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(24) This compound melts around 150 °C, but resolidifies on further heating to give yellow crystals, mp 211–214 °C.
(25) This absorption disappears if the compound is dried at 120 °C for 70 min to give yellow-colored crystals, which, according to NMR, do not contain methylene chloride.
(26) The high-melting modification can be obtained from the low-melting modification by melting and resolidification.
(27) No attempts were made to optimize the yields.
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Anodic Cyanation of Tertiary Aliphatic and Heterocyclic Amines

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Electrochemical cyanation of tertiary aliphatic and heterocyclic amines in sodium cyanide–aqueous methanol solution using platinum electrodes was studied. Cyanation occurred at the carbon α to the nitrogen atom in each case to form corresponding α-cyano amines in reasonable yields. Some of the unsymmetrical aliphatic and heterocyclic amines gave two isomers. From the relative amounts of the isomers, it was found that the order of ease of the cyanation at the α position of the alkyl group is $(CH_2)_4 > (CH_2)_5 > CH_3 > C_2H_5 > n\text{-}C_3H_7 > i\text{-}C_3H_7$, and that the substitution occurs at the α-carbon situated in positions easily accessible to the electrode.

Electrochemical cyanation of organic compounds has been studied by various investigators,[1-3] but there are only a few reports on the anodic cyanation of amines. Previously, Andreades and Zahnow[4] found that the anodic oxidation of *N,N*-dialkylanilines and benzylamines gave rise to cyanation at the alkyl carbon atom α to the amino nitrogen. Yoshida and Fueno[5] pointed out that the anodic oxidation of diphenylamines in methanol containing sodium cyanide gave *p*-cyanodiphenylamines in good yields. However, no systematic reports are available on the cyanation of tertiary aliphatic amines. We have now studied anodic cyanation of tertiary aliphatic and heterocyclic amines in aqueous methanol containing sodium cyanide at a platinum electrode, and have examined whether this reaction could be used for the preparation of α-cyano amines on a macro scale.

Results

Prior to the preparative studies, current–potential measurements were carried out with triethylamine and α-diethylaminopropionitrile in 0.5 M sodium cyanide–aqueous methanol solution at a platinum anode.

As shown in Figure 1, triethylamine initiated a discharge at approximately 0.7 V (SCE) and then the current rose steeply at 0.9 V or over, whereas α-diethylaminopropionitrile was oxidized at about 0.3 V more anodic than triethylamine. Generally, oxidation potentials of the cyanated products are substantially higher than the values for the corresponding amines. In aqueous methanolic sodium cyanide without triethylamine, a deviation from the ohmic current was observed in the vicinity of 1.0 V, and the electrolytic current gradually increased through the potential of 1.7 V.[6-8] Despite the high concentration of cyanide ion, the degree of increase in the current was very low. Therefore, in the presence of amine, the oxidation of amine itself would be insignificantly affected below 1.4 V.

According to controlled potential electrolyses of triethylamine in 2.0 M sodium cyanide solution, the number of electrons, n, involved in the overall electrode reaction amounted to ca. 2 at 1.2 V.

In a similar manner, relative discharge potentials of other amines were read from the current–potential curves. Each amine employed, except for diisopropylmethylamine and *N-tert*-butylpyrrolidine, was significantly oxidized in a potential range from 0.97 to 1.05 V.

On the basis of the data, preparative constant current electrolyses were carried out under such conditions as to maintain the potential at a convenient range.

In Table I, representative results of anodic cyanation of several kinds of tertiary amines on a macro scale are summarized.

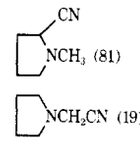
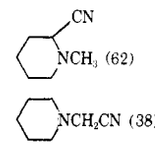
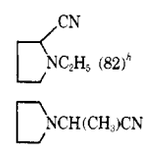
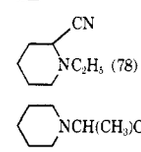
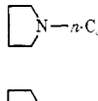
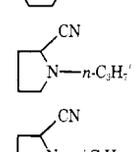
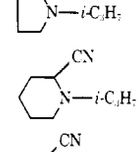
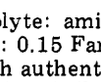
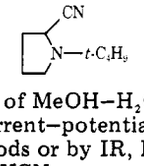
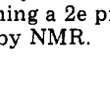
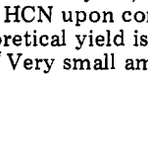
In each case, cyanation occurred exclusively at the carbon atom α to the nitrogen atom and the corresponding α-cyano amines were produced in reasonable yields. Unsymmetrical tertiary aliphatic amines with the methyl group were mainly cyanated at the methyl group, and the amount of cyanation at the methylene group decreased as the length of the alkyl group increased. No cyanated products at the methine group were obtained from dimethylisopropylamine and diisopropylmethylamine.

On the other hand, some of the *N*-alkylpiperidine and pyrrolidine derivatives gave two isomers, one of which was a product substituted at the ring and the other was a product cyanated at the side chain, and it was ascertained that the former product invariably formed in preference to the latter. For example, *N*-methylpiperidine gave *N*-methyl-2-cyanopiperidine in a yield of 41% and α-piperidineacetonitrile in a 25% yield according to GLC analysis (62:38). In the case of *N*-ethylpiperidine, the ratio of cyanation at the ring to the side chain was 78:22, and in *N*-isopropylpiperidine, no side chain substituted product was detected. A similar tendency was observed for *N*-alkylpyrrolidine derivatives, although the substitution showed more precedence to the ring α position than the corresponding piperidine derivatives. Apparently, the order of ease of the cyanation at the α position of the alkyl group is as follows: $(CH_2)_4 > (CH_2)_5 > CH_3 > C_2H_5 > n\text{-}C_3H_7 > i\text{-}C_3H_7 = 0$. This order is compatible with that of steric hindrance around the nitrogen atom of amine.

Table II shows the results of the constant potential electrolysis of *N*-methylpiperidine at various anode potentials.

The current efficiency for the formation of the cyanated products was about 95% even at a potential of 1.4 V. In addition, the relative amount of the isomers was hardly affected by the potentials.

Table I. Anodic Cyanation of Tertiary Aliphatic and Heterocyclic Amines[a]

Expt	Amine	Registry no.	Discharged[b] potential, V vs. SCE	Anode potential, V vs. SCE	Products[c]	Material[d] yield, %	Current[g] efficiency, %
1	$(CH_3)_3N$	75-50-3	1.03	1.2–1.4	$(CH_3)_2NCH_2CN$	[53]	[70]
2	$(C_2H_5)_3N$	121-44-8	0.97	1.1–1.2	$(C_2H_5)_2NCH(CH_3)CN$	36[e] [53][f]	48 [70]
3	$(CH_3)_2NC_2H_5$	598-56-1	1.02	1.0–1.3	$(C_2H_5)(CH_3)NCH_2CN$ (79) $(CH_3)_2NCH(CH_3)CN$ (21)	31 [44]	41 [58]
4	$(C_2H_5)_2NCH_3$	616-39-7	1.02	1.0–1.2	$(C_2H_5)_2NCH_2CN$ (57) $(C_2H_5)(CH_3)NCH(CH_3)CN$ (43)	32 [37]	43 [49]
5	n-$C_3H_7N(CH_3)_2$	926-63-6	1.02	1.1–1.3	(n-C_3H_7)$(CH_3)NCH_2CN$ (84) $(CH_3)_2NCH(C_2H_5)CN$ (16)	40 [53]	54 [70]
6	i-$C_3H_7N(CH_3)_2$	996-35-0	1.01	1.1–1.2	(i-C_3H_7)$(CH_3)NCH_2CN$	40 [54]	54 [73]
7	$(i$-$C_3H_7)_2NCH_3$	10342-97-9	0.90	0.9–1.1	$(i$-$C_3H_7)_2NCH_2CN$	43 [55]	57 [73]
8		120-94-5	0.99	1.0–1.3		46 [59]	62 [79]
9		626-67-5	1.05	1.1–1.4		57 [66]	76 [88]
10		7335-06-0	1.00	1.0–1.2		57	76
11		766-09-6	1.05	1.1–1.3		61	82
12		7335-07-1	0.98	1.0–1.2		59	79
13		17544-07-9	0.99	1.0–1.1		57	75
14		766-79-0	1.00	1.0–1.2		62	82
15		15185-01-0	0.92	0.9–1.0		63	84

[a] Anolyte: amine (0.10 mol) and NaCN (0.15 mol) in 75 mL of MeOH–H_2O (1:1). Constant current: 0.5 A. Consumed current: 0.15 Faraday. Temperature: 3 °C. [b] Read from the current–potential curve. [c] Identified either by direct comparison with authentic samples prepared by the Knoevenagel methods or by IR, NMR, and mass spectrum. Elemental analyses of α-aminonitriles are uncertain because they easily eliminated HCN upon combustion. Their picrates were analyzed. [d] Calculated by not considering recovery of unchanged amine. Theoretical yield is 75%. [e] Isolated yield. [f] According to GLC. [g] Assuming a 2e process. [h] The ratio was determined by NMR. [i] Very small amounts of α-pyrrolidinebutyronitrile were detected by NMR.

Discussion

The reaction mechanism for the present electrolysis appears to be analogous to that of anodic oxidation of tertiary amine, because amine is exclusively oxidized in preference to the cyanide ion. Anodic oxidation of aliphatic amines at a platinum electrode in nonaqueous media was studied extensively by Mann and his co-workers,[9] and Masui and Sayo[10] also investigated the electrochemical dealkylation of aliphatic tertiary amines in alkaline aqueous solution at a glassy carbon electrode. According to their reports, the generalized mechanism is as follows.

In the initial step, adsorbed amine undergoes one-electron transfer to form a cation radical (1), followed by deprotonation to give a neutral radical (2) which can undergo a second electron transfer to form the iminium cation (3), or can disproportionate to form the enamine (4). When a sufficient potential for a two-electron oxidation of amine is employed in the presence of sodium cyanide, the former reaction would be favorable and the produced iminium cation (3) would react with the cyanide ion to give α-cyano amine (5). Masui and Sayo[10] also described that the relative amount of dealkylation in unsymmetrical tertiary amines is predominantly governed by acidity and the number of α protons. Similar tendencies were recognized in our experimental results; namely, the order of increasing difficulty of the cyanation at the α carbon was

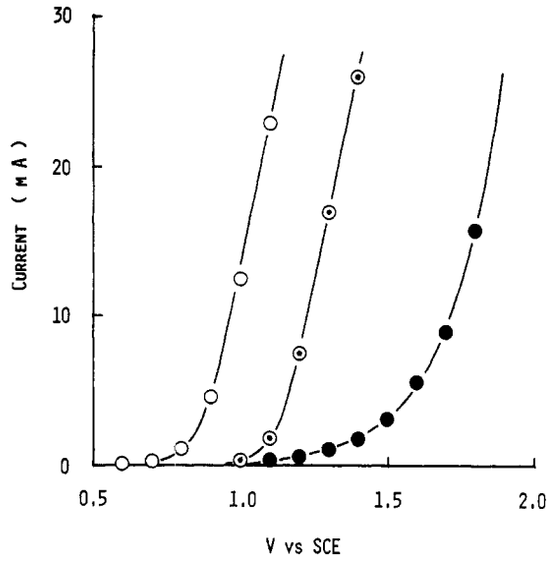
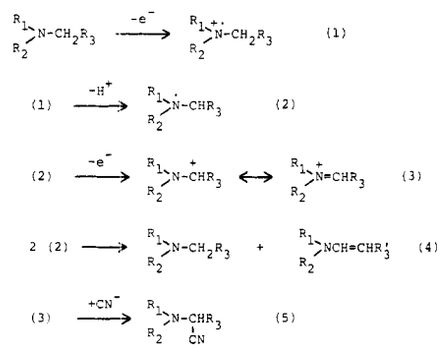


Figure 1. Current–potential curves: ●, 0.5 M NaCN MeOH–H_2O (1:1) solution; ○, in the presence of 0.1 M of $(C_2H_5)_3N$; ⊙, in the presence of 0.1 M of $(C_2H_5)_2NCH(CH_3)CN$ (at 25 °C).

Scheme I



methyl, ethyl, *n*-propyl, and isopropyl. However, it seems insufficient to explain the difference in the relative amount of isomers between five- and six-membered heterocyclic compounds, or in the reactivities of the alkyl group between the ring and the side chain.

It is known that amines are adsorbed through their lone pair of electrons of the nitrogen atom on an anode surface,[11] and that the degree of adsorption of an amine can affect its anodic oxidation.[12] Therefore, it is necessary to take into account the orientation of the amino molecule on the electrode surface. The steric configuration of the adsorbed amine must be appreciably restricted to the site of the electrode by interactions between the alkyl groups around the amino nitrogen and the electrode. As can be seen from the results in Table I, the cyanation at the alkyl groups with a greater steric hindrance was more difficult. Particularly, the isopropyl group should form a stable radical in a homogeneous system; however, the substituted products at the methine group could not be detected by NMR spectrum analysis of the crude product. (A strong singlet adsorption spectra arising from two isolated methyl groups at 1.4 ppm is expected.) Consequently, the deprotonation must occur at the α carbon situated in positions easily accessible to the electrode.

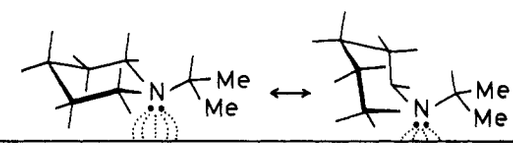
α carbons in the rings with limited free rotation can approach closer to the electrode than those of the side chain; especially it was noted that the five-membered ring has a nearly planar structure for access. Thus it would be preferable to make a substitution at the α carbon in the ring rather than in the side chain, and especially in a five-membered ring, the substitution would be strongly favored. On the contrary, for example, adsorbed *N*-isopropylpiperidine would be forced into such a configuration as to prevent access of the methine group to the electrode by a mutual repulsion between the two methyl groups and axial hydrogen atoms in the ring, and by a steric interaction between the alkyl groups and the electrode as shown in Scheme II.

Table II. Anodic Cyanation of *N*-Methylpiperidine at Various Potentials[a]

Applied potential, V vs. SCE	Conversion, %	Current[d] efficiency, %	Mol ratio of isomers 9a:9b
1.0	1.35	97.5	60[b]:40[c]
1.1	3.1	95.5	61:39
1.2	6.2	93.9	62:38
1.3	8.0	95.7	63:37
1.4	10.8	94.9	61:39

[a] Anolyte: amine (40 mmol) and NaCN (40 mmol) in 20 mL of MeOH–H_2O (1:1). Temperature: 3 °C. [b] *N*-Methyl-2-cyanopiperidine. [c] α-Piperidineacetonitrile. [d] According to GLC.

Scheme II



It may be concluded that the chief determining factor of the end products is steric based on the actual configuration of the adsorbed amine on the electrode surface and the molecular structure itself, rather than the applied potential. This electrolytic method seems to be suitable for the introduction of the cyano group into the ring of heterocyclic amines even though other products are formed.

Experimental Section

Reagents. All amines except for trimethylamine and triethylamine were prepared by the usual methods[13–16] and their purities were checked by GLC analysis. Methanol was purified by fractional distillation. Reagent grade sodium cyanide was used without purification.

Analytical Methods. Gas chromatographic analyses were conducted with a Hitachi Model 163 gas chromatograph using glass columns packed with 20% Apiezon grease and 10% potassium hydroxide on 60–80 mesh Chromosorb W AW. Infrared spectra were recorded on a Hitachi EPI-G2 double beam recording spectrophotometer. Samples were prepared and scanned as a neat liquid between sodium chloride crystals. NMR spectra were recorded on a Hitachi 20-A recording spectrometer as an approximate 20% solution in carbon tetrachloride. Mass spectra were obtained with a Hitachi M-52 instrument.

Potentiostatic Electrolyses. All potentials were referred to a saturated calomel electrode. Controlled potential electrolyses and current–potential measurements were carried out in a H-type cell with a glass frit diaphragm separating two compartments. The anode compartment (25 mL) contained a smooth platinum plate (4.0 cm^2) and was rapidly stirred by a magnetic stirring bar. The cathode compartment (15 mL) contained a platinum wire. This cell was provided with a reference electrode. Anode potential was controlled by using a Nichia HP-500 type potentiostat.

A. Controlled Potential Electrolysis of *N*-Methylpiperidine. A solution consisting of 990 mg (40 mmol) of amine in 20 mL of 2.0 M sodium cyanide–aqueous methanol (1:1) solution was electrolyzed at various anode potentials at 3 °C. The consumed current was estimated from the current–time curve. After the electrolysis, the percent of the products was determined by GLC analysis.

B. Current–Anode Potential Relationships. Current–potential measurements were made in 20 mL of 0.5 M sodium cyanide–aqueous methanol (1:1) solution containing 2 mmol of reactant at 25 °C. Each discharge potential was read from the current–potential curve plotted from the current values after 1 min from adjustment of the potentials for each 10-mV rise from 0.4 to 2.0 V.

Constant Current Electrolyses for Preparative Studies. Large-scale electrolyses were carried out in a 100-mL separable flask shielded from the cathode compartment using a porous cup. A cylindrical platinum net (4.5 cm in height, 11.0 cm in circumference, 55 mesh) was used at the anode and the cathode was a coil of platinum wire (0.8 mm ϕ, 20 cm). A reference electrode was connected to the working electrode. The cell was thermostated at 3 °C, and was stirred by a magnetic stirring bar.

The experimental procedure is as follows. The anolyte contained 0.1 mol of amine and 0.15 mol of sodium cyanide dissolved in 75 mL of 1:1 methanol–water solution (for expt 7–15, 2:1 solution was used). The catholyte was an aqueous methanol solution of sodium cyanide. Electrolysis was carried out under a constant current at 0.5 A for 8 h. Total consumed current was 0.15 Faraday. During the electrolysis, the anode potential was gradualy increased up to 0.3 V above the initial potential. After completion of the reaction, the anolyte was concentrated under reduced pressure at 35 °C on a rotary evaporator, and the remaining crude liquid was saturated with 25 g of anhydrous potassium carbonate. The organic layer was separated, and the aqueous layer was extracted twice with 30-mL portions of ether. The combined extracts were dried with potassium carbonate, and then analyzed by GLC.

Trimethylamine (Expt 1). The anolyte (contained 4.4 g of *N,N*-dimethylaminoacetonitrile[17–19] according to the GLC analysis) was saturated with anhydrous potassium carbonate without evaporation. Then the oily layer was worked up as above and distilled. The portion collected at 35–67 °C (60 mm) was additionally dried and redistilled. The purified sample (bp 134–136 °C) was identical with an authentic sample as shown by IR and NMR. The nonvolatile residue in the first distillation was extracted with ether. The ether solution was decanted and concentrated to ½ volume. A small amount of white, needle crystals of α-dimethylaminoacetamide,[18] mp 94–96 °C, was obtained.

Triethylamine (Expt 2). The product was isolated by distillation. A colorless liquid of α-(*N,N*-dimethylamino)propionitrile[17,22] was obtained at 63–65 °C (17 mm) in a yield of 4.5 g. This was identified with an authentic sample by IR and NMR.

Dimethylethylamine (Expt 3). The crude undistilled liquid product was shown to be 3.3 g of *N*-methyl-*N*-ethylaminoacetonitrile (**3a**) and 1.0 g of α-dimethylaminopropionitrile (**3b**)[17] by GLC analysis (79:21). The aminonitriles were concentrated by distillation [3.0 g, bp 78–83 °C (74 mm)] and each nitrile for the analytical sample was isolated by preparative GLC. **3a**: IR ν 2220 cm^{-1} (CN); NMR δ 1.02 (t, 3 H), 2.30, 2.46 (s, q, 5 H), 3.42 ppm (s, 2 H); mass spectrum *m/e* (rel intensity) 98 (M$^+$, 15), 83 (M$^+$ − 15, 100), 71 (M$^+$ − 27, 9), 42 (38). Picrate of **3a**: yellowish needles from ethanol–acetone, mp 156–157.5 °C. Anal. Calcd for $C_{11}H_{13}N_5O_7$: C, 40.37; H, 4.00; N, 21.40. Found: C, 40.0; H, 3.9; N, 21.5. **3b** was identified with an authentic sample by IR and NMR.

Diethylmethylamine (Expt 4). After evaporation of the solvent, the remainder of the crude liquid exhibited two principal peaks arising from *N,N*-diethylaminoacetonitrile (**4a**)[17,19,20] and α-(*N*-methyl-*N*-ethylamino)propionitrile (**4b**) by GLC analysis. The mole ratio of the products was 57:43. The distillation of the mixture gave 3.6 g of colorless liquid at 64–67 °C (23 mm) and analytical samples were obtained by preparative GLC. The IR and NMR spectra of **4a** were identical with those of an authentic sample. **4b**: IR ν 2225 cm^{-1} (CN); NMR δ 1.05 (t, 3 H), 1.37 (d, 3 H), 2.21 (s, 3 H), 3.59 ppm (q, 1 H); mass spectrum *m/e* (rel intensity) 112 (M$^+$, 3), 97 (M$^+$ − 15, 11), 85 (M$^+$ − 27, 28), 70 (M$^+$ − 42, 82), 42 (100). Picrate of **4b**: yellowish prisms from ethanol–acetone, mp 120–122 °C dec. Anal. Calcd for $C_{12}H_{15}N_5O_7$: C, 42.23; H, 4.43; N, 20.52. Found: C, 42.1; H, 4.4; N, 20.6.

Dimethyl-*n*-propylamine (Expt 5). The distillation gave 4.5 g of colorless liquid at 55–64 °C (15 mm). GLC analysis showed 84% of *N*-methyl-*N*-*n*-propylaminoacetonitrile (**5a**) and 16% of α-dimethylaminobutylonitrile (**5b**).[17] Analytical samples were obtained by preparative GLC. **5a**: IR ν 2230 cm^{-1} (CN); NMR δ 0.94 (t, 3 H), 1.50 (sextet, 2 H), 2.33, 2.42 (s, t, 5 H), 3.45 ppm (s, 2 H); mass spectrum *m/e* (rel intensity) 112 (M$^+$, 7), 85 (M$^+$ − 27, 8), 84 (M$^+$ − 28, 14), 83 (M$^+$ − 29, 100), 42 (25). Picrate of **5a**: yellowish, rodlike crystals from ethanol–acetone, mp 97–98.5 °C. Anal. Calcd for $C_{12}H_{15}N_5O_7$: C, 42.23; H, 4.43; N, 20.52. Found: C, 42.5; H, 4.4; N, 20.9. **5b**: The IR and NMR spectrum were compared with those of an authentic sample, respectively.

Dimethylisopropylamine (Expt 6). The crude product was distilled. A fraction with bp 63–65 °C (15 mm) was obtained in a yield of 4.5 g. *N*-Methyl-*N*-isopropylaminoacetonitrile: IR ν 2225 cm^{-1} (CN); NMR δ 1.10 (d, 6 H), 2.35 (s, 3 H), 2.73 (sextet, 1 H), 3.52 ppm (s, 2 H); mass spectrum *m/e* (rel intensity) 112 (M$^+$, 9), 97 (M$^+$ − 15, 100), 85 (M$^+$ − 27, 12), 70 (M$^+$ − 42, 71), 42 (57). Picrate: yellowish leaflets from ethanol, mp 163.5–165.5 °C dec. Anal. Calcd for $C_{12}H_{15}N_5O_7$: C, 42.23; H, 4.43; N, 20.52. Found: C, 42.5; H, 4.4; N, 20.9. The NMR spectrum of the rough product was shown to be devoid of the cyanated isomer at the methine group.

Diisopropylmethylamine (Expt 7). Similarly, the combined ether layers were dried and distilled. *N,N*-Diisopropylaminoacetonitrile[17] was obtained in a yield of 6.0 g at 98–102 °C (35 mm). The isomer was not detected by NMR.

***N*-Methylpyrrolidine (Expt 8).** The crude product was concentrated by distillation. A fraction with bp 69–78 °C (18 mm) was obtained in a yield of 5.1 g. According to GLC analysis, the fraction consisted of 81% of *N*-methyl-2-cyanopyrrolidine (**8a**)[21] and 19% of 1-pyrrolidineacetonitrile (**8b**).[19,23] Each nitrile for analysis was isolated by fractional distillation and purified by preparative GLC. **8a**: bp 99–100 °C (64 mm); IR ν 2225 cm^{-1} (CN); NMR δ 2.42 (s, 3 H), 3.58 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 83 (M$^+$ − 27, 79), 82 (M$^+$ − 28, 100), 42 (45). **8b**: bp 74–76 °C (15 mm); IR ν 2230 cm^{-1} (CN); NMR δ 1.80 (m, 4 H), 2.59 (m, 4 H), 3.58 ppm (s, 2 H); mass spectrum *m/e* (rel intensity) 110 (M$^+$, 55), 109 (M$^+$ − 1, 84), 83 (M$^+$ − 27, 38), 82 (100), 42 (95). Picrate of **8a**: yellowish needles from ethanol–acetone, mp 134–137 °C dec. Anal. Calcd for $C_{12}H_{13}N_5O_7$: C, 42.48; H, 3.86; N, 20.64. Found: C, 42.4; H, 3.8; N, 20.4. Picrate of **8b**: yellowish prisms from ethanol–acetone, mp 156.5–157 °C dec. Anal. Found: C, 42.7; H, 3.8; N, 20.7.

***N*-Methylpiperidine (Expt 9).** The distillation of the products gave 7.1 g of colorless liquid at 104–120 °C (38 mm). The fraction was shown to be 62% of *N*-methyl-2-cyanopiperidine (**9a**)[21] and 38% of 1-piperidineacetonitrile (**9b**)[17,19,24,25] by GLC. Each nitrile was isolated by fractional distillation and was purified by preparative GLC. **9a**: bp 73.5–74 °C (12 mm); IR ν 2220 cm^{-1} (CN); NMR δ 2.28 (s, 3 H), 3.68 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 97 (M$^+$ − 27, 98), 96 (M$^+$ − 28, 100), 82 (M$^+$ − 42, 86), 42 (96). **9b**: bp 85 °C (12 mm); IR ν 2250 cm^{-1} (CN); NMR δ 3.37 ppm (s, 2 H); mass spectrum *m/e* (rel intensity) 124 (M$^+$, 45), 123 (M$^+$ − 1, 100), 97 (M$^+$ − 27, 39), 96 (62), 42 (58). Picrate of **9a**: yellowish crystal powder from ethanol–acetone, mp 153–155 °C dec. Anal. Calcd for $C_{13}H_{15}N_5O_7$: C, 44.19; H, 4.28; N, 19.83. Found: C, 43.9; H, 4.1; N, 19.7. Picrate of **9b**: yellowish crystal powder, mp 159.5–161 °C dec. Anal. Found: C, 44.1; H, 4.2; N, 20.2.

***N*-Ethylpyrrolidine (Expt 10).** The crude product was distilled. A fraction with bp 100–105 °C (39 mm) was obtained in a yield of 7.1 g. The gas chromatogram of the fraction showed a peak with a discernible shoulder. The chief product was *N*-ethyl-2-cyanopyrrolidine (**10a**). The retention time of the shoulder peak was checked against an authentic sample of α-pyrrolidinepropionitrile (**10b**)[26] and the identity of the product was confirmed by the peak enhancement method. NMR showed that the fraction was a mixture of 82% of **10a** and 18% of **10b**. **10a** could be isolated by preparative GLC but **10b** could not be purified. **10a**: IR ν 2220 cm^{-1} (CN); NMR δ 1.09 (t, 3 H), 3.84 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 97 (M$^+$ − 27, 97), 82 (M$^+$ − 42, 100). Picrate of **10a**: yellowish needles from ethanol, mp 114–116.5 °C dec. Anal. Calcd for $C_{13}H_{15}N_5O_7$: C, 44.19; H, 4.28; N, 19.83. Found: C, 44.3; H, 4.2; N, 19.9.

***N*-Ethylpiperidine (Expt 11).** The crude product was distilled. GLC analysis of the distillate [bp 116–121 °C (47 mm), 8.1 g] showed it to be 78% of *N*-ethyl-2-cyanopiperidine (**11a**) and 22% of α-piperidinepropionitrile (**11b**).[21] Analytical samples were obtained by preparative GLC. **11a**: IR ν 2220 cm^{-1} (CN); NMR δ 1.09 (t, 3 H), 3.84 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 111 (M$^+$ − 27, 54), 96 (M$^+$ − 42, 100). **11b**: IR ν 2220 cm^{-1} (CN); NMR δ 1.42, 1.56 (d, broad, 9 H), 3.47 (broad, 4 H), 3.53 ppm (q, 1 H); mass spectrum *m/e* (rel intensity) 111 (M$^+$ − 27, 100), 110 (M$^+$ − 28, 67), 96 (M$^+$ − 42, 82). Picrate of **11a**: yellowish prisms from ethanol–acetone, mp 124–128 °C dec. Anal. Calcd for $C_{14}H_{17}N_5O_7$: C, 45.77; H, 4.76; N, 19.07. Found: C, 45.5; H, 4.7; N, 19.2. Picrate of **11b**: yellowish prisms from ethanol–acetone, mp 121–125 °C dec. Anal. Found: C, 45.8; H, 4.6; N, 19.4.

***N*-*n*-Propylpyrrolidine (Expt 12).** The distillation of the crude product gave 8.2 g of colorless liquid at 114–119 °C (40 mm). Although the NMR spectrum of the distillate showed very weak signals which suggested the presence of α-pyrrolidinebutyronitrile, it consisted of almost pure *N*-*n*-propyl-2-cyanopyrrolidine: IR ν 2220 cm^{-1} (CN); NMR δ 0.91 (t, 3 H), 3.62 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 111 (M$^+$ − 27, 39), 82 (100). Picrate: yellowish, rodlike crystals from methanol, mp 103–104 °C dec. Anal. Calcd for $C_{14}H_{17}N_5O_7$: C, 45.77; H, 4.67; N, 19.07. Found: C, 45.9; H, 4.7; N, 19.4.

***N*-Isopropylpyrrolidine (Expt 13).** The distillation gave 7.8 g of *N*-isopropyl-2-cyanopyrrolidine at 95–98 °C (22 mm). NMR analysis showed that the distillate was free of the side-chain substi-

tuted product: IR ν 2220 cm^{-1} (CN); NMR δ 1.13 (d, 6 H), 3.91 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 111 (M^+ − 27, 43), 96 (M^+ − 42, 100). Picrate: yellowish leaflets from ethanol–acetone, mp 106–111 °C dec. Anal. Calcd for $C_{14}H_{17}N_5O_7$: C, 45.77; H, 4.67; N, 19.07. Found: C, 45.6; H, 4.6; N, 18.8.

***N*-Isopropylpiperidine (Expt 14).** The ether extracts were distilled. Unchanged amine (1.3 g) was recovered at about 55–60 °C (24 mm) and then 9.4 g of *N*-isopropyl-2-cyanopiperidine was obtained at 108–110 °C (24 mm): IR ν 2210 cm^{-1} (CN); NMR δ 1.10 (double d, 6 H, J = 6 Hz), 3.94 ppm (t, 1 H); mass spectrum *m/e* (rel intensity) 125 (M^+ − 27, 33), 110 (M^+ − 42, 100). Picrate: yellowish leaflets from ethanol–acetone, mp 105.5–109 °C dec. Anal. Calcd for $C_{15}H_{19}N_5O_7$: C, 47.24; H, 5.02; N, 18.37. Found: C, 47.0; H, 5.0; N, 18.0.

***N*-*tert*-Butylpyrrolidine (Expt 15).** The distillation gave 2.0 g of starting amine and 9.6 g of *N*-*tert*-butyl-2-cyanopyrrolidine [bp 98 °C (13 mm)]: IR ν 2225 cm^{-1} (CN); NMR δ 1.09 (s, 9 H), 1.95 (broad, 4 H), 2.75 (broad, 2 H), 3.73 ppm (broad, 1 H); mass spectrum *m/e* (rel intensity) 152 (M^+, 3), 137 (M^+ − 15, 85), 125 (M^+ − 27, 40), 110 (M^+ − 42, 100), 68 (74). Picrate: yellowish prisms from ethanol–acetone, mp 177–179 °C dec. Anal. Calcd for $C_{15}H_{19}N_5O_7$: C, 47.24; H, 5.02; N, 18.37. Found: C, 47.4; H, 5.0; N, 18.0.

Registry No.—**3a,** 62842-25-5; **3a** picrate, 62842-26-6; **4b,** 62842-27-7; **4b** picrate, 62842-28-8; **5a,** 62842-29-9; **5a** picrate, 62842-30-2; **6a,** 62842-31-3; **6a** picrate, 62842-32-4; **8a,** 20297-37-4; **8a** picrate, 18747-97-2; **8b,** 29134-29-0; **8b** picrate, 62842-33-5; **9a,** 18747-95-0; **9a** picrate, 18747-96-1; **9b,** 3010-03-5; **9b** picrate, 25283-66-3; **10a,** 62842-34-6; **10a** picrate, 62842-35-7; **11a,** 62842-36-8; **11a** picrate, 62842-37-9; **11b,** 62842-38-0; **11b** picrate, 62842-39-1; **12a,** 62842-40-4; **12a** picrate, 62842-41-5; **13a,** 62842-42-6; **13a** picrate, 62842-43-7; **14a,** 62842-44-8; **14a** picrate, 62842-45-9; **15a,** 62842-46-0; **15a** picrate, 62842-47-1; α-dimethylaminoacetamide, 6318-44-1; NaCN, 143-33-9; *N,N*-diisopropylaminoacetonitrile, 54714-49-7.

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The Mechanism of Indeno[1,2,3-*de*]quinolin-2-one Formation

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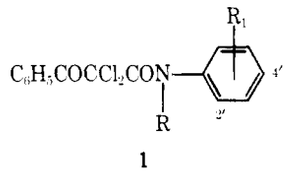
The unambiguous synthesis of 1,6-dichloro-3-ethylindeno[1,2,3-*de*]quinolin-2(3*H*)-one (**7**) was undertaken. Product **7** was found to be identical with that derived by sulfuric acid catalyzed cyclization of 2,2,4′-trichloro-*N*-ethylbenzoylacetanilide (**4**). This is evidence that **7** arises from **4** via a "direct" cyclization intermediate. A convenient modification of the Cook and Koelsch indenoquinolinone synthesis, which afforded **7** by a shorter route, is reported. The diagnostically useful anisotropic deshielding of the C-7 and C-10 protons by the halogen at C-1 and C-6 in the ^1H NMR spectrum of **7** is described.

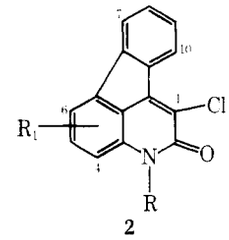
We report further developments relating to the mode of cyclization of 2,2-dichlorobenzoylacetanilides **1** to indeno[1,2,3-*de*]quinolin-2-ones **2.** In our earlier work,[1] a "direct" ring closure was tacitly assumed. The recent findings of Harcourt and Taylor[2] with 4′-methoxybenzylaminoacetonitrile prompted us to consider the intervention of a similar, appropriately modified "spiro" intermediate during the cyclization of **1,** in helping to explain the migrations encountered with certain methyl-substituted substrates.[1]

It is evident (Scheme I) that closure of the relatively uncomplicated **4** via a "spiro" intermediate i in which bond a breaks would lead to the 5-chloroindenoquinolinone **6,** whereas rearrangement of i to the "direct" intermediate ii,[3] and/or closure in a "direct" fashion, would result in the 6-chloroindenoquinolinone **7.** Competitive cleavage of both carbon and nitrogen bonds in related "spiro" species has been described by Hey; for example, treatment of the spirodienol **8** with acid gave a mixture of benzophenanthridinones in which the product of nitrogen migration, **9,** predominated.[4] The sole indenoquinolinone product derived from **4** has now been unequivocally identified as **7,** and accordingly, pathway 1 (Scheme I) for this cyclization can be discounted.



1

3, R = H; R_1 = 4′-Cl
4, R = C_2H_5; R_1 = 4′-Cl



2

5, R = H; R_1 = 6-Cl
6, R = C_2H_5; R_1 = 5-Cl
7, R = C_2H_5; R_1 = 6-Cl