

## Synthesis and Structure of Unsymmetrical Cross-Conjugated Dienones with Thienyl Substituents

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**Abstract**—By condensation of thiophenecarbaldehyde and *m*-nitrobenzaldehyde with furyl-, thienylmethylene-cyclohexanones in basic medium 2-(het)arylmethylene-6-thienylmethylene-cyclohexanones were prepared. Under the conditions of acid catalysis analogously built dienones were synthesized containing 5-nitrothiophene fragment. Based on the data of IR and <sup>1</sup>H NMR spectroscopy their *E,E*-configuration was established.

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Nowadays the chemistry of symmetric dienone derivatives of cyclic ketones is sufficiently well documented, and the opportunities are presented for practical applications of these compounds to the synthesis of biologically active substances [1], new polymer materials [2], and other practically useful compounds [3].

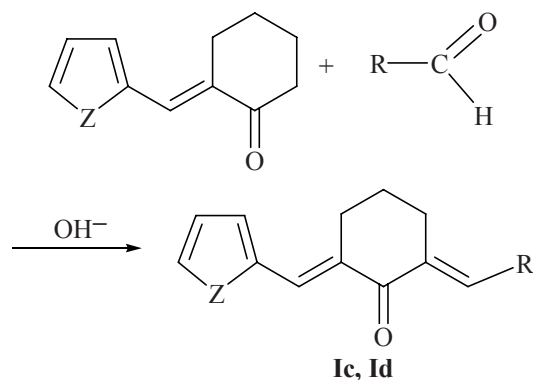
Their unsymmetrical analogs with different substituents in the  $\alpha$ -positions to the carbonyl group are less understood. The introduction into the structure of these compounds of heterocyclic fragments creates additional and unequal reaction sites calling for establishment of the regiodirection of reactions and extending the range of their applications.

We formerly reported on the synthesis of 6-arylmethylene-2-furylmethylenecyclohexanones [4] and on the regiospecificity of their reactions with hydrazines leading to the formation of *trans*-3-arylmethylene-7-furylmethylene-3,3a,4,5,6,7-NH(Ph)-hexahydroindazoles [5]. In extension of these studies and in order to evaluate the effect of the nature of the heterocyclic substituent on the stereo- and regiochemistry of reactions with binucleophilic reagents we carried out a synthesis of thienyl-substituted cross-conjugated dienones of the analogous structure and of dienone with two heteryl substituents (furyl and thienyl).

It was formerly reported [6] on preparation of 2-thienylmethylene-6-phenylmethylenecyclohexanone (**1a**) and 2-thienylmethylene-6-(4-methoxyphenylmethylene)-cyclohexanone (**1b**). Here we discuss the structure and

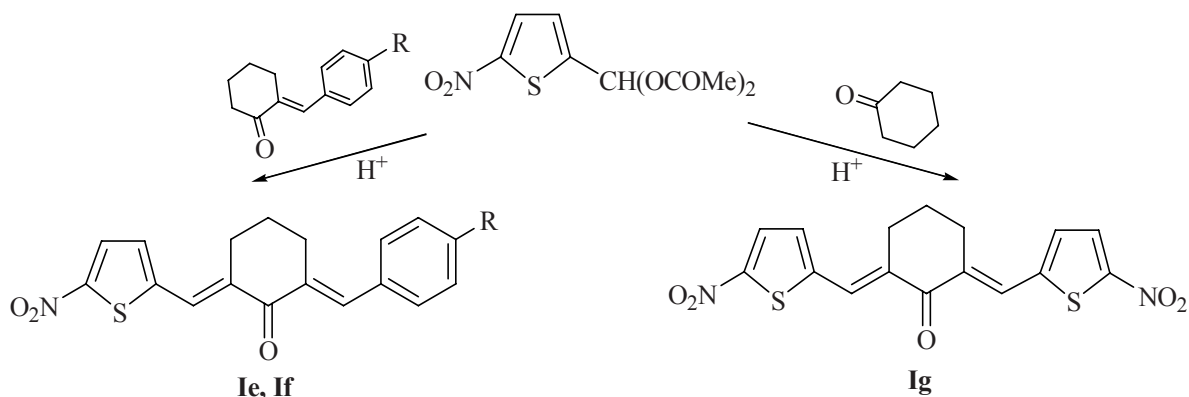
describe the synthesis of new thienyl(5-nitrothienyl)-methylene-containing cyclohexanones **1c–1g** by crotonic condensation under conditions of acid or base catalysis.

2-Thienylmethylene-6-(3-nitrophenylmethylene)-cyclohexanone (**1c**) and 2-thienylmethylene-6-furylmethylene-cyclohexanone (**1d**) were obtained in high yields (92 and 85% respectively) by the condensation of hetarylmethylenecyclohexanones with thiophenecarbaldehyde and 3-nitrobenzaldehyde in alkaline medium.



Z = S, R = Ph (**a**), 4-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub> (**b**), 3-NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub> (**c**);  
Z = O, R = 2-thienyl (**d**).

The use as a carbonyl component of 5-nitrothiophenecarbaldehyde in the alkaline medium proved to be impossible because of strong tarring of the reaction mixture. 5-Nitrothienyl-substituted dienones **1e–1g** we synthesized under conditions of the acid catalysis (glacial acetic acid with addition of concn. H<sub>2</sub>SO<sub>4</sub>) employing



R = H (**e**), 4-OMe (**f**).

as the carbonyl component a commercial product, 5-nitrothiophenecarbaldehyde diacetate that under the reaction conditions readily hydrolyzed to the corresponding aldehyde.

Symmetric dienone **1g** has a higher melting point (by 40–90°C) compared with unsymmetrical analogs **1a–1f** evidently because of tighter packing of molecules in the crystal. We synthesized the compound as a model for assigning the vinyl protons in the  $^1\text{H}$  NMR spectra.

The thin-layer chromatography indicated that in all cases individual compounds were obtained.

The IR spectra of thienyl-containing dienones **1a–1g** like the furan analogs [4] contain absorption bands at 1674–1655 and 1597–1558  $\text{cm}^{-1}$  characteristic of the conjugated system of the carbonyl group and ethylene bonds. The presence of bands of out-of-plane bending vibrations of the C=C–H bond at 968–984  $\text{cm}^{-1}$  indicates the location of substituents and the carbonyl group on the different sides of the ethylene bond [7, 8]; thus the dienones have *E,E*-configuration.

$^1\text{H}$  NMR spectra are in agreement with the assumed structure of the obtained compounds. It should only be emphasized that the chemical shifts of vinyl protons are close for the structures =CH–Ar and =CH–Ht. However the analysis of the obtained spectral findings with the use of published data (for 2,6-dithienylmethylene-cyclohexanone [9]) and our earlier results [4] permitted some conclusions.

The position of the vinyl proton signal (7.83 ppm) in the spectrum of symmetric ketone 2,6-bis(5-nitrothienylmethylene)cyclohexanone (**1g**) is conserved also in the spectra of unsymmetrical analogs containing the 5-nitrothienylmethylene fragment (7.81–7.83 ppm). In thienyl-containing ketones **1a–1d** this signal is shifted downfield (7.97–8.02 ppm). The chemical shifts of vinyl protons

in the substituents comparable in the electron-donor characteristics (ketone **1e**) are virtually identical (7.81 and 7.82 ppm).

The signal of the arylmethylene proton (=CH–Ar) is located slightly upfield (7.77–7.79 ppm) compared with the (nitro)thienylmethylene one (=CH–Ht); therewith the electron-donor 4-OMe group (compounds **1b** and **1f**) and electron-acceptor 3-NO<sub>2</sub> group (compound **1c**) practically do not affect its position (7.77, 7.79, and 7.79 ppm respectively). The proton signals of the alicycle appear as multiplets (1.79–2.09 ppm, 2H, at C<sup>4</sup>; 2.83–3.03 ppm, 4H, at C<sup>3</sup>, C<sup>5</sup>).

We plan further to study the reactions of the newly synthesized dienones with hydrazines and establish their regiodirection.

## EXPERIMENTAL

$^1\text{H}$  NMR spectra of compounds **1a–1g** were registered on a spectrometer Bruker AC-400 (400 MHz) in CDCl<sub>3</sub>, internal reference TMS. IR spectra were recorded on an infrared Fourier spectrometer FSM-1201. The reaction progress was monitored and the purity of compounds obtained was checked by TLC on Silufol UV-254 plates, eluent hexane–diisopropyl ether–chloroform, 3:1:1, spots visualized in iodine vapor or under UV irradiation. Melting points were determined in unsealed capillaries.

Compounds **1a** and **1b** were described in [6].

**(E,E)-2-Thienylmethylene-6-phenylmethylene-cyclohexanone (1a).**  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.79–2.03 m (2H, CH<sub>2</sub>), 2.85–2.99 m (4H, CH<sub>2</sub>), 7.25 d (1H, H<sub>Th</sub><sup>β</sup>, *J* 4.0 Hz), 7.16 d (1H, H<sub>Th</sub><sup>β'</sup>, *J* 4.0 Hz), 7.31–7.58 m (6H, H<sub>Th</sub><sup>α</sup>, Ph), 7.81 s (1H, =CH–Ph), 8.01 s (1H, =CH–Th).

**(E,E)-2-Thienylmethylene-6-(4-methoxyphenylmethylene)cyclohexanone (1b).**  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.67–1.94 m (2H, CH<sub>2</sub>), 2.83–2.98 m (4H, CH<sub>2</sub>),

3.84 s (1H, CH<sub>3</sub>), 6.93 d (2H, H<sup>m</sup><sub>Ph</sub>, *J* 8.7 Hz), 7.47 d (2H, H<sup>o</sup><sub>Ph</sub>, *J* 8.7 Hz), 7.55 m (1H, H<sup>α</sup><sub>Th</sub>), 7.23 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.2 Hz), 7.14 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.2 Hz), 7.77 C (1H, =CH–Ar), 7.98 s (1H, =CH–Th).

**(E,E)-2-Thienylmethylene-6-(3-nitrophenylmethylene)cyclohexanone (Ic).** In 20 ml of 2-propanol was dissolved 2 g (10.4 mmol) of thienylmethylene-cyclohexanone and 1.58 g (10.4 mmol) of 3-nitrobenzaldehyde and to the solution was added dropwise 5 ml of 20% NaOH solution. Yield 3.11 g (92%), yellow crystals, mp 145–146°C (from 2-propanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3157 [CH(Th)], 753–695 (C–S), 3080 [CH(Ph)], 2953 (CH<sub>2<sub>as</sub></sub>), 2866 (CH<sub>2<sub>s</sub></sub>), 1524 (NO<sub>2<sub>as</sub></sub>), 1346 (NO<sub>2<sub>s</sub></sub>), 1655 (C=O), 1600 (C=C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.88–1.94 m (2H, CH<sub>2</sub>), 2.89–2.96 m (4H, CH<sub>2</sub>), 7.16 m (1H, H<sup>β</sup><sub>Th</sub>), 7.41 m (1H, H<sup>m</sup><sub>Ph</sub>), 7.72 d (1H, H<sup>o</sup><sub>Ph</sub>, *J* 8.0 Hz), 8.18 d (H<sup>p</sup><sub>Ph</sub>, *J* 8.0 Hz), 8.28 s (1H, H<sup>o</sup><sub>Ph</sub>), 7.56–7.78 m (2H, H<sup>β</sup><sub>Th</sub>, H<sup>α</sup><sub>Th</sub>), 7.79 s (1H, =CH–Ar), 8.02 s (1H, =CH–Th). Found, %: C 66.42; H 5.03; N 4.32; S 9.66. C<sub>18</sub>H<sub>15</sub>NSO<sub>3</sub>. Calculated, %: C 66.46; H 4.61; N 4.31; S 9.85.

**(E,E)-2-Thienylmethylene-6-furylmethylene-cyclohexanone (Id)** was prepared similarly to compound **Ic**. Yield 1.47 g (85%), yellow crystals, mp 132°C (from 2-propanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3115 [CH(Th)], 752–722 (C–S), 3080, 3028 [CH(Ph)], 2938 (CH<sub>2<sub>as</sub></sub>), 2832 (CH<sub>2<sub>s</sub></sub>), 1024 [C–O–C(Fu)], 1645 (C=O), 1589 (C=C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.88–1.95 m (2H, CH<sub>2</sub>), 2.89–3.03 m (4H, CH<sub>2</sub>), 6.50 m (1H, H<sup>β</sup><sub>Fu</sub>), 6.67 d (1H, H<sup>β</sup><sub>Fu</sub>, *J* 4.0 Hz), 7.13 m (1H, H<sup>β</sup><sub>Th</sub>), 7.36 d (H<sup>α</sup><sub>Fu</sub>, *J* 4.0 Hz), 7.52 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.8 Hz), 7.55 br.s (2H, H<sup>α</sup><sub>Th</sub>, =CH–Fu), 7.97 s (1H, =CH–Th). Found, %: C 71.59; H 5.67; S 11.36. C<sub>16</sub>H<sub>14</sub>SO<sub>2</sub>. Calculated, %: C 71.11; H 5.18; S 11.85.

**(E,E)-2-(5-Nitrothienylmethylene)-6-phenylmethylene-cyclohexanone (Ie).** In 15 ml of acetic acid was dissolved 3 g (11.6 mmol) of 5-nitrothiophenecarbaldehyde diacetate and 2.16 g (11.6 mmol) of 2-phenylmethylene-cyclohexanone, to the solution was added 1 ml of water and 1–2 drops of concn. H<sub>2</sub>SO<sub>4</sub>. Yield 2.35 g (62%), dark-yellow crystals, mp 158–159°C (from acetic acid and 2-propanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3108 [CH(Th)], 773–696 (C–S), 3080, 3028 [CH(Ph)], 2957 (CH<sub>2<sub>as</sub></sub>), 2900 (CH<sub>2<sub>s</sub></sub>), 1526 (PO<sub>2<sub>as</sub></sub>), 1342 (PO<sub>2<sub>s</sub></sub>), 1660 (C=O), 1572 (C=C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.83–1.94 m (2H, CH<sub>2</sub>), 2.89–2.95 m (4H, CH<sub>2</sub>), 7.24 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.0 Hz), 7.34–7.45 m (5H, Ph), 7.82 br.s (2H, =CH–Ph, =CH–Th), 7.92 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.0 Hz). Found, %: C 66.02; H 4.49; N 4.24; S 9.59. C<sub>18</sub>H<sub>15</sub>NSO<sub>3</sub>. Calculated, %: C 66.46; H 4.61; N 4.31; S 9.85.

**(E,E)-2-(5-Nitrothienylmethylene)-6-(4-methoxyphenylmethylene)cyclohexanone (If)** was prepared similarly to compound **Ie**. Yield 2.35 g (63%), dark-yellow crystals, mp 162–163°C (from acetic acid and 2-propanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3113 [CH(Th)], 756–722 (C–S), 3016, 3090 [CH(Ph)], 2957 (CH<sub>2<sub>as</sub></sub>), 2841 (CH<sub>2<sub>s</sub></sub>), 1530 (PO<sub>2<sub>as</sub></sub>), 1342 (PO<sub>2<sub>s</sub></sub>), 1662 (C=O), 1570 (C=C), 2889 (CH<sub>3<sub>s</sub></sub>), 1256 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.91–1.94 m (2H, CH<sub>2</sub>), 2.90–2.96 m (4H, CH<sub>2</sub>), 3.85 s (1H, CH<sub>3</sub>), 6.94 d (2H, H<sup>m</sup><sub>Ph</sub>, *J* 8.4 Hz), 7.24 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.4 Hz), 7.45 d (2H, H<sup>o</sup><sub>Ph</sub>, *J* 8.4 Hz), 7.79 s (1H, =CH–Ar), 7.82 s (1H, =CH–Th), 7.92 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.4 Hz). Found, %: C 64.55; H 5.02; N 3.91; S 8.38. C<sub>19</sub>H<sub>17</sub>NSO<sub>4</sub>. Calculated, %: C 64.22; H 4.79; N 3.94; S 9.01.

**(E,E)-2,6-Bis(5-nitrothienylmethylene)cyclohexanone (Ig)** was prepared similarly to compound **Ie**. Yield 5.29 g (35%), brown crystals, mp 225–227°C (from acetic acid and 2-propanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3113 [CH(Th)], 764–731 (C–S), 3080, 3028 [CH(Ph)], 2953 (CH<sub>2<sub>as</sub></sub>), 2870 (CH<sub>2<sub>s</sub></sub>), 1519 (PO<sub>2<sub>as</sub></sub>), 1334 (PO<sub>2<sub>s</sub></sub>), 1662 (C=O). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.04–2.09 m (2H, CH<sub>2</sub>), 2.95–2.98 m (4H, CH<sub>2</sub>), 7.27 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.0 Hz), 7.83 s (2H, =CH–Th), 7.93 d (1H, H<sup>β</sup><sub>Th</sub>, *J* 4.0 Hz). Found, %: C 51.31; H 3.29; N 7.60; S 17.15. C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>S<sub>2</sub>O<sub>5</sub>. Calculated, %: C 51.06; H 3.19; N 7.45; S 17.02.

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