

Preparation of New Nitrogen-Bridged Heterocycles. 37.¹⁾ Synthesis and Rearrangement of Full-Conjugated Oxepino[2,3-*b*]indolizine Derivatives

Akikazu KAKEHI,* Suketaka ITO, and Hideyuki MURANAKA

Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380

(Received April 12, 1994)

The title compounds were first synthesized in considerably good yields by acid-catalyzed dehydration of the corresponding ethyl 2-arylcarbonyl-3-hydroxy-3-phenyl-2,3-dihydrooxepino[2,3-*b*]indolizin-4-carboxylate derivatives with methanesulfonic acid in boiling chloroform. Although these full-conjugated oxepino[2,3-*b*]indolizines with a nonaromatic 16 π electron system were stable at room temperature, upon heating them in boiling ethanol, they were smoothly rearranged to ethyl 2-arylcarbonyl-1-oxo-2-phenyl-1,2-dihydropyrido[1,2-*a*]indole-3-carboxylates in good yields. The structures of these oxepino[2,3-*b*]indolizines and the rearranged pyrido[1,2-*a*]indol-1(2*H*)-ones were distinctly determined by physical and spectral means, including X-ray analyses.

In our preceding paper²⁾ we reported that the acid-catalyzed dehydration of 4-acetyl-2-arylcarbonyl-3-methyl-2,3-dihydrooxepino[2,3-*b*]indolizin-3-ol derivatives, such as **A** (see Fig. 1), did not form any full-conjugated oxepino[2,3-*b*]indolizines **C**, but, instead of them, provided the corresponding 3-methylene compounds **B**. The latter compounds **B** were formed via dehydration between the 3-hydroxyl group and one of the less acidic 3-methyl protons, rather than the more acidic 2-methine proton in **A**. This finding strongly suggested that the *exo*-methylene type of compound **B** has a higher stability than does the full-conjugated type of compound **C**, and, if any reaction routes which lead to the other types of compounds are possible, the isolation of full-conjugated oxepino[2,3-*b*]indolizines, such as **C** with nonaromatic 16 π electron system, might be very difficult. Based on these facts and our interest in the reactivity of new heterocycles having a nonaromatic 4 π electron system,³⁾ we focussed our attention on the preparation of 2,3-dihydrooxepino[2,3-*b*]indolizin-3-ols having a 3-substituent in which there is no easily abstracted proton, and thus selected a phenyl group as the 3-substituent for this purpose. In this paper we wish to report first on the syntheses of full-conjugated oxepino[2,3-*b*]indolizines from the acid-catalyzed dehydrations of the ethyl 2-arylcarbonyl-3-hydroxy-3-phenyl-2,3-dihydrooxepino[2,3-*b*]indolizine-4-carboxylates and their smooth rearrangement in boiling ethanol to ethyl 2-arylcarbonyl-1-oxo-2-phenyl-1,2-dihydropyrido[1,2-*a*]indole-3-carboxylates.

Results and Discussion

Preparations of 2,3-Dihydrooxepino[2,3-*b*]indolizin-3-ols. Ethyl 2-arylcarbonyl-3-hydroxy-3-phenyl-2,3-dihydrooxepino[2,3-*b*]indolizine-4-carboxylates (**4a—f**) were obtained in low yields (2—5%) from a treatment of 1-(ethoxycarbonylmethyl)-2-ethylpyridinium bromide **1a** and 1-(ethoxycarbonylmethyl)-2-propylpyridinium bromide **1b** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), followed by reactions of the resulting 2(3*H*)-indolizinones with ethyl (ethoxy-

methylene)benzoylacetate **2**, and then phenacyl bromides **3a—c** in the presence of a base, together with the formation of 3-benzoyl-2*H*-pyrano[2,3-*b*]indolizin-2-ones **5a,b** and 2-(arylcarbonyl)furo[2,3-*b*]indolizines **6a—f** (Scheme 1). Products **4a—f** and **6a—f** must be formed from the common intermediates, 2-arylcarbonylmethoxy-3-[2-benzoyl-2-(ethoxycarbonyl)vinyl]indolizines, by similar means described earlier by us.^{2,4)} On the other hand, 2*H*-pyrano[2,3-*b*]indolizin-2-ones **5a,b** seem to be provided via an intramolecular nucleophilic attack of the 2-hydroxyl oxygen on the ester carbonyl carbon in 3-[2-benzoyl-2-(ethoxycarbonyl)vinyl]-2-indolizinols with the elimination of an ethanol. A similar reaction route has already been reported concerning the formation of pyrano[3,2-*a*] and pyrano[2,3-*b*]indolizin-2-ones from the acid-catalyzed deacylations of 2-acyloxy-1- and 3-[2-(ethoxycarbonyl)vinyl]indolizine derivatives.⁵⁾

The structures of products **4a—f** were determined by inspections of their physical and spectral data, and by comparisons of their IR and ¹H NMR (for those for **4a—f**, see Table 1) spectral data with those for known 2,3-dihydrooxepino[2,3-*b*]indolizines.²⁾ In particular, the chemical shifts and signal patterns for the skeletal protons in the ¹H NMR spectra of **4a—f** were very similar to those for 4-acetyl-2-arylcarbonyl-3-methyl-2,3-dihydrooxepino[2,3-*b*]indolizin-3-ols.²⁾ Furthermore, the *cis* configuration at the 2- and 3-positions in **4a—f** could be determined based on the crystallographic data for compound **4e**.⁶⁾ The structures of compounds **5a,b** were identified by the analytical data, the very strong fluorescence,⁵⁾ and by the presence of benzoyl proton signals and the absence of ethoxycarbonyl proton signals in the ¹H NMR spectra. On the other hand, compounds **6a—f** were concluded to be 2-(arylcarbonyl)furo[2,3-*b*]indolizines by a comparison with authentic samples.^{2,4,7)}

Acid-Catalyzed Dehydrations of 2,3-Dihydrooxepino[2,3-*b*]indolizin-3-ols. When ethyl 2-benzoyl-3-hydroxy-11-methyl-3-phenyl-2,3-dihydrooxepino[2,3-*b*]indolizine-4-carboxylate **4a** was heated in chloro-

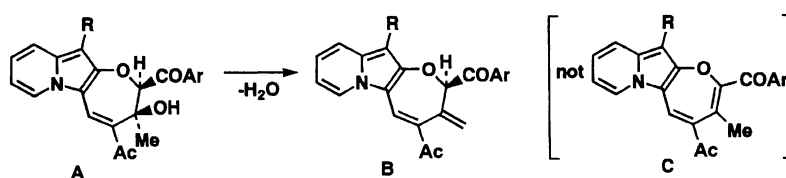
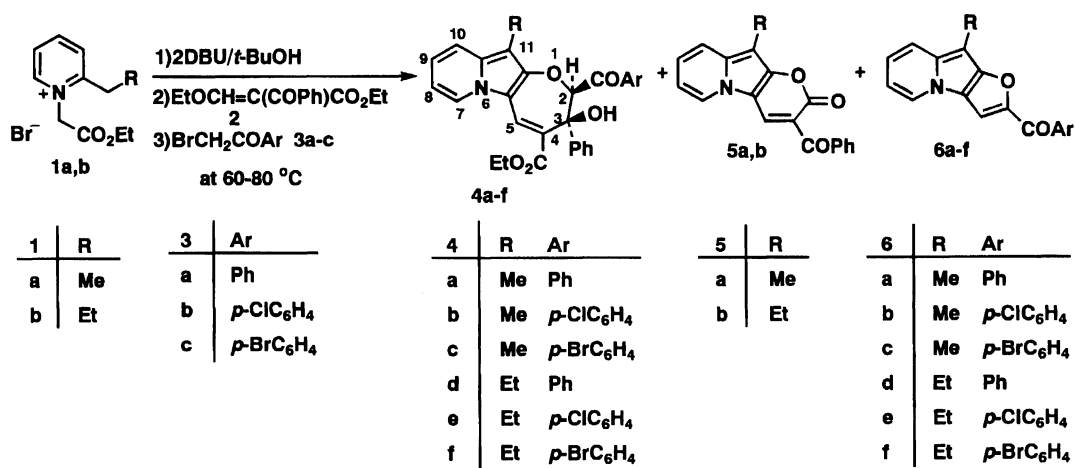


Fig. 1.

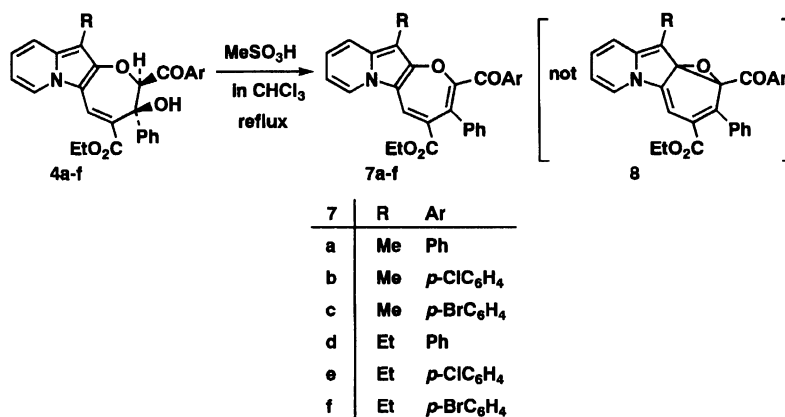


Scheme 1.

Table 1. ¹H NMR Spectral Data for Oxepino[2,3-*b*]indolizines

Compd No. ^{a)}	δ (CDCl ₃)											
	C-2	C-5	C-7	C-8	C-9	C-10	11-R	CO ₂ Et		3-OH	Ar and 3-Ph	
4a	5.55 s	8.36 s	8.28 br d	6.68 dt	7.09 br t	b)	1.73 s		1.29 t	4.21 q	6.33 s	7.1—8.2 m
4b	5.45 s	8.32 s	8.25 br d	6.65 dt	7.06 br t	b)	1.75 s		1.26 t	4.19 q	6.30 s	7.1—8.1 m
4c	5.48 s	8.22 s	8.15 br d	6.63 dt	7.04 br t	b)	1.80 s		1.31 t	4.24 q	6.24 s	7.1—8.0 m
4d	5.58 s	8.34 s	8.26 br d	6.71 dt	7.02 br t	b)	0.72 t	2.33 q	1.30 t	4.25 q	6.33 s	7.1—8.2 m
4e	5.46 s	8.26 s	8.19 br d	6.69 dt	7.03 br t	b)	0.77 t	2.34 q	1.33 t	4.23 q	6.32 s	7.1—8.1 m
4f	5.57 s	8.34 s	8.30 br d	6.68 dt	7.03 br t	b)	0.77 t	2.38 q	1.31 t	4.25 q	6.38 s	7.1—8.0 m
7a	—	8.34 s	8.22 br d	6.81 dt	b)	b)	1.74 s		0.77 t	3.87 q	—	6.9—8.1 m
7b	—	8.29 s	8.20 br d	6.76 dt	b)	b)	1.80 s		0.79 t	3.91 q	—	6.9—8.1 m
7c	—	8.30 s	8.22 br d	6.77 dt	b)	b)	1.77 s		0.77 t	3.88 q	—	6.9—8.0 m
7d	—	8.32 s	8.21 br d	6.81 dt	b)	b)	0.87 t	2.30 q	0.77 t	3.91 q	—	6.9—8.1 m
7e	—	8.28 s	8.15 br d	6.73 dt	b)	b)	0.86 t	2.27 q	0.74 t	3.83 q	—	6.9—8.1 m
7f	—	8.30 s	8.20 br d	6.70 dt	b)	b)	0.91 t	2.34 q	0.79 t	3.91 q	—	6.9—8.0 m

a) The coupling constants are as follows: $J_{7,8}=J_{8,9}=7.0$, $J_{9,10}=9.0$, and $J_{Et}=7.0$ Hz. b) Overlapped with the proton signals of the 2-arylcarbonyl and the 4-phenyl groups.



Scheme 2.

form including a small amount of methanesulfonic acid for 15 min, and the resulting reaction mixture was separated by column chromatography, the corresponding crystalline product **7a** was obtained in 61% yield as red prisms. Similarly, a treatment of 2,3-dihydrooxepino[2,3-*b*]indolizin-3-ols **4b–f** with the same reagent provided compounds **7b–f** in 68, 69, 92, 99 and 87% yields, respectively (Scheme 2).

The structures of compounds **7a–f** could be determined with ease by spectral and analytical inspections. The elemental analyses for all products **7a–f** were in good accord with our proposed compositions, and the ¹H NMR spectra (Table 1) exhibited no signal for the 3-hydroxyl proton or the 2-methine proton. The absence of a 3-hydroxyl group could also be confirmed based on the IR spectra of **7a–f**. In comparison with the dihydro compounds **4a–f**, a considerably higher magnetic shift ($\delta=0.3–0.6$) of the proton signals for the 4-ethoxycarbonyl group was observed in the ¹H NMR spectra of **7a–f**. Since the distance between the 3-phenyl group and the 4-ethoxycarbonyl group in these full-conjugated oxepino[2,3-*b*]indolizines **7a–f** becomes nearer than that in 2,3-dihydrooxepino[2,3-*b*]indolizin-3-ols **4a–f**, this shielding effect must be caused by the aromatic ring current of the 3-phenyl group. On the other hand, the chemical shifts for the protons and alkyl proton signals on the indolizine ring in compounds **7a–f** were very similar to those in the starting material **4a–f** and other oxepino[2,3-*b*]indolizine derivatives.²⁾ Furthermore, the chemical shifts of the skeletal protons on the indolizine ring in compounds **7a–f** are also parallel to those in aromatic indolizine derivatives,^{4,7,8)} except for that of the C₁₁-alkyl (*R*) group.⁹⁾ These spectral data completely negated the presence of possible valence isomers, such as **8**,³⁾ bearing an oxanorcaradiene structure for compounds **7a–f**.

The single-crystal X-ray crystallography for compound **7a** unambiguously exhibited that its structure is a full-conjugated oxepino[2,3-*b*]indolizine. The crystal and structure analysis data, as well as selected bond lengths and bond angles for ethyl 2-benzoyl-11-methyl-3-phenyloxepino[2,3-*b*]indolizine-4-carboxylate

7a, are summarized in Tables 2 and 3.¹²⁾ An ORTEP drawing^{13,14)} for **7a** is shown in Fig. 3. As can be seen from this drawing and the least-squares plane (mean deviation 0.0089 Å and $\chi^2=12.0$) of the indolizine ring, this molecule **7a** comprises on almost plane indolizine ring and a nonplanar and tub-shaped oxepine ring (mean deviation 0.2756 Å and $\chi^2=7334.0$), and also has a stacking structure between the respective three substituents at the 2-, 3-, and 4-positions. The bond alteration in the oxepine ring is much more remarkable than that in indolizine ring (see Table 3 and Fig. 2). The crystal data for the indolizine ring in **7a** are grossly similar to those for the indolizines reported earlier by us and other investigators.¹⁵⁾ Eventually, these crystal data also showed that those full-conjugated indolizines **7a–f** comprise an aromatic indolizine ring and a nonaromatic and nonplanar oxepine ring.

Rearrangements of Full-Conjugated Oxepino[2,3-*b*]indolizines. These thus-obtained full-conjugated oxepino[2,3-*b*]indolizines **7a–f** were stable at room temperature; however, we observed a smooth transformation in the recrystallization of **7a** from hot ethanol. When a reddish ethanolic solution of ethyl 2-benzoyl-11-methyl-3-phenyloxepino[2,3-*b*]indolizine-4-carboxylate **7a** was heated under reflux for 10 h, and the reaction mixture was then cooled to room temperature, compound **9a** was separated from the reaction solution in 92% yield as orange prisms. Similar treatments of compounds **7b–f** in boiling ethanol gave the corresponding products **9b–f** in good yields (70–99%) (Scheme 3).

The analytical data for products **9a–f** showed that they have the same molecular compositions as materials **7b–f**, and the IR spectra exhibited each two carbonyl bands in the ranges of 1688–1701 and 1657–1669 cm⁻¹. Furthermore, all of the chemical shifts for the skeletal protons and the alkyl protons in the ¹H NMR spectra (Table 4) of compounds **9a–f** are quite similar to those in aromatic indolizine derivatives.^{4,7,8)} The values of the chemical shifts for the ethoxycarbonyl protons were intermediate between those for 2,3-dihydro-

Table 2. Crystal and Structure Analysis Data of Compounds **7a** and **9a**

	7a	9a
Formula	C ₂₉ H ₂₃ NO ₄	C ₂₉ H ₂₃ NO ₄
Formula weight	449.51	449.51
Crystal system	Monoclinic	Triclinic
Space group	<i>P</i> 2 ₁ / <i>c</i> ; <i>Z</i> =4	<i>P</i> $\bar{1}$; <i>Z</i> =2
Lattice parameter		
<i>a</i> /Å	16.628(7)	11.631(3)
<i>b</i> /Å	8.216(6)	12.519(4)
<i>c</i> /Å	17.408(10)	8.946(4)
α /°	90	110.67(3)
β /°	94.01(4)	109.91(3)
γ /°	90	83.44(2)
<i>V</i> /Å ³	2372(2)	1145.9(7)
<i>D</i> _{calcd} /g cm ⁻³	1.258	1.303
Crystal size/mm ³	0.28×0.26×1.00	0.26×0.48×1.00
Diffractometer	Rigaku AFC5S	Rigaku AFC5S
Radiation	Mo <i>K</i> α (λ =0.71069 Å)	Mo <i>K</i> α (λ =0.71069 Å)
Monochromator	Graphite	Graphite
Scan type	ω -2 θ	ω -2 θ
2 θ Max	55.1°	55.1°
Computer program	TEXSAN system ^{a)}	TEXSAN system ^{a)}
Structure solution	MITHRIL ^{b)}	MITHRIL ^{b)}
Hydrogen atom treatment	Observed, isotropic	Calculated, not refined
Refinement	Full-matrix, anisotropic	Full-matrix, anisotropic
Least-squares weight	4 <i>F</i> _o ² / σ ² (<i>F</i> _o ²)	4 <i>F</i> _o ² / σ ² (<i>F</i> _o ²)
No. of measurement ref.	Total: 5718 Unique: 5524	Total: 5547 Unique: 5285
No. of observations ^{c)}	1350	2002
No. of variables	307	307
Residuals <i>R</i> ; <i>R</i> _w	0.065; 0.098	0.071; 0.076
Max Shift/Error	0.27	0.04
$\Delta\rho_{\max}$ /e ⁻ Å ⁻³	0.24	0.36

a) See Ref. 10. b) Direct method, see Ref. 11. c) $I > 3.00\sigma(I)$.

drooxepinoindolizin-3-ols **4a–f** and for full-conjugated oxepinoindolizines **7a–f**, indicating a decrease in the shielding effect due to the phenyl group. Based on the considerations of the well-known ring-contraction trend (thermal oxepine-phenol rearrangement) of oxepine derivatives¹⁶⁾ and of the thermal stability of the products, we initially thought these products **9a–f** to be ethyl 1-arylcarbonyloxy-2-phenylpyrido[1,2-*a*]indole-3-carboxylates **10**. Because of the high planarity of the aromatic benzene ring, however, the smaller shielding effect to the ethoxycarbonyl protons attributable to the adjacent phenyl group in their ¹H NMR spectra could not skillfully explain this structure **10**. Taking into account this fact, other possible rearranged products, ethyl 2-arylcarbonyl-1-oxo-2-phenyl-1,2-dihydropyrido[1,2-*a*]indole-3-carboxylates, were newly considered as candidates for these products **9a–f**. The final structures for **9a–f** were established based on an analogy of a single-crystal X-ray analysis for compound **9a**. The crystal and structure analysis data, as well as selected bond lengths and bond angles for ethyl 2-benzoyl-10-methyl-1-oxo-2-phenylpyrido[1,2-*a*]indole-3-carboxylate **9a**, are summarized in Tables 2 and 3.¹²⁾ An ORTEP drawing¹³⁾ for **9a** is shown in Fig. 4. The crystal data for the indolizine ring of **9a** were also parallel to those

for other indolizine and fused indolizines.¹⁵⁾

Mechanisms. Possible mechanisms for the formations of full-conjugated oxepino[2,3-*b*]indolizines **7a–f** and pyrido[1,2-*a*]indol-1(2*H*)-ones **9a–f** are summarized in Scheme 4. The formation of compounds **7a–f** must be proceeded via protonation on the 3-hydroxyl oxygen of 2,3-dihydrooxepino[2,3-*b*]indolizin-3-ols **4a–f**, dehydration giving cationic intermediates **11**, followed by an elimination of the 2-methine proton from **11**. As first described, it is clear that the introduction of a phenyl group, in which there is no proton to abstract with ease, to the 3-position of 2,3-dihydrooxepino[2,3-*b*]indolizin-2-ol derivatives played an important role regarding the access of such full-conjugated oxepino[2,3-*b*]indolizines with a nonaromatic 4*n* π electron system. On the other hand, pyrido[1,2-*a*]indol-1(2*H*)-ones **9a–f** must be formed due to the valence isomerization of the oxepine ring in **7a–f**, followed by ring opening of the resulting tetracyclic oxiranes **8** along with a rearrangement of the arylcarbonyl group to the adjacent carbon atom.¹⁷⁾ The latter step is also a recovery of the aromaticity of the indolizine ring. In general, a smooth thermal and acid-catalyzed rearrangement from 2-unsubstituted oxepines to phenol derivatives^{3,16)} and a thermal re-

Table 3. Selected Bond Lengths and Bond Angles for Compounds **7a** and **9a** (esd's where given, are in parentheses)

	7a	9a		7a	9a
Bond lengths ^{a)}					
a	1.37(1)	1.412(6)	k	1.40(1)	1.427(6)
b	1.40(1)	1.389(7)	l	1.36(1)	1.333(6)
c	1.41(1)	1.376(5)	m	1.49(1)	1.537(7)
d	1.40(1)	1.360(6)	n	1.33(1)	—
e	1.36(2)	1.337(7)	o	1.42(1)	—
f	1.39(2)	1.412(8)	p	1.37(1)	—
g	1.36(2)	1.342(8)	q	—	1.579(7)
h	1.42(1)	1.421(7)	r	—	1.440(7)
i	1.41(1)	1.377(7)	s	—	1.212(6)
j	1.39(1)	1.420(6)			
Bond angles ^{a)}					
ab	112(1)	108.7(4)	fg	120(1)	120.5(5)
ai	106(1)	106.7(4)	gh	121(1)	121.0(5)
ap	125(1)	—	hi	136(1)	135.2(5)
ar	—	131.7(5)	hj	117(1)	115.9(5)
bc	104(1)	108.4(4)	ij	108(1)	108.9(4)
bk	127(1)	124.5(4)	kl	124(1)	119.5(5)
bp	123(1)	—	lm	123(1)	122.7(4)
br	—	119.6(4)	mn	123(1)	—
cd	128(1)	130.6(4)	mq	—	112.3(4)
cj	110(1)	107.3(4)	no	123(1)	—
ck	128(1)	127.1(5)	op	111.7(8)	—
de	118(1)	120.4(5)	qr	—	116.8(5)
dj	122(1)	122.1(4)	qs	—	118.1(5)
ef	122(1)	120.1(5)	rs	—	125.1(5)

a) For the alphabetical symbols of the bond lengths and angles, see Fig. 2.

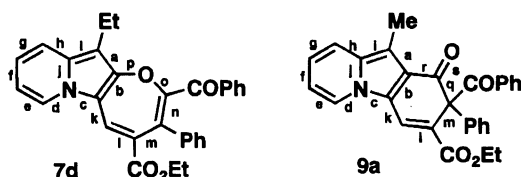


Fig. 2.

arrangement from 2,7-disubstituted oxepines or oxabridged annulenes to other oxepine compounds¹⁸⁾ have been well documented. In all reactions of the oxepine series, the corresponding valence isomers, oxanorcaradiene compounds, are presumed to be a key intermediate.^{3,16,18)} The reason why the products in these reactions were 2-(arylcarbonyl)pyrido[1,2-*a*]indol-1(2*H*)-ones **9a**—**f**, but not 1-(arylcarbonyloxy)pyrido[1,2-*a*]indoles **10**, is still unclear. However, this migration aptitude is very interesting, because such a rearrangement of an arylcarbonyl group is no precedent; in similar rearrangements of 6-substituted 2-arylcarbonyl-1,4-thiazines and -1,3,4-thiadiazines having the same 8 π electron system, the arylcarbonyl group is moved only on the sulfur atom, but not on the adjacent carbon atom at all.¹⁹⁾

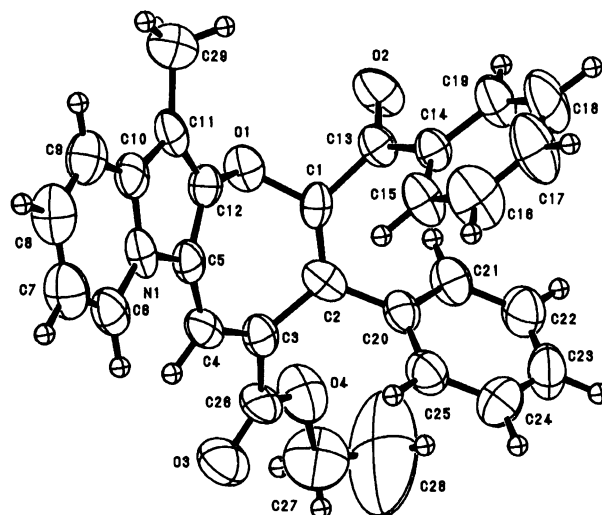


Fig. 3. ORTEP drawing of ethyl 2-benzoyl-11-methyl-3-phenyloxepino[2,3-*b*]indolizine-4-carboxylate (**7a**) showing the atom labeling scheme and 50% probability thermal ellipsoids.

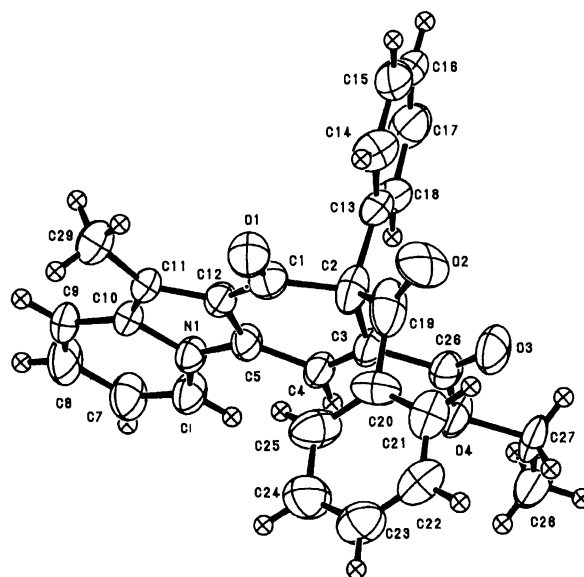
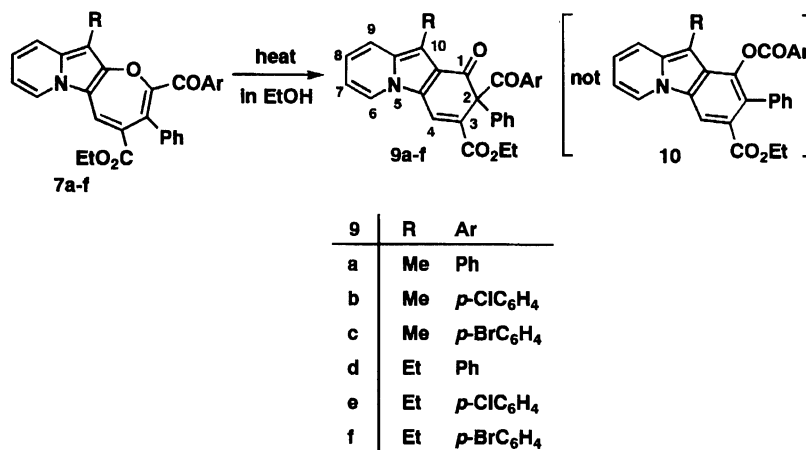


Fig. 4. ORTEP drawing of ethyl 2-benzoyl-10-methyl-2-phenyl-1-oxo-1,2-dihydropyrido[1,2-*a*]indole-3-carboxylate (**9a**) showing the atom labeling scheme and 50% probability thermal ellipsoids.

Experimental

The melting points were measured with a Yanagimoto micro-melting-point apparatus and were not corrected. Microanalyses were performed on a Perkin-Elmer 2400 elemental analyzer. The ¹H NMR spectra (60 MHz) were measured with a Varian EM360A spectrometer in deuteriochloroform with tetramethylsilane used as an internal standard; the chemical shifts are expressed in δ values. The IR spectra were taken with a JASCO FT/IR-5300 infrared spectrophotometer.

Preparations of 2,3-Dihydrooxepino[2,3-*b*]indolizine-3-ols. General Method. To an ethanolic so-

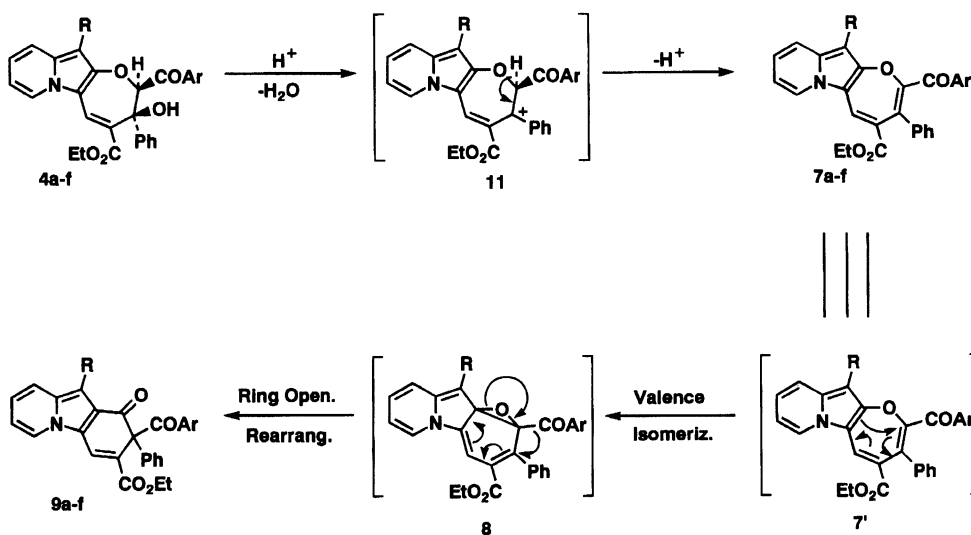


Scheme 3.

Table 4. ¹H NMR Spectral Data for Pyrido[1,2-*a*]indol-1(2*H*)-ones

Compd. No. ^{a)}	δ (CDCl ₃)								
	C-4	C-6	C-7	C-8	C-9	10-R	CO ₂ Et	Ar and 2-Ph	
9a	8.48 s	8.22 br d	-6.6—7.2- m	b)	2.50 s		1.03 t	4.06 q	7.2—7.9 m
9b	8.47 s	8.24 br d	-6.6—7.2- m	b)	2.50 s		1.04 t	4.06 q	7.2—7.9 m
9c	8.48 s	8.23 br d	-6.6—7.2- m	b)	2.50 s		1.07 t	4.06 q	7.2—7.8 m
9d	8.53 s	8.29 br d	-6.6—7.2- m	b)	1.11 t	2.97 q	1.01 t	4.03 q	7.2—7.9 m
9e	8.43 s	8.24 br d	-6.6—7.2- m	b)	1.12 t	2.96 q	1.06 t	4.05 q	7.2—7.9 m
9f	8.38 s	8.16 br d	-6.6—7.2- m	b)	1.07 t	2.96 q	1.01 t	4.02 q	7.2—7.8 m

a) The coupling constants are as follows; $J_{6,7}=7.0$ and $J_{Et}=7.0$ Hz. b) Overlapped with the proton signals of the 2-phenyl and 2-arylcarbonyl groups.



Scheme 4.

Table 5. Some Data for Oxepino[2,3-*b*]indolizines

Reactants	Products(%) ^{a)}	Mp ^{b)} /°C	ν (KBr) ^{b)} /cm ⁻¹			Formula ^{b,c)}
1a,2,3a	4a(5),5a(8),6a(4)	195—197	3309	1699	1651	C ₂₉ H ₂₅ NO ₅
1a,2,3b	4b(4),5a(6),6b(9)	213—215	3382	1701	1655	C ₂₉ H ₂₄ ClNO ₅
1a,2,3c	4c(5),5a(7),6c(9)	211—215	3391	1701	1655	C ₂₉ H ₂₄ BrNO ₅
1b,2,3a	4d(2),5b(4),6d(3)	167—168	3416	1699	1655	C ₃₀ H ₂₇ NO ₅
1b,2,3b	4e(2),5b(10),6e(10)	184—186	3306	1701	1649	C ₃₀ H ₂₆ ClNO ₅
1b,2,3c	4f(5),5b(4),6f(3)	151—153	3308	1701	1649	C ₃₀ H ₂₆ BrNO ₅
4a	7a(61)	168—170		1694	1667	C ₂₉ H ₂₃ NO ₄
4b	7b(68)	135—137		1696	1671	C ₂₉ H ₂₂ ClNO ₄
4c	7c(69)	113—115		1698	1672	C ₂₉ H ₂₂ BrNO ₄
4d	7d(92)	184—185		1692	1657	C ₃₀ H ₂₅ NO ₄
4e	7e(99)	92—94		1698	1669	C ₃₀ H ₂₄ ClNO ₄
4f	7f(87)	147—148		1688	1669	C ₃₀ H ₂₄ BrNO ₄

a) Compounds **4a—f** were obtained as yellow needles, **5a,b** as orange flakes, **6a—f** as red needles, and **7a—f** as red prisms. b) This value is for oxepino[2,3-*b*]indolizine. c) Satisfactory analytical data (within $\pm 0.3\%$ for C, H, and N) were obtained for compounds **4a—f** and **7a—f**.

Table 6. Some Data for Pyrido[1,2-*a*]indol-1(2*H*)-ones

Reactant	Product ^{a)}	Yield %	Mp °C	ν (KBr) cm ⁻¹		Formula ^{b)}
7a	9a	92	184—185	1692	1657	C ₂₉ H ₂₃ NO ₄
7b	9b	99	92—94	1698	1669	C ₂₉ H ₂₂ ClNO ₄
7c	9c	87	147—148	1688	1669	C ₂₉ H ₂₂ BrNO ₄
7d	9d	71	234—235	1698	1667	C ₃₀ H ₂₅ NO ₄
7e	9e	70	225—226	1701	1663	C ₃₀ H ₂₄ ClNO ₄ +1/2EtOH
7f	9f	78	189—192	1696	1657	C ₃₀ H ₂₄ BrNO ₄ +1/2EtOH

a) Compounds **9a—f** were obtained as orange prisms. b) Satisfactory analytical data (within $\pm 0.3\%$ for C, H, and N) were obtained for compounds **9a—f**.

lution (30 ml) of 1-(ethoxycarbonylmethyl)pyridinium bromide (**1a** or **1b**, 3 mmol) DBU (1.83 g, 7 mmol) was added under heating (60—80 °C) in a water bath; after 15 min, ethyl (ethoxymethylene)benzoylacetate (**2**, 0.74 g, 3 mmol), and then phenacyl bromide (**3**, 3 mmol), were added to the resulting 2(3*H*)-indolizinone solution. The reaction solution was allowed to react for an additional 3—4 h under these conditions. From the cooled reaction solution, insoluble substances were removed by filtration, and the filtrate was concentrated at reduced pressure. The thus-obtained residue was separated by repeating column chromatography on alumina using benzene, and then chloroform, as eluents to give the corresponding ethyl 2-arylcarbonyl-3-hydroxy-3-phenyl-2,3-dihydrooxepino[2,3-*b*]indolizine-4-carboxylates **4**, 3-benzoyl-2*H*-pyrano[2,3-*b*]indolizin-2-ones **5**, and 2-(arylcarbonyl)furo[2,3-*b*]indolizines **6**. All products **4a—f**, **5a,b**, and **6a—f** were recrystallized from ethanol.

Products **6a—f** were in accord with authentic samples in all respects, and some data for new compounds, 3-benzoyl-2*H*-pyrano[2,3-*b*]indolizin-2-ones **5a,b**, are as follows:

5a, orange flakes, mp 242—243 °C, ν (KBr) 1703 and 1624 (CO) cm⁻¹, δ (CDCl₃)=2.35 (3H, s, 10-Me), 6.85 (1H, br t, $J=7.0$ and 7.0 Hz, 7-H), 7.0—8.0 (8H, m, 6-, 8-, 9-H and phenyl protons), 8.29 (1H, br d, $J=7.0$ Hz, 6-H), and 8.59 (1H, s, 4-H). Anal. (C₁₉H₁₃NO₃) C,H,N.

5b, orange flakes, mp 260—261 °C, ν (KBr) 1713 and 1624 (CO) cm⁻¹, δ (CDCl₃)=1.30 (3H, t, $J=7.0$ Hz, 10-CH₂CH₃), 2.81 (2H, q, $J=7.0$ Hz, 10-CH₂CH₃), 6.85 (1H,

dt, $J=7.0$, 7.0, and 2.0 Hz, 7-H), 7.0—8.0 (8H, m, 6-, 8-, 9-H and phenyl protons), 8.27 (1H, br d, $J=7.0$ Hz, 6-H), and 8.60 (1H, s, 4-H). Anal. (C₂₀H₁₅NO₃) C,H,N.

These results and some physical and spectral data are summarized in Tables 1 and 5.

Preparations of Full-Conjugated Oxepino[2,3-*b*]indolizines. General Method. To a chloroform solution (20 ml) of 2,3-dihydrooxepino[2,3-*b*]indolizin-3-ol (**4**, 1 mmol) methanesulfonic acid (0.5 ml) was added; the resulting mixture was heated under reflux in a water bath for 15—20 min. The reaction solution, which turned from yellow to red, was quickly concentrated at reduced pressure at below 30 °C. The residue was separated by column chromatography on alumina using chloroform as an eluent. Evaporation of the solvent at below 30 °C and recrystallization from ethanol without heating provided the dehydrated products **7a—f**.

These data are listed in Tables 1 and 5.

Rearrangements of Full-Conjugated Oxepino[2,3-*b*]indolizines to Pyrido[1,2-*a*]indol-1(2*H*)-ones. General Method. Full-conjugated oxepino[2,3-*b*]indolizine (**7**, 0.5 mmol) was dissolved in 50 ml of ethanol,

and the resulting solution was heated under reflux in a water bath until the starting material **7** disappeared (by TLC monitoring, about 7—20 h). After the reaction was completed, the reaction solution was cooled to room temperature and the precipitates of compound **9** which separated were collected by suction. The crude product was then re-

crystallized from ethanol. These data are given in Tables 4 and 6.

References

- 1) For part 36 of this series, see: A. Kakehi, S. Ito, M. Mitani, and M. Kanaoka, *Bull. Chem. Soc. Jpn.*, **67**, 1646 (1994).
- 2) A. Kakehi, S. Ito, and H. Muranaka, *J. Fac. Eng. Shinshu Univ.*, No. **74**, 31 (1994).
- 3) E. Vogel and H. Gunther, *Angew. Chem.*, **79**, 429 (1967).
- 4) A. Kakehi, S. Ito, H. Furuta, and K. Todoroki, *J. Fac. Eng. Shinshu Univ.*, No. **58**, 1 (1985).
- 5) A. Kakehi, S. Ito, S. Murakami, and H. Sano, *Bull. Chem. Soc. Jpn.*, **57**, 548 (1984).
- 6) X-Ray crystallography of compound **4e** was carried out on a Rigaku AFC5S diffractometer. The diffraction data were collected with the use of Mo $K\alpha$ radiation and 5329 independent reflection were used for solving the structure by direct method (MITHRIL, see Ref. 11) in the TEXSAN program (see Ref. 10). Crystal data: yellow prisms (from ethanol), $C_{30}H_{26}ClNO_5$, FW=515.99, monoclinic, space group $P2_1/n$, $a=12.472(17)$ Å, $b=13.052(5)$ Å, $c=16.198(6)$ Å, $\beta=100.38(6)^\circ$, $V=2594(6)$ Å³, $Z=4$, $D_{\text{calcd}}=1.321$ g cm⁻³, $R=0.057$, $R_w=0.059$.
- 7) A. Kakehi, S. Ito, T. Ohizumi, and M. Ito, *Bull. Chem. Soc. Jpn.*, **56**, 1219 (1983).
- 8) A. Kakehi, S. Ito, K. Nakanishi, K. Watanabe, and M. Kitagawa, *Bull. Chem. Soc. Jpn.*, **53**, 1115 (1980); A. Kakehi, S. Ito, B. Wada, K. Watanabe, K. Nishimura, and A. Kumagai, *Bull. Chem. Soc. Jpn.*, **55**, 3590 (1982).
- 9) The proton signals for the 1-methyl or the 1-ethyl group of aromatic indolizine derivatives are usually exhibited at δ (CDCl₃)=2.1–2.4 (3H, s) or δ =1.1–1.3 (3H, t, $J=7.0$ Hz) and 2.6–2.9 (2H, q, $J=7.0$ Hz). See Refs. 4, 7, and 8. However, the reason for this large high magnetic shift to the C₁₁-methyl or C₁₁-ethyl protons in **4a–f** and **7a–f** is still unclear.
- 10) "TEXSAN TEXRAY, Structure Analysis Package," Molecular Structure Corporation (1985).
- 11) C. J. Gilmore, *J. Appl. Crystallogr.*, **17**, 42 (1984).
- 12) Tables of the coordinates, bond lengths, bond and torsion angles, and F_o-F_c tables for compounds **7a** and **9a** are deposited as Document No. 67061 at the Office of the Editor of Bull. Chem. Soc. Jpn.
- 13) C. K. Johnson, "ORTEP II, Report ORNL-5138," Oak Ridge National Laboratory, Oak Ridge, Tennessee (1976).
- 14) The large β_{eq} value for the C(28) atom in ORTEP drawing for **7a** is principally owing to the high flexibility of the 4-ethoxycarbonyl group in the crystal lattice, and the resulting low accuracy for this analysis seemed to be caused by this fact and the X-ray labile property of compound **7a**.
- 15) R. G. Pritchard, *Acta Crystallogr., Sect. C*, **C44**, 1150 (1988); A. Kakehi, K. Kitajima, S. Ito, and N. Takusagawa, *Acta Crystallogr., Sect. C*, **C49**, 604 (1993); A. Kakehi, K. Kitajima, S. Ito, and N. Takusagawa, *Acta Crystallogr., Sect. C*, **C49**, 1230 (1993).
- 16) E. Vogel, W. A. Boll, and H. Günther, *Tetrahedron Lett.*, **1965**, 609.
- 17) In this rearrangement, the nucleophilic movement of the 2-arylcarbonyl group to the adjacent position must be involved. Although such migration of an acyl group is not like and not known, we can not give any other plausible explanation for this rearrangement at present.
- 18) E. Vogel, M. Biskup, W. Pretzer, and W. A. Böll, *Angew. Chem.*, **76**, 785 (1964).
- 19) A. Kakehi, S. Ito, M. Ito, T. Yotsuya, and K. Nagata, *Bull. Chem. Soc. Jpn.*, **58**, 1432 (1985); A. Kakehi, S. Ito, S. Yonezu, K. Maruta, K. Yuito, M. Shiohara, and K. Adachi, *Bull. Chem. Soc. Jpn.*, **60**, 1867 (1987).