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Synthesis of Methylpyridine Derivatives. XXXII.[1] Reaction of Pyridine, Quinoline, and Isoquinoline with 4-Bromoacetoacetic Acid Derivatives and Synthesis of Indolizine Derivatives

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Reaction of 4-bromoacetoacetanilide (II) with pyridine (Ia), 4-methylpyridine (Ib), and 3-methylpyridine (Ic) gave pyridinium (IVa), 4-methylpyridinium (IVb), and 3-methylpyridinium (N-phenylcarbamoyl) acetonylide (IVc), respectively. These ylides (IVa, b, c) were allowed to react with diethyl acetylenedicarboxylate (DEAC) to give diethyl 3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIa), and its methyl derivatives (VIb, VIc, and VId).

Reaction of ethyl 4-bromoacetoacetate (III) with pyridines (Ia, b, c) followed by treatment with DEAC afforded the pyrrolo[1,2-*a*]pyridine derivatives (VIIa, b, c, d).

Similarly, quinoline (VIIIa) and 4-methylquinoline (VIIIb) reacted with II (III) to give the corresponding N-ylides, IXa and IXb (Xa and Xb), respectively. These ylides were converted to the pyrrolo[1,2-*a*]quinoline derivatives (XIa, b and XIIa, b). Similar reaction of isoquinoline gave the pyrroloisoquinoline derivatives (XIII, XIV).

Keywords——N-ylide; methylpyridine; methylquinoline; acetoacetic acid derivative; cycloaddition; acetylenedicarboxylate; indolizine derivative

It is a well documented fact that pyridine reacts with α-haloketone to give the quaternary ammonium salt, which, on treatment with base, is transformed into the N-ylide.[3] At the same time, dipolar cycloaddition reactions of some ylides with diethyl acetylenedicarboxylate (DEAC) have been studied by several groups of workers.[4] For example, the reaction of N-phenacylpyridinium ylide with DEAC was reported to give the pyrrolopyridine derivative.[5] In this paper we wish to report that the reaction of 4-bromoacetoacetic acid derivatives with pyridine, quinoline and isoquinoline gives the corresponding N-ylides, which are converted to the indolizine derivatives by dipolar cycloaddition reaction.

Equimolar quantities of pyridine (Ia) and 4-bromoacetoacetanilide (II) were brought into reaction in ethanol at room temperature. The oily product obtained was then neutralized with sodium ethoxide to give yellow crystals, pyridinium (N-phenylcarbamoyl)acetonylide (IVa) in 26% yield.

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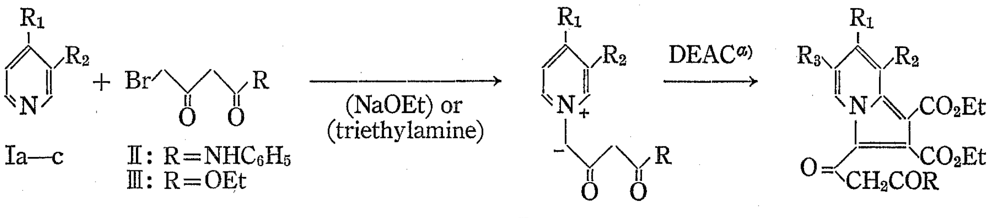
Similarly, 4 and 3-methylpyridine (Ib and Ic) reacted with II to give the corresponding ylides, 4-methylpyridinium (IVb) and 3-methylpyridinium (N-phenylcarbamoyl)acetonylide (IVc) in 20% and 36% yields, respectively.

Cycloaddition reaction of ylides (IVa, b, c) was attempted. Thus, the ylide (IVa) was allowed to react with DEAC in dimethylformamide (DMF) giving the product, which was assigned as diethyl 3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIa).

When the ylide (IVb) was allowed to react with DEAC, diethyl 7-methyl-3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIb) was obtained in 8% yield. Similar reaction of 3-methylpyridinium ylide (IVc) with DEAC gave rise to diethyl 8-methyl-3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIc) and the 6-methyl isomer (VId) in 8% and 5% yields, respectively.

When ethyl 4-bromoacetoacetate (III) was used instead of compound II, the ylides (V) were not isolated as the crystalline substance. However, ring closure reaction of the crude product (V) with DEAC afforded the pyrrolo[1,2-*a*]pyridine derivatives (VII). Thus, pyridine was allowed to react with the bromoester (III) followed by treatment with triethylamine to give the oily product (Va), which reacted with DEAC in DMF to give diethyl 3-(ethoxycarbonyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIIa) in 12% yield. Similar reaction of 4-methylpyridine (Ib) afforded the 7-methylpyrrolo[1,2-*a*]pyridine derivative (VIIb) in 10% yield. Similarly, 3-methylpyridine (Ic) reacted with the bromoester (III) to give the ylide (Vc), which was, without purification, treated with DEAC to afford the isomeric pyrrolo[1,2-*a*]pyridine derivatives (VIIc and VIId).

Reaction of 2-methylpyridine with compound II and III followed by ring closure with DEAC did not give any crystalline product corresponding to the pyrrolo[1,2-*a*]pyridine derivatives.



Ia—c

II: $R=NHC_6H_5$
III: $R=OEt$

IVa—c: $R=NHC_6H_5$
Va—c: $R=OEt$

VIa—d: $R=NHC_6H_5$
VIIa—d: $R=OEt$

a : $R_1=R_2=H$
b : $R_1=CH_3$, $R_2=H$
c : $R_1=H$, $R_2=CH_3$

a : $R_1=R_2=H$
b : $R_1=CH_3$, $R_2=H$
c : $R_1=H$, $R_2=CH_3$

a : $R_1=R_2=R_3=H$
b : $R_1=CH_3$, $R_2=R_3=H$
c : $R_1=R_3=H$, $R_2=CH_3$
d : $R_1=R_2=H$, $R_3=CH_3$

Chart 1

a) **DEAC; diethyl acetylenedicarboxylate**

Reaction of quinoline (VIIIa) with the bromoanilide (II) and the bromoester (III) gave rise to the corresponding quinolinium ylides (IXa and Xa) in 55% and 53% yields, respectively. Similar reaction of 4-methylquinoline (VIIIb) with II and III gave rise to the corresponding ylides (IXb and Xb) in 10% and 13% yields, respectively.

Heating of the ylide (IXa) in acetic anhydride afforded a 30% yield of 2-acetoxypyrrolo[1,2-*a*]quinoline-3-carboxanilide (XIa). Similarly, the ylides (IXb, Xa, and Xb) were refluxed in acetic anhydride to afford the corresponding pyrrolo[1,2-*a*]quinoline derivatives (XIb, XIIa, b) in 40%, 28%, and 61% yields, respectively.

Equimolar quantities of isoquinoline and bromoacetoacetanilide (II) were brought into reaction, and the resulting oily product was heated with triethylamine in acetic anhydride. The crystalline substance obtained was assigned as ethyl 2-acetoxy-3-acetylpyrrolo[2,1-*a*]isoquinoline (XIII).

Similarly, reaction of isoquinoline with the ester (III) followed by treatment with triethylamine in acetic anhydride afforded a 20% yield of ethyl 2-acetoxy-3-acetylpyrrolo[2,1-*a*]isoquinoline-1-carboxylate (XIV).

Ring closure of the pyridinium ylides (IV and V) with acetic anhydride failed. Also reaction of quinolinium and isoquinolinium ylides (IX, X) with DEAC did not give the corresponding cycloaddition products.

Structural assignments of the products obtained in the present investigation were made on the basis of elemental analyses and the spectroscopic data detailed in the experimental section.

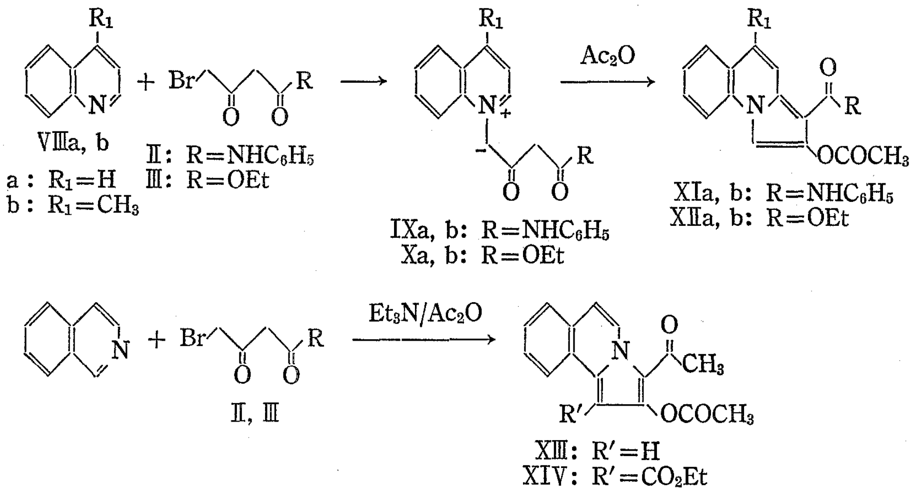


Chart 2

The formation of the indolizine derivatives (VI, VII) can be explained by the 1,3-dipolar cycloaddition of the pyridinium ylides (IV, V) with DEAC accompanied with oxidation.

Reaction of quinolinium ylide (IX, X) with acetic anhydride to give the pyrroloquinoline derivatives (XI, XII) might well involve the intermolecular cyclization. Namely, the ylide (IX, X) is acetylated with acetic anhydride to give the quaternary ammonium intermediate (A), which is converted to the dipolar intermediate (B). Cyclization gives the dehydro intermediate of pyrroloquinoline (C), which is oxidized to give the product (XI, XII).

In the case of isoquinoline derivative, the 3-position of intermediate (D) is acetylated with ease to give the product (XIV). In the case of the amide intermediate (D, where R is NHC_6H_5), the carbamoyl group is readily hydrolyzed, presumably by steric hindrance, to give the product XIII.

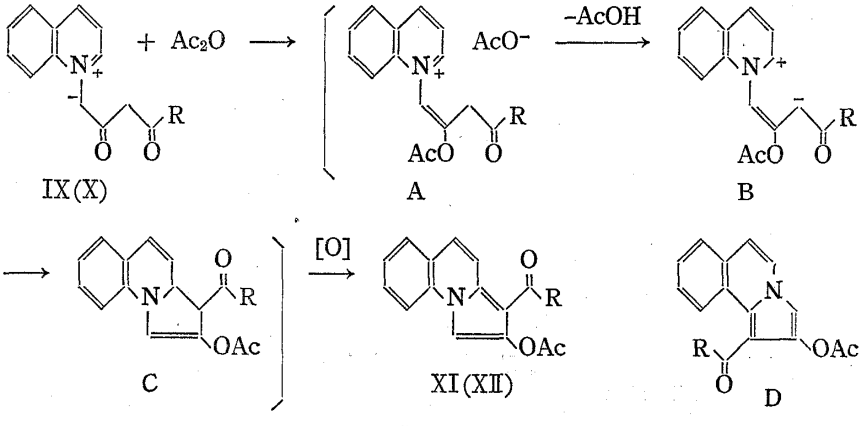


Chart 3

Experimental

Pyridinium (N-Phenylcarbamoyl)acetonylide (IVa)——A solution of pyridine (Ia) (1.6 g, 0.02 mol) and 4-bromoacetoacetanilide (II) (4.7 g, 0.02 mol) in abs. ethanol (20 ml) was allowed to stand at room temperature for a day. The reaction mixture was condensed *in vacuo* to give an oily residue, to which was added a sodium ethoxide solution prepared from sodium metal (0.5 g, 0.02 atom) and abs. ethanol (20 ml). Crystals separated were collected by suction. Recrystallization from ethanol gave 2.0 g (26%) of yellow needles, mp 176—178°. *Anal.* Calcd. for $C_{15}H_{14}N_2O_2$ (IVa): C, 70.85; H, 5.55; N, 11.02. Found: C, 70.79; H, 5.57; N, 10.66. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3450, 1655 (sh), 1631. NMR (CF_3CO_2H) δ: 4.20 (2H, s, CH_2), 5.91 (2H, s, N–CH_2, protonated by CF_3CO_2H), 7.37 (5H, s, benzene ring proton), 7.95—8.30 (2H, m, 3,5-H), 8.45—8.82 (3H, m, 2,4,6-H), 9.07—9.32 (1H, br., NH).

4-Methylpyridinium (N-Phenylcarbamoyl)acetonylide (IVb)——According to the procedure described above, 4-methylpyridine (Ib) (1.9 g, 0.02 mol) was allowed to react with compound II (4.7 g, 0.02 mol) in abs. ethanol (20 ml), followed by treatment with sodium ethoxide prepared from sodium (0.5 g, 0.02 atom) in ethanol (20 ml) to give yellow crystals. Recrystallization from ethanol gave 1.0 g (20%) of colorless needles, mp 191—193° (dec.). *Anal.* Calcd. for $C_{16}H_{16}N_2O_2$ (IVb): C, 71.62; H, 6.01; N, 10.44. Found: C, 71.45; H, 6.03; N, 10.14. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3450, 1655 (sh), 1635. NMR (CF_3CO_2H) δ: 2.77 (3H, s, CH_3), 4.17 (2H, s, CH_2), 5.79 (2H, s, N–CH_2), 7.35 (5H, s, ring proton), 7.87 (2H, d, J=6.0 Hz, 3,5-H), 8.45 (2H, d, J=6.0 Hz, 2,6-H), 9.05 (1H, br., NH).

3-Methylpyridinium (N-Phenylcarbamoyl)acetonylide (IVc)——According to the similar fashion given for the ylide (IVa), 3-methylpyridine (Ic) (3.8 g, 0.04 mol) was allowed to react with II (9.4 g, 0.04 mol) in abs. ethanol (40 ml). Treatment of the resulting residue with sodium ethoxide (sodium 1.0 g, ethanol 40 ml) gave yellow crystals. Recrystallization from ethanol gave 3.7 g (36%) of yellow needles (hygroscopic), mp 177—180° (dec.). *Anal.* Calcd. for $C_{16}H_{16}O_2N_2 \cdot 1/4H_2O$ (IVc): C, 70.44; H, 6.10; N, 10.27. Found: C, 70.45; H, 5.98; N, 10.17. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1640, 1598. NMR (CF_3CO_2H) δ: 2.60 (3H, s, CH_3), 4.17 (2H, s, CH_2), 5.82 (2H, s, N–CH_2), 7.32 (5H, s, ring proton), 7.70—8.07 (1H, m, 4-H), 8.27—8.55 (3H, m, 2,4,6-H), 9.10—9.30 (1H, br., NH).

Diethyl 3-(N-Phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIa)——To a solution of the ylide (IVa) (0.25 g, 0.001 mol) in dimethylformamide (DMF) (5 ml), was added diethyl acetylenedicarboxylate (DEAC) (0.17 g, 0.001 mol). After allowing to stand at room temperature overnight, the reaction mixture was condensed under reduced pressure. The resulting residue was extracted with *n*-hexane, ether, and then with benzene. From the benzene extract, crystalline product was obtained. Recrystallization from acetone gave colorless fine needles, mp 169—170°. Yield, 46 mg (11%). *Anal.* Calcd. for $C_{23}H_{24}N_2O_6$ (VIa): C, 65.08; H, 5.70; N, 6.60. Found: C, 65.11; H, 5.22; N, 6.43. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3300, 1725 (sh), 1706, 1666, 1640. NMR ($CDCl_3$) δ: 1.38 (3H, t, J=6.7 Hz, CH_3), 1.45 (3H, t, J=6.7 Hz, CH_3), 3.93 (2H, s, CH_2), 4.38 (2H, q, J=6.7 Hz, CH_2), 4.56 (2H, q, J=6.7 Hz, CH_2), 6.90—7.80 (7H, m, 6,7-H, benzene ring), 8.29—8.60 (1H, m, 8-H), 9.0—9.3 (1H, br., NH), 9.88—10.05 (1H, m, 5-H).

Diethyl 7-Methyl-3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIb)——Employing the similar procedure described in the above run, the ylide (IVb) (0.27 g, 0.001 mol) was allowed to react with DEAC (0.17 g, 0.001 mol) in DMF (5 ml). Crystals obtained from the ether extract were purified by recrystallization from ethanol giving colorless small needles, mp 170—171°. Yield, 35 mg (8%). *Anal.* Calcd. for $C_{24}H_{26}N_2O_6$ (VIb): C, 65.74; H, 5.98; N, 6.39. Found: C, 65.55; H, 5.80; N, 6.15. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3300, 1725 (sh), 1705, 1668, 1630. NMR ($CDCl_3$) δ: 1.38 (3H, t, J=6.7 Hz, CH_3), 1.45 (3H, t, J=6,7 Hz, CH_3), 2.48 (3H, s, CH_3), 3.90 (2H, s, CH_2), 4.36 (2H, q, J=6.7 Hz, CH_2), 4.54 (2H, q, J=6.7 Hz, CH_2), 6.80—7.75 (6H, m, 6-H, benzene ring), 8.09—8.25 (1H, m, 8-H), 9.05—9.45 (1H, br., NH), 9.82 (1H, d, J=6.7 Hz, 5-H).

Diethyl 8-Methyl (and 6-Methyl)-3-(N-phenylcarbamoyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIc and VId)——According to the similar procedure described above, the ylide (IVc) (0.57 g, 0.002 mol) was allowed to react with DEAC (0.42 g, 0.003 mol) in DMF (10 ml). The resulting oily product was purified by silica gel column chromatography using *n*-hexane–ether (1 : 1) as an eluant to give a crystalline substance, which was submitted to column chromatography, once again. Crystals obtained from the first elution were recrystallized from methanol to give 70 mg (8%) of compound VIc, yellow prisms of mp 136—137°. The second elution gave 40 mg (5%) of compound VId, colorless prisms (from methanol) of mp 164—165°, depressed to 110° on admixture with a sample of VIc obtained above. *Anal.* Calcd. for $C_{24}H_{26}N_2O_6$ (VIc): C, 65.74; H, 5.98; N, 6.39. Found: C, 65.88; H, 5.59; N, 6.41. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3355, 1718, 1688, 1628. NMR ($CDCl_3$) δ: 1.40 (3H, t, J=6.7 Hz, CH_3), 1.45 (3H, t, J=6.7 Hz, CH_3), 2.64 (3H, s, CH_3), 3.95 (2H, s, CH_2), 4.35 (2H, q, J=6.7 Hz, CH_2), 4.52 (2H, q, J=6.7 Hz, CH_2), 6.90—7.64 (7H, m, 6,7-H, benzene ring), 9.1—9.2 (1H, br., NH), 9.83 (1H, d, J=7.5 Hz, 5-H). *Anal.* Calcd. for $C_{24}H_{26}N_2O_6$ (VId): C, 65.74; H, 5.98; N, 6.39. Found: C, 66.04; H, 5.75; N, 6.74. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 3280, 1728, 1700, 1660, 1638. NMR ($CDCl_3$) δ: 1.48—1.70 (6H, m, $2 \times CH_3$), 2.48 (3H, s, CH_3), 3.96 (2H, s, CH_2), 4.30—4.70 (4H, m, $2 \times CH_2$), 7.10—7.66 (6H, m, 7-H, benzene ring), 8.30 (1H, d, J=9 Hz, 8-H), 9.16—9.20 (1H, br. s, 5-H), 9.72—9.80 (1H, br., NH).

Diethyl 3-(Ethoxycarbonyl)acetylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIIa)——A solution of pyridine (Ia) (0.8 g, 0.01 mol) and ethyl 4-bromoacetoacetate (III) (2.1 g, 0.01 mol) in dry benzene (10 ml) was allowed to stand at room temperature for a day. The reaction mixture was condensed under reduced pressure, and the resulting oily residue was dissolved in DMF (5 ml), to which solution was added triethylamine (1 g, 0.01 mol) and DEAC (1.7 g, 0.01 mol). After allowing to stand overnight, the mixture was condensed *in vacuo*. The residue was purified by silica gel column chromatography. The ether elution gave a crystalline substance, which was recrystallized from ether to colorless prisms, mp 104—105°. Yield, 0.45 g (12%). *Anal.* Calcd. for $C_{19}H_{21}NO_7$ (VIIa): C, 60.79; H, 5.64; N, 3.73. Found: C, 60.54; H, 5.42; N, 3.67. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1734, 1703, 1628. NMR ($CDCl_3$) δ: 1.38 (3H, t, $J=6.7$ Hz, CH_3), 1.44 (3H, t, $J=6.7$ Hz, CH_3), 1.49 (3H, t, $J=6.7$ Hz, CH_3), 3.87 (2H, s, CH_2), 4.23 (2H, q, $J=6.7$ Hz, CH_2), 4.37 (2H, q, $J=6.7$ Hz, CH_2), 4.48 (2H, q, $J=6.7$ Hz, CH_2), 6.90—7.65 (2H, m, 6,7-H), 8.25—8.50 (1H, m, 8-H), 9.85—10.07 (1H, m, 5-H).

Diethyl 3-(Ethoxycarbonyl)acetyl-7-methylpyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIIb)——According to the procedure described in the above run, 4-methylpyridine (Ib) (0.93 g, 0.01 mol) was treated with III (2.1 g, 0.01 mol) and then with DEAC (1.7 g, 0.01 mol) in the presence of triethylamine (1 g, 0.01 mol) and DMF (5 ml). The reaction mixture was condensed, and the residue was extracted with ether. The ether extract was submitted to silica gel column chromatography. The *n*-hexane–ether (4: 1) elution gave a crystalline substance. Recrystallization from ether afforded colorless needles, mp 119—120°. Yield, 0.39 g (10%). *Anal.* Calcd. for $C_{20}H_{23}NO_7$ (VIIb): C, 61.69; H, 5.95; N, 3.60. Found: C, 61.94; H, 5.82; N, 3.73. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1732, 1689, 1625. NMR ($CDCl_3$) δ: 1.28 (3H, t, $J=6.7$ Hz, CH_3), 1.38 (3H, t, $J=6.7$ Hz, CH_3), 1.43 (3H, t, $J=6.7$ Hz, CH_3), 2.48 (3H, s, CH_3), 3.86 (2H, s, CH_2), 4.23 (2H, q, $J=6.7$ Hz, CH_2), 4.36 (2H, q, $J=6.7$ Hz, CH_2), 4.47 (2H, q, $J=6.7$ Hz, CH_2), 6.80—7.05 (1H, m, 6-H), 8.09—8.25 (1H, m, 8-H), 9.85 (1H, d, $J=6.7$ Hz, 5-H).

Diethyl 3-(Ethoxycarbonyl)acetyl-8-methyl(and 6-methyl)pyrrolo[1,2-*a*]pyridine-1,2-dicarboxylate (VIIc and VIId)——Employing the similar fashion described above, 3-methylpyridine (0.95 g, 0.01 mol) was treated with III (2.1 g, 0.01 mol), DMF (10 ml), triethylamine (1 g), and DEAC (1.7 g). The resulting residue, after evaporation of the solvent, was submitted to silica gel column chromatography using a mixture of *n*-hexane–ether (4: 1) as an eluant. The first elution gave 0.18 g (5%) of colorless prisms (from petroleum ether), mp 50—51° (VIIc). The second elution gave 0.15 g (4%) of colorless prisms (from ethanol), mp 86—87° (VIId). *Anal.* Calcd. for $C_{20}H_{23}O_7N$ (VIIc): C, 61.69; H, 5.95; N, 3.60. Found: C, 61.45; H, 5.86; N, 3.46. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1740, 1728, 1630. NMR ($CDCl_3$) δ: 1.26 (3H, t, $J=6.7$ Hz, CH_3), 1.38 (3H, t, $J=6.7$ Hz, CH_3), 1.40 (3H, t, $J=6.7$ Hz, CH_3), 2.61 (3H, s, CH_3), 3.91 (2H, s, CH_2), 4.20 (2H, q, $J=6.7$ Hz, CH_2), 4.30 (2H, q, $J=6.7$ Hz, CH_2), 4.42 (2H, q, $J=6.7$ Hz, CH_2), 6.90—7.26 (2H, m, 6,7-H), 9.85 (1H, d, $J=6.5$ Hz, 5-H). *Anal.* Calcd. for $C_{20}H_{23}NO_7$ (VIId): C, 61.69; H, 5.95; N, 3.60. Found: C, 61.92; H, 6.20; N, 3.47. IR $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1748, 1738, 1708, 1630. NMR ($CDCl_3$) δ: 1.28 (3H, t, $J=6.7$ Hz, CH_3), 1.36 (3H, t, $J=6.7$ Hz, CH_3), 1.41 (3H, t, $J=6.7$ Hz, CH_3), 2.38 (3H, s, CH_3), 3.85 (2H, s, CH_2), 4.22 (2H, q, $J=6.7$ Hz, CH_2), 4.37 (2H, q, $J=6.7$ Hz, CH_2), 4.46 (2H, q, $J=6.7$ Hz, CH_2), 7.36 (1H, d, $J=8$ Hz, 7-H), 8.25 (1H, d, $J=8$ Hz, 8-H), 9.80 (1H, s, 5-H).

Quinolinium (N-Phenylcarbamoyl)acetonylide (IXa)——A solution of quinoline (VIIIa) (1.29 g, 0.01 mol) and 4-bromoacetoacetanilide (II) (2.56 g, 0.01 mol) in abs. ethanol (10 ml) was allowed to stand at room temperature for a day. Triethylamine (1 g, 0.01 mol) was added to the solution with stirring, and crystals separated were collected by suction. Recrystallization from ethanol gave yellow needles, mp 271—273° (dec.). Yield, 1.68 g (55%). *Anal.* Calcd. for $C_{19}H_{16}N_2O_2$ (IXa): C, 74.98; H, 5.30; N, 9.21. Found: C, 74.76; H, 5.41; N, 9.31. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 3300 (sh), 1658. NMR (CF_3CO_2H) δ: 5.41 (2H, s, CH_2), 7.39 (5H, s, benzene ring), 7.50—8.20 (7H, m, aromatic H), 8.40—8.61 (1H, br., NH), 8.49 (1H, s, $\equiv$N–CH=).

4-Methylquinolinium (N-Phenylcarbamoyl)acetonylide (IXb)——According to the procedure described above, reaction of 4-methylquinoline (VIIIb) (1.43 g, 0.01 mol) with II (2.56 g, 0.01 mol) followed by treatment with triethylamine (1 g) gave the ylide (IXb), mp 240° (dec.) yellow needles (ethanol). Yield, 0.3 g (10%). *Anal.* Calcd. for $C_{20}H_{18}N_2O_2$ (IXb): C, 75.49; H, 5.70; N, 8.80. Found: C, 75.19; H, 5.15; N, 8.78. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1670, 1600. NMR (CF_3CO_2H) δ: 2.58 (3H, s, CH_3), 4.45 (2H, s, CH_2), 6.80—7.80 (11H, m, aromatic H), 8.23 (1H, s, =CH–N$\equiv$), 10.08—10.22 (1H, br., NH). Mass Spectrum *m/e*: 318 (M^+).

Quinolinium (Ethoxycarbonyl)acetonylide (Xa)——According to the procedure given for the ylide (IXa), reaction of quinoline (VIIIa) (1.29 g, 0.01 mol) with the bromoester (III) (2.1 g, 0.01 mol) and triethylamine (1 g) in ethanol gave the ylide (Xa), yellow needles (ethanol), mp 173—175°. Yield, 1.36 g (53%). *Anal.* Calcd. for $C_{15}H_{15}NO_3$ (Xa): C, 70.02; H, 5.88; N, 5.44. Found: C, 70.28; H, 5.68; N, 5.35. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1655. NMR (CF_3CO_2H) δ: 1.46 (3H, t, $J=6.3$ Hz, CH_3), 4.54 (2H, q, $J=6.3$ Hz, CH_2), 5.79 (2H, s, CH_2), 7.70—8.50 (6H, m, aromatic H), 8.38 (1H, s, =CH–N$\equiv$), 8.75—8.96 (1H, m, 2-H).

4-Methylquinolinium (Ethoxycarbonyl)acetonylide (Xb)——According to the procedure described above, 4-methylquinoline (VIIIb) (2.9 g, 0.02 mol) was allowed to react with III (4.2 g, 0.02 mol) and triethylamine (2 g) to give 0.9 g (16%) of the ylide (Xb), mp 188—189° (dec.), yellow needles (ethanol). *Anal.* Calcd. for $C_{16}H_{17}O_3N$ (Xb): C, 70.83; H, 6.32; N, 5.16. Found: C, 70.78; H, 5.82; N, 5.01. IR $\nu_{\max}^{\text{CHCl}_3}$ cm^{-1}: 1706, 1657. NMR ($CDCl_3$) δ: 1.38 (3H, t, $J=7.0$ Hz, CH_3), 2.62 (3H, s, CH_3), 4.34 (2H, q, $J=7$ Hz, CH_2), 4.40 (2H, s, CH_2), 7.12—7.92 (6H, m, aromatic H), 8.06 (1H, s, =CH–N$\equiv$).

2-Acetoxypyrrolo[1,2-*a*]quinoline-3-carboxanilide (XIa)——A mixture of the ylide (IXa) (0.3 g, 0.001 mol) and acetic anhydride (5 ml) was refluxed for 1 hr. After removal of acetic anhydride by vacuum distillation, the residual solid was purified by recrystallization from benzene to give yellow prisms, mp 186—188°. Yield, 0.1 g (30%). *Anal.* Calcd. for $C_{21}H_{16}N_2O_3$ (XIa): C, 73.24; H, 4.68; N, 8.14. Found: C, 72.96; H, 4.53; N, 8.28. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 3430, 1775, 1654. NMR ($CDCl_3$) δ: 2.42 (3H, s, $COCH_3$), 7.05—7.80 (10H, m, aromatic H), 8.06 (1H, s, 1-H), 8.34 (1H, d, J=9.7 Hz, 4-H), 8.46 (1H, br., NH).

2-Acetoxy-5-methylpyrrolo[1,2-*a*]quinoline-3-carboxanilide (XIb)——According to the procedure described above, reaction of the ylide (IXb) (0.1 g) with acetic anhydride (5 ml) gave the pyrroloquinoline derivative (XIb), mp 212—214° (dec.), pale green needles (benzene). Yield, 45 mg (40%). *Anal.* Calcd. for $C_{22}H_{18}N_2O_3$ (XIb): C, 73.73; H, 5.06; N, 7.82. Found: C, 73.44; H, 5.15; N, 7.86. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1782, 1660, 1628. NMR ($CDCl_3$) δ: 2.43 (3H, s, CH_3CO), 2.62 (3H, d, J=1 Hz, CH_3), 7.05—7.89 (9H, m, aromatic H), 8.08 (1H, s, 1-H), 8.23 (1H, d, J=1 Hz, 4-H), 8.40—8.55 (1H, br., NH).

Ethyl 2-Acetoxypyrrolo[1,2-*a*]quinoline-3-carboxylate (XIIa)——According to the procedure given for compound XIa, reaction of the ylide (Xa) (0.26 g, 0.001 mol) with acetic anhydride (5 ml) gave 83 mg (28%) of compound XIIa, mp 162—163°, yellow prisms (benzene). *Anal.* Calcd. for $C_{17}H_{15}NO_4$ (XIIa): C, 68.67; H, 5.08; N, 4.71. Found: C, 68.55; H, 4.83; N, 4.65. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1763, 1687. NMR ($CDCl_3$) δ: 1.42 (3H, t, J=6.3 Hz, CH_3), 2.40 (3H, s, CH_3CO), 4.38 (2H, q, J=6.3 Hz, CH_2), 7.29—7.97 (5H, m, aromatic H), 7.78 (1H, s, 1-H), 8.15 (1H, d, J=9 Hz, 4-H).

Ethyl 2-Acetoxy-5-methylpyrrolo[1,2-*a*]quinoline-3-carboxylate (XIIb)——According to the procedure described above, reaction of the ylide (Xb) (0.27 g) with acetic anhydride (10 ml) gave 0.19 g (61%) of compound XIIb, mp 174—175°, green needles (benzene). *Anal.* Calcd. for $C_{18}H_{17}NO_4$ (XIIb): C, 69.44; H, 5.50; N, 4.50. Found: C, 69.61; H, 5.72; N, 4.39. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1770, 1690. NMR ($CDCl_3$) δ: 1.38 (3H, t, J=6.7 Hz, CH_3), 2.34 (3H, s, CH_3CO), 2.52 (3H, d, J=1 Hz, CH_3), 4.33 (2H, q, J=6.7 Hz, CH_2), 7.22—7.90 (5H, m, aromatic H), 7.90 (1H, d, J=1 Hz, 4-H).

2-Acetoxy-3-acetylpyrrolo[2,1-*a*]isoquinoline (XIII)——A solution of isoquinoline (1.29 g, 0.01 mol) and II (2.56 g) in abs. ethanol (20 ml) was allowed to stand at room temperature for a day. The reaction mixture was condensed *in vacuo*, and the residue was dissolved in acetic anhydride (20 ml), to which solution was added triethylamine (1 g). The mixture was refluxed for 2 hr. After removal of acetic anhydride by vacuum distillation, the resulting residue was dissolved in chloroform. The chloroform solution was washed with water, dried over sodium sulfate, and condensed. The residue was purified by alumina chromatography. The benzene elution afforded 0.15 g (6%) of compound XIII, mp 142—143°, pale yellow leaves (benzene). *Anal.* Calcd. for $C_{16}H_{13}NO_3$ (XIII): C, 71.90; H, 4.90; N, 5.24. Found: C, 72.13; H, 5.19; N, 5.47. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1768, 1708. NMR ($CDCl_3$) δ: 2.40 (3H, s, CH_3), 2.55 (3H, s, CH_3), 7.00 (1H, d, J=7.7 Hz, 5-H), 7.03 (1H, s, 1-H), 7.30—8.20 (4H, m, aromatic H), 9.50 (1H, d, J=7.7 Hz, 4-H).

Ethyl 2-Acetoxy-3-acetylpyrrolo[2,1-*a*]isoquinoline-1-carboxylate (XIV)——According to the procedure described above, reaction of isoquinoline (1.29 g) and III (2.1 g) in ethanol (10 ml) followed by treatment with acetic anhydride (15 ml) and triethylamine (1 g) afforded a crystalline substance. Recrystallization with benzene gave colorless needles, mp 152—153°. Yield, 0.7 g (20%). *Anal.* Calcd. for $C_{19}H_{17}NO_5$ (XIV): C, 67.25; H, 5.05; N, 4.13. Found: C, 67.35; H, 5.03; N, 4.15. IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1774, 1699. NMR ($CDCl_3$) δ: 1.43 (3H, t, J=6.3 Hz, CH_3), 2.45 (3H, s, CH_3), 2.56 (3H, s, CH_3), 4.44 (2H, q, J=6.3 Hz, CH_2), 7.19 (1H, d, J=7.7 Hz, 5-H), 7.40—7.89 (3H, m, aromatic H), 8.90—9.25 (1H, m, 9-H). 9.70 (1H, d, J=7.7 Hz, 4-H).

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