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Radziszewski-Type Oxidation of 3,5-di(α-Cyanostiryl)-1,2,4-Thiadiazoles [†]

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Abstract: Due to the presence of two acrylonitrile fragments, 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles prone to react under Radziszewski reaction conditions (oxidative hydrolysis of nitriles to amides) with simultaneous epoxidation and formation of epoxyamides. Thus, the prepared 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles were oxidized under Radziszewski conditions (H_2O_2, KOH) with the involvement of only one of acrylonitrile fragments and formation of corresponding epoxyamides.

Keywords: arylmethylenecyanothioacetamides; 1,2,4-thiadiazoles; Radziszewski oxidation; epoxyamides

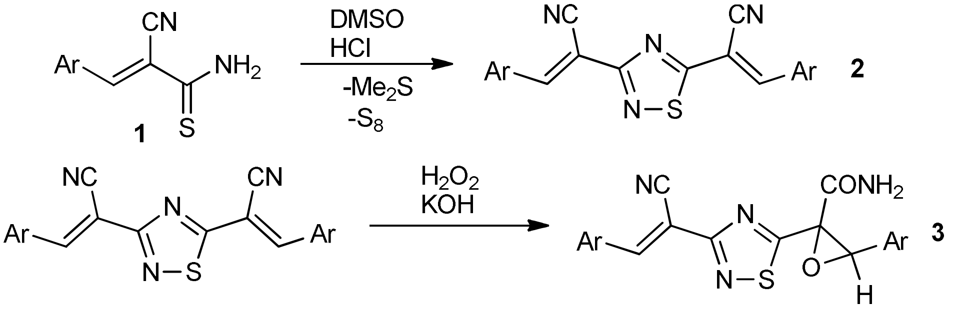
1. Introduction

Earlier we reported the synthesis of substituted 1,2,4-thiadiazoles resulted from oxidative dimerization of arylmethylene cyanothioacetamides upon treatment with DMSO-HCl system [1]. These compounds have highly reactive acrylonitrile moieties so that they can be further transformed to give a plethora of new heterocyclic products.

Radziszewski reaction is widely used in organic practice to prepare primary carboxamides from nitriles under mild oxidative conditions. It is known [2–7] that acrylonitriles react under Radziszewski conditions with simultaneous epoxidation of C=C double bond. So due to the presence of two reactive C=C-C≡N fragments, 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles appeared to be suitable substrates for the synthesis of new epoxyamides. The aim of our study was to determine the structure of oxidation products as well as optimal reaction conditions. The resulting amides may be of interest as reagents for heterocyclic and supramolecular synthesis.

2. Results and Discussion

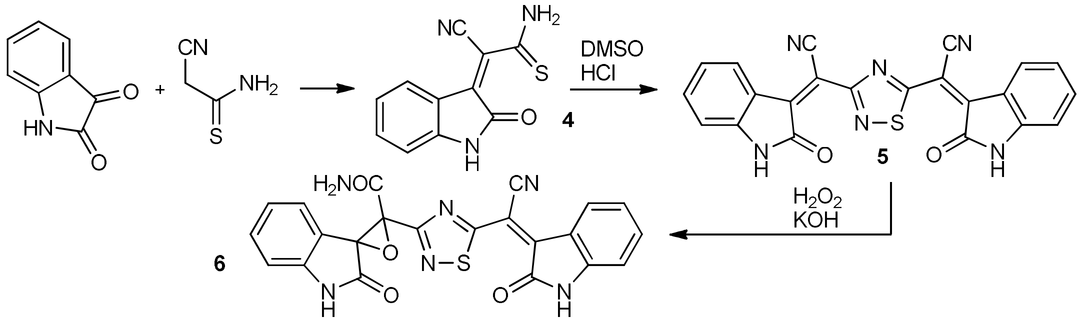
The starting 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles **2** were prepared by oxidative dimerization of arylmethylene cyanothioacetamides **1** in DMSO-HCl system [1] (Scheme 1). We found that upon treatment of compounds **2** with an excess of H_2O_2 in the presence of catalytic amounts of aq. KOH in EtOH, epoxyamides **3** isolated in moderate yields (up to 50%).



Scheme 1. Synthesis and oxidation of 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles **2**.

Compounds **3** are white or yellowish powders, insoluble in water or EtOH. The reaction proceeds very slow at room temperature. The use of larger amounts of KOH favors the oxidation rate, but generally resulted in a decrease in the yields of epoxyamides **3**, probably due to partial hydrolysis of both precursors and the reaction products.

Next, the condensation product of cyanothioacetamide with isatin, thioacrylamide **4**, was oxidized with DMSO–HCl to give thiadiazole **5**. The latter react under Radziszewski reaction conditions to give epoxyamide **6**. As for **3**, only one of acrylonitrile fragments react to afford. We suppose this is due to the lower solubility of monoepoxyamides **3** and **6** resulted in the precipitation and elimination of a molecule from the oxidation process.



Scheme 2. Synthesis and oxidation of thioamides **4**.

The structure of the obtained compounds was confirmed by spectral data. Thus, the IR spectra of the compounds exhibit characteristic absorption bands corresponding to stretching vibrations of N–H bonds, amide C=O and conjugated C≡N group (Figure 1). It was concluded that only one acrylonitrile fragment is involved in the Radziszewski reaction.

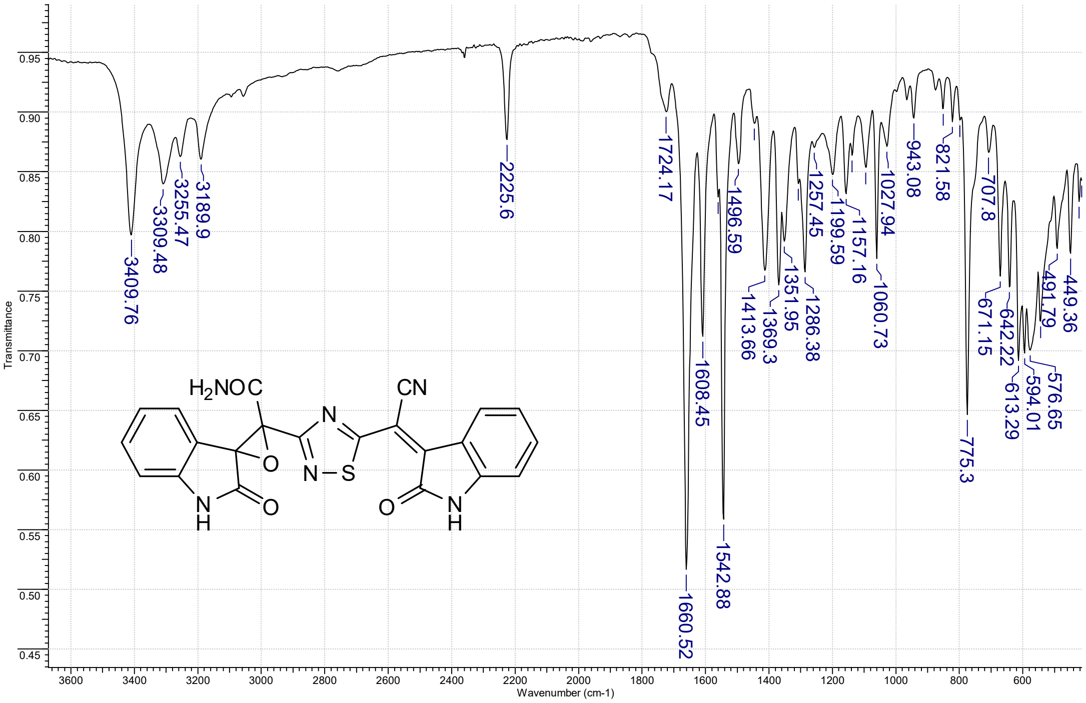
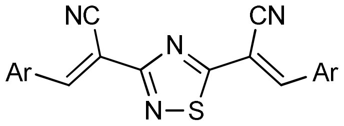


Figure 1. FT-IR (ATR mode) spectrum of compound **6**.

3. Experimental

3.1. *Method for the Synthesis of Thiadiazoles* **2**



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Arylmethylidene cyanothioacetamide **1** (1.5 mmol) was placed in a beaker, and acetone or EtOH (3–5 mL) and DMSO (0.6 mL, 8.45 mmol) were added. To complete dissolution of thioamide, the mixture was gently heated. To the solution formed, conc. HCl (0.5 mL, 4.7 mmol) was added dropwise with constant stirring. The reaction mixture turned red for a moment, then discolored and became turbid (formation of colloidal sulfur). Within a few seconds, the product precipitated (*Caution! Dimethyl sulfide extensively evolved!*). The suspension was diluted with EtOH (5 mL), maintained for 24 h at 20 °C, the solid product was filtered off. To remove the traces of elemental sulfur, the obtained products were purified by recrystallization from acetone, AcOH or by reprecipitation from DMSO with aqueous EtOH.

3.2. *Method for the Synthesis of Compounds* **3** *and* **6**

10% aqueous KOH solution (1.5 mmol) was added in one portion to a mixture of the corresponding thiadiazole (3 mmol), thoroughly ground to a fine powder, and 32% H_2O_2 (d = 1.1 g/mL) (2.7 mL, 0.03 mol) in EtOH. The reaction mixture was heated until an exothermic reaction started, with vigorous stirring. After reaction complete and evolution of oxygen ceased, the crystalline solid was filtered off and washed with cold aq. EtOH to give pure epoxyamides.

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