Synthesis of photochromic 2,3-bis(2,5-dimethyl-3-thienyl)-3-cyanoacrylates by the Beckmann rearrangement of a cyclobutenedione derivative

Valerii Z. Shirinian,[a] Mikhail M. Krayushkin,*[a] Valerii A. Barachevskii,[b] Leonid I. Belen'kii,[a] Aleksei A. Shimkin[a] and Yuri P. Strokach[b]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 095 135 5328; e-mail: mkray@mail.ioc.ac.ru*

[b] *Photochemistry Center, Russian Academy of Sciences, 119421 Moscow, Russian Federation. E-mail: barva@photonics.ru*

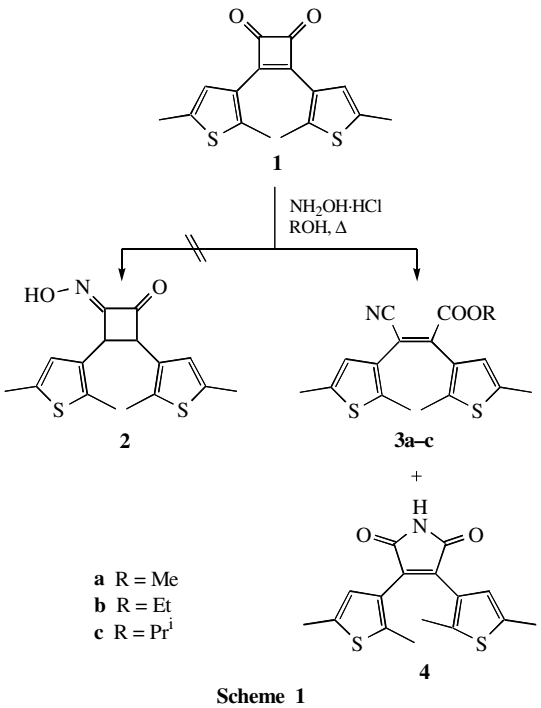
DOI: 10.1070/MC2004v014n05ABEH001916

An unusual Beckmann rearrangement was discovered in the reaction of 3,4-bis(2,5-dimethyl-3-thienyl)cyclobut-3-ene-1,2-dione with hydroxylamine hydrochloride to give esters of 2,3-bis(2,5-dimethyl-3-thienyl)-3-cyanoacrylic acid.

In a continuation of our studies[1] of the synthesis of new photochromic systems based on dithienylethenes, we examined the reaction of 3,4-bis(2,5-dimethyl-3-thienyl)cyclobut-3-ene-1,2-dione **1** with hydroxylamine in order to prepare 3-cyanoacrylic acid derivatives *via* the Beckmann rearrangement. The dithienyl derivatives of acrylic acid are important intermediates in the synthesis of photochromic dithienylethenes based on maleic anhydride and maleimide,[2] and they are also of interest as photochromes.[3]

Although numerous examples of the Beckmann rearrangement of various oximes of carbonyl compounds were reported,[4,5] no data on cyclobutenedione derivatives are available. The Beckmann rearrangement of 3,4-bis(2,5-dimethyl-3-thienyl)cyclobut-3-ene-1,2-dione monooxime **2** can result in cyclobutenedione ring opening, which can be used for the synthesis of new dihetarylethene systems. However, our attempts to prepare compound **2** by refluxing diketone **1** with free hydroxylamine in various solvents (ethanol, dioxane and acetonitrile) were unsuccessful. Heating of compound **1** with hydroxylamine hydrochloride in aqueous dioxane or acetonitrile for 20 h was also unsuccessful. However, it was found that diketone **1** reacts with hydroxylamine hydrochloride in primary alcohols to give alkyl 2,3-bis(2,5-dimethyl-3-thienyl)-3-cyanoacrylates **3a–c**† in good yields (70–80%). In all cases, maleimide **4**‡ (7–10%) was isolated as a by-product (Scheme 1).

A feature differentiating this reaction from known examples of the Beckmann rearrangement[5] is the opening of a cyclobutenedione ring under mild conditions under the action of hydroxylamine hydrochloride to give ester and nitrile groups. Note that the reaction does not proceed without an alcohol, *i.e.*, an alcohol acts as both a solvent and a reagent.



Scheme 1

The mechanism of this transformation remains obscure. Apparently, the reaction includes a step of formation of monooxime **6**, which is a key compound for the Beckmann rearrangement (Scheme 2). Presumably, first, semiketal **5** is formed, in which strain in the four-membered ring decreases due to the sp^3 hybridization of a carbon atom. The subsequent reaction of compound **5** with hydroxylamine affords monooxime **6**. We can assume the formation of two oximes with *Z*- and *E*-configurations (**6a** and **6b**, respectively). The Beckmann

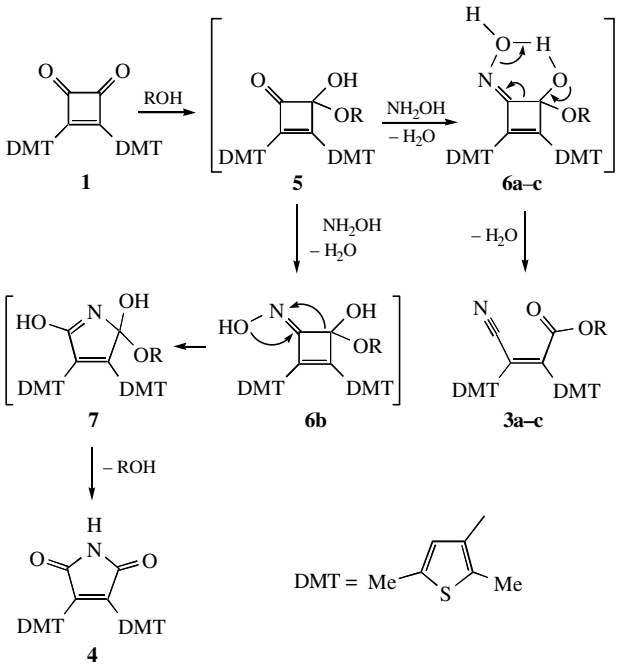
† *The reaction of diketone* **1** *with hydroxylamine hydrochloride (general procedure).* Hydroxylamine hydrochloride (5 mmol) was added to a solution of 3,4-bis(2,5-dimethyl-3-thienyl)cyclobut-3-ene-1,2-dione **1** (1 mmol) in 5 ml of an alcohol, and the reaction mixture was refluxed until the starting thiophene completely disappeared (TLC monitoring). Then the reaction mixture was cooled to room temperature, filtered to remove the unreacted hydroxylamine hydrochloride, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel [elution with EtOAc–petroleum ether (40–70 °C) mixtures, 1:6 to 1:4] to give corresponding cyanoesters **3a–c** and 3,4-bis(2,5-dimethyl-3-thienyl)-pyrrole-2,5-dione **4**.

Methyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl) acrylate **3a**: yield 73%, mp 87–89 °C (methanol). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.96 (s, 3H, Me), 2.13 (s, 3H, Me), 2.32 (s, 3H, Me), 2.35 (s, 3H, Me), 3.90 (s, 3H, OMe), 6.30 (s, 1H, $H_{thioph.}$), 6.33 (s, 1H, $H_{thioph.}$). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 13.99, 14.07, 14.99, 15.04 (4Me), 53.00 (OMe), 113.65 (C–CN), 116.86 (CN), 125.54, 125.81 ($2C_{thioph.}H$), 129.04, 129.91 ($2C_{thioph.}$), 136.52, 136.66, 138.14, 138.25 ($4C_{thioph.}Me$), 141.77 ($C_{thioph.}COO$), 166.28 (COO). MS, *m/z* (%): 331 (74) [M$^+$], 316 (61). IR (KBr, ν/cm^{-1}): 1724 (C=O), 2208 (CN). Found (%): C, 61.60; H, 5.17; N, 4.23; S, 19.35. Calc. for $C_{17}H_{17}NO_2S_2$ (%): C, 61.65; H, 5.38; N, 4.46; S, 19.04.

Ethyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl)acrylate **3b**: yield 80%, mp 95–97 °C (ethanol). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.40 (t, 3H, CH_2Me, ^3J 7.09 Hz), 1.95 (s, 3H, Me), 2.13 (s, 3H, Me), 2.30 (s, 3H, Me), 2.32 (s, 3H, Me), 4.40 (q, 3H, CH_2Me, ^3J 7.09 Hz), 6.35 (s, 1H, $H_{thioph.}$), 6.39 (s, 1H, $H_{thioph.}$). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 14.02 (CH_2Me), 14.10, 14.15, 15.08, 15.16 (4Me), 62.52 (OCH_2), 113.13 (*C*–CN), 116.97 (CN), 125.57, 125.82 ($2C_{thioph.}H$), 129.06, 129.97 ($2C_{thioph.}$), 136.45, 136.67, 138.15, 138.20 ($4C_{thioph.}Me$), 142.05 (*C*–COO), 165.95 (COO). MS, *m/z* (%): 345 (96) [M$^+$], 330 (68). IR (KBr, ν/cm^{-1}): 1720 (C=O), 2216 (CN). Found (%): C, 62.66; H, 5.55; N, 4.04; S, 18.55. Calc. for $C_{18}H_{19}NO_2S_2$ (%): C, 62.77; H, 5.70; N, 4.08; S, 18.04.

Isopropyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl)acrylate **3c**: yield 78%, mp 93–95 °C (ethanol). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.39 (d, 6H, $CHMe_2$, ^3J 6.65 Hz), 1.96 (s, 3H, Me), 2.13 (s, 3H, Me), 2.31 (s, 3H, Me), 2.32 (s, 3H, Me), 5.25 (m, 1H, $CHMe_2$), 6.30 (s, 2H, $H_{thioph.}$). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 14.08, 15.03, 15.09, 15.83 (4Me), 21.55 ($OCHMe_2$), 70.65 ($OCHMe_2$), 112.40 (*C*–CN), 116.99 (CN), 124.67, 125.57 ($2C_{thioph.}H$), 129.06, 130.04 ($2C_{thioph.}$), 136.33, 136.58, 137.93, 138.12 ($4C_{thioph.}Me$), 142.50 (*C*–COO), 165.95 (COO). MS, *m/z* (%): 359 (43) [M$^+$], 344 (16). IR (NaCl, ν/cm^{-1}): 1720 (C=O), 2216 (CN). Found (%): C, 63.48; H, 5.89; N, 3.90; S, 17.84. Calc. for $C_{19}H_{21}NO_2S_2$ (%): C, 63.52; H, 6.08; N, 4.10; S, 16.92.

‡ *3,4-Bis(2,5-dimethyl-3-thienyl)pyrrole-2,5-dione* **4**: yield 8%, mp 195–197 °C (lit.,[6] mp 196–198 °C). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.89 (s, 6H, Me), 2.43 (s, 6H, Me), 6.72 (s, 2H, $H_{thioph.}$), 7.49 (br. s, 1H, NH). MS, *m/z* (%): 317 (81) [M$^+$], 302 (100) [M$^+$ – Me].



Scheme 2

rearrangement of *Z*-oxime **6a** results in cyanoesters **3a–c**, while that of *E*-oxime **6b** gives maleimide **4**. The high yields of compounds **3a–c** compared to those of **4** can be attributed to a higher stability of the closed (ring) form of *Z*-oxime **6a** caused by hydrogen bonding between the oxime oxygen and the hydroxyl hydrogen in the semiketal fragment.

Esters **3a–c** were identified by ^{1}H and ^{13}C NMR and IR spectroscopy, mass spectrometry and elemental analysis and by chemical transformation into a known compound. As expected, cyanoesters are produced as *Z*-isomers, *i.e.*, the two thiophene rings occupy *cis* positions relative to the double bond. This structure is additionally confirmed by the transformation, under mild conditions, of ethyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl)-acrylate **3b** into pyrrole-2,5-dione monooxime **9**§ (the reaction was carried out by refluxing **3b** with free hydroxylamine in anhydrous ethanol until the starting compound disappeared). Acid hydrolysis of **9** furnishes furandione **4** (Scheme 3). Presumably, the reaction starts with the formation of amidoxime **8**, whose cyclization yields product **9**, which was characterised by ^{1}H NMR and mass spectra. Our attempts to prepare samples of this compound pure for analysis by recrystallization or preparative chromatography failed because the product is unstable, and it was always contaminated with imide **4**.¶ The structure of furandione **4** was established by ^{1}H NMR spectroscopy, mass spectrometry and a comparison of its physicochemical properties with those of the imide prepared previously.

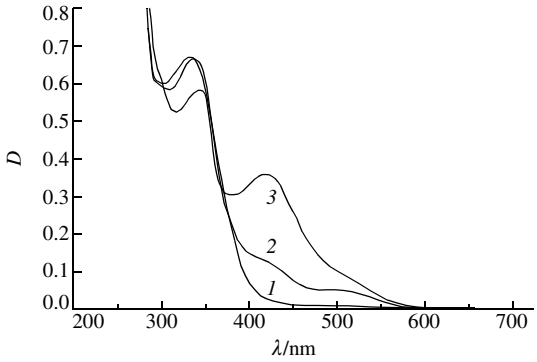
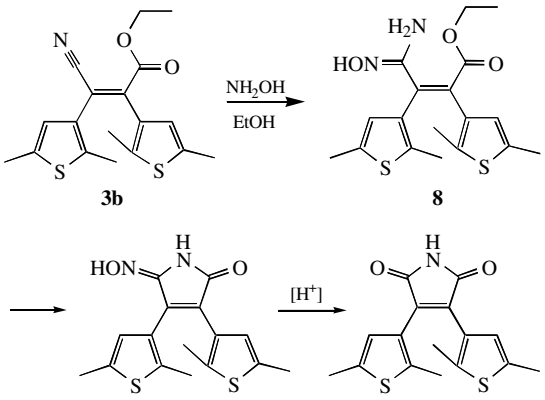


Figure 1 Absorption spectra of **3b** in toluene: (*1*) initial solution and (*2*), (*3*) after irradiation at 313 nm.

We studied the photochromic properties of cyanoester **3b**.†† The spectral and kinetic data of photochromic transformations are shown in Figures 1 and 2. The absorption band for the open form of compound **3b** occurs at λ_{max} = 313 nm, while the photo-induced closed form has two absorption bands at λ_{max} = 420 and 510 nm (Figure 1). The lifetime of the ring form does not exceed 10 s.

Thus, we discovered an unusual Beckmann rearrangement in the reaction of 3,4-bis(2,5-dimethyl-3-thienyl)cyclobut-3-ene-1,2-dione **1** with hydroxylamine hydrochloride, which results in cyclobutenedione ring opening to give alkyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl)acrylates, which are difficult to prepare by other routes. The photochromic properties of cyanoester **3b** were studied; under exposure to UV radiation, it converted into a ring form whose absorption maximum is shifted to the short-wavelength part of the visible region.

This study was supported by the Russian Foundation for Basic Research (grant no. 04-03-32878).



Scheme 3

§ *Monooxime of 3,4-bis(2,5-dimethyl-3-thienyl)pyrrole-2,5-dione* **9**. Hydroxylamine hydrochloride (0.05 g, 0.72 mmol) and ammonium acetate (0.057 g, 0.7 mmol) were added to a solution of ethyl 3-cyano-2,3-bis(2,5-dimethyl-3-thienyl)acrylate **3b** (0.1 g, 0.3 mmol) in 7 ml of ethanol. The reaction mixture was refluxed until the starting cyanoester was completely consumed (TLC monitoring) and cooled to room temperature. The solvent was evaporated, and the solid residue was purified by chromatography [elution with a EtOAc–petroleum ether (40–70 °C) mixture, 1:6 to 1:4] to give imidooxime **9** (70 mg, 70%) as pinkish crystals, mp 232–234 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.86 (s, 3H, Me), 1.89 (s, 3H, Me), 2.41 (s, 3H, Me), 2.43 (s, 3H, Me), 6.68 (s, 1H, $H_{thioph.}$), 6.71 (s, 1H, $H_{thioph.}$), 7.64 (br. s, 1H, NH), 7.97 (br. s, 1H, NOH). MS, *m/z* (%): 332 (31) [M$^+$], 316 (63), 315 (99), 301 (45).

¶ *3,4-Bis(2,5-dimethyl-3-thienyl)pyrrole-2,5-dione* **4** *from imidoxime* **9**. Concentrated hydrochloric acid (0.5 ml) was added to a solution of 3,4-bis(2,5-dimethyl-3-thienyl)pyrrole-2,5-dione monooxime **9** (0.07 g, 0.21 mmol) in 5 ml of ethanol, and the reaction mixture was refluxed until compound **9** completely disappeared (TLC monitoring). Then the reaction mixture was cooled to room temperature, and the solvent was evaporated. The solid residue was recrystallised from ethanol to give 56 mg (84%) of a yellow powder, mp 197–198 °C (lit.,[6] mp 196–198 °C).

†† The absorption spectra for the open and closed forms of photochromic compounds were measured on a Shimadzu UV-VIS spectrophotometer in the range 200–800 nm. The closed form was obtained after photo-excitation of the solution with a DRSh-250 mercury lamp through a UV light filter which separates radiation with λ = 313 nm. The kinetics of photocolouration of solutions of diarylethenes was measured at the absorption maximum wavelength during irradiation of preliminarily decolourised solutions of these compounds. The photo-decolouration kinetics was measured during irradiation of preliminarily coloured solutions with visible mercury lines of a DRSh-250 lamp separated by means of appropriate light filters.

The photodecomposition kinetic curves obtained for photochromic compounds were used to estimate the number of cycles of photochromic transformations under high-intensity radiation. The photodecomposition of solutions was characterised by the time it took for the optical density of the photostationary state at the absorption maximum to halve under continuous irradiation with unfiltered light from a DRSh-250 lamp.

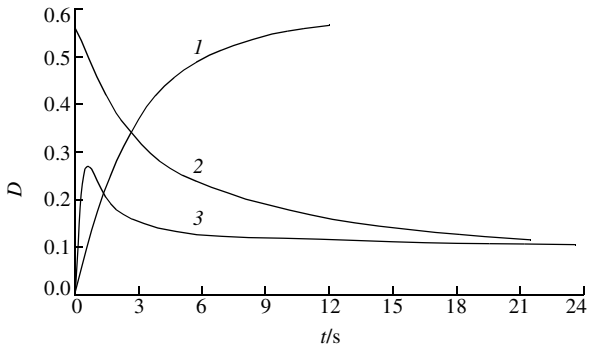


Figure 2 Kinetics of (*1*) photocolouration under exposure to radiation at 365 nm, (*2*) photobleaching under exposure to radiation at 436 nm and (*3*) photodegradation under irradiation with full light from a DRSh-250 mercury lamp in the solutions of **3b** in toluene.

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Received: 12th March 2004; Com. 04/2242