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### Chiral, Hinged, and Functionalized Multiheteromacrocycles<sup>1</sup>

Sir:

The pioneering "Pedersen Papers"<sup>2</sup> on crown ether chemistry and the remarkable properties of Simmons and Park's *out-in* bicyclic amines<sup>3</sup> and of Lehn's cryptates<sup>4</sup> stimulated us to turn from the study of effects of crown ethers on ion-pair phenomena<sup>5</sup> to synthesizing multiheteromacrocycles with cavities shaped to complex selected species. Host cycles that exhibit properties of chiral recognition of potential guest molecules would be particularly interesting. This paper reports syntheses of crowns containing chiral steric barriers, some with transannularly located functionalized side chains.

Without high dilution,  $\beta, \beta'$ -dihydroxy- $\alpha, \alpha'$ -binaphthyl (1), ditosylates of polyethylene glycols and potassium *tert*-butoxide<sup>6a</sup> in tetrahydrofuran<sup>6b</sup> (or sodium or potassium hydroxide in dioxane-butanol)<sup>2a</sup> gave cycles<sup>7</sup> 2, 3, and 4. Intermediate 5 treated under similar conditions with catechol (derivatives or analogs) gave 6-10. With Na<sub>2</sub>S in butanol-dioxane, 5 gave 11. From catechol, 12 was prepared similarly to 5. From 12 and 1, 6 was synthesized (50%). Conventional reactions converted 9 to 13. Biphenylcrown 14 was prepared from *o, o'*-dihydroxybiphenyl and the dichloride of pentaethylene glycol.

All cycles tested (2, 3, 6, 13, and 14) dissolved in chloroform the otherwise insoluble *tert*-butylammonium tetraphenylborate. Complexation (1:1) produced marked chemical shifts and multiplicity changes of nmr spectral bands. The 1:1 complex<sup>7a</sup> of 2 crystallized (chloroform), mp 118-120° dec. Cycles 3 and 6 (only ones tested) dissolved hydronium tosylate (1 mol) in

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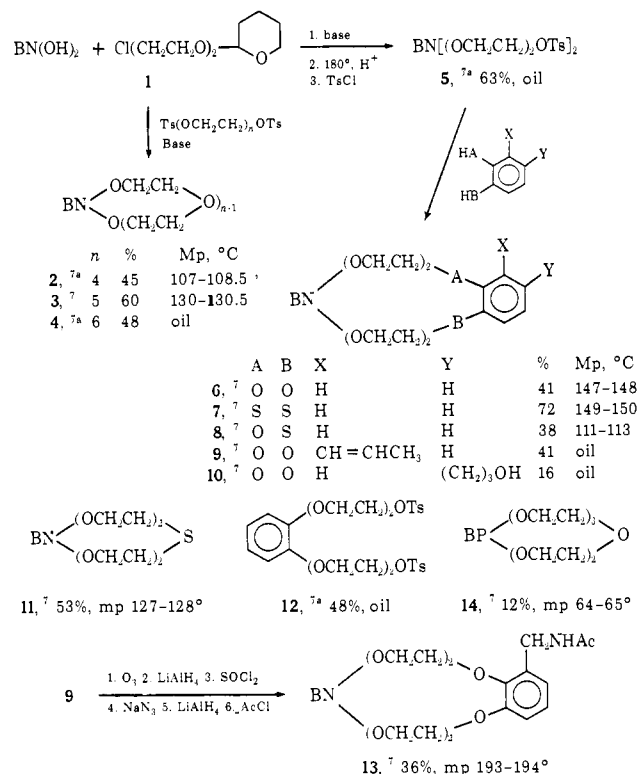
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(7) (a) Carbon and hydrogen analyses were within 0.30% of theory. Nmr spectra were consistent with assigned structures. (b) Mass spectra exhibited substantial molecular ion peaks.

### Scheme I<sup>a</sup>



<sup>a</sup> BN =  $\beta, \beta'$ -substituted  $\alpha, \alpha'$ -binaphthyl; BP = 2,2'-substituted biphenyl.

chloroform by complexation. Similarly, 3 dissolved potassium permanganate in benzene.<sup>8</sup> Tetrabutylammonium hydroxide when substituted for metal bases reduced yields (factor ~2 to 3) in preparations of cycles 3 and 6. Apparently metal ion templating of open-chain starting material produced the higher yields.

Macroreticular resin<sup>9a</sup> was used to characterize the cycles' complexing power for cations at the resin-solvent interface.<sup>9b</sup> For each cation and cycle, the resin became saturated with cycle to an extent ( $\pm 5\%$ ) independent of cycle concentration in dichloromethane, and  $K_s = 100 \times (\text{moles adsorbed cycle}) / (\text{moles cation present})$ . For tribenzylamine against resin-H<sub>3</sub>O<sup>+</sup>,  $K_s = 18.6$ . Values of  $K_s$  for resin-H<sub>3</sub>O<sup>+</sup>, -Na<sup>+</sup>, -K<sup>+</sup>, -NH<sub>4</sub><sup>+</sup>, and -Cs<sup>+</sup> complexing the cyclic ethers were respectively: benzo[15]crown-5,<sup>2a</sup> 1.3, 1.2, 0.69, 0.43, 0.19; benzo[18]crown-6,<sup>2a</sup> 3.6, 1.1, 1.3, 1.05, 0.69; dibenzo[18]crown-6,<sup>2a</sup> 1.35, 0.89, 0.97, 0.65, 0.40; 2, 0.40, 0.59, 0.21, 0.096, 0.027; 3, 0.91, 0.67, 0.57, 0.47, 0.23; 4, 0.92, 0.61, 0.49, 0.45, 0.29; 6, 0.54, 0.55, 0.43, 0.30, 0.095; 11, 0.95, 0.19, 0.029, 0.017, 0.000; 8, 0.83, 0.29, 0.13, 0.057, 0.007; 13, 1.14, 0.54, 0.31, 0.30, 0.047; 14, 1.4, 0.74, 0.56, 0.43, 0.19. The trends indicate: aromatic rings decrease  $K_s$ 's;  $K_s$  for resin-H<sub>3</sub>O<sup>+</sup> > -Na<sup>+</sup> > -K<sup>+</sup> > -NH<sub>4</sub><sup>+</sup> > -Cs<sup>+</sup>, except for 2 (-Na<sup>+</sup> > -H<sub>3</sub>O<sup>+</sup>) and for benzo- and dibenzo[18]crown-6 (-K<sup>+</sup> > -Na<sup>+</sup>); six-oxygen cycles complex better than five; S substituted for O lowers  $K_s$ , except for resin-H<sub>3</sub>O<sup>+</sup>; the side chain of 13 de-

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(9) (a) Amberlyst-15, polystyrenesulfonic acid, Rohm and Haas, 40-60 mesh, average pore diameter, 200-600 Å. (b) Dry resin saturated with H<sub>3</sub>O<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>, NH<sub>4</sub><sup>+</sup>, or Cs<sup>+</sup> (25-50 mg) was mixed with 5 to 12  $\times 10^{-3}$  M solution of cycle in dry dichloromethane. The solution's optical density ( $\lambda$  250-340 nm) was measured before mixing and monitored until constant (mixture shaken at 25°).

creases  $K_s$  for resin- $\text{Cs}^+$ , increases  $K_s$  for resin- $\text{H}_3\text{O}^+$ , but has little effect on the other three. Dibenzo[18]crown-6's  $K_s$  order of resin- $\text{K}^+ > -\text{Na}^+ > -\text{Cs}^+$  parallels Frensdorff's<sup>10</sup> stability constant order for dibenzo[18]crown-6's complexation of metal chlorides in methanol. Others noted that substitution of O by S decreases the complexation of alkaline earth metals by crown ethers,<sup>2d, 2f</sup> and that [18]crown-6 derivatives complex  $\text{K}^+ > \text{NH}_4^+ > \text{Cs}^+$ .<sup>10</sup> Binaphthyl crown ether CPK models suggest hole diameters of 2.6–3.1 Å that change with naphthyl-naphthyl dihedral angles (45–135°). "Hinged" cycles adapt somewhat differently to guest-cation size and character.

The maximum cycle adsorption on cationic resin occupies ~4% of the potential sites. Smid,<sup>11</sup> with benzo[18]crown-6 units included in polystyrene polymer, observed 70% maximal crown site utilization by  $\text{K}^+$ . Resin-crown's steric requirements for complexing  $\text{K}^+$  are less than resin- $\text{K}^+$ 's requirements for complexing crown.

Chiral crowns 2–4, 6, and 7 contain  $C_2$  symmetry axes. Chiral alkylammonium salt's complexation to either face of  $C_2$ -crowns generates indential species. Crowns 10 and 13 possess "sidedness," since binding to different faces generates diastereomers. The side chain of 10 is located closer to the  $C_2$  axis of parent cycle 6 than is the side chain of 13. Thus the two faces that 13 presents to potential chiral guest molecules differ more than the two faces of 10. This work demonstrates feasibility of synthesizing a variety of chiral crown ethers capable of complexing ammonium, alkylammonium, hydronium, and metal cations.

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## Chiral Recognition in Molecular Complexing<sup>1</sup>

Sir:

Crown ether compounds containing binaphthyls as potential chiral barriers were reported.<sup>2</sup> Chiral recognition properties of optically pure crown ethers complexing (*R*)- and (*S*)- $\alpha$ -phenylethylammonium hexafluorophosphate are described here.

Binaphthol (1), resolved to optical purity through its mono-*l*-menthoxyacetic ester, gave  $[\alpha]^{25\text{D}} - 33.6^\circ$ .<sup>3a</sup> The (superior) reported method<sup>4</sup> gave  $[\alpha]^{25\text{D}} - 33.9^\circ$ <sup>3a</sup> and  $[\alpha]^{25\text{D}} + 33.8^\circ$ .<sup>3a</sup> Although optically stable (100°,

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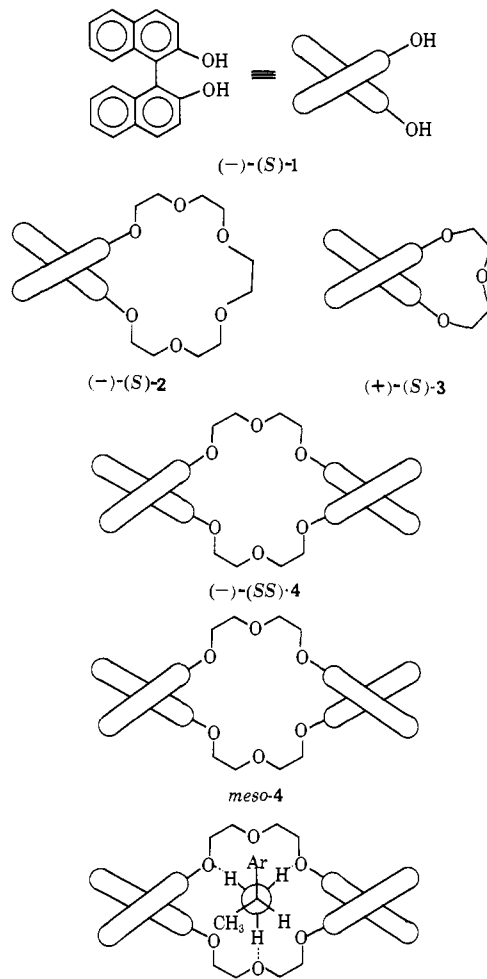
(3) (a) *c* 0.87–1.0, tetrahydrofuran; (b) carbon and hydrogen analyses were within 0.30 of theory; new compounds gave expected pmr spectra and molecular ions in their mass spectra; (c) *c* 0.81–0.87,  $\text{CH}_2\text{Cl}_2$ .

(4) J. Jacques and C. Fouquay, *Tetrahedron Lett.*, 4617 (1971).

24 hr) in dioxane-water, (–)-1 racemized 72% with HCl (~1.2 *N*) present and 69% (118°, 23 hr) in butanol–0.667 *M* KOH. Molecular models (CPK) indicate that protonation or hydroxylation of the 1 or 8 positions of (–)-1 lowers the steric barrier to Ar–Ar rotation. Charge at these positions probably makes bond angles more deformable.

With pentaethylene glycol ditosylate in tetrahydrofuran–potassium *tert*-butoxide (66°, 5 hr), optically pure (–)-1 gave (–)-2<sup>3b</sup> (64%, oil,  $[\alpha]^{25\text{D}} - 70.5^\circ$ <sup>3a</sup>). In oxygen-free diethylene glycol (sealed tube, 205°), (–)-2 underwent 0% rotational loss in 6, and 8.6% in 202 hr.

With diethylene glycol ditosylate in tetrahydrofuran–potassium *tert*-butoxide (15 hr, 66°), optically pure (–)-1 gave (+)-3<sup>3b</sup> (5%, mp 230–231°,  $[\alpha]^{25\text{D}} + 71^\circ$ <sup>3c</sup>)



projection looking down C–N of (*R*)-5  
cation complexed with (SS)-4; Ar =  $\text{C}_6\text{H}_5$

and (–)-4<sup>3b</sup> (31%,  $[\alpha]^{25\text{D}} - 221^\circ$ ,<sup>3c</sup> mp 123–126°, cyclohexane solvate). Similarly, (+)-1 gave (+)-4 ( $[\alpha]^{25\text{D}} + 221^\circ$ ,<sup>3c</sup> mp 123–126°, solvate). Similarly, (±)-1 gave (±)-3<sup>3b</sup> (8%, mp 227–228°), (±)-4<sup>3b</sup> (25%, mp 260–260.5°), and *meso*-4<sup>3b</sup> (2%, mp 283–284°). The identity of the pmr spectra of (+)-4 and (±)-4 and the substantial difference between these spectra and that of *meso*-4 established (±)-4 and *meso*-4 structures. Whereas (+)-4 exemplifies the rarely encountered chiral  $D_2$  point group, that of *meso*-4 is  $C_s$ . Since (+)-1 is  $R$ ,<sup>5</sup> all configurations are assignable.

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