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Preparation of New Nitrogen-Bridged Heterocycles. XIII.[1] Syntheses of Some Tricyclic and Tetracyclic Indolizine Derivatives with Antiallergic Activity

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Alkaline treatment of 2,3-annelated 1-ethoxycarbonylmethylpyridinium bromides was investigated as a method for the preparation of 1,8-annelated indolizine derivatives. The reaction of 1-ethoxycarbonylmethyl-2,3-cyclopentenopyridinium bromide (**1**) with ethanolic sodium ethoxide did not afford any significant products, but similar treatment of 1-ethoxycarbonylmethyl-2,3-cyclohexenopyridinium bromide (**8**) gave the expected 1,8-annelated 2(3*H*)-indolizinone, 8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-one (**9**), in 53% yield. The reactions of the salt **8** with a base in the presence of some vinylating and alkylating or acylating agents afforded the corresponding 1-alkoxy- or 1-acyloxy-2-vinylpyrroloquinoline derivatives (**26**—**35**), which were further transformed to tetracyclic indolizines fused with a furan or a pyran ring. Some of these tricyclic and tetracyclic indolizines showed antiallergic activity.

Keywords——indolizine; pyrrolo[3,2,1-*ij*]quinoline; cyclopent[*hi*]indolizine; furo[2′,3′:4,5]-pyrrolo[3,2,1-*ij*]quinoline; pyrano[2′,3′:4,5]pyrrolo[3,2,1-*ij*]quinoline; antiallergic activity

Previous studies in our laboratory have demonstrated that some polyfunctionalized indolizines can be synthesized smoothly *via* the allylidenedihydropyridine[2] and 2(3*H*)-indolizinone[3] routes, and can be transformed further to the corresponding 1,2- and 2,3-fused indolizine derivatives.[4] Since these methods are applicable to pyridinium salts having a methyl or a methylene group at the 2-position, the use of 2,3-annelated pyridinium salts in these reactions should lead to the formation of 1,8-annelated indolizine derivatives, which are not easily accessible by other methods. Recently, increased attention has been paid to such 1,8-annelated indolizines from the physicochemical and pharmaceutical viewpoints.[5] In this paper we wish to report the preparation of some 1,8-annelated indolizines, cyclopent-[*hi*]indolizine and pyrrolo[3,2,1-*ij*]quinoline, starting from 1-ethoxycarbonylmethyl-2,3-cyclopenteno- and 2,3-cyclohexenopyridinium (5,6,7,8-tetrahydroquinolinium) bromides, and further cyclization of the 1-acyloxy- and 1-(aroylmethoxy)-2-vinylpyrrolo[3,2,1-*ij*]quinolines thus obtained to tetracyclic indolizine derivatives.

Results and Discussion

Reactions of 2,3-Cyclopentenopyridinium Salt

The reaction of 1-ethoxycarbonylmethyl-2,3-cyclopentenopyridinium bromide (**1**) with ethanolic sodium ethoxide was examined according to our previous procedure,[3a] but the expected 1,2,7,8-tetrahydrocyclopent[*hi*]indolizine-1-one (**2**) could not be obtained. Similar treatment of the salt **1** in the presence of an alkylating or an acylating agent did not give any significant product. However, the reaction of the salt **1** with excess potassium carbonate in ethanol in the presence of a vinylating agent such as ethyl (ethoxymethylene)cyanoacetate (**3**,

Z form) or (ethoxymethylene)malononitrile (**4**) afforded the 7-vinylated compound **5** or **6** in 63 or 41% yield, respectively. The reason why the alkaline treatment of salt **1** did not give the indolizinone **2** is presumably the severe ring strain involved in the formation of the azapentalene skeleton in **2**. This interpretation was also supported by the following findings: reactions of **5** and **6** under basic conditions[6] or under heating [2c] did not afford the expected ethyl 7,8-dihydrocyclopent[*hi*]indolizine-2-carboxylate (**7**) at all, though the smooth transformation of 1-ethoxycarbonylmethyl-1,2-dihydropyridine having an acyclic 2-allylidene group to ethyl 3-indolizinecarboxylate under such reaction conditions is well known.[2c,6] However, the conversion of **5** to **7** could be accomplished in 41% yield only under more drastic conditions (refluxing in acetic anhydride). This method for preparing cyclopent[*hi*]indolizines such as **7** is very useful because of the inaccessibility of similar compounds in the reactions of 1-phenacyl-2,3-cyclopentenopyridinium salt with various bases.[5e]

The structures of compounds **5**, **6**, and **7** were assigned on the basis of comparisons of their physical and spectral data with those of 2-allylidene-1-ethoxycarbonylmethyl-1,2-dihydropyridine[2] and ethyl 3-indolizinecarboxylates[2c,6b] reported earlier by us. For example, the proton nuclear magnetic resonance (^{1}H-NMR) spectra of products **5** and **6** clearly showed a two proton singlet (δ near 4.7) due to the methylene group in the 1-ethoxycarbonylmethyl group and a four proton multiplet (δ 2.7—3.5) due to the 5- and 6-methylene groups. In particular, the presence of an intact ethoxycarbonylmethyl group and the absence of the 7-methylene group supported the proposed structures for **5** and **6**. On the other hand, the ^{1}H-NMR spectrum of **7** exhibited signals at δ 1.38 (3H, t, J=7.0 Hz) and 4.32 (2H, q, J=7.0 Hz) due to protons of only one ethoxycarbonyl group and at δ 3.0—3.7 (4H, m) due to the 7- and 8-methylene protons, together with four aromatic proton signals (δ 6.4—8.6), and its infrared (IR) spectrum showed an α,β-unsaturated carbonyl absorption (1671 cm^{-1}) but no cyano or acetoxyl carbonyl absorption bands. From these spectral data and the elemental analysis, we concluded that compound **7** is ethyl 7,8-dihydrocyclopent[*hi*]indolizine-2-carboxylate and not a possible alternative,[2b,c] 1-acetoxy-7,8-dihydrocyclopent[*hi*]indolizine.

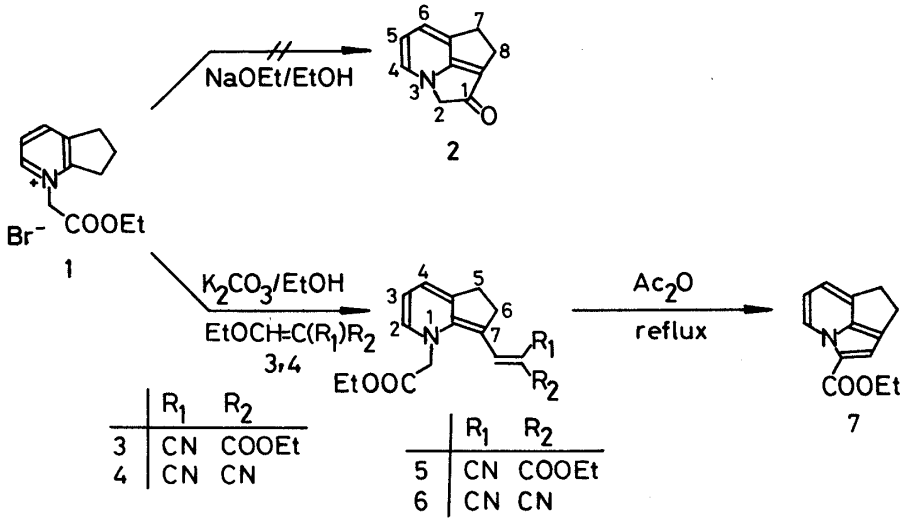
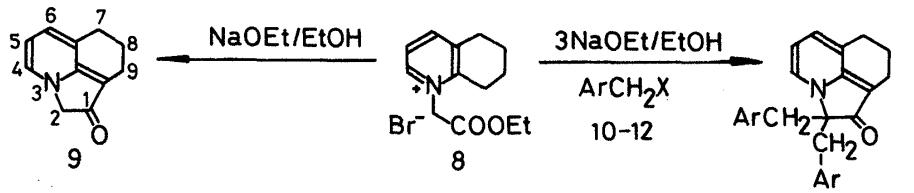


Chart 1

Reactions of 5,6,7,8-Tetrahydroquinolinium Salt

Although **2** could not be obtained from **1**, the reaction of 1-ethoxycarbonylmethyl-5,6,7,8-tetrahydroquinolinium bromide (**8**) with ethanolic sodium ethoxide smoothly gave the expected 1,8-annelated 2(3*H*)-indolizinone, 8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-one (**9**), in 53% yield as unstable black prisms, mp 65—68 °C (dec.). Furthermore, the reactions of **8** with a 3-fold molar amounts of base in the presence of excess benzyl halide such

as benzyl bromide **10**, *p*-chlorobenzyl chloride **11**, or *p*-nitrobenzyl chloride **12**, provided the corresponding 2,2-dibenzyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-one derivatives (**13**—**15**) in 51—57% yields (see Chart 2).

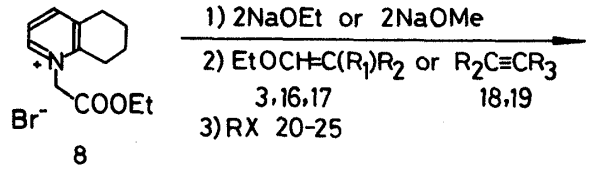


	Ar	X
10	Ph	
11	*p*-ClC$_6$H$_4$	Cl
12	*p*-NO$_2$C$_6$H$_4$	Cl

	Ar
13	Ph
14	*p*-ClC$_6$H$_4$
15	*p*-NO$_2$C$_6$H$_4$

Chart 2

On the other hand, the reactions of the pyrroloquinolone **9** generated *in situ* with some vinylating agents **3** and **16**—**19**, followed by alkylation or acylation with some phenacyl bromides **20**—**24** and acetic anhydride **25** afforded the corresponding 1-aroylmethoxy-(**26**—**30**) or 1-acetoxy-2-vinyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinoline derivatives (**31**—**35**) in moderate to good yields (Chart 3).



	R_1	R_2
16	COOEt	COOEt
17	Ac	COOEt

	R_2=R_3
18	COOMe
19	COOEt

	RX
20	BrCH$_2$COPh
21	BrCH$_2$COC$_6$H$_4$Cl-*p*
22	BrCH$_2$COC$_6$H$_4$Br-*p*
23	BrCH$_2$COC$_6$H$_4$Me-*p*
24	BrCH$_2$COC$_6$H$_4$Ph-*p*
25	Ac$_2$O

	R_1	R_2	R_3	R
26	CN	COOEt	H	CH$_2$COPh
27	CN	COOEt	H	CH$_2$COC$_6$H$_4$Cl-*p*
28	CN	COOEt	H	CH$_2$COC$_6$H$_4$Br-*p*
29	CN	COOEt	H	CH$_2$COC$_6$H$_4$Me-*p*
30	CN	COOEt	H	CH$_2$COC$_6$H$_4$Ph-*p*
31	COOEt	COOEt	H	Ac
32	Ac	COOEt	H	Ac
33	CN	COOEt	H	Ac
34	H	COOMe	COOMe	Ac
35	H	COOEt	COOEt	Ac

Chart 3

The elemental analyses of **9**, **13**—**15**, and **26**—**35** were in good accord with the proposed compositions, and the physical and spectral data were grossly similar to those of 2(3*H*)-indolizinones, 3,3-dialkyl-2(3*H*)-indolizinones, and 2-alkoxy- and 2-acyloxy-3-vinylindolizines.[3,4c] For example, the ^{1}H-NMR spectrum of pyrroloquinolone **9** showed signals at δ 4.19 (2H, s, 2-H), 6.10 (1H, t, J=7.0, 7.0 Hz, 5-H), 6.85 (1H, br d, J=7.0 Hz, 6-H), and 7.27 (1H, d, J=7.0 Hz, 4-H) together with the trimethylene signals at δ 1.5—2.0 (2H, m, 8-H) and 2.2—2.8 (4H, m, 7 and 9-H). In particular, the chemical shifts of 4-H, 5-H, and 6-H (δ 6.10—7.27) and of the 2-methylene protons (δ 4.19) are similar to those (δ 6.1—7.6 and 4.0—4.4) of known 2(3*H*)-indolizinones.[3a] Similarly, the chemical shifts and the signal patterns due to the protons at the 4—9 positions of 2,2-dibenzylpyrroloquinolones **13**—**15** are

also parallel to those of **9** (see Experimental). On the other hand, the structures of 2-aroylmethoxy-(**26**—**30**) and 2-acetoxy-1-vinylpyrrolo[3,2,1-*ij*]quinolines (**31**—**35**) were determined mainly on the basis of the presence of the vinyl moiety derived from the vinylating agent employed (from their ^{1}H-NMR spectra; see Table II) and their IR spectra (absence of characteristic carbonyl absorption near 1600 cm^{-1} of 2(3*H*)-indolizinones).[3)]

Cyclization to Tetracyclic Indolizine Derivatives

Since smooth transformations of 2-(aroylmethoxy)- and 2-acyloxy-3-vinylindolizine derivatives to furo[2,3-*b*]indolizines and pyrano[2,3-*b*]indolizines were recently established,[1,4c,d)] we examined the possibility of transforming the 1,8-annelated indolizines **26**—**35** obtained above to novel tetracyclic indolizines. The reactions of 1-aroylmethoxy-2-vinylpyrroloquinolines (**26**—**30**) with 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) in chloroform[1)] proceeded smoothly even at room temperature to afford the corresponding 8-aroyl-5,6-dihydro-4*H*-furo[2′,3′: 4,5]pyrrolo[3,2,1-*ij*]quinolines (**36**—**40**) in 43—64% yields. The presence of the furo[3,2-*b*]indole skeleton in these products **36**—**40** is very interesting because of the pharmaceutical activity of similar types of compounds.[7)] The reaction of 1-acetoxy-2-[2,2,-bis(ethoxycarbonyl)vinyl]pyrroloquinoline (**31**) with concentrated sulfuric acid at room temperature afforded ethyl 5,6-dihydro-4*H*,8*H*-pyrano[2′,3′: 4,5]pyrrolo[3,2,1-*ij*]quinolin-8-one-9-carboxylate (**41**) in 73% yield, but that of the 2-[2-acetyl-2-(ethoxycarbonyl)vinyl] derivative (**32**) gave only a very small amount of **42**. Similarly, treatment of 1-acetoxy-2-[2-cyano-2-(ethoxycarbonyl)vinyl]pyrroloquinoline (**33**) with sulfuric acid at 90—100 °C gave the unsubstituted pyranopyrroloquinolone (**43**) in 30% yield. On the other hand, the reactions of 1-acetoxy-2-[1,2-bis(ethoxycarbonyl)vinyl]pyrroloquinolines (**34** and **35**) with sulfuric acid at room temperature afforded the expected 9-alkoxycarbonylmethylene-5,6-dihydro-4*H*-furo[2′,3′: 4,5]pyrrolo[3,2,1-*ij*]quinolin-8(9*H*)-ones (**44** and **45**) in low yields. These conversions are summarized in Chart 4.

The structures of these tetracyclic indolizines **36**—**45** were detemined by physical and spectral means, and by IR and ^{1}H-NMR spectral comparisons with tricyclic compounds such as furo[2,3-*b*]indolizines[1,4c)] and pyrano[2,3-*b*]indolizines[4d)] prepared earlier by us. In particular, all elemental analyses of **36**—**45** were in good accord with the proposed compositions, and in the ^{1}H-NMR spectra, the chemical shifts (see Table IV and Experimental) of the skeletal protons except those due to the furan or pyran moiety were very similar to each other and also to those of tricyclic indolizines.[4c,d)]

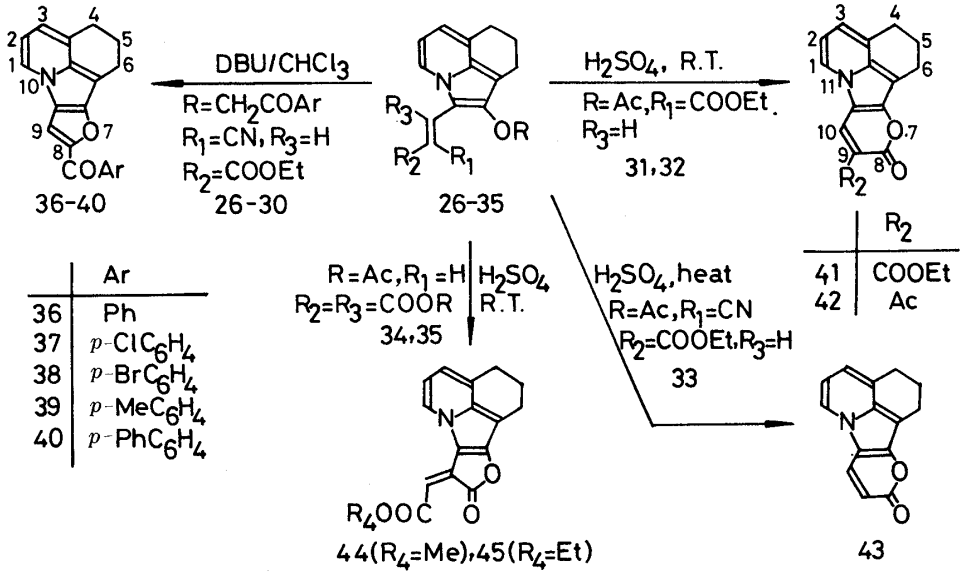


Chart 4

Pharmaceutical Activity

As seen in furo[3,2-*b*]indole derivatives,[7] 8-aroyl-5,6-dihydro-4*H*-furo[2′,3′:4,5]pyrrolo[3,2,1-*ij*]quinolines (**36**—**40**) showed considerable antiallergic activity. Interestingly, the same activity was also observed in their precursors, 1-acylmethoxy-2-vinyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolines (**26**—**30**).

Experimental[8]

1-Ethoxycarbonylmethyl-2,3-cyclopentenopyridinium Bromide (1) and 1-Ethoxycarbonylmethyl-5,6,7,8-tetrahydroquinolinium Bromide (8)——The pyridinium salt **1** or **8** was prepared by the reaction of 2,3-cyclopentenopyridine or 5,6,7,8-tetrahydroquinoline with ethyl bromoacetate according to the procedure described in our previous paper.[9] Some physical data for these salts are as follows. **1**, 89%, colorless prisms (from acetone), mp 155—156 °C, IR (KBr): 1739 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.33 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 2.1—2.8 (2H, m, 6-H), 3.0—3.7 (4H, m, 5 and 7-H), 4.31 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.17 (2H, s, NCH_2), 7.91 (1H, q, J=7.0, 6.0 Hz, 3-H), 6.77 (1H, br d, J=7.0 Hz, 4-H), 9.55 (1H, dd, J=6.0, 1.0 Hz, 2-H). *Anal.* Calcd for $C_{12}H_{16}BrNO_2$: C, 50.37; H, 5.64; N, 4.89. Found: C, 50.23; H, 5.60; N, 4.92. **8**, colorless needles (from ethanol–ether), mp 152—153 °C, IR (KBr): 1738 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.33 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 1.6—2.3 (4H, m, 6 and 7-H), 2.8—3.3 (4H, m, 5 and 8-H), 4.31 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.20 (2H, s, NCH_2), 7.89 (1H, q, J=7.0, 6.0 Hz, 3-H), 8.30 (1H, br d, J=7.0 Hz, 4-H), 9.72 (1H, dd, J=6.0, 1.5 Hz, 2-H). *Anal.* Calcd for $C_{13}H_{18}BrNO_2$: C, 52.01; H, 6.04; N, 4.67. Found: C, 51.88; H, 6.09; N, 4.51.

1-Ethoxycarbonylmethyl-7-vinyl-5,6-dihydro-1*H*-cyclopenta[*b*]pyridines (5 and 6)——General Method: An ethanolic solution (50 ml) of **1** (1.43 g, 5 mmol) was allowed to react with an ethoxymethylene compound **3** or **4** (5 mmol) in the presence of anhydrous potassium carbonate (5 g) at room temperature for 1 d under stirring. The resulting mixture was filtered to remove inorganic substances and the filtrate was concentrated under reduced pressure. The residue was separated by column chromatography (alumina) using ether and then chloroform as eluents, and evaporation of the chloroform layer gave the product. Recrystallization from ethanol afforded the pure compound. Some data for products **5** and **6** are as follows. **5**, 63%, red prisms, mp 158—159 °C, IR (KBr): 2185 (CN), 1752 (CO), 1642 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.30 and 1.38 (each 3H, J=7.0 Hz, 2 × $OCH_2\underline{CH_3}$), 2.7—3.5 (4H, m, 5 and 6-H), 4.21 and 4.38 (each 2H, q, J=7.0 Hz, 2 × $O\underline{CH_2}CH_3$), 4.78 (2H, s, NCH_2), 6.40 (1H, t, J=7.0, 7.0 Hz, 3-H), 7.00 (2H, br d, J=7.0 Hz, 2 and 4-H), 7.57 (1H, s, vinyl-H). *Anal.* Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 66.00; H, 6.13; N, 8.38. **6**, 41%, red prisms, mp 191—193 °C, IR (KBr): 2195 (CN), 2170 (CN), 1745 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.40 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 2.7—3.5 (4H, m, 5 and 6-H), 4.38 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 4.73 (2H, s, NCH_2), 6.53 (1H, t, J=7.0, 7.0 Hz, 3-H), 6.79 (1H, s, vinyl-H), 7.08 (1H, br d, J=7.0 Hz, 2 or 4-H), 7.13 (1H, br d, J=7.0 Hz, 4 or 2-H). *Anal.* Calcd for $C_{16}H_{15}N_3O_2$: C, 68.31; H, 5.37; N, 14.94. Found: C, 68.25; H, 5.36; N, 15.01.

Ethyl 7,8-Dihydrocyclopent[*hi*]indolizine-2-carboxylate (7)——A mixture of **5** (328 mg, 1 mmol) and acetic anhydride (3 ml) was heated under reflux until the disappearance of **5** was confirmed by thin layer chromatographic monitoring (12 h). The resulting solution was concentrated under reduced pressure and the residual oil was separated by column chromatography on alumina using ether as an eluent. The combined ether layer was concentrated and recrystallization of the residue from ethanol gave **7** (88 mg, 41%), colorless needles, mp 73 °C, IR (KBr): 1671 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.38 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 3.0—3.7 (4H, m, 7 and 8-H), 4.37 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.4—6.9 (2H, m, 5 and 6-H), 7.11 (1H, s, 1-H), 8.57 (1H, dd, J=6.0, 1.5 Hz, 4-H). *Anal.* Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.55; H, 6.15; N, 6.42.

On the other hand, thermolysis at the refluxing temperature in xylene or the treatment of **5** with a base such as potassium carbonate did not yield the corresponding **7** at all.

8,9-Dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-one (9)——An ethanolic solution (50 ml) of **8** (1.500 g, 5 mmol) was treated with ethanolic sodium ethoxide (5 mmol in 5 ml of ethanol) at 50—60 °C in a water bath for 5 min. The resulting dark red solution was concentrated under reduced pressure at below 50 °C. Since this product was very unstable, the residue was quickly separated twice by column chromatography on alumina using ether and chloroform as eluents, and the combined chloroform layer was concentrated under reduced pressure at below 30 °C. Recrystallization of the crude product from tetrahydrofuran (THF) afforded pure **9** (0.506 g, 53% as monohydrate) as very unstable black prisms, mp 65—68 °C (dec.), IR (KBr): 1595 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.5—2.0 (2H, m, 8-H), 2.2—2.8 (4H, m, 7 and 9-H), 4.19 (2H, s, 2-H), 6.10 (1H, t, J=7.0, 7.0 Hz, 5-H), 6.85 (1H, br d, J=7.0 Hz, 6-H), 7.27 (1H, d, J=7.0 Hz, 4-H). *Anal.* Calcd for $C_{11}H_{11}NO \cdot H_2O$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.73; H, 6.85; 7.68.

2,2-Dibenzylpyrrolo[3,2,1-*ij*]quinolin-1(2*H*)-ones (13—15)——General Method: An ethanolic solution (50 ml) of the quinolinium bromide **8** (1.500 g, 5 mmol) and benzyl halide (30 mmol) was treated with ethanolic sodium ethoxide (15 mmol in 15 ml of ethanol) at 60—80 °C in a water bath for 2 h. The reaction mixture was concentrated under

TABLE I. Physical Data for 2-Vinylpyrrolo[3,2,1-*ij*]quinolines

Compd. No.	Reactants			Yield (%)	mp (°C)	IR ν_{max}^{KBr} cm^{-1}	Formula	Analysis (%) Calcd (Found)		
								C	H	N
26	**8**	**3**	**20**	79	155	1691 2208	$C_{25}H_{22}N_2O_4$	72.45	5.35	6.76
								(72.18	5.47	6.85)
27	**8**	**3**	**21**	30	206—208	1701 1689 2200	$C_{25}H_{21}ClN_2O_4$	66.89	4.72	6.24
								(66.96	4.78	6.11)
28	**8**	**3**	**22**	30	210—211	1699 1687 2199	$C_{25}H_{21}BrN_2O_4$	60.86	4.29	5.68
								(61.16	4.34	5.38)
29	**8**	**3**	**23**	31	188—189	1689 2205	$C_{26}H_{24}N_2O_4$	72.88	5.65	6.54
								(73.02	5.69	6.36)
30	**8**	**3**	**24**	48	144—146	1690 2203	$C_{31}H_{26}N_2O_4$	75.90	5.34	5.71
								(75.69	5.30	5.81)
31	**8**	**16**	**25**	17	93—95	1774 1708	$C_{21}H_{23}NO_6$	65.44	6.02	3.63
								(65.48	5.91	3.70)
32	**8**	**17**	**25**	65	150—152	1768 1694	$C_{20}H_{21}NO_5$	67.59	5.96	3.94
								(67.54	5.95	4.00)
33	**8**	**3**	**25**	92	102	1774 1699 2215	$C_{19}H_{18}N_2O_4$	67.45	5.36	8.28
								(67.20	5.49	8.32)
34	**8**	**18**	**25**	46	155—158	1736 1697	$C_{19}H_{19}NO_6$	63.86	5.36	3.92
								(63.83	5.35	3.96)
35	**8**	**19**	**25**	61	147—149	1728 1696	$C_{21}H_{23}NO_6$	65.44	6.02	3.63
								(65.48	5.91	3.70)

TABLE II. ^{1}H-NMR Spectral Data for 2-Vinylpyrrolo[3,2,1-*ij*]quinolines in $CDCl_3$

Compd.[a] No.	4-H	5 and 6-H	7 and 9-H	8-H	R			Vinyl-H	Others	
26	[b]	6.7—7.0 m	2.6—3.0 m	1.7—2.2 m	5.60 s	7.4—8.3 m		8.34 s	1.38 t	4.33 q
27	[b]	6.6—7.0 m	2.6—3.0 m	1.7—2.2 m	5.53 s	7.3—8.3 m		8.31 s	1.38 t	4.34 q
28	8.22 q	6.6—7.0 m	2.6—3.0 m	1.6—2.2 m	5.54 s	7.5—8.1 m		8.33 s	1.39 t	4.34 q
29	8.23 q	6.6—7.0 m	2.6—3.0 m	1.6—2.1 m	5.58 s	7.1—8.1 m	2.43 s	8.34 s	1.37 t	4.34 q
30	[b]	6.6—7.0 m	2.6—3.0 m	1.6—2.2 m	5.63 s	7.3—8.4 m		8.34 s	1.37 t	4.33 q
31	7.85 q	6.6—6.8 m	2.5—3.0 m	1.7—2.2 m	2.32 s			7.97 s	1.24 t	1.32[c] t
32[d]	7.82 q	6.6—6.9 m	2.5—3.0 m	1.6—2.2 m	2.28 s			7.98 s	1.21 t	4.30[e] q
(32)[f]	[g]	[g]	[g]	[g]	2.28 s			7.94 s	1.34 t	4.28[h] q
33	8.18 q	6.7—7.0 m	2.5—3.1 m	1.7—2.2 m	2.50 s			8.29 s	1.38 t	4.35 q
34	8.11 q	6.5—6.9 m	2.5—3.1 m	1.7—2.2 m	2.34 s			6.18 s	3.80 s	3.98 s
35	8.10 q	6.4—6.8 m	2.5—3.1 m	1.7—2.2 m	2.32 s			6.14 s	1.31 t	1.38[i] t

a) The coupling constants were as follows: $J_{4,5}=5.0$, $J_{4,6}=3.0$, and $J_{Et}=7.0$ Hz. *b*) Overlapped with the phenyl proton signals. *c*) Plus 4.29 (q) and 4.32 (q). *d*) Major isomer in *cis–trans* mixture for the 2-vinyl group in **32**. *e*) Plus 2.38 (s). *f*) Minor isomer in **32**. *g*) Overlapped with the signals due to the major isomer. *h*) Plus 2.46 (s). *i*) Plus 4.33 (q) and 4.41 (q).

TABLE III. Physical Data for 8-Aroylfuropyrroloquinolines

Compd. No.	React.	Yield (%)	mp (°C)	IR ν_{max}^{KBr} cm^{-1}	Appearance	Formula	Analysis (%) Calcd (Found)		
							C	H	N
36	**26**	43	150—152	1609	Yellow prisms	$C_{20}H_{15}NO_2$	79.72	5.02	4.65
							(79.53	5.15	4.72)
37	**27**	64	155—158	1607	Red prisms	$C_{20}H_{14}ClNO_2$	71.54	4.20	4.17
							(71.46	4.15	4.17)
38	**28**	58	179—182	1605	Red prisms	$C_{20}H_{14}BrNO_2$	63.13	3.71	3.68
							(63.00	3.60	3.61)
39	**29**	46	149—151	1597	Orange prisms	$C_{21}H_{17}NO_2$	79.98	5.43	4.44
							(80.13	5.64	4.18)
40	**30**	52	174—175	1613	Yellow prisms	$C_{26}H_{19}NO_2$	82.74	5.07	3.71
							(82.93	5.10	3.43)

TABLE IV. ^{1}H-NMR Spectral Data for 8-Aroylfuropyrroloquinolines in $CDCl_3$

Compd. No.	1-H	2 and 3-H	4 and 6-H	5-H	Ar		9-H
36	*a)*	6.3—6.7 m	2.7—3.2 m	1.8—2.3 m	7.3—8.1 m		7.56 s
37	*a)*	6.4—6.8 m	2.7—3.2 m	1.8—2.3 m	7.3—8.1 m		7.60 s
38	*a)*	6.3—6.7 m	2.7—3.2 m	1.7—2.3 m	7.4—8.0 m		7.55 s
39	*a)*	6.3—6.7 m	2.7—3.2 m	1.7—2.3 m	7.1—8.1 m	2.47 s	7.58 s
40	*a)*	6.3—6.7 m	2.7—3.2 m	1.8—2.3 m	7.3—8.2 m		*a)*

a) Overlapped with the phenyl proton signals.

reduced pressure and the residual oil was purified by column chromatography on alumina using chloroform as an eluent. The combined chloroform layer was concentrated, and recrystallization of the crude product from chloroform–ether gave the corresponding 2,2-dibenzylpyrroloquinolone. Some data for **13**—**15** are as follows. **13**, 72%, orange prisms, mp 209—212 °C (dec.), IR (KBr): 1600 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.0—1.6 (2H, m, 8-H), 2.0—2.4 (4H, m, 7 and 9-H), 3.04 and 3.45 (each 2H, d, J=14.0 Hz, 2×benzyl-H), 5.99 (1H, t, J=7.0, 7.0 Hz, 5-H), 6.59 (1H, br d, J=7.0 Hz, 6-H), 6.8—7.5 (11H, m, 4-H and 2×phenyl-H). *Anal.* Calcd for $C_{25}H_{23}NO$: C, 84.95; H, 6.56; N, 3.96. Found: C, 84.78; H, 6.69; N, 4.00. **14**, 75%, orange needles, mp 164—167 °C, IR (KBr): 1602 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.0—1.6 (2H, m, 8-H), 2.0—2.6 (4H, m, 7 and 9-H), 2.97 and 3.41 (each 2H, d, J=14.0 Hz, 2×benzyl-H), 6.08 (1H, t, J=7.0, 7.0 Hz, 5-H), 6.63 (1H, br d, J=7.0 Hz, 6-H), 6.7—7.4 (9H, m, 4-H and 2×phenyl-H). *Anal.* Calcd for $C_{25}H_{21}Cl_2NO$: C, 71.10; H, 5.01; N, 3.32. Found: C, 70.83; H, 5.25; N, 3.30. **15**, 51%, red prisms, mp 185—188 °C, IR (KBr): 1610 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.0—1.5 (2H, m, 8-H), 1.9—2.5 (4H, m, 7 and 9-H), 2.85 and 3.70 (each 2H, d, J=14.0 Hz, 2×benzyl-H), 6.23 (1H, t, J=7.0, 7.0 Hz, 5-H), 6.68 (1H, br d, J=7.0 Hz, 6-H), 7.0—8.3 (9H, m, 4-H and 2×phenyl-H). *Anal.* Calcd for $C_{25}H_{21}N_3O_5$: C, 67.71; H, 4.77; N, 9.48. Found: C, 67.70; H, 4.85; N, 9.40.

1-Alkoxy- (26—30) and 1-Acetoxy-2-vinyl-8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolines (31—35)——These 2-vinylpyrroloquinoline derivatives were synthesized from the reactions of the quinolinium bromide **8**, vinylating agents, **3** and **16**—**19**, and phenacyl bromides **20**—**24** or acetic anhydride **25** according to the procedure reported by us.[3b] Recrystallizations from ethanol gave the pure compounds as yellow needles (**26**—**31** and **33**—**35**) or red needles (**32**). Some data are summarized in Tables I and II.

8-Aroyl-5,6-dihydro-4*H*-furo[2′,3′:4,5]pyrrolo[3,2,1-*ij*]quinolines (36—40)——General Method: A chloroform solution (50 ml) of 1-aroylmethoxy-2-vinylpyrroloquinoline (200 mg) and DBU (0.5 g) was stirred at room

temperature for 1 d. The resulting red solution was concentrated under reduced pressure and the residue was separated by column chromatography on alumina using hexane and ether as eluents. The ether layer was concentrated and recrystallization of the crude product from ethanol afforded a pure sample. Some data for compounds **36**—**40** are listed in Tables III and IV.

Acidic Treatment of 1-Acetoxy-2-vinylpyrrolo[3,2,1-*ij*]quinolines (31—35)——5,6-Dihydro-4*H*,8*H*-pyrano-[2′,3′:4,5]pyrrolo[3,2,1-*ij*]quinolin-8-ones (**41**—**43**) and 9-methylene-5,6-dihydro-4*H*-furo[2′,3′:4,5]pyrrolo[3,2,1-*ij*]-quinolin-8(9*H*)-ones (**44** and **45**) were synthesized according to the procedures described in our previous paper[4d] and the crude products were purified by recrystallization from ethanol (**41** , **43**, and **45**) or methanol (**44**). Some physical and spectral data are as follows. **41**, 73%, brown prisms, mp 235—237 °C, IR (KBr): 1731 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.42 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 1.8—2.3 (2H, m, 5-H), 2.7—3.1 (4H, m, 4 and 6-H), 4.40 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.6—7.1 (2H, m, 2 and 3-H), 8.11 (1H, dd, J=6.0, 2.0 Hz, 1-H). *Anal.* Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.62; H, 5.09; N, 4.77. **42**, trace, IR (KBr): 1710 cm^{-1} (CO).[10] **43**, 30%, brown prisms, mp 194—196 °C, IR (KBr): 1690 cm^{-1} (CO), ^{1}H-NMR ($CDCl_3$) δ: 1.9—2.4 (2H, m, 5-H), 2.8—3.3 (4H, m, 4 and 6-H), 5.94 (1H, d, J=10.0 Hz, 9-H), 6.5—6.9 (2H, m, 2 and 3-H), 7.94 (1H, d, J=10.0 Hz, 10-H), and 7.95 (1H, dd, J=6.0, 2.0 Hz, 6-H). *Anal.* Calcd for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.63; H, 5.18; N, 5.98. **44**, 34%, red needles, mp 201—203 °C, IR (KBr): 1722 and 1703 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.6—2.3 (2H, m, 5-H), 2.7—3.1 (4H, m, 4 and 6-H), 4.07 (3H, s, OMe), 6.33 (1H, s, vinyl-H), 6.5—6.9 (2H, m, 2 and 3-H), 8.73 (1H, dd, J=6.0, 2.0 Hz, 1-H). *Anal.* Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 68.03; H, 4.88; N, 4.64. **45**, 27%, red needles, mp 193—195 °C, IR (KBr): 1723 and 1710 cm^{-1} (CO), ^{1}H-NMR (in $CDCl_3$) δ: 1.44 (3H, t, J=7.0 Hz, $OCH_2\underline{CH_3}$), 1.7—2.3 (2H, m, 5-H), 2.7—3.1 (4H, m, 4 and 6-H), 4.48 (2H, q, J=7.0 Hz, $O\underline{CH_2}CH_3$), 6.30 (1H, s, vinyl-H), 6.4—6.8 (2H, m, 2 and 3-H), 8.70 (1H, dd, J=6.0 and 2.0 Hz, 1-H). *Anal.* Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.55; H, 4.96; N, 4.78.

References and Notes

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10) A pure sample of **42** for analysis could not be obtained because of the low yield.