

# Reactions with Hydrazonoyl Halides. Part 15.<sup>1</sup> A Synthetic Approach to 2,3-Dihydrothiadiazoles

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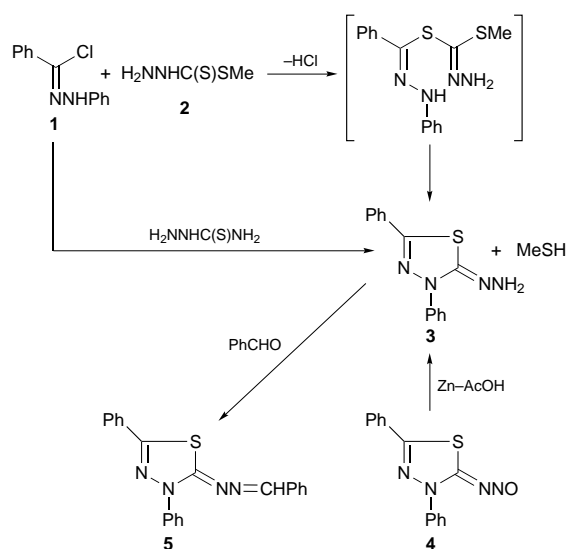
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*J. Chem. Research (S),*  
1998, 12–13  
*J. Chem. Research (M),*  
1998, 0169–0179

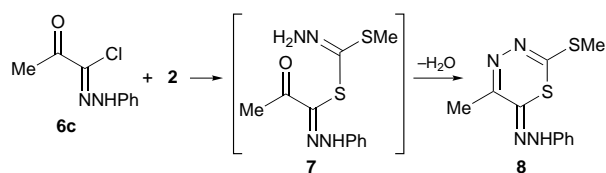
Hydrazonoyl halides **1** and **6a–f** reacted with methyl hydrazinecarbodithioate (**2**) and methyl 3-[1-(aryl)alkylmethylidene]hydrazinecarbodithioates (**9a–d** or **10a,b**), in ethanolic triethylamine solution, to afford the corresponding 2-hydrazono-3,5-diphenyl-2,3-dihydro-1,3,4-thiadiazoles (**3**), 5-methyl-2-methylsulfanyl-6-phenylhydrazono-1,3,4-thiadiazine (**8**) and 2,3-dihydro-1,3,4-thiadiazoles **17–20a–f**, respectively.

It has been reported that dithiocarbazoic acid reacts with haloacetophenones<sup>2</sup> and  $\alpha$ -halo compounds<sup>3</sup> to give 1,3,4-thiadiazines and 2-halomethyl-1,3,4-thiadiazoles, which have been reported to exhibit antiprotozoal,<sup>4</sup> antiviral,<sup>5</sup> bactericidal<sup>6</sup> and fungicidal<sup>7</sup> properties. However, the reaction of hydrazonoyl halides with dithiocarbazoate has not yet been reported.<sup>8</sup> In this paper, we report a study of this reaction.

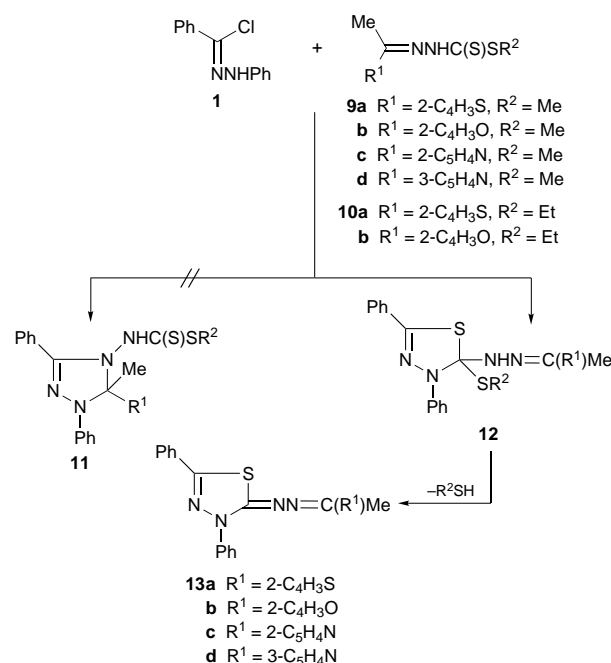
Treatment of *N*-phenylbenzohydrazonoyl chloride (**1**) with methyl hydrazinecarbodithioate (**2**) in ethanolic triethylamine afforded a product which gave analytical and spectral data in accord with its formulation as 2-hydrazono-3,5-diphenyl-2,3-dihydro-1,3,4-thiadiazole (**3**). Compound **3** was authentically obtained by other routes: (a) *via* reaction<sup>9</sup> of **1** with thiosemicarbazide; (b) by reduction of 2-nitrosoimino-3,5-diphenyl-2,3-dihydro-1,3,4-thiadiazole<sup>10</sup> (**4**). Also, **3** reacted with benzaldehyde to give the corresponding hydrazone **5** (see Scheme 1). In contrast to the above results,



1-chloro-2-phenylhydrazonopropan-2-one (**6c**) reacted with **2** to give a product formulated as 5-methyl-2-methylsulfanyl-6-phenylhydrazono-1,3,4-thiadiazine (**8**) according to elemental analysis and spectral data (see Scheme 2).



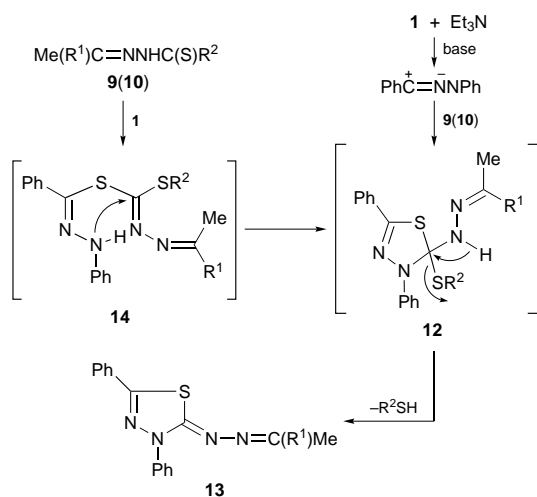
Treatment of *N*-phenylbenzohydrazonoyl chloride (**1**) with methyl 3-[1-(2-thienyl)ethylidene]hydrazinecarbodithioate (**9a**) in ethanolic triethylamine at room temperature gave the 2,3-dihydro-1,3,4-thiadiazole **13a** (see Scheme 3). In contrast, treatment of **1** with ethyl 3-[1-(2-thienyl)ethylidene]hydrazinecarbodithioate (**10a**), at room temperature, produced the same product (**13a**). These results indicate the following facts: (a) structure **12** is not the final product; (b) **13a** is formed *via* loss of methane-(or ethane-)thiol; (c) structure **11** is ruled out (see Scheme 3).



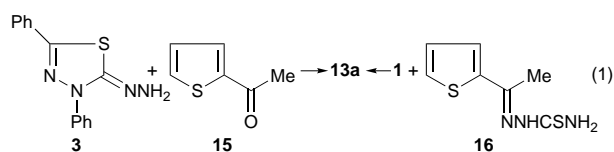
Similarly, compounds **9b–d** reacted with **1** to give 2,3-dihydro-1,3,4-thiadiazole derivatives **13b–d**, respectively. The products **13a–d** are assumed to be formed *via* elimination of alkanethiol from the corresponding cycloadduct **12**, resulting from 1,3-dipolar cycloaddition of nitrile imide to the C=S of the methyl or ethyl dithiocarbazoate [similar to the reaction of hydrazonoyl halides with substituted thiourea<sup>9</sup>] (see Scheme 4). The formation of **13a–d** can also be explained by the reaction of a dithiocarbazoate of general formula **9** (or **10**) with the hydrazonoyl chloride **1**, in the presence of a base such as triethylamine or potassium hydroxide. The corresponding 2,3-dihydro-1,3,4-thiadiazole can be easily obtained through the nucleophilic attack of the thiolate group followed by ring closure and methane-(or ethane-)thiol elimination.

The elimination of the thiole moiety was confirmed by isolation of the same product (**13a**) when using **10a** and **1**, respectively. All attempts to isolate the hydrazone **14** were

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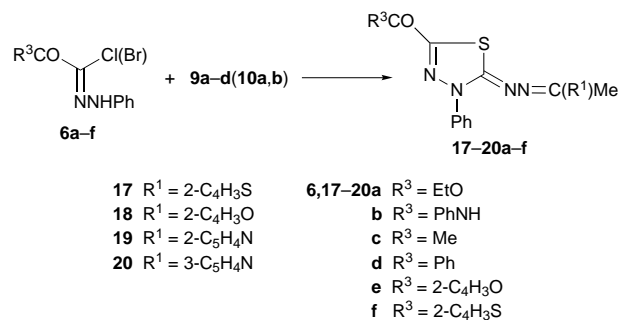


Scheme 4



unsuccessful. Unequivocal support for structure **13** was provided by the preparation of **13a** via two routes. The first involves the reaction of 5-hydrazino-2,4-diphenyl-1,3,4-thiadiazole **3** with 2-acetylthiophene (**15**), in propan-2-ol, the second by the reaction of *N*-phenylbenzohydrazonoyl chloride (**16**), in boiling ethanol. All the products were identical with **13a** [see eqn. (1)].

In order to study the effect of a carbonyl group on the reactivity of the hydrazonoyl halides, the reaction of  $\alpha$ -oxohydrazonoyl halides **6a–f** with **9a–d**, in ethanolic triethylamine at room temperature, was investigated and found to give the corresponding 2,3-thiadiazoles **17–20a–f**. The structures of the products were confirmed by their spectra and alternative synthesis. Thus, the reaction of **10a,b** with **6a,b** in ethanol containing equimolar amounts of triethylamine gave products identical with **17a,b** and **18a,b** respectively (see Scheme 5).



Scheme 5

Techniques used:  $^1\text{H}$  NMR, IR, mass spectrometry

Tables: 2

References: 23

Received, 16th July 1997; Accepted, 19th September 1997  
Paper E/7/05088G

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