Nitrile Sulphide Formation from the Thermal Fragmentation of 1,3,4-Oxathiazoles: a Retro-1,3-dipolar Cycloaddition

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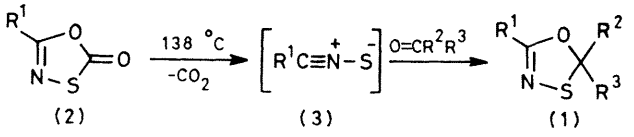
Summary 1,3,4-Oxathiazoles, on thermolysis, undergo retro-1,3-dipolar cycloaddition to afford carbonyl compounds and nitrile sulphides, which may be trapped by cycloaddition with alkynes and nitriles

1,3,4-OXATHIAZOLES (**1**) have recently been synthesised[1] by heating 1,3,4-oxathiazol-2-ones (**2**) in the presence of aldehydes and ketones possessing electron-withdrawing substituents, the reaction being assumed to proceed *via* the initial decarboxylation of (**2**) to the nitrile sulphide (**3**), which subsequently undergoes 1,3-dipolar cycloaddition to the carbonyl group



(2) (3) (1)

We now report that (**1**) are themselves thermally labile and, on more vigorous heating, fragment to regenerate the nitrile sulphides and carbonyl compounds *via* a retro-1,3-dipolar cycloaddition reaction Heating (**1a**) in mesitylene under reflux for 1 h resulted in its complete disappearance and the formation of the corresponding nitrile (**4a**) (98%), sulphur, and hexachloroacetone (99%) Repeating the thermolysis in the presence of the established[2] dipolarophile dimethyl acetylenedicarboxylate (DMAD) [10 mol per mol of (**1a**)] afforded the isothiazole 1,3-dipolar cycloadduct (**5a**) (87%), together with (**4a**) (8%), sulphur, and hexachloroacetone (99%), strongly indicating the involvement of a nitrile sulphide intermediate Further evidence was provided when ethyl cyanoformate (ECF) yielded the cycloadduct (**6a**) (92%), other oxathiazoles exhibited similar behaviour (see Table)

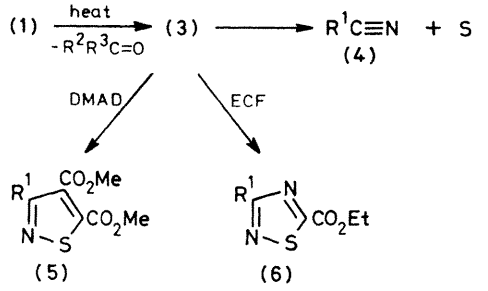
The oxathiazoles prove to be similar in many ways to the oxathiazolones as sources of nitrile sulphides For example, nitriles are formed as by-products owing to the fragmentation of (**3**) competing with the cycloaddition (Scheme 1), the balance between the two processes being dependent[3] on the electronic nature of R^1 Likewise, the rate of oxathiazole disappearance is greater for electron-donating than for electron-withdrawing substituents [2] There are, however, significant differences in stability within the oxathiazole series, with reaction times increasing as the ketone fra ment varies from hexachloroacetone through trifluoroacetophenone to chloral

The variety of nitrile sulphide sources provided by the series of 5-(*p*-methoxyphenyl)oxathiazoles (**1a**—**c**) and the corresponding oxathiazolone (**2a**) presented an opportunity to test for any variation in regioselectivity in the cycloaddition reactions, and thereby establish if the cycloadducts were being formed *via* a free nitrile sulphide intermediate or by direct interaction of the precursor with the dipolarophile Accordingly (**1a**—**c**) and (**2a**) were heated in mesitylene at 160 °C in the presence of ethyl propiolate (EP) [10 mol per mol of (**1**) or (**2**)] and the

TABLE. Products and reaction conditions for the thermolyses of 1,3,4-oxathiazoles (**1**) at 161 ± 1 °C in the presence of dipolarophiles.

Oxathiazole	Dipolarophile	Reaction time/h	Cycloadduct (%)[a]	Nitrile (%)[a]
(**1a**)	DMAD	0·8	(**5a**) (88)	(**4a**) (8)
	ECF	1	(**6a**) (92)	—[b]
	EP	1	(**7**) (47)	(**4a**) (16)
			(**8**) (35)	
(**1b**)	DMAD	4	(**5a**) (80)	(**4a**) (12)
	EP	4	(**7**) (44)	(**4a**) (23)
			(**8**) (33)	
(**1c**)	DMAD	18	(**5a**) (60)	(**4a**) (33)
	EP	19	(**7**) (17)	(**4a**) (68)
			(**8**) (13)	
(**1d**)	DMAD	2	(**5b**) (64)	—[b]
(**1e**)	DMAD	22	(**5b**) (52)	—[b]
	ECF	26	(**6b**) (75)	—[b]
(**1f**)	DMAD	2·8	(**5c**) (69)	—[b]
	ECF	3	(**6c**) (70)	—[b]
(**1g**)	DMAD	0·6	(**5d**) (92)	—[b]
(**1h**)	DMAD	10·5	(**5d**) (34)	—[b]

[a] Yields measured by h.p.l.c. [b] Not determined.

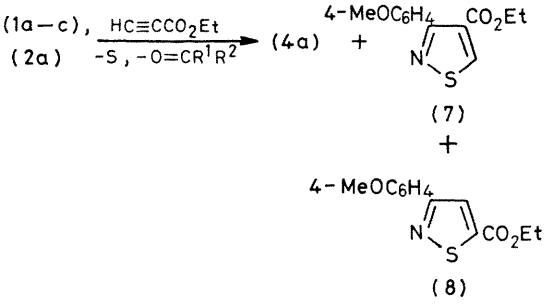


(**1**)**a**; $R^1 = 4\text{-MeOC}_6H_4$, $R^2 = R^3 = CCl_3$
b; $R^1 = 4\text{-MeOC}_6H_4$, $R^2 = CF_3$, $R^3 = Ph$
c; $R^1 = 4\text{-MeOC}_6H_4$, $R^2 = CCl_3$, $R^3 = H$
d; $R^1 = Ph$, $R^2 = R^3 = CCl_3$
e; $R^1 = Ph$, $R^2 = CCl_3$, $R^3 = H$
f; $R^1 = 4\text{-ClC}_6H_4$, $R^2 = R^3 = CCl_3$
g; $R^1 = Me$, $R^2 = R^3 = CCl_3$
h; $R^1 = Me$, $R^2 = CCl_3$, $R^3 = H$

(**2**—**6**)**a**; $R^1 = 4\text{-MeOC}_6H_4$
b; $R^1 = Ph$
c; $R^1 = 4\text{-ClC}_6H_4$
d; $R^1 = Me$

SCHEME 1. DMAD = dimethyl acetylenedicarboxylate, ECF = ethyl cyanoformate.

products analysed by h.p.l.c. (Scheme 2). From (**2a**) the ratio of the resulting isomeric isothiazoles (**7**) and (**8**) was found to be 1·32, while the corresponding values from (**1a**—**c**) were 1·34, 1·33, and 1·31, respectively (Table); this constant regioselectivity is consistent with cycloadduct formation *via* a free nitrile sulphide and supports the conclusions drawn from recent kinetic studies.[2] However, the yield of the by-product (**4a**) increased from 12% from (**2a**) to 63% from (**1c**). This variation is not consistent with straightforward cleavage of the precursor and



SCHEME 2.

subsequent competition between the fragmentation and cycloaddition reactions of (**3a**), because such a scheme requires the nitrile yield to be independent of the source of the nitrile sulphide. The possibility that there exists an alternative pathway to the nitrile cannot be discounted and is currently under investigation.

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[1] R. M. Paton, J. F. Ross, and J. Crosby, *J. Chem. Soc., Chem. Commun.*, 1979, 1146.
[2] R. K. Howe, T. A. Gruner, L. G. Carter, L. L. Black, and J. E. Franz, *J. Org. Chem.*, 1978, **43**, 3736.
[3] R. K. Howe and J. E. Franz, *J. Org. Chem.*, 1974, **39**, 962.