiolactams and adducts were estimated from peak areas in the spectra. For the nitrone (1a), percentages of the thiolactam (5a) and total adducts (4a + 6a) are shown in Table I. In a few cases adducts of either type were isolated. For the nitrone (1b), no isothiocyanate adducts (4b) were observed, and percentages of the thiolactam (5b) and isocyanate adducts (6b) are shown in Table II.

To some extent it is possible to explain the direction of dipolar addition to arylisothiocyanates in terms of the electronic disturbance brought to the phenyl ring by the various substituents. Thus, the resonance structures for both electron donating and electron withdrawing substituents indicate that both types of substituent cause a reduction of the C=N bond

TABLE I

Cycloaddition of arylisothiocyanates to 5,5-dimethyl-1-pyrroline 1-oxide (1a)

Ar-N=C=S Ar=	Estimated percentage composition (p.m.r.)		Percentage yields of isolated adducts	
	5a	4a + 6a	4a	6a
2,4-Dichlorophenyl-	5	95		
1-Naphthyl-	5	95		80
4-Fluorophenyl-	23	77		68
3-Nitrophenyl-	26	74		
4-Nitrophenyl-	33	67		
4-Carbethoxyphenyl-	34	66	22	
4-Ethoxyphenyl-	44	56		
4-Chlorophenyl-	45	55		
4-Methylphenyl-	45	55		
2,6-Dimethylphenyl-	50	50		
2-Nitrophenyl-	52	48		

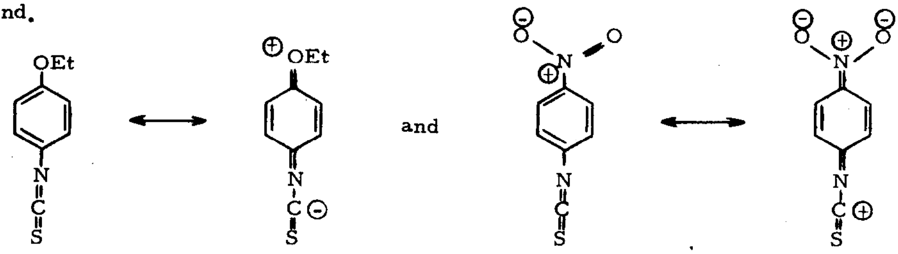
TABLE II

Cycloaddition of arylisothiocyanates to 3,3,5,5-tetramethyl-1-pyrroline 1-oxide (1b)

Ar-N=C=S Ar=	Estimated percentage composition (p.m.r.)		Percentage yields of isolated products	
	5b	6b	5b	6b
2,4-Dichlorophenyl-	69	31	40	
1-Naphthyl-	76	24	65	
4-Fluorophenyl-	74	26		
3-Nitrophenyl-	54	46		
4-Nitrophenyl-	72	28	62	20
4-Carbethoxyphenyl-	75	25	55	20
4-Ethoxyphenyl-	80	20	39	
4-Chlorophenyl-	75	25		14
4-Methylphenyl-	78	22	63	
2,6-Dimethylphenyl-	83	17	46	
2-Nitrophenyl-	84	16	80	

order relative to the C=S bond order of the isothiocyanate. This acts in favour of addition to the C=S bond.

e.g.



Steric factors can also be important in directing cycloaddition across the C=S bond. This is demonstrated for the tetramethyl nitrone (1b), the reactions of which show a marked preference for addition to the C=S bond of all aryl isothiocyanates other than phenylisothiocyanate.

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