Acid-Catalyzed Reactions of 3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridines

Yasuyoshi Miki*, Osamu Tomii, Hayami Nakao, Mayumi Kubo,
Hiroko Hachiken, and Shoji Takemura

Faculty of Pharmaceutical Sciences, Kinki University, 3-4-1, Kowakae,
Higashi-Osaka 577, Japan

Masazumi Ikeda

Kyoto Pharmaceutical University, Misasagi, Yamashina,
Kyoto 607, Japan

Received July 17, 1987

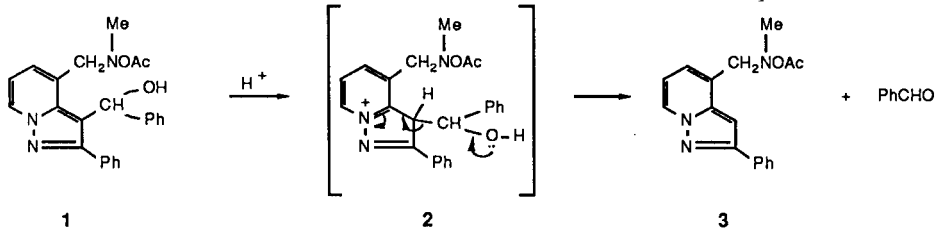
Treatment of 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]pyridines with trifluoroacetic acid in dichloromethane resulted in the formation of pyrazolo[1,5-*a*]pyridines, bis[α-(pyrazolo[1,5-*a*]pyrid-3-yl)benzyl] ethers, and phenylbis(pyrazolo[1,5-*a*]pyrid-3-yl)methanes, depending upon the presence or absence of the substituents at the 2- and/or 4-positions and the reaction conditions employed.

J. Heterocyclic Chem., **25**, 327 (1988).

In a previous paper [1] we described that the reaction of 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]pyridine **1** with a dilute acid resulted in the extrusion of benzaldehyde to give the pyrazolo[1,5-*a*]pyridine **3** in quantitative yield. This reaction is assumed to proceed *via* initial protonation at the 3-position of the pyrazolo[1,5-*a*]pyridine ring followed by retro-aldol-like reaction of the resulting intermediate **2** to give **3** (Scheme 1). We now examined the effect of the substituents at the 2- and/or 4-positions on this reaction. In this paper we report the sharply contrasting behavior of various substituted 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]-pyridine derivatives.

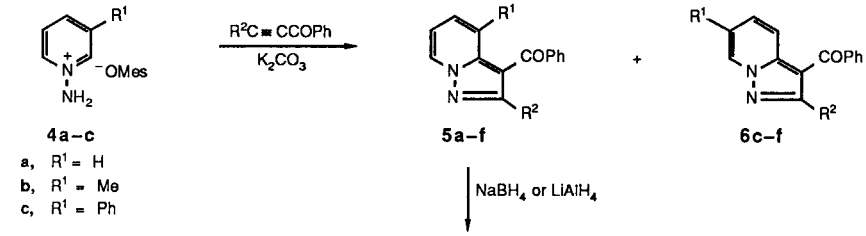
The starting 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]pyridines **7a-f** were prepared by using well established procedure [2] as outlined in Scheme 2. Although the 3-benzoylpyrazolo[1,5-*a*]pyridines **5a-c,e** were smoothly

Scheme 1



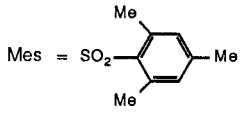
1 **2** **3**

Scheme 2



4a–c

a, R^1 = H
b, R^1 = Me
c, R^1 = Ph

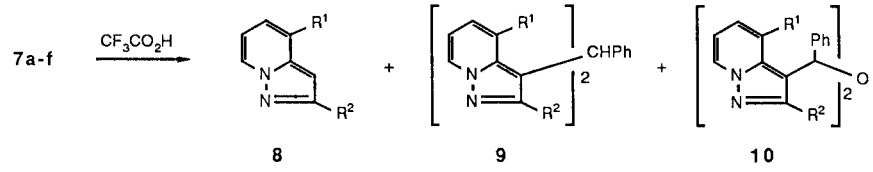
Mes = 

5a–f **6c–f**

7a–f

a, R^1 = R^2 = H; **b**, R^1 = H, R^2 = Ph
c, R^1 = Me, R^2 = H; **d**, R^1 = Me, R^2 = Ph
e, R^1 = Ph, R^2 = H; **f**, R^1 = R^2 = Ph

Scheme 3



reduced with sodium borohydride in methanol to give the corresponding alcohols **7a-c,e**, conversion of the ketones **5d** and **5f** to the alcohols **7d** and **7f** was achieved only by reduction with lithium aluminium hydride in tetrahydrofuran.

Treatment of 4-methyl-2-phenyl derivative **7d** with trifluoroacetic acid (0.01 equivalent) in refluxing dichloromethane gave only the pyrazolo[1,5-*a*]pyridine **8d** (83%) with the extrusion of benzaldehyde. The 2,4-diphenyl derivative **7f** also underwent conversion to **8f** in 94% yield.

On the other hand, similar treatment of **7a** led only to the bis[α-(3-pyrazolo[1,5-*a*]pyrid-3-yl)benzyl] ether **10a** in 94% yield. Interestingly, when treated with 2.5 equivalents of trifluoroacetic acid in refluxing dichloromethane, **7a** gave the phenylbis(pyrazolo[1,5-*a*]pyrid-3-yl)methane **9a** in 96% yield. It was then found that the ether **10a** was completely transformed into **9a** under the same conditions. Similar behavior was also observed with the 4-methyl derivative **7c** and the 4-phenyl derivative **7e**, which gave the ethers **10c,e** and the phenylbis(pyrazolo-[1,5-*a*]pyrid-3-yl)methanes **9c,e**, respectively, depending upon the reaction conditions. The 2-phenyl derivative **7b** showed the intermediate behavior between **7a** and **7d**. These results are summarized in Table 1.

The structures of these products were assigned on the basis of the elemental analyses and the spectroscopic evidence (see Experimental). The stereochemistry of **10** is unclear at present time.

A plausible mechanism for the formation of **8-10** is outlined in Scheme 4. The types of products observed depend upon the presence or absence of the substituents at

Scheme 4

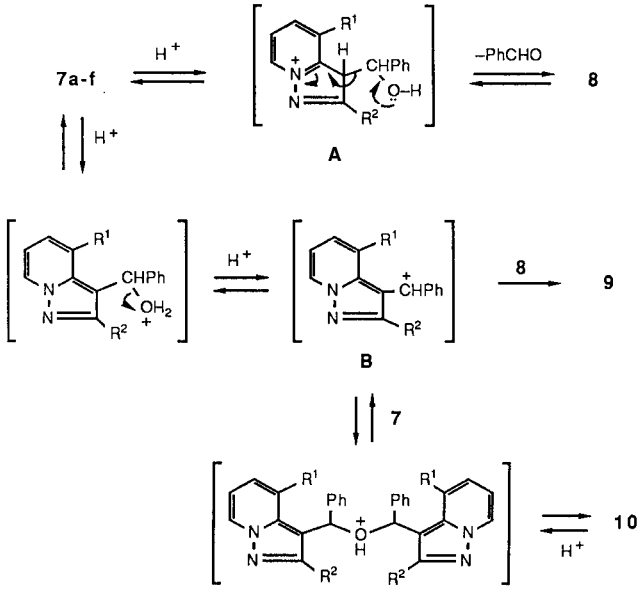


Table 1

Reaction of 3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridines **7a-f** with Trifluoroacetic Acid

7	R^1	R^2	CF_3COOH (equivalents)	Reaction Conditions [a] Temperature	Time (hours)	Yield (%) **8**	**9**	**10**
a	H	H	2.5	reflux	1	–	96	–
			0.01	reflux	1	–	–	94
b	H	Ph	2.5	rt	1	5	94	–
			0.01	reflux	2	57	28	–
c	CH_3	H	2.5	rt	1	–	75	–
			0.01	reflux	30	–	–	87
d	CH_3	Ph	2.5	rt	2	80	–	–
			0.01	reflux	0.5	83	–	–
e	Ph	H	2.5	[b]		–	68	–
			0.01	[b]		–	–	98
f	Ph	Ph	2.5	rt	0.5	92	–	–
			0.01	reflux	1.5	94	–	–

[a] All reactions were carried out in dichloromethane. [b] After refluxed for 3 hours, the reaction mixture was stirred at room temperature for 20 hours.

the 2- and/or 4-positions and the reaction conditions employed. 3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridine derivatives lacking phenyl group at the 2-position, the formation of **9** and **10** is the favored reaction pathways. Both processes involve the benzylic carbenium ion intermediates **B** which combine with either **7** or **8**. However, in the case of **7d** and **7f** the bulky substituents at the 2- and 4-positions inhibit an attack of **7** or **8** on the benzylic carbenium ion intermediates **B** and thus the extrusion of benzaldehyde becomes the sole reaction course. In mechanistic details, the behavior of 3-(α-hydroxybenzyl)pyrazolo-[1,5-*a*]pyridines toward acid is closely related to that of well documented behavior of 3-hydroxymethylindoles under the acidic conditions [3].

EXPERIMENTAL

All melting points 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 a Hitachi EPI-G2 spectrophotometer. The low resolution mass spectra were recorded on a M-70 JMX-HX100 spectrometer at 70 eV.

N-Amino-3-phenylpyridinium Mesitylenesulfonate (**4c**).

To a stirred solution of 3-phenylpyridine (3.10 g, 20 mmoles) in dichloromethane (40 ml) was added a solution of *O*-mesitylenesulfonylhydroxylamine [4] (6.14 g, 70% assay, 20 mmoles) in dichloromethane (40 ml) under ice-cooling and the reaction mixture was left at room temperature for 1 hour. Addition of ether to the mixture gave a precipitate, which was collected and recrystallized from ethyl acetate-methanol to give **4c** (6.88 g, 93%), mp 103-104°.

Anal. Calcd. for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99; N, 7.56. Found: C, 65.01; H, 5.83; N, 7.55.

3-Benzoylpyrazolo[1,5-*a*]pyridines **5** and **6**. General Procedure.

To a suspension of the *N*-aminopyridinium mesitylenesulfonate **4a-c** (10 mmoles) and potassium carbonate (12 mmoles) in tetrahydrofuran (100 ml) was added 1-phenyl-2-propyn-1-one or 1,3-diphenyl-2-propyn-1-one (10 mmoles). The reaction mixture was stirred at room temperature overnight. The insoluble material was filtered off and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel.

3-Benzoylpyrazolo[1,5-*a*]pyridine (**5a**).

Compound **5a** was obtained in 64% yield, mp 100-101° (methanol); ir (Nujol): 1635 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.07 (dt, 1H, J = 7, 1.5 Hz, H-6), 7.5-7.6 and 7.8-7.9 (m, 6H, H-5 and Ph), 8.30 (s, 1H, H-2), 8.48 (dt, 1H, J = 9, 1.5 Hz, H-4), and 8.60 (dt, 1H, J = 7, 1.5 Hz, H-7).

Anal. Calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.59; H, 4.52; N, 12.62.

3-Benzoyl-2-phenylpyrazolo[1,5-*a*]pyridine (**5b**).

Compound **5b** was obtained in 61% yield, mp 110-111° (lit [5] mp 110°).

3-Benzoyl-4-methyl- (**5c**) and 3-Benzoyl-6-methyl-pyrazolo[1,5-*a*]pyridines (**6c**).

Reaction of **4b** (1.54 g, 5 mmoles) and 1-phenyl-2-propyn-1-one (0.65 g, 5 mmoles) as described in General Procedure afforded a mixture of **5c** and **6c**, which was separated by column chromatography on silica gel. Elution with *n*-hexane/ether (2:1) gave **5c** (0.48 g, 41%) and **6c** (0.21 g, 18%).

Compound **5c** had mp 79-80° (*n*-hexane); ir (Nujol): 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.72 (s, 3H, CH_3), 6.97 (t, 1H, J = 7 Hz, H-6), 7.24 (br d, 1H, J = 7 Hz, H-5), 7.5-7.7 and 7.9-8.0 (m, 5H, Ph), 8.12 (s, 1H, H-2), and 8.48 (br d, 1H, J = 7 Hz, H-7).

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.30; H, 4.94; N, 11.89.

Compound **6c** had mp 135-136° (methanol); ir (Nujol): 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.44 (s, 3H, CH_3), 7.40 (dd, 1H, J = 9, 1.5 Hz, H-5), 7.5-7.6 and 7.8-7.9 (m, 5H, Ph), 8.24 (s, 1H, H-2), 8.38 (br d, 1H, J = 9 Hz, H-4), and 8.40 (br s, 1H, H-7).

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.34; H, 5.18; N, 11.88.

3-Benzoyl-4-methyl- (**5d**) and 3-Benzoyl-6-methyl-2-phenyl-pyrazolo[1,5-*a*]-pyridines (**6d**).

Reaction of **4b** (9.37 g, 30.4 mmoles) and 1,3-diphenyl-2-propyn-1-one (6.30 g, 30.6 mmoles) as described in General Procedure gave a mixture of **5d** and **6d**, which was separated by column chromatography on silica gel. Elution with *n*-hexane containing gradually increasing amounts of ethyl acetate yielded **5d** (5.40 g, 57%) and **6d** (2.40 g, 25%).

Compound **5d** had mp 163-164° (ethanol); ir (Nujol): 1640 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.34 (s, 3H, CH_3), 6.87 (t, 1H, J = 7 Hz, H-6), 7.06 (dq, 1H, J = 7, 1 Hz, H-5), 7.2-7.6 and 7.75-7.85 (m, 10H, 2 x Ph), and 8.48 (br d, 1H, J = 7 Hz, H-7).

Anal. Calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.92; H, 5.24; N, 9.04.

Compound **6d** had mp 160-162° (methanol); ir (Nujol): 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.43 (s, 3H, CH_3), 7.1-7.6 (m, 11H, H-5 and 2 x Ph), 7.98 (dd, 1H, J = 9, 1 Hz, H-4), and 8.40 (dd, 1H, J = 2, 1 Hz, H-7).

Anal. Calcd. for $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.94; H, 5.28; N, 9.17.

3-Benzoyl-4-phenyl- (**5e**) and 3-Benzoyl-6-phenylpyrazolo[1,5-*a*]pyridines (**6e**).

Reaction of **4c** (2.20 g, 6 mmoles) and 1-phenyl-2-propyn-1-one (0.78 g, 6 mmoles) as described in General Procedure afforded a mixture of **5e** and **6e**, which was separated by column chromatography on silica gel. Elution with *n*-hexane containing gradually increasing amounts of ethyl acetate gave **5e** (0.85 g, 48%) and **6e** (0.17 g, 10%).

Compound **5e** had mp 142-143° (methanol); ir (Nujol): 1650 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.12 (t, 1H, J = 7 Hz, H-6), 7.25-7.75 (m, 11H, H-5 and 2 x Ph), 8.25 (s, 1H, H-2), and 8.65 (dd, 1H, J = 7, 1 Hz, H-7).

Anal. Calcd. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.82; H, 4.65; N, 9.33.

Compound **6e** had mp 238-239° (benzene); ir (Nujol): 1630 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.5-8.0 (m, 10H, 2 x Ph), 7.84 (dd, 1H, J = 9, 2 Hz, H-5), 8.36 (s, 1H, H-2), 8.56 (dd, 1H, J = 9, 2 Hz, H-4), and 8.84 (dd, 1H, J = 2, 1 Hz, H-7).

Anal. Calcd. for $C_{20}H_{14}N_2O$: C, 80.52; H, 4.73; N, 9.39. Found: C, 80.38; H, 4.76; N, 9.33.

3-Benzoyl-2,4-diphenyl- (**5f**) and 3-Benzoyl-2,6-diphenylpyrazolo[1,5-*a*]-pyridines (**6f**).

Reaction of **4c** (1.48 g, 4 mmoles) and 1,3-diphenyl-2-propyn-1-one (0.82 g, 4 mmoles) as described in General Procedure yielded a mixture of **5f** and **6f**, which was separated by column chromatography on silica gel. Elution with benzene containing gradually increasing amounts of ethyl acetate afforded **5f** (0.66 g, 44%) and **6f** (0.34 g, 23%).

Compound **5f** had mp 142-143° (methanol); ir (Nujol): 1660 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.01 (t, 1H, J = 7 Hz, H-6), 7.1-7.75 (m, 16H, H-5 and 3 x Ph), and 8.64 (dd, 1H, J = 7, 1 Hz, H-7).

Anal. Calcd. for $C_{26}H_{18}N_2O$: C, 83.40; H, 4.85; N, 7.48. Found: C, 83.26; H, 4.66; N, 7.53.

Compound **6f** had mp 166-167° (ethanol); ir (Nujol): 1635 (C=O) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 6.74 (dd, 1H, J = 9, 1.5 Hz, H-5), 7.2-7.8 (m, 15H, 3 x Ph), 8.15 (dd, 1H, J = 9, 1 Hz, H-4), and 8.86 (dd, 1H, J = 1.5, 1 Hz, H-7).

Anal. Calcd. for $C_{25}H_{18}N_2O$: C, 83.40; H, 4.85; N, 7.48. Found: C, 83.64; H, 4.71; N, 7.48.

3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridines **7a-f**. General Procedure.

Method A: To a solution of the 3-benzoylpyrazolo[1,5-*a*]pyridine **5a-c,e** (5 mmoles) in methanol (20 ml) was added sodium borohydride (30 mmoles) and the reaction mixture was stirred at room temperature for 1 hour. The mixture was diluted with water and extracted with chloroform. The extract was dried over sodium sulfate and concentrated. The residue was recrystallized from an appropriate solvent to give the corresponding alcohol **7a-c,e**.

3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridine (**7a**).

Compound **7a** was obtained in 97% yield, mp 84-85° (cyclohexane); ir (Nujol): 3300 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.58 (br d, 1H, J = 3 Hz, OH), 6.15 (br d, 1H, J = 3 Hz, C*H*-Ph), 6.73 (dt, 1H, J = 7, 2 Hz, H-6), 7.05 (ddd, 1H, J = 9, 7, 1 Hz, H-5), 7.3-7.5 (m, 6H, H-4 and Ph), 7.75 (s, 1H, H-2), and 8.40 (dt, 1H, J = 7, 1 Hz, H-7).

Anal. Calcd. for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39; N, 12.49. Found: C, 74.87; H, 5.64; N, 12.49.

3-(α-Hydroxybenzyl)-2-phenylpyrazolo[1,5-*a*]pyridine (**7b**).

Compound **7b** was obtained in 95% yield, mp 139-140° (cyclohexane-ethyl acetate); ir (Nujol): 3200 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.52 (d, 1H, J = 4 Hz, OH), 6.27 (d, 1H, J = 4 Hz, C*H*-Ph), 6.71 (dt, 1H, J = 7 , 1.5 Hz, H-6), 6.94 (ddd, 1H, J = 9, 7, 1 Hz, H-5), 7.1-7.8 (m, 11H, H-4 and 2 x Ph), and 8.42 (dt, 1H, J = 7, 1 Hz, H-7).

Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33. Found: C, 79.80; H, 5.27; N, 9.29.

3-(α-Hydroxybenzyl)-4-methylpyrazolo[1,5-*a*]pyridine (**7c**).

Compound **7c** was obtained in 98% yield, mp 93-94° (cyclohexane); ir (Nujol): 3200 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.37 (d, 1H, J = 4 Hz, OH), 2.64 (s, 3H, CH_3), 6.37 (d, 1H, J = 4 Hz, C*H*-Ph), 6.68 (t, 1H, J = 7 Hz, H-6), 6.90 (br d, 1H, J = 7 Hz, H-5), 7.3-7.5 (m, 5H, Ph), 7.59 (s, 1H, H-2), and 8.31 (d, 1H, J = 7 Hz, H-7).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.55; H, 6.04; N, 11.68.

3-(α-Hydroxybenzyl)-4-phenylpyrazolo[1,5-*a*]pyridine (**7e**).

Compound **7e** was obtained in 90% yield, mp 135-137° (dichloromethane-ether): ir (Nujol): 3250 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.87 (d, 1H, J = 4 Hz, OH), 5.61 (d, 1H, J = 4 Hz, C*H*-Ph), 6.84 (t, 1H, J = 7 Hz, H-6), 7.02 (dd, 1H, J = 7, 1 Hz, H-5), 7.1-7.5 (m, 10H, 2 x Ph), 7.82 (s, 1H, H-2), and 8.50 (dd, 1H, J = 7, 1 Hz, H-7).

Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 79.98; H, 5.37; N, 9.33. Found: C, 79.77; H, 5.48; N, 9.41.

Method B: A suspension of **5d,f** (1 mmole) and lithium aluminium hydride (2 mmoles) in tetrahydrofuran (10 ml) was stirred at room temperature for 0.5-1 hour. After an excess of lithium aluminium hydride was destroyed by addition of a saturated Rochelle salt solution, the precipitate was filtered off and the filtrate was concentrated. The residue was purified by column chromatography [silica gel: benzene/ethyl acetate (10:1)].

3-(α-Hydroxybenzyl)-4-methyl-2-phenylpyrazolo[1,5-*a*]pyridine (**7d**).

Compound **7d** was obtained in 96% yield, mp 192-194° (benzene); ir (Nujol): 3150 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 2.18 (s, 3H, CH_3), 2.42 (d, 1H, J = 4 Hz, OH), 6.42 (d, 1H, J = 4 Hz, C*H*-Ph), 6.73 (t, 1H, J = 7 Hz, H-6), 6.86 (dq, 1H, J = 7, 1 Hz, H-5), 7.2-7.6 (m, 10H, 2 x Ph), and 8.42 (br d, 1H, J = 7 Hz, H-7).

Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91. Found: C, 80.36; H, 5.92; N, 8.94.

3-(α-Hydroxybenzyl)-2,4-diphenylpyrazolo[1,5-*a*]pyridine (**7f**).

Compound **7f** was obtained in 81% yield, mp 158-159° (cyclohexane); ir (Nujol): 3400 (OH) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.86 (d, 1H, J = 8 Hz, OH), 5.81 (d, 1H, J = 8 Hz, C*H*-Ph), 6.88 (t, 1H, J = 7 Hz, H-6), 6.97 (dd, 1H, J = 7, 1.5 Hz, H-5), 7.1-7.6 (m, 15H, 3 x Ph), and 8.60 (dd, 1H, J = 7, 1.5 Hz, H-7).

Anal. Calcd. for $C_{26}H_{20}N_2O$: C, 82.95; H, 5.36; N, 7.44. Found: C, 83.23; H, 5.40; N, 7.50.

Reaction of 3-(α-Hydroxybenzyl)pyrazolo[1,5-*a*]pyridines (**7**) with Trifluoroacetic Acid. General Procedure.

A solution of the 3-(α-hydroxybenzyl)pyrazolo[1,5-*a*]pyridine **7a-f** (1 mmole) and trifluoroacetic acid (0.01 mmole or 2.5 mmoles) in dichloromethane (10 ml) was stirred at room temperature or refluxed. After the reaction mixture was neutralized with 5% sodium bicarbonate 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 preparative thin layer chromatography (silica gel, benzene-ethyl acetate). These results are summarized in Table 1.

Phenylbis(pyrazolo[1,5-*a*]pyrid-3-yl)methane (**9a**).

Compound **9a** was obtained as an oil [monopicrate, mp 187-188° (acetone)]; ^{1}H-nmr (deuteriochloroform): δ 5.80 (s, 1H, C*H*-Ph), 6.69 (dt, 2H, J = 7, 1.5 Hz, 2 x H-6), 6.93 (ddd, 2H, J = 9, 7, 1 Hz, 2 x H-5), 7.10 (ddd, 2H, J = 9, 1.5, 1 Hz, 2 x H-4), 7.2-7.3 (m, 5H, Ph), 7.60 (s, 2H, 2 x H-2), and 8.42 (dt, 2H, J = 7, 1 Hz, 2 x H-7); ms: m/z 324 M^+.

Anal. Calcd. for $C_{27}H_{19}N_7O_7$ (monopicrate): C, 58.58; H, 3.47; N, 17.72. Found: C, 58.38; H, 3.40, N, 17.66.

Bis[α-(pyrazolo[1,5-*a*]pyrid-3-yl)benzyl] Ether (**10a**).

Compound **10a** had mp 149-151° (benzene-*n*-hexane); ^{1}H-nmr (deuteriochloroform): δ 5.72 and 5.74 (s each, 2 x 1H, 2 x O-C*H*-Ph), 6.70 (br t, 2H, J = 7 Hz, 2 x H-6), 6.93 and 6.97 (ddd each, 2 x 1H, J = 9, 7, 1 Hz, 2 x H-5), 7.18 (br d, 2H, J = 9 Hz, 2 x H-4), 7.2-7.5 (m, 10H, 2 x Ph), 7.80 and 7.82 (s each, 2 x 1H, 2 x H-2), and 8.42 (dt, 2H, J = 7, 1 Hz, 2 x H-7); ms: m/z 430 M^+.

Anal. Calcd. for $C_{28}H_{22}N_4O$: C, 78.12; H, 5.15; N, 13.01. Found: C, 78.09; H, 5.20; N, 13.11.

2-Phenylpyrazolo[1,5-*a*]pyridine (**8b**).

Compound **8b** had mp 109-111° (methanol) (lit [6] mp 109°).

Phenylbis(2-phenylpyrazolo[1,5-*a*]pyrid-3-yl)methane (**9b**).

Compound **9b** had mp 125-126° (cyclohexane); ^{1}H-nmr (deuteriochloroform): δ 6.10 (s, 1H, C*H*-Ph), 6.52 (ddd, 2H, J = 9, 1.5, 1 Hz, 2 x H-4), 6.68 (dt, 2H, J = 7, 1.5 Hz, 2 x H-6), 6.82 (ddd, 2H, J = 9, 7, 1 Hz, 2 x H-5), 7.1-7.4 (m, 15H, 3 x Ph), and 8.45 (dt, 2H, J = 7, 1 Hz, 2 x H-7); ms: m/z 476 M^+.

Anal. Calcd. for $C_{33}H_{24}N_4$: C, 83.17; H, 5.08; N, 11.76. Found: C, 83.38; H, 5.34; N, 11.65.

Phenylbis(4-methylpyrazolo[1,5-*a*]pyrid-3-yl)methane (**9c**).

Compound **9c** had mp 196-197° (cyclohexane); ^{1}H-nmr (deuteriochloroform): δ 2.43 (s, 6H, 2 x CH_3), 6.46 (s, 1H, C*H*-Ph), 6.62 (t, 2H, J = 7 Hz, 2 x H-6), 6.74 (br d, 2H, J = 7 Hz, 2 x H-5), 7.1-7.3 (m, 5H, Ph), 7.34 (s, 2H, 2 x H-2), and 8.32 (br d, 2H, J = 7 Hz, 2 x H-7); ms: m/z 352 M^+.

Anal. Calcd. for $C_{23}H_{20}N_4$: C, 78.38; H, 5.72; N, 15.90. Found: C, 78.53; H, 5.91; N, 15.60.

Bis[α-(4-methylpyrazolo[1,5-*a*]pyrid-3-yl)benzyl] Ether (**10c**).

Compound **10c** had mp 62-65° (ether-petroleum ether); ^{1}H-nmr (deuteriochloroform): δ 2.02 and 2.05 (s each, 2 x 3H, 2 x CH_3), 5.97 and 6.01 (s each, 2 x 1H, 2 x O-C*H*-Ph), 6.5-6.8 (m, 4H, 2 x H-5 and 2 x H-6), 7.1-7.5 (m, 10H, 2 x Ph), 7.97 and 8.01 (s each, 2 x 1H, 2 x H-2), and 8.26 and 8.31 (br d each, 2 x 1H, J = 7 Hz, 2 x H-7); ms: m/z 458 M^+.

Anal. Calcd. for $C_{30}H_{26}N_4O$: C, 78.58; H, 5.71; N, 12.22. Found: C, 78.70; H, 5.92; N, 11.76.

4-Methyl-2-phenylpyrazolo[1,5-*a*]pyridine (**8d**).

Compound **8d** had mp 77-78° (*n*-hexane) (lit [7] mp 77-78°).

Phenylbis(4-phenylpyrazolo[1,5-*a*]pyrid-3-yl)methane (**9e**).

Compound **9e** had mp 180-181° (cyclohexane); ^{1}H-nmr (deuteriochloroform): δ 4.85 (s, 1H, C*H*-Ph), 6.26 (br d, 2H, J = 7 Hz, 2 x H-5), 6.7-7.3 (m, 17H, 2 x H-6 and 3 x Ph), 7.40 (s, 2H, 2 x H-2), and 8.45-8.55 (m, 2H, 2 x H-7); ms: m/z 476 M$^+$.

Anal. Calcd. for $C_{33}H_{24}N_4$: C, 83.17; H, 5.08; N, 11.76. Found: C, 83.47; H, 4.96; N, 11.82.

Bis[α-(4-phenylpyrazolo[1,5-*a*]pyrid-3-yl)benzyl] Ether (**10e**).

Compound **10e** had mp 183-186° (*n*-hexane-ethyl acetate); ^{1}H-nmr (deuteriochloroform): δ 5.04 and 5.13 (s each, 2 x 1H, 2 x O-C*H*-Ph), 6.5-7.2 (m, 24H, 2 x H-5, 2 x H-6, and 4 x Ph), 8.12 and 8.15 (s each, 2 x 1H, 2 x H-2), and 8.4-8.55 (m, 2H, 2 x H-7); ms: m/z 582 M$^+$.

Anal. Calcd. for $C_{40}H_{30}N_4O$: C, 82.45; H, 5.19; N, 9.62. Found: C, 82.50; H, 5.13; N, 9.63.

2,4-Diphenylpyrazolo[1,5-*a*]pyridine (**8f**).

Compound **8f** had mp 150-151° (benzene-*n*-hexane); ^{1}H-nmr (deuteriochloroform): δ 6.88 (t, 1H, J = 7 Hz, H-6), 7.00 (d, 1H, J = 1 Hz, H-3), 7.16 (dd, 1H, J = 7, 1 Hz, H-5), 7.3-7.8 and 7.95-8.05 (m, 10H, Ph), and 8.54 (br d, 1H, J = 7 Hz, H-7).

Anal. Calcd. for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22; N, 10.36. Found: C, 84.32; H, 5.22; N, 10.28.

Transformation of **10a,c,e** into **9a,c,e**. General Procedure.

To a solution of **10a** (43 mg, 0.1 mmole) in dichloromethane (1 ml) was added trifluoroacetic acid (0.25 mmole) and the reaction mixture was stirred at room temperature for 24 hours. 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 preparative thin layer chromatography (silica gel, benzene-ethyl acetate) to give **9a** (32 mg, 99%).

Similar treatment of **10c** (46 mg) with trifluoroacetic acid in hot dichloromethane for 8 hours gave **9c** (30 mg, 86%).

Similar treatment of **10e** (58 mg) with trifluoroacetic acid in hot dichloromethane for 12 hours gave **9e** (31 mg, 65%) and **10e** (10mg, 17%).

REFERENCES AND NOTES

[1] Y. Miki, O. Tomii, M. Utsunomiya, S. Takemura, and M. Ikeda, *Chem. Pharm. Bull.*, **34**, 3588 (1986).

[2] Y. Miki, N. Nishikubo, Y. Nomura, H. Kinoshita, S. Takemura, and M. Ikeda, *Heterocycles*, **22**, 2467, (1984) and references cited therein.

[3] W. A. Demers and T. F. Spande, in "The Chemistry of Heterocyclic Compounds", Vol **25** Part **III**, W. J. Houlihan, ed, John Wiley and Sons, Inc, New York, NY, 1979, p 174.

[4] Y. Tamura, J. Minamikawa, Y. Miki, S. Matsugashita, and M. Ideda, *Tetrahedron Letters*, 4133, (1972).

[5] K. T. Potts, U. P. Singh, and J. Bhattacharyya, *J. Org. Chem.*, **33**, 3766 (1968).

[6] J. D. Bower and G. R. Ramaga, *J. Chem. Soc.*, 4506 (1957).

[7] Y. Miki, M. Uragi, S. Takemura, and M. Ikeda, *J. Chem. Soc., Perkin Trans. I*, 379 (1985).