Table I. Intermolecular Coupling Reaction of 2-Pyridyllithium with Ethyl 2-Pyridyl Sulfoxide

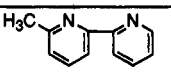
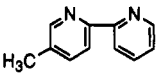
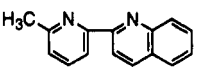
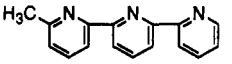
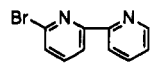
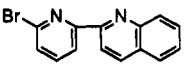
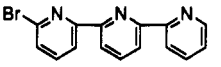
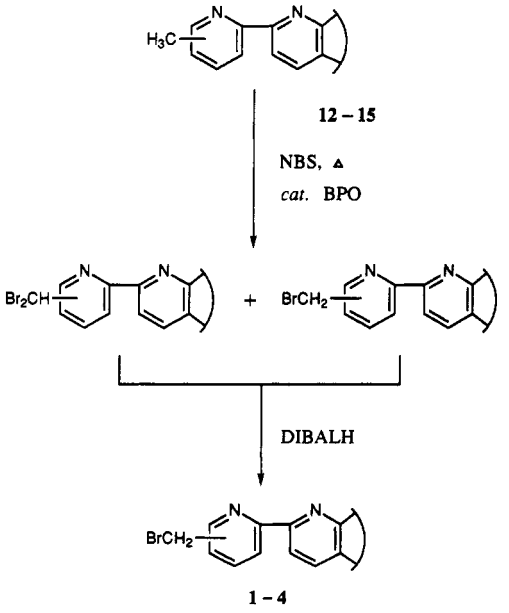
entry	2-bromopyridine	sulfoxide	product		yield (%)
1	6-methyl	9		12	60
2	5-methyl	9		13	70
3	6-methyl	10		14	35
4	6-methyl	11		15	54
5	6-bromo	9		16	80
6	6-bromo	10		17	80
7	6-bromo	11		18	76

Table II. Bromination of Picolyl Derivatives 12–16

		yields (%)			
entry	substrate	monobromide	dibromide[a]		product[b]
1	12	26	39	1	54
2	13	20	40	2	45
3	14	21	47	3	56
4	15	27	44	4	60
5	23	0	0	5	0

[a] Isolated yields. [b] Totally converted yields of monobromide after reduction.

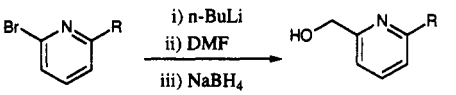
Scheme II



ridine (19) was brominated with carbon tetrabromide and triphenylphosphine to give 1[18] in 90% yield. By using the same procedure, 3 and 4 were obtained in 85 and 40% yields, respectively, by two steps from 17 and 18. These results are summarized in Table III.

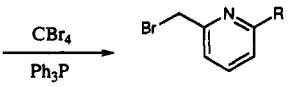
Preparation of 2-methyl-6-(2-pyrazinyl)pyridine (23) was unsuccessful by intermolecular ligand coupling reaction of 2-(6-methylpyridyl)lithium and ethyl 2-pyrazinyl sulfoxide or of 2-pyrazinyllithium and ethyl 2-(6-methylpyridyl) sulfoxide. In this case, the intramolecular ligand

Scheme III



16 – 18 19 – 21

16 R = 2-pyridyl 19 R = 2-pyridyl
17 R = 2-quinolyl 20 R = 2-quinolyl
18 R = 6-(2,2'-bipyridyl) 21 R = 6-(2,2'-bipyridyl)



1, 3, 4

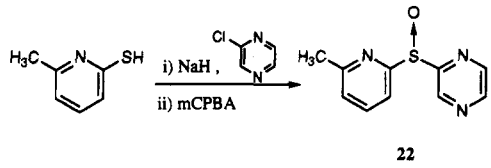
1 R = 2-pyridyl
3 R = 2-quinolyl
4 R = 6-(2,2'-bipyridyl)

Table III. Functional Transformation of Bromopyridine to Bromomethylpyridine

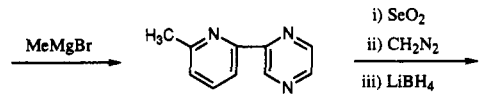
entry	substrate	(hydroxymethyl)-pyridine	yield (%)	(bromomethyl)-pyridine	yield (%)
1	16	19	63	1	90
2	17	20	88	3	92
3	18	21	54	4	74

coupling reaction of 2-(6-methylpyridyl) 2-pyrazinyl sulfoxide (22) was employed and gave the desired coupling product 23. The sulfoxide 22 was prepared in two steps as follows: sodium salt of 6-mercapto-2-picoline was treated with 2-chloropyrazine in HMPA to give pyrazinyl picolyl sulfide, which was immediately oxidized with MMPP (magnesium monoperhydroxyphthalate) to lead to sulfoxide 22 in 76% yield by the two steps. This sulfoxide was subjected to the intramolecular ligand coupling by the use of methylmagnesium bromide in THF to afford 23 in 36% yield. Since 23 could not be brominated under the free-radical bromination condition (see Table II), an alternative transformation was required for the synthesis of 2-(bromomethyl)-6-(2-pyrazinyl)pyridine (5). First, oxidation of the methyl group in 23 to the corresponding carboxylic acid was performed by treatment of

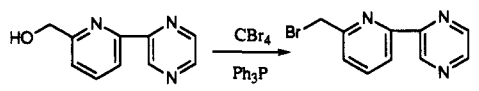
Scheme IV



22

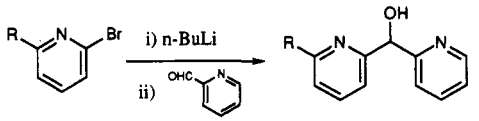


23

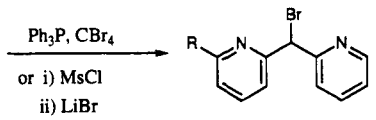


24 5

Scheme V



25 R = H 86 %
26 R = THPOCH$_2$ 53 %



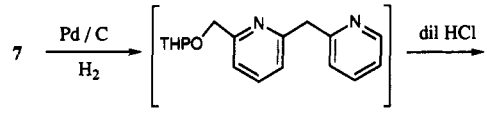
6 R = H 46 %
7 R = THPOCH$_2$ 63 %

23 with selenium dioxide in refluxing benzene. Without purification, the crude acid was esterified with diazomethane in chloroform and methanol to give methyl ester. Upon successive treatment with $LiBH_4$, the ester was reduced to 2-(6-(hydroxymethyl)pyridyl)pyrazine (24) in 87% yield. Then 24 was brominated with carbon tetrabromide and triphenylphosphine to give 2-(6-bromomethyl)pyridyl)-2-pyrazine (5) in 87% yield.

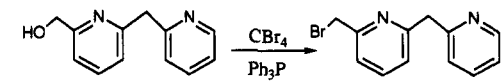
Synthesis of Bromo(2,2′-bipyridyl)methane: Preparation of Type II Compounds. Addition of 2-pyridyllithium to 2-pyridinecarboxaldehyde at −78 °C gave bis(2-pyridyl)methanol (25)[18] in 86% yield. Bromination of the alcohol with carbon tetrabromide and triphenylphosphine afforded the desired bromide 6 in 46% yield. Pyridyllithium prepared from 2-bromo-6-((2-tetrahydropyranyloxy)methyl)pyridine was treated with 2-pyridinecarboxaldehyde at −78 °C to give secondary alcohol 26 in 53% yield. Although bromination of the alcohol with carbon tetrabromide and triphenylphosphine did not give 7 in satisfactory yield, the compound 26 was mesylated once with methanesulfonyl chloride in pyridine. Then replacement of the mesylate to bromide anion was carried out by treating the methanesulfonate with LiBr in HMPA to give the bromide 7 in 67% yield. The bromides 6 and 7 are both rather unstable and are preferable to be used in a day.

Synthesis of 6-(Bromomethyl)-2-(2-pyridylmethyl)-pyridine: Preparation of Type III Compounds. The bromide 7 was subjected to reductive hydrogenolysis under

Scheme VI



27



28 8

hydrogen atmosphere in the presence of Pd charcoal. This reduction gave 27 along with a partially hydrolyzed product of THP ether 28. Treatment of the crude mixtures with dilute hydrochloric acid in methanol eventually gave 2-(hydroxymethyl)-6-(2-pyridylmethyl)pyridine (28) in 98% yield in two steps. The hydroxymethyl group was brominated in the same manner as described in Scheme III to give 8 in 69% yield.

Conclusion

We have developed novel preparations of ω-(bromomethyl)pyridinoheteroaromatic compounds 1–8. The current methods would be applicable in many types of substrates. These ω-(bromomethyl)pyridinoheteroaromatic compounds promise to be useful synthetic tools not only for new double-armed crown ethers but also for a wider range of newly designed functional molecules, which may possess physically or biologically interesting properties. Their synthetic use in the cases of the armed azacrown ethers and the characteristic features are discussed in the following paper in this issue.

Experimental Section

General. Melting points were uncorrected. ^1H and ^{13}C NMR were taken in $CDCl_3$ for ^1H (400 or 300 MHz) and for ^{13}C (100 or 75 MHz). The chemical shifts were shown as δ value (ppm) using tetramethylsilane (0 ppm) for proton spectra and $CHCl_3$ (77.0 ppm) for carbon spectra as an internal standard. Infrared spectra (IR) were recorded as liquid films on NaCl plates or as tablets. Low- and high-resolution mass spectra (LRMS and HRMS) were obtained at 10 or 70 eV using the direct inlet method at the Analytical Center in Okayama University of Science. Only significant peaks are described here for IR and MS. Analytical TLC was carried out on 0.25-mm precoated silica gel plates. Silica gel (70–300 mesh) was used for gravity column chromatography and silica gel (230–400 mesh) for flash column chromatography. All air-sensitive reactions were conducted in flame-dried glassware under an Ar atmosphere. THF, ether, and benzene used as solvents for reactions were dried over sodium benzophenone ketyl, and methylene chloride was dried over phosphorus pentoxide. These solvents were freshly distilled just before use.

Ethyl 6-(2,2′-Pyridyl) Sulfoxide (11). To a stirred solution of ethylmercaptan sodium salt (32 mmol) in HMPA (13 mL), prepared from ethylmercaptan (2.37 mL, 32 mmol) and sodium hydride (1.28 g, 60%, 32 mmol), was added 6-bromo-2,2′-bipyridine (3.0 g, 12.8 mmol) slowly at room temperature. The mixture was stirred for 20 min and then poured into ice–water (50 mL) and extracted with ether and hexane (1:1, 200 mL). Organic layer was washed with water (4 mL × 5) and brine (4 mL) and dried over $MgSO_4$. Evaporation of the solvent gave crude sulfide: oil; R_f = 0.35 (7.5% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 1.36 (t, J = 7.4 Hz, 3H), 3.20 (q, J = 7.4 Hz, 2H), 7.08 (dd, J = 7.9, 0.8 Hz, 1H), 7.18 (ddd, J = 4.8, 2.6, 1.1 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 7.70 (ddd, J = 7.9, 7.5, 1.8 Hz, 1H), 8.01 (dd, J = 7.7, 0.9 Hz, 1H), 8.34 (d, J = 8.0 Hz, 1H), 8.56 (dm, J = 4.8

Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.6, 24.4, 116.3, 120.9, 122.2, 123.6, 136.7, 136.7, 150.0, 155.5, 155.9, 158.4. To the crude sulfide dissolved in methanol (30 mL) was added magnesium monoperoxyphthalate (3.96 g, 6.4 mmol) in several portions at 0 °C. After the addition, the mixture was warmed to room temperature and stirred for 1 h. The solution was condensed to 10 mL of the volume under reduced pressure, poured into ice–water (15 mL), and extracted with $CHCl_3$ (30 mL × 3). The combined extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude material was purified by column chromatography on silica gel eluted with 60% EtOAc in hexane to give 11 (2.8 g) in 94% yield by two steps. Recrystallized from benzene/hexane (1:5): mp 91–92 °C; R_f = 0.36 (3% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.25 (t, J = 7.3 Hz, 3H), 3.01 (dq, J = 13.6, 7.3 Hz, 1H), 3.25 (dq, J = 13.6, 7.3 Hz, 1H), 7.36 (ddd, J = 7.7, 4.8, 1.1 Hz, 1H), 7.85 (td, J = 7.7, 1.8 Hz, 1H), 8.00 (dd, J = 7.1, 1.1 Hz, 1H), 8.06 (t, J = 7.7 Hz, 1H), 8.37 (dt, J = 8.1, 1.1 Hz, 1H), 8.50 (dd, J = 7.7, 1.1 Hz, 1H), 8.70 (dm, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 5.3, 47.4, 120.0, 121.1, 121.6, 124.3, 136.9, 138.5, 149.2, 154.5, 156.1, 163.4; IR (KBr) 1038 cm^{-1}; MS (70 eV) m/z (rel intensity) 232 (M^+, 26), 204 (13), 184 (54), 156 (75), 155 (80), 78 (60), 44 (base). Anal. Calcd for $C_{12}H_{12}N_2OS$: C, 62.04; H, 5.21; N, 12.06. Found: C, 62.26; H, 5.25; N, 12.18.

General Coupling Reaction of Pyridyllithium and Ethyl Heteroaromatic Sulfoxide. To a stirred solution of bromopyridine (3.3 mmol) in a mixture of ether, hexane, and THF (2:1:1, 12 mL) was added dropwise n-BuLi (3.1 mmol, 1.66 M in hexane solution) at −78 °C during 5–10 min. To the resulting dark brown solution was added ethyl heteroaromatic sulfoxide (3 mmol) in THF (2 mL) drop-by-drop at the same temperature. After being stirred for 5 min, the reaction mixture was quenched with water (5 mL) and extracted with EtOAc (150 mL). The organic layer was washed with water (3 mL × 3) and brine (5 mL) and dried over $MgSO_4$. Solvent was evaporated under reduced pressure, and residue was purified by flash column chromatography on silica gel. The spectroscopic and analytical data were as follows.

6-Methyl-2,2′-bipyridine (12).[13] Recrystallized from hexane/benzene (4:1): mp 50–51 °C; ^1H NMR ($CDCl_3$) δ 2.60 (s, 3H), 7.20 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 5.0 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 8.20 (d, J = 7.6 Hz, 1H), 8.42 (d, J = 7.6 Hz, 1H), 8.70 (d, J = 4.0 Hz, 1H).

5-Methyl-2,2′-bipyridine (13):[13] oil; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H), 7.28 (ddd, J = 6.0, 4.8, 1.2 Hz, 1H), 7.63 (dd, J = 8.1, 1.6 Hz, 1H), 7.80 (td, J = 7.7, 1.6 Hz, 1H), 8.28 (d, J = 8.1 Hz, 1H), 8.35 (dt, J = 7.0, 1.1 Hz, 1H), 8.51 (dd, J = 1.4, 0.8 Hz, 1H), 8.66 (dm, J = 4.9 Hz, 1H).

6-Methyl-2-(2-quinolyl)pyridine (14).[13] Recrystallized from hexane/benzene (3:1): mp 97–99 °C; ^1H NMR ($CDCl_3$) δ 2.66 (s, 3H), 7.18 (d, J = 7.7 Hz, 1H), 7.51 (td, J = 8.0, 0.7 Hz, 1H), 7.71 (td, J = 8.1, 1.5 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.81 (dd, J = 8.2, 0.9 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.1 Hz, 1H), 8.42 (d, J = 8.1 Hz, 1H), 8.57 (d, J = 8.4 Hz, 1H).

6-Methyl-2,2′:6′,2″-terpyridine (15).[14] Recrystallized from hexane: mp 111.5–113.0 °C; ^1H NMR ($CDCl_3$) δ 2.64 (s, 3H), 7.18 (d, J = 7.7 Hz, 1H), 7.30 (td, J = 7.7, 1.8 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.84 (td, J = 7.7, 1.8 Hz, 1H), 7.94 (t, J = 7.9 Hz, 1H), 8.39 (dt, J = 8.1, 1.1 Hz, 1H), 8.43 (dd, J = 7.7, 1.1 Hz, 1H), 8.47 (dd, J = 7.7, 1.1 Hz, 1H), 8.61 (dd, J = 8.1, 1.1 Hz, 1H), 8.68 (dm, J = 4.1 Hz, 1H).

6-Bromo-2,2′-bipyridine (16).[15] Recrystallized from hexane: mp 69–70 °C; ^1H NMR ($CDCl_3$) δ 7.33 (ddd, J = 6.1, 4.7, 1.3 Hz, 1H), 7.49 (dd, J = 7.7, 0.7 Hz, 1H), 7.67 (t, J = 7.7 Hz, 1H), 7.83 (td, J = 7.7, 1.8 Hz, 1H), 8.39 (dd, J = 7.7, 0.7 Hz, 1H), 8.41 (dd, J = 8.1, 1.1 Hz, 1H), 8.67 (dm, J = 4.8 Hz, 1H).

6-Bromo-2-(2-quinolyl)pyridine (17). Recrystallized from benzene: mp 162–164 °C; R_f = 0.31 (5% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 7.54 (dd, J = 7.9, 1.5 Hz, 1H), 7.57 (ddd, J = 8.6, 7.0, 1.1 Hz, 1H), 7.72 (t, J = 7.7 Hz, 1H), 7.74 (ddd, J = 8.4, 7.4, 1.5 Hz, 1H), 7.86 (dd, J = 8.2, 1.3 Hz, 1H), 8.15 (dd, J = 8.2, 1.3 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.56 (d, J = 8.8 Hz, 1H), 8.65 (dd, J = 7.9, 0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 119.0, 120.4, 127.0, 127.6, 128.3, 128.4, 129.6, 129.7, 146.9, 139.2, 141.5, 147.7, 154.4, 157.4; MS m/z (rel intensity) 286, 284 (M^+, 21, 19), 205 (base), 128 (26). Anal. Calcd for $C_{14}H_9N_2Br$: C, 58.97; H, 3.18; N, 9.82. Found: C, 59.07; H, 3.23; N, 9.99.

6-Bromo-2,2′:6′,2″-terpyridine (18). Recrystallized from hexane: mp 155.0–156.5 °C; R_f = 0.39 (3% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.34 (ddd, J = 6.3, 5.9, 2.1 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 7.86 (td, J = 7.8, 1.9 Hz, 1H), 7.96 (t, J = 7.9 Hz, 1H), 8.45 (d, J = 7.8 Hz, 1H), 8.47 (d, J = 7.9 Hz, 1H), 8.58 (d, J = 7.8 Hz, 1H), 8.58 (d, J = 7.8 Hz, 1H), 8.71 (dm, J = 3.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 119.7, 121.0, 121.3, 121.5, 123.8, 127.9, 136.8, 137.9, 139.1, 141.5, 149.1, 153.6, 155.3, 155.8, 157.3; MS m/z (rel intensity) 313, 311 (M^+, 93, 92), 233 (base), 232 (98). Anal. Calcd for $C_{15}H_{10}N_3Br$: C, 57.71; H, 3.23; N, 13.46. Found: C, 57.99; H, 3.49; N, 13.67.

Preparation of (Bromomethyl)pyridine Derivatives by Radical Reaction. A mixture of methylpyridine derivative (2 mmol), N-bromosuccinimide (10 mmol), and dibenzoyl peroxide (0.5 mmol) in CCl_4 (60 mL) was heated under reflux until the starting material was consumed as evidenced by TLC, which generally required 1–2 h. After the mixture was cooled, precipitate was filtered off through a Celite pad. The filtrate was condensed and purified roughly by silica gel column chromatography to give a mixture of monobromide and dibromide. At this stage it was possible to isolate the both products by careful chromatography, but further purification was unnecessary for the next reduction of dibromide to monobromide. The mixture was dissolved in CH_2Cl_2 (30 mL), and DIBALH (1 M in n-hexane solution) was dropped to the mixture at −78 °C until all dibromide was reduced to monobromide, with monitoring by TLC. The reaction mixture was diluted with EtOAc (150 mL) and aqueous ammonium chloride (10 mL) and stirred for 10 min at room temperature. The whole was filtered through a Celite pad by reduced pressure, and the residue was washed with EtOAc (25 mL × 2). The combined extracts were washed with water (4 mL × 3) and brine and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel. The spectroscopic and analytical data were as follows.

6-(Bromomethyl)-2,2′-bipyridine (1).[16] Recrystallized from hexane/benzene (5:1): mp 65.5–67.0 °C; ^1H NMR ($CDCl_3$) δ 4.63 (s, 2H), 7.32 (ddd, J = 6.0, 4.9, 1.3 Hz, 1H), 7.45 (dd, J = 7.7, 1.1 Hz, 1H), 7.82 (t, J = 7.7 Hz, 1H), 7.83 (td, J = 7.7, 1.1 Hz, 1H), 8.32 (dd, J = 7.9, 0.9 Hz, 1H), 8.45 (dt, J = 8.1, 1.1 Hz, 1H), 8.68 (dm, J = 5.0 Hz, 1H).

5-(Bromomethyl)-2,2′-bipyridine (2). Recrystallized from hexane: mp 72–3 °C; R_f = 0.33 (5% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.52 (s, 2H), 7.30 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.80 (td, J = 7.9, 1.6 Hz, 1H), 7.83 (dd, J = 8.4, 2.2 Hz, 1H), 8.39 (d, J = 8.1 Hz, 2H), 8.67 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 29.6, 121.0, 121.1, 121.2, 123.9, 133.6, 137.6, 149.2, 149.3, 155.4, 156.0; MS m/z (rel intensity) 250, 248 (M^+, 78, 76), 204 (13), 170 (base), 142 (77), 141 (75). Anal. Calcd for $C_{11}H_9N_2Br$: C, 53.04; H, 3.64; N, 11.25. Found: C, 53.30; H, 3.86; N, 11.53.

6-(Bromomethyl)-2-(2-quinolyl)pyridine (3). Recrystallized from benzene/hexane (1:1): mp 145–146 °C; R_f = 0.34 (7.5% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 4.68 (s, 2H), 7.52 (dd, J = 7.5, 0.9 Hz, 1H), 7.56 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.74 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.86 (dd, J = 8.1, 1.5 Hz, 1H), 7.88 (td, J = 7.7, 1.5 Hz, 1H), 8.17 (dd, J = 8.4, 0.7 Hz, 1H), 8.28 (d, J = 8.8 Hz, 1H), 8.59 (dd, J = 7.9, 0.9 Hz, 1H), 8.62 (d, J = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 34.2, 119.0, 120.9, 123.7, 126.8, 127.6, 128.2, 129.5, 129.7, 136.7, 137.9, 147.8, 155.6, 156.0, 156.1; MS (70 eV) m/z (rel intensity) 300, 298 (M^+, 23, 24), 219 (57), 109 (10), 44 (base). Anal. Calcd for $C_{15}H_{11}N_2Br$: C, 60.22; H, 3.71; N, 9.36. Found: C, 60.27; H, 3.57; N, 9.14.

6-(Bromomethyl)-2,2′:6′,2″-terpyridine (4). Recrystallized from benzene/hexane (1:2): mp 124–125 °C; R_f = 0.33 (2% triethylamine in EtOAc); ^1H NMR ($CDCl_3$) δ 4.68 (s, 2H), 7.33 (ddd, J = 5.9, 4.8, 1.1 Hz, 1H), 7.48 (dd, J = 7.7, 1.1 Hz, 1H), 7.85 (t, J = 7.7 Hz, 1H), 7.85 (td, J = 7.7, 1.6 Hz, 1H), 7.95 (t, J = 7.9 Hz, 1H), 8.45 (dd, J = 7.7, 1.1 Hz, 1H), 8.50 (dd, J = 7.7, 1.1 Hz, 1H), 8.53 (dd, J = 7.9, 1.1 Hz, 1H), 8.60 (dt, J = 8.1, 1.1 Hz, 1H), 8.70 (dm, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 34.2, 120.3, 121.1, 121.1, 121.2, 123.4, 123.8, 136.9, 137.8, 137.9, 149.1, 154.8, 155.2, 155.9, 156.1, 156.2; MS m/z (rel intensity) 327 and 325 (M^+, base and 96), 246 (62), 155 (9). Anal. Calcd for $C_{16}H_{12}N_3Br$: C, 58.91; H, 3.71; N, 12.88. Found: C, 58.86; H, 3.46; N, 12.56.

Introduction of the Hydroxymethyl Group to Pyridinoheteroaromatic Derivatives. 2-Lithiopyridine (3.1 mmol) was

prepared in the same manner as the coupling reaction for the compounds 12–18 and then quenched with DMF (0.57 mL, 7.75 mmol) at −78 °C. The mixture was allowed to warm to 0 °C and diluted with MeOH (6 mL). $NaBH_4$ (190 mg, 5 mmol) was added to the mixture and the resulting mixture stirred for 15 min at 0 °C. The reaction mixture was condensed to 10 mL, extracted with EtOAc (70 mL), and washed with water (3 mL × 3) and brine (3 mL). The extract was dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel. The spectroscopic and analytical data were as follows.

6-(Hydroxymethyl)-2,2′-bipyridine (19): oil, R_f = 0.30 (10% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.86 (s, 2H), 7.26 (dd, J = 7.7, 0.7 Hz, 1H), 7.34 (ddd, J = 6.0, 4.8, 1.1 Hz, 1H), 7.83 (t, J = 7.7 Hz, 1H), 7.85 (td, J = 7.7, 1.8 Hz, 1H), 8.32 (d, J = 7.7 Hz, 1H), 8.41 (dd, J = 8.1, 1.1 Hz, 1H), 8.71 (dm, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 64.1, 119.3, 120.2, 120.9, 123.5, 136.7, 137.3, 148.8, 154.5, 155.4, 157.9; IR (film) 3370 cm^{-1}, MS m/z (rel intensity) 186 (98), 38 (base), 137 (85). Anal. Calcd for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.04. Found: C, 71.19; H, 5.46; N, 15.04.

6-(Hydroxymethyl)-2-(2-quinolyl)pyridine (20). Recrystallized from ether/CH_2Cl_2 (1:1): mp 131.5–133.0 °C; R_f = 0.35 (5% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.01 (t, J = 4.9 Hz, 1H), 4.88 (d, J = 4.9 Hz, 2H), 7.30 (d, J = 8.1 Hz, 1H), 7.57 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.75 (ddd, J = 8.4, 7.0, 1.5 Hz, 1H), 7.86 (dd, J = 8.1, 1.1 Hz, 1H), 7.88 (t, J = 7.7 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H), 8.58 (d, J = 8.8 Hz, 1H), 8.59 (dd, J = 7.7, 0.7 Hz, 1H); IR (KBr) 3408 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 64.0, 118.8, 120.4, 120.7, 126.8, 127.6, 128.2, 129.6, 129.7, 136.8, 137.6, 147.8, 155.0, 155.5, 158.2; MS (70 eV) m/z (rel intensity) 236 (M^+, base), 235 (97), 207 (28), 178 (40), 128 (45), 85 (70), 29 (68). Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.11; N, 11.86. Found: C, 76.15; H, 5.19; N, 11.69.

6-(Hydroxymethyl)-2,2′:6′,2″-terpyridine (21). Recrystallized from benzene/hexane (1:4): mp 111–112 °C; R_f = 0.34 (50% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 4.87 (s, 2H), 7.28 (d, J = 8.8 Hz, 1H), 7.36 (ddd, J = 7.4, 5.3, 1.1 Hz, 1H), 7.88 (t, J = 7.7 Hz, 1H), 7.89 (t, J = 7.7 Hz, 1H), 7.99 (t, J = 7.7 Hz, 1H), 8.48 (d, J = 8.0 Hz, 1H), 8.49 (d, J = 7.6 Hz, 1H), 8.55 (d, J = 7.8 Hz, 1H), 8.62 (dd, J = 8.2, 1.6 Hz, 1H), 8.72 (dm, J = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 64.0, 119.5, 120.3, 120.7, 120.9, 121.0, 123.6, 136.7, 137.3, 137.6, 148.9, 154.6, 154.7, 155.0, 155.9, 158.4; MS (70 eV) m/z (rel intensity) 263 (M^+, base), 234 (67), 232 (53), 185 (35), 155 (90); IR (KBr) 3367 cm^{-1}. Anal. Calcd for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.99. Found: C, 72.79; H, 5.14; N, 15.83.

Bromination of the ω-(Hydroxymethyl) Group of 16–18. To a mixture of ω-(hydroxymethyl)pyridine (1 mmol) and carbon tetrabromide (2 mmol) in CH_2Cl_2 (4 mL) was added triphenylphosphine (1.1 mmol) at 0 °C by several portions during 15 min. It was stirred for 0.5–1.5 h at the same temperature, and in order to remove triphenylphosphine oxide the mixture was passed through a short silica gel (10 g) column eluted with CH_2Cl_2. After removal of solvent, the residue was purified by flash chromatography on silica gel eluted with 10–25% EtOAc in hexane to give the corresponding bromide. The yields are described in Table III.

2-(6-Methylpyridyl) 2-Pyrazinyl Sulfoxide (22). To a suspension of NaH (797 mg, 19.3 mmol) in HMPA (10 mL) was dropped 6-mercapto-2-picoline (2.5 g, 19.3 mmol) in HMPA (10 mL) at 0 °C during 10 min. After evolution of hydrogen gas was ceased, 2-chloropyrazine (4.57 g, 39.86 mmol) was added, and the mixture was heated at 70 °C for 1 h. It was cooled to room temperature and diluted with EtOAc (130 mL) and hexane (130 mL). The solution was washed with water (6 mL × 4) and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residue was dissolved in MeOH (50 mL). To this solution was added MMPP (5.58 g, 9.0 mmol) at 0 °C by several portions during 15 min. Then, after 30 min of stirring, solvent was evaporated under reduced pressure and extracted with $CHCl_3$ (500 mL). The $CHCl_3$ layer was washed with water (10 mL × 4) and dried over $MgSO_4$. $CHCl_3$ was removed under reduced pressure, and residue was purified by flash chromatography on silica gel eluted with 40% EtOAc in hexane to give sulfoxide (3.32 g) in 76% yield: mp 105–107 °C, recrystallized from CH_2Cl_2; R_f = 0.25 (70% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 2.56 (s, 3H), 7.22 (d, J = 7.7 Hz, 1H), 7.79 (t, J = 7.7 Hz, 1H), 7.88 (d, J = 7.7 Hz, 1H), 8.60 (dd, J = 2.4, 1.7 Hz, 1H), 8.65 (d, J = 2.6 Hz, 1H), 9.20 (d, J = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 24.1, 116.7, 125.1, 138.2, 142.2, 144.3, 145.9, 159.8, 159.9, 162.2; IR (KBr) 1030 cm^{-1}; MS (70 eV) m/z (rel intensity) 219 (M^+); HRMS calcd for $C_{10}H_9N_3OS$ 219.0466, found 219.0450.

6-Methyl-2-(2-pyrazinyl)pyridine (23). To a stirred THF (25 mL) solution of sulfoxide **22** (1.0 g, 4.87 mmol) was added methylmagnesium bromide (5 mmol, 0.92 M in THF solution) at −50 °C under an argon atmosphere. The mixture was stirred for 15 min at the same temperature, and then silica gel (1 g) was added to the mixture. It was allowed to warm to room temperature, and the whole mixture was passed through a silica gel (8 g) column eluted with ether. The eluent was collected and evaporated. The residual oil was purified by flash chromatography on silica gel eluted with 10% EtOAc in hexane to give **23** (280 mg) in 36% yield, mp 57–59 °C, recrystallized from CH_2Cl_2/ether (1:1): R_f = 0.39 (30% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 2.65 (s, 3H), 7.22 (d, J = 7.7 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 8.13 (d, J = 8.1 Hz, 1H), 8.58 (d, J = 2.6 Hz, 1), 8.60 (dd, J = 2.6, 1.5 Hz, 1H), 9.68 (d, J = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.4, 118.4, 124.0, 137.1, 143.3, 143.5, 144.2, 151.3, 153.5, 158.3; MS (70 eV) m/z (rel intensity) 171 (M^+, 46), 119 (64), 40 (80), 29 (53), 28 (base). Anal. Calcd for $C_{10}H_9N_3$: C, 70.16; H, 5.30; N, 24.54. Found: C, 69.97; H, 5.23; N, 24.51.

6-(Hydroxymethyl)-2-(2-pyrazinyl)pyridine (24). A mixture of **23** (890 mg, 5.20 mmol) and selenium dioxide (1.15 g, 10.38 mmol) was refluxed in pyridine (25 mL) for 43 h. After the mixture was cooled, remaining selenium dioxide was removed by filtration, and the filtrate was diluted with a mixture of $CHCl_3$ (150 mL) and MeOH (150 mL). To this solution was added an ethereal solution of diazomethane at 0 °C until carboxylic acid was consumed as indicated by TLC. An excess of diazomethane was decomposed with acetic acid. Solvent was removed under reduced pressure, and the residue was roughly purified by chromatography on silica gel eluted with 40% EtOAc in hexane to give methyl ether, which was contaminated with some inorganic material. Without further purification the impure material was dissolved in a 2:1 mixture of MeOH and methylene chloride (7.5 mL), and $LiBH_4$ (71 mg, 3.25 mmol) was added at room temperature. The mixture was stirred for 20 min at room temperature. An excess of $LiBH_4$ was decomposed with acetone (0.5 mL), and solvent was removed under reduced pressure. Residue was chromatographed on aluminum oxide eluted with 2.5% MeOH in $CHCl_3$ to give **24** (289 mg) in 87% yield: mp 108.0–109.0 °C, recrystallized from hexane; R_f = 0.38 (10% MeOH in $CHCl_3$); ^1H NMR ($CDCl_3$) δ 4.87 (s, 2H), 7.34 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 7.7 Hz, 1H), 8.30 (d, J = 8.2 Hz, 1H), 8.63 (s, 2H), 9.65 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 64.0, 120.1, 121.2, 137.8, 143.1, 143.6, 144.5, 150.6, 152.9, 158.9; IR (film) 3380 cm^{-1}; MS (70 eV) m/z (rel intensity) 187 (M^+, 25), 186 (22), 158 (4), 17 (base); HRMS calcd for $C_{10}H_9N_3O$ 187.0746, found 187.0782.

6-(Bromomethyl)-2-(2-pyrazinyl)pyridine (5). By the same bromination procedure in Scheme III described for the substrates 19–21 was obtained **5** (404 mg) in 95% yield from **24** (320 mg) as unstable crystal. Recrystallized from benzene/hexane (1:4): mp 135–145 °C; R_f = 0.46 (50% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 4.87 (s, 2H), 7.34 (d, J = 8.1 Hz, 1H), 7.87 (t, J = 7.5 Hz, 1H), 8.30 (d, J = 8.2 Hz, 1H), 8.60 (s, 2H), 9.66 (s, 1H).

(2-(6-((2-Tetrahydropyranyloxy)methyl)pyridyl))(2-pyridyl)methanol (26). To a stirred THF (6 mL) solution of 6-bromo-2-((2-tetrahydropyranyloxy)methyl)pyridine (530 mg, 1.95 mmol) was added n-BuLi (1.2 mL, 1.61 M in hexane) at −78 °C under an argon atmosphere. After being stirred for 5 min, the reaction was quenched with 2-pyridinecarboxaldehyde (250 mg, 2.34 mmol) at the same temperature. The whole was stirred for 15 min. After the cooling bath was removed, the mixture was diluted with water (3 mL) and EtOAc (180 mL). The organic layer was washed with water (3 mL × 3) and dried over $MgSO_4$. Solvent was removed under reduced pressure, and the residual oil was purified by flash chromatography on silica gel eluted with 30% EtOAc in hexane to give an oily product (312 mg) in 53% yield: oil; R_f = 0.20 (2.5% MeOH in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.50–1.97 (m, 6H), 3.56 (m, 1H), 3.91 (ddd, J = 11.4, 8.4, 2.7 Hz, 1H), 4.69 (dd, J = 13.7, 1.3 Hz, 1H), 4.78 (q, J = 3.2 Hz, 1H), 4.92 (dt, J = 13.6, 0.7 Hz, 1H), 5.94 (s, 1H), 7.21 (ddd, J = 6.0, 4.7,

1.1 Hz, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.67 (t, J = 7.7 Hz, 1H), 7.68 (td, J = 7.5, 1.5 Hz, 1H), 8.55 (d, J = 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 19.3, 25.4, 30.5, 62.2, 69.6, 74.9, 98.4, 119.6, 120.1, 121.1, 122.5, 136.8, 137.4, 148.2, 157.2, 159.6, 161.0; IR (film) 3402 cm^{-1}; MS m/z (rel intensity) 300 (M^+, 3), 216 (14), 212 (20), 200 (base), 182 (28). Anal. Calcd for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found: C, 67.71; H, 6.49; N, 9.45.

Bis(2-pyridyl)methanol (25).[19] This compound was prepared from 2-bromopyridine and 2-bromopyridinecarboxaldehyde by the same manner described for **26**: mp 39–41 °C, recrystallized from hexane; R_f = 0.35 (10% MeOH in $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.88 (s, 1H), 7.19 (td, J = 7.3, 1.1 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.66 (td, J = 7.7, 1.8 Hz, 2H), 8.55 (dm, J = 4.8 Hz, 2H).

(2-(6-((2-Tetrahydropyranyloxy)methyl)pyridyl))(2-pyridyl)methyl Bromide (7). To a mixture of alcohol **26** (1.275 g, 4.25 mmol) and triethylamine (1.72 g, 17 mmol) in methyl chloride (16 mL) was dropped methanesulfonyl chloride (584 mg, 5.1 mmol) at 5 °C under Ar atmosphere. After the addition, the bath was removed, and the mixture was stirred for 5 min at room temperature. Then the mixture was diluted with EtOAc (80 mL) and washed with water (2 mL × 3). The organic layer was dried over $MgSO_4$, and residual oil was purified roughly by chromatography on silica gel to give the mesylate (1.35 g) in 85% yield, which was used for next reaction in 1 day: oil; R_f = 0.45 (2.5% MeOH in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.48–1.96 (m, 6H), 3.04 (s, 3H), 3.53 (m, 1H), 3.89 (m, 1H), 4.60 (dd, J = 13.9, 2.6 Hz, 1H), 4.74 (t, J = 6.2 Hz, 1H), 4.85 (dd, J = 13.7, 3.1 Hz, 1H), 6.72 (s, 1H), 7.26 (ddd, J = 6.2, 5.1, 1.1 Hz, 1H), 7.39 (d, J = 7.9 Hz, 1H), 7.45 (d, J = 7.9 Hz, 1H), 7.57 (dd, J = 7.7, 3.7 Hz, 1H), 7.74 (t, J = 7.9 Hz, 1H), 7.75 (td, J = 7.7, 1.5 Hz, 1H), 8.58 (d, J = 4.8 Hz, 1H). A mixture of the mesylate (1.35 g, 3.57 mmol) and LiBr (2.5 g, 29.8 mmol) was stirred in DMF (10 mL) for 3 h. The mixture was diluted with EtOAc (90 mL) and hexane (90 mL), washed with water (5 mL × 3), and dried over $MgSO_4$. Solvent was removed under reduced pressure, and residual oil was purified by flash chromatography on silica gel eluted with 30% EtOAc in hexane to give bromide (1.03 g) as an oil in 80% yield. Since this bromide is not stable enough for long storage, it should be used in 1 day: oil; R_f = 0.40 (30% EtOAc in hexane); ^{1}H NMR ($CDCl_3$) δ 1.50–1.90 (m, 6H), 3.53 (m, 1H), 3.89 (m, 1H), 4.63 (d, J = 13.6 Hz, 1H), 4.76 (t, J = 2.9 Hz, 1H), 4.86 (dd, J = 14.1, 1.6 Hz, 1H), 6.25 (s, 1H), 7.19 (ddd, J = 6.8, 5.0, 2.0 Hz, 1H), 7.39 (dd, J = 7.7, 0.7 Hz, 1H), 7.62 (dd, J = 7.9, 0.4 Hz, 1H), 7.66–7.74 (m, 3H), 8.58 (dt, J = 4.8, 1.3 Hz, 1H).

(19) Klosa, J. *J. Prakt. Chem.* **1960**, *10*, 335.

Bis(2-pyridyl)methyl Bromide (6). This compound was prepared from **24** in 46% yield by the same manner described for **7**. As this bromide was unstable, it should be used in 1 day. Recrystallized from hexane: mp 84.0–84.5 °C; R_f = 0.38 (70% EtOAc in hexane); ^{1}H NMR ($CDCl_3$) δ 6.28 (s, 1H), 7.20 (ddd, J = 5.7, 4.9, 2.4 Hz, 2H), 7.68–7.74 (m, 4H), 8.58 (td, J = 4.8, 1.3 Hz, 2H).

2-(Hydroxymethyl)-6-(2-pyridylmethyl)pyridine (28). A mixture of bromide **7** (1.03 g, 2.84 mmol) and palladium (50 mg, 10% on charcoal) was stirred in EtOH (10 mL) under a hydrogen atmosphere for 1.5 h. Palladium charcoal was filtered off and washed with ethanol (5 mL × 2). To the ethanol solution was added hydrochloric acid (0.5 mL), and the whole was stirred for 30 min at room temperature. Solvent was removed under reduced pressure, and the residue was made basic with aqueous NaOH (1 M) and extracted with $CHCl_3$ (50 mL × 2). The $CHCl_3$ layer was dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by flash chromatography on silica gel eluted with 2.5% MeOH in $CHCl_3$ to give alcohol (532 mg) in 94% yield: mp 76–78 °C, recrystallized from CH_2Cl_2/ether (1:1); R_f = 0.38 (20% MeOH in $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.33 (s, 2H), 4.72 (s, 2H), 7.12 (t, J = 7.2 Hz, 3H), 7.24 (d, J = 8.1 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.59 (td, J = 7.7, 1.8 Hz, 1H), 8.51 (dm, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 46.8, 63.9, 118.2, 121.5, 121.9, 123.6, 136.7, 137.2, 149.2, 149.2, 158.1, 159.1; IR (KBr) 3082 cm^{-1}; MS (70 eV) m/z (rel intensity) 200 (M^+, base), 199 (97), 182 (69), 169 (50), 117 (15), 93 (23), 78 (31), 32 (46). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.16; H, 6.04; N, 13.69.

2-(Bromomethyl)-6-(2-pyridylmethyl)pyridine (8). By the same bromination procedure in Scheme III, 2-(hydroxymethyl)-6-(2-pyridylmethyl)pyridine (**28**) was brominated to **8** in 69% yield: oil; R_f = 0.30 (2.5% MeOH in $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.35 (s, 2H), 4.52 (s, 2H), 7.14 (d, J = 7.3 Hz, 2H), 7.28 (t, J = 8.1 Hz, 2H), 7.60 (t, J = 7.7 Hz, 1H), 7.61 (td, J = 7.5, 1.8 Hz, 1H), 8.55 (dm, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 33.5, 54.2, 111.4, 122.8, 123.0, 123.1, 123.8, 128.3, 137.0, 137.9, 149.3, 156.2; MS (70 eV) m/z (rel intensity) 264 and 262 (M^+, 20 and 19). Anal. Calcd for $C_{12}H_{11}N_2Br$: C, 54.75; H, 4.21; N, 10.65. Found: C, 55.08; H, 4.31; N, 10.40.

Supplementary Material Available: NMR spectra of **22** and **24** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Side Arm Effects on Cation Binding, Extraction, and Transport Functions of Oligopyridine-Functionalized Aza-Crown Ethers

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A new series of lariat ethers and double-armed crown ethers was prepared in which oligopyridine-functionalized side arms were attached as secondary donor sites. A novel preparative method of oligopyridine derivatives was successfully applied to the synthesis of these crown ethers. Introduction of an oligopyridine-functionalized side arm into the crown ether system, if of the proper chain length and geometrical arrangement, significantly offered three-dimensional complexation with various metal cations suitable for extraction and transport. Liquid–liquid extraction, ^{13}C-NMR binding, and liquid membrane transport experiments revealed that the present type of double-armed crown ethers exhibited cation-binding abilities superior to corresponding lariat ethers.

Introduction

Lariat ethers, double-armed crown ethers, and related armed macrocycles were designed to enhance the cation-binding ability of common macrocyclic ligands by attachment of cation-ligating side arms and also to offer three-dimensional complexation suitable for extraction and transportation.[1] As we and several other research groups have reported, ester, amide, ether, and other oxygen donor-functionalized side arms have readily been attached to the aza- and diaza-crown ethers.[2] These often exhibited different cation-binding properties from those observed with the parent crown ethers via side arm participation. Since their cation-binding behaviors were strongly dependent on the coordination characters of their side arms, introduction of a potential binding site on the side arm is a promising strategy for functionalization of crown ether compounds.

Here, we report the synthesis and cation-binding properties of a new series of lariat ethers and double-armed crown ethers having oligopyridine-functionalized side arms. Although oligopyridine derivatives have potential as specific metal binders,[3] incorporation of these moieties into the crown ether system poses many synthetic difficulties, which has kept the examples reported to date to a limited number. We recently developed a general preparation of functionalized 2,2′-bipyridine derivatives by the reaction of 2-(alkylsulfinyl)pyridines with 2-pyridyllithium reagents.[4] This reaction was successfully employed in the synthesis of various armed aza-crown ethers which contained oligopyridine-functionalized side arms. We systematically introduced bipyridine, terpyridine, and their derivatives on the side arms of aza- and diaza-18-crown-6 rings. The molecular structures of lariat ethers and double-armed crown ethers prepared are summarized in Chart I. They were found to exhibit enhanced binding abilities toward "hard" metal cations, though oligopyridines are potential ligands of "soft" metal cations.[5] In particular, double-armed crown ethers had great advantages in extraction and transport processes. A combination of soft oligopyridine and hard crown ring donor groups offered unique metal recognition phenomena. Side arm effects on the cation binding, extraction, and transport functions of the oligopyridine-armed crown ethers are discussed below.

Results and Discussion

Synthesis of Oligopyridine-Armed Aza-Crown Ethers. Three kinds of oligopyridine-armed crown ethers were prepared: double-armed crown ethers, lariat ethers, and their thia analogs (see Chart I). Pyridine-armed diaza-crown ether **1a** has been demonstrated to be an effective metal cation binder/carrier.[6] 2,2′-Bipyridine and oligopyridine derivatives are known to form coordination complexes with various metal cations, and other armed crown ethers prepared here are also expected to offer interesting cation recognition via crown ring–side arm cooperation.[7] Since the syntheses of unsymmetrical oligopyridine derivatives presented earlier are too long and complicated for scale-up, we developed a new synthetic route which provides ready access to multigram quantities of oligopyridine precursors for synthesis of these armed crown ethers (see Scheme I).

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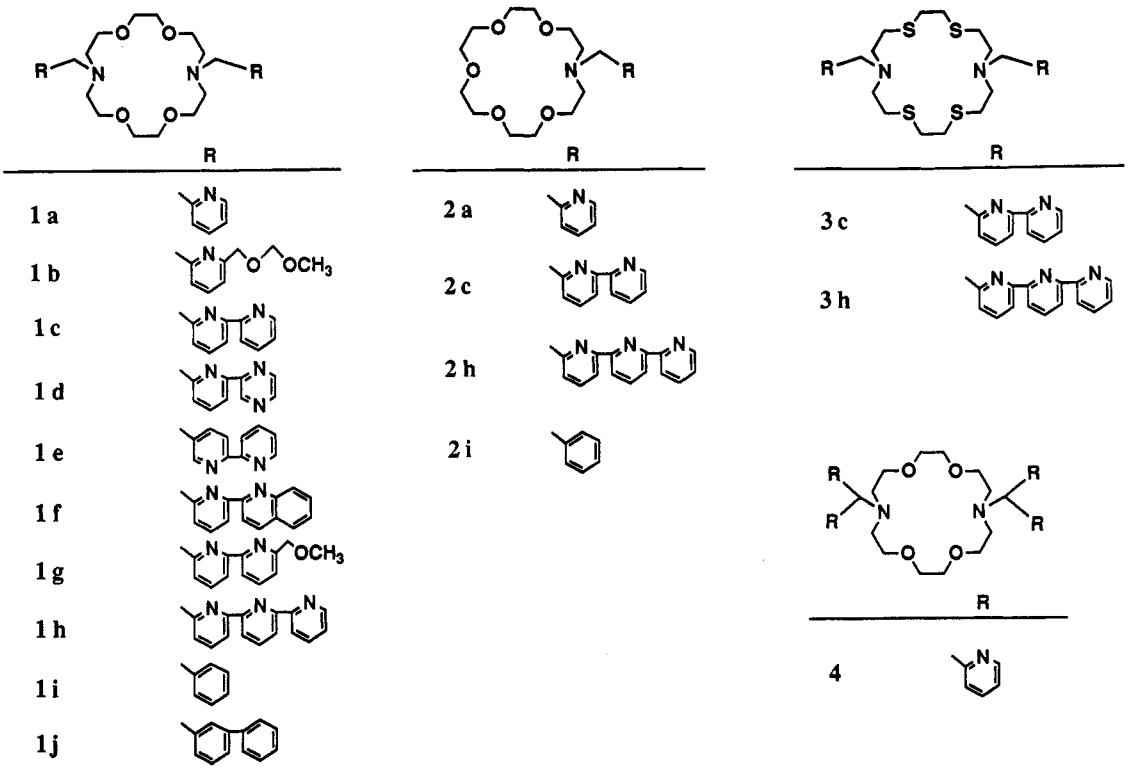
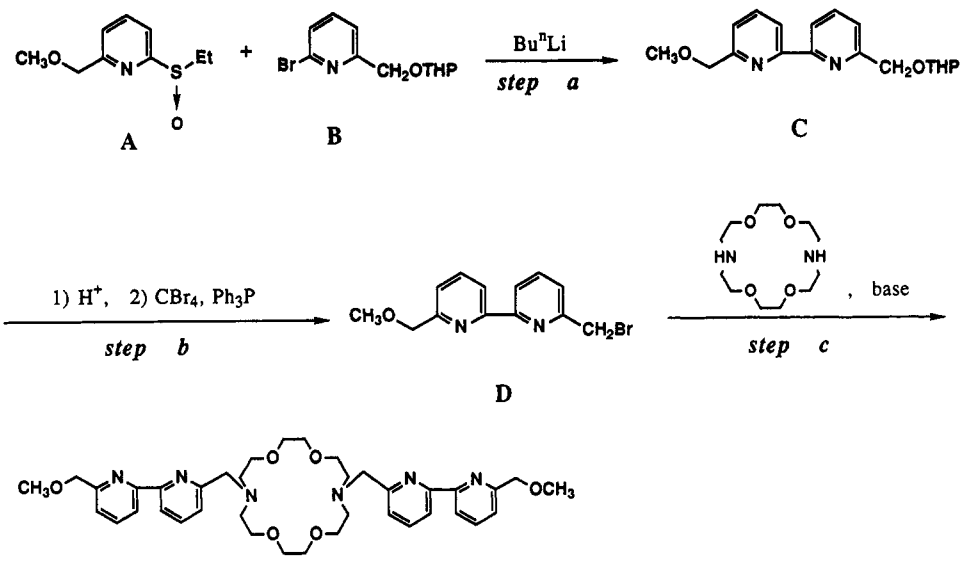
Chart I. Structures of Employed Crown Ethers



Scheme I. Typical Synthesis of Double-Armed Crown Ether



Our synthetic strategy was to prepare oligopyridine precursors via *ipso* substitution of 2-(alkylsulfinyl)pyridines by 2-pyridyllithiums and then react them with aza- and diaza-18-crown-6 rings. Typical synthesis of double armed crown ether **1g** is illustrated in Scheme I. In step a, 2-pyridyllithium was generated by halogen–metal exchange of 2-bromopyridine **B** with *n*-butyllithium in ether or THF at −78 °C and subsequently treated with 2-pyridyl sulfoxide **A**, giving protected bipyridine **C**. The THP group was easily removed by the standard procedure (HCl in MeOH), and the hydroxymethyl group formed was brominated by carbon tetrabromide with triphenylphosphine to give (bromomethyl)bipyridine **D** (step b). Finally, double-armed diaza-crown ether **1g** was prepared by alkylation (step c). We used various (bromomethyl)-oligopyridines[8] to prepare a new series of armed crown ethers having oligopyridine-functionalized side arms (see Experimental Section).

Cation Extraction Profile. Cation-binding abilities of the armed aza-crown ethers prepared were assessed by solvent extraction of alkali, alkaline earth, heavy, and transition-metal perchlorates. Nine double-armed diaza-crown ethers **1a–h** and **4**, three lariat ethers **2a–h**, two thia anaolgs **3c** and **3h**, and three reference compounds **1i**, **1j**, and **2i** were examined. The extraction percentages, defined as percent metal cation extracted in the organic phase, were calculated from the concentrations of metal

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