

# Synthesis and Stereochemistry of Selected 2-Thienylethylene Derivatives

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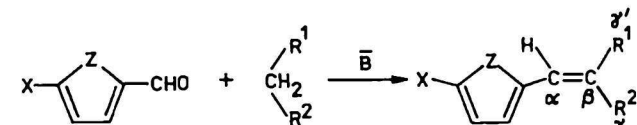
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The preparation of 5-X-2-thienylidene derivatives by Knoevenagel condensation method is described. The stereochemistry of target derivatives was studied by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectroscopy and the results were confronted with those obtained in the furan series.

The presented results supplement our earlier data on the stereochemistry of 2-furylethylene and some 2-thienylethylene derivatives [1–5].

The studied 5-X-2-thienylidene derivatives I–XIII have been prepared by the Knoevenagel condensation, using  $\beta$ -alanine as catalyst (Scheme 1), and the derivatives XIV and XV according to Ref. [6].



For I–XV Z = S,  
XVI–XX Z = O.

	X	R <sup>1</sup>	R <sup>2</sup>
I	NO <sub>2</sub>	COOEt	COOEt
II	NO <sub>2</sub>	COMe	COOEt
III	NO <sub>2</sub>	COMe	COMe
IV	NO <sub>2</sub>	CN	CN
V	NO <sub>2</sub>	CN	CQOMe
VI	Br	COOEt	COOEt
VII	Br	COMe	COOEt
VIII	Br	COMe	COMe
IX	Br	CN	CN
X	Br	CN	COOMe
XI	SO <sub>2</sub> —Ph	COOEt	COOEt
XII	SO <sub>2</sub> —Ph	COMe	COOEt
XIII	SO <sub>2</sub> —Ph	COMe	COMe
XIV	SO <sub>2</sub> —Ph	CN	CN
XV	SO <sub>2</sub> —Ph	CN	COOMe
XVI	NO <sub>2</sub>	COOEt	COOEt
XVII	NO <sub>2</sub>	COMe	COOEt
XVIII	NO <sub>2</sub>	COMe	COMe
XIX	NO <sub>2</sub>	CN	CN
XX	NO <sub>2</sub>	CN	COOMe

Scheme 1

The structures of the synthesized thienylidene compounds I–XV and furan analogues XVI–XX prepared according to [7, 8] were inferred from their respective IR, UV,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra (Tables 1–4). The stretching vibrations of carbonyl groups of 5-X-2-thienylidene derivatives were found at  $\tilde{\nu} = 1700\text{--}1715\text{ cm}^{-1}$ , those of C=C bonds at  $1600\text{--}1610\text{ cm}^{-1}$  (Table 1).

The IR spectra of the compounds II, VII, XII, and XVII displayed a complex band in the region of  $\tilde{\nu} = 1700\text{--}1715\text{ cm}^{-1}$ ; the band incorporated two distinct maxima and has been ascribed to the interaction of  $\nu(\text{C}=\text{O})$  of carbonyl and esters groups. The ultraviolet spectra of the title compounds displayed three or four absorption maxima (Table 1), the first one at  $\lambda = 200\text{--}210\text{ nm}$ , the second at  $216\text{--}270$  and the third one at  $276\text{--}300\text{ nm}$ . The fourth maximum extends to the visible part of the spectrum. The absorption maxima have been assigned to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  electron transitions localized in the thiophene ring, the phenylsulfonyl group and in the molecular orbital extending over the entire conjugated  $\pi$ -system.

The  $^1\text{H}$  NMR chemical shifts and coupling constants are given in Table 2. For a group of selected compounds  $^{13}\text{C}$  NMR spectra were taken and compared with those of the furan analogues (Tables 3 and 4).

The geometrical isomerism of trisubstituted ethylene derivatives was studied by  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral methods. Special attention was paid to the mutual position of the thiophene ring and the exocyclic double bond.

The preferred conformation of such ethylenic system was ascertained by analysis of  $^1\text{H}$  NMR long-range coupling constants between the heterocyclic H-4 proton and the alkenic H- $\alpha$  proton  $^5J_{4,\alpha}$ . The somewhat higher value of this constant (0.4–0.6 Hz) was in some furylethylene derivatives an indication for the preferred *s-cis* conformation, whereby the orientation of the furan ring depended on the character and position of substituents at the exocyclic double bond [2, 3, 5]. In the series of 5-X-2-thienylidene derivatives no interaction between H-4 and H- $\alpha$  was observed – a fact which seems to suggest that now the *s-trans* conformation may be preferred.

It has been established by  $^1\text{H}$  NMR spectra that compounds II, V, VII, X, XII, and XV exist as a mixture of Z- and E-isomers in the ratio 5 : 1. The differences in chemical shifts of alkenic protons in

**Table 1.** Characterization, IR and UV ( $\lambda/\text{nm}$ ,  $\epsilon/(\text{m}^2 \text{mol}^{-1})$ ) Spectral Data of 5-X-2-Thienylidene Derivatives

Compound	Formula $M_r$	$w_s(\text{calc.})/\%$ $w_s(\text{found})/\%$	M.p./ $^{\circ}\text{C}$ Yield/%	$\tilde{\nu}/\text{cm}^{-1}$				$\lambda_{\text{max}}$	$\lambda_{\text{max}}$	$\lambda_{\text{max}}$	$\lambda_{\text{max}}$
				$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{C})$	$\nu_s(\text{NO}_2)$	$\nu_{\text{as}}(\text{NO}_2)$	log $\epsilon$	log $\epsilon$	log $\epsilon$	log $\epsilon$
I	$\text{C}_{12}\text{H}_{13}\text{NO}_6\text{S}$ 299.3	10.70	82–84	1705	1610	1325	1510	208.3	255.1		355.9
		10.49	72					2.88	2.89		3.25
II	$\text{C}_{11}\text{H}_{11}\text{NO}_5\text{S}$ 269.26	11.89	108–109	1700	1605	1325	1510	207.5	253.2		357.1
		11.62	71					2.89	2.89		3.29
III	$\text{C}_{10}\text{H}_9\text{NO}_4\text{S}$ 239.26	13.39	130–131	1705	1605	1330	1510	206.6	247.5		359.7
		13.17	89					2.86	2.89		3.27
IV	$\text{C}_8\text{H}_3\text{N}_3\text{O}_2\text{S}$ 205.15	15.61	147–148	–	1600	1325	1500	206.6	254.5		359.7
		15.36	82					2.83	2.83		3.21
V	$\text{C}_9\text{H}_6\text{N}_2\text{O}_4\text{S}$ 238.22	13.44	136–137	1705	1605	1320	1505	204.5	257.1		363.6
		13.08	94					2.78	2.84		3.30
VI	$\text{C}_{12}\text{H}_{13}\text{BrO}_4\text{S}$ 333.2	9.61	62–63	1710	1605	–	–	206.2	268.1	298.5	–
		9.35	48					3.01	3.22	3.30	–
VII	$\text{C}_{11}\text{H}_{11}\text{BrO}_3\text{S}$ 303.18	10.56	78–80	1710	1610	–	–	200.2	264.6	–	333.3
		10.27	48					2.95	3.26	–	2.79
VIII	$\text{C}_{10}\text{H}_9\text{BrO}_2\text{S}$ 273.15	11.74	70–73	1710	1605	–	–	204.1	268.8	–	336.7
		11.52	51					3.05	3.14	–	3.40
IX	$\text{C}_8\text{H}_3\text{BrN}_2\text{S}$ 239.09	13.41	139–140	–	1610	–	–	202.4	223.2	281.7	357.1
		13.11	87					2.92	2.97	3.13	3.45
X	$\text{C}_9\text{H}_6\text{O}_2\text{BrNS}$ 272.12	11.78	134–135	1715	1610	–	–	204.1	216.5	284.9	354.6
		11.51	95					3.16	3.11	3.19	3.49
XI <sup>a</sup>	$\text{C}_{18}\text{H}_{18}\text{O}_6\text{S}_2$ 394.47	16.26	122–124	1715	1610	–	–	–	245.6	276.6	319.1
		16.03	58					–	3.23	3.34	3.31
XII <sup>a</sup>	$\text{C}_{17}\text{H}_{16}\text{O}_5\text{S}_2$ 364.44	17.60	174–175	1715	1605	–	–	–	247.2	278.1	321.5
		17.49	59					–	3.40	3.47	3.13
XIII <sup>a</sup>	$\text{C}_{16}\text{H}_{14}\text{O}_4\text{S}_2$ 334.41	19.18	153–154	1710	1605	–	–	–	245.8	276.9	322.7
		18.90	62					–	3.41	3.44	3.43

a) For XI–XIII  $\tilde{\nu}(\nu_s(\text{SO}_2)) = 1150, 1150, \text{ and } 1155 \text{ cm}^{-1}$ , respectively;  $\tilde{\nu}(\nu_{\text{as}}(\text{SO}_2)) = 1330 \text{ cm}^{-1}$ .

*E*- and *Z*-isomers are too small to allow meaningful application of additive increments method [9]

for calculation of chemical shifts of alkenic protons. The calculated difference between *E*- and

**Table 2.**  $^1\text{H}$  NMR Data ( $\delta$ ,  $J_{\text{C,H}}/\text{Hz}$ ) of Compounds I–XX

Compound	H-3 dd	H-4 d	H- $\alpha$ d	$\text{CH}_2$	$\text{CH}_3$	$J_{3,4}$	$J_{3,\alpha}$
I	7.63	8.04	7.88	4.42, 4.30	1.35, 1.30	4.3	0.6
( <i>Z</i> )-II	7.62	8.04	7.87	4.41	1.38, 2.44	4.3	0.6
( <i>E</i> )-II	7.61	8.02	7.82	4.41	1.33, 2.49	4.3	0.6
III	7.56	8.03	7.83	–	2.37, 2.47	4.3	0.6
IV	8.60	8.12	8.59	–	–	4.4	0.6
V	8.04	8.16	8.56	–	3.90	4.3	0.6
VI	7.42	7.08	7.76	4.37, 4.25	1.32, 1.28	4.0	0.6
VII	7.45	7.10	7.76	4.37	2.37, 2.45	4.0	0.6
VIII	7.34	7.05	7.68	–	2.33, 2.40	4.0	0.6
IX	7.85	7.34	8.39	–	–	4.2	0.6
X	7.88	7.31	8.42	–	–	4.2	0.6
XI	7.60	7.92	7.71	4.38, 4.30	–	4.1	0.5
XII	7.62	7.94	7.70	2.37 ( $\text{OCH}_3$ )	1.38, 2.44 ( $\text{OCH}_2\text{CH}_3$ )	4.1	0.5
XIII	7.58	7.93	7.75	2.35, 2.36 ( $\text{OCH}_3$ )	–	4.1	0.5
XIV	7.92	7.96	8.54	–	–	4.1	0.5
XV	8.0	7.90	8.51	–	3.87 ( $\text{OCH}_3$ )	4.1	0.5
XVI	7.34	7.75	7.63	4.38	1.28	3.9	0.4
XVII	7.31	7.77	7.70	2.40 ( $\text{OCH}_3$ ) 4.37	1.35	3.9	0.4
XVIII	7.24	7.74	7.55	2.41	2.39 ( $\text{OCH}_3$ )	3.9	0.4
XIX	7.46	7.62	7.64	–	–	3.9	0.4
XX	7.52	7.60	8.14	–	3.90 ( $\text{OCH}_3$ )	3.9	a

a) Unresolved, measured in  $\text{DMSO}-d_6$ . For XI–XV  $\delta(\text{H}_{\text{arom}}) = 7.65\text{--}8.25 \text{ m}$ .  $J_{4,\alpha}$  for I–XV = 0, XVI–XVIII 0.3, XIX, XX unresolved.

**Table 3.**  $^{13}\text{C}$  NMR Data ( $\delta$ ) of Compounds I–VI

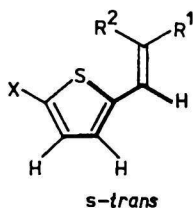
Compound	C-2	C-3	C-4	C-5	C- $\alpha$	C- $\beta$	C- $\gamma$	C- $\gamma'$	Other signals		
I	141.53	133.33	128.01	154.56	132.53	126.02	162.81	165.75	–		
(Z)-II	141.57	133.52	128.03	154.80	132.78	133.54	193.81	166.14	62.52	13.90	26.54
									(CH <sub>2</sub> )	(CH <sub>3</sub> )	(COCH <sub>3</sub> )
III	141.34	132.37	128.06	154.54	130.73	142.81	195.83	202.92	31.03	26.37	(CH <sub>3</sub> )
(E)-A	145.91	134.90	130.52	151.29	130.34	123.27	166.54	–			
IV	149.65	120.75	114.03	152.50	125.50	126.79	162.67	164.44			
(Z)-V	150.00	120.77	114.18	152.62	125.28	134.53	195.15	165.73			
VI	150.42	119.76	114.19	152.73	123.31	142.44	196.86	203.00			

A – 3-(5-nitro-2-thienyl)-2-propenoic acid, measured in DMSO-*d*<sub>6</sub>.

**Table 4.** Coupling Constants  $J_{\text{C,H}}$ /Hz of Compounds I–VI

Compound	C- $\gamma$ ,H- $\alpha$	C- $\gamma'$ ,H- $\alpha$	C-3,H-3	C-4,H-4	C- $\alpha$ ,H- $\alpha$	C- $\beta$ ,H- $\beta$	Other constants <sup>a</sup>				
I	7.8	10.7	175.4	178.9	159.8	3.9	4.8 (C-4,H-3), 3.9 (C-3,H-4), 12.7 (C-5,H-4)				
II	7.7	11.6	175.3	179.2	159.4	3.9	4.8 (C-4,H-3), 3.9 (C-3,H-4), 12.7 (C-5,H-4)				
III	7.8	10.7	174.8	178.2	159.2	3.9	4.8 (C-4,H-3), 3.9 (C-3,H-4), 12.7 (C-5,H-4)				
A	5.8	–	177.0	178.7	165.0	<i>b</i>	166.5 (C- $\beta$ ,H- $\beta$ )				
IV	7.8	10.7	184.6	188.5	166.0	<i>b</i>	–				
V	7.7	11.7	182.6	187.5	163.1	2.9	4.8 (C- $\alpha$ ,H- $\alpha$ )				
VI	7.7	10.7	184.6	188.5	165.0	<i>b</i>	5.8 (CO,CH <sub>3</sub> )				

a) For compounds IV–VI: 8.8 (C-2,H-3), (C-2,H-4), 2.9 (C-4,H-3), (C-3,H- $\alpha$ ); b) unresolved.



Z-isomers was  $\Delta\delta(\text{calc.}) = 0.38$ ;  $\Delta\delta(\text{exp}) = 0.05$ .

In case of derivative II the major isomer was unequivocally identified by the value of its vicinal coupling constant  $^3J_{\text{C,H}}$  which was compared with the data of other ethylene derivatives [4].

The assignment of carbon signals in  $^{13}\text{C}$  NMR spectra of selected derivatives was based on proton-coupled spectra and the respective  $^1J_{\text{C,H}}$  coupling constants. It was also supported by the characteristic splitting caused by long-range coupling and by comparison with the published data of other thiophene derivatives [10, 11].

## EXPERIMENTAL

Infrared spectra of the prepared compounds were measured using KBr discs (0.8 mg/300 mg of KBr) on the spectrometer RB-577 (Perkin) calibrated with a 25  $\mu\text{m}$  polystyrene film. Ultraviolet spectra of ethanolic solutions ( $c = 3 \times 10^{-5}$  mol  $\text{dm}^{-3}$ ) in 1 cm cells were recorded on Specord UV–VIS spectrometer (Zeiss, Jena). The  $^1\text{H}$  NMR spectral studies were performed with a 80 MHz spectrometer BS 487 C (Tesla) at 25 °C and with

tetramethylsilane as internal standard.  $^{13}\text{C}$  NMR spectra were recorded on the spectrometer FX-100 (Jeol) in 10 mm tubes, the measurements were performed in deuteriochloroform at 21 °C and 25.05 MHz. Spectral data of the compounds XIV–XX are in Ref. [6, 4, 8].

## 5-X-2-Thienylidene Derivatives I–XIII

To the solution of 5-X-2-thiophenecarbaldehyde (0.05 mol) dissolved in ethanol (30  $\text{cm}^3$ ) the component with the active methylene group (0.05 mol) was added, followed by the catalytic amount of  $\beta$ -alanine (10–30 mg) and enough water to dilute ethanol to 70 per cent. The reaction mixture was then stirred at laboratory temperature and progress of reaction monitored by TLC checks. After completion of the reaction the separated crystalline portion was filtered off and recrystallized from ethanol.

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## Interactions of $\beta$ -Cyclodextrin with 4-Alkylmorpholine *N*-Oxide Surfactants

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Interactions of  $\beta$ -cyclodextrin (CD) with nonionic surfactants of the 4-alkylmorpholine *N*-oxide type (alkyl = C<sub>9</sub>—C<sub>16</sub>) in aqueous solutions were investigated using the spectrophotometric method with methyl orange and the solubilization method, respectively. Results from both the methods confirmed that the process of surfactant association in aqueous solutions is affected by the formation of water-soluble CD surfactant inclusion complexes. In the presence of CD each phase of this process (*i.e.*: monomers, fractional micelle formation range, micellar zone) is shifted towards higher surfactant concentrations. The ratio  $\Delta\text{CMC}/c(\text{CD})$  expressing the measure of the CD surfactant interaction decreases with prolongation of the alkyl chain. It seems that the CD interacts with the alkyl chain of the surfactant molecule and not with its polar head group.

Several studies on inclusion complexes of organic molecules with cyclodextrin (CD) indicate that the cavity of CD forms in aqueous medium a hydrophobic environment [1—6].  $\beta$ -Cyclodextrin interacts with both ionic as well as nonionic surfactants containing an alkyl chain in their molecule, which is demonstrated *e.g.* by a shift in critical micellar concentration (CMC) of the surfactant to higher values [7—11]. The goal of our work was the study of interactions between  $\beta$ -cyclodextrin and a series of nonionic 4-alkylmorpholine *N*-oxide surfactants in aqueous solutions. The spectrophotometric method using methyl orange as well as the solubilization method were adopted for this study. The spectrophotometric method utilized the characteristic changes of the methyl orange absorbance values by inter-

action with the surfactants in molecular and associate state, respectively.

### EXPERIMENTAL

The homologous series of 4-alkylmorpholine *N*-oxides (alkyl = nonyl (I), decyl (II), undecyl (III), dodecyl (IV), tridecyl (V), tetradecyl (VI), pentadecyl (VII), and hexadecyl (VIII)) was synthesized according to [12].

$\beta$ -Cyclodextrin (CD) (Chinoin, Budapest), methyl orange (MO), and pyrene (Lachema, Brno) were used. Pyrene was purified by multiple crystallization from benzene.

For determination of the CMC of 4-alkylmorpholine *N*-oxides in aqueous solutions (pH approxi-