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Studies on the Reactions of Heterocyclic Compounds. IV.[1] Preparations and Reactions of Heterocyclic N-Ylides[2]

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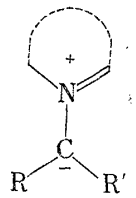
The reaction of di-substituted methyl bromides such as dimethyl bromomalonate (IIa), bromomalonamide (IIb), bromocyanoacetamide (IIc), and methyl bromocyanoacetate (IId) with aromatic amines (pyridine, isoquinoline, and 1,6-naphthyridine) gave stable N-ylides, IVa—IVd, VIa, VIb, and VIIa. From the reaction of bromomalononitrile (IIe) and quinoline or isoquinoline afforded diquinolinium-(VIII) and diisoquinolinium pentacyanopropenide (IX). From the reaction of IId with quinolines in MeOH, azirino[1,2-*a*]-cyclopropa[*c*]quinoline derivatives (Xa and Xc) with new ring system were given. When treated with hydrogen chloride in MeOH, Xa was converted to dimethyl 3-quinolinemalonate (XII). When IVd was treated with sodium methoxide in DMF, methyl α-cyano-[1,(4*H*),4′-bipyridine]-$\Delta^{\alpha,4}$-acetate (XVI) was produced. VIc, VIb, and VIIb, when treated with sodium methoxide in MeOH, gave fused imidazole derivatives (XVIII, XIX, and XX).



I

The syntheses of N-ylides stabilized by CN, COOMe, and $CONH_2$ were attempted in order to compare the reactivity of N-ylides (I, R, R′=$COOCH_3$, CN, and $CONH_2$) of aromatic amines with that of N-oxide[4] and N-imine.[5] This paper reports the syntheses using the methyl bromides with two electronegative groups, some chemical behaviors of the N-ylides obtained, and other observations made during the process.

First, the general synthetic procedure of treating quaternary salt with base was carried out. Dimethyl bromomalonate (IIa), bromomalonamide (IIb), and bromocyanoacetamide (IIc) reacted with pyridine and gave each corresponding quarternary salt (IIIa—IIIc). These salts, when treated with potassium carbonate or Amberlite IRA-410, gave each corresponding ylide (IVa—IVc). With methyl bromocyanoacetate (IId), however, the corresponding ylide (IVd), instead of the quaternary salt, was obtained at the reaction with pyridine. In the cases of isoquinoline and 1,6-naphthyridine, the reaction gave similar ylides (VIb and VIIa).

However, the reaction of bromomalononitrile (IIe) with aromatic amines did not give the corresponding ylides. In the reaction with quinoline and isoquinoline, IIe gave yellow crystals of diquinolinium (VIII, mp 149—150°) and diisoquinolinium pentacyanopropenide (IX, mp 153—154°) possessing the specific absorption of pentacyanopropenide anion (397 and 414 mμ), besides the absorption of respective bases in ultraviolet (UV) spectrum. VIII is reported to have been prepared by Middleton and others[6] from the reaction of quinoline with tetracyanoethylene,[7] but no mention is found about its structure. The composition of VIII and IX both agrees with the 2:1 adducts of each base and pentacyanopropane in elemental analysis.

1) Part III: Y. Kobayashi, I. Kumadaki, and H. Sato, *Chem. Pharm. Bull.* (Tokyo), **17**, 2614 (1969).
2) Presented at the 89th Meeting of Pharmaceutical Society of Japan, Nagoya, April 1969.
3) Location: *600, Kashiwagi-4, Shinjuku-ku, Tokyo.*
4) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., Amsterdam, 1967.
5) T. Okamoto and M. Hirobe, *Yuki Gosei Kagaku Kyokai Shi*, **26**, 746 (1968).
6) W.J. Middleton, E.L. Little, D.D. Coffman, and V.A. Engelhardt, *J. Am. Chem. Soc.*, **80**, 2795 (1958).
7) VIII was prepared by an improved method on that described in ref. 6.

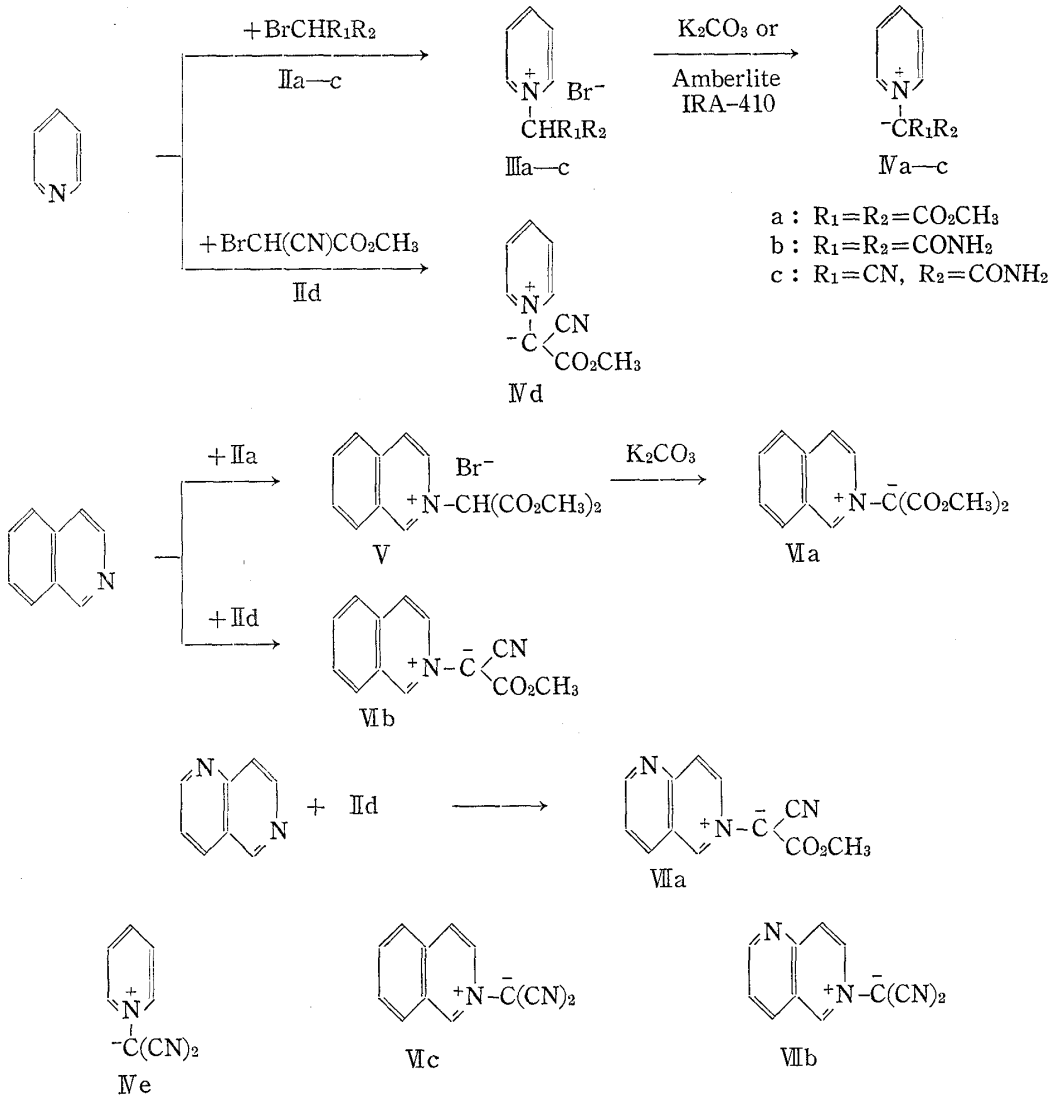


Chart 1

And their nuclear magnetic resonance (NMR) spectra showed signals corresponding to single quinolinium and isoquinolinium salts; the two bases in VIII and IX, respectively, are found to be combined in the same manner against one pentacyanopropene. Infrared (IR) spectra of VIII and IX showed an absorption corresponding to the cyano group at 2238 cm^{-1}. From the results of the spectra described above and by assuming the structure of the reaction product with 1-methyl-2-pyridone,[8] the formula in Chart 2 is proposed as the structure of VIII and IX.

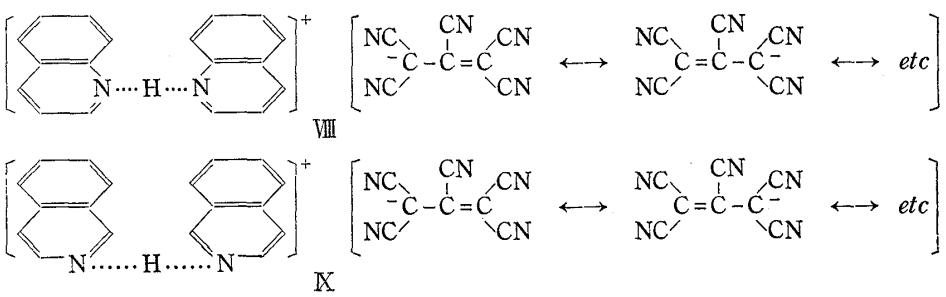


Chart 2

8) B.S. Thyagarajan, K. Rajagopalan, and P.V. Gopalakrishnan, *Chem. Ind.* (London), **1966**, 1887.

As to the reason why VIII and IX were produced, the following is our explanation: following one of the routes shown in Chart 3, IIe was dimerized by ionic mechanism (route a)[9] or *via* carbene (route b) and gave tetracyanoethylene as intermediate, which reacted with bases to produce VIII[6] and IX.

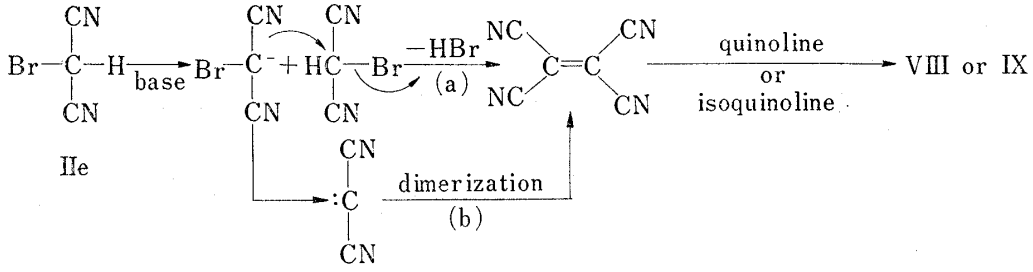


Chart 3

The corresponding dicyanomethylides, therefore, could not be obtained by this method; so tetracyanoethylene oxides and amines were treated according to Linn's method to synthesize the corresponding dicyanomethylides (IVe,[10] VIc,[10] and VIIb in Chart 1). On the other hand, when IId, which gave the desired product with pyridines, was treated with quinoline as base, dimethyl 1,2-dicyano-1a,1b,2,-7b-tetrahydro-1*H*-azirino[1,2-*a*]-cyclopropa[*c*]quinoline-1,2-dicarboxylate (Xa) was obtained (Chart 4).

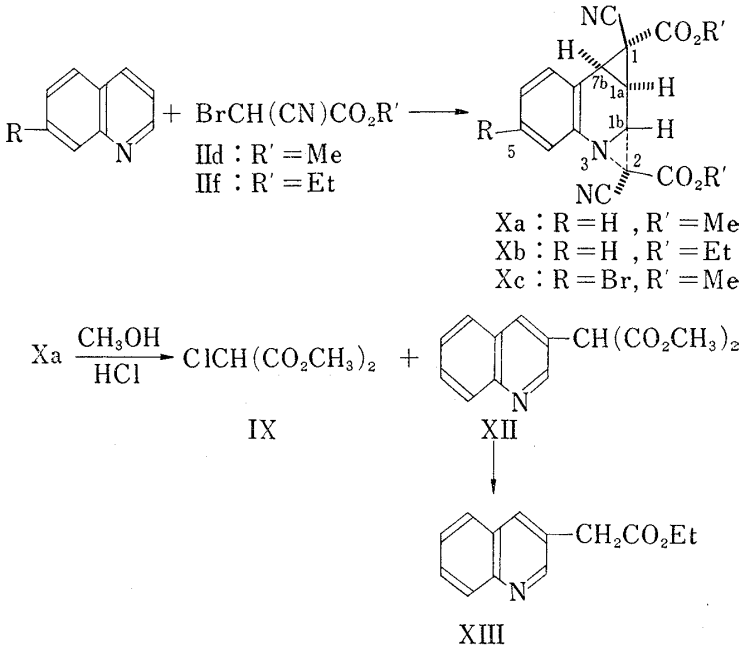


Chart 4

The elemental analysis of Xa agreed with that of $C_{17}H_{13}O_4N_3$. By the data of NMR, IR, and UV spectra, the structure of Xa is suggested: that is, NMR spectrum suggests that 1a-H and 1b-H are in *trans*-configuration. From ethyl bromocyanoacetate (IIf), Xb wasobtained in the same manner. The perfect steric configuration was determined by X-ray diffraction analysis with heavy atom method using 5-bromo derivative (Xc).[11]

When Xa was allowed to stand in anhydrous methanol saturated with dry hydrogen chloride, it was converted into dimethyl chloromalonate (XI)[12] and dimethyl 3-quinolinemalonate (XII). XII was identified by being derived to ethyl 3-quinolineacetate (XIII).[13]

Then, the mechanism of formation of Xa is considered. Polymerization of bromomethanes with two strong electronegative groups such as IId and IIf or their addition or insertion to

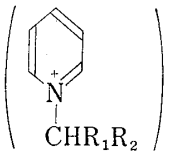
9) J.P. Ferris and L.E. Orgel, *J. Org. Chem.*, **30**, 2365 (1965).
10) W.J. Linn, O.W. Webster, and R.E. Benson, *J. Am. Chem. Soc.*, **87**, 3633 (1965).
11) Y. Kobayashi, T. Kutsuma, Y. Hanzawa, Y. Iitaka, and H. Nakamura, *Tetrahedron Letters*, **1969**, 5337.
12) E.L. Hirst and A.K. Mcbeth, *J. Chem. Soc.*, **121**, 2177 (1922).
13) R.G. Jones, Q.F. Soper, O.K. Behrens, and J.W. Corse, *J. Am. Chem. Soc.*, **70**, 2843 (1948).

olefins by base is reported to proceed by ionic mechanism[14] or *via* carbene[15] or *via* radical.[16] Although the mechanism of the production of Xa in the reaction of IId with quinoline is not clear, since the reaction easily proceeded in the nitrogen atmosphere in the dark in the presence of hydroquinone or *p*-(*tert*-butyl)catechol, the mechanism *via* radical must be denied and the reaction is supposed to proceed by ionic mechanism or *via* carbene.

This reaction is interesting not only as a case of the formation of a new ring system but also as a method to introduce a carbon substituent into 3-position of quinoline, since its yield was better than 50% over all.

Next, the natures of the obtained ylides were investigated. Comparison of pK_a values of the conjugated acids of disubstituted methylides of pyridine is shown in Table I. As is clear from Table I and as can be expected from electron theory, the effect of the substituent to stability of ylides decreases as follows: CN>COOMe>$CONH_2$. This fact explains the point that IVd can be directly synthesized without base treatment.

Table I. pK_a Values of Conjugated Acids of Pyridinium Ylides



Ylide	R_1	R_2	pK_a[a]
IVd	CN	CO_2CH_3	1>
IVc	CN	$CONH_2$	4.19
IVa	CO_2CH_3	CO_2CH_3	4.85
IVb	$CONH_2$	$CONH_2$	7.95

a) pK_a value is measured in water by titration method and uncorrected.

The following are the discoveries about the reactivity. Pyridinium dicyanomethylide (IVe), reacting with sodium methoxide in methanol, gave imidazo[1,2-*a*]pyridine derivative (XIV), as was reported before.[17] Cyclization of ylides containing cyano substituent synthesized as above by the similar reaction with methoxide ion was investigated. Isoquinolinium (VIc) and 1,6-naphthyridinium (VIIb) ylides react more readily than pyridinium ylide (IVe) and give cyclized compounds (XVIII and XX).

When IVe and VIc were treated with dry hydrogen chloride in methanol to convert one of the two cyano groups into the ester group,[18] the corresponding monomethyl esters (IVd and VIb) were given. When the reaction was applied to 1,6-naphthyridine dicyanomethylide (VIIb), however, cyclization rather than esterification proceeded to give XX. This is considered to be caused by the effect of the positive-charged nitrogen atom at 1-position in protonated VIIb, which lessens the electron density of the carbon atom at 5-position and may promote the nucleophilic cyclization reaction.

Although the pyridinium ylide containing cyanoester group (IVd) does not react with methoxide ion in methanol, it does so in dimethylformamide to give crystals of XVI, mp 275°. The elemental analysis of XVI agreed with that of $C_{14}H_{11}O_2N_3$. IR spectrum showed charac-

14) R.T. Coutts and K.W. Hindmargh, *Can. J. Chem.*, **44**, 2092 (1966); A.P. Krapcho and P.S. Huyffer, *J. Org. Chem.*, **28**, 2904 (1963).
15) J.S. Swenson and D.J. Renand, *J. Am. Chem. Soc.*, **87**, 1394 (1965).
16) *a*) P. Boldt, L. Schulz, and J. Etzemüller, *Chem. Ber.*, **100**, 1281 (1967); *b*) P. Boldt and L. Schulz, *Tetrahedron Letters*, **1967**, 4351.
17) T. Kutsuma, K. Sato, T. Chida, and Y. Tsukuno, *Yakugaku Zasshi*, **90**, 251 (1970).
18) A. Riech and P. Dietrich, *Chem. Ber.*, **96** 3044 (1963).

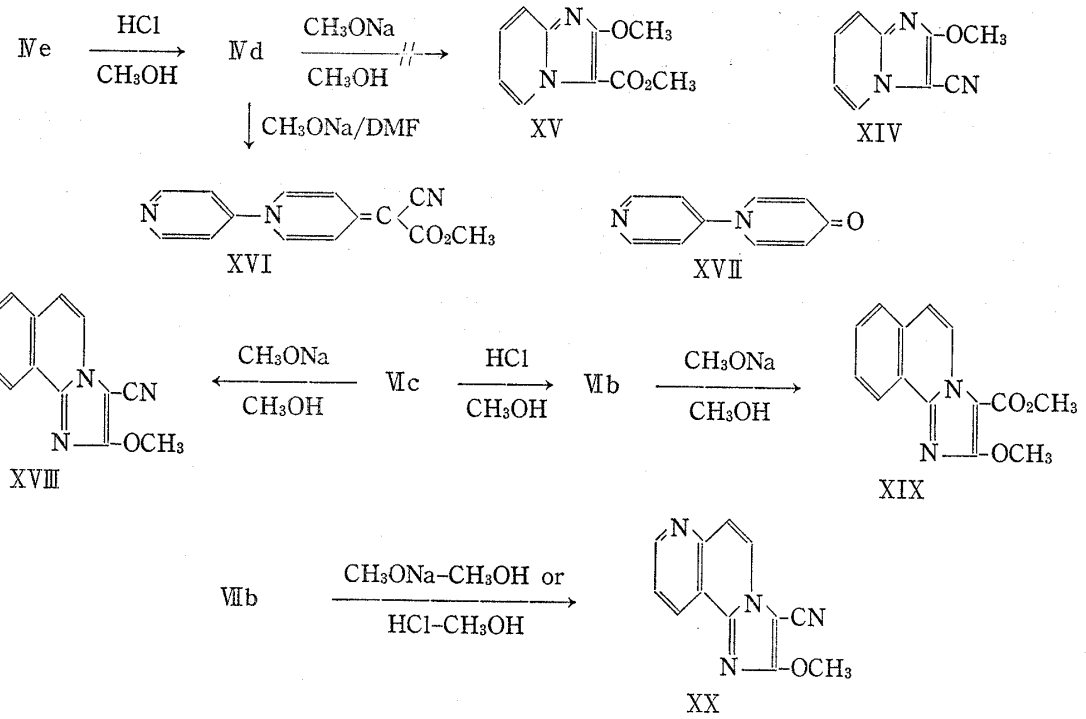


Chart 5

teristic absorption at 2220 ($\nu_{C\equiv N}$), 1654, 1315 (conjugated methyl ester), and 816 cm^{-1} (two adjacent aromatic protons). UV spectrum showed absorption at 437 mμ (ε=24300). Its NMR spectrum is very similar to that of [1(4*H*),4'-bipyridine]-4-one (XVII).[19] From the above data, the structure of XVI was estimated. A mechanism of its formation was presumed to be as shown in Chart 6.

Isoquinolinium ylide (VIb), unlike the pyridinium one (IVd), forms a cyclized compound (XIX) in the reaction with methoxide ion in methanol. The above fact shows that the order

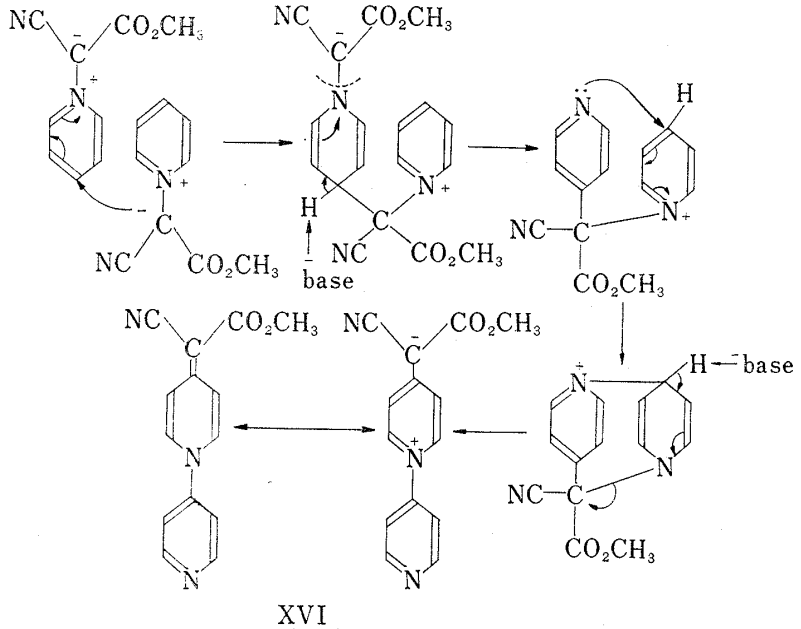


Chart 6

19) M. Hamana and H. Yoshimura, *Yakugaku Zasshi*, **72**, 1051 (1962).

of activities of the α-position of nitrogen atom upon the nucleophilic cyclization of ylides by methoxide ion is as follows: 1,6-naphthyridine>isoquinoline>pyridine.

The spectral data of polyazabenz[*e*]indenes obtained from isoquinolinium ylides and sodium methoxide mentioned above are shown in Table II. The UV spectra of XVIII, XIX, and XX resemble to that of trimethyl benzo[*g*]pyrrocoline-1,2,3-tricarboxylate.[20] In IR spectrum, the absorption band of carbonyl group in the ester group at 3-position in XIX appears at a considerably low wave number region. As was shown in the case of imidazo-[1,2-*a*]pyridines,[17] this is supposed to be due to the contribution of resonance forms like XIXA and XIXB as the electron density of the carbon atom at 3-position is increased by the effects of the nitrogen atom at 4-position[21] and the methoxyl group at 2-position.

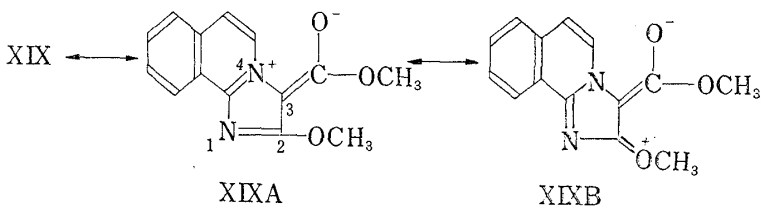


Chart 7

Table II. Spectral Data of Azabenz[*g*]indolizines

Compound	UV $\lambda_{max}^{95\%\ EtOH}$ mμ (ε×10⁻⁴)	IR cm⁻¹ $\nu_{C\equiv N}^{KBr}$	IR cm⁻¹ $\nu_{C=O}^{KBr}$	NMR[a] H-5	H-6	H-7	H-8	H-9	H-10	CH_3
XVIII	221.5 (1.35) 255 (3.06)[b] *262 (4.30)* 270.5 (2.19) 301—309[c] (1.00) 330 (0.11) 343 (0.10)	2220	—	7.89	7.22	7.80	~	7.60	8.50	4.18
				$J_{5,6}=7.3$						
XIX	224 (1.56) 232 (1.54) 265 (4.27) 274 (3.34) 305 (1.44) 3.12 (1.45) 331 (0.56) 345 (0.10)	—	1678	9.02	7.17	7.77	~	7.53	8.52	4.23 3.95
				$J_{5,6}=7.5$						
XX	223.5 (2.18) 246.5 (1.98) 271 (2.96) 276 (2.78) 321 (0.88) 337 (0.54)	2230	—	8.18	7.57	—	9.01	7.60	8.83	4.21
				$J_{5,6}=7.2$ $J_{8,9}=4.0$ $J_{8,10}=2.0$ $J_{9,10}=8.7$						

a) Nuclear magnetic resonance spectra (δ-values; *J* in Hz) are measured at 100 MHz by JNM-4H-100 (Japan Electron Optics Lab. Co., Ltd.) in deuteriochloroform with tetramethylsilane as internal standard
b) italics indicate inflexion c) broad absorption band

In the NMR spectrum of XIX, the signal of the proton at 5-position appears in a considerably low magnetic field. This is attributed to the rather strong anisotropic effect[22] of the ester group at the *peri*-position.

Experimental

Pyridinium Bis(methoxycarbonyl)methylide (IVa)——To a solution of pyridine (0.88 g, 1.1 mmole) in acetone (15 ml), methyl bromomalonate (IIa, 2.11 g, 1.0 mmole) was added and the mixture was allowed

20) R.H. Wiley and L.H. Knabeschuh, *J. Org. Chem.*, **18**, 836 (1953).
21) W.W. Paudler and H.L. Bewitt, *J. Org. Chem.*, **30**, 4081 (1965); J.P. Paolini, *J. Org. Chem.*, 30, 4085 (1965).
22) R.M. Acheson and W.R. Tulby, *J. Chem. Soc.* (*C*), **1968**, 1263; R.M. Acheson and D.A. Robinson, *J. Chem. Soc.* (*C*), **1968**, 1633.

to stand for 24 hr at room temperature. The precipitated colorless crystals were filtered and recrystallized from a mixture of iso-PrOH and iso-Pr_2O to give colorless needles of a bromide (IIIa), mp 137—138°. Yield, 2.35 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 248 (9640). *Anal.* Calcd. for $C_{10}H_{12}O_4NBr$: C, 41.39; H, 4.17; N, 4.38. Found: C, 40.92; H, 4.10; N, 4.80.

The bromide (IIIa, 2.30 g) was dissolved in H_2O and the solution was basified with K_2CO_3 and extracted with $CHCl_3$. After the solution was dried over Na_2SO_4, the solvent was evaporated to afford yellow crystals. Recrystallization from acetone gave yellow needles of IVa, mp 183—184°. Yield, 1.56 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 246 (19100), 398 (1200). IR ν_{max}^{KBr} cm^{-1}: 1680—1620 (broad), (–$COOCH_3$). NMR ($CDCl_3$) δ: 8.61 (2H, d, J=6.8 Hz, 2- and 6-H), 8.21 (1H, m, 4-H), 7.78 (2H, t, J=6.8 Hz, 3- and 5-H), 3.71 (6H, s, CH_3OOC). *Anal.* Calcd. for $C_{10}H_{11}O_4N$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.17; H, 5.39; N, 6.69.

Pyridinium Dicarbamoylmethylide (IVb)——To a solution of pyridine (1.60 g) in MeOH (30 ml), bromomalonamide (IIb, 1.81 g) was added with stirring at room temperature and the stirring was continued for 13 hr at the same temperature. When the precipitated crystals were filtered and washed with cold MeOH, colorless crystals were obtained. Recrystallization from MeOH gave colorless needles of a bromide (IIIb), mp 228—229° (decomp.). Yield, 1.90 g. *Anal.* Calcd. for $C_8H_{10}O_2N_3Br$: C, 36.94; H, 3.88; N, 16.16. Found: C, 36.64; H, 3.97; N, 16.62.

The bromide (IIIb, 1.30 g) was dissolved in 40% MeOH and the solution was mixed well with Amberlite IRA-410 (5.0 ml) and the resin was filtered off; the filtrate was concentrated *in vacuo*. Recrystallization of the residue from 95% EtOH gave orange–yellow crystals of IVb, mp 134°. Yield, 0.75 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 254 (18300), 430 (900). IR ν_{max}^{KBr} cm^{-1}: 3420, 3310, 3270, 3175 (–NH_2 of amide), 1665, 1621, 1550, 1530 (>C=O of amide). *Anal.* Calcd. for $C_8H_9O_2N_3$: C, 53.62; H, 5.06; N, 23.45. Found: C, 53.40; H, 5.16; N, 23.37.

Pyridinium Carbamoylcyanomethylide (IVc)——A mixture of pyridine (8.0 g), bromocyanoacetamide (IIc, 8.15 g), and acetone (80 ml) was allowed to stand for 18 hr at room temperature. After removal of the acetone *in vacuo*, the residue was dissolved in MeOH (200 ml) and the solution was mixed well with Amberlite IRA–410 (100 ml). The resin was filtered off and washed well with hot MeOH. Concentration of the combined MeOH solution gave a dark red solid and this solid was dissolved in hot H_2O (100 ml). The solution was treated with a decolorizing carbon and was concentrated *in vacuo*. Recrystallization of the residue from 90% EtOH (60 ml) gave yellow–brown needles of IVc, mp 167—168° (decomp). Yield, 2.6 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 236 (17100), 401 (9800). IR ν_{max}^{KBr} cm^{-1}: 3325, 3280, 3175 (–NH_2 of amide), 2165 (–C≡N), 1618, 1568 (>C=O of amide). *Anal.* Calcd. for $C_8H_7ON_3$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.99; H, 4.63; N, 25.71.

Pyridinium Cyano(methoxycarbonyl)methylide (IVd)——i) A solution of pyridine (1.60 g), methyl bromocyanoacetate (IId, 1.78 g), and acetone (15 ml) was allowed to stand for 24 hr at room temperature. The precipitated colorless hygroscopic pyridine hydrobromide (1.1 g) was filtered off, whose picrate was identified with the authentic sample by the mixture melting point, mp 164°; the filtrate was concentrated to give a dark brown solid. The solid was dissolved in $CHCl_3$ and chromatographed over Al_2O_3 (30 g). Its elute gave yellow crystals (IVd, 1.63 g), which were recrystallized from iso-PrOH (20 ml) to give yellow needles, mp 140°. Yield, 1.30 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 230 (17900), 392 (11400). IR $\nu_{max}^{CHCl_3}$ 2195 (–C≡N), 1650 (–$COOCH_3$). NMR ($CDCl_3$) δ: 9.29 and 9.27 (2H, a pair of doublets, J=5.10 Hz, 2- and 6-H), 7.68—7.61 (3H, m, 3-, 4-, and 5-H), 3.73 (3H, s, CH_3OOC). *Anal.* Calcd. for $C_9H_8O_2N_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.43; H, 4.88; N, 16.28.

ii) To a suspension of pyridinium dicyanomethylide (IVe, 1.50 g) in abs. MeOH (15 ml), dry HCl gas was saturated under ice-NaCl cooling and the mixture was allowed to stand overnight in an ice-NaCl bath. The precipitated colorless crystals were filtered and dissolved in ice–water. The solution was basified with K_2CO_3 and extracted with $CHCl_3$; after the solution was dried over Na_2SO_4, the solvent was evaporated to give yellow crystals. Recrystallization from iso-PrOH gave yellow needles, mp 139—140°. Yield, 1.32 g. The compound was identified with IVd by the mixture melting point.

Isoquinolium Bis(methoxycarbonyl)methylide (VIa)——To a solution of IIa (4.22 g) in acetone (30 ml), isoquinoline (5.20 g) was added and the mixture was allowed to stand for 24 hr at room temperature. The precipitated colorless crystals (V) were filtered, washed with acetone, and dissovled in H_2O. The solution was basified with K_2CO_3 and extracted with $CHCl_3$. After the solution was dried over Na_2SO_4, the evaporation of $CHCl_3$ gave yellow crystals (VIa). Recrystallization from acetone gave yellow needles, mp 235—236° (decomp.). Yield, 4.25 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 238 (52500), 318 (2480), 330 (3370), 342 (3700), 424 (2400). IR ν_{max}^{KBr} cm^{-1}: 1675, 1595 (–$COOCH_3$). *Anal.* Calcd. for $C_{14}H_{13}O_4N$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.45; H, 5.15; N, 5.36.

Isoquinolinium Cyano(methoxycarbonyl)methylide (VIb)——i) To a solution of isoquinoline (12.9 g) in ethyl acetate (15 ml), a solution of (IId, 8.9 g) in ethyl acetate (15 ml) was added and the mixture was allowed to stand for 24 hr at room temperature. After the reaction mixture was cooled with ice, the precipitated crystals and brown tar were filtered. After washing off the tar with cold acetone, the resulting pale yellow solid was treated with cold H_2O to remove isoquinoline hydrobromide, which was identified as picrate with the authentic sample by the mixture melting point, and dark yellow crystals were obtained.

Recrystallization from MeOH gave yellow needles, mp 158—159°. Yield, 3.34 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 227 (48200), 257 (6000), 305 (5900), 372 (infl.) (5600), 427 (13600). IR ν_{max}^{KBr} cm^{-1}: 2185 (–CN), 1665—1635 (broad) ($COOCH_3$). *Anal.* Calcd. for $C_{13}H_{10}O_2N_2$: C, 69.01; H, 4.46; N, 12.38. Found: C, 69.31; H, 4.57; N, 12.49.

ii) Dry HCl was passed through a suspension of VIe (1.93 g) in abs. MeOH (40 ml) under ice-cooling and the mixture was allowed to stand overnight with ice-cooling. The solvent was evaporated *in vacuo* and the residue was added to ice-water (100 ml). The precipitated crystals were filtered and washed with cold H_2O. Recrystallization from MeOH gave yellow needles, mp 158—159°. Yield, 0.88 g. The compound was identified with VIb, which was obtained by i) method by the mixture melting point.

1,6-Naphthyridinium 6-Cyano(methoxycarbonyl)methylide (VIIa)——To a solution of IId (0.89 g) in ether (10 ml), 1,6-naphthyridine[23] (0.65 g) was added and heated under reflux for 6 hr. The solvent was evaporated; the dark brown residue was dissolved in $CHCl_3$ and chromatographed over Al_2O_3 (20 g). The column was eluted with $CHCl_3$ and a yellow solid (VIIa) was obtained from the yellow fraction. Recrystallization from EtOH gave yellow needles, mp 208—209°. Yield, 0.04 g. UV $\lambda_{max}^{Tetrahydrofuran}$ mμ (ε): 296 (5960), 384 (6830), 468 (12800). IR ν_{max}^{KBr} cm^{-1}: 2205 (–C≡N), 1670—1635 (broad) (–$COOCH_3$). NMR ($CDCl_3$) δ: 10.30 (1H, s, 5-H), 9.18 (1H, d, $J_{2,3}$=4.5 Hz, 2-H), 9.11 (1H, d, $J_{3,4}$=8.7 Hz, 4-H), 8.29 (1H, d, $J_{7,8}$=8.0 Hz, 7-H), 8.13 (1H, d, $J_{7,8}$=8.0 Hz, 8-H), 7.68 (1H, q, $J_{2,3}$=4.5 Hz, $J_{3,4}$=8.7 Hz, 3-H), 3.76 (3H, s, CH_3OOC). *Anal.* Calcd. for $C_{12}H_9O_2N_3$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.04; H, 4.17; N, 18.82.

1,6-Naphthyridinium 6-Dicyanomethylide (VIIb)——To a solution of 1,6-naphthyridine (2.60 g) in tetrahydrofuran (10 ml), a solution of tetracyanoethylene oxide[10] (2.88 g) in tetrahydrofuran (20 ml) was added dropwise with the temperature kept under 5° and the mixture was allowed to stand for 24 hr in an ice-bath. The precipitated crystals were filtered and washed with cold tetrahydrofuran to afford yellow crystals. Recrystallization from chlorobenzene gave yellow crystals (VIIb), mp 273—274° (decomp.). Yield, 2.46 g. UV $\lambda_{max}^{Tetrahydrofuran}$ mμ (ε): 295 (5730), 388 (9000), 475 (14800). IR ν_{max}^{KBr} cm^{-1}: 2205, 2170 (–C≡N). *Anal.* Calcd. for $C_{11}H_6N_3$: C, 68.03; H, 3.11; N, 28.85. Found: C, 67.91; H, 3.04; N, 29.42.

Diquinolinium Pentacyanopropenide (VIII)——i) To a solution of quinoline (2.58 g, 20 mmole) in ether (10 ml), a solution of bromomalononitrile[16a] (IIe, 1.45 g, 10 mmole) in ether (10 ml) was added under ice-cooling. After the mixture was allowed to stand for 24 hr, the ether was evaporated. To the dark brown solid residue, H_2O (20 ml) was added and the water-insoluble part was filtered. UV spectrum of the filtrate showed the identical absorption with quinoline and UV spectrum of the water-insoluble part had an absorption at 396 and 414 mμ besides that of quinoline. The water-insoluble part was extracted twice with hot 40% MeOH and filtered. The MeOH solution was treated with charcoal and cooled to give yellow needles, mp 149—150°. Yield, 0.59 g. The compound was identified with VIII obtained by ii) method by the mixture melting point. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 397 (21800), 415 (21100). IR ν_{max}^{KBr} cm^{-1}: 2240 (–C≡N), 1515 (>C=C̈–C̄–). NMR (DMSO-d_6) δ: 9.35 (1H, d, $J_{2,3}$=5.0 Hz, 2-H), 9.20 (1H, d, $J_{3,4}$=8.2 Hz, 4-H), 8.44—7.90 (5H, m, ar-H).

ii) To a solution of quinoline (0.26 g) in tetrahydrofuran (5 ml), a solution of tetracyanoethylene (0.26 g) in tetrahydrofuran (5 ml) was added and the mixture was allowed to stand for 0.5 hr at room temperature. When H_2O was added to this solution, yellow crystals were obtained. Recrystallization from 30% MeOH gave small yellow needles, mp 149—150°.

Diisoquinolinium Pentacyanopropenide (IX)——i) To a solution of isoquinoline (2.58 g, 20 mmole) in ether (10 ml), a solution of IIe (1.45 g, 10 mmole) in ether (10 ml) was added and the mixture was treated in the same way as VIII. Orange-yellow needles were obtained, mp 154—155°. Yield, 0.57 g. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): 397 (20200), 414 (19400). IR ν_{max}^{KBr} cm^{-1}: 2240 (–C≡N), 1514 (>C=C̈–C̄<). NMR (DMSO-d_6) δ: 9.64 (1H, s, 1-H), 8.63 (1H, d, $J_{3,4}$=7.2 Hz, 3-H), 8.40—7.80 (5H, m, ar-H). *Anal.* Calcd. for $C_{26}H_{15}N_7$: C, 73.40; H, 3.55; N, 23.06. Found: C, 73.28; H, 3.55; N, 23.40.

ii) To a solution of isoquinoline (0.26 g) in tetrahydrofuran (5 ml), a solution of tetracyanoethylene (0.26 g) in tetrahydrofuran (5 ml) was added; immediately, the mixture changed from orange to dark red. When the solution was diluted with H_2O, yellow crystals were obtained. Recrystallization from 30% MeOH gave yellow needles, mp 153—154°. This compound was identified with the salt which was obtained by i) method by the mixture melting point.

Dimethyl 1,2-Dicyano-1a,1b,2,7b-tetrahydro-1*H*-azirino[1,2-*a*]cyclopropa[*c*]quinoline-1,2-dicarboxylate (Xa)——i) To a solution of quinoline (10.4 g, 80 mmole) in MeOH (25 ml), a solution of IId (7.12 g, 40 mmole) in MeOH (25 ml) was added and the mixture was allowed to stand for 2 days. The precipitated faintly yellow prisms were filtered and recrystallized from acetone–MeOH (1:1) to give colorless prisms (Xa). Yield, 3.95 g. This substance had no constant melting point, namely, it changed to brown at around 180° and gradually decomposed at around 200°. UV $\lambda_{max}^{95\%EtOH}$ mμ (ε): *ca.* 245 (infl.) (7400). IR ν_{max}^{KBr} cm^{-1}: 2280 (–C≡N), 1750 (–$COOCH_3$). NMR (DMSO-d_6) δ: 7.65—7.25 (4H, m, ar-H), 3.83 (3H, s, CH_3OOC),

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3.80 (3H, s, CH_3OOC), 3.78 (1H, s, 1b-H), 3.36 (1H, d, J=8.7 Hz, 7b-H), 3.12 (1H, d, J=8.7 Hz, 1a-H). *Anal.* Calcd. for $C_{17}H_{13}O_4N_3$: C, 63.15; H, 4.05; N, 13.00. Found: C, 63.19; H, 4.20; N, 13.16.

ii) In a solution of quinoline (5.20 g, 40 mmole) and 4-(*tert*-butyl)catechol (0.16 g, 1 mmole) in MeOH (15 ml), N_2 gas was bubbled for 10 min in the dark. To this, a solution of IId(3.56 g) in MeOH (15 ml) was added in the dark and N_2 atmosphere, and the mixture was allowed to stand for 2 days. It was worked up in the same manner as in i) to give white prisms of Xa. Yield, 1.90 g. The crystals changed to brown gradually at 180° and decomposed at around 200°. IR spectrum was identical with that of Xa obtained by i) method. When hydroquinone was used in the place of 4-(*tert*-butyl)catechol, the same result was given.

Diethyl 1,2-Dicyano-1a,1b,2,7b-tetrahydro-1*H*-azirino[1,2-*a*]cyclopropa[*c*]quinoline-1,2-dicarboxylate (Xb)——To a solution of quinoline (12.9 g, 0.1 mole) in MeOH (40 ml), a solution of ethyl bromocyanoacetate (IIf) in MeOH (40 ml) was added and the mixture was allowed to stand for 2 days at room temperature. The precipitated white crystals were filtered and recrystallized from MeOH to give colorless needles, mp 140—143° (decomp.). Yield, 3.0 g. UV $\lambda_{max}^{95\%\,EtOH}$ mμ (ε): *ca.* 245 (infl.) (6800). IR ν_{max}^{KBr} cm^{-1}: 2280 (–C≡N), 1745 (–$COOCH_3$). *Anal.* Calcd. for $C_{19}H_{17}O_4N_3$: C, 69.45; H, 4.88; N, 11.96. Found: C, 64.55; H, 4.70; N, 12.15.

Dimethyl 5-Bromo-1,2-dicyano-1a,1b,2,7b-tetrahydro-1*H*-azirino[1,2-*a*]cyclopropa[*c*]quinoline-1,2-dicarboxylate (Xc)——To a solution of 7-bromoquinoline[24] (2.08 g, 10 mmole) in MeOH (10 ml), a solution of IId (0.89 g, 5 mmole) in MeOH (10 ml) was added and the mixture was allowed to stand for 10 days at room temperature. The precipitated crystals were filtered and recrystallized from acetone–MeOH mixture to give colorless prisms. Yield, 0.41 g. This substance had no constant melting point like Xa, and it changed to brown at around 170° and gradually decomposed at around 210°. UV $\lambda_{max}^{CH_3CN}$ mμ (ε): 226.5 (22200), *ca.* 250 (infl.) (7600). IR ν_{max}^{KBr} cm^{-1}: 2270 (–C≡N), 1745 (–$COOCH_3$). NMR (DMSO-d_6) δ: 7.60—7.50 (3H, m, ar-H), 3.83 (3H, s, CH_3OOC), 3.82 (3H, s, CH_3OOC), 3.77 (1H, s, 1b-H), 3.37 (1H, d, J=8.5 Hz, 7b-H), 3.12 (1H, d, J=8.5 Hz, 1a-H). *Anal.* Calcd. for $C_{17}H_{12}O_4N_3Br$: C, 50.76; H, 3.01; N, 10.45. Found: C, 50.94; H, 3.08; N, 10.42.

Methyl 3-Quinolinemalonate (XII)——A suspension of finely ground Xa (3.23 g) in abs. MeOH (50 ml) was saturated with dry HCl gas in an ice–salt bath and the mixture was allowed to stand overnight in this condition. The reaction mixture was poured into an excess ice water and extracted with benzene. After the benzene layer was washed with H_2O and dried over Na_2SO_4, the solvent was evaporated to give faintly yellow stimulative liquid (1.50 g). The liquid was distilled *in vacuo* to give colorless liquid (XI), bp 135—140° (30 mmHg) (bath temperature). Yield, 1.25 g. The compound was identified with dimethyl chloromalonate[12] by comparing the IR spectra. The acid layer, which was isolated from benzene layer of XI, was basified with K_2CO_3 and extracted with $CHCl_3$. Evaporation of the solvent gave faintly yellow viscous oil (2.20 g). This substance was dissolved in $CHCl_3$ and chromatographed over Al_2O_3. Elution with $CHCl_3$ gave colorless crystals (1.82 g), which were recrystallized from cyclohexane to give colorless needles (XII), mp 87—88°. UV $\lambda_{max}^{95\%\,EtOH}$ mμ (ε): 233 (41800), 280 (3150), 290 (infl.) (2900), 304.5 (2550), 317.5 (2480). IR ν_{max}^{KBr} cm^{-1}: 1743 (–$COOCH_3$). NMR ($CDCl_3$) δ: 8.93 (1H, d, $J_{2,4}$=1.7 Hz, 2-H), 8.30 (1H, d, $J_{2,4}$=1.7 Hz, 4-H), 8.30 (1H, d, $J_{7,8}$=8.3 Hz, 8-H), 7.90—7.50 (3H, m, 5-, 6-, and 7-H), 3.78 (6H, s, two CH_3OOC). *Anal.* Calcd. for $C_{14}H_{13}O_4N$: C, 64.86; H, 5.05; N, 5.40. Found: C, 64.28; H, 5.08; N, 5.40.

Picrate, yellow needles, mp 188—189°. *Anal.* Calcd. for $C_{20}H_{16}O_{11}N_4$: C, 49.19; H, 3.30; N, 11.47. Found: C, 49.26; H, 3.43; N, 11.82.

Ethyl 3-Quinolineacetate (XIII)——A solution of XII (0.20 g) in 20% HCl (10 ml) was heated at 100° for 6 hr and after it was evaporated *in vacuo* the colorless residue was dissolved in EtOH (20 ml). This solution was saturated with dry HCl gas and was allowed to stand for 2 days. After the solvent was evaporated, the residue was basified with K_2CO_3 and extracted with benzene. After it was dried over Na_2SO_4, benzene was evaporated and a colorless oily residue (XIII) was obtained. Yield, 0.14 g. The residue was led to a picrate for identification and the picrate was recrystallized from EtOH to give yellow needles, mp 152—153°. *Anal.* Calcd. for $C_{19}H_{16}O_9N_4$: C, 51.35; H, 3.63; N, 12.61. Found: C, 51.32; H, 3.68; N, 12.55. This picrate was identified with that derived from ethyl 3-quinolineacetate[13] by the mixture melting point.

Methyl α-Cyano-[1(4*H*),4′-bipyridine]-$\Delta^{\alpha,4}$-acetate (XVI)——A solution of Na (0.5 g) in abs. MeOH (10 ml) was evaporated *in vacuo*. To this residue, DMF (20 ml) and IVd (0.88 g) were added and heated on a water bath for 0.5 hr. The reaction mixture became dark red. After it was cooled, the mixture was neutralized with AcOH (1 ml) and the insoluble brown powder was filtered. The filtrate was extracted with $CHCl_3$ (200 ml). The $CHCl_3$ layer was washed well with H_2O and the solvent was evaporated. The obtained brown residue was dissolved in $CHCl_3$ and chromatographed over Al_2O_3 (30 g). Its elution with 5% acetone–AcOEt gave orange–red solid, which was recrystallized from a large amount of MeOH to give orange–yellow crystals (XVI), mp 275°. Yield, 0.033 g. UV $\lambda_{max}^{CH_3CN}$ mμ (ε): 231 (20500), 437 (24300). IR ν_{max}^{KBr} cm^{-1}: 2220 (–C≡N), 1654 (–$COOCH_3$), 1315 (CH_3), 816 (4-substituted pyridine). NMR (CF_3COOH) δ: 9.44 and

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8.82 (4H, a pair of doublets, $J=6.75$ Hz), 9.26 and 8.68 (4H, a pair of doublets, $J=6.5$ Hz). *Anal.* Calcd. for $C_{14}H_{11}O_2N_3$: C, 66.39; H, 4.38; N, 16.59. Found: C, 66.66; H, 4.48; N, 16.67.

[1(4*H*),4′-Bipyridine]-4-one (XVII)——By the method of Hamana,[19] faintly yellow needles (XVII), mp 177—178°, were obtained from 4-nitropyridine and phosphoryl chloride. UV $\lambda_{max}^{95\%\ EtOH}$ mμ (ε): 291 (3260). NMR (CF_3COOH) δ: 9.23 and 8.51 (4H, a pair of doublets, $J=6.75$ Hz), 8.80 and 7.67 (4H, a pair of doublets, $J=7.25$ Hz).

2-Methoxyimidazo[2,1-*a*]isoquinoline-3-carbonitrile (XVIII)——To a solution of Na (0.55 g) in abs. MeOH, VIc (1.93 g) was added and heated for 11 hr with stirring. After the reaction mixture was cooled with ice, the precipitated crystals were filtered. Recrystallization from EtOH gave colorless needles, mp 178—179°. Yield, 0.68 g. *Anal.* Calcd. for $C_{13}H_9ON_3$: C, 69.94; H, 4.06; N, 18.83. Found: C, 69.64; H, 4.25; N, 19.26.

Methyl 2-Methoxyimidazo[2,1-*a*]isoquinoline-3-carboxylate (XIX)——To a solution of Na (0.5 g) in abs. MeOH (40 ml), VIb (1.70 g) was added and heated under reflux for 6 hr. MeOH was evaporated; the residue was neutralized with a solution of AcOH (1.7 ml) in H_2O (100 ml) and extracted with CH_2Cl_2. After the CH_2Cl_2 layer was dried, the solvent was evaporated. The residue was dissolved in CH_2Cl_2–C_6H_6 (1:1) and chromatographed over Al_2O_3 (50 g). Recrystallization of the elute from EtOH gave colorless needles (XIX), mp 169—171°. Yield, 0.45 g. *Anal.* Calcd. for $C_{14}H_{12}O_3N_2$: C, 65.62; H, 4.72; N, 10.93. Found: C, 65.67; H, 4.74; N, 11.31.

2-Methoxyimidazo[2,1-*f*]-1,6-naphthyridine-3-carbonitrile (XX)——i) To a solution of Na (0.35 g) in abs. MeOH (70 ml), ylide (VIIb) (0.98 g) was added and heated under reflux for 1 hr. After the mixture was cooled, AcOH (1 ml) was carefully added to neutralize the mixture and MeOH was evaporated *in vacuo*. The dark brown residue obtained was dissolved in $CHCl_3$; the insoluble solid was filtered off and the filtrate was chromatographed over Al_2O_3 (30 g). Its elution with $CHCl_3$ gave colorless crystals, which were recrystallized from MeOH–$CHCl_3$ mixture to give colorless needles (XX), mp 213—214°. Yield, 0.12 g. *Anal.* Calcd. for $C_{12}H_8ON_4$: C, 64.29; H, 3.60; N, 24.99. Found: C, 64.59; H, 3.81; N, 24.41.

ii) A suspension of ylide (0.39 g) (VIIb) in abs. MeOH (15 ml) was saturated with dry HCl gas under icecooling and the mixture was allowed to stand overnight in this condition. The solvent was evaporated *in vacuo* and ice–water (10 ml) was added to the residue. This mixture was basified with K_2CO_3 and extracted with $CHCl_3$. After it was dried over K_2CO_3, a part of the $CHCl_3$ layer was concentrated and chromatographed over Al_2O_3 (10 g). Its elution with $CHCl_3$ gave colorless powder, which was recrystallized from MeOH to give colorless needles, mp 213—214°. Yield, 0.18 g. This compound was identified with XX, which was obtained by i) method by the mixture melting point and comparing IR spectra.

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