

NITRILES IN ORGANIC SYNTHESIS: A NOVEL SYNTHESIS OF 2-THIENYLBIARYLS

Abdel Ghani A. ELAGAMEY^a, Mamdouh A. SOFAN^a, Zaghloul E. KANDEEL^b
and MOHAMED H. ELNAGDI^b

^a Chemistry Department, Faculty of Science, Damietta, Egypt and

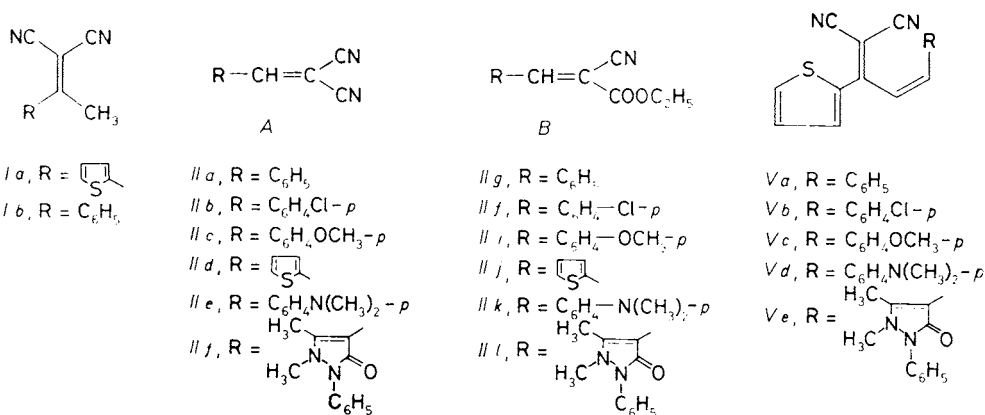
^b Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt

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A novel synthesis of 2-thienylbiaryls *via* the reaction of the 2-cyano-3-(2-thienyl)crotonitrile with cinnamitriles is reported. The same products were also obtained from the reaction of 1,1-dicyano-2-thienyl-4-arylbuta-1,3-dienes with malonitrile or ethyl cyanoacetate.

Nitriles are versatile reagents and their utility in organic synthesis is now receiving considerable interest¹⁻³. In conjunction of previous work directed for exploring the synthetic potential of nitriles⁴⁻⁶, the reaction of 2-cyano-3-(2-thienyl)crotonitrile (*Ia*) with cinnamitriles *II* was investigated. Previously we have reported several novel syntheses of heterocycles utilizing the reaction of *II* with active methylene reagents^{5,6}. The present work resulted in developing a new high-yield approach to the substituted 2-thienylbiaryl derivatives. These derivatives are difficult to obtain by known synthetic approaches of biaryls.

Compounds *Ia,b* were prepared *via* condensation of malonitrile with 2-acetylthiophene or acetophenone following literature procedure⁷. Compound *Ia* reacted readily with *IIa-d* to yield products of condensation *via* hydrogen cyanide elimina-



In place at *IIh* read *IIh* below the formula B.

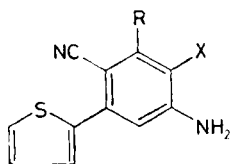
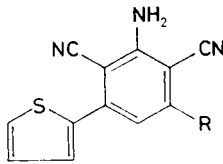
tion. Two isomeric structures seemed possible for the reaction products (*cf.* structures *III* and *IV*) and logical mechanisms could be suggested to account for the formation of either products. Although the possible formation of *III* through addition of the active methyl to cyano group, subsequent intramolecular Diels–Alder cyclization and HCN elimination seemed least likely, independent proof seemed necessary.

In order to establish the structure of the reaction products, compound *Ia* was condensed with aldehydes to yield the corresponding ylidenes *Va–c*. Compounds *Va–c* reacted with malononitrile to yield the same products of reaction of *Ia* and *Ila–c*. Thus, it was believed that reaction proceed *via* addition of methyl function to the α,β -unsaturated linkage in *Ila–c* followed by cyclization and hydrogen cyanide elimination.

TABLE I
Data of the synthesized compounds

Compound	M.p., °C (Yield, %) ^a	Formula (Mol. wt.)	Calculated/found			
			% C	% H	% N	% S
<i>IVa</i>	235 (85)	C ₁₈ H ₁₁ N ₃ S (301.4)	71.74	3.68	13.94	10.64
			71.58	3.75	14.02	10.65
<i>IVb</i>	268 (88)	C ₁₈ H ₁₀ ClN ₃ S (335.8)	64.38	3.00	12.51	9.55
			64.23	3.14	12.35	9.82
<i>IVc</i>	218 (80)	C ₁₉ H ₁₃ N ₃ OS (331.4)	68.86	3.95	12.69	9.68
			68.85	3.92	12.61	9.77
<i>IVd</i>	257 (75)	C ₁₆ H ₉ N ₃ S ₂ (307.4)	62.52	2.95	13.67	20.86
			62.51	2.89	13.88	20.82
<i>Va</i>	140 (55)	C ₁₆ H ₁₀ N ₂ S (262.3)	73.25	3.84	10.68	12.22
			73.41	3.98	10.75	12.16
<i>Vb</i>	290 (59)	C ₁₆ H ₉ ClN ₂ S (296.8)	64.75	3.06	9.44	10.81
			64.72	3.15	9.62	10.70
<i>Vc</i>	150 (52)	C ₁₇ H ₁₂ N ₂ OS (292.4)	69.84	4.14	9.58	10.97
			69.82	4.17	9.55	10.86
<i>Vd</i>	228 (65)	C ₁₈ H ₁₅ N ₃ S (305.4)	70.79	4.95	13.76	10.50
			70.93	5.03	13.78	10.61
<i>Ve</i>	255 (80)	C ₂₁ H ₁₆ N ₄ OS (372.4)	67.72	4.33	15.04	8.61
			67.79	4.45	15.23	8.42

Compounds *IVa–c* prepared by different methods were obtained nearly in the same yields.

III, X = CN, COOC₂H₅IV a, R = C₆H₅IV b, R = C₆H₄-Cl-*p*IV c, R = C₆H₄-OCH₃-*p*

IV d, R =

Structure IV could be established based on the fact that *Ilg-j* reacted with *Ia* to yield the same product obtained from reaction of *Ia* and *Iia-d*. Also the ethyl cyanoacetate reacted with *Va-c* to yield the same reaction products. In this case compounds *IIIa-d* resulting *via* ethyl formate elimination would have not been formed. In addition compound *IVa* could be prepared from reaction of *Ib* with *Iid* or *Iij*.

The successful formation of *IVa-c* *via* different routes prompted us to try a convenient preparation of *IVa-c*. Consequently, a sample of *IVa* was prepared by refluxing a mixture of *Ia*, benzaldehyde and malononitrile or ethyl cyanoacetate in ethanol and in presence of catalytic amount of piperidine.

In contrast to *Iia-d* and *Ilg-j*, compounds *Iie,k* and *Iif,l* reacted with *Ia* under the same conditions to ylidene derivatives *Vd* and *Ve*. Compounds *Vd* and *Ve* were obtained *via* direct condensation of *Ia* with *p*-dimethylaminobenzaldehyde and 4-formylantipyrine, respectively, as has been previously reported for the formation of *Va-c*. The formation of *Vd* and *Ve* from reaction of *Ia* with *Iie,k* or *Iif,l* is as-

TABLE II

Selected bands in the IR spectra of the synthesized compounds

Compound	$\tilde{\nu}(\text{KBr}), \text{cm}^{-1}$
<i>IVa</i>	3 500, 3 390 (NH ₂); 2 220 (CN); 1 640 (NH ₂)
<i>IVb</i>	3 500, 3 400 (NH ₂); 2 220 (CN); 1 650 (NH ₂)
<i>IVc</i>	3 490, 3 350 (NH ₂); 2 220 (CN); 1 650 (NH ₂)
<i>IVd</i>	3 500, 3 390 (NH ₂); 2 220 (CN); 1 640 (NH ₂)
<i>Va</i>	2 200 (CN); 1 630 (C=C)
<i>Vb</i>	2 200 (CN); 1 640 (C=C)
<i>Vc</i>	2 200 (CN); 1 620 (C=C)
<i>Vd</i>	2 200 (CN); 1 620 (C=C)
<i>Ve</i>	3 050 (CH ₃); 2 200 (CN); 1 680 (C=O); 1 620 (C=C)

sumed to proceed *via* initial Michael addition of *Ia* to the activated double bond in *II* followed by elimination of either malononitrile (in case of *IIf,f*) or ethyl cyanoacetate (in case of *IIh,l*). Similar mechanism has been suggested earlier^{8,9} to account for the formation of ylidenes on addition of active methylene reagents to some derivatives of *II*.

EXPERIMENTAL

Melting points were determined with a Thomas Hoover melting point apparatus and are uncorrected. The infrared spectra were determined utilizing KBr discs, with a Beckman IR spectrometer. Satisfactory analytical data ($\pm 0.3\%$ in agreement with the molecular formulas given) were performed by the Microanalytical unit at Cairo University.

3-Amino-2,4-dicyano-5-thienylbiaryls (*IVa-d*)

From Ia and IIa-d or IIg-j: A suspension of *Ia* 1.74 g (0.01 mol) and (0.01 mol) of *IIa-d* or *IIg-j* in ethanol (30 ml) was refluxed in the presence of (0.1 ml) of piperidine for 1 h. The solvent was concentrated and the remaining solids were collected by filtration and crystallized from dimethylformamide (Tables I and II).

From Va-c and malonitrile or ethyl cyanoacetate: A suspension of *Va-c* (0.01 mol) and 0.66 g (0.01 mol) of malononitrile or 1.13 g (0.01 mol) of ethyl cyanoacetate in ethanol (30 ml) and (0.1 ml) of piperidine was refluxed for 2 h. The solvent was then evaporated and the resulting solids were collected by filtration and crystallized from dimethylformamide.

Compound IVa from Ib and IIj or IIj: A suspension of 1.68 g (0.01 mol) of *Ib* and (0.01 mol) of *IIj* or *IIj* in ethanol (30 ml) was refluxed in the presence of (0.1 ml) piperidine for 1 h. The solvent was then evaporated and the remaining solid *IVa* was collected by filtration and crystallized from dimethylformamide.

Compound IVa from Ia, benzaldehyde and malononitrile or ethyl cyanoacetate: A mixture of 1.74 g (0.01 mol) of *Ia*, benzaldehyde 1.06 g (0.01 mol) and (0.01 mol) of malononitrile or ethyl cyanoacetate was refluxed in ethanol (30 ml) with (0.1 ml) of piperidine for 2 h. The solid was collected by filtration and crystallized from dimethylformamide.

1,1-Dicyano-2-thienyl-4-arylbuta-1,3-dienes *Va-e*

A solution of *Ia* 1.74 g (0.01 mol), and (0.01 mol) of the appropriate aldehyde in ethanol (30 ml), and (0.1 ml) piperidine was refluxed for 4 h. The solvent was then removed *in vacuo* and the remaining products were triturated with a little water. The resulting solid obtained on standing were collected by filtration and crystallized from ethanol (Tables I and II).

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