CYCLOCONDENSATION REACTIONS OF 3-ARYL-2-BENZYLIDENE-3-OXOPROPANENITRILES WITH ACETYLAROMATIC DERIVATIVES

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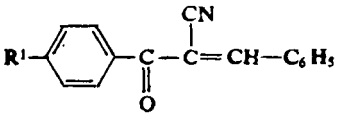
Cyclocondensation of 3-aryl-2-benzylidene-3-oxopropanenitriles *Ia* and *Ib* with acetyl aromatic derivatives *IIa—IIc* in the presence of ammonium acetate affords 2,6-diaryl-4-phenyl-3-cyanopyridines *IV* and *V*. Reaction of the nitrile *Ib* with 1,2-diphenylethanone (*III*) gave 2-(4-biphenylyl)-4,5,6-triphenyl-3-cyanopyridine (*VI*). The relation between the structure of the synthesized pyridine derivatives *IV— VI* and their spectral properties is discussed.

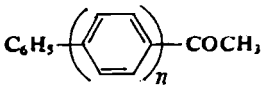
The hitherto known syntheses of 2,4,6-triaryl-3-cyanopyridines are based on cyclocondensation of 1,3-diaryl-2-propen-1-ones with 3-phenyl-3-oxopropanenitrile[1,2] or 3-amino-3-phenyl-2-propenenitrile[3,4]. Another method, used for the preparation of the parent pyridine *IVa*, starts from 2,4,6-triphenyl-3-azapyrylium[5] or thiopyrylium perchlorates[6,7] and 3-phenyl-3-oxopropanenitrile. In our preceding communication[8] we reported that cyclocondensation of β-oxonitriles *I* with cycloalkanones in the presence of ammonium acetate affords cycloalkeno[*b*]pyridines. In the present paper we describe an extension of this reaction to acetylaromatic compounds as the carbonylmethylene component in order to develop a novel approach to 2,4,6-triaryl-3-cyanopyridines containing in positions 2 and 6 higher polyphenylyl residues. Derivatives of this type might exhibit interesting optical properties.

Cyclocondensation of 3-aryl-2-benzylidene-3-oxopropanenitriles *Ia* and *Ib* with acetyl derivatives *IIa—IIc* in the presence of ammonium acetate afforded 2,6-diaryl-4-phenyl-3-cyanopyridines *IV* and *V* in 13—42% yields (Table I). Analogously, reaction of 1,2-diphenylethanone (*III*) with oxonitrile *Ib* gave 2-(4-biphenylyl)-4,5,6-triphenyl-3-cyanopyridine (*VI*). Contrary to the previously described analogous cyclocondensation of 1,3-diphenylpropene-1-one (*IXb*) with 3-phenyl-3-oxopropanenitrile leading to a mixture of the 1,4-dihydropyridine derivative and the corresponding pyridine *IVa*, we did not isolate any primarily arising dihydro derivative. This fact may be due to formation of an unstable intermediate (*VIII*) from 3-azahexatriene *VII*; this intermediate then undergoes dehydrogenation rather than tautomerization to the 1,4-dihydro isomer (Scheme 1). The suggested mechanism may be supported

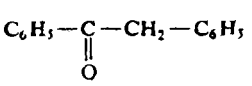
by the finding[9] that 3-azahexatrienes of the type *VII* undergo a facile thermal cyclization to give pyridines, the initial reaction step being the formation of an unstable 3,4-dihydropyridine. The described preparation of 2,4,6-triaryl-3-cyanopyridines *IV* and *V* is more advantageous than the already published methods[1-7] since it makes use of better accessible starting compounds *I* (ref.[10-13]) and *II* (ref.[14]), particularly in the case of the most important compounds, where R^1 and R^2 are not hydrogen atoms. In common solvents, the obtained pyridines *IVb* – *Vc* show a marked blue fluorescence; the fluorescence occurs also when the solid compounds are irradiated with UV light.



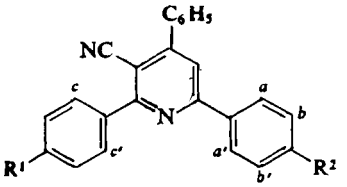
Ia, $R^1 = H$
Ib, $R^1 = C_6H_5$



IIa, $n = 0$
IIb, $n = 1$
IIc, $n = 2$

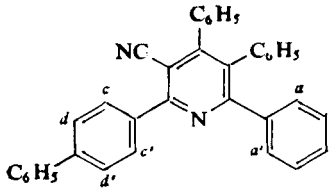


III

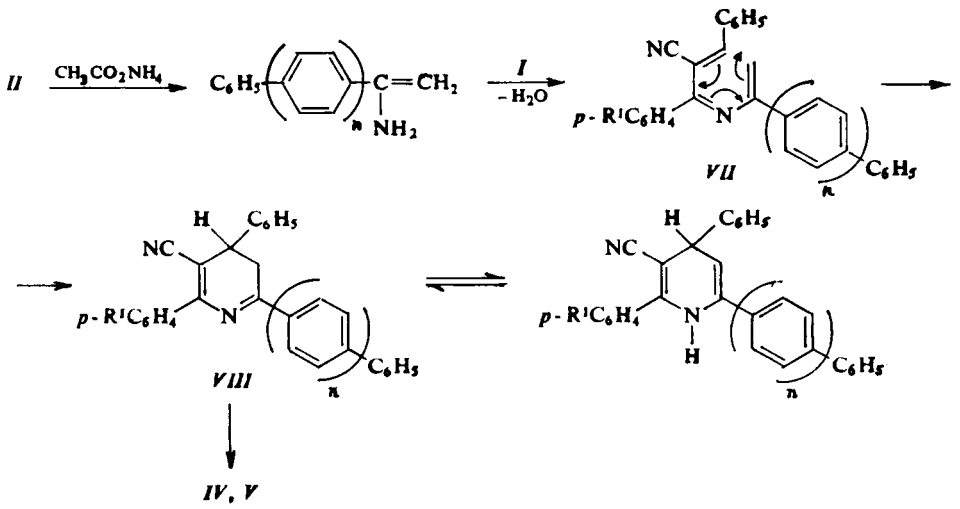


IVa, $R^1 = H$, $R^2 = H$
IVb, $R^1 = H$, $R^2 = C_6H_5$
IVc, $R^1 = H$, $R^2 = p\text{-}C_6H_5C_6H_4$

Va, $R^1 = C_6H_5$, $R^2 = H$
Vb, $R^1 = C_6H_5$, $R^2 = C_6H_5$
Vc, $R^1 = C_6H_5$, $R^2 = p\text{-}C_6H_5C_6H_4$



VI



SCHEME 1

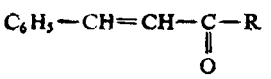
TABLE I

2,6-Diaryl-4-phenyl-3-cyanopyridines *IV* and *V*

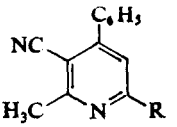
Compound (yield, %)	R^1	R^2	M.p., °C[a]	Formula (mol.wt.)	Calculated/Found		
					% C	% H	% N
IVa (42)	H	H	227–228[b]	$C_{24}H_{16}N_2$ (332·4)	86·71 86·83	4·86 4·83	8·43 8·26
IVb (40)	H	C_6H_5	210–212	$C_{30}H_{20}N_2$ (408·5)	88·20 88·12	4·94 5·07	6·86 6·95
IVc (13)	H	p-$C_6H_5C_6H_4$	237–238	$C_{36}H_{24}N_2$ (484·6)	89·22 89·20	5·00 5·34	5·78 5·87
Va (39)	C_6H_5	H	231–232	$C_{30}H_{20}N_2$ (408·5)	88·20 88·19	4·94 5·02	6·86 6·95
Vb (37)	C_6H_5	C_6H_5	240–242	$C_{36}H_{24}N_2$ (484·6)	89·22 89·14	5·00 4·97	5·78 5·83
Vc (36)	C_6H_5	p-$C_6H_5C_6H_4$	269–271	$C_{42}H_{28}N_2$ (560·7)	89·96 89·23	5·04 5·13	5·00 4·91

[a] Compounds *IVa*–*IVc*, *Ia*, and *Vb* were crystallized from ethanol–benzene and *Vc* from benzene
[b] reported[1] m.p. 222–223°C.

The structure of the products *IV*–*VI* has been confirmed by their spectral characteristics. Their IR spectra (Table II) exhibit (C≡N) stretching vibration bands at 2 214–2 228 cm^{-1}, $\nu(C{=}C)_{arom}$ bands and bands due to the pyridine skeleton. Also the ^1H NMR spectra agree with the structures *IV*–*VI*. In addition to the complex multiplet in the region δ 6·80–7·96, the spectrum displays characteristic signals at δ 8·05–8·28 and δ 8·01–8·14 corresponding to the *ortho* protons H_a, $H_{a'}$, H_c and $H_{c'}$ of the phenyl nuclei in the positions 2 and 6 of the pyridine skeleton. These signals were assigned on the basis of different multiplicity in the spectra of the unsymmetrically substituted derivatives *IVb*, *IVc*, *Va* and *Vc* and comparison with ^1H NMR spectra of the model compounds *Xa*–*Xc* (Table II), prepared by cyclocondensation of 3-phenyl-2-propen-1-ones *IXa*–*IXc* with 3-amino-2-butenenitrile ac-



IXa, R = H
IXb, R = C_6H_5
IXc, R = *p*-$C_6H_5C_6H_4$



Xa, R = H
Xb, R = C_6H_5
Xc, R = *p*-$C_6H_5C_6H_4$

cording to the described procedure[15,16]. The simple shape of the signals indicates that in solution compounds *IV*–*VI* assume a non-planar conformation in which the phenyl rings in positions 2 and 6 markedly deviate from the plane and consequently the protons H_a, $H_{a'}$ and H_c, $H_{c'}$ are approximately chemically equivalent. A similar effect was observed in the ^1H NMR spectra of 4-aryl-2-(4-biphenylyl)-3-cyanocycloalkeno[*b*]pyridines[8].

EXPERIMENTAL

Temperature data are uncorrected. Melting points were determined on a Boetius block. Spectral characteristics were measured on the following instruments: Perkin–Elmer 325 (IR), Varian XL-100 (^1H NMR) and AEI MS 902S (mass spectra, 70 eV). The 2-benzylidene-3-oxopropanenitriles *I* were prepared by the method of Kauffmann[10]; *Ia*: m.p. 84–85°C (reported[12] m.p. 83·5 - 85·5°C) and *Ib* (see ref.[13]). The acetyl derivatives *IIb* and *IIc* were synthesized by Friedel–Crafts acetylation of biphenyl and *p*-terphenyl, respectively[14]; 4-acetyl-*p*-terphenyl (*IIc*) m.p. 235 - 237°C (dioxane), reported m.p. 230°C (ref.[17]), 207–209°C (ref.[14]) and 185–186°C (ref.[18]). For $C_{20}H_{16}O$ (272·4) calculated: 88·19% C, 5·93% H; found: 87·85% C, 5·96% H. IR spectrum (KBr), ν_{max} (cm^{-1}): 1 682 s (C=O). ^1H NMR spectrum (C^2HCl_3), δ (ppm): 2·65 (s, 3 H, CH_3), 7·30–7·84 (m, 11 H, H arom.), 8·03 (d, 2 H, H *ortho*). The compound *Xa* was prepared by cyclocondensation of 3-amino-2-butenenitrile and *IXa* in an alkaline medium according to ref.[15]; m.p. 105–107°C (reported[15] m.p. 105–106°C); compound *Xb* was obtained analogously from 1,3-diphenyl-2-propen-1-one (*IXb*): m.p. 117–118°C (reported[16] m.p. 116°C).

TABLE II

Infrared and ^{1}H NMR data for 4-phenyl-3-cyanopyridines *IV*–*VI* and *X*

Compound	$\tilde{\nu}_{max}$, cm^{-1} ($CHCl_3$)[a]					δ_H, ppm (C^2HCl_3, 31°C)[b]		
	ν(=C—H)	ν(C≡N)	ν(C=C) and ν(C=N)			$H_{a,a'}$	$H_{c,c'}$	H_{arom}
IVa	3 068 w	2 222 m	1 603 w	1 575 s	1 499 m	8·13 dd	8·03 dd	7·30–7·72 m
	3 017 m		1 588 s	1 535 s	1 447 w			7·77 s (H—$C_{(5)}$)
IVb	3 064 w	2 222 m	1 607 w	1 573 s	1 494 w	8·22 d	8·01 dd	7·30–7·88 m
	3 016 m		1 600 w	1 563 m	1 488 m	J = 8·2 Hz		
			1 585 s	1 532 s	1 446 m			
IVc	3 070 w	2 228 m	1 608 w	1 574 s	1 506 w	8·25 d	8·03 dd	7·31–7·93 n
	3 040 w		1 600 w	1 532 m	1 494 m	J = 8·2 Hz		
	3 019 w		1 585 s	1 524 s	1 486 s			
Va	3 070 w	2 228 m	1 613 w	1 578 s	1 497 m	8·05–8·27 m		7·30–7·88 m
	3 040 w		1 502 w	1 559 w	1 492 s		8·11 d	
	3 022 m		1 587 s	1 536 s	1 450 m		J = 8·2 Hz	
Vb	3 070 w	2 224 m	1 613 m	1 579 s	1 500 w	8·22 d	8·10 d	7·27–7·85 m
	3 040 w		1 603 m	1 566 m	1 492 s	J = 8·2 Hz	J = 8·2 Hz	
	3 019 m		1 587 s	1 535 s	1 450 m			

Vc	3 030 w	2 214 m	1 606 m 1 577 s 1 554 m	1 520 s 1 495 w	1 485 s 1 450 m	8.28 d $J = 8{\cdot}2$ Hz	8·14 d $J = 8{\cdot}2$ Hz	7·32—7·96 m
VI	3 100 w 3 070 w 3 030 m	2 228 m	1 612 w 1 604 w 1 584 w	1 563w 1 536 s 1 490 s	1 484 s 1 449 m	[c]	8·17 d[d] $J = 8{\cdot}2$ Hz	6·80—7·68 m
Xa	3 070 w 3 020 m	2 224 s	1 588 s 1 548 m	1 502 m	1 449 m	2·61 s[e]	2·80 s[f]	7·10 s (H—$C_{(5)}$) 7·35—7·75 m
Xb	3 070 w 3 019 m	2 221 s	1 602 w 1 587 s 1 578 s	1 543 s 1 495 m	1 458 w 1 447 m	8·06 dd	2·90 s[f]	7·42—7·61 m 7·65 s (H—$C_{(5)}$)
Xc	3 064 w 3 018 m	2 221 s	1 600 w 1 585 s 1 579 s	1 563 m 1 538 s 1 499 w	1 490 m 1 447 m	8·13 d[g] $J = 8{\cdot}2$ Hz	2·90 s[f]	7·30—7·68 m

[a] Compound *Vc* was measured by the KBr technique; [b] internal standard tetramethylsilane; [c] signal in the H_{arom} region; [d] 77·5 (d, 2 H, $H_{d,d'}$, $J = 8{\cdot}2$ Hz); [e] methyl group in position 6; [f] methyl in position 2; [g] 7·67 (d, 2 H, $H_{b,b'}$, $J = 8{\cdot}2$ Hz).

2,4,6-Triaryl-3-cyanopyridines *IV* and *V*

A mixture of 3-aryl-2-benzylidene-3-oxopropanenitrile *I* (1·7 mmol), the corresponding acetal derivative *II* (1·7 mmol) and ammonium acetate (1·7 mmol) in ethanol (7 ml) was refluxed for 8 h. The precipitate was filtered, washed with ethanol, the product purified by chromatography on silica gel with chloroform as eluant (detection with iodine vapours and UV light) and crystallized from appropriate solvent (see Table I).

2-(4-Biphenylyl)-4,5,6-triphenyl-3-cyanopyridine (*VI*)

A mixture of 2-benzylidene-3-(4-biphenylyl)-3-oxopropanenitrile (*Ib*; 0·52 g), compound *III* (0·33 g), ammonium acetate (0·13 g), and ethanol (7 ml) was refluxed for 12 h. After standing for several days, the precipitate was filtered and processed as described for the pyridines *IV* and *V*. Crystallization from ethanol-benzene afforded 0·31 g (38%) of the pyridine *VI*, m.p. 249–250°C. For $C_{36}H_{24}N_2$ (484·6) calculated: 89.22% C 5·00% H, 5·78% N; found: 89·24% C, 5·13% H, 5·49% N.

6-(4-Biphenylyl)-4-phenyl-2-methyl-3-cyanopyridine (*Xc*)

3-Phenyl-2-propen-1-one (*IXc*; 2·85 g) and 3-amino-2-butenenitrile (0·82 g) were added to a solution of sodium methoxide, prepared from 0·5 g of sodium and 30 ml of methanol, and the mixture was heated for 6 h on a water bath. After standing overnight, the precipitate was filtered, washed with a small amount of ethanol and crystallized from ethanol–benzene, affording 1·6 g of compound which was subjected to column chromatography on silica gel (200 g) in chloroform. Crystallization from ethanol–benzene gave 0·98 g (28%) of the pure product *Xc*, m.p. 159–160°C, which in solution exhibited a marked blue fluorescence. For $C_{25}H_{18}N_2$ (356·5) calculated: 86·67% C, 5·25% H, 8·09% N; found: 86·67% C, 5·28% H, 8·19% N. Mass spectrum, *m/z* (rel. intensity, %): 348 (4), 347 (28), 346 (100, $[M]^{\ddagger}$), 345 (21), 344 (3), 343 (2), 331 (2), 269 (5), 178 (2), 174 (2), 173 (9, $[M]^{2+}$), 172 (3), 171 (2), 165 (2), 152 (3), 139 (2), 79 (2).

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