Scheme II). Crown **3** was prepared with some modifications by the method developed by Bradshaw and co-workers for obtaining similar crowns.[6,11] A mixture of 401 mg (1.31 mmol) of **7**, 256 mg (1.31 mmol) of dimethyl 2,6-pyridinedicarboxylate, and 35 mg (0.65 mmol) of $NaOCH_3$ was combined with 120 mL of dry benzene in a flask equipped with a Soxhlet apparatus. Molecular sieves (4 Å, 10 g) were placed in the extraction thimble, and the mixture was refluxed through the Soxhlet for 32 h. Because the TLC (THF/isopropyl ether (1/8)) showed that the diester was consumed but not the diol, another 100 mg (0.51 mmol) of diester was added and the mixture was refluxed for another 24 h. The cold mixture was acidified with 0.2 mL of glacial acetic acid, and the solvent was removed under reduced pressure. Ice (10 g) and 50 mL of CH_2Cl_2 were added to the residue, the resulting mixture was shaken, and the phases were separated. The organic phase was dried ($MgSO_4$) and filtered, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (THF/toluene (1/8)). The resulting solid was recrystallized from hexane to give 85 mg (15%) of white crystals: mp 96-97 °C; $[\alpha]^{25}_D$ -24.33° (c = 0.825, benzene); ^1H NMR δ 1.05 (18 H, s), 3.38-3.87 (12 H, m), 5.2 (2 H, t, J = 8 Hz), 7.95 (1 H, t), 8.12 (2 H, d, J = 10 Hz); MS m/e 437 (M^+). Anal. Calcd for $C_{23}H_{35}NO_7$: C, 63.14; H, 8.06. Found: C, 63.18; H, 8.13.

Determination of ΔG_c^* Values. ΔG_c^* values listed in Table I were determined as reported.[5-8,15]

Determination of log K Values by the Direct ^1H NMR Method. The log K values listed in Table II were determined as reported.[10] A sample containing a few milligrams of macrocycle in a known volume of solvent was first loaded into the probe, and a spectrum was taken. The sample was then unloaded, added to the sample tube with a small amount of the ammonium salt, and reloaded into the probe, and another spectrum was taken. This process was repeated until no significant change was observed in successive ^1H NMR spectra. Usually 8-12 spectra were taken for each log K determination. The crown ether concentrations were ~0.01-0.015 M and the ammonium salt concentrations varied from 0.0 M to ~0.06 M for each of the experiments. In such experiment, an accurately weighed quantity of the crown ether was dissolved in a known volume of solvent at 25.0 °C. The analytical balance used was calibrated for accuracy using a standard weight from the National Institute of Standards and Technology. The salt concentrations were calculated on the basis of the integral ratio of a particular ammonium salt signal to a particular crown ether signal in the spectra. In order to obtain a quantitative integration, the time delay between the two pulses for each NMR acquisition was set long enough to allow sufficient relaxation of the signals of interest. The log K values were then calculated from the differences in chemical shift values as reported.[10]

Acknowledgment. This work was supported by the Office of Naval Research.

Supplementary Material Available: ^1H NMR spectra for compounds **6-8**, **11-18**, and **20** (12 pages). Ordering information is given on any current masthead page.

Base-Catalyzed Alkylation of 2-Naphthol with Glyoxal

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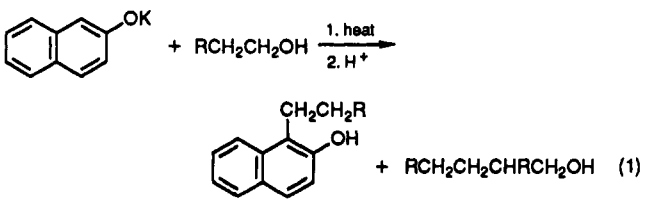
Received June 28, 1990

Alkylation of potassium 2-naphthyl oxide with glyoxal in aqueous media formed 1,2-dihydronaphtho[2,1-*b*]furan-1,2-diol (**1**). Without isolation of **1**, acidification of this reaction mixture with aqueous HCl led to three products, i.e., the lactone of (2-hydroxy-1-naphthyl)acetic acid (**2**), the hemiacetal of bis(2-hydroxy-1-naphthyl)acetaldehyde (**3**), and the corresponding acetal (**4**). Mutual interconversions of **1** and these three products revealed the reaction pathway and the mechanisms of formation of the lactone and the acetal.

Introduction

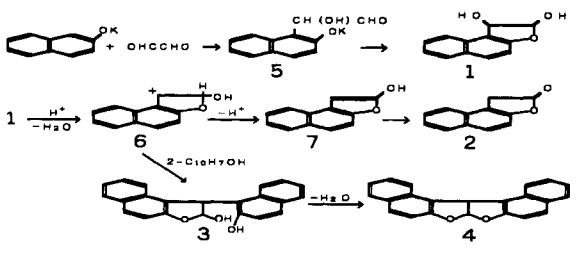
We have reported the base-catalyzed reaction of 2-naphthol with a primary alcohol (e.g., 1-butanol) to form 1-alkyl-2-naphthols and 2-alkyl-substituted alkanols.[2]



Use of benzyl alcohol as the primary alcohol produces only 1-benzyl-2-naphthol. Based on the isolation of three precursors for this reaction, we proposed an aldehyde mechanism, i.e., benzaldehyde as the key intermediate to initiate the reaction.[3] In an extension of our project to the use of dialdehydes, we here report the base-catalyzed alkylation of 2-naphthol with glyoxal.

The reaction of either phenols or naphthols with glyoxal has been reported by several investigators, including

Scheme I



Dischendorfer,[4] McGowan, Anderson, and Walker,[5] and Coxworth.[6] Although there had been discrepancies in structural analyses for the condensation products, Coxworth finally characterized them as the acetal type, rather than the ether type, by means of ^1H NMR spectroscopy.[6] For example, the reaction of glyoxal with 2-naphthol in acidic media gave 7a,14c-dihydronaphtho[2,1-*b*]naphtho-[2′,1′:5,6]furo[3,2-*d*]furan (**4**).[6]

Recently, Maravigna synthesized thermally stable polymers containing the furofuran skeleton by condensa-

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0022-3263/91/1956-3336$02.50/0 © 1991 American Chemical Society

tion of glyoxal with 2,6- and 2,7-dihydroxynaphthalenes.[7] However, these reported reactions were all carried out in acidic rather than basic media.

Results and Discussion

In our investigation of the base-catalyzed alkylation of 2-naphthol with glyoxal, we were able to isolate four products. By IR, NMR, and mass spectral analyses, their structures were determined as 1,2-diol **1**, lactone **2**, hemiacetal **3**, and furofuran **4** (see Scheme I). The structures of **1** and **2** were confirmed by conversion to their respective diacetate (**8**) and methyl ester (**9**) derivatives.

The ratios of these four products varied widely with the reaction conditions and workup procedures. For example, **2** was the only product (73% yield) when an aqueous solution of potassium 2-naphthyl oxide was added dropwise to aqueous glyoxal and this mixture was treated with aqueous hydrochloric acid. On the other hand, **4** was the sole product when aqueous glyoxal was added to a tetrahydrofuran (THF) solution of potassium 2-naphthyl oxide, followed by acidification. Interconversions among products **1**, **2**, **3**, and **4** under various conditions were carried out as follows:

(a) Product **1** was heated in the presence of aqueous hydrochloric acid at 50 °C to give only **2** (92%).

(b) Product **1** was heated neat for 3 h at 80 °C to give **2** in 8% yield.

(c) A chloroform solution of **1** and 2-naphthol was refluxed with stirring for 2 h in the presence of aqueous hydrochloric acid to give a mixture of **2**, **3**, and **4**. The combined yield of **3** and **4** increased with increasing concentration of 2-naphthol.

(d) Heat treatment of **3** in aqueous hydrochloric acid gave only **4**, which was stable and remained unchanged under these conditions.

These experimental results are explained in Scheme I. Product **1** is a common precursor for **2** and **3**, which was confirmed experimentally. In the reaction of potassium 2-naphthyl oxide with glyoxal, none of **2**, **3**, or **4** were formed before addition of aqueous HCl. Formation of **5** is reasonable because, as reported before,[3] the reaction of potassium 2-naphthyl oxide with benzaldehyde gave 1-(α-hydroxybenzyl)-2-naphthol in good yield; **5**, in turn, is converted into the corresponding hemiacetal **1**. The unique feature of **1** is that it carries two hydroxyl groups, one being an alcoholic hydroxyl group on position 1 and the other a hemiacetal hydroxyl group on position 2. The oxygen atom of C_1-OH, more basic than that of C_2-OH, is susceptible to attack by an acid to yield, after removal of water, the carbonium ion **6**, a common intermediate for **2** and **3**. In the absence of 2-naphthol, **6** is readily converted into **7**, the enol form of **2**. With 2-naphthol, on the other hand, **6** is transformed into hemiacetal **3**, which gives acetal **4** in the presence of acid.

Another possible route for the formation of **2** via (2-hydroxy-1-naphthyl)acetic acid (**10**) was suggested by Laws' study.[8] In fact, **10** was found in our THF reaction mixture as a minor product, and the same product was almost exclusively converted into **2** when refluxed for 1 h in the presence of hydrochloric acid. However, this route is improbable because **1** cannot give **10** directly. The latter must be formed by hydrolysis of **2** (moisture slowly converts **2** into **10**[8]).

In the reactions of glyoxal with 2-naphthol reported by Dischendorfer (using glyoxal sodium bisulfite in place of glyoxal)[4] and Coxworth,[6] products **1** and **3** were not detected. However, it is reasonable that their reactions must proceed according to Scheme I, with 2-naphthol rather than potassium 2-naphthyl oxide. In their procedures, the reaction was carried out in acidic media in the presence of excess 2-naphthol. Under these conditions **1** must be a transient species to be converted chiefly via **3** into **4**, and not into **2**. The formation of **2** was, however, confirmed, indicating the intervention of **1**.

Gaseous glyoxal, in place of aqueous glyoxal solution, was introduced into a THF solution of 2-naphthol in the presence of sulfuric acid. In this experiment, a 42% conversion to bis(2-hydroxy-1-naphthyl)methane (**11**) was observed. It was reported that phenols having a free para position (e.g., phenol, 2,6-dimethylphenol, and thymol) give 1,1,2,2-tetrakis(4-hydroxyphenyl)ethane (**12**) or its derivatives, rather than the product corresponding to **11**, from condensations with glyoxal.[5,9,10] In our reaction, however, the product corresponding to **12**, a more sterically crowded product, was not detected.

Experimental Section

Proton and ^{13}C NMR spectra were recorded on a JEOL JNM-FX-60 spectrometer. MS spectra were obtained at 70 eV. Liquid chromatography was performed with an EYELA PLC-7 (Tokyo Rikakikai) chromatograph (column, Cica-MERCK RP-18). Melting points are uncorrected.

Typical examples are shown and the reaction conditions and products are summarized in Table I.

1,2-Dihydronaphtho[2,1-*b*]furan-1,2-diol (1). In a flask equipped with a mechanical stirrer was placed 40% aqueous glyoxal (120 g, 0.83 mol). A solution of 2-naphthol (20.0 g, 0.139 mol) in 280 mL of H_2O containing KOH (0.139 mol) was added dropwise at 30 °C over 1.5 h. The mixture was stirred at 30 °C for 3 h.

The precipitate formed during the reaction was collected on a filter, washed successively with $CHCl_3$ and H_2O, and dried in a vacuum oven to give **1** (29.9 g, 98%).

Addition of aqueous glyoxal to an aqueous solution of potassium 2-naphthyl oxide also gave **1** (24.7 g) in 81% yield.

1: mp 60 °C (from *n*-hexane); IR (KBr, cm^{-1}) 3400 (with a shoulder at 3500, broad and strong, ν_{OH}), 1140 (s), 800 (m), 740 (m) (the last two are characteristic of a 1,2-disubstituted naphthalene); ^1H NMR (DMSO-d_6) δ 5.25 (d, 1 H, J = 6.3 Hz, ArC*H*(OH)–) (This doublet changed into a singlet, whose top is not sharp upon addition of D_2O.), 5.7–5.9 (multiplet, 2 H, ArCH(OH)C*H*(OH)O- + 1 O*H*) (This multiplet changed into a narrow doublet (1 H) centered at 5.80 ppm after exchange with D_2O.), 7.1–7.9 (m, 7 H, Ar*H* + ArCH(OH)CH(O*H*)O-); ^{13}C NMR (DMSO-d_6) δ 76.9 (d, ArCH(OH)-), 108.9 (d), 112.6 (d), 119.7 (s), 122.7 (d), 123.1 (d), 127.0 (d), 128.7 (d), 129.0 (s), 130.8 (s), 131.1 (d), 156.9 (s) (The signal for ArCH(OH)CH(OH)-O- is in the aromatic region); MS *m/e* 202 (M^+, 48), 184 (53), 173 (87), 156 (55), 128 (base peak, 100), 127 (70). Anal. Calcd for $C_{12}H_{10}O_3 \cdot H_2O$: C, 65.44; H, 5.49. Found: C, 65.32; H, 5.39.

No **2**, **3**, or **4** were formed via **1** unless the reaction medium was made acidic with aqueous HCl.

Naphtho[2,1-*b*]furan-2(1*H*)-one (2). Method A. A mixture of $CHCl_3$ (20 mL), **1** (1.06 g, 0.00482 mol), and aqueous HCl (3 N, 25 mL) was stirred at 50 °C for 1 h. The $CHCl_3$ layer was separated from the mixture and analyzed by liquid chromatography. No products but **2** were detected. Evaporation of $CHCl_3$ gave **2** (0.815 g, 92%).

Method B. A mixture of $CHCl_3$ (30 mL), **1** (2.20 g, 0.01 mol), 2-naphthol (varied from 0.005 to 0.04 mol), and aqueous HCl (3 N, 20 mL) was refluxed with stirring for 2 h. After cooling, a precipitate of **3** was obtained by filtration (**3** was partially soluble in $CHCl_3$) and the aqueous layer was extracted with ether. The $CHCl_3$ layer and ether extract were combined and evaporated to

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Table I. Reaction Conditions and Products (Summary)

reaction[a]	solvent	conditions[b] °C/h	product (%)
2-Naph-OK + Gly →	H_2O	30/4.5	1 (98)
1 $\xrightarrow{HCl}$	$CHCl_3$/H_2O	50/1	2 (92)
1 + 2-Naph $\xrightarrow{HCl}$	$CHCl_3$/H_2O	refl/2	2, 3, 4[c]
2-Naph-OK + Gly →	H_2O	30/4	2 (73)
$\xrightarrow{HCl}$	$CHCl_3$/H_2O	50/2	
1 →	neat	80/3	2 (8)
10 $\xrightarrow{HCl}$	$CHCl_3$/H_2O	refl/1	2 (36)
2-Naph-OK + Gly →	H_2O–THF	30/4	2 (52), 3 (45), 4 (2)
$\xrightarrow{HCl}$	$CHCl_3$/H_2O	rt	
2-Naph-OK + Gly →	H_2O–THF	30/4	2 (47), 4 (48)
$\xrightarrow{acidification}$			
2-Naph-OK + Gly →	H_2O–THF	30/3.5	4 (92)
3 $\xrightarrow{HCl}$	H_2O	50/1	4 (43)
1 + Ac_2O →	pyridine	refl/2	8 (68)
2 + MeOH →	MeOH	refl/8	9 (77)
$\xrightarrow{H_2SO_4}$			
2-Naph-OK + Gly →	THF	40/2	10 (22)
$\xrightarrow{NaOH}$	H_2O–MeOH	refl/3	10 (93)
2-Naph-OH + Gly $\xrightarrow{H_2SO_4}$	THF	40/70 (min)	4 (27), 11 (42)

[a] 2-Naph-OH, 2-naphthol; Gly, glyoxal; glyoxal; symbol →→ means a two-step reaction. [b] refl, refluxed. [c] Yields varied depending on 2-naphthol/1 mol ratio.

dryness. Washing the residue with ether gave 4, an ether-insoluble product. The amounts of 2 and 3 dissolved in the ether were determined by liquid chromatography.

The amount of 2-naphthol (mol) and yields (%) of 2, 3, and 4 were 0.005, 10, 13, 9; 0.01, 12, 22, 9; 0.04, 1, 0, 52, respectively.

Method C. 2-Naphthol (12.6 g, 0.0875 mol) in 140 mL of H_2O containing KOH (0.0875 mol) was added dropwise to 40% aqueous glyoxal (60.4 g, 0.417 mol) at 30 °C over 1 h, and the resulting mixture was stirred at 30 °C for 3 h and then adjusted to pH 2 with HCl. After addition of $CHCl_3$, the mixture was stirred at 50 °C for 2 h. Evaporation of the $CHCl_3$ gave 2 (11.8 g, 73%) (63% after recrystallization from ethanol).

Method D. One gram of 1 was heated neat for 3 h at 80 °C to give 2. The yield (8%) was determined by liquid chromatography.

Method E. A mixture of 10 (0.31 g, 0.0015 mol), $CHCl_3$ (30 mL), and aqueous HCl (3 N, 20 mL) was refluxed with stirring for 1 h. After evaporation of the $CHCl_3$, neutralization with aqueous $NaHCO_3$ followed by extraction with ether gave only 2 (0.10 g, 36%).

2: mp 103 °C (from ethanol; lit.[8] mp 102–103 °C); IR (KBr, cm^{-1}) 1800 (s, $\nu_{C=O}$ of lactone), 860 (m), 805 (m), 760 (m), 750 (m); ^1H NMR ($CDCl_3$) δ 3.45 (s, 2 H, $ArCH_2CO$-), 6.9–7.7 (m, 6 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 31.9 (t, $ArCH_2CO$-), 111.3 (d), 116.5 (s), 122.8 (d), 124.8 (overlapping doublet and singlet), 127.5 (d), 129.0 (d), 129.5 (d), 130.3 (s), 152.0 (s), 174.3 (s, -*C*O-); MS *m/e* 184 (M^+, 58), 156 (44), 128 (base peak, 100). Anal. Calcd for $C_{12}H_8O_2$: C, 78.25; H, 4.38. Found: C, 78.12; H, 4.38.

1-(2-Hydroxy-1,2-dihydronaphtho[2,1-*b*]furan-1-yl)-2-naphthol (3). A THF solution (200 mL) of potassium 2-naphthyl oxide (31.4 g, 0.173 mol) was added dropwise to aqueous glyoxal (150 g, 1.03 mol) at 30 °C over 1 h and the resulting mixture stirred at 30 °C for 3 h. The upper (THF) layer was separated and dried (over $MgSO_4$) and the THF was evaporated. $CHCl_3$ and aqueous HCl were added to the residue and the mixture was stirred. The precipitate was collected by filtration to give 3 (12.7 g, 45%). After evaporation of the $CHCl_3$, 4 (0.54 g, 2%, as an ethanol-insoluble product) and 2 (16.6 g, 52%, recrystallized from ethanol) were also obtained.

In a second parallel experiment, aqueous HCl was added without separation of the THF layer. The resulting mixture was extracted with ether and then with $CHCl_3$. After evaporation of the combined extracts, 4 was obtained as an ether- and ethanol-insoluble product (12.9 g, 48%) and the residue was recrystallized from ethanol to give 2 (15.0 g, 47%). After evaporation of the ethanol, a trace amount of 10 was observed in the residue.

Hemiacetal 3: mp 152 °C; IR (KBr, cm^{-1}) 3400 (strong and broad), 870 (m), 800 (m), 740 (s, with a shoulder at 760); ^1H NMR (DMSO-d_6) δ 5.93 (d, J = 3 Hz, 1 H, ArC*H*Ar), 6.29 (d, J = 3 Hz, 1 H, ArOC*H*(OH)-), 7.0–8.6 (m, 12 H, Ar*H*), 9.46 (s, 1 H, O*H*), 10.37 (s, 1 H, O*H*) (The last two signals disappeared upon addition of D_2O.); ^{13}C NMR (DMSO-d_6) δ 47.0 (d, ArCHAr), 48.4 (d, weak), 107.2–133.4 (m), 152.8 (s), 155.6 (s) (The signal for the hemiacetal carbon is in the aromatic region.); MS *m/e* 328 (M^+, 46), 310 (base peak, 100), 281 (48), 144 (73).

Since compound 3 is readily converted into 4, it was impossible to obtain elemental analysis for the compound.

7a,14c-Dihydronaphtho[2,1-*b*]naphtho[2',1':5,6]furo[3,2-*d*]furan (4). To a THF solution (200 mL) of potassium 2-naphthyl oxide (15.0 g, 0.0824 mol) was added dropwise 40% aqueous glyoxal (71.7 g, 0.494 mol) at 30 °C over 30 min. The mixture was stirred for 3 h, acidified with aqueous HCl, and extracted successively with ether and $CHCl_3$. After evaporation of the solvent from the combined solution, the residue was washed with ethanol to give 4 (11.8 g, 92%).

Heating 3 (0.52 g, 0.00159 mol) at 50 °C for 1 h in the presence of aqueous HCl (3 N, 3 mL) gave only 4 (0.21 g, 43%).

4: mp 234 °C (from acetone; lit. mp 235 °C[4] and 236.5–238 °C[6]); IR (KBr, cm^{-1}) 845 (w), 805 (m), 735 (m); ^1H NMR (DMSO-d_6, at 80 °C) δ 5.82 (d, 1 H, J = 6.0 Hz, ArC*H*Ar), 7.2–8.4 (m, 13 H, Ar*H* + ArOC*H*OAr); ^{13}C NMR (DMSO-d_6) δ 48.5 (d, ArCHAr), 111.5 (d), 114.4 (d), 118.6 (s), 122.9 (d), 123.3 (d), 126.4 (d), 128.7 (d), 129.5 (s), 129.7 (s), 130.1 (d), 155.6 (s) (The signal for the acetal carbon is in the aromatic region.); MS *m/e* 310 (M^+, base peak, 100), 281 (39). Anal. Calcd for $C_{22}H_{14}O_2$: C, 85.14; H, 4.55. Found: C, 85.13; H, 4.60.

Diacetate of 1,2-Dihydronaphtho[2,1-*b*]furan-1,2-diol (8). A mixture of 1 (1.00 g, 0.00455 mol), acetic anhydride (50 mL), and pyridine (10 mL) was refluxed for 2 h. After cooling, the mixture was extracted with ether. The ether solution was washed successively with aqueous $NaHCO_3$, water, and dilute HCl and then dried (over $MgSO_4$) to give the diacetate of 1 (0.92 g, 68%).

Diacetate of 1: mp 157 °C (from ethanol); IR (KBr, cm^{-1}) 1735 (s, shoulder at 1750), 1215 (s), 810 (w, with a shoulder at 800), 740 (w); ^1H NMR ($CDCl_3$) δ 2.11 (s, 6 H, CH_3COO-), 6.68 (s, 2 H, AcOC*H*C*H*OAc, signals for the two protons are overlapped), 7.1–7.9 (m, 6 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 20.8 (q, CH_3COO-), 77.1 (d, ArCHCHOAr), 102.0 (d), 112.5 (d), 114.6 (s), 122.7 (d), 124.3 (d), 128.2 (d), 129.1 (d), 130.2 (two overlapping singlets), 133.3 (d), 158.9 (s), 169.3 (s, one of the two *C*=O), 170.6 (s, one of the two *C*=O) (The signal for ArCH-*C*H-OAr is in the aromatic region.); MS *m/e* 286 (M^+, 27), 184 (79), 173 (base peak, 100), 128 (24). Anal. Calcd for $C_{16}H_{14}O_5$: C, 67.12; H, 4.93. Found: C, 66.83; H, 5.02.

Methyl (2-Hydroxy-1-naphthyl)acetate (9). A mixture of 2 (0.52 g, 0.00283 mol), methanol (30 mL), and sulfuric acid (5 mL) was refluxed for 8 h. After cooling, the mixture was neutralized with aqueous Na_2CO_3 to afford the ester (0.40 g, 77%).

9: mp 135 °C (from *n*-hexane); IR (KBr, cm^{-1}) 3380 (s), 1710 (s), 1210 (s), 810 (m), 740 (m); ^1H NMR (DMSO-d_6) δ 3.59 (s, 3 H, $COOCH_3$), 4.05 (s, 2 H, $ArCH_2COOCH_3$), 7.1–7.8 (m, 6 H, Ar*H*), 9.83 (s, 1 H, ArO*H*); ^{13}C NMR (DMSO-d_6) δ 30.2 (t, $ArCH_2$-), 51.6 (q, $ArCH_2COOCH_3$), 112.4 (s), 117.9 (d), 122.4 (d), 122.5 (d), 126.4 (d), 128.0 (s), 128.3 (d), 128.4 (d), 133.5 (s), 153.0 (s), 171.9 (s, $ArCH_2COOCH_3$); MS *m/e* 216 (M^+, 28), 184 (63), 156 (61), 128 (base peak, 100). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.06; H, 5.59.

(2-Hydroxy-1-naphthyl)acetic Acid (10). To a cooled solution (−10 °C) of potassium 2-naphthyl oxide (6.26 g, 0.0344 mol)

in THF (40 mL) was introduced glyoxal gas, generated by heating glyoxal polymer (10.2 g) in the presence of phosphorus pentoxide (14 g).[11] The mixture was stirred at 40 °C for 2 h to produce **10** (1.53 g, 22%), together with recovered 2-naphthol (2.28 g, 46%) and a trace amount of **1**.

An improved procedure for preparing **10** is as follows. A mixture of **2** (0.53 g, 0.0029 mol), methanol (50 mL), and aqueous NaOH (0.5 N, 10 mL) was refluxed for 3 h. After cooling, the mixture was acidified with aqueous HCl to pH 2 and extracted with ether. Evaporation of the ether gave **10** (0.55 g, 93%).

10: mp 150 °C (from $CHCl_3$, lit.[12] mp 147 °C); IR (KBr, cm^{-1}) 3350 (strong and broad), 1705 (s), 1210 (s), 815 (w), 740 (m); ^1H NMR (DMSO-d_6) δ 3.97 (s, 2 H, $ArCH_2COOH$), 7.1–7.8 (m, 7 H, ArH + ArOH), 9.74 (s, broad, COOH); ^{13}C NMR (DMSO-d_6) δ 30.7 (t, $ArCH_2COOH$), 113.3 (s), 118.1 (d), 122.4 (d), 122.8 (d), 126.4 (d), 128.2 (strong signal with a shoulder; this may be composed of two doublets and one singlet), 133.7 (s), 152.9 (s), 173.0 (s, $ArCH_2COOH$); MS *m/e* 202 (M^+, 11), 184 (65), 156 (56), 128 (base peak, 100). Anal. Calcd for $C_{12}H_{10}O_3$: C, 71.28; H, 4.99. Found: C, 70.99; H, 5.09.

Bis(2-hydroxy-1-naphthyl)methane (11). To a stirred THF solution (100 mL) of 2-naphthol (5.12 g, 0.0356 mol) at −10 °C was introduced glyoxal gas generated as described above, followed by a dropwise addition of concd sulfuric acid (3 mL) in THF (5 mL). The resulting mixture was stirred at 40 °C for 70 min. Aqueous NaOH (2%, 200 mL) was added and the precipitate (crude **4**) was filtered off (1.50 g, 27%). The filtrate was acidified with aqueous HCl to afford **11** (2.24 g, 42%) as a precipitate. The filtrate contained unreacted 2-naphthol (1.28 g, 25%) with a small amount of **2** (<1%).

The yield of **11** was 18% (0.96 g) when the same reaction was carried out at 20 °C.

11: mp 207 °C (from toluene, lit.[12] mp 200 °C); ^1H NMR (acetone-d_6) δ 4.90 (s, 2 H, $ArCH_2Ar$), 7.1–7.8 (m, 12 H, ArH), 8.3–8.4 (m, 2 H, ArOH); ^{13}C NMR (acetone-d_6) δ 22.2 (t, $ArCH_2Ar$), 119.2 (d), 120.7 (s), 123.7 (d), 125.3 (d), 127.0 (d), 129.2 (d), 129.6 (d), 130.7 (s), 135.5 (s), 153.1 (s); MS *m/e* 300 (M^+, base peak, 100), 157 (71), 145 (64), 144 (96). Anal. Calcd for $C_{21}H_{16}O_2$: C, 83.98; H, 5.37. Found: C, 84.04; H, 5.42.

The IR spectrum was identical with that of an authentic sample.[13]

Supplementary Material Available: ^{13}C NMR and MS spectra for compounds 1–4 (8 pages). Ordering information is given on any current masthead page.

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Synthesis and Structure of Macrocyclic Amides Containing a 2,2′-Dipyridylmethane Unit. A New Class of Chiral Macrocyclic Ligands

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Received June 19, 1990

A novel class of 13-membered tetraaza rings containing dipyridylmethaneamide units was obtained by condensation of 1,2-diamines with 1,1-bis[6-(chloroformyl)-2-pyridyl]-1-methoxypropane. By use of *trans*-1,2-diaminocyclohexane, a chiral macrocyclic amide was obtained, while the cis isomer afforded two diastereomeric pseudochiral compounds. The chiral ligand yielded a square-planar complex with Ni(II) by loss of the amide protons, with the chirality close to the metal center. The structures of the two macrocyclic dipyridylmethane amides derived from (*R*,*R*)- and (*R*,*S*)-diaminocyclohexane (**5a** and **6a**, respectively), and that of 1,1-bis(6-carboxy-2-pyridyl)-1-methoxypropane (**1**) were studied by X-ray diffraction. In the crystal of **1**-monohydrate, the dipyridylmethane moiety adopts an anti conformation with the two aromatic rings nearly perpendicular to one another. The crystal of **5a** and that of **6a** contain two and three crystallographically independent molecules, respectively. These five macrocycles are very similar in their overall bowllike shape but exhibit minor conformational differences. ^1H NMR studies demonstrate that similar conformations are maintained in solution.

Introduction

Synthetic macrocyclic ligands have attracted considerable attention due to their widespread chemical and biochemical applications.[1] Of particular importance are dissymmetric ligands capable of chiral recognition for use in asymmetric synthesis and chiral separations.[2]

Pyridine and bipyridine have commonly been incorporated into macrocyclic frameworks, affording ligands which readily complex transition-metal ions.[3] An extensively used method for the construction of macrocyclic ligands with these heterocycles as subunits involves condensation of heterocyclic biscarboxylic acid derivatives with diamines, affording macrocyclic pyridine[4] or bipyridine diamides.[5] Chiral amide derivatives have been obtained analogously by incorporation of amino acid derivatives in the macrocycles.[6] Amides are able to form both strong complexes with metal ions by substitution of the amide hydrogen for a metal ion and weaker complexes where the metal ion

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0022-3263/91/1956-3339$02.50/0 © 1991 American Chemical Society