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Nitroenamines. Part 9[1]. The enaminic reactivity of 2-nitromethylenethiazolidine[2]

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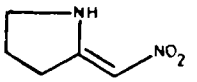
Abstract. 2-Nitromethylenethiazolidine has been synthesised and found to be a weak enamine. It reacts with acyl isothiocyanates but not with phenyl isothiocyanate. Oxidative cyclization of the acyl isothiocyanate adducts leads to isothiazolo [3,2-b] thiazole derivatives. The 2-benzoylimino compound 8 undergoes base catalysed fragmentation to give the nitronitrile 9.

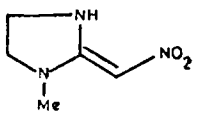
Keywords. Nitroenamine ; enaminic reactivity ; cyanolation ; push-pull ethylene.

1. Introduction

In the past, we have compared the nucleophilic reactivity of cyclic nitrovinylamines such as 1 and nitroketeneaminals such as 2 (Rajappa 1981). The latter were found to be more reactive than the former towards electrophiles. We wanted to extend our investigation to 2-nitromethylenethiazolidine 3 to find out if the sulfur lone-pairs would effectively conjugate with the nitrovinyl system.



(1)



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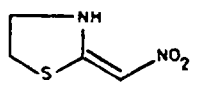

(3)

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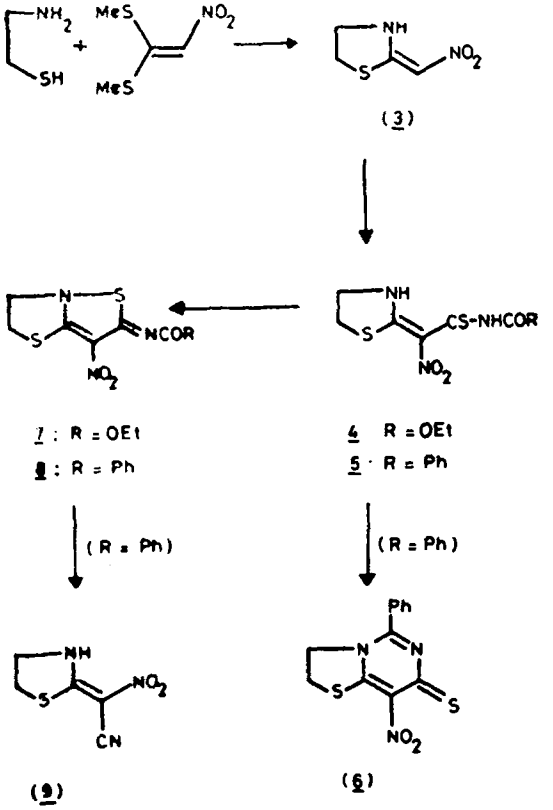
[1] Part 8. Rajappa and Sreenivasan 1979.

[2] Contribution No. 672 from CIBA-GEIGY Research Centre.

Scheme 1



2. Results and discussion

2-Nitromethylenethiazolidine (3) has been synthesised earlier from 2-methylthiazoline by nitration with *n*-propyl nitrate in liquid ammonia in presence of sodium amide (Feuer and Lawrence 1972). We have now prepared the compound by the action of cysteamine on 1,1-bis (methyl-mercapto)-2-nitroethylene (scheme 1).

We had earlier concluded that isothiocyanates constituted ideal probes to delineate the enaminic reactivity of nitroenamines. Accordingly, we set out to map the reactivity of 3 towards various isothiocyanates. The compound was recovered unreacted after refluxing for 16 hr with phenyl isothiocyanate in acetonitrile solution. However, the more reactive acyl isothiocyanates formed adducts with 3. Thus carbethoxy isothiocyanate gave the adduct 4, while benzoyl isothiocyanate gave 5. Although these adducts could not be obtained in crystalline form, their subsequent reactions left no doubt as to their identity. It turns out thus that in its enaminic reactivity, 2-nitromethylene thiazolidine 3 resembles the nitrovinylamine 1 rather than the nitroketeneaminal 2.

Acyl isothiocyanate adducts of nitroenamines have served as useful starting materials for other types of nitro derivatives (Rajappa 1977). We have subjected

the products derived from 2-nitromethylenethiazolidine also to some of these transformations. For instance, the adduct 5 can be easily cyclized to 4-nitro-1-phenyl-6,7-dihydro-3H-thiazolo [3, 2-c] pyrimidine-3-thione (6) ; in fact, this conversion takes place even during the work-up of (5). Both (4) and (5) could be oxidized by bromine to produce the 2-acylimino-3-nitro-5, 6-dihydro-2H-isothiazolo [3,2-b] thiazoles (7) and (8) respectively ; in this reaction, a bond is created between the ring nitrogen and the sulfur atom of the thiocarbonyl group.

A reaction of special significance to nitroenamine chemistry is the base-catalysed fragmentation of 5-benzoylimino-4-nitroisothiazolines with extrusion of sulfur (Rajappa *et al* 1977). The presence of this moiety in (8) prompted us to examine its behaviour towards sodium ethoxide. It was gratifying to find that the isothiazolo [3, 2-b] thiazole (8) also undergoes this characteristic fragmentation reaction, leading to 2-(α-cyano- α-nitro) methylenethiazolidine (9) in 19% yield. The net result of the three step sequence comprising of adduct formation (5), oxidative cyclization (8) and fragmentation is thus the " cyanolation " of 2-nitromethylene-thiazolidine ; This is equivalent to reaction of enamine with CN^+. The product (9) is a novel push–pull ethylene.

3. Experimental

Melting points are uncorrected. Mass spectra were recorded on a Varian Mat CH 7 instrument at 70 eV utilizing direct insertion.

3.1. *Synthesis of 2-nitromethylene thiazolidine* (3)

A suspension of 1,1-bis (methylmercapto)-2-nitroethylene (16 g) in ethanol (180 ml) was stirred under nitrogen with cysteamine (10 g) for 18 hr at 30°C and then left for 2 days. The solid was filtered and extracted with boiling isopropanol. The insoluble residue was discarded. The product (3) crystallized from isopropanol ; yield 6 g, m.p. 141–143°C (Found : C, 32·85 ; H, 4·28 ; N, 18·90. $C_4H_6N_2O_2S$ requires C, 32·88 ; H, 4·14 ; N, 19·18%). MS : 146 (M^+).

3.2. *Reaction of* (3) *with acyl isothiocyanates*

3.2a. *With carbethoxy isothiocyanate* : A solution of 3 (1·5 g) in acetonitrille (25 ml) was treated with carbethoxy isothiocyanate (1·3 g) at 30° and left for 3 hr. The solvent was removed *in vacuo* and the residue dissolved in ethyl acetate. The small amount of insoluble material was discarded and the solution containing (4) used as such for the oxidative cyclization (see below).

3.2b. *With benzoyl isothiocyanate* : A solution of 3 (4·5 g) in acetonitrile (75 ml) was treated with benzoyl isothiocyanate (4·8 g) at 30°, and left for 16 hr. The solvent was removed *in vacuo*, the residue digested with chloroform and filtered. The filtrate containing the adduct (5) was used as such for the oxidative cyclization (see below). The chloroform-insoluble solid was recrystallized from methylene chloride–hexane to give 6, (3 g), m.p. 193–194° (Found : C, 49·70; H, 3·22 ; N, 14·09. $C_{12}H_9N_3O_2S_2$ requires C, 49·47 ; H, 3·12 ; N, 14·43%).

3.3. *Oxidative cyclization of the adducts* 4 *and* 5

The ethyl acetate solution containing the adduct 4 was cooled to 10° and treated dropwise with stirring with bromine (1·4 g) in ethyl acetate (10 ml). After the addition was over, ether was added and the precipitated solid filtered. This was basified with $NaHCO_3$ and the base recrystallized from acetonitrile to give the isothiazolo [3,2-b] thiazole 7 (0·9 g), m.p. 220–221°C (Found : C, 35·31 ; H, 3·46 ; N, 15·25. $C_8H_9N_3O_4S_2$ requires C, 34·92 ; H, 3·30 ; N, 15·27%). MS : 275 (M^+).

The chloroform solution containing the adduct 5 was similarly oxidized with bromine (3·5 g) in chloroform (15 ml). Saturated $NaHCO_3$ solution (100 ml) was added after 15 min, stirred for 30 min, and the solid filtered. Trituration with ethanol gave the isothiazolo [3,2-b] thiazole 8 (2·0 g), m.p. 250–255°. A sample was recrystallized from acetic acid to give the pure 8, m.p. 265–268° (Found : C, 46·86 ; H, 3·16 ; N, 13·48. $C_{12}H_9N_3O_3S_2$ requires C, 46·91 ; H, 2·95 ; N, 13·68%). MS : 307 (M^+).

3.4. 2-(α-*cyano*-α-*nitro*) *methylene thiazolidine* (9)

Sodium ethoxide was prepared by dissolving sodium metal (0·3 g) in absolute ethanol (50 ml). To this solution was added 2-benzoylimino-3-nitro-5,6-dihydro-2H-isothiazolo [3,2-b] thiazole (8) (2·8 g), and the mixture refluxed with stirring for 2 hr. The solvent was then removed *in vacuo*, and the residue dissolved in water and filtered. The filtrate was extracted with ether to remove ethyl benzoate. The aqueous solution was cooled and acidified with acetic acid. The solid, that separated, was filtered and recrystallized from acetonitrile-methanol to give the nitronitrile 9 (0·3 g), m.p. 227–230°C (d), after becoming black at 200°C (Found : C, 34·95 ; H, 3·35 ; N, 24·38. $C_5H_5N_3O_2S$ requires C, 35·09 ; H, 2·95 ; N, 24·56%). IR (nujol) : 2220 cm^{-1} (CN). MS : 171 (M^+).

Acknowledgement

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