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NOVEL CYCLIZATION OF 2-(HYDROXYIMINO)-2-PHENYLETHYL DITHIOCARBOXYLATES

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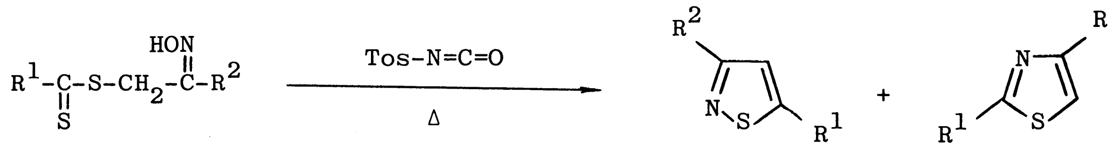
2-(Hydroxyimino)-2-phenylethyl arenedithiocarboxylates were cyclized to isothiazoles by the treatment with tosyl isocyanate.

In the course of our research to develop new synthetic applications of dithiocarboxylic acid derivatives,1) we have been interested in the nucleophilicity of sulfur atom of the thiocarbonyl moiety.2) In this paper, we describe a novel cyclization of 2-(hydroxyimino)-2-phenylethyl arenedithiocarboxylates (1) to form 3,5-diarylisothiazoles (2) by the treatment with tosyl isocyanate.



1 2 3

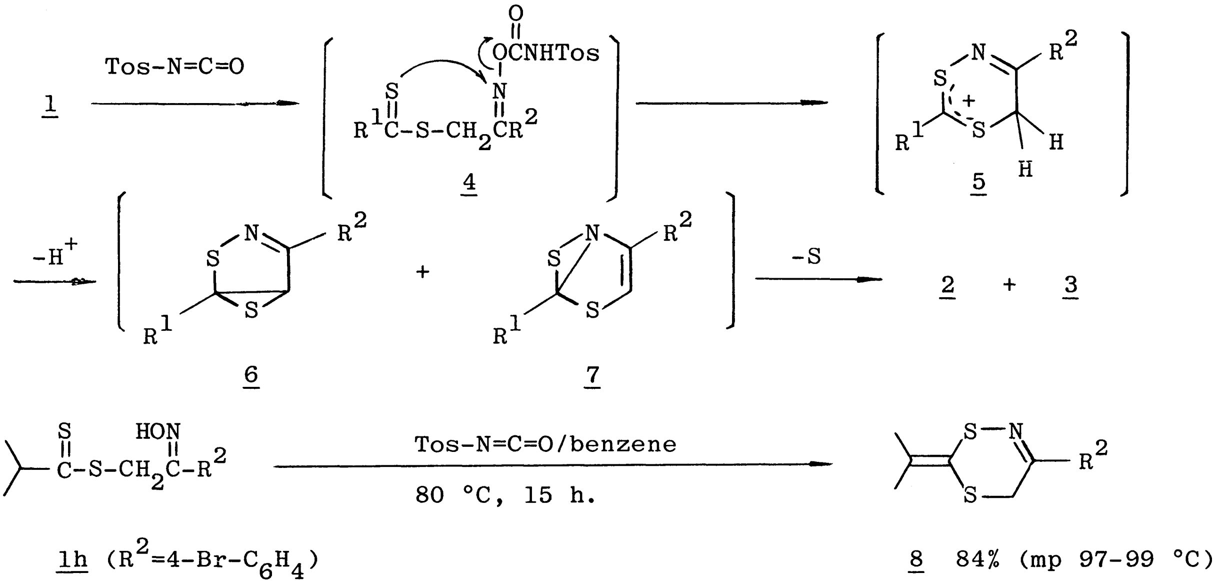
The typical procedure is exemplified by the synthesis of 3,5-diphenylisothiazole (2a). A mixture of the oxime (1a) (0.287 g, 1 mmol)3) and tosyl isocyanate (0.394 g, 2 mmol) in 20 mL of toluene in a sealed tube was heated to 120 °C for 20 h. After evaporation, the residue was chromatographed on silica-gel (benzene as eluant) followed by preparative TLC (Wako-gel BW-5F, CH_2Cl_2/n-hexane=1/1) to give the isothiazole (2a) (0.155 g, 65%; mp 80-81 °C)4) together with a small amount of 2,4-diphenylthiazole (3a) (0.025 g, 11%; mp 91-92 °C). Similar treatment of the oximes (1b-e) yielded the corresponding isothiazoles (2b-e) with small amounts of the thiazoles (3b-d). The alkyl substituted isothiazole, 3-methyl-5-phenylisothiazole (2f), was also obtained in 49% yield by the treatment of 2-(hydroxyimino)propyl dithiobenzoate (1f) with tosyl isocyanate5) (Table 1). In all cases, Beckmann rearrangement products such as amides were not detected.

The reaction seems to proceed as depicted in Scheme 1. At first, the hydroxy group of the oxime (1) reacts with tosyl isocyanate to form the urethane (4). Then, nucleophilic attack of the thiocarbonyl sulfur to nitrogen occurs to give the 6H-1,3,4-thioniathiazine (5). Deprotonation of (5) from C-6 carbon resulted in the formation of the episulfides (6 and 7), which extrude sulfur to yield the isothiazole (2) and the thiazole (3).6) Formation of the 6H-2-isopropylidene-1,3,4-dithiazine (8) from the oxime (1h) also suggests this mechanism.

Application of this ring contraction reaction for the synthesis of other 5-membered hetero aromatics is now in progress.

Table 1.

Oximes 1	R^1	R^2	Product yield/% 2	3
1a	C_6H_5	C_6H_5	65	11
1b	$4\text{-}CH_3\text{-}C_6H_4$	C_6H_5	72	6
1c	$4\text{-}CH_3O\text{-}C_6H_4$	C_6H_5	64	10
1d	$4\text{-}Cl\text{-}C_6H_4$	C_6H_5	73	8
1e	$2\text{-}CH_3\text{-}C_6H_4$	C_6H_5	60	-
1f	C_6H_5	CH_3	49	-
1g	$4\text{-}Cl\text{-}C_6H_4$	CH_3	43	-



Scheme 1.

References

1) S. Kato, S. Yamamoto, K. Ando, K. Itoh, M. Mizuta, and M. Ishida, Z. Naturforsch., B, 36, 739 (1981); M. Ishida, H. Sato, and S. Kato, Synthesis, 1982, 927.

2) M. Ishida, S. Kato, and M. Mizuta, Z. Naturforsch., B, 36, 1047 (1981).

3) The oxime (1a) was prepared from α-chloroacetophenone oxime and piperidinium dithiobenzoate in 86% yield (mixture of geometrical isomers; syn/anti=9/1).

4) M. Maeda and M. Kojima, J. Chem. Soc., Perkin Trans. 1, 1978, 685.

5) The reaction was carried out at 80 °C for 5 h in benzene.

6) Extrusion of sulfur from 1,4,2-dithiazines; E. Fanghaenel, J. Prakt. Chem., 318, 127 (1976).

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