2,2-DIMETHYL-5-(5-R-2-FURFURYLIDENE)-1,3-DIOXANE-4,6-DIONES.

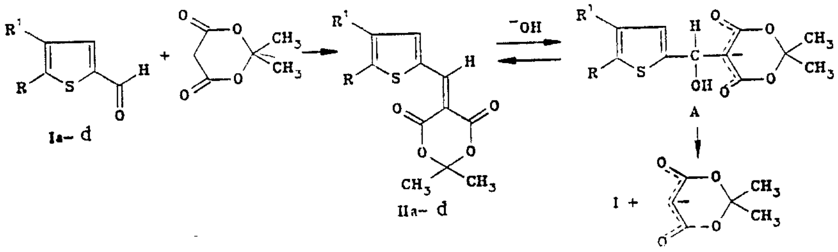
4.* SYNTHESIS, STEREOSTRUCTURES, AND PROPERTIES OF THIOPHENE ANALOGS

G. D. Krapivin, V. G. Kul'nevich,
and N. I. Val'ter

UDC 547.7.841'734.07:541.634:543.422.25

The reaction of 2-formylthiophenes with Meldrum's acid gave the corresponding thenylidenedioxanediones, which, in contrast to the furfurylidene derivatives, have an s-trans conformation of the mutual orientation of the thiophene ring and the exocyclic double bond. Thenyldioxanediones were synthesized by the selective hydrogenation of the exocyclic double bond.

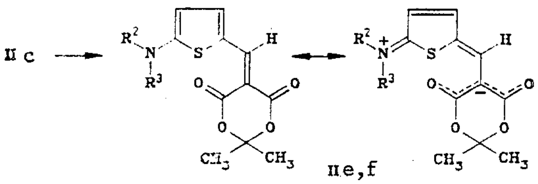
It has been shown [2] that furan aldehydes react with 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid) under mild conditions. These conditions were also used for the synthesis of thenylidene derivatives IIa-d, which were isolated in rather high yields in the form of colored crystals when the reaction mixtures were cooled (Table 1).



I, II a $R=R^1=H$; b $R=C_2H_5$, $R^1=H$; c $R=Br$, $R^1=H$; d $R=R^1=Br$

"Hard" nucleophiles ($^{-}$OH, $^{-}$OR) add reversibly to the α-carbon atom of the exocyclic double bond. However, attempts to determine the pK_a values of II were unsuccessful; in aqueous solutions with pH > 7, II decomposes rapidly to the anion of Meldrum's acid and the corresponding 2-formylthiophene I.

"Soft" nucleophiles smoothly replace halogen atoms in the 5 (but not the 4!) position of the thiophene ring of IIc, d. In particular, the corresponding amino derivatives IIe, f were obtained by the reaction of bromo derivative IIc with a twofold excess of dimethylamine or morpholine.



II e $R^2=R^3=CH_3$; f $R^2+R^3=(CH_2CH_2)_2O$

The electronic absorption spectra (Table 1) of the thenylidenedioxanediones are similar to the spectra of the corresponding furan derivatives. The differences between the wavelengths of the maxima of the K bands of IIa-f and their furan analogs are 0, −10, −3, 2, 15, and 3 nm, respectively.

---

*See [1] for Communication 3.

Krasnodar Polytechnical Institute, Krasnodar 350680. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1338-1342, October, 1989. Original article submitted February 23, 1988.

0009-3122/89/2510-1118$12.50

TABLE 1. Characteristics of II and III

Compound	Empirical formula	mp, °C	UV spectrum (ethanol), λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		Yield, %
				ν_{CO}^{s}	ν_{CO}^{as}	
IIa	$C_{11}H_{10}O_4S$	190...191 [3, 4]	264 (3,76), 313 (3,80), 364 (4,26)	1720	1750	93
IIb	$C_{13}H_{14}O_4S$	78...79	265 (3,83), 310 (3,70), 386 (4,38)	1708	1740	98
IIc	$C_{11}H_9BrO_4S$	130...131	207 (4,32), 259 (4,00), 307 (3,86), 376 (4,66)	1721	1755	95
IId	$C_{11}H_8Br_2O_4S$	180...182	258 (4,14), 316 (3,59), 382 (3,99)	1720	1755	86
IIe	$C_{13}H_{15}NO_4S$	>180 (dec.)	265 (4,17), 471 (4,76)	1690	1710	75
IIf	$C_{15}H_{17}NO_5S$	220...221	266 (4,03), 467 (4,92)	1680	1715	60
IIIa	$C_{11}H_{12}O_4S$	97...98	244 (3,98), 269 (4,25)	1741	1776	98
IIIb	$C_{13}H_{16}O_4S$	77...79	269 (4,25)	1750	1792	93
IIIc	$C_{11}H_{11}BrO_4S$	96...97	267 (4,27)	1746	1796	98
IIId	$C_{11}H_{10}Br_2O_4S$	129...130	262 (4,23)	1750	1795	96

Compounds IIa-d have broad ($\Delta\nu_{1/2}$ ~ 4000 cm^{-1}), smooth, and symmetrical long-wave absorption bands that undergo a bathochromic shift with an increase in the polarity of the solvent (positive solvatochromism).

Amino derivatives IIe,f, like merocyanine dyes, have, in the visible region of the spectrum, a narrow ($\Delta\nu_{1/2}$ 1600 cm^{-1}) more intense band, on the shortwave slope of which one observes a second maximum (in the form of a shoulder) that is associated with a vibrational 0—1' transition. The latter, like the 0—0' transition, is polarized along the conjugation chain. (The absorption bands of 5-aminofurfurylidenedioxanediones also have a similar form [2].) The longwave absorption of IIe,f has negative solvatochromism; this is characteristic for compounds, the ground state of which is more polar than the excited state.

The IR spectra of thenylidene compounds II contain two bands of stretching vibrations of C=O groups – asymmetrical and symmetrical; the ν_{CO}^{s} band is approximately twice as intense as the ν_{CO}^{as} band (Table 1).

In previous communications [2, 5, 6] it has been demonstrated by PMR spectroscopy and x-ray diffraction analysis that furfurylidenedioxanediones have an s-cis conformation that is stabilized by conjugation and an intramolecular hydrogen bond between the furan 3-H proton and the oxygen atom of the more closely located carbonyl group. In the PMR spectra this shows up in the form of a paramagnetic anisotropic shift of the signal of the 3-H proton to the 8.3-8.9 ppm region; the constant of spin-spin coupling between the 4-H and α-H protons is 0.6-0.8 Hz [2, 5].

In the PMR spectra of thenylidene derivatives II (Table 2) the signal of the 3-H proton does not undergo an anisotropic shift and is located at 7.75-7.90 ppm; spin-spin coupling (SSC) between the 4-H and α-H protons also is not observed. On the other hand, the spectrum of unsubstituted thenylidene derivative IIa contains long-range SSC between the 5-H and α-H protons (J = 1.2 Hz), which constitutes evidence for a W_5-shaped orientation of the bonds between these rings, i.e., an s-transoid orientation of the thiophene ring and the exocyclic double bond. The low-temperature PMR spectra (−80°C) do not reveal broadening of the signals of the protons of the thiophene ring, and, consequently, in solution there is only one rotational conformer. The absence of a paramagnetic anisotropic effect of the carbonyl group on the 3-H proton and the existence of a long-range stereospecific SSC between the α-H and 5-H protons make it possible to conclude that II exist in the form of s-trans conformers. This difference in the conformational structures between the thenylidene and furfurylidene derivatives may be due to the possibility of specific intramolecular interaction beween the sulfur atom and the oxygen atom of the carbonyl group, which is apparently energically more favorable than the formation of an intramolecular hydrogen bond in 2,2-dimethyl-5-(5-R-furfurylidene)-1,3-dioxane-4,6-diones.

We have previously shown [2, 5] that the transfer of electron density in aminofurfurylidenedioxanedione molecules leads to an increase in the difference between the chemical shifts of the B protons of the furan ring and the constants of SSC between these rings.

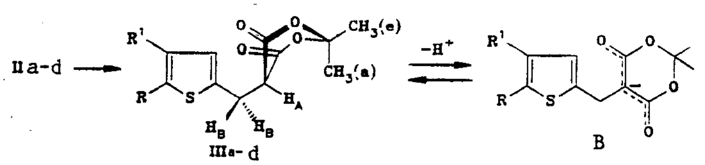
Only an increase in the difference in the chemical shifts of the B protons of the thiophene ring (from 0.6 ppm for IIa-d to 1.3 ppm for IIe,f; Table 2) is observed in the PMR spectra of aminothiophenes IIe,f.

TABLE 2. Spectra of II and III ($CDCl_3$)

Compound	Chemical shift, ppm, SSCC, Hz
IIa	1,68 (s, 6H, $C(CH_3)_2$); 7,17 (1H, 4-H); 7,80 (1H, 3-H); 7,87 (1H, 5-H); 8,56 (1H, α-H); $J_{3.4}=4.1$; $J_{4.5}=5,0$; $J_{3.5}=1.2$; $J_{\alpha 5}=1,2$; $J_{\alpha 3}=0,8$
IIb	1.30 (t, 3H, $J=7,5$, CH_2CH_3); 1.68 (s 6H, $C(CH_3)_2$); 2.88 (q, 2H, $J=7,5$, CH_2CH_3); 6,93 (1H, 4-H); 7,70 (1H, 3-H); 8,48 (1H, α-H); $J_{3,4}=4,0$; $J_{\alpha,3}==0,5$
IIc	1,67 (s, 6H, $C(CH_3)_2$); 7,37 (1H, 4-H); 7,90 (1H, 3-H); 8,48 (1H, α-H); $J_{3\,4}=4,2$; $J_{\alpha,3}=0,3$
IId	1.60 (s, 6H, $C(CH_3)_2$); 7,91 (d, 1H. 3-H); 8.37 (d 1H, α-H); $J_{\alpha,3}=0,4$
IIe	1,55 (s 6H, $C(CH_3)_2$); 3.25 (s 6H, $N(CH_3)_2$); 6,40 (d, 1H, 4-H); 7,75 (br., 1H, 3-H): 8,08 (s, 1H, α-H): $J_{3.4}=5.0$
IIf	1,55 (s 6H, $C(CH_3)_2$); 3.53 (m, 4H) and 3,73 (m, 4H) — $N(CH_2CH_2)O$; 6,48 (d 1H, 4-H): 7,75 (d 1H, 3-H): 8,12 (s 1H, α-H); $J_{3,4}=5,0$
IIIa	1,52 (s 3H, $CH_{3(e)}$): 1.68 (s 3H, $CH_{3(a)}$); 3.60 (2H, H_B); 3.73 (1H, H_A); $J_{AB}=5,4$; 6,87 (1H, 3-H); 6,88 (1H, 4-H); 7,27 (1H, 5-H); $J_{3,4}=2,0$; $J_{4,5}==4.6$; $J_{3.5}=1,6$
IIIb	1.18 (t 3H, $J=7,2$, CH_2CH_3); 1,50 (s, 3H, $CH_{3(e)}$); 1,67 (s 3H, $CH_{3(a)}$); 2,67 (q, 2H, $J=7.2$, CH_2CH_3): 3.52 (2H, H_B); 3,73 (1H, H_A); $J_{AB}=5,0$; 6,48 (d, 1H, 4-H); 6,67 (d, 1H, 3-H); $J_{3,4}=3,4$
IIIc	1,60 (s 3H. $CH_{3(e)}$); 1,70 (s 3H, $CH_{3(a)}$): 3,50 (2H, H_B); 3,77 (1H, H_A); $J_{AB}=4,8$; 6.67 (d, 1H, 3-H); 6,77 (d 1H, 4-H); $J_{3,4}=3,0$
IIId	1,63 (s, 3H. $CH_{3(e)}$); 1,72 (s, 3H, $CH_{3(a)}$); 3,48 (2H, H_B); 3,72 (1H, H_A); $J_{AB}=5,1$; 6,76 (s 1H, 3-H)

Let us also note the characteristic (but not stereospecific) SSC between the 3-H and α-H protons (^4J = 0.3-0.8 Hz), which is observed in both the spectra of thenylidene (Table 2) and furan [2, 5] derivatives.

The reaction of IIa-d with sodium borohydride in ethanol leads to selective hydrogenation of the exocyclic double bond (Table 1). Amino derivatives IIe,f do not undergo the reaction under these conditions.



The UV spectra of solutions of III (Table 1) in ethanol contain a broad absorption band at 260-270 nm of a π—π* transition in mesomeric ion B — the product of dissociation of monosubstituted Meldrum's CH acid. This band masks the less intense absorption of the thiophene ring at 230-240 nm. Only a band of the π—π* transition of the thiophene fragments of III molecules is observed in nondissociating solvents such as hexane and in acidic alcohol solutions.

Hydrogenation of the exocyclic C=C bond leads to a shift of both bands of the carbonyl absorption in the IR spectra of III to the high-frequency region of the spectrum (Table 1); this was also observed in the case of furfuryldioxanediones [6].

The PMR spectra of thenyldioxanediones III are similar to the spectra of the corresponding furfuryldioxanediones [6] and have (Table 2) two singlet signals of anisochronic protons of methyl groups of an isopropylidene link, a multiplet signal of the AB_2 system of the protons of the $CH—CH_2$ grouping, and signals of protons of a thiophene ring (and the substituent in it). Consequently, it may be assumed that thenyldioxanediones III have a stereostructure that is similar to the structure of furfuryldioxanediones [6]: the dioxane ring has a rigid boat conformation, the methyl groups are situated at axial and equatorial bonds (hence the nonequivalence of the signals of the protons of the methyl groups), and the thenyl substituent is situated at an equatorial bond in the plane of mirror symmetry of the dioxanedione ring.

It is most probable that the multiple bond of the thiophene ring is eclipsed by the saturated bond, as occurs in solutions of furfuryl derivatives [6] and other alkenes [7, 8].

The following conclusions can be drawn on the basis of a comparison of the results of the present research with the data in [1, 2, 5, 6]. Thenylidene- and furfurylidenedioxanediones have different conformations, viz., s-trans and s-cis, respectively. On the other hand, thenyl- and furfuryldioxanedione molecules have the same geometry, which is determined primarily by the conformation of the dioxanedione ring.

EXPERIMENTAL

The UV spectra of the compounds were recorded with a Specord UV-Vis spectrophotometer. The IR spectra were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ were recorded with a Tesla BS-467A spectrometer with hexamethyldisiloxane as the internal standard. The course of the reactions and the individuality of the synthesized compounds were monitored by means of TLC on Silufol UV-254 plates in a toluene–ethanol system (20:3).

The results of elementary analysis of II and III for C, H, and N were in agreement with the calculated values.

2,2-Dimethyl-5-(2-thenylidene)-1,3-dioxane-4,6-dione (IIa). A 1.12-g (10 mmole) sample of 2-formylthiophene and 1.44 g (10 mmole) of Meldrum's acid were dissolved in 40 ml of ethanol, three drops of triethylamine were added, and the mixture was allowed to stand at room temperature for 3 h.

Compounds IIb-d were similarly obtained.

2,2-Dimethyl-5-(5-N,N-dimethylamino-2-thenylidene)-1,3-dioxane-4,6-dione (IIe). A 0.7-g (2.2 mmole) sample of IIc was dissolved in 50 ml of ethanol, 0.66 g (4.4 mmole) of 30% aqueous dimethylamine was added, and the mixture was allowed to stand at room temperature for 5 h. The solvent was evaporated, and the residue was extracted with ether. The ether fractions were combined and dried over Na_2SO_4, the ether was removed, and the residual oil was crystallized by trituration with heptane.

Compound IIf was similarly obtained.

2,2-Dimethyl-5-(2-thenyl)-1,3-dioxane-4,6-dione (IIIa). Finely ground $NaBH_4$ was added in small portions (~100 mg) with vigorous stirring to a solution of 1.5 g (63 mmole) of IIa in 150 ml of ethanol until the color of the solution vanished, after which 50 g of crushed ice was added, and the aqueous mixture was acidified to pH ~ 5 with dilute HCl (1:10). The resulting colorless precipitate was washed with water and recrystallized from alcohol.

Compounds IIIb-d were similarly obtained.

LITERATURE CITED

1. G. D. Krapivin, V. E. Zavodnik, N. I. Val'ter, V. K. Bel'skii, and V. G. Kul'nevich, Khim. Geterotsikl. Soedin., No. 9, 1201 (1989).
2. G. D. Krapivin, V. G. Kul'nevich, and N. I. Val'ter, Khim. Geterotsikl. Soedin., No. 10, 1325 (1986).
3. P. Schuster, O. E. Polansky, and F. Wessely, Monatsh. Chem., 95, 53 (1964).
4. D. Vellemin, Chem. Ind., 478 (1983).
5. G. D. Krapivin, N. I. Val'ter, and V. G. Kul'nevich, Khim. Geterotsikl. Soedin.
6. G. D Krapivin, V. E. Zavodnik, V. K. Bel'skiii, N. I. Val'ter, and V. G. Kul'nevich, Khim. Geterotsikl. Soedin., No. 11, 1453 (1988).
7. E. E. Eliel, N. Allinger, S. Angyal, and H. Morrison, Conformational Analysis [Russian translation], Mir, Moscow (1969).
8. U. Burkert and N. Allinger, Molecular Mechanics [Russian translation], Mir, Moscow (1986).