

THIOPHENE DERIVATIVES. I.

PREPARATION OF SUBSTITUTED 5-PHENYL-2-THIOPHENECARBALDEHYDES

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In the present paper the authors deal with the arylation of 2-thiophenecarbaldehyde with X-benzenediazonium salts (where X = 4-NO₂, 3-NO₂, 2-NO₂, 4-Br, 3-Br, 4-OCH₃, 4-CH₃, H, and 4-Cl) under conditions of a modified Meerwein reaction. Further, they describe the preparation of some substituted 5-phenyl-2-thiophenecarbaldehydes under conditions of a modified Vilsmeier reaction and interpret the infrared and ultraviolet spectra of the synthesised compounds.

The Meerwein reaction for arylation of α,β -unsaturated carbonyl compounds with benzenediazonium salts¹, also successfully applied for the arylation of furan derivatives²⁻⁹, was in the case of thiophenes only used to arylate β -2-thienylacrylic acid with *p*-nitrobenzenediazonium salt¹⁰ and thiophene with *o*-arsonophenyldiazonium salt¹¹. The arylation of 2-thiophenecarbaldehyde has not been described in the literature. In the present paper are given the arylation results of 2-thiophenecarbaldehyde by using the above method together with the most favourable reaction conditions. The substituted 5-phenyl-2-thiophenecarbaldehydes were also prepared by a modification of the Vilsmeier reaction.

From Table I it is to be seen that the substituent on the benzene ring affects appreciably the reaction yield. Diazonium salts with electron acceptor substituents give higher yields than those with electron donor substituents. In a preceding study⁷ we succeeded in the preparation of phenylfuranaldehydes with activating substituents by a modification of the Meerwein reaction, using extracting agents for separation the reaction products from the acid medium. In the present case the acid medium was adjusted by addition of sodium acetate. Under these conditions it was possible to prepare arylthiophenecarbaldehydes with activating substituents. In contrast to the arylation of 2-furanaldehyde, where the position of the substituent in respect to the diazo group does not affect the yield⁴, on arylation of 2-thiophenecarbaldehyde we noted an increasing yield in the order $o < m < p$ (I, II, III). These findings are in accord with the literature¹². The decrease of the diene character of the thiophene ring compared with that of the furan ring results in lower yields when arylating 2-thiophenecarbaldehyde^{4,7}.

As the most advantageous solvents have proved themselves acetone, methyl ethyl ketone, and acetonitrile. In these solvents the reaction takes place in a homogeneous medium. As catalyst were used divalent copper salts. For diazonium salts with electron donor substituents the amount of the catalyst had to be increased from 0.15 mol to 0.24 mol per 1 mol thiophenecarbaldehyde, and for halogen derivatives even to 0.28 mol (by using 0.15 mol catalyst the yield of compound *VIII* was 4.4% and by using 0.24 mol, 7.4%). With derivatives carrying electron acceptor substituents the reaction took place in strong acid medium and with derivatives carrying electron donor substituents at pH 3–4 in the presence of sodium acetate, in both cases at 40–55°C.

As the diazonium salts with electron donor substituents gave only small yields, we prepared more advantageously the corresponding 5-(X-phenyl)-2-thiophenecarbaldehydes (where X = H, 4-CH₃, and 4-OCH₃) from the 2-(X-phenyl)thiophenes using a modification of Vilsmeier's formylation reaction. The substituted 2-phenylthiophenes were prepared by the method of Gomberg and Bachman¹³.

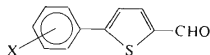
The data obtained by studying the infrared absorption spectra of the synthesised 5-(X-phenyl)-2-thiophenecarbaldehydes are listed in Table II. The 1687–1670 cm⁻¹ region shows very strong absorption bands characteristic for the carbonyl group.

TABLE I
Synthesised 5-(X-Phenyl)-2-thiophenecarbaldehydes

Number	Formula (mol.wt.)	Calculated/Found				M.p., °C yield (method) ^a
		% N(Hal)	% S	% C	% H	
<i>I</i>	C ₁₁ H ₇ NO ₃ S	6.01	13.73	56.70	3.03	149–150
4-NO ₂	(233)	6.11	13.71	56.78	3.00	24(A)
<i>II</i>	C ₁₁ H ₇ NO ₃ S	6.01	13.73	56.70	3.03	119–120
3-NO ₂	(233)	6.29	13.43	56.72	2.91	16(A)
<i>III</i>	C ₁₁ H ₇ NO ₃ S	6.01	13.73	56.70	3.03	107–107.5
2-NO ₂	(233)	5.94	13.75	56.81	2.88	11.2(A)
<i>IV</i>	C ₁₁ H ₇ BrOS	30.12	11.98	49.47	2.64	111–112
4-Br	(267.1)	30.37	12.00	49.61	2.81	25(A), 47(C)
<i>VI</i>	C ₁₁ H ₇ BrOS	30.12	11.98	49.47	2.64	103–105 ^b
3-Br	(267.1)	30.21	11.77	49.58	2.60	19(A)
<i>VII</i>	C ₁₂ H ₁₀ OS	—	15.84	71.23	4.97	85–87
4-CH ₃	(202.3)	—	15.78	71.46	5.09	6.7(B) ^a , 35.5(C)
<i>IX</i>	C ₁₂ H ₁₀ O ₂ S	—	14.68	66.01	4.61	119–120
4-OCH ₃	(218.3)	—	14.64	66.15	4.38	11.4(B) ^a , 36.2(C)

^a Yields by method *A* and *B* are calculated on the reacted 2-thiophenecarbaldehyde. *V* Yield by method *A* 23%, by method *C* 37%; m.p. in accord with the literature¹⁷. *VIII* Yield by method *B* 7.4%, by method *C* 51.8%; m.p. in accord with the literature¹⁸. Compounds *I*–*IX* were crystallised from ethanol; compounds *VII* and *VIII* can be steam-distilled. ^b B.p. at 12 Torr.

The wave number of the carbonyl group depends on the nature of the substituent. In the $980\text{--}850\text{ cm}^{-1}$ and $1115\text{--}1065\text{ cm}^{-1}$ regions appear absorption bands of medium intensity which can be assigned to the deformation vibrations of the C—H bonds¹⁴. The stretching vibrations of the C—C and C—S bonds¹⁴ are in the



$1358\text{--}1350\text{ cm}^{-1}$, $1460\text{--}1427\text{ cm}^{-1}$, and $1621\text{--}1590\text{ cm}^{-1}$ regions. As expected, the frequencies of the bonds of the nitro group in compound *III* are observed at higher values than in compound *I*. The higher values for the nitro group in compound *III* than in compound *I* can be explained by the non-coplanar structure of the *ortho*-

TABLE II
Values of Ultraviolet (λ_{\max} nm) and Infrared Spectra (cm^{-1}) of 5-(X-Phenyl)-2-thiophene-carbaldehydes

Num-ber	λ_{\max}	$\log \epsilon$	$\frac{J(\text{CH})}{\beta(\text{CH})}$	$\tilde{\nu}(\text{C—C})(\text{C—S})$	$\tilde{\nu}(\text{C=O})$
<i>I</i> ^a	311	4.16	903 (13)	1 457 (26)	1 682 (76)
	276	3.97	1 115 (20)	1 607 (42)	
<i>II</i> ^a	284	4.22	950 (11)	1 427 (18)	1 673 (63)
	223	4.27	1 100 (11)	1 590 (14)	
<i>III</i> ^a	298	4.25	973 (12)	1 459 (39)	1 681 (81)
	278	4.20	1095 (10)	1 614 (23)	
<i>IV</i>	231	4.42	967 (17)	1456 (53)	1 679 (87)
	238	3.98	1100 (10)	1598 (16)	
<i>V</i>	331	4.37	965 (14)	1455 (53)	1674 (79)
	236	3.97	1100 (42)	1604 (16)	1 687 (77)
<i>VI</i>	287	4.18	980 (39)	1460 (35)	1 679 (62)
	262	4.03	1088 (31)	1599 (73)	
<i>VII</i>	336	4.35	967 (12)	1458 (26)	1674 (87)
	236	3.92	1065 (20)	1621 (17)	
<i>VIII</i>	329	4.31	967 (12)	1459 (48)	1674 (86)
	232	3.78	1067 (19)	1607 (13)	
<i>IX</i>	349	4.39	968 (13)	1459 (68)	1670 (86)
	242	4.00	1066 (27)	1615 (55)	

^a Values for $\tilde{\nu}_{\text{as}}(\text{NO}_2)$ and $\tilde{\nu}_{\text{sym}}(\text{NO}_2)$: 1550 (19) and 1350 (80) cm^{-1} (*I*); 1560 (18) and 1358 (60) cm^{-1} (*II*); 1556 (23) and 1359 (44) cm^{-1} (*III*).

derivative^{15,16}. However, the corresponding differences in the wave numbers of the NO₂ groups are smaller than in the case of the furancarbaldehyde nitrophenyl derivatives^{15,16}.

From the ultraviolet spectra it follows that in the *para*-derivatives the first band in the region of longer wavelengths is against that of the *meta*-derivative subject to a bathochromic shift ($\Delta\lambda_{\max}$ between *I* and *II* is 27 nm and between *IV* and *VI* 44 nm). The difference of 14 nm between *I* and *III* might be explained by means of the non-coplanar structure of the *o*-nitro derivative. The higher λ_{\max} of compound *III* against that of compound *II* points to the fact that in these compounds electric effects have a greater influence than steric effects, what we had not noted with some *ortho*-substituted phenylfurancarbaldehyde derivatives^{15,16}. This explanation follows also from the infrared spectra, $\tilde{\nu}(\text{C}=\text{O})$ at 1681 cm⁻¹ (*I*), 1673 cm⁻¹ (*II*), and 1681 cm⁻¹ (*III*), and also from the mentioned anomalous frequencies of the nitro groups.

EXPERIMENTAL

Preparation of 5-(X-phenyl)-2-thiophenecarbaldehydes

Method A: A mixture of the arylamine (0.1 mol), concentrated hydrochloric acid (26.5 ml) and water (35 ml) is treated with aqueous sodium nitrite (7.2 g; 0.104 mol) at 0–5°C. To the filtrated solution of the diazonium salt are added 2-thiophenecarbaldehyde (11.2 g; 0.1 mol) in acetone (60 ml) and, after warming the mixture to 25°C, with stirring CuCl₂·2 H₂O, namely for the derivatives *I–III* 2.54 g (0.015 mol) and for the derivatives *IV–VI* 4.7 g (0.028 mol), in both cases in 20 ml of water. The temperature is then raised to 40°C, in the case of the derivatives *IV–VI* to 50–55°C, and the mixture stirred for 4 h. Then it is allowed to stand for 16 h, whereupon the oily layer is separated, washed with aqueous sodium carbonate and steam distilled. The 5-(X-phenyl)-2-thiophenecarbaldehyde is obtained from the residue by crystallisation.

Method B: To the mixture of the diazonium salt solution (0.1 mol) and 2-thiophenecarbaldehyde (0.1 mol) in acetone (60 ml) are successively added sodium acetate (25 g) and CuCl₂·2 H₂O (4.0 g; 0.024 mol) in 20 ml of water. The further procedure is identical with that of method *A*.

Method C: POCl₃ (0.168 mol) is added dropwise to a stirred mixture of 2-(X-phenyl)-thiophene (0.1 mol), dimethylformamide (0.168 mol), and toluene (60 ml). The resulting mixture is stirred at room temperature for 30 min and on a boiling water bath for 4½ h, and is then allowed to stand overnight, whereupon it is shaken with a hot saturated sodium acetate solution. The toluene layer is separated and the solvent distilled off *in vacuo*. The crude product is purified by crystallisation from ethanol. By method *C* were prepared compounds *IV*, *V*, *VII*, *VIII*, and *IX*.

Spectral measurements. Infrared spectra were measured in the 3600–700 cm⁻¹ region on a Zeiss (Jena) IR spectrophotometer using 0.01M chloroform solutions of the compounds in NaCl cells of 1.02 mm thickness. The calibration of the spectrophotometer was carried out by means of a polystyrene foil of 25 µm thickness. The accuracy of reading of the wave numbers was ±1 cm⁻¹. Ultraviolet spectra were taken on a spectrophotometer Specord UV VIS using 5 · 10⁻⁵M methanol solutions in cells of 1 cm thickness; measuring accuracy ±1 nm.

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