Photochromic dihetarylethenes

14.* Synthesis of symmetrical and unsymmetrical dihetarylcyclobutene-1,2-diones

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A procedure was developed for the synthesis of symmetrical and unsymmetrical cyclobutene-1,2-dione derivatives bearing thiophene and thieno[3,2-*b*]thiophene substituents by the Friedel—Crafts reaction of the corresponding heterocyclic compounds with squaric acid dichloride in the presence of $AlCl_3$. In addition to the target dihetarylcyclobutenediones, monoacylation products of methyl (2,5-dimethylthiophen-3-yl)acetate and methyl 5-methylthieno[3,2-*b*]thiophene-2-carboxylate with squaric acid dichloride were isolated and characterized.

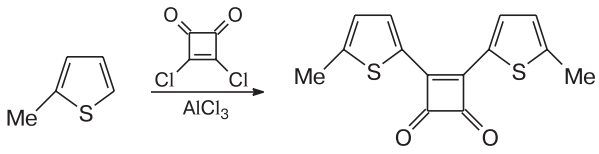
Key words: 2,5-dimethylthiophene, 2-methylthiophene, methyl (2,5-dimethylthiophen-3-yl)acetate, methyl 5-methylthieno[3,2-*b*]thiophene-2-carboxylate, squaric acid dichloride, Friedel—Crafts reaction, dithienylcyclobutenediones.

In the previous study,[1] we have found the optimum conditions for the Friedel—Crafts reaction of 2,5-dimethylthiophene with squaric acid dichloride in the presence of $AlCl_3$ and demonstrated that the use of a dichloroethane—heptane mixture as the solvent prevented side processes and made it possible to prepare 3,4-bis(2,5-dimethylthiophen-3-yl)cyclobut-3-ene-1,2-dione in satisfactory yield. In the present study, we applied analogous conditions to the synthesis of a series of dihetarylcyclobutene-1,2-diones bearing thiophene and thieno[3,2-*b*]thiophene fragments as hetaryl substituents.

Thus the reaction of 2-methylthiophene (**1**) with squaric acid dichloride (Scheme 1) was carried out in two steps. In the first step, heptane was used as the solvent and the temperature was maintained at −20 °C (presumably, 4-chloro-3-(5-methylthiophen-2-yl)cyclobut-3-ene-1,2-dione was formed in this step and precipitated as a heptane-insoluble complex with $AlCl_3$). In the second step, dichloroethane was added (heptane : dichloroethane ratio was 2 : 1, v/v) and the reaction was completed at 0 °C. To prevent accumulation of HCl, inert gas was passed through the reaction mixture. 3,4-Bis(5-methylthiophen-2-yl)cyclobut-3-ene-1,2-dione (**2**) was obtained in 78% yield.

Different unsymmetrical and symmetrical dithienylcyclobutenediones were synthesized under analogous conditions (Scheme 2). The use of the procedure developed in our previously study[1] allowed us to separate the first step in which more reactive squaric acid dichloride served

Scheme 1



1 **2**

as the reagent from the second step involving less reactive 4-chloro-3-hetarylcyclobutene-1,2-dione. As a result, we succeeded in isolating the reaction products of squaric acid dichloride with one molecule of methyl 5-methylthieno[3,2-*b*]thiophene-2-carboxylate (**3**) and with one molecule of methyl (2,5-dimethylthiophen-3-yl)acetate (**4**), *viz.*, methyl 6-(2-chloro-3,4-dioxocyclobut-1-enyl)-5-methylthieno[3,2-*b*]thiophene-2-carboxylate (**5**) and methyl [4-(2-chloro-3,4-dioxocyclobut-1-enyl)-2,5-dimethylthiophen-3-yl]acetate (**6**), respectively. Then, we used the latter compounds in the synthesis of both symmetrical 3,4-bis(5-methoxycarbonyl-2-methylthieno[3,2-*b*]thiophen-3-yl)cyclobutene-1,2-dione (**7**) and unsymmetrical dihetarylcyclobutene-1,2-diones, *viz.*, 3-(2,5-dimethyl-3-thienyl)-4-(5-methoxycarbonyl-2-methylthieno[3,2-*b*]thiophen-3-yl)cyclobutene-1,2-dione (**8**) and 3-(4-methoxycarbonylmethyl-2,5-dimethyl-3-thienyl)-4-(5-methoxycarbonyl-2-methylthieno[3,2-*b*]thiophen-3-yl)cyclobutene-1,2-dione (**9**).

Compounds **5** and **6** proved to be unstable and were characterized by ^1H NMR spectroscopy and mass spec-

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Scheme 2

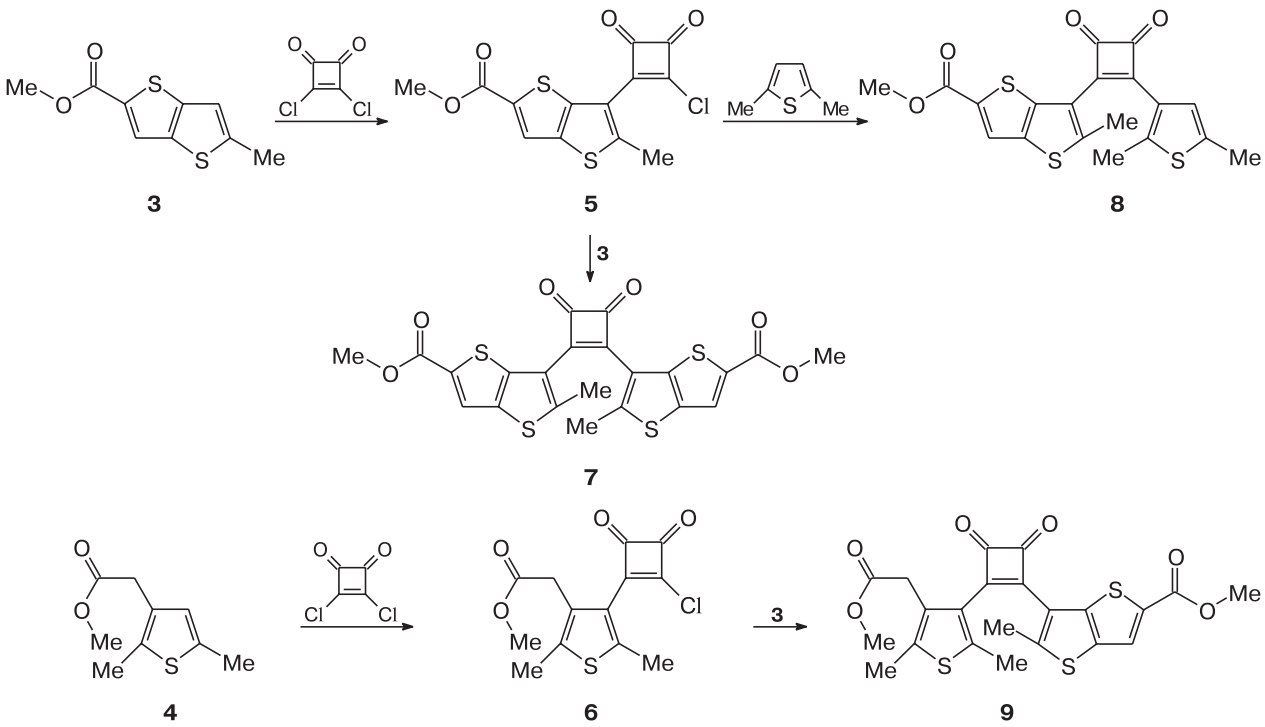

Table 1. Reaction conditions and physicochemical characteristics of the compounds

Compound	T_1[a] °C	T_2[b] °C	Solvent ratio[c]	M.p./°C (solvent)	Yield[d] (%)	Found / Calculated (%) C	H	S	Molecular formula
2	−20	0	1 : 2	181—182 (heptane—benzene)	78	61.89 / 61.29	3.77 / 3.67	22.83 / 23.37	$C_{14}H_{10}O_2S_2$
5	−10	−5	7 : 1	172—173 (heptane—benzene)	52	—	—	—	—
6	−20	−5	6 : 1	185—186 (heptane—benzene)	48	—	—	—	—
7	0	20	10 : 1	232—233 (MeOH—benzene)	77	52.51 / 52.57	3.12 / 2.81	24.06[e] / 25.52	$C_{20}H_8O_6S_4$
8	−10	−5	4 : 1	185—186 (MeOH—benzene)	64	55.45[f] / 56.70	3.42 / 3.51	23.81 / 23.90	$C_{18}H_8O_4S_3$
9	0	20	10 : 1	71—73 (MeOH—benzene)	70	55.94 / 55.86	3.67 / 3.82	19.47 / 20.27	$C_{22}H_{18}O_6S_3$

[a] The lowest reaction temperature.
[b] The highest reaction temperature.
[c] Dichloroethane : heptane.
[d] Yields are given for the samples obtained by recrystallization without preliminary purification by preparative chromatography.
[e] Attempts to prepare a sample characterized by satisfactory analysis for S failed.
[f] Attempts to prepare a sample characterized by satisfactory analysis for C failed.

Table 2. Spectroscopic characteristics of the compounds

Compound	NMR, δ		Mass spectrum, *m/z*
	^{1}H	^{13}C	
2	2.75 (s, 6 H, Me); 7.10 (d, 2 H, H(3′), *J* = 3.9 Hz); 8.27 (d, 2 H, H(4′))	16.04 (Me); 127.36 (C(2)); 128.09 (C(3)); 134.48 (C(4)); 151.68 (C(5)); 171.51 (C=C); 192.91 (C=O)	274 $[M]^+$, 218 $[M - 2\,CO]^+$
5	2.93 (s, 3 H, Me); 3.92 (s, 3 H, MeO); 7.90 (s, 1 H, CH)	—	326, 328 $[M]^+$, 291 $[M - Cl]^+$
6	2.38 (s, 3 H, Me); 2.50 (s, 3 H, Me); 3.60 (s, 3 H, MeO); 3.70 (s, 2 H, CH_2)	—	298, 300 $[M]^+$, 263 $[M - Cl]^+$
7	2.74 (s, 6 H, 2 Me); 3.82 (s, 6 H, 2 MeO); 7.85 (s, 2 H, CH of thienothiophene)	17.45 (Me); 52.53 (MeO); 120.39 (CMe); 125.28 (CH); 135.04; 136.13; 142.54; 154.76; 162.57; 181.96 (C=C); 193.95 (MeOC=O); 199.19 (C=O)	502 $[M]^+$, 446 $[M - 2\,CO]^+$
8	2.31 (s, 3 H, Me); 2.45 (s, 3 H, Me); 2.76 (s, 3 H, Me); 3.89 (s, 3 H, MeO); 6.91 (s, 1 H, CH of thiophene); 7.92 (s, 1 H, CH of thienothiophene)	15.08, 15.68, 17.23, 52.36, 125.05, 126.49, 135.01, 136.02, 138.54, 141.99, 147.26, 152.28, 162.59, 180.48, 183.90, 194.49, 195.11	402 $[M]^+$, 346 $[M - 2\,CO]^+$
9	1.98 (s, 3 H, Me); 2.42 (s, 3 H, Me); 2.80 (s, 3 H, Me); 3.58 (s, 3 H, MeO); 3.75 (s, 2 H, CH_2); 3.92 (s, 3 H, MeO); 7.89 (s, 1 H, CH of thienothiophene)	13.23 (Me); 15.19 (Me); 17.46 (Me); 33.18 (CH_2); 52.00 (MeO); 52.37 (MeO); 121.16; 124.77 (CH); 128.03; 129.48; 135.15; 135.47; 136.10; 141.19; 154.35; 162.61; 170.65; 182.99 (C=C); 185.99 (C=C); 194.35 (C=O); 195.54 (C=O)	474 $[M]^+$, 446 $[M - CO]^+$, 418 $[M - 2\,CO]^+$

trometry. The structures of dithienylcyclobutenediones **2** and **7—9** were confirmed by the data from ^{1}H and ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis (Tables 1 and 2). The mass spectra of this class of compounds have peaks of molecular ions along with peaks of the fragmentation ions $[M - 28]^+$ and $[M - 56]^+$ corresponding to fragmentation with liberation of one or two CO molecules, respectively. The ^{13}C NMR spectra of dihetarylcyclobutenediones are characterized by signals for the C atoms of the keto groups of the cyclobutenedione ring (δ 190—195) and signals for the C atoms of the double bond of the cyclobutenedione ring (δ 180—186), which agrees with the known data[2] for various substituted diphenylcyclobutenediones.

To summarize, we developed procedures for the synthesis of symmetrical and unsymmetrical cyclobutene-1,2-dione derivatives bearing thiophene and thieno[3,2-*b*]thiophene fragments as substituents. Variations in the temperature and the solvent ratio in the individual steps of the process enables one to control the rate of the reaction of squaric acid dichloride with thiophene derivatives and synthesize both the target dihetarylcyclobutene-1,2-diones and the reaction products of the dichloride with one molecule of the substrate.

Experimental

The ^{1}H and ^{13}C NMR spectra were recorded on Bruker AC-200, Bruker WM-250, and Bruker AM-300 spectrometers in $CDCl_3$. The mass spectra (EI) were measured on a Kratos instrument (70 eV) with direct inlet of the sample into the ion source. The melting points were determined on a Boetius stage and were not corrected.

The completion of the reactions was judged from the TLC data (Silufol UV-254 plates, light petroleum—AcOEt as the solvent system). Column chromatography was carried on Al_2O_3 (Brockmann activity II, neutral) and silica gel Acros (0.060—0.200 mm).

2-Methylthiophene (**1**), 2,5-dimethylthiophene, squaric acid, and $AlCl_3$ were purchased from Aldrich. Dichloroethane was dried by refluxing over P_2O_5 for 3 h followed by distillation. Heptane was used without purification. Squaric acid dichloride was prepared according to a modified procedure[3] (DMF and a catalytic amount of a NaCl—KCl mixture were used as the catalysts; dichloroethane was used as the solvent) and recrystallized from heptane. Methyl 5-methylthieno[3,2-*b*]thiophene-2-carboxylate (**3**)[4] was synthesized according to a modified procedure[5] (2-mercapto-3-(5-methyl-2-thienyl)acrylic acid[6] was oxidized with *N*-bromosuccinimide in dichloroethane at 60 °C). Methyl (2,5-dimethylthiophen-3-yl)acetate (**4**) was prepared from 2,5-dimethylthiophene according to a known procedure.[7]

Synthesis of dithienylcyclobutene-1,2-diones (general procedure). A solution of a substrate (0.02 mol) in heptane (25 mL) (for compounds **2** and **9**) or dichloroethane (25 mL) (for compounds **7** and **8**) and a solution of squaric acid dichloride (or compounds **5** and **6**) (0.01 mol) in dichloroethane (25 mL) were added dropwise with stirring to a suspension of $AlCl_3$ (0.04 mol) in heptane (15 mL) under a stream of argon at the lowest temperature indicated in Table 1. The reaction mixture was stirred for 3—4 h. Then dichloroethane was added to the

required solvent ratio (see Table 1) and the temperature of the reaction mixture was raised (see Table 1). The reaction mixture was stirred at this temperature until the starting compound was completely consumed (TLC data). Then the reaction mixture was poured onto ice and the aqueous phase was extracted with $CHCl_3$. The extracts and the organic layer were combined, washed with a 3% $NaHCO_3$ solution and water until the washing water became neutral, and dried with $MgSO_4$. The solvent was distilled off and the residue was recrystallized from the corresponding solvent. For analytical purposes, chromatography was carried out on a silica gel—Al_2O_3 mixture (light petroleum (60—80 °C)—AcOEt mixture, 6 : 1).

Synthesis of 4-chloro-3-hetarylcyclobutene-1,2-diones (general procedure). A solution of a substrate (0.01 mol) in dichloroethane (25 mL) and a solution of squaric acid dichloride (0.01 mol) in dichloroethane (25 mL) were added dropwise with stirring to a suspension of $AlCl_3$ (0.01 mol) in heptane (25 mL) at the lowest temperature indicated in Table 1. The reaction mixture was stirred for 5—6 h and dichloroethane was added to the required solvent ratio (see Table 1). Then the reaction temperature was raised (see Table 1) and the mixture was kept at this temperature until the starting compound was completely consumed (TLC data). The reaction mixture was worked up as described above, the solvent was distilled off, and the residue was recrystallized from a heptane—benzene mixture.

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