

The Reactions of *N,N'*-Diphenyldithiomalonamide with Michael Acceptors [†]

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Abstract: *N,N'*-diphenyldithiomalonamide (dithiomalonidianilide) smoothly reacts with various Michael acceptors to give either stable Michael adducts or products of their further heterocyclization. The structure of the products was confirmed by 2D NMR experiments and X-ray data. The mechanisms of the reactions are discussed.

Keywords: dithiomalonidianilide; heterocyclization; 2-cyanoacrylates; Meldrum's acid; Michael adducts

1. Introduction

N-Substituted thioamides play an important role in the synthesis of nitrogen- and sulfur-containing heterocyclic compounds. They are widely used in organic synthesis to prepare compounds with new, previously unknown core structures. *N,N'*-diphenyl malondithioamide (dithiomalonidianilide) **1** is a promising compound to build new heterocyclic systems, since it has two thioanilide fragments and CH-acidity due to the methylene bridge (Figure 1).

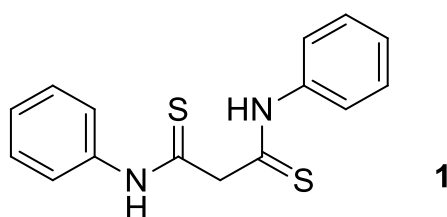
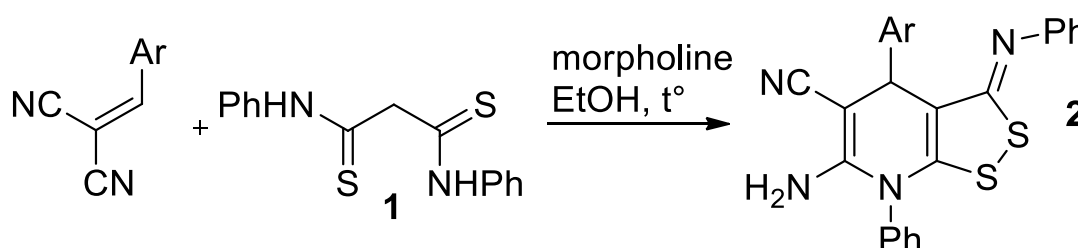


Figure 1. The structure of dithiomalonidianilide.

Earlier, we described the reported the reaction of *N,N'*-diphenyldithiomalonidiamide **1** with arylmethylenemalononitriles [1]. The products of the reaction were [1,2]dithiolo[3,4-*b*]pyridines **2**, as it was shown by means of X-ray analysis (Scheme 1).

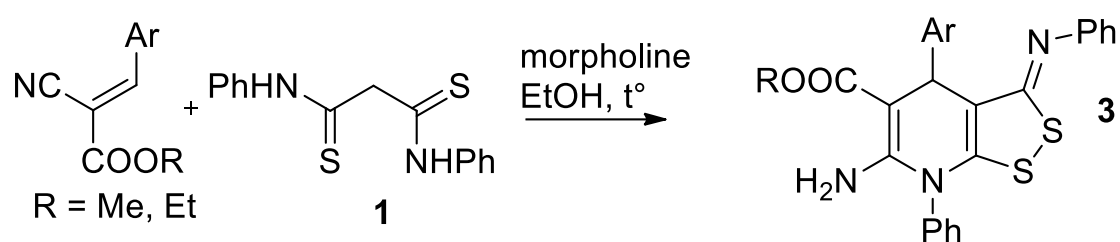


Scheme 1. The reaction of *N,N'*-diphenyldithiomalonamide **1** with arylmethylenemalononitriles.

N,N'-Diphenyldithiomalonamide **1** is an active methylene compound that is rarely used in heterocyclization reactions. In continuation of our studies in this field, we decided to study the reactions of dithioamide **1** with other Michael acceptors.

2. Results and Discussion

We found that the reaction of dithiomalonamide **1** with arylmethylenecyanoacetates proceeds readily in the presence of a basic catalyst and, in the presence of an oxidizing agent (atmospheric oxygen), gives [1,2]dithiolo[3,4-*b*]pyridines **3** in modest yields (Scheme 2). The structure of the obtained compounds was confirmed by a complex of spectral data, including 2D NMR spectroscopy (HSQC, HMBC), as well as X-ray data (Figures 1 and 2).



Scheme 2. The reaction of *N,N'*-diphenyldithiomalonamide **1** with arylmethylenecyanoacetates.

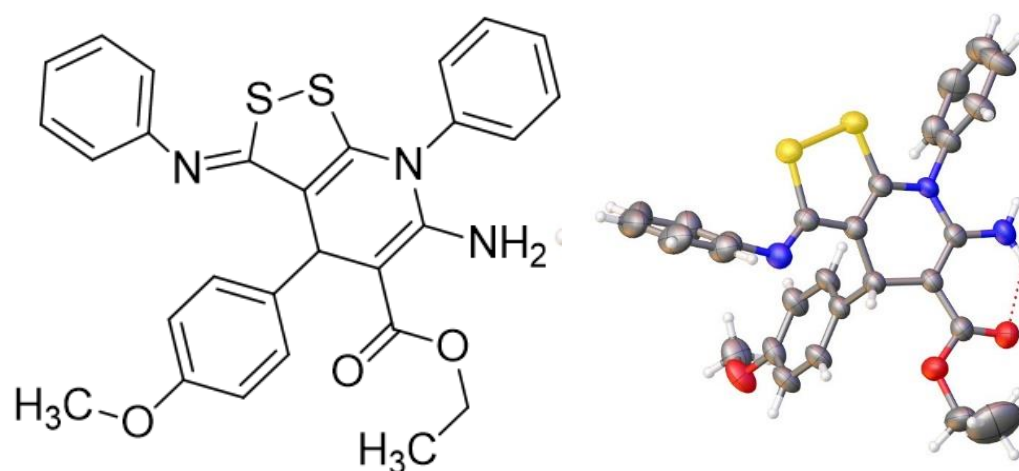


Figure 1. Structure of the reaction product of (4-methoxyphenyl)methylidenecyanoacetic ester and dithiomalonamide **1** (according to X-ray diffraction data).

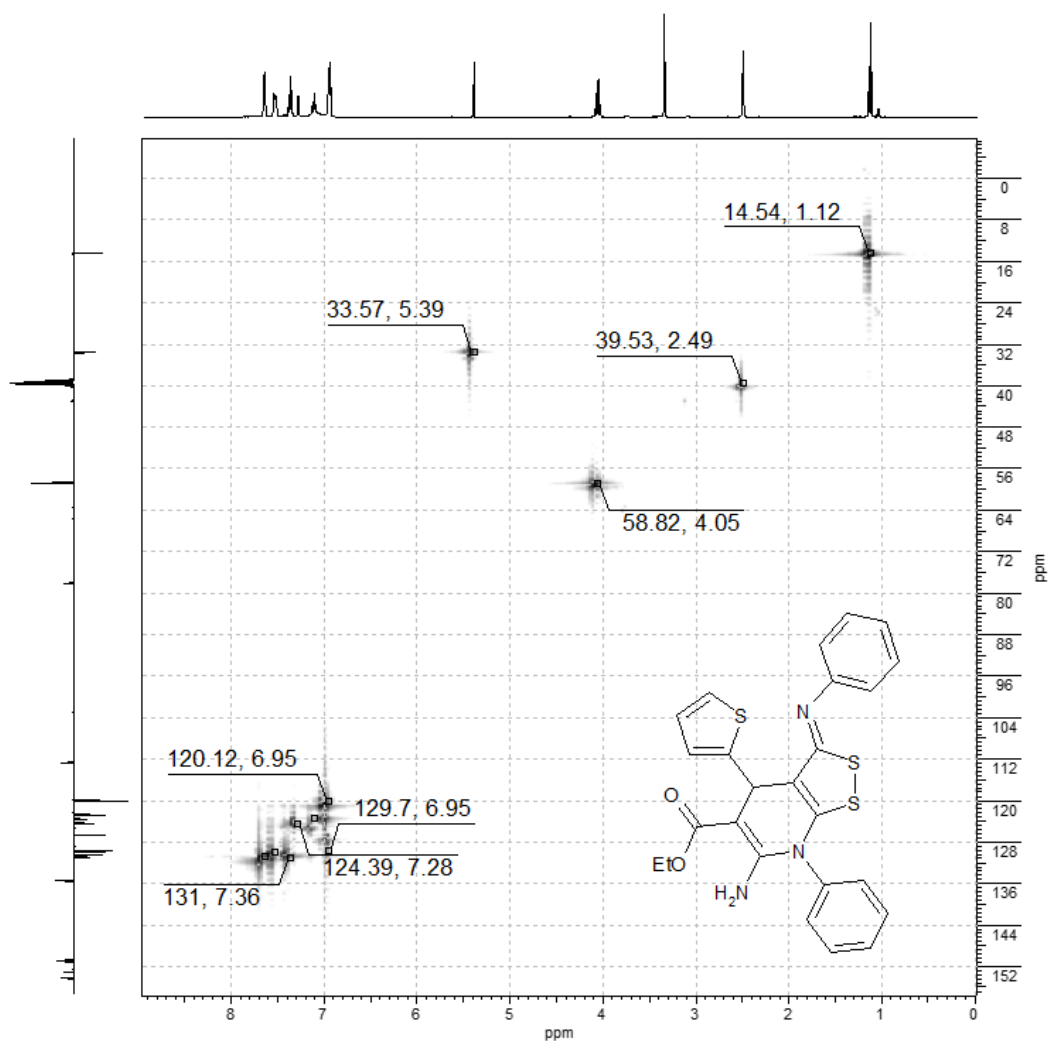
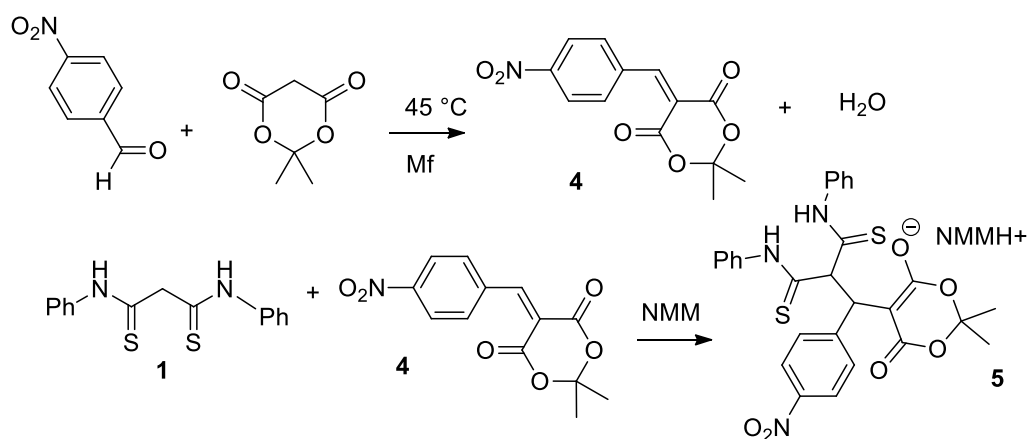


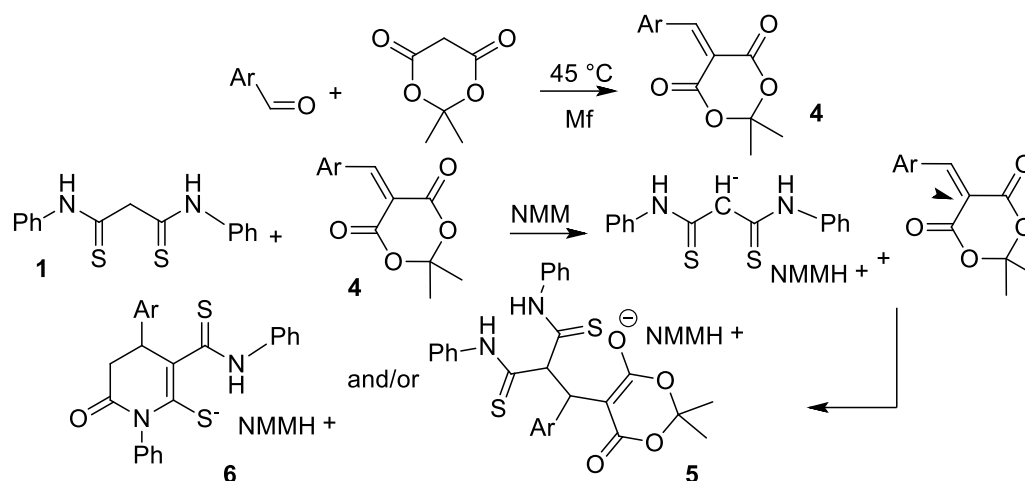
Figure 2. NMR $^1\text{H}/^{13}\text{C}$ HSQC spectrum (400/101 MHz, DMSO-d_6) of **3b**.

Next, we decided to study the reaction of **1** with arylmethylene Meldrums' acids **4**. It was found, that with 4-nitrobenzylidene derivative the reaction proceeds smoothly to give the Michael adduct **5** (Scheme 3):



Scheme 2. The reaction of *N,N'*-diphenyldithiomalonamide **1** with 4-nitrobenzylidene Meldrum's acid.

We decided to expand the base of similar Michael adducts, using various aromatic aldehydes to prepare arylidene Meldrum's acids. However, we found that, along with the formation of the Michael adducts **5**, in most cases the by-process of further cyclization occurs giving rise to formation of tetrahydropyridine-2-thiolates **6**. In these cases, the isolated crystalline products are mixtures of adducts **5** and their cyclization products **6** in various ratios. The plausible mechanism consists of two stages. At the first stage, the arylidene Meldrum's acid **4** is formed. The reaction proceeds as a Knoevenagel-type condensation [2]. Next, the aforementioned activated alkene undergoes the Michael addition with dithiomaldonamide **1**, to form Michael adducts **5** and, followed by subsequent by-process, their cyclization products **6** (Scheme 3).



Scheme 3. The reaction of *N,N'*-diphenyldithiomaldonamide **1** with arylidene Meldrum's acids.

The structure of the products was confirmed by a complex of spectral methods (NMR ^1H , ^{13}C DEPTQ), IR spectroscopy; the structures of the adducts (**5a** and **5d**) were also proved using X-ray diffraction data (Figure 3):

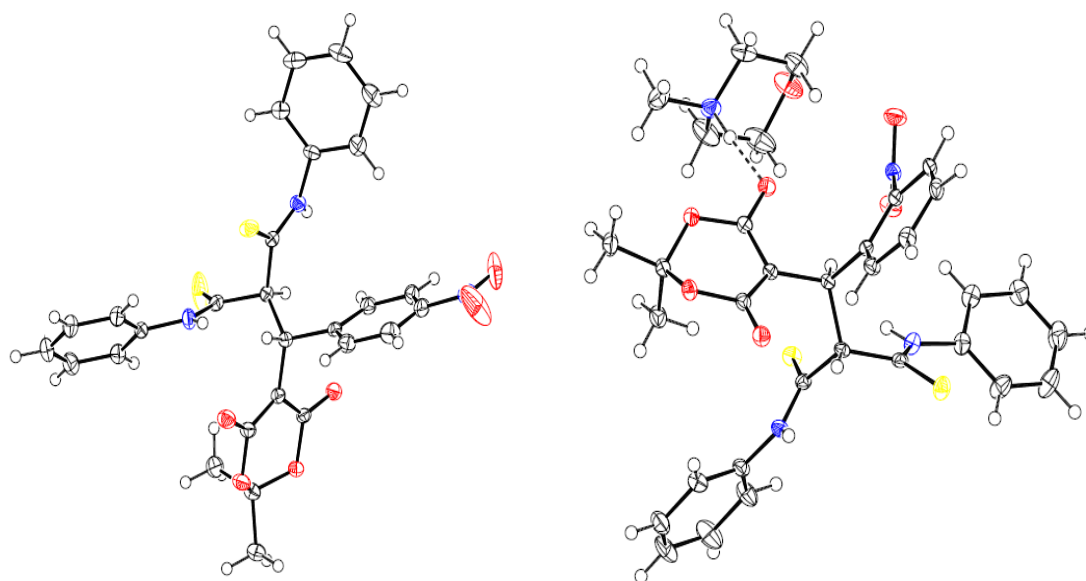
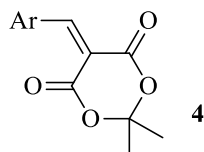


Figure 3. Structures of the Michael adducts **5** (according to X-ray diffraction data).

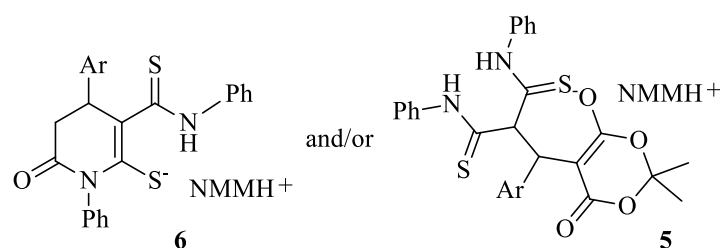
3. Experimental

3.1. Method for the Synthesis of Arylidene Derivatives of Meldrum's Acid 4



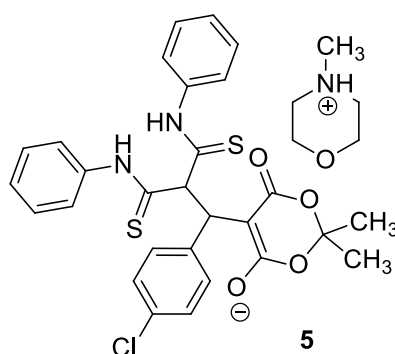
A beaker was charged with 15 ml of ethanol-water mixture (1: 2), 0.5 g (0.0035 mol) of Meldrum's acid, 0.0035 mol of the corresponding aldehyde and a catalytic amount of morpholine (1-2 drops). The mixture was stirred at 45 °C. Precipitation of the product was observed in the first 10 minutes. The reaction proceeds within 2 hours, then the product is filtered off, washed with aqueous alcohol.

3.2. Method for the Synthesis of Michael Adducts 5 and Their Cyclization Products 6



A mixture of 0.25 g of arylidene Meldrum's acid and an equimolar amount of dithiomalondianilide 1 was refluxed in 15 ml of dry acetone. The resulted solution was filtered through a paper filter to remove insoluble impurities. The filtrate was transferred into a flat-bottom flask and a 1.5-fold excess of base was added. The mixture was refluxed under vigorous stirring. A bright-yellow crystals begin to precipitate from the hot solution within 5 min. The crystals obtained were filtered off, washed with cold acetone.

N-Methylmorpholinium 5-[3-Anilino-2-(anilinothiocarbonyl)-1-(4-chlorophenyl)-3-thioxopropyl]-2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-olate 5a



The resulting product is soluble in DMF and DMSO, and insoluble in ethanol, ethyl acetate, acetone. The product contains an admixture (about 15% mol) of the cyclization product. The yield is 52%.

IR spectrum, ν , cm^{-1} : 3190-3128 (N – H), 3024-2862 (C – H), 1654 (C = O), 1595-1494 (C = C). The NMR ^1H spectrum is given in the Figure 4.

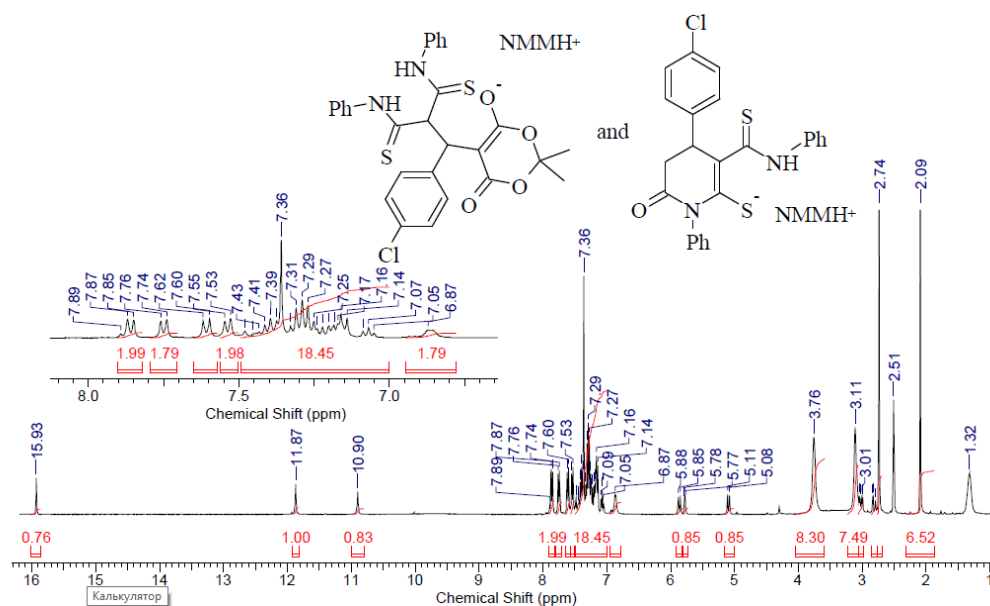


Figure 4. NMR ¹H spectrum (400 MHz, DMSO-d₆) of compound 5a.

References

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