Acid-Catalyzed Reactions of 1- and 3-(α-Hydroxybenzyl)indolizines

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Treatment of 1-(α-hydroxybenzyl)- and 3-(α-hydroxybenzyl)indolizines with trifluoroacetic acid in dichloromethane gave phenylbis(α-indolizinyl)methanes, bis[α-(indolizinyl)benzyl] ethers and indolizines, depending upon the presence or absence of the substituent at the 2- or 5-position and the reaction conditions used.

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In a previous paper [1] we described the reaction of 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]pyridines **1** with trifluoroacetic acid to give the bis(pyrazolo[1,5-*a*]pyrid-3-yl)-methanes **2** and pyrazolo[1,5-*a*]pyridines **3**, depending upon the substituent at the 2- and/or 4-positions and the reaction conditions used. The reaction is probably initiated by protonation at the 3-position of the pyrazolo[1,5-*a*]-pyridine which is followed by the extrusion of benzaldehyde to afford the products **2** and **3** (Scheme 1). Indolizines [2], carbon analogues of pyrazolo[1,5-*a*]pyridines [3], show similar reactivities but differ in possessing two electrophilically reactive sites (positions 1 and 3) from the latter which has only one reactive site (position 3). In continuation of our studies on the chemistry of indolizines and related compounds we report here the behavior of the 1-(α-hydroxybenzyl)- **6** and 3-(α-hydroxybenzyl)indolizines **7** toward trifluoroacetic acid.

The 1-(α-hydroxybenzyl)-**6a,b** and 3-(α-hydroxybenzyl)-indolizines **7a-c**, were synthesized by using well established procedure [4] as outlined in Scheme 2.

In general, the acid-catalyzed reaction of indolizines was carried out by stirring at room temperature or refluxing a solution of **6** or **7** in dichloromethane containing trifluoroacetic acid (2.5 and 0.01 molar equivalents).

In this manner the 1-(α-hydroxybenzyl)indolizines **6a,b** [5] were treated with trifluoroacetic acid to give the bis(indolizin-1-yl)methanes **8a,b** and the ether **9**. Further treatment of the ether **9** with 2.5 molar equivalents of trifluoroacetic acid completely converted into **8b**. Similar treatment of 3-(α-hydroxybenzyl)indolizines **7a-c** [5] gave the bis(indolizin-3-yl)methanes **10a-c** and the indolizines **11b,c** (Scheme 3). The results were summarized in Tables 1 and 2. The structures of these products were assigned on the basis of the elemental analyses and spectroscopic evidence (see Experimental). The stereochemistry of **9** is not clear at the present time.

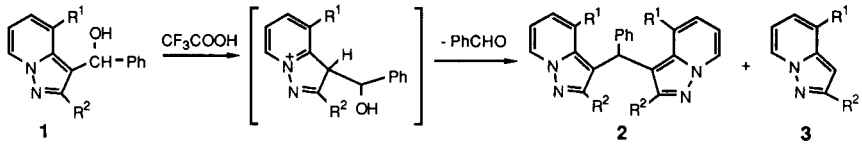
Table 1

Reaction of 1-(α-Hydroxybenzyl)indolizines 6 with Trifluoroacetic Acid

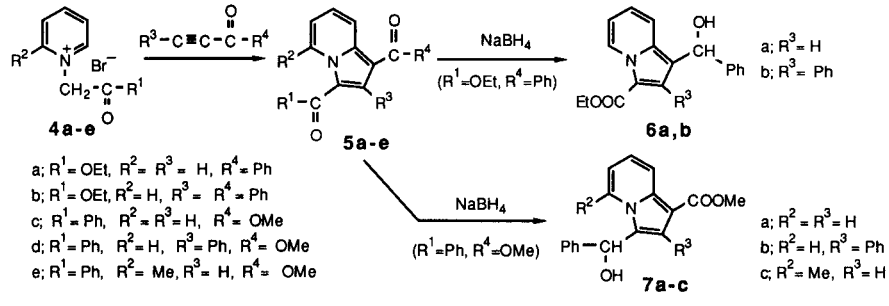
6	R^3	CF_3COOH (equivalents)	Reaction Conditions [a] Temperature	Time	Yield(%) 8	9
a	H	0.01	reflux	1 hour	87	---
		2.5	rt	1.5 hour	71	---
b	Ph	0.01	reflux	5 hours	27	55
		2.5	rt	1.5 hour	48	---

[a] All reactions were carried out in dichloromethane.

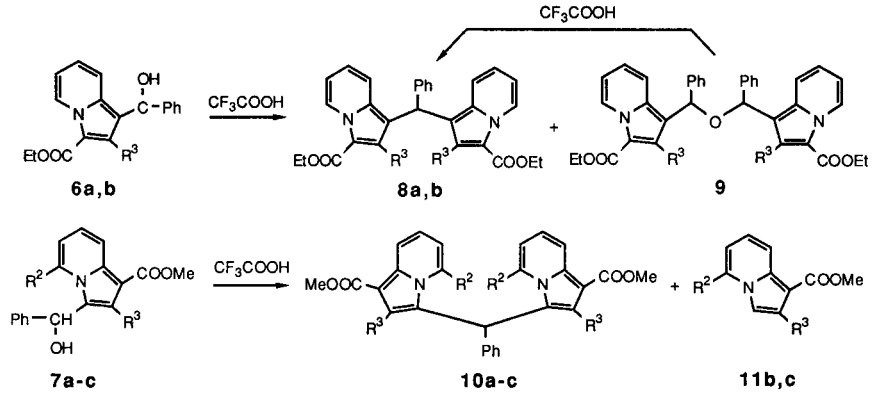
Scheme 1



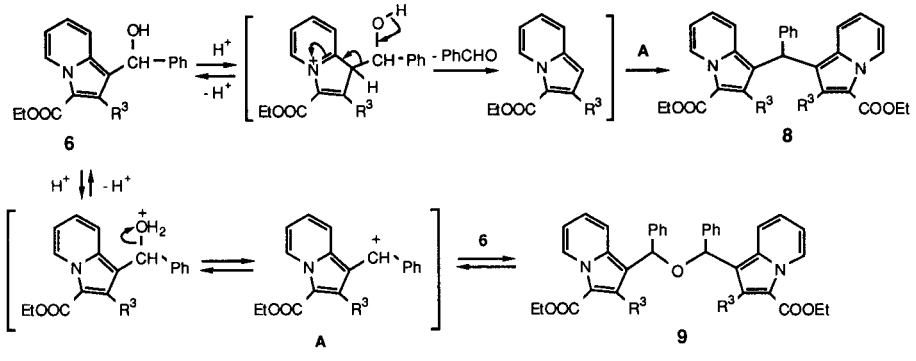
Scheme 2



Scheme 3



Scheme 4



Scheme 5

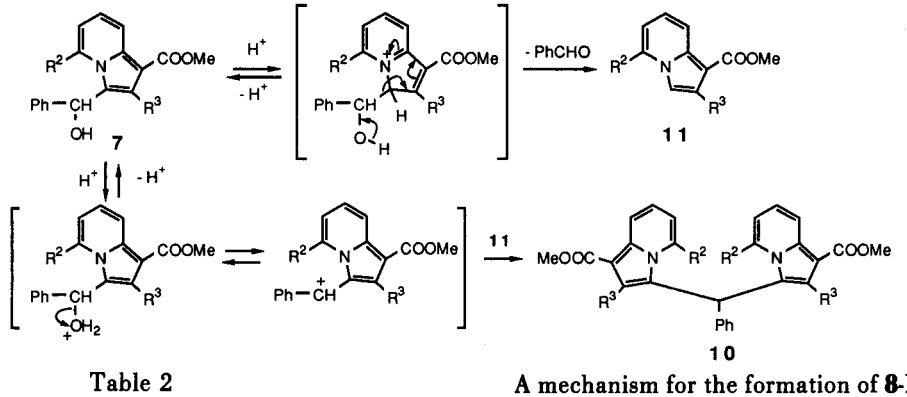


Table 2

Reaction of 3-(α-Hydroxybenzyl)indolizines 7 with Trifluoroacetic Acid

7	R^2	R^3	CF_3COOH (equivalents)	Reaction Conditions [a] Time (minutes)	Yield(%) 10	11
a	H	H	0.01	60	87	--
			2.5	10	93	--
b	H	Ph	0.01	90	2	87
			2.5	30	85	--
c	Me	H	0.01	5	--	79
			2.5	5	41	40

[a] All reactions were carried out in dichloromethane at room temperature.

A mechanism for the formation of **8-11** is very similar to the previously proposed one for the formation of **2** and **3** [1] and outlined in Schemes 4 and 5.

In conclusion, the behavior of the indolizines **6** and **7** toward trifluoroacetic acid is closely related to that of pyrazolo[1,5-*a*]pyridines **2** and **3**.

EXPERIMENTAL

All mps are uncorrected. The ^{1}H-nmr spectra were determined on a JEOL FX200 spectrometer using tetramethylsilane as an internal standard. The ir spectra were recorded with Hitachi EPI-G2 spectrophotometer. The low resolution mass spectra were recorded on a M-70 JMX-HX100 spectrometer at 70 eV.

Ethyl 1-Benzoylindolizine-3-carboxylates and Methyl 3-Benzoylindolizine-1-carboxylates (**5**). General Procedure.

To a suspension of the *N*-ethoxycarbonylmethyl- or *N*-phenacylpyridinium bromide (**4**) (10 mmoles) and potassium carbonate (12 mmoles) in tetrahydrofuran (100 ml) was added 1-phenyl-2-propyn-1-one (10 mmoles), 1,3-diphenyl-2-propyn-1-one (10 mmoles), methyl propiolate (15 mmoles), or methyl phenylpropiolate (10 mmoles). The reaction mixture was stirred at room temperature overnight (In the case of the reaction with methyl phenylpropiolate the reaction mixture was refluxed for twelve hours to complete the reaction after stirring). The insoluble material was filtered off and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel. Elution with *n*-hexane/ethyl acetate (20:1-10:1) gave **5**.

Ethyl 1-Benzoylindolizine-3-carboxylate (**5a**).

Compound **5a** was obtained in 50% yield, mp 115-116° (*n*-hexane-benzene); ir (nujol): 1625 and 1690 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.38 (t, 3H, J = 7 Hz, CH_3), 4.38 (q, 2H, J = 7 Hz, CH_2), 7.06 (dt, 1H, J = 7, 1.5 Hz, H-6), 7.42 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.5-7.9 (m, 5H, Ph), 7.78 (s, 1H, H-2), 8.62 (dt, 1H, J = 9, 1.5 Hz, H-8), and 9.56 (dt, 1H, J = 7, 1 Hz, H-5).

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.58; H, 5.27; N, 4.75.

Ethyl 1-Benzoyl-2-phenylindolizine-3-carboxylate (**5b**).

Compound **5b** was obtained in 90% yield, mp 115-116° (ethanol); ir (nujol): 1625 and 1665 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.94 (t, 3H, J = 7 Hz, CH_3), 4.10 (q, 2H, J = 7 Hz, CH_2), 6.99 (dt, 1H, J = 7, 1 Hz, H-6), 7.0-7.5 (m, 11H, H-7 and 2 x Ph), 8.04 (br d, 1H, J = 9 Hz, H-8), and 9.62 (br d, 1H, J = 7 Hz, H-5).

Anal. Calcd. for $C_{24}H_{19}NO_3$: C, 78.03; H, 5.18; N, 3.79. Found: C, 78.07; H, 4.96; N, 3.76.

Methyl 3-Benzoylindolizine-1-carboxylate (**5c**).

Compound **5c** was obtained in 70% yield, mp 162-163° (*n*-hexane-benzene); ir (nujol): 1620 and 1690 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.88 (s, 3H, CH_3), 7.06 (dt, 1H, J = 7, 1 Hz, H-6), 7.4-7.6 (m, 5H, Ph), 7.43 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.79 (s, 1H, H-2), 8.34 (dt, 1H, J = 9, 1 Hz, H-8) and 9.95 (dt, 1H, J = 7, 1 Hz, H-5).

Anal. Calcd. for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.02. Found: C, 73.34; H, 4.79; N, 4.90.

Methyl 3-Benzoyl-2-phenylindolizine-1-carboxylate (**5d**).

Compound **5d** was obtained in 48% yield, mp 165-166° (methanol); ir (nujol): 1610 and 1685 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.70 (s, 3H, CH_3), 6.9-7.5 (m, 12H, H-6, H-7, and 2 x Ph), 8.41 (dt, 1H, J = 9, 1 Hz, H-8), and 9.56 (dt, 1H, J = 7, 1 Hz, H-5).

Anal. Calcd. for $C_{23}H_{17}NO_3$: C, 77.73; H, 4.82; N, 3.94. Found: C, 77.86; H, 4.93; N, 3.89.

Methyl 3-Benzoyl-5-methylindolizine-1-carboxylate (**5e**).

Compound **5e** was obtained in 41% yield, mp 115-116° (ether); ir (nujol): 1630 and 1700 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.62 (s, 3H, CH_3), 3.90 (s, 3H, CH_3), 6.92 (br d, 1H, J = 7 Hz, H-6), 7.4-8.1 (m, 5H, Ph), 7.44 (dd, 1H, J = 9, 7 Hz, H-7), 7.72 (s, 1H, H-2), and 8.36 (br d, 1H, J = 9 Hz, H-8).

Anal. Calcd. for $C_{18}H_{15}NO_3$: C, 73.70; H, 5.15; N, 4.78. Found: C, 73.63; H, 5.24; N, 4.71.

1-(α-Hydroxybenzyl)- **6a,b** and 3-(α-Hydroxybenzyl)indolizines **7a-c**. General Procedure.

Sodium borohydride (30 mmoles) was added to a solution of ethyl 1-benzoylindolizine-3-carboxylates **5a,b** (5 mmoles) in ethanol (25 ml) or a solution of methyl 3-benzoylindolizine-1-carboxylates **5c-e** (5 mmoles) in methanol (25 ml) and the reaction mixture was stirred at room temperature overnight (In the case of **5c-e** the reaction time is 5-60 minutes). Water was added to the reaction mixture and the aqueous solution was extracted with chloroform. The extract was washed with water, dried over sodium sulfate, and concentrated to dryness *in vacuo*. The residue was purified by silica gel column chromatography. Elution with *n*-hexane/ethyl acetate (10:1-5:1) yielded **6a,b** or **7a-c**.

Ethyl 1-(α-Hydroxybenzyl)indolizine-3-carboxylate (**6a**).

Compound **6a** was obtained in 100% yield, mp 89-90° (*n*-hexane-benzene); ir (nujol): 3400 (OH) and 1660 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.35 (t, 3H, J = 7 Hz, CH_3), 2.2-2.3 (br s, 1H, OH), 4.31 (q, 2H, J = 7 Hz, CH_2), 6.14 (s, 1H, CH), 6.76 (dt, 1H, J = 7, 1 Hz, H-6), 6.96 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.2-7.5 (m, 6H, H-2 and Ph), 7.53 (dt, 1H, J = 9, 1 Hz, H-8), and 9.36 (dt, 1H, 7, 1 Hz, H-5).

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.48; H, 6.04; N, 4.63.

Ethyl 1-(α-Hydroxybenzyl)-2-phenylindolizine-3-carboxylate (**6b**).

Compound **6b** was obtained in 86% yield, mp 134-135° (*n*-hexane-benzene); ir (nujol): 3350 (OH) and 1680 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.88 (t, 3H, J = 7 Hz, CH_3), 2.12 (s, 1H, OH), 4.04 (q, 2H, J = 7 Hz, CH_2), 5.88 (s, 1H, CH), 6.77 (dt, 1H, J = 7, 1.5 Hz, H-6), 6.91 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.1-7.4 (m, 10H, 2 x Ph), 7.42 (br d, 1H, J = 9 Hz, H-8), and 9.51 (br d, 1H, J = 7 Hz, H-5).

Anal. Calcd. for $C_{24}H_{21}NO_3$: C, 77.60; H, 5.70; N, 3.77. Found: C, 77.79; H, 5.86; N, 3.69.

Methyl 3-(α-Hydroxybenzyl)indolizine-1-carboxylate (**7a**).

Compound **7a** was obtained in 84% yield, mp 146-147° (*n*-hexane-ether); ir (nujol): 3380 (OH) and 1665 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.64 (d, 1H, J = 5 Hz, OH), 3.81 (s, 3H, CH_3), 6.11 (d, 1H, J = 5 Hz, CH), 6.68 (dt, 1H, J = 7, 1.5 Hz, H-6), 6.83 (s, 1H, H-2), 7.05 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.3-7.5 (m, 5H, Ph), 8.14 (br d, 1H, J = 9 Hz, H-8), and 8.18 (br d, 1H, J = 7 Hz, H-5).

Anal. Calcd. for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.57; H, 5.50; N, 4.92.

Methyl 3-(α-Hydroxybenzyl)-2-phenylindolizine-1-carboxylate (**7b**).

Compound **7b** was obtained in 87% yield, mp 147-148° (*n*-hexane-ethyl acetate): ir (nujol): 3450 (OH) and 1660 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.1-2.5 (br s, 1H, OH), 3.67 (s, 3H, CH_3), 6.08 (s, 1H, CH), 6.50 (dt, 1H, J = 7, 1.5 Hz, H-6), 7.01 (ddd, 1H, J = 9, 7, 1 Hz, H-7), 7.2-7.4 (m, 11H, H-5 and 2 x Ph), and 8.22 (br d, 1H, J = 9 Hz, H-8).

Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.29; H, 5.36; N, 3.92. Found: C, 77.47; H, 5.53; N, 3.93.

Methyl 3-(α-Hydroxybenzyl)-5-methylindolizine-1-carboxylate (**7c**).

Compound **7c** was obtained in 100% yield, mp 150-151° (ether-*n*-hexane); ir (nujol): 3450 (OH) and 1665 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.58 (d, 1H, J = 6 Hz, OH), 3.02

(s, 3H, CH_3), 3.78 (s, 3H, CH_3), 6.46 (d, 1H, J = 6 Hz, CH), 6.54 (br d, 1H, J = 7 Hz, H-6), 6.71 (s, 1H, H-2), 6.98 (dd, 1H, J = 9, 7 Hz, H-7), 7.3-7.5 (m, 5H, Ph) and 8.16 (br d, 1H, J = 9 Hz, H-8).

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.20; H, 5.80; N, 4.74. Found: C, 73.21; H, 5.88; N, 4.72.

Reaction of Ethyl 1-(α-Hydroxybenzyl)indolizine-3-carboxylates **6** and Methyl 3-(α-Hydroxybenzyl)indolizine-1-carboxylates **7** with Trifluoroacetic Acid. General Procedure.

A solution of the ethyl 1-(α-hydroxybenzyl)indolizine-3-caboxylates **6** or the methyl 3-(α-hydroxybenzyl)indolizine-1-carboxylates **7** (1 moles) in dichloromethane (10 ml) containing trifluoroacetic acid (0.01 mmole or 2.5 mmoles) was stirred at room temperature or refluxed. After the reaction mixture was neutralized with 5% sodium hydrogen carbonate solution, the organic layer was separated and the aqueous layer was extracted with dichloromethane. The combined organic extract was washed with water, dried over sodium sulfate, and concentrated. The crude products were separated by column chromatography or preparative thin layer chromatography on silica gel (*n*-hexane or dichloromethane/ethyl acetate). These results are summarized in Table 1.

Phenylbis (3-ethoxycarbonylindolizin-1-yl)methane (**8a**).

Compound **8a** had mp 123-124° (ethanol); ir (nujol): 1680 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform); δ 1.34 (t, 6H, J = 7 Hz, 2 x CH_3), 4.28 (q, 4H, J = 7 Hz, 2 x CH_2), 5.85 (s, 1H, CH), 6.75 (dt, 2H, J = 7, 1.5 Hz, 2 x H-6), 6.85 (ddd, 2H, J = 9, 7, 1.5 Hz, 2 x H-7), 7.09 (s, 2H, 2 x H-2), 7.2-7.4 (m, 7H, 2 x H-8 and Ph), and 9.38 (dt, 2H, J = 7, 1.5 Hz, 2 x H-5).

Anal. Calcd. for $C_{29}H_{26}N_2O_4$: C, 74.66; H, 5.62; N, 6.00. Found: C, 74.39; H, 5.46; N, 5.76.

Phenylbis(3-ethoxycarbonyl-2-phenylindolizin-1-yl)methane (**8b**).

Compound **8b** had mp 161-162° (*n*-hexane-benzene); ir (nujol): 1670 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.74 (t, 6H, J = 7 Hz, 2 x CH_3), 3.92 (q, 4H, J = 7 Hz, 2 x CH_2), 5.56 (s, 1H, CH), 6.3-6.7 (m, 4H, 2 x H-6 and 2 x H-7), 6.9-7.2 (m, 17H, 2 x H-8 and 3 x Ph), and 9.4-9.5 (m, 2H, J = 7, 2 x H-5); ms: m/z 618 M^+.

Anal. Calcd. for $C_{41}H_{34}N_2O_4$: C, 79.59; H, 5.54; N, 4.53. Found: C, 79.72; H, 5.74; N, 4.47.

Bis[α-(3-ethoxycarbonyl-2-phenylindolizin-1-yl)benzyl] Ether (**9**).

Compound **9** had mp 167-168° (ether); ir (nujol): 1670 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 0.83 (t, 6H, J = 7 Hz, 2 x CH_3), 3.99 (q, 4H, J = 7 Hz, 2 x CH_2), 5.48 (s, 2H, 2 x CH), 6.7-6.9 (m, 4H, 2 x H-6 and 2 x H-7), 6.9-7.3 (m, 20H, 4 x Ph), 7.53 (br d, 2H, J = 8 Hz, 2 x H-8), and 9.49 (br d, 2H, J = 7 Hz, 2 x H-5); ms: m/z 724 M^+.

Anal. Calcd. for $C_{48}H_{40}N_2O_5$: C, 79.53; H, 5.56; N, 3.87. Found: C, 79.48; H, 5.68; N, 3.83.

Phenylbis(1-methoxycarbonylindolizin-3-yl)methane (**10a**).

Compound **10a** had mp 210-211° (methanol); ir (nujol): 1685 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.81 (s, 6H, 2 x CH_3), 5.67 (s, 1H, CH), 6.60 (s, 2H, 2 x H-2), 6.64 (dt, 2H, J = 7, 1.5 Hz, 2 x H-6), 7.06 (ddd, 2H, J = 9, 7, 1 Hz, 2 x H-7), 7.1- 7.2 (m, 5H, Ph), 7.60 (br d, 2H, J = 7 Hz, 2 x H-5), and 8.23 (dt, 2H, J = 9, 1.5 Hz, 2 x H-8).

Anal. Calcd. for $C_{27}H_{22}N_2O_4$: C, 73.96; H, 5.06; N, 6.39. Found: C, 73.94; H, 4.81; N, 6.18.

Phenylbis(1-methoxycarbonyl-2-phenylindolizin-3-yl)methane (**10b**).

Compound **10b** had mp 222-224° (ethyl acetate); ir (nujol): 1680 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.64 (s, 6H, 2 x CH_3), 6.00 (s, 1H, CH), 6.23 (br t, 2H, J = 7 Hz, 2 x H-6), 6.7-7.2 (m, 19H, 2 x H-5, 2 x H-7, and 3 x Ph), and 8.12 (br d, 2H, J = 9 Hz, 2 x H-8).

Anal. Calcd. for $C_{39}H_{30}N_2O_4$: C, 79.30; H, 5.12; N, 4.74. Found: C, 79.38; H, 5.13; N, 4.70.

Methyl 2-Phenylindolizine-1-carboxylate (**11b**).

Compound **11b** had mp 105-106° (methanol); ir (nujol): 3450 (OH) and 1660 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 3.76 (s, 3H, CH_3), 6.69 (br t, 1H, J = 9 Hz, H-6), 7.04 (br dd, 1H, J = 9, 7 Hz, H-7), 7.20 (s, 1H, H-3), 7.3-7.5 (m, 5H, Ph), 7.94 (br d, 1H, J = 7 Hz, H-5), and 8.19 (br d, 1H, J = 9 Hz, H-8).

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.47; H, 5.22; N, 5.57. Found: C, 76.55; H, 5.24; N, 5.54.

Phenylbis(1-methoxycarbonyl-5-methylindolizin-3-yl)methane (**10c**).

Compound **10c** had mp 262-264° dec, (methanol); ir (nujol): 1690 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.74 (s, 6H, 2 x CH_3), 3.78 (s, 6H, 2 x CH_3), 6.36 (br d, 2H, 2 x H-6), 6.38 (s, 2H, 2 x H-2), 6.8-7.0 (m, 5H, CH, 2 x H-7, and Ph), 7.2-7.3 (m, 3H, Ph) and 8.22 (br d, 2H, J = 9 Hz, 2 x H-8).

Anal. Calcd. for $C_{29}H_{26}N_2O_4$: C, 74.66; H, 5.62; N, 6.01. Found: C, 74.47; H, 5.74; N, 5.93.

Methyl 5-Methylindolizine-1-carboxylate (**11c**).

Compound **11c** had mp 104-105°, (*n*-hexane); ir (nujol): 1685 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.56 (s, 3H, CH_3), 3.89 (s, 3H, CH_3), 6.56 (br d, 1H, J = 7 Hz, H-6), 7.02 (dd, 1H, J = 9, 7 Hz, H-7), 7.12 (d, 1H, J = 3 Hz, H-2 or H-3), 7.29 (d, 1H, J = 3 Hz, H-3 or H-2) and 8.12 (br d, 1H, J = 9 Hz, H-8).

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; H, 7.40. Found: C, 69.82; H, 5.97; N, 7.36.

Transformation of Bis[α-(3-ethoxycarbonyl-2-phenylindolizin-1-yl)benzyl] Ether (**9**) into phenylbis(3-ethoxycarbonyl-2-phenylindolizin-1-yl)methane (**8b**).

To a solution of **9** (72 mg, 0.1 mole) in dichloromethane (2 ml) was added trifluoroacetic acid (29 mg, 0.25 mmole) and the reaction mixture was stirred at room temperture for one hour. After the reaction mixture was neutralized with 5% sodium carbonate solution, the mixture was extracted with dichloromethane. The extract was washed with water, dried over sodium sulfate, and concentrated. The residue was purified by column chromatography (silica gel, *n*-hexane-ethyl acetate) to give **8b** (54 mg, 87%) and methyl 3-(α-hydroxybenzyl)-2-phenylindolizine-1-carboxylate **7b** (3 mg, 8%).

REFERENCES AND NOTES

[1] Y. Miki, O. Tomii, H. Nakao, M. Kubo, H. Hachiken, S. Takemura and M. Ikeda, *J. Heterocyclic Chem.*, **25**, 327 (1988).

[2] A. R. Katritzky and C. W. Rees, in Comprehensive Heterocyclic Chemisry, Vol. **4**, Pergamon Press Ltd., Oxford, London, 1984, p 443.

[3] A. R. Katritzky and C. W. Rees, in Comprehensive heterocyclic Chemistry, Vol. **5**, Pergamon Press Ltd., Oxford, London, 1984, p 305.

[4] Y. Miki, H. Kinoshita, T. Yoshimaru, and S. Takemura, *Heterocycles*, **26**, 199 (1987).

[5] Under the nmr measurement conditions (in deuteriochloroform at 35°), **7a** was completely transformed into a mixture of **10a** and benzaldehyde within thirty minutes, whereas **6a** was stable and remained unchanged after several hours.