Reaction of 1,3-Dithiane Anions with Nitriles: Generation of Primary Aminoketene Thioacetals

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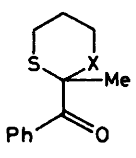
The anions derived from 1,3-dithiane and 2-trimethylsilyl-1,3-dithiane react with simple nitriles to provide primary aminoketene thioacetals.

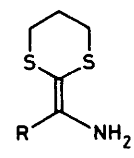
The chemistry of the anions derived from 1,3-dithiane and 1,3-oxathiane has been extensively studied and reviewed,[1] particularly with regard to the use of these materials as acyl anion equivalents. However, although the corresponding 2-trimethylsilyl derivatives have found application in ketene thioacetal generation[2] they have generally received much less attention.

In 1983 Fuji reported that the anion derived from 2-trimethylsilyl-1,3-oxathiane reacted with benzonitrile to provide an anionic species which further reacted with methyl iodide to give the carbon-quenched material (**1**), X = O, and other products, in poor yield.[3]

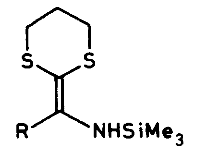
In these laboratories we have shown that 2-lithio-2-



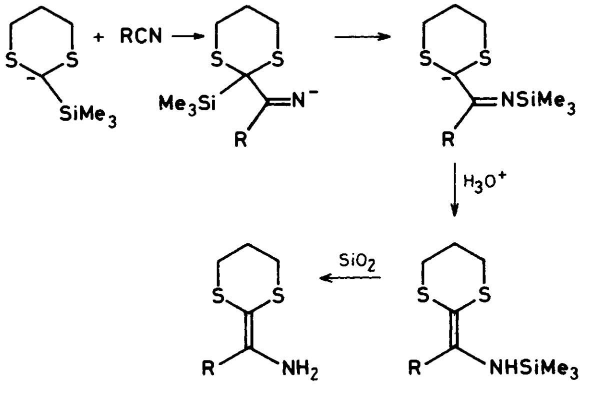
(1)



(2)

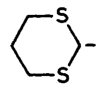
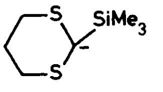
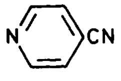
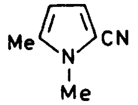
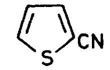
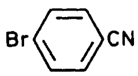


(3)



Scheme 1

Table 1. % Yields of primary aminoketene thioacetals derived from reactions of nitriles RCN with dithiane anions.[a]

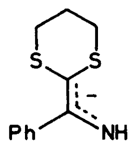
RCN		
PhCN	90	67
	81	78
	69	61
	66	96
	65	27
	60	48
Me_3CCN [b]	55	40

[a] All new compounds were characterised spectroscopically and/or by elemental analysis. [b] Product exists in tautomeric equilibrium with imine (7).

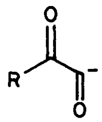
trimethylsilyl-1,3-dithiane reacts at low temperature with simple nitriles cleanly to provide primary aminoketene thioacetals (**2**) in reasonable yields after aqueous work-up and chromatography (Table 1).

The reaction may proceed *via* an inter- or intra-molecular shift of the silicon moiety[3,4] (Scheme 1), and indeed the *N*-silylated materials (**3**) can be isolated from the reaction mixture if acidic conditions are avoided.

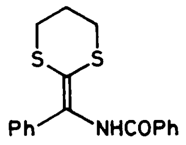
An unexpected[5] further discovery is that the silicon atom is quite unnecessary in this procedure. The parent 2-lithio-1,3-dithiane undergoes similar reactions, with substantially improved yields, presumably *via* an analogous proton transfer (Table 1).



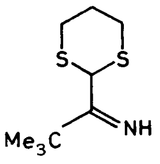
(**4**)



(**5**)



(**6**)



(**7**)

Lithiodithianes were generated from the corresponding dithianes and n-butyl-lithium at −40 °C and added to the nitriles at −78 °C using tetrahydrofuran as solvent. Reactions were allowed to reach room temperature, and then quenched with saturated aqueous ammonium chloride solution. Normal work-up and silica gel chromatography (Merck 9385) gave the primary aminoketene thioacetals, usually as crystalline solids.

Primary aminoketene thioacetals are stable materials which may be stored indefinitely. They exhibit the expected ambident nucleophilicity. Hence, treatment of (**2**), R = Ph, with n-butyl-lithium at −78 °C produces anion (**4**) which reacts with methyl iodide at the carbon atom to give (**1**), X = S, upon hydrolytic work-up. This behaviour is interesting as it provides an example of an α-ketoacyl anion equivalent (**5**).[3]

In contrast, acylation of compound (**2**), R = Ph, with benzoyl chloride occurs at the nitrogen atom to yield the corresponding amide (**6**).

This pattern of reactivity appears to be of considerable potential in heterocyclic synthesis.

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