The Syntheses of Nitrogen-Oxygen Donor Macrocycles Containing Pyridine Ring

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Five new nitrogen-oxygen mixed donor macrocycles have been prepared by condensation of 2,6-bis [(2-formylphenyl)oxymethyl]pyridine with different diamino compounds in hot methanol, followed by a one-pot reduction of the intermediate bis-Schiff base. All the macrocycles were identified by elemental analysis, and ir, uv, and nmr spectroscopy.

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Introduction.

There is great interest in macrocyclic host ligands capable of selective recognition of metal cations, anions and neutral molecules[1]. Oxygen donor macrocycles such as crown ethers are well known to make strong complexation with alkali and alkaline earth ions. On the other hand, polyazamacrocycles show a high affinity for transition metal ions. Nitrogen-oxygen mixed donor macrocycles can form stable complexes with both alkali and transition metal ions. Therefore, mixed donor macrocycles have received much attention as receptors for a range of metal ions and other cations [2-5]. Most of the macrocycles with mixed donor sites bearing oxygen and sp^3 nitrogen atoms, oxygen and sp^2 nitrogen atoms, or oxygen and sp^3 and sp^2 nitrogen atoms have shown very interesting behavior in metal ion discrimination.

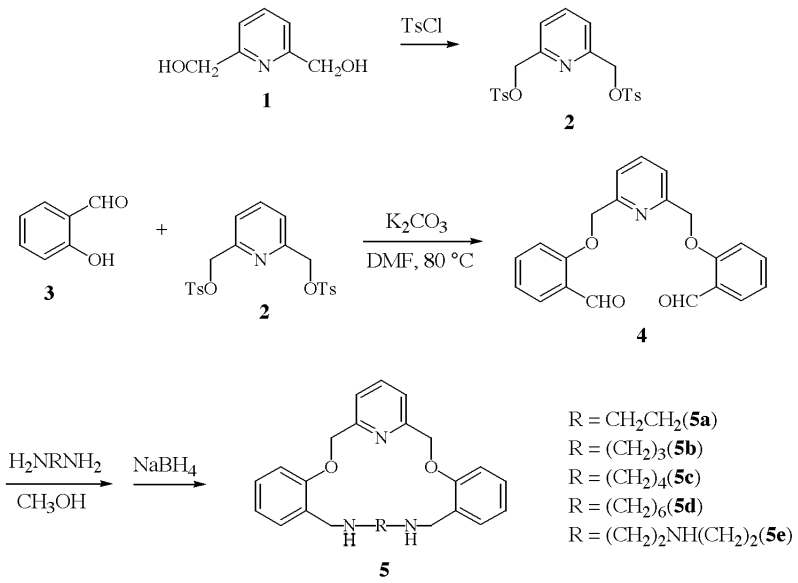
In this paper, five new nitrogen-oxygen donor macrocycles incorporating sp^2 and sp^3 nitrogen atoms were synthesized in six steps from commercially available starting materials. The synthetic route for the synthesis of the five new macrocycles containing pyridine ring and secondary amine functions is shown in Scheme 1. We plan to study the complexation properties and their transport of cations. This paper only describes the synthesis of these compounds.

Results and Discussion.

The dialdehyde, 2,6-bis[(2-formylphenyl)oxymethyl]-pyridine, which was used for the final ring closure steps in the preparation of the macrocycles was obtained by the reaction of 2,6-ditosyloxymethylpyridine with salicylaldehyde in the presence of potassium carbonate in dimethylformamide under nitrogen. A little excess of salicylaldehyde was used in order to ensure the formation of the dialdehyde.

In the syntheses of **5a-5e**, the dialdehyde was condensed with diamines in hot methanol. The corresponding Schiff-base derivatives were not isolated but instead reduction was carried out *in situ* by slow addition of sodium borohydride to the reaction solution. The

Scheme 1



condensation reaction can be performed at room temperature with a long period of time, but the yields are usually low. The reduction step can also be carried out at room temperature without lowering the yields of macrocycles. It is not necessary to carry out the ring closure step under high dilution conditions or in the presence of template ions.

The structures proposed for the new macrocycles **5a-5e** are consistent with data obtained from their elemental analyses, and ir, uv, and nmr spectra.

EXPERIMENTAL

Melting points were measured on an XT4-100^{x}A and X_4 microscopic apparatus and are uncorrected. Elemental analyses were determined on a PE-2400 (II) Elemental Analyser. Ir spectra were recorded on an IR-810 Spectrophotometer as potassium bromide pellets. ^{1}H nmr and ^{13}C nmr spectra were recorded on a DPX-400 spectrometer in deuterated chloroform. Chemical shift (δ) are given in ppm relative to that of chloroform (δ = 7.24ppm). Uv-vis spectra were measured on a WFZ900-D4 spectrophotometer.

All solvents were of analytical grade and used without further purification. Ethylene diamine, 1,3-diaminopropane, 1,4-diaminobutane, 1,6-diaminohexane, diethylenetriamine were purified by normal distillation or by distillation under reduced pressure before use. Starting materials were purchased from commercial sources where available.

2,6-Ditosyloxymethylpyridine was prepared from 2,6-bis(hydroxymethyl)pyridine[6] according to the literature method[7,8].

Preparation of 2,6-Bis[(2-formylphenyl)oxymethyl]pyridine (**4**) (Scheme 1).

Salicylaldehyde **3** (8.5 g, 0.07 mole), 11g of potassium carbonate and 80 ml of dimethylformamide were placed in a three-necked flask. The mixture was warmed to 80° under nitrogen, and then 13.4 g of 2,6-ditosyloxymethylpyridine (**2**) was added. The reaction mixture was stirred vigorously at 80° for 10 hours. After cooling, the reaction mixture was poured into ice-water (200 ml). The pale yellow solid was filtered, washed with water and dried. The crude product was decolored by active carbon and recrystallized from methanol to give 9.11 g (75%) of white crystals of dialdehyde **4**, mp 136-138°; ir: 2850 (C-H), 1700 (CHO), 1252, 1080 (Ar-O-C), 1611 (Py), 862 (1,3-Py), 760 (1,2-Ar); ^{1}H nmr: δ 10.62 (s, 2H, CHO); 7.60-7.88 (m, 3H, PyH); 7.09-7.56 (m, 8H, ArH); 5.36 (s, 4H, OCH_2); ^{13}C nmr: δ 189.56 (CHO); 155.97, 138.20, 128.98 (Py); 160.42, 136.01, 125.03, 121.36, 120.53, 112.87 (Ar); 70.75 (OCH_2).

Anal. Calcd. for $C_{21}H_{17}NO_4$: C, 72.61; H, 4.93; N, 4.03. Found: C, 72.60; H, 4.92; N, 4.01.

Preparation of Macrocycles **5a**.

To a refluxing solution of dialdehyde **4** (1.40 g, 0.004 mole) in 150 ml of methanol was added 0.24 g (0.004 mole) of ethylenediamine in 50 ml of methanol. After the addition, the reaction solution was stirred for 5 minutes, and then a small amount of borax followed by sodium borohydride (0.8 g) were added slowly to the stirred solution, and then the mixture was stirred for 3 hours. The reaction solution was filtered and reduced to a small volume on a rotary evaporator. The residue was dissolved in water (60 ml), and extracted with chloroform (3 x 50 ml). The chloroform extracts were mixed and washed with water, dried over anhydrous sodium sulphate and then evaporated to dryness to afford a crude oily product, which eventually crystallized to form a white solid. Recrystallization from ether gave 1.05 g (70%) of **5a**, mp 138-140°; ir: 3480, 3300 (N-H); 2900 (C-H); 1610 (Py); 1310, 1140 (C-N-C); 1258, 1080 (Ar-O-C); 860 (2,6-Py); 760 (1,2-Ar); ^{1}H nmr: δ 2.66 (s, 2H, NH), 2.78 (s, 4H, NCH_2CH_2), 3.85 (s, 4H, $ArCH_2$), 5.16 (s, 4H, OCH_2), 6.89-7.35 (m, 8H, ArH), 7.37-7.78 (m, 3H,PyH); uv: 286, 317 nm.

Anal. Calcd. for $C_{23}H_{25}N_3O_2$: C, 73.57; H 6.71; N, 11.19. Found: C, 72.98; H, 6.75; N, 11.30.

Preparation of Macrocycles **5b-5e**.

5b-5e were prepared in a similar manner to the procedure described above for **5a**.

Compound **5b** was obtained in 72% yield (white crystals, recrystallized from dichloromethane–ether); mp 128-130°; ir: 3420, 3254 (N-H); 2900 (C-H); 1610 (Py); 1305, 1120 (C-N-C); 1250, 1080 (Ar-O-C); 860 (2,6-Py); 755 (1,2-Ar). ^{1}H nmr: δ 1.77 (t, 2H, CCH_2C); 2.13 (br, 2H, NH), 2.74 (t, 4H, NCH_2); 3.82 (s, 4H, $ArCH_2$); 5.06 (s, 4H, OCH_2); 6.85-7.27 (m, 8H, ArH); 7.35-7.66 (m, 3H, PyH); ^{13}C nmr: δ 156.13, 137.61, 128.40 (Py); 157.18, 130.09, 128.27, 120.99, 119.55, 111.29 (Ar); 69.92 (OCH_2); 49.61 ($ArCH_2$); 48.29 ($NHCH_2$); 29.84 (CH_2); uv: 288, 317 nm.

Anal. Calcd. for $C_{24}H_{27}N_3O_2$: C, 74.00; H, 6.99; N, 10.79. Found: C, 73.59; H, 7.08; N, 10.62.

Compound **5c** was obtained in 68% yield (recrystallized from ether); mp 63-65°; ir: 3420, 3250 (N-H); 2900, 2827 (C-H); 1605 (Py); 1300, 1130 (C-N-C); 1250, 1060 (Ar-O-C); 860 (2,6-Py); 760 (1,2-Ar); ^{1}H nmr: δ 1.22 (m, 4H, CH_2CH_2); 2.39 (br, 2H, NH); 2.62 (t, 4H, NCH_2), 3.73 (s, 4H, $ArCH_2$); 5.16 (s, 4H, OCH_2); 6.92-7.30 (m, 8H, ArH); 7.50-7.87 (m, 3H, PyH); ^{13}C nmr: δ 156.12, 137.86, 128.60 (Py); 157.18, 130.90, 123.00, 121.24, 111.87 (Ar), 71.59 (OCH_2), 50.22 ($ArCH_2$), 48.47 ($NHCH_2$), 26.95 (CH_2); uv: 290, 317 nm.

Anal. Calcd for $C_{25}H_{29}N_3O_2$: C, 74.41; H, 7.24; N, 10.42. Found: C, 74.20; H, 7.09; N, 9.98.

Compound **5d** was obtained in 74% yield (recrystallized from ether); mp 72-76°; ir: 3425 (N-H); 2920, 2848 (C-H); 1610 (Py); 1310, 1138 (C-N-C); 1258, 1062 (Ar-O-C); 866 (2,6-Py); 766 (1,2-Ar); ^{1}H nmr: δ 0.90-1.24 (m, 8H, CH_2); 2.13 (s, 2H, NH); 2.60 (t, 4H, NCH_2); 3.80 (s, 4H,$ArCH_2$); 5.20 (s, 4H, OCH_2); 6.95-7.32 (m, 8H, ArH); 7.57-7.90 (m, 3H, PyH); uv: 286, 315 nm.

Anal. Calcd. for $C_{27}H_{33}N_3O_2$: C, 75.14; H, 7.70; N, 9.74. Found: C, 75.21; H, 7.78; N, 9.87.

Compound **5e** was obtained in 65% as an oil; ir: 3420 (br, N-H); 2920, 2835 (C-H); 1611 (Py); 1310,1136 (C-N-C); 1257,1064 (Ar-O-C); 860 (2,6-Py); 760 (1,2-Ar); ^{1}H nmr: δ 2.54 (s, 3H, NH); 2.64-2.70 (m, 8H, NCH_2); 3.76 (s, 4H, $ArCH_2$); 5.19 (s, 4H, OCH_2); 6.95-7.28 (m, 8H, ArH); 7.46-7.83 (m, 3H, PyH); uv: 291 nm.

Anal. Calcd. for $C_{25}H_{30}N_4O_2$: C, 71.74; H, 7.22; N, 13.39. Found: C, 71.62; H, 7.36; N, 13.51.

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