

Thiophene derivatives. II.*

α,β -Unsaturated ketones of phenylthiophene series

^aJ. KOVÁČ, ^aL. FIŠERA, and ^bR. FRIMM

^aDepartment of Organic Chemistry, Slovak Technical University,
880 37 Bratislava

^bResearch Institute of Drugs,
801 00 Bratislava

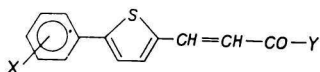
Received 3 February 1972

Accepted for publication 21 July 1972

The preparation is described of α,β -unsaturated ketones of the phenylthiophene series by condensation of 5-(X-phenyl)-2-thiophenecarbaldehydes ($X = 4\text{-NO}_2$, 4-Cl, 3-Cl, 4-Br, H, 4-CH₃, 3-CH₃, 4-OCH₃) with acetone, 2-acetylfuran, 2-acetylthiophene, and acetophenone. Infrared and ultraviolet spectra of the prepared derivatives are interpreted. The presence of individual conformers is discussed by means of the stretching vibrations of a carbonyl group and those of the C=C bonds.

Heterocyclic analogs of α,β -unsaturated ketones $R^1\text{—CH=CH—COR}^2$, where R^1 and R^2 are five-membered rings with one heteroatom (heterocyclic chalcone analogs) were the subject of many studies [1–6]. Chalcones of the phenylthiophene series are described in [7]; here the derivatives *V* and *XVII* were prepared by Claisen–Schmidt condensation of 5-phenyl-2-thiophenecarbaldehyde with ketones.

The modified Meerwein reaction [8] was used for arylation of 2-thiophenecarbaldehyde with substituted benzenediazonium salts. This reaction afforded substituted phenylthiophenecarbaldehydes, from which new α,β -unsaturated ketones of the phenylthiophene series were obtained by base-catalyzed condensation with acetone, 2-acetylfuran, 2-acetylthiophene, and acetophenone, respectively (Scheme 1).



Scheme 1

The papers on chalcones of the phenylfuran series reported certain anomalies concerning the conformation of these compounds [6, 21], which fact made the chalcones of phenylthiophene series interesting.

Experimental

Table 1 presents the synthesized compounds *I–XXIV* and their characterization. Tables 2–4 contain the spectral data. The i.r. spectra of *I–XIX* were recorded on a UR-20 Zeiss apparatus and those of *XX–XXIV* on a Unicam SP-100 instrument

* For Part I see Ref. [8].

in the 1800–1400 cm^{-1} region (concentration 0.01 mol l^{-1} in CHCl_3 and CCl_4). The calibration was done with a polystyrene foil 25 μm thick. Reading accuracy was $\pm 1 \text{ cm}^{-1}$. The u.v. spectra were obtained using a Specord UV VIS Zeiss spectrophotometer in 1-cm cells (concentration $10^{-5} \text{ mol l}^{-1}$ in methanol). CCl_4 , anal. grade, was used for measurements without further purification; CHCl_3 was dried by passing several times through the column filled with blue silica gel. Methanol, spectral grade, was employed.

3-*Y*-1-[5-(*X*-Phenyl)-2-thienyl]propene-3-ones (I–XIX)

To a mixture of 5-(*X*-phenyl)-2-thiophenecarbaldehyde (0.001 mole) and acetophenone (0.12 g; 0.001 mole), 2-acetylfuran (0.11 g; 0.001 mole), or 2-acetylthiophene (0.126 g; 0.001 mole) in ethanol 20% NaOH solution (0.2–0.4 ml) was added while boiling and stirring. After 2-hour stirring the reaction mixture was allowed to stand for 24 hours at room temperature. The separated solid was sucked off, washed with aqueous-alcoholic solution, and crystallized from ethanol.

1-[5-(*X*-Phenyl)-2-thienyl]-1-butene-3-ones (XX–XXIV)

To a mixture of the corresponding substituted 5-phenyl-2-thiophenecarbaldehyde (0.001 mole) in acetone (10 ml) and in water (10 ml) 33% NaOH solution (0.5 ml) was added at 10°C. After 4-hour vigorous shaking the solid was sucked off and crystallized from ethanol at room temperature.

Results and discussion

α,β -Unsaturated ketones and derivatives *V* and *XVII* described in [7] were prepared by the Claisen–Schmidt condensation. The obtained physical constants of the starting 5-phenyl-2-thiophenecarbaldehyde and of the two above-mentioned derivatives did not agree with the data reported; this supports the fact that the products described in literature and those prepared by us are not identical. When using the procedure described in [7] we found that the condensation did not take place, for the starting aldehydes were again obtained. This led us to the assumption that the mentioned authors prepared different compounds. To solve this contradiction we prepared 5-phenyl-2-thiophenecarbaldehyde by two methods [8].

Using benzaldehyde and 2-furancarbaldehyde for condensation [9], the so-called Michael adducts were isolated. In case the substituted 5-phenyl-2-thiophenecarbaldehydes were employed, the reaction proceeded under the same conditions as the Claisen–Schmidt condensation and the products of further addition were not separated. In the preparation of *X* and *XIV* (where *X* = 3- CH_3) an addition product was formed and a chalcone liberated on acidifying the reaction mixture with dilute acetic acid.

The i.r. spectra of the studied chalcone analogs of the phenylthiophene series show the intense absorption bands at 1688–1647 cm^{-1} assigned to the stretching vibrations of the carbonyl group (Table 2). With chalcones *VIII*, *IX*, *XI–XIV*, *XV–XIX*, where *Y* = 2-furyl or 2-thienyl in the solution of organic solvent, no splitting of the band belonging to the C=O stretching vibrations observed with chalcones [10] took place. ($\bar{\nu}(\text{C}=\text{O})$ 1670 and 1655 cm^{-1} in CCl_4 and 1665 and 1639 cm^{-1} in CHCl_3 .) The presence of two absorption bands in the carbonyl region of the spectrum points to the existence of 2 conformers (*s-cis* and *s-trans*).

As a result of interactions of the stretching vibrations of the C=O and C=C bonds the higher wavenumber is assigned to the *cis* conformer. In our case, where *Y* is 2-thienyl

Table 1

Characterization of the synthesized derivatives

Compound	X	Y	Formula	M	Calculated/found					Yield [%]	M.p. [°C]
					% C	% S	% H	% Hal	% N		
I	4-NO ₂	Phenyl	C ₁₉ H ₁₃ O ₃ NS	335.1	68.12 68.03	9.58 9.56	4.81 4.72	—	4.26 4.23	89.4	202—204
II	4-Cl	Phenyl	C ₁₉ H ₁₃ OSCl	324.3	68.57 68.77	9.85 9.87	4.01 4.10	10.91 10.82		78.2	152—153
III	3-Cl	Phenyl	C ₁₉ H ₁₃ OSCl	324.3	68.57 68.65	9.85 10.04	4.01 4.23	10.91 10.89		71	133—134
IV	4-Br	Phenyl	C ₁₉ H ₁₃ OSBr	368.2	61.98 62.05	8.64 8.88	3.54 3.78	21.6 21.31		81.6	166—167
V	H	Phenyl	C ₁₉ H ₁₄ OS	291.0	78.7 78.6	11.03 11.05	4.84 4.87			93	124—125*
VI	4-CH ₃	Phenyl	C ₂₀ H ₁₆ OS	304.1	79.10 79.05	10.52 10.58	5.27 5.33			83.2	137—138
VII	4-OCH ₃	Phenyl	C ₂₀ H ₁₆ O ₂ S	320.2	75.10 74.97	10.00 10.10	5.01 5.05			93.5	154—156
VIII	4-NO ₂	2-Furyl	C ₁₇ H ₁₁ NO ₄ S	325.3	62.82 62.87	9.83 9.92	3.41 3.58	—	4.31 4.40	55.4	222—223
IX	4-Cl	2-Furyl	C ₁₇ H ₁₁ ClO ₂ S	315.4	64.85 64.90	10.18 10.23	3.49 3.40	11.27 11.30		69.7	155—158
X	3-CH ₃	Phenyl	C ₂₀ H ₁₆ OS	304.1	79.10 79.31	10.52 10.41	5.27 5.15			38.1	202—205
XI	4-Br	2-Furyl	C ₁₇ H ₁₁ BrO ₂ S	359.9	56.71 56.83	8.95 9.00	3.09 3.00	22.28 22.25		69.5	159—160
XII	H	2-Furyl	C ₁₇ H ₁₂ SO ₂	281.2	72.4 72.12	11.4 11.36	4.27 4.37			65	118—120

Table 1 (Continued)

Compound	X	Y	Formula	M	Calculated/found					Yield [%]	M.p. [°C]
					% C	% S	% H	% Hal	% N		
<i>XIII</i>	4-CH ₃	2-Furyl	C ₁₈ H ₁₃ SO ₂	295.0	73.41 73.35	10.80 10.94	4.43 4.69			64.4	128—130
<i>XIV</i>	3-CH ₃	2-Furyl	C ₁₈ H ₁₃ SO ₂	295.0	73.41 73.42	10.80 10.85	4.43 4.69			52.8	89—91
<i>XV</i>	4-NO ₂	2-Thienyl	C ₁₇ H ₁₁ NO ₃ S ₂	341.3	59.82 60.10	18.77 18.66	3.22 3.41		4.11 4.05	58.6	184—186
<i>XVI</i>	4-Br	2-Thienyl	C ₁₇ H ₁₁ BrS ₂ O	375.9	54.31 54.25	17.08 17.13	2.93 3.07	21.38 21.20		61.2	181—183
<i>XVII</i>	H	2-Thienyl	C ₁₇ H ₁₂ S ₂ O	297.1	68.91 68.79	21.65 21.55	4.06 4.13			50.5	148—150 ^b
<i>XVIII</i>	3-Cl	2-Thienyl	C ₁₇ H ₁₁ ClS ₂ O	331.4	61.68 61.61	19.35 19.38	3.42 3.30	10.74 10.81		75.5	122—123
<i>XIX</i>	4-OCH ₃	2-Thienyl	C ₁₈ H ₁₃ S ₂ O ₂	327.0	66.25 66.31	19.67 19.79	4.31 4.48			58.1	147—148
<i>XX</i>	4-NO ₂	Methyl	C ₁₄ H ₁₁ NSO ₃	273.3	61.58 61.77	11.54 11.31	4.03 4.21			54.9	146—147
<i>XXI</i>	4-Br	Methyl	C ₁₄ H ₁₁ BrSO	307.2	55.09 55.21	10.43 10.39	3.69 3.80	26.05 25.95		91.4	139—140
<i>XXII</i>	H	Methyl	C ₁₄ H ₁₂ SO	228.3	73.75 73.62	14.02 13.94	5.27 5.21			52.6	129—130
<i>XXIII</i>	4-CH ₃	Methyl	C ₁₅ H ₁₃ SO	241.3	74.42 74.41	13.23 13.22	5.78 5.68			78.8	122—125
<i>XXIV</i>	3-Cl	Methyl	C ₁₄ H ₁₁ ClSO	262.7	63.94 64.05	12.21 12.43	4.19 4.08			51.8	91—93

a) Ref. [7] gives m.p. 110—111°C.*b*) Ref. [7] gives m.p. 137—141°C.

Table 2

Infrared spectral data of 3-Y-1-[5-(X-phenyl)-2-thienyl]propene-3-ones in CHCl_3

Compound	$\tilde{\nu}(\text{C}=\text{C})$ [cm^{-1}]	$\log T/T_0$	<i>s-cis</i>		<i>s-trans</i>	
			$\tilde{\nu}(\text{C}=\text{O})$ [cm^{-1}]	$\log T/T_0$	$\tilde{\nu}(\text{C}=\text{O})$ [cm^{-1}]	$\log T/T_0$
I	1596	0.9542	1667	0.7404	1645	0.4150
II	1594	0.9294	1665	0.7324	1641	0.4150
III	1595	0.9345	1663	0.7404	1640	0.3979
IV	1593	0.9294	1665	0.7243	1641	0.4150
	1602*	0.8372	1648	0.3979	1648	0.3979
V	1595	0.9294	1664	0.7324	1640	0.4314
	1606*	0.7781	1671	0.7404	1647	0.4150
VI	1594	0.9395	1663	0.7324	1639	0.4150
VII	1593	0.9494	1664	0.7243	1639	0.4150
VIII	1596	0.9678	1663	0.7634		
IX	1596	0.9685	1658	0.7993		
X	1607	0.8325	1666	0.6812	1644	0.4150
XI	1595	0.9685	1658	0.7993		
	1604*	0.8573	1666	0.8129		

* Measured in CCl_4 .

Table 2 (Continued)

Compound	$\tilde{\nu}(\text{C}=\text{C})$ [cm^{-1}]	$\log T/T_0$	$\tilde{\nu}(\text{C}=\text{O})$ [cm^{-1}]	$\log T/T_0$
XII	1594	0.9590	1667	0.8062
XIII	1594	0.9731	1658	0.8861
XIV	1594	0.8751	1657	0.6232
XV	1590	0.9243	1649	0.8129
XVI	1587	0.9542	1647	0.7708
XVII	1589	0.9395	1648	0.8195
XVIII	1590	0.8976	1648	0.7324
XIX	1585	0.8568	1647	0.6434

and 2-furyl only one band appeared, which showed the presence of one conformer. This fact may be accounted for by dipolar interactions between the carbonyl oxygen atom and the heteroatom of thiophene or furan ring. According to Bellamy [11] this kind of interaction may take place also with sulfur atoms; the appropriate heteroatom is not inevitably bound in α -position with regard to the carbonyl oxygen. These anomalies appeared also with the phenylfuran chalcone analogs [6]. The higher intensity of the bands belonging to the stretching vibrations of the $\text{C}=\text{C}$ bonds observed on the spectra of I–XIX when compared with the intensity of the $\text{C}=\text{O}$ bonds indicates that the compounds VIII–XIX exist only in the *s-cis* conformation [16], which predominates with the compounds I–VII.

As expected, the wavenumbers of the $\text{C}=\text{O}$ bonds measured in chloroform are by 7–8 cm^{-1} lower than those measured in tetrachloromethane. These small changes in wavenumbers may be explained by different solvation ability of the solvents used [11].

Table 3

Infrared spectral data of 1-[5-(X-phenyl)-2-thienyl]-1-butene-3-ones

Compound	<i>s-cis</i>		<i>s-trans</i>		<i>s-cis</i>		<i>s-trans</i>	
	$\bar{\nu}(\text{C=O})$ [cm ⁻¹]	log T/T_0	$\bar{\nu}(\text{C=O})$ [cm ⁻¹]	log T/T_0	$\bar{\nu}(\text{C=C})$ [cm ⁻¹]	log T/T_0	$\bar{\nu}(\text{C=C})$ [cm ⁻¹]	log T/T_0
Measured in CCl ₄								
XX	1698	0.2041	1678	0.2369	1611 sh	0.2041	1604	0.3763
XXI	1697	0.2817	1677	0.3213	1614	0.3110	1606	0.3213
XXII	1695	0.1664	1674	0.2202	1615	0.2041	1604	0.1664
XXIII	1693	0.1664	1674	0.2455	1612	0.2202	1604	0.2121
XXIV	1696	0.1184	1676	0.1737	1613 sh	0.1316	1604	0.1664
Measured in CHCl ₃								
XX	1688	0.1100	1671	0.1906	1610 sh	0.2787	1598	0.6255
XXI	1687	0.1326	1670	0.2374	1604	0.3623	1595	0.6021
XXII	1686	0.1174	1670	0.2276	1613	0.4494	1597	0.5006
XXIII	1685	0.0746	1668	0.1648	1612	0.3245	1595	0.3894
XXIV	1687 sh	0.0746	1669	0.1648	1612	0.2897	1597	0.5384

sh — shoulder.

Table 4
Ultraviolet spectral data of the synthesized derivatives

Compound	λ_{\max} [nm]	$\log \epsilon$	λ_{\max} [nm]	$\log \epsilon$	Compound	λ_{\max} [nm]	$\log \epsilon$	λ_{\max} [nm]	$\log \epsilon$
I	294	4.44	404	4.97	XIV	287	4.62	405	4.90
III	276	4.07	390	4.50	XV	316	4.88	388	4.98
IV	279	4.57	397	4.93	XVI	278	4.62	403	4.85
V	277	4.56	396	4.94	XVII	279	4.50	403	4.88
VI	279	4.54	404	4.90	XVIII	286	4.54	394	4.98
VII	284	4.66	415	4.99	XIX	300	4.53	410	4.85
VIII	303	4.62	409	4.98	XX	257	4.41	369	4.76
IX	285	4.41	403	4.90	XXI	260	4.76	372	5.75
	306	4.43							
XI	293	4.14	408	4.56	XXII	253	4.54	370	5.00
						290	4.17		
XII	304	4.46	405	4.91	XXIII	260	4.20	378	4.59
						298	4.04		
XIII	297	4.39	411	4.79	XXIV	310	4.59	368	4.66

With derivatives where $Y = 2\text{-furyl}$ or 2-thienyl the values of wavenumbers of the band of $\bar{\nu}(\text{C}=\text{O})$ decrease in comparison with phenyl derivatives. It is due to the conjugation of electron-donor heterocyclic rings with carbonyl group; on the oxygen of this group the electron density increases [12]. (*I-VII*: $\bar{\nu}(\text{C}=\text{O})$ 1667–1663 cm^{-1} ; *VIII-XIV*: 1658–1657 cm^{-1} ; and *XV-XX*: 1649–1647 cm^{-1} ; Table 2.) The wavenumber of the carbonyl group ($\Delta\bar{\nu}(\text{C}=\text{O}) \sim 1-4 \text{ cm}^{-1}$) is only little influenced by the substituent.

In the case of derivatives *I-VII* and *XX-XXIV* where Y is phenyl and CH_3 , respectively, the splitting of the bands corresponding to the stretching vibrations of the carbonyl group and those of the $\text{C}=\text{C}$ bonds was observed. This type of the band splitting often occurs with the carbonyl group-containing compounds [13, 18]. According to *Brown* [18] this splitting is caused by the presence of conformers; according to others [19] by the Fermi resonance. The differences in wavenumbers arisen by splitting of the band belonging to the stretching vibrations of the CO group are 16–18 cm^{-1} in chloroform and 19–21 cm^{-1} in tetrachloromethane. Therefore it cannot be assumed that this splitting is due to the addition of the *cis* isomer, in which case the differences in wavenumbers would be maximally 5–6 cm^{-1} [14]. The spectra of phenyl vinyl ketone, on which no geometrical isomers have been observed, reveal two absorption bands assigned to the stretching vibrations of the carbonyl group [15, 17]. The i.r. spectrum of *XXI* measured in KBr showed several bands belonging to $\text{C}=\text{C}$ and $\text{C}=\text{O}$ vibrations ($\bar{\nu}(\text{C}=\text{C})$ 1592 and 1617 cm^{-1} , $\bar{\nu}(\text{C}=\text{O})$ 1646 and 1668 cm^{-1}) and that of *XXII* in nujol ($\bar{\nu}(\text{C}=\text{C})$ 1591 (sh) and 1615 cm^{-1} and $\bar{\nu}(\text{C}=\text{O})$ 1640 and 1665 cm^{-1}). Since it is generally supposed that the α,β -unsaturated ketones may in the solid state exist only in the form of one conformer (although some authors [20] assume the formation of two conformers also in the solid phase), one could expect that two bands assigned to the stretching vibrations of the carbonyl group are due to the Fermi reaction. The presence of two $\bar{\nu}(\text{C}=\text{O})$ as well as of two $\bar{\nu}(\text{C}=\text{C})$ on the spectra of the compounds *I-VII* and *XX-XXIV* (Tables 3 and 4) cannot be explained by the Fermi resonance [10] but the existence of the two conformers (Scheme 2). This statement is supported by the shape of



Scheme 2

split bands which are very intensive. It has been known that with the five-membered heterocyclic chalcone analogs the splitting of the $\text{C}=\text{O}$ band may be found only in the cases when the methyl group has been attached to the carbonyl group. The existence of the two bands assigned to $\bar{\nu}(\text{C}=\text{O})$ points to the unambiguous orientation of a heterocyclic ring with regard to the carbonyl group.

It ensues from the first absorption band of the u.v. spectra (Table 4) in the range of longer wavelengths that with derivatives where Y is 2-furyl, the furan ring eliminates the effect of a substituent bound to the benzene ring and nitro group is of reverse character; the conjugated system is decreased (*XV*: λ_{max} 388 nm, *XVII*: λ_{max} 403 nm).

Acknowledgements. We are grateful to Dr K. Špírková and D. Horvátová for elementary analyses and to S. Markusová, N. Bakošová, and L. Livařová for taking the i.r. and u.v. spectra.

References

1. Tsukerman, S. V., Nikitchenko, V. M., and Lavrushin, V. F., *Zh. Obshch. Khim.* **32**, 2324 (1962).
2. Lavrushin, V. F., Tsukerman, S. V., and Artemenko, A. M., *Zh. Obshch. Khim.* **31**, 3037 (1961).
3. Lavrushin, V. F., Tsukerman, S. V., and Artemenko, A. M., *Zh. Obshch. Khim.* **32**, 1324 (1962).
4. Tsukerman, S. V., Chan Kuok Shon, and Lavrushin, V. F., *Zh. Obshch. Khim.* **34**, 2881 (1964).
5. Nikitchenko, V. M., Tsukerman, S. V., and Lavrushin, V. F., *Zh. Obshch. Khim.* **33**, 2563 (1963).
6. Frimm, R., Kováč, J., and Krutošíková, A., *Chem. Zvesti* **27**, 101 (1973).
7. Lipkin, A. E., Putokhin, N. I., and Borisov, S. I., *Khim. Geterotsykl. Soedin.* **1967**, 1020.
8. Frimm, R., Fišera, L., and Kováč, J., *Collect. Czech. Chem. Commun.* **38**, 1809 (1973).
9. Steinkopf, W. and Popp, W., *Justus Liebigs Ann. Chem.* **540**, 27 (1939).
10. Hayes, W. P. and Timmons, C. J., *Spectrochim. Acta* **24A**, 323 (1968).
11. Bellamy, L. J., *Advances in Infrared Group Frequencies*, p. 172. Methuen, 1968.
12. Tsukerman, S. V., Artemenko, A. M., Lavrushin, V. F., and Rozum, J. S., *Zh. Obshch. Khim.* **34**, 2309 (1964).
13. Zaitsev, B. E. and Sheiker, Yu. N., *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1962**, 408.
14. Kuhn, P. L., Lutz, C., and Bauer, R., *J. Amer. Chem. Soc.* **72**, 5058 (1950).
15. Kossany, J., *Bull. Soc. Chim. Fr.* **1965**, 704.
16. Aleksaian, M. V. and Sobolev, E. V., *Dokl. Akad. Nauk SSSR* **150**, 118 (1961).
17. Noack, K., *Spectrochim. Acta* **18**, 1625 (1962).
18. Brown, T., *J. Amer. Chem. Soc.* **80**, 3513 (1958).
19. Allen, G., Ellington, P., and Meaking, G., *J. Chem. Soc.* **1960**, 1909.
20. Hoyr, H. and Hensel, W., *Z. Elektrochem.* **64**, 958 (1960).
21. Frimm, R., Kováč, J., and Závodská, E., *Zborník prác Chemickotechnologickej fakulty SVŠT.* (Collection of Communications, Section Chemistry, Slovak Technical University.) P. 41, Bratislava, 1967.

Translated by A. Lukáčová