chemistry proceedings

Proceedings

Radziszewski-type oxidation of 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles †

Polina G. Dahno,1 Arina G. Levchenko,1 Victor V. Dotsenko1-3*

[1] Kuban State University, 149 Stavropolskaya str, Krasnodar, 350040 Russia； e-mail: p.dahno@yandex.ru
[2] ChemEx Lab, Vladimir Dal' Lugansk National University, 20A/7 Molodezhny, Lugansk, 91034 Russia
[3] Department of Chemistry, North Caucasus Federal University, 1a Pushkin St., 355009 Stavropol, Russia
* Correspondence: e-mail@e-mail.com; Tel.: (optional; include country code; if there are multiple corresponding authors, add author initials)

† Presented at the 25th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2021; Available online: https://ecsoc-25.sciforum.net/.

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. It is established that the reaction proceeds nonselectively,and gives a mixture of products of regioisomeric oxidation. Only in one of the cases, it was possible to isolate the product of double epoxidation. The structure of the epoxyamides products was confirmed by IR and NMR spectroscopy data.

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

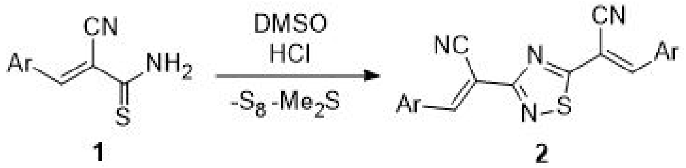
1. Introduction

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.

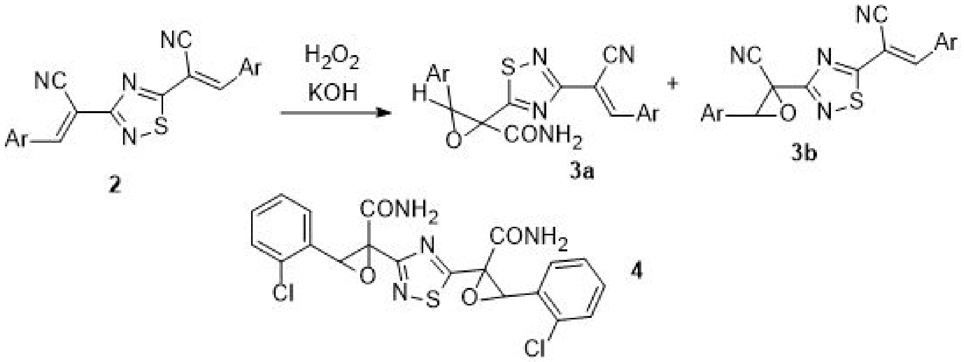
2. Results and discussion

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).



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

The derivatives of 1,2,4-thiadiazole 2 obtained by us were oxidized under the conditions of the Radzishevsky reaction (H2O2, KOH) with the involvement of one of the acrylonitrile fragments and the formation of epoxyamides 3a and 3b with moderate yields (up to 50%). It is established that the reaction proceeds nonselectively,and gives a mixture of products of regioisomeric oxidation. Only in one of the cases, it was possible to isolate the product of double epoxidation 4. The resulting amides are of interest as reagents for heterocyclic and supramolecular synthesis. The structure of the obtained compounds is confirmed by spectral data.



Scheme 2. Oxidation of 3,5-di(α-cyanostiryl)-1,2,4-thiadiazoles 2

Compounds 3a and 3b 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 3a and 3b, probably due to partial hydrolysis of both precursors and the reaction products.

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 (Fig. 1). It was concluded that only one acrylonitrile fragment is involved in the Radziszewski reaction. The 1H NMR spectrum of epoxyamides is characterized by the presence of two narrow singlets of protons of the oxirane ring in the range 4.72–4.81 ppm. The signal of the amide group and signals of the aromatic substituent are resolved as a multiplet at 7.35–7.71 ppm. The signals of the CH protons of the acrylonitrile fragment are found in the range 8.14–8.42 ppm.

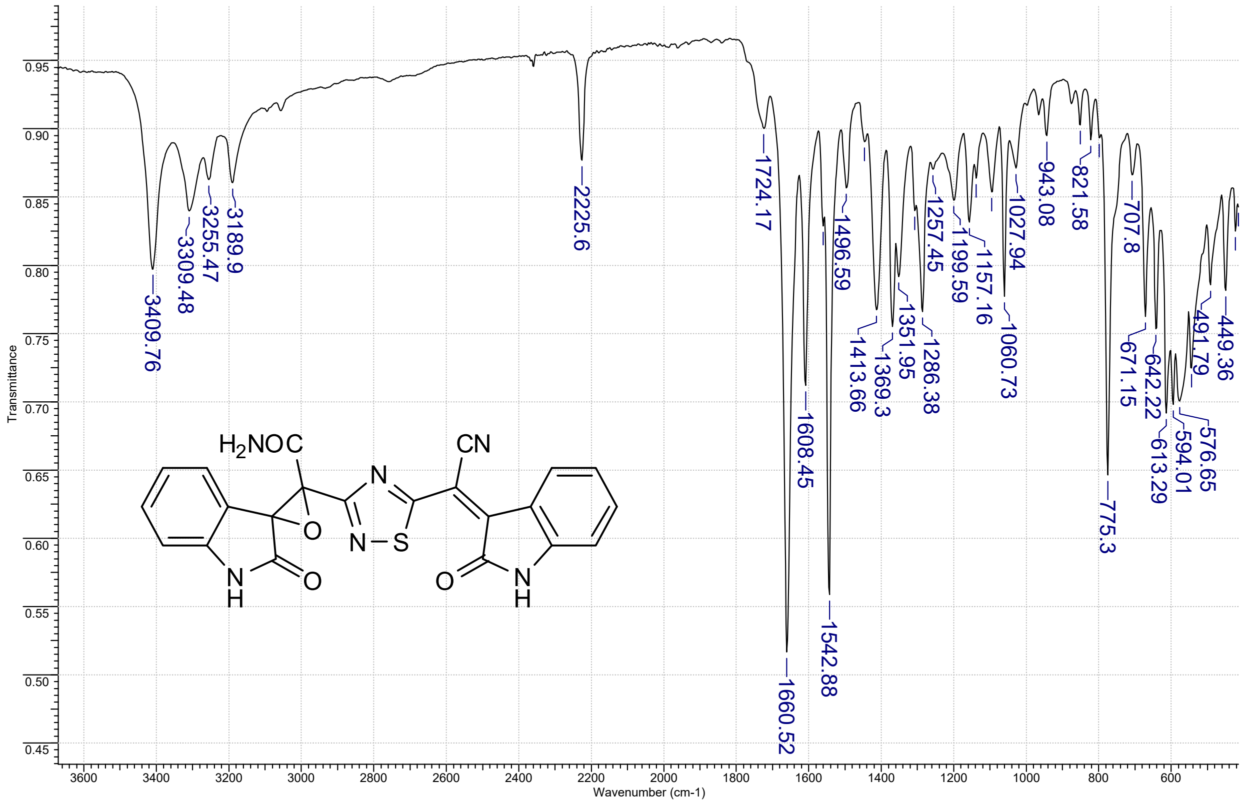
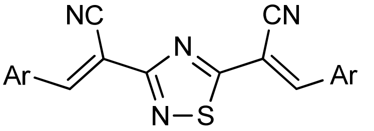


Figure 1. FT-IR (ATR mode) spectrum of compound

3. Experimental

3.1. Method for the synthesis of thiadiazoles 2



2

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 3a and 3b

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% H2O2 (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.

References

1. Dotsenko, V.V. and Krivokolysko, S.G., 2013. Oxidation of thioamides with the DMSO–HCl system: a convenient and efficient method for the synthesis of 1,2,4-thiadiazoles, isothiazolo[5,4-b]pyridines, and heterocyclic disulfides // Chemistry of Heterocyclic Compounds, 49(4), pp.636-644.
2. Murray, J.V. and Cloke, J.B., 1934. The Formation of Glycidamides by the Action of Hydrogen Peroxide on α,β-Ethylenic Nitriles // Journal of the American Chemical Society, 56(12), pp.2749-2751.
3. Payne, G.B., 1961. Reactions of hydrogen peroxide. VIII. Oxidation of isopropylidenemalononitrile and ethyl isopropylidenecyanoacetate // The Journal of Organic Chemistry, 26(3), pp.663-668.
4. Igarashi, M. and Midorikawa, H., 1961. Syntheses of alpha-keto amides and acids from ethyl alkylidenecyanoacetate // Bulletin of the chemical society of Japan, 34(10), pp.1543-1544.
5. Dotsenko, V.V., Krivokolysko, S.G., Litvinov, V.P. and Gutov, A.V., 2007. The Radziszewski oxidation of (E)-3-aryl-2-(thiazol-2-yl)acrylonitriles: A convenient diastereoselective synthesis of (2S,3S)-3-aryl-2-(thiazol-2-yl) oxirane-2-carboxamides // Doklady Chemistry, Vol. 412, No. 2, pp. 29-32.
6. Dotsenko, V.V., Krivokolysko, S.G. and Litvinov, V.P., 2005. Oxidation of 2-(thiazol-2-yl)acrylonitrile derivatives with an H2O2-KOH system: Convenient route to new oxirane-2-carboxamides // Russian chemical bulletin, 54(10), pp.2394-2397.
7. Dotsenko, V.V., Krivokolysko, S.G. and Litvinov, V.P., 2011. The Radziszewski oxidation of cycloalkylidene-α-(thiazol-2-yl) acetonitriles: A new approach toward spirooxiranes // Journal of Heterocyclic Chemistry, 48(1), pp.162-167.