

THE REACTION OF 2-CYANO-3-(5-PHENYLSULPHONYL-2-THIENYL)ACRYLONITRILE WITH NUCLEOPHILES

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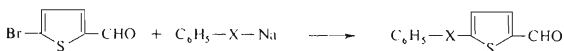
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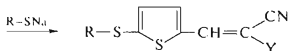
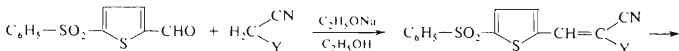
5-Phenylsulphonyl- and 5-phenylthio-2-thiophenylaldehydes react with malonodinitrile and methyl cyanoacetate under the conditions of Knoevenagel reaction to give the corresponding condensation products. It has been found that when 2-cyano-3-(5-phenylsulphonyl-2-thienyl)-acrylonitrile is treated with nucleophiles the phenylsulphonyl group is substituted.

It is known¹⁻⁴ that nucleophilic substitution of arylthio-, heteroarylthio- and arylsulphonyl groups with N- and S-nucleophiles takes place readily in 5-substituted furfurylidene malononitriles and methyl 2-cyano-3-(5-arylthio-2-furyl)-, 2-cyano-3-(5-heteroarylthio-2-furyl)- and 2-cyano-3-(5-phenylsulphonyl-2-furyl)acrylates.

The present work describes syntheses and S_N reactions of analogous thiophene derivatives, *i.e.* 2-cyano-3-(5-phenylthio-2-thienyl)- and 2-cyano-3-(5-phenylsul-



X = SO₂; S



- Ia*, Y = CN; R = C₆H₅
IIa, Y = COOCH₃; R = C₆H₅
IIIa, Y = CN; R = CH₃
IIIb, Y = CN; R = *i*-C₃H₇
IIIc, Y = CN; R = *i*-C₆H₁₁
IIId, Y = CN; R = 4-Cl-C₆H₄

- Ib*, Y = CN
IIb, Y = COOCH₃

phonyl-2-thienyl)acrylonitriles, and methyl 2-cyano-3-(5-phenylthio-2-thienyl)- and 2-cyano-3-(5-phenylsulphonyl-2-thienyl)acrylates. The compounds were prepared by treatment of 5-phenylthio- and 5-phenylsulphonyl-2-thiophenylaldehydes with malonodinitrile and methyl cyanoacetate under the conditions of Knoevenagel condensation (Scheme 1). 5-Phenylsulphonyl-2-thiophenylaldehyde was obtained by reacting 5-bromo-2-thiophenylaldehyde with sodium benzenesulphinate in dimethylformamide at 140°C, and 5-phenylthio-2-thiophenylaldehyde was prepared from 5-bromo-2-thiophenylaldehyde and sodium thiophenolate by a reaction in acetone at room temperature.

The studied thiophene derivatives, *i.e.* 2-cyano-3-(5-phenylsulphonyl-2-thienyl)acrylonitrile and methyl 2-cyano-3-(5-phenylsulphonyl-2-thienyl)acrylate do not react with N-nucleophiles (piperidine, morpholine, pyrrolidine) to give products of substitution of the phenylsulphonyl group. Their reactions were carried out in various solvents (sulpholane, dimethyl sulphoxide, ethanol, acetone, tetrahydrofuran) and under a variety of reaction conditions (25–80°C, 2–24 h). A mixture of products was formed from which, occasionally, unreacted substrate could be recovered. It has been found, by monitoring the reactions spectrophotometrically, that the last UV absorption band of 2-cyano-3-(5-phenylsulphonyl-2-thienyl)acrylonitrile (λ_{max} 344 nm) disappeared immediately upon the addition of the nucleophile, but the band indicative of the formation of the expected substitution product has not appeared even after prolonged reaction time.

It is probable that, with furan type substrates, the determining role in the nucleophilic substitution of the phenylsulphonyl group is played by the more electronegative oxygen hetero atom, in the presence of which the electron deficiency at the position 5 becomes more pronounced, as compared with the corresponding thiophene derivatives. Therefore, we have carried out reactions with S-nucleophiles (sodium thiolates) with which the reactions took place readily. Apart from acetone, sulpholane and dimethyl sulphoxide could be used as solvents, and in all cases the yields of the products were confirmed also by mass spectrometry.

EXPERIMENTAL

Electron spectra for $3 \cdot 10^{-5}$ – $7 \cdot 10^{-5}$ M solutions in methanol were measured in 1 cm cells with the accuracy of ± 1 nm using a Specord UV VIS spectrometer.

5-Phenylsulphonyl-2-thiophenylaldehyde

A mixture of sodium benzenesulphinate (0.1 mol) and 5-bromo-2-thiophenylaldehyde (0.1 mol) in dimethylformamide (300 ml) was heated at 130–140°C for 4–5 h. After cooling, the mixture was poured into water (600 ml), the separated oil was extracted with chloroform, the extract dried with anhydrous sodium sulphate and concentrated. Crystallization from ethanol gave 18.7 g (74.5%) of the title product, m.p. 72–73°C. For $C_{11}H_8O_3S_2$ (252.2) calculated: 52.36% C, 3.20% H, 25.42% S; found: 52.41% C, 3.14% H, 25.24% S.

TABLE I
Physico-Chemical Characteristics for the Prepared Substances

Compound X or R	Formula (m.w.)	M.p., °C (yield, %)	Calculated/Found				λ_{\max} , nm (log ϵ)			
			% C	% H	% N	% S				
<i>Ia</i> C ₆ H ₅ S	C ₁₄ H ₈ N ₂ S ₂ (268.4)	65 (92)	62.66 62.47	3.00 2.85	10.44 10.26	23.90 23.75	205 (4.33)	249 (3.86)	299 (3.78)	412 (4.30)
<i>Ib</i> C ₆ H ₅ SO ₂	C ₁₄ H ₈ N ₂ O ₂ S ₂ (300.4)	165–167 (86.5)	55.98 55.64	2.68 2.57	9.33 9.28	21.35 21.12	205 (4.17)	241 (3.88)	—	344 (4.40)
<i>IIa</i> C ₆ H ₅ S	C ₁₅ H ₁₁ NO ₂ S ₂ (301.4)	89–90 (88)	59.78 59.65	3.68 3.51	4.65 4.62	21.28 21.08	205 (4.32)	247 (4.09)	303 (4.00)	400 (4.25)
<i>Ib</i> C ₆ H ₅ SO ₂	C ₁₅ H ₁₁ NO ₄ S ₂ (333.4)	173–174 (88)	54.03 53.88	3.33 3.25	4.20 4.08	19.24 19.09	205 (4.22)	242 (3.90)	—	341 (3.38)
<i>IIIa</i> R = CH ₃	C ₉ H ₆ N ₂ S ₂ (206.3)	168–170 (58)	52.39 52.44	2.93 2.81	13.58 13.58	31.08 31.87	206 (3.95)	244 (3.69)	283 (3.54)	347 (4.18)
<i>IIIb</i> R = i-C ₃ H ₇	C ₁₁ H ₁₀ N ₃ S ₂ (234.3)	154–156 (63)	56.37 56.20	4.30 4.23	11.95 11.79	27.36 27.22	205 (4.08)	245 (3.76)	282 (3.60)	346 (4.25)
<i>IIIc</i> R = i-C ₅ H ₁₁	C ₁₃ H ₁₄ N ₂ S ₂ (262.4)	162–163 (61)	59.50 59.34	5.37 5.25	10.67 10.48	24.44 24.31	206 (4.05)	242 (3.77)	284 (3.63)	343 (4.30)
<i>IIId</i> R = 4-Cl-C ₆ H ₄	C ₁₄ H ₇ ClN ₂ S ₂ (302.8)	108–110 (91)	55.52 55.39	2.33 2.19	9.25 9.13	21.17 21.10	205 (4.38)	228 (4.15)	252 (3.97)	306 (3.87)

5-Phenylthio-2-thiophenylaldehyde

A mixture of sodium thiophenolate (0.05 mol) and 5-bromo-2-thiophenylaldehyde (0.05 mol) in acetone (50–100 ml) was stirred at room temperature for 2–3 h, filtered, decolorized with charcoal, and concentrated. The crude product was recrystallized from ethanol to give 7.1 g (65%) of material melting at 86–88°C. For $C_{11}H_8OS_2$ (220.2) calculated: 59.99% C, 3.66% H, 29.12% S; found: 59.72% C, 3.55% H, 29.02% S.

2-Cyano-3-(5-X-2-thienyl)acrylonitriles (*Ia*, *Ib*) and Methyl 2-Cyano-3-(5-X-2-thienyl)acrylates (*IIa*, *IIb*)

A solution of malonodinitrile (0.02 mol) in ether (10 ml), or methyl cyanoacetate (0.02 mol) in ethanol (10 ml) was added to a solution of 5-X-2-thiophenylaldehyde (0.02 mol) in the same solvent. Ethanolic 10% sodium ethoxide (5–10 drops) was added with stirring and the product, separated during a reaction period of 2 h, was filtered and recrystallized from a suitable solvent. Physico-chemical constants of thus prepared substances are given in Table I.

2-Cyano-3-(5-R-S-2-thienyl)acrylonitriles

A solution of a thiol (0.001 mol) in acetone was added to a mixture of 2-cyano-3-(5-phenylsulphonyl-2-thienyl)acrylonitrile (0.001 mol) and anhydrous sodium carbonate (0.001 mol) in acetone (20–30 ml). Depending upon the nucleophilic reagent, the mixture was stirred for 0.5–3 h during which time sodium benzenesulphinat separated. The mixture was filtered, the filtrate treated with charcoal, concentrated and the product was crystallized from a suitable solvent. For physico-chemical constants and elemental analyses of the prepared substances see Table I.

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