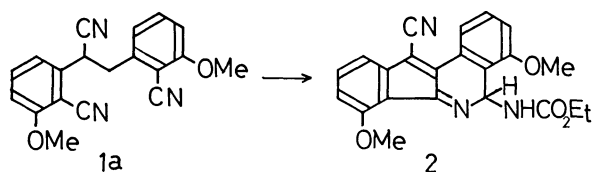


Cyclization Reactions of 2,3-Bis(2-cyanophenyl)propionitriles. III.¹⁾ Substituent Effect on the Carbanion Reactivities of the Propionitriles and Tautomerism of 5-Acetamido- 11-cyanoindeno[1,2-*c*]isoquinolines

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The substituent effect in the base-catalyzed cyclization reaction of 2,3-bis(2-cyanophenyl)propionitriles (**1**) to 5-amino-11-cyano-11*H*-indeno[1,2-*c*]isoquinolines has been studied and the result is discussed in terms of the dichotomic carbanion reactivities of **1**. Preparation of **1** and the tautomerism of 5-acetamido-11-cyanoindeno[1,2-*c*]isoquinolines between 5*H* and 11*H* structures are described.

When 2,3-bis(2-cyano-3-methoxyphenyl)propionitrile (**1a**) was allowed to react with sodium ethoxide and diethyl carbonate in ethanol, a red pigment was obtained in 79.3% yield, to which we assigned the structure **2** (Scheme 1).²⁾



Scheme 1.

The formation of **2** from **1a** involves the preferential attack of C-3 carbanion to the cyano group on aromatic ring.

The cause for the less stable C-3 carbanion participating exclusively in the cyclization deserves further study. We have confirmed that the cyclization product derived from the more stable C-2 carbanion is also obtained and examined the relative reactivity of the dichotomic carbanions in terms of the substituent effect. We have found an interesting tautomerism between 11*H*- and 5*H*-indeno[1,2-*c*]isoquinoline systems, which is markedly influenced by the substitution patterns of the aryl rings.

Results and Discussion

Preparation of 2,3-Bis(2-cyanophenyl)propionitriles (**1**).

The reaction of 2-cyano-3-methoxybenzyl bromide (**3a**) with sodium cyanide afforded 2,3-bis(2-cyano-3-methoxyphenyl)propionitrile (**1a**) in variable ratios to the normal product, 2-cyano-3-methoxybenzyl cyanide (**5a**), depending on the conditions.³⁾ Formation of the former compound is accelerated in the case of low cyanide concentration and in a polar aprotic medium such as DMSO. Since the reactivity of the benzyl cyanides (**4**) initially produced is affected to a large extent by the substituents in aryl rings, a proper

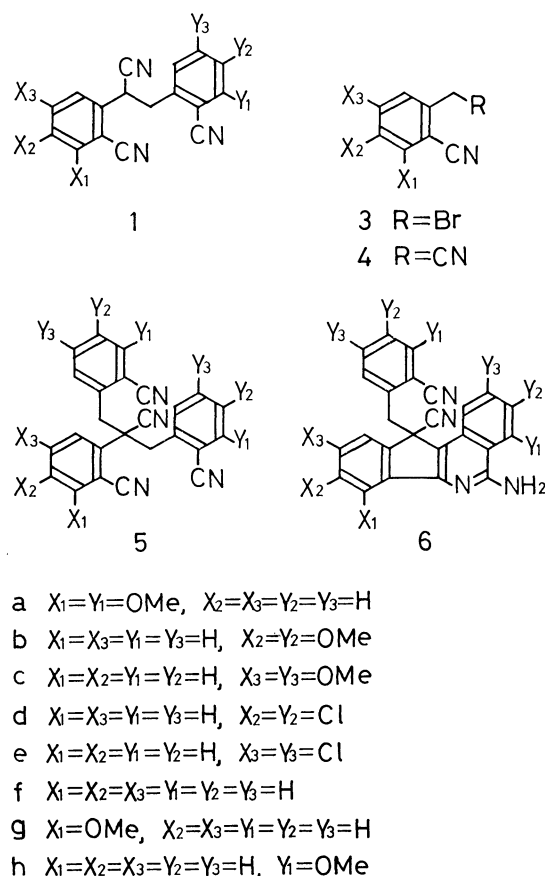


Fig. 1.

modification of the reaction procedure was necessary in order to prepare propionitriles (**1**) in acceptable yields. The following methods were investigated.

- A solution of a bromide and NaCN in ethanol-water (2: 1) was allowed to stand at -20 °C for 48 h.
- A solution of a bromide and NaCN in ethanol-water (4: 1) was refluxed for 6 h.
- A mixture of a bromide, NaCN, a trace of NaI, and acetone was stirred at room temperature for 48 h.
- A mixture of a bromide, NaCN, a trace of NaI, and acetone was stirred and refluxed for 24 h.

The results obtained in the reactions of the substrates **3a**—**3f** are summarized in Table 1. Method D was generally applicable (**3a**, **3b**, **3c**, and **3f**) except when

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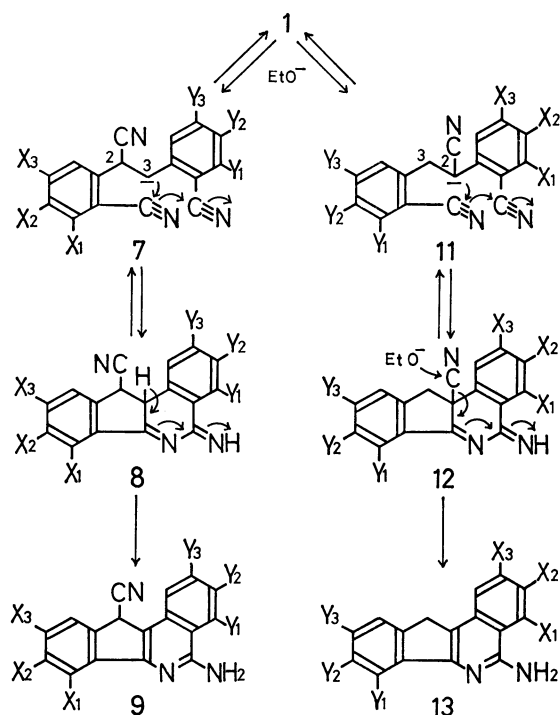
TABLE 1. PREPARATION OF 2,3-BIS(2-CYANOPHENYL)PROPIONITRILES (**1**)

Entry	Substrate	Reaction conditions		Yield (%)			
		Method	Ratio (NaCN/3)	1	4	5	6
1	3a	B	1.5	17.2	58.8	0	0
2	3a	D	2.0	78.0	0	0	0
3	3b	D	3.5	58.9	18.9	0	0
4	3c	D	5.5	42.4	0	7.4	0
5	3d	A	12.7	54.0	25.0	0	0
6	3d	C	4.7	0	0	27.0	22.8
7	3e	A	19.7	71.5	20.0	0	0
8	3f	D	3.0	77.0	0	0	0

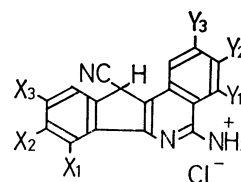
the intermediary benzyl cyanides (**4**) were unusually reactive as in the case of compounds **3d** and **3e** with chlorosubstituents. For example, the reaction of **3d** by method C (entry 6) gave only the disubstituted compound **5d** and **6d**, which would be formed by cyclization of **5d**. Method A was introduced in such cases. Use of protic solvents and a large excess of sodium cyanide suppressed the disubstitution.

Cyclization Reactions of 2,3-Bis(2-cyanophenyl)propionitriles (1). Of the reactants used in the original red pigment formation,² diethyl carbonate does not seem to be essential for the cyclization reaction.

Thus, when a solution of the propionitrile (**1a**) in ethanol was refluxed in the presence of two molar equivalents of sodium ethoxide under nitrogen atmosphere for 2 h, a dark brown reaction mixture was obtained. This mixture was warmed with 1% sodium hydroxide solution for a short time in order to confirm the dissolution of the acidic product. It was then filtered. After acidification of the filtrate with dil. hydrochloric

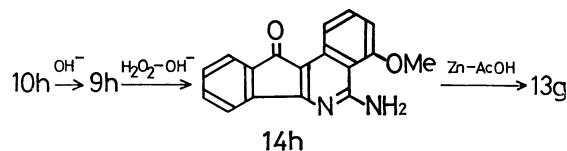


Scheme 2.



10

Fig. 2.



Scheme 3.

acid solution, the cyclized product **9a** was isolated as a colorless hydrochloride (**10a**) in 55% yield.⁴ The undissolved material was separated by silica gel chromatography to afford a product in 3% yield, identified as **13a**. **13a** was obtained from **2** by treatment with alkaline hydrogen peroxide and the subsequent reduction with zinc-acetic acid.^{2a} The formation of **13** is best interpreted by the cyclization of **1** via C-2 anion **11** followed by aromatization of the resulting heterocyclic ring with loss of the cyano group (Scheme 2). The possibility of the formation of **13** via **9** was excluded by the fact that cyclization of the propionitrile (**1g**) afforded **13g** and not **13h**. The substitution pattern was confirmed by the derivation of **13g** from **9h** through the reaction sequence used for the conversion of **2** into **13a** (Scheme 3). Thus the cyclization reaction of the 2,3-bis(2-cyanophenyl)propionitriles (**1**) with a base is dichotomic.

Cyclization experiments carried out in the same way as above for variously substituted 2,3-bis(2-cyanophenyl)propionitriles (**1**) have confirmed this to be the case.

TABLE 2. CYCLIZATION REACTIONS OF 2,3-BIS(2-CYANOPHENYL)PROPIONITRILES (**1**)

Substrate	Reaction conditions		Yield (%)		Ratio 9/13
	NaOEt (mol eq.)	Time (h)	9	13	
1a	2	2	55	3	18.3
1b	14	2	0	81	0
1c	2	2	66	7	9.4
1d	2	2	34	40	0.85
1e	2	2	61	6	10.2
1f	2	2	32	45	0.71
1g	4	4	23	46	0.50
1h	2	2	27	50	0.54

The results are summarized in Table 2. Formation of the dual products **9** and **13** takes place, with the exception of **1b**, which is extremely nonreactive, giving only **13b** upon reaction with use of excess base (14 molar equiv.). In the case of the propionitrile with unsubstituted aryl rings (**1f**) and the *p*-substituted analog (**1d**), the molar ratios of **9** to **13** are smaller than 1.

On the other hand, the molar ratios of *m*-substituted compounds (**1a**, **1c**, and **1e**) are larger than 1. Thus the formation ratios of **9** to **13** are considerably affected by the substitution patterns of the aryl rings, especially by the position of the substituents.

This should be interpreted in terms of the substituent effect on the relative reactivity of the intermediate anions **7** and **11**. The C-3 carbanion **7** would be formed in much smaller amount as compared to the C-2 carbanion **11**.

However, the cyclization of **7** gives the product **9**, which is in turn converted into a stabilized anion **15**.

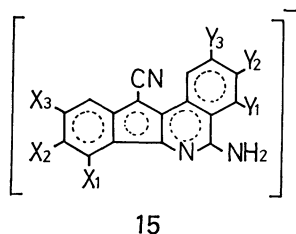
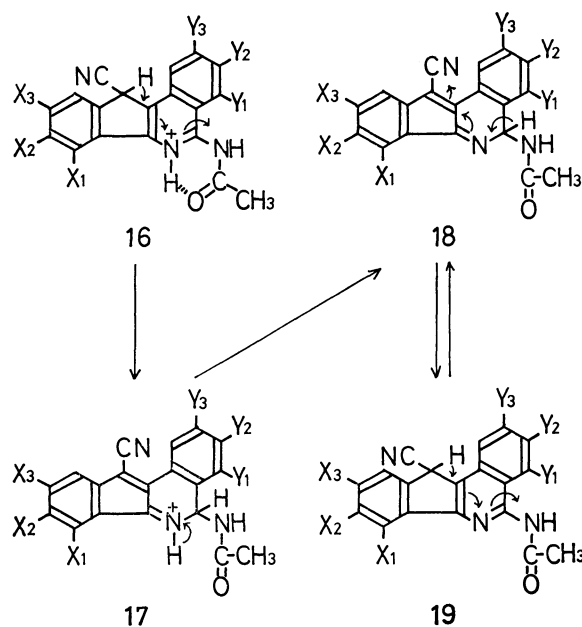


Fig. 3.

In contrast, the reaction of **11** leads to the formation of unstable cyclization product **12**, which could be aromatized only by the loss of the angular cyano group; **12** would be mostly reverted to **11**. The results obtained for the compounds **1g** and **1h**, in which the two aromatic rings are substituted in different ways, indicate that the formation ratios of **9** to **13** can not be explained by the substituent effect on the relative stability of the intermediate anions **7** and **11**. Unless the C-3 carbanion formation is extremely depressed by the presence of an electron-releasing group in para position as in the case of **7b**, the formation of **9** is considered to become comparable to that of **13** (**1d** and **1f**). The promoting effect of *m*-substituents, especially *m*-methoxyl group for the cyclization to **9** is remarkable (**1a**, **1c**, and **1e**) but it is difficult to give an explanation entirely in terms of inductive effect.

Tautomerism of the Acetamides 18 and 19 Derived from 9. For the purpose of identification, analogs **9** substituted in various ways were converted into acetamides by treatment with acetic anhydride and a catalytic amount of concd. sulfuric acid. The resulting solution of isoquinolinium salt (**16**) was poured into ice-water, yielding the colored acetamides (**18**). The 5*H*-indeno[1,2-*c*]isoquinoline structures (**18**) were characterized by coloration and strong absorption near 2160 cm⁻¹. The specific formation of **18** from **16** can be accounted for by the mechanism shown in Scheme 4. The hydrolysis of **16** is initiated by the release of the proton at position 11 rather than that on ring nitrogen atom, which is trapped by strong hydrogen bonding.

When compounds **18** were dissolved in chloroform, one of them gave a colorless solution, while the others gave solutions with the same color as the original compound or a different one. Crystallization from the solutions gave either the original 5*H*-indeno[1,2-*c*]isoquinolines (**18**), or a colorless compound. The IR spectrum of the latter compound exhibits a weak absorption band due to the nitrile group at 2250 cm⁻¹,



Scheme 4.

TABLE 3. TAUTOMERISM OF 5-ACETAMIDO-11-CYANOINDENO[1,2-*c*]ISOQUINOLINES

Group	Parent amino compd.	5 <i>H</i> -isomer (18)		Coloration of CHCl ₃ soln.	11 <i>H</i> -isomer (19)	
		Color	ν/cm^{-1} ^{a)}		Color	ν/cm^{-1} ^{a)}
(i)	9a	red	2165(s)	red		
(ii)	9d	dark	2160(s)	pale		
	9e	green		yellow		
		red	2160(s)	pale yellow		
(iii)	9f	purple	2180(s)	colorless	colorless	2250(w)

a) (s): strong, (w): weak.

indicating that it represents the 11*H*-indeno[1,2-*c*]isoquinoline structure (**19**), tautomeric with **18**. The behavior of **9** by the above treatment in relation to the substitution patterns of the aryl rings can be classified into three groups (Table 3).

(i) No color change on dissolution in chloroform and recovery of the 5*H*-isomer on crystallization.

(ii) Color change to pale yellow and recovery of the 5*H*-isomer.

(iii) Change to colorless and conversion into 11*H*-isomer.

The correlation between the relative stability of 5*H*- and 11*H*-isomers, and the substitution patterns of the aryl rings is not clear from the data available.

Experimental

Melting points were uncorrected. IR spectra were measured in Nujol mull. NMR spectra were determined at 60 MHz unless otherwise stated. Chemical shifts are given in δ -values, using TMS as an internal standard. The instruments used are the same as those reported.^{2a)}

2,3-Bis(2-cyano-3-methoxyphenyl)propionitrile (1a). Method B: A solution of **3a** (8.93 g) and NaCN (2.9 g) in ethanol-

TABLE 4. 2,3-Bis(2-CYANOPHENYL)PROPIONITRILES (**1**) AND 2-CYANOBENZYL CYANIDES (**4**)

Compd No.	Mp/°C (Solv. for recryst.) ^{a)}	Formula	Calcd (Found) (%)			IR ν/cm^{-1} -CN	Solv. ^{a)}	NMR			
			C	H	N			δ/ppm (J/Hz)			
								ArH	>CH	-OCH	>CH ₂
1a	161—162 (M)	C ₁₉ H ₁₅ N ₃ O ₂	71.91 (71.93)	4.76 4.88	13.24 13.12)	2225	CDCl ₃	7.73— 6.81m	4.48t (7.5)	3.93 s 3.90 s	3.42d (7.5)
1b	133.5—134.5 (B-P)	C ₁₉ H ₁₅ N ₃ O ₂	71.91 (71.91)	4.76 4.84	13.24 13.26)	2230	TFA	7.67— 7.20m	4.67t (7.0)	3.93 s	3.57d (7.0)
1c	152—152.5 (B)	C ₁₉ H ₁₅ N ₃ O ₂	71.91 (71.79)	4.76 4.78	13.24 13.16)	2220	CDCl ₃	7.63— 6.77m	4.50t (7.5)	3.87 s	3.50d (7.5)
1d^{b)}	147—148 (B-P)	C ₁₇ H ₉ N ₃ Cl ₂	62.60 (62.47)	2.78 2.85	12.88 12.76)	2230	CDCl ₃	7.68— 7.36m	4.54t (7.5)		3.56dd, 3.36dd (7.5, 14.0)
1e^{b)}	197—198 (M)	C ₁₇ H ₉ N ₃ Cl ₂	62.60 (62.64)	2.78 2.92	12.88 12.93)	2230	TFA	7.68— 7.36m	4.73t (7.0)		3.68dd, 3.52dd (7.0, 14.0)
1f^{c)}	114 (M)					2250 2230	TFA	8.17— 7.23m	4.80t (7.0)		3.72d (7.0)
1g	187.5 (C-M)	C ₁₈ H ₁₃ N ₃ O	75.24 (74.94)	4.56 4.65	14.63 14.71)	2240 2230					
1h	136—137 (M)	C ₁₈ H ₁₃ N ₃ O	75.24 (75.13)	4.56 4.69	14.63 14.34)	2240 2230					
4a	114—116 (C-T)	C ₁₀ H ₈ N ₂ O	69.75 (69.62)	4.68 4.79	16.27 16.16)	2265 2225					
4b	83.5—84.5 (B-P)	C ₁₀ H ₈ N ₂ O	69.75 (69.71)	4.68 4.74	16.27 16.05)	2250 2230					
4d	67—67.5 (D-P)	C ₉ H ₅ N ₂ Cl	61.21 (61.23)	2.85 2.92	15.86 15.50)	2230					
4e	119—120 (D)	C ₉ H ₅ N ₂ Cl	61.21 (61.31)	2.85 2.98	15.86 15.45)	2235					

a) B: benzene, C: chloroform, D: diethyl ether, M: methanol, P: petroleum ether, T: tetrachloromethane, TFA: trifluoroacetic acid. b) The NMR spectra of **1d** and **1e** were measured at 100 MHz. c) Ref. 5, mp 114 °C.

water (4 : 1, 250 ml) was refluxed for 6 h. After extraction with chloroform and evaporation of the solvent, the residue was chromatographed on silica gel. Elution with benzene-chloroform (1 : 1) afforded **4a** (4.02 g). Further elution with the same eluent gave **1a** (1.08 g). The physical data of **1a—1h**, **4a**, **4b**, **4d**, and **4e** are summarized in Table 4.

Method D: A mixture of **3a** (1 g), NaCN (434 mg), NaI (45 mg), and dry acetone (12 ml) was stirred and refluxed for 24 h. After addition of water, extraction with chloroform and evaporation of the solvent, the residue on crystallization from methanol gave **1a** (547 mg).

2,3-Bis(2-cyano-4-methoxyphenyl)propionitrile (1b). **Method D:** A mixture of **3b** (7.0 g), NaCN (5.25 g), NaI (420 mg), and dry acetone (60 ml) was treated in the same way as described for **1a**. After evaporation of the solvent, the residue was chromatographed on silica gel.

Elution with benzene afforded **4b** (1.06 g). Elution of the column with benzene-chloroform (1 : 1) gave **1b** (2.89 g).

2,3-Bis(2-cyano-5-methoxyphenyl)propionitrile (1c). **Method D:** **3c** (6.76 g) was cyanated as above. After evaporation of the solvent, the residue was crystallized from methanol-benzene to give 2-cyano-1,2,3-tris(2-cyano-5-methoxyphenyl)propane (**5c**) (307 mg), mp 211—212 °C; ν_{max} 2220 cm⁻¹ (-CN); $\delta(\text{CF}_3\text{CO}_2\text{H})$ 4.12 (4H, s, 2 × ArCH₂), 3.89 (3H, s, ArOCH₃), and 3.85 (6H, s, 2 × ArOCH₃). Found: C, 72.80; H, 4.87; N, 12.00%. Calcd for C₂₈H₂₂N₄O₃: C, 72.71; H, 4.79; N, 12.12%. The filtrate was chromatographed on silica gel.

Elution with benzene-chloroform (1 : 1) gave **1c** (4.0 g).

2,3-Bis(2-cyano-4-chlorophenyl)propionitrile (1d). **Method A:** A solution of **3d** (5.74 g) in ethanol (92 ml) was added to a solution of NaCN (15.5 g) in water-ethanol (1 : 1, 186 ml)

and mixed. The resulting solution was allowed to stand at -20 °C for 48 h. After addition of water (300 ml), extraction with chloroform and evaporation of the solvent, the residue was chromatographed on silica gel. Elution with benzene-petroleum ether (1 : 1) gave **4d** (1.1 g). Further elution with the same eluent gave **1d** (2.19 g).

Method C: A mixture of **3d** (1 g), NaCN (1 g), NaI (20 mg), and dry acetone (10 ml) was stirred at room temperature for 48 h. After addition of water, extraction with chloroform and evaporation of the solvent, the residue was chromatographed on silica gel. Elution with benzene gave 2-cyano-1,2,3-tris(2-cyano-4-chlorophenyl)propane (**5d**) (186 mg), mp 210—211 °C (from benzene-petroleum ether); ν_{max} 2230 cm⁻¹ (-CN); $\delta(\text{CDCl}_3)$ 4.22, 3.80 (4H, ABq, $J=14.0$ Hz, 2 × >CH₂). Found: C, 63.41; H, 2.90; N, 11.59%. Calcd for C₂₅H₁₃N₄Cl₃: C, 63.11; H, 2.75; N, 11.78%. Elution of the column with chloroform gave 5-amino-11-cyano-3,8-dichloro-11-(2-cyano-4-chlorobenzyl)-11H-indeno[1,2-c]isoquinoline (**6d**) (157 mg), mp 209—210 °C (from methanol); $\lambda_{\text{max}}^{\text{H}_2\text{SO}_4-\text{EtOH}}$ 208 ($\epsilon \times 10^{-3}$, 61.4), 225 (55.9), 233 sh (49.6), 341 (18.2), 372 (13.2), and 390 nm (10.0); ν_{max} 3490 and 3380 (-NH₂) and 2230 cm⁻¹ (-CN); $\delta(\text{CDCl}_3)$ 8.10—6.77 (9H, m, ArH), 5.57 (2H, s, -NH₂, disappears on D₂O exchange), 4.00 (1H, d, $J=14.0$ Hz, >CH_AH_B) and 3.45 (1H, d, $J=14.0$ Hz, >CH_AH_B). Found: C, 62.66; H, 2.76; N, 11.63%.

Calcd for C₂₅H₁₃N₄Cl₃: C, 63.11; H, 2.75; N, 11.78%.

2,3-Bis(2-cyano-5-chlorophenyl)propionitrile (1e). **Method A:** **3e** (1.58 g) was treated in the same way as described for **1d**. Elution of the silica gel column with benzene-petroleum ether (1 : 1) gave **4e** (245 mg). Elution of the column with benzene-chloroform (1 : 1) gave **1e** (800 mg).

2,3-Bis(2-cyanophenyl)propionitrile (1f). **Method D:** **3f**

TABLE 5. 5-AMINO-11-CYANO-11*H*-INDENO[1,2-*c*]ISOQUINOLINE HYDROCHLORIDES (**10**) AND 5-AMINO-11*H*-INDENO[1,2-*c*]ISOQUINOLINES (**13**)

Compd No.	Mp/°C ^b	Formula	Calcd (Found) (%)			IR ν/cm^{-1}		NMR ($\text{CF}_3\text{CO}_2\text{H}$) ^a δ/ppm		
			C	H	N	$-\text{NH}_3^+$ or $-\text{NH}_2$	$-\text{CN}$	ArH	$>\text{CH}$ $>\text{or CH}_2$	$-\text{OCH}_3$
10a	249dec	$\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}_2\text{Cl}$	64.50 (64.15)	4.56 4.76	11.88 11.72	3300 3080—2760	2245	8.27— 7.20m	5.30s	4.34s 4.13s
10c	268dec	$\text{C}_{19}\text{H}_{16}\text{N}_3\text{O}_2\text{Cl}$	64.50 (64.27)	4.56 4.72	11.88 11.66	3290, 3190 2620	2245	8.42— 7.17m	5.27s	4.13s 4.05s
10d	290dec	$\text{C}_{17}\text{H}_{10}\text{N}_3\text{Cl}_3$	56.30 (56.64)	2.78 2.80	11.59 11.44	3405, 3180 2760	2240	8.42— 7.52m	5.27s	
10e	290dec	$\text{C}_{17}\text{H}_{10}\text{N}_3\text{Cl}_3$	56.30 (56.24)	2.78 2.89	11.59 11.57	3280, 3120 2640	2240	8.48— 7.64m	5.34s	
10f	278dec	$\text{C}_{17}\text{H}_{12}\text{N}_3\text{Cl}$	69.51 (69.43)	4.12 4.25	14.30 14.27	3240, 3100 2580	2240	8.55— 7.57m	5.32s	
10g	279dec	$\text{C}_{18}\text{H}_{14}\text{N}_3\text{OCl}$	66.77 (66.61)	4.36 4.48	12.98 12.68	3180—2740	2240	8.58— 7.25m	5.40s	4.33s
10h	275dec	$\text{C}_{18}\text{H}_{14}\text{N}_3\text{OCl}$	66.77 (66.74)	4.36 4.53	12.98 12.76	3420, 3260 3160, 2440	2245	8.27— 7.28m	5.27s	4.27s
13a	229—230 dec	$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$	73.95 (73.73)	5.52 5.63	9.58 9.35	3500, 3370		8.03— 6.90m	3.75s	4.13s 4.03s
13b	262dec	$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$	73.95 (73.95)	5.52 5.57	9.58 9.54	3460, 3370 3290, 3130		8.08— 6.95m	3.95s	4.07s
13c	207—208 dec	$\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_2$	73.95 (73.50)	5.52 5.33	9.58 9.32	3460, 3360 3160		7.86— 6.88m	3.80s	3.92s 3.84s
13d	244—245 dec	$\text{C}_{16}\text{H}_{10}\text{N}_2\text{Cl}_2$	63.81 (63.53)	3.35 3.32	9.30 9.36	3480, 3380 3280, 3140		8.20— 7.26m	3.98s	
13e	295	$\text{C}_{16}\text{H}_{10}\text{N}_2\text{Cl}_2$	63.81 (63.70)	3.35 3.42	9.30 9.29	3480, 3280 3140		8.34— 7.48m	4.06s	
13f	207—208 dec	$\text{C}_{16}\text{H}_{12}\text{N}_2$	82.73 (82.61)	5.21 5.32	12.06 12.06	3300, 3100		8.32— 7.32m	3.85s	
13g	193.5— 195.5	$\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$	77.84 (77.79)	5.38 5.49	10.68 10.49	3480, 3280 3160		8.03— 7.00m	3.73s	4.08s
13h	209—211	$\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}$	77.84 (77.51)	5.38 5.49	10.68 10.41	3360, 3200		8.27— 6.87m	3.97s	4.03s

a) The spectrum of **13c** was measured in CDCl_3 . b) Recrystallized from methanol. dec: decomposition.TABLE 6. 5-ACETAMIDO-11-CYANO-5*H*-INDENO[1,2-*c*]ISOQUINOLINES (**18**) AND 5-ACETAMIDO-11-CYANO-11*H*-INDENO[1,2-*c*]ISOQUINOLINE (**19f**)

Compd No.	Mp/°C ^a	Formula	Calcd (Found) (%)			IR ν/cm^{-1} ^b			NMR ($\text{CF}_3\text{CO}_2\text{H}$) δ/ppm			
			C	H	N	$>\text{NH}$	$-\text{CN}$	$>\text{CO}$	ArH	$>\text{CH}$	$-\text{OCH}_3$	$-\text{COCH}_3$
18a	292—293 dec	$\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_3$	70.18 (69.84)	4.77 4.86	11.69 11.77	3300	2165s	1680 w	8.40— 7.20m	5.53s	4.37s 4.27s	2.73s
18d	263—264 dec	$\text{C}_{19}\text{H}_{11}\text{N}_3\text{O}_3\text{Cl}_2$	61.20 (60.99)	3.01 2.90	11.41 10.94	3210	2160s	1695 w	8.72— 7.74m	5.62s		2.74s
18e	280.5— 281dec	$\text{C}_{19}\text{H}_{11}\text{N}_3\text{OCl}_2$	61.20 (61.06)	3.01 2.92	11.41 11.26	3200 3120	2160s	1690 w	8.74— 7.76m	5.60s		2.74s
19f	269—270 dec	$\text{C}_{19}\text{H}_{13}\text{N}_3\text{O}$	76.24 (75.81)	4.38 4.64	14.04 13.93	3180 3100	2250 w	1690s	8.70— 7.72m	5.58s		2.74s

a) Recrystallized from chloroform. b) s: strong, w: weak.

(10.5 g) was treated in the same way as described for **1a** to give **1f** (5.54 g).

2-(2-Cyano-3-methoxyphenyl)-3-(2-cyanophenyl)propionitrile (**1g**) and 2-(2-Cyanophenyl)-3-(2-cyano-3-methoxyphenyl)propionitrile (**1h**). A mixture of **4a** (2.0 g), **3f** (2.27 g), K_2CO_3 (1.6 g), NaI (150 mg, and dry acetone (30 ml) was refluxed for 24 h. After filtration and evaporation, the residue was crystallized to give **1g** (2.76 g, 82.6%). **1h** was similarly prepared in 72% yield from **4f**⁶ and **3a**.

Cyclization Reactions of the Propionitriles (**1**). General

Procedure: A solution of sodium ethoxide (2 mmol; **14** and 4 mmol for **1b** and **1g** respectively) in ethanol (5 ml) was added to a mixture of **1** (1 mmol) and ethanol (10 ml). The mixture was stirred and refluxed for 2 h (4 h for **1g**). When the reaction was completed,⁷ 1% NaOH aqueous solution (30 ml) was added and warmed for 30 min. The solution was then cooled and allowed to stand in a refrigerator overnight. The precipitates were collected by filtration and chromatographed on silica gel. Elution with chloroform gave **13**. By acidification of the filtrate with an excess of dilute hydrochloric

TABLE 7. UV SPECTRAL DATA OF **10**, **13**, **18**, AND **19**

	10 (H ₂ SO ₄ -EtOH) ^{c)}	$\lambda_{\max}^{\text{a)}}$ /nm ($\epsilon \times 10^{-3}$) 13 (H ₂ SO ₄ -EtOH) ^{c)}	18 or 19^{b)} (EtOH)
a	220 (32.5), 263 (19.6) 332s(10.3), 344 (13.2) 380 (16.3), 398 (15.0)	220 (36.9), 259 (21.3) 328 (13.5), 342 (16.2) 386 (17.6), 405 (16.5)	217 (23.8), 250 (36.2), 279s(24.3), 286 (25.4) 325 (15.3), 384 (17.1), 520 (4.5),
b		228 (41.4), 327 (19.0) 340 (19.4), 392 (11.6) 410 (10.7)	
c	216 (25.2), 252 (21.8) 280 (38.0), 338 (18.8) 354s(16.2), 370s(14.3)	212 (25.9), 253 (22.5) 280 (38.7), 340 (20.3) 370 (15.7)	
d	223 (41.0), 233 (36.7) 325s(16.0), 337 (17.2) 372 (11.0), 390 (8.3)	223 (53.0), 234s(35.4) 324 (22.9), 338 (23.5) 380 (13.0), 400 (10.8)	220 (30.7), 234 (29.9), 265 (32.2), 282 (28.0) 303 (20.3), 320 (16.8), 330 (15.7), 366 (8.4) 428 (3.6), 460s(2.5)
e	213 (27.8), 260 (32.2) 327s(18.2), 335 (19.7) 366 (13.4), 384 (10.6)	212 (28.4), 258 (29.6) 324 (19.3), 337 (20.8) 375 (13.8), 392 (10.5)	230s(27.6), 243s(28.2), 272 (42.0), 330 (15.3) 356s (8.3), 422s(3.8), 458s(2.8), 540s(1.0)
f	213 (31.4), 239 (27.4) 316 (16.0), 330 (16.5) 364 (11.3), 382 (9.6)	213 (33.0), 244 (23.5) 316 (14.7), 330 (14.9) 374 (10.0), 388s (8.2)	212 (30.2), 261 (33.9), 293 (12.8), 301 (13.0) 314 (13.7), 357 (6.7), 420 (1.8), 460s(1.3)
g	218 (40.5), 245 (28.9) 342 (19.8), 372 (12.6) 388s(10.0)	216 (30.7), 225s(29.4) 250 (19.7), 257 (18.9) 318 (13.4), 332 (14.4) 380 (18.4), 400 (17.9)	
h	227 (29.8), 248 (16.6) 262 (16.9), 320 (10.5) 334 (11.7), 372 (16.6) 392 (15.8)	216 (35.0), 245 (25.7) 329 (16.6), 341 (18.5) 381 (10.7), 396s(8.8)	

a) s: shoulder. b) **18**: **a**, **d** and **e**; **19**: **f**. c) Containing two drops of 0.5 mol dm⁻³ H₂SO₄ per 10 ml.

acid, **10**, a hydrochloride of **9**, was obtained as a colorless precipitate. The physical data of **10** and **13** are given in Tables 5 and 7.

Oxidative Degradation of **10h** with Alkaline Hydrogen Peroxide.

To a solution of **10h** (600 mg) in a mixture of 10% NaOH-EtOH (1: 4, 50 ml) was added 3% H₂O₂ (40 ml) and the mixture was stirred at 0 °C for 30 min. After dilution with water (400 ml) the resulting red precipitate was collected by filtration and recrystallized from chloroform to afford 5-amino-4-methoxy-11*H*-indeno[1,2-*c*]isoquinolin-11-one (**14h**) (396 mg, 77.5%), mp 247.5–248 °C; $\nu_{\max}$ 3500, 3290, and 3130 (–NH₂) and 1685 cm⁻¹ (>CO); δ (CF₃CO₂H) 8.47–7.17 (7H, m, ArH) and 4.22 (3H, s, ArOCH₃). Found: C, 73.74; H, 4.46; N, 10.19%. Calcd for C₁₇H₁₂N₂O₂: C, 73.90; H, 4.38; N, 10.14%.

Zinc Dust Reduction of 14h. **14h** (440 mg), zinc dust (2.2 g), and glacial acetic acid (20 ml) were mixed and refluxed for 2 h. The insoluble material was removed by filtration. The filtrate was made basic by the addition of ammonia solution under ice-cooling. The resulting precipitate was collected by filtration and recrystallized from methanol to give pure 5-amino-4-methoxy-11*H*-indeno[1,2-*c*]isoquinoline (375 mg, 90%), mp 193.5–194.5 °C, which was identical with **13g** produced by the cyclization of **1g** in comparison of their TLCs, mps, and IR spectra.

Acetylation of **9**.

General Procedure: To a mixture of **10** (100 mg) and Ac₂O (10 ml) was added a few drops of concd. H₂SO₄ at room temperature. After being left to stand for a certain time (1 h for **10a**, **10d**, and **10f**; a few min for **10e**), the mixture was poured into ice-water. The precipitated pigment was collected by filtration and crystallized from chloroform. The physical data of the acetamides **18** and **19** are summarized in Tables 6 and 7.

References

- 1) The numbering of the title compounds appearing in Parts I and II should be corrected as indicated in this paper.
- 2) a) Part I: K. Ando, T. Tokoroyama, and T. Kubota, *Bull. Chem. Soc. Jpn.*, **47**, 1008 (1974); b) Part II: K. Ando, T. Tokoroyama, and T. Kubota, *ibid.*, **47**, 1014 (1974).
- 3) T. Tokoroyama, T. Nishikawa, K. Ando, M. Nomura, and T. Kubota, *Nippon Kagaku Kaishi*, **1974**, 136.
- 4) The free amine (**9**) is liable to be oxidized in the air.²⁾
- 5) D. G. Buckley, E. Ritchie, and W. C. Taylor, *Aust. J. Chem.*, **22**, 577 (1969).
- 6) 2-Cyanobenzyl cyanide (**4f**) was prepared by treating **3f** with KCN in aqueous ethanol; T. S. Osdene and G. M. Timmis, *J. Chem. Soc.*, **1955**, 2214.
- 7) Completion of the reaction was checked by TLC (silica gel, benzene, or chloroform).