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Synthesis of Photochromic 1,2-Dihetarylethene Using Regioselective Acylation of Thienopyrroles

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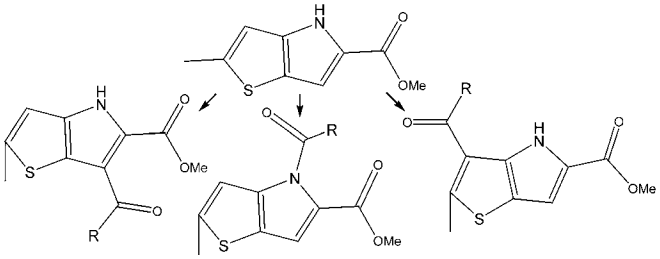
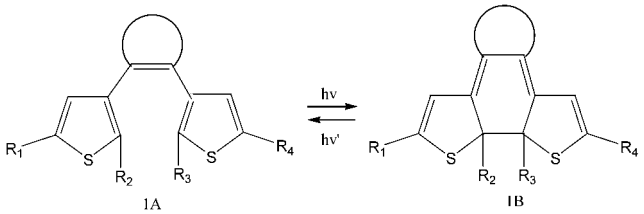
ABSTRACT



The influence of catalysts, acid chlorides, and solvents in the acylation of methyl 2-methyl-4*H*-thieno[3,2-b]pyrrole-5-carboxylate was studied. Conditions for the regioselective acylation processes were found. Thienopyrrole-based photochrome was synthesized for the first time.

Thermally stable photochromic 1,2-dihetarylethenes with high cyclicity are of considerable interest as promising elements for optical memory.[1]



It is known that high cyclicity is demonstrated by photochromic products containing fused heterocycles: benzothiophene, indole, and thieno[3,2-b]thiophene.[1] Note that 1,2-dihetarylethenes containing indole rings not only are photochromes[2] but also exhibit a wide spectrum of biological activity and are intensely studied as promising drugs and cosmetic makeup preparations.[2,3]

In this connection, it was of interest to synthesize previously undescribed dihetarylethenes containing thienopyrrole fragments, which are rather close heterocyclic analogues of all three indicated types of substituents, and to study their properties.

In this work, we studied the possibility of regioselective acylation reactions of methyl 2-methyl-4*H*-thieno[3,2-b]-pyrrole-5-carboxylate (**1a**) (Scheme 1). As we showed[4] and the authors described,[5] the acyl moiety that formed is of interest for subsequent transformation into the bridging fragments of 1,2-dihetarylethenes.

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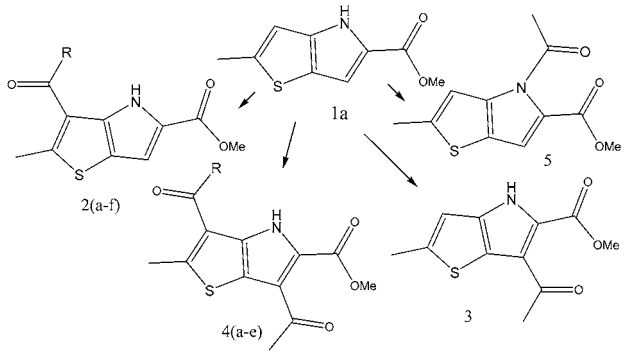
Scheme 1

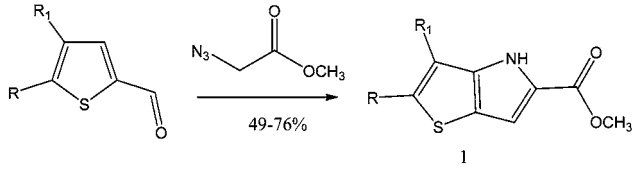


2a: R = CH_3, 2b: R = CH_3CH_2, 2c: R = $ClCH_2$, 2d: R = Cl_2CH, 2e: R = Cl_3C, 2f: R = $(CH_3)_2CH$

4a: R = CH_3, 4b: R = CH_3CH_2 4c: R = $ClCH_2$, 4d: R = Cl_2CH 4e: Cl_3C

We synthesized thienopyrroles (**1a**−**c**) by the condensation of the corresponding thiophenaldehydes with esters of azidoacetic acid (Hemetsberger−Knittel reaction)[6] (Scheme 2). Compounds **1b**,**c** were synthesized for the unambiguous

Scheme 2



1a: R = CH_3, R_1 = H; 1b: R = CH_3, R_1 = Br; 1c: R = H, R_1 = H

interpretation of the ^1H and ^{13}C NMR spectra of isomers **2** and **3**.

It should be mentioned that the acylation of thieno[3,2-b]pyrrole carboxylates was poorly studied, and only the reaction of ethyl 4*H*-thieno[3,2-b]pyrrole-5-carboxylate with acetyl chloride resulting in the insertion of the keto group into position 2 of thienopyrrole was described.[7]

We studied the influence of the nature of catalysts, reactants, and solvents on thienopyrrole **1a** acylation. The results of compound **1a** acylation in dichloroethane, nitromethane, and ionic liquid in the presence of different equivalents of $AlCl_3$ and $SnCl_4$ are presented in Table 1.

It can be seen in Table 1 that when two or more $AlCl_3$ equivalents are used, acylation in dichloroethane occurs regioselectively at the thiophene ring (entries 1 and 2). The introduction of electron-withdrawing substituents into aliphatic acid chlorides has no effect on the position selectivity of the process (entries 3−7). Acylation of thienopyrrole in ionic liquid, 1-butyl-3-methylimidazolium heptachlorodialuminate(III), led to introduction of one acyl group into the thiophene ring (entries 8 and 9). The application of equimolar amounts of $AlCl_3$ enhances the probability of the reaction at the pyrrole ring because, in this case, complex-free thienopyrrole can be attacked (entries 10 and 11). However, it is impossible to perform the selective acetylation of the

Table 1. Acylation Products of Thienopyrrole **1a**

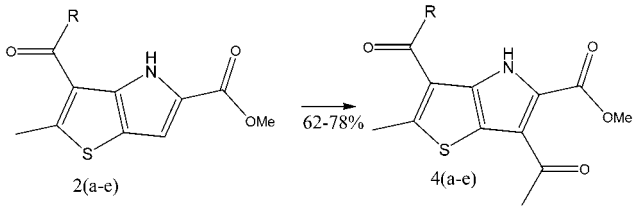
entry	reagent	molar ratio of **1a**:Lewis acid	solvent	product ratio of **2a**:**4a**:**3**	yield, %
1	A	1:2.1[c]	a	100:0:0	95
2	2.1A	1:3.1[c]	a	100:0:0	93
3	B	1:2.1[c]	a	100 (**2b**)	67
4	C	1:2.1[c]	a	100 (**2c**)	77
5	D	1:2.1[c]	a	100 (**2d**)	67
6	E	1:2.1[c]	a	100 (**2e**)	66
7	F	1:2.1[c]	a	100 (**2f**)	63
8	1.1A	1:2[c]	c	100:0:0	92
9	1.1C	1:2[c]	c	100:0:0	90
10	A	1:1.1[c]	a	25:0:75	91
11	A	1:1.1[c]	b	15:0:85	89
12	A	1:2.1[d]	a	0:0:100	93
13	A	1:2.1[d]	b	0:25:75	91
14	2.1A	1:2.1[d]	a	0:20:80	92

[a] Reagents: A, CH_3COCl; B, CH_3CH_2COCl; C, $ClCH_2COCl$; D, $Cl_2CHCOCl$; E, Cl_3CCOCl; F, $(CH_3)_2CHCOCl$. [b] Solvents: a, $ClCH_2CH_2Cl$; b, CH_3NO_2; c, 1-butyl-3-methylimidazolium heptachlorodialuminate(III). [c] $AlCl_3$. [d] $SnCl_4$.

pyrrole ring in the presence of $AlCl_3$. The use of $SnCl_4$, which is a weaker Lewis acid than $AlCl_3$, decreases the electron-withdrawing character of the complexes formed with thienopyrrole and allows the regioselective synthesis of ketone 3 (entry 12). At the same time, in the presence of $SnCl_4$, the acetyl group cannot be selectively introduced into the thiophene ring (entries 13 and 14).

We also showed that the target synthesis of various mixed diketones (**4a**−**e**) can be performed in nitromethane by the successive selective introduction of one acyl group into the thiophene ring in the presence of $AlCl_3$ and then of another into the pyrrole ring in the presence of $SnCl_4$ (Scheme 3).

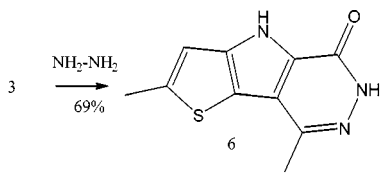
Scheme 3



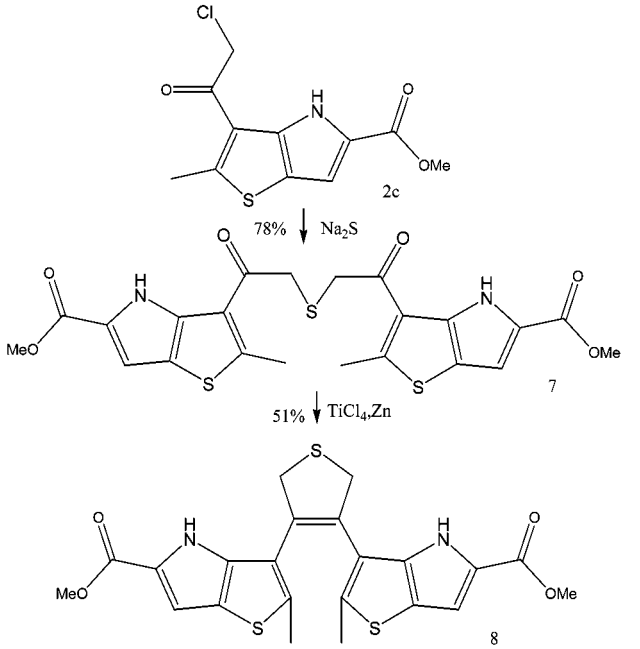
When compound (**3**) was used as the substrate, the second acylation did not occur.

We also investigated the possibility of acetylating the pyrrole nitrogen atom. The reaction was performed in the

Scheme 4



Scheme 5



presence of different bases, and the highest yield of the corresponding amide (**5**) was achieved for potassium *tert*-butylate. As should be expected, even trace amounts of this compound are absent from the acylation products of thienopyrrole **1a** under the Friedel−Crafts conditions. However, when amide **5** is acylated in the presence of $AlCl_3$, only ketone **2a** is formed instead of the corresponding diacyl derivative.

The structure of the obtained compounds was proved from the ^1H and ^{13}C NMR spectra of compounds **1b**,**c** and acylation products of thienopyrrole and chemical transformations (Scheme 4).

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Thus, we showed the possibility of the regioselective introduction of acyl groups into different positions of thienopyrrole **1a**.

For the first time, we synthesized photochromic 1,2-dihetarylethene (**8**) in which thienopyrrole fragments are linked by the tetrahydrothiophene. The transformations were carried out by analogy to a described procedure[5] (Scheme 5).

The photochromic properties of compound **8** were studied in an acetonitrile solution. Compound **8** (Figure 1) exhibits

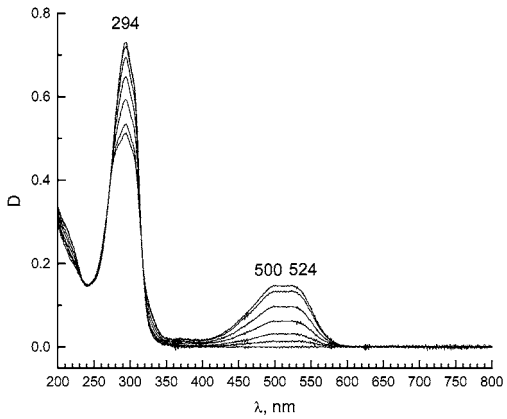

Figure 1. Absorption spectra of **8** and in the photostationary state under irradiation with 254 nm light.

typical photochromic properties and undergoes at least 20 cycles of the photoinduced transition from the open form 1A to the cyclic form 1B and back. Without irradiation (in the dark), the cyclic form of compound **8** is stable for at least 200 h.

Supporting Information Available: Procedures for synthesis of acylthienopyrroles and photochromic 1,2-dihetarylethene. This material is available free of charge via the Internet at http://pubs.acs.org.

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