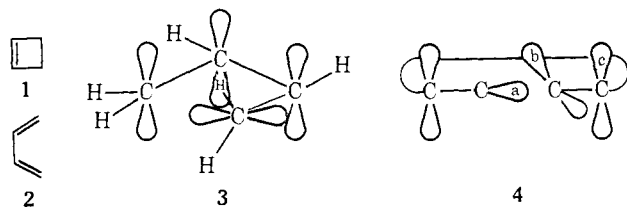


size using MINDO/3 and without making any assumptions, is now trivial,<sup>12</sup> we were able to impose a less rigorous constraint on the system to enforce disrotatory reaction. We assumed only that as one of the methylene groups in **1** rotates, the other is prevented from rotating in a conrotatory sense, being, however, free to rotate disrotatorily. Under these conditions the reaction followed a course entirely different from that<sup>7,10</sup> previously assumed, involving the formation of the orthogonal biradical **3**. The transition state of the reaction lies between **1** and **3**, its structure (Fig. 1b) corresponding to rotation of one of the methylene groups in **1** through 45° while the other remains orthogonal to the C<sub>4</sub> plane. All previous calculations for the reaction must therefore be disregarded. The calculated activation energy (55.6 kcal/mol) leads to an estimate of the difference between the conrotatory and disrotatory paths of 16.6 kcal/mol, in good agreement with a recent experimental estimate ( $\geq 15$  kcal/mol<sup>17</sup>).

The reaction therefore follows the pattern predicted by our recent discussion<sup>6</sup> of the course of "forbidden" reactions in terms of orbital isomerism. Such a reaction involves the interconversion of lumomers and must therefore involve an orbital crossing and an intermediate biradical. The reaction will try to cross the biradical barrier at its lowest point, *i.e.*, one corresponding to the most stable form of the biradical. Here that would be expected to be **3** since any interaction between the in-plane 2p AO and the MO's of the allyl moiety will be antibonding.<sup>4</sup>



It is easy to see why an energy barrier should separate **1** from **3**. As one of the methylene groups in **1** begins to rotate, the interaction between the AO's (a and b in **4**) forming the H<sub>2</sub>C-CH<sub>2</sub> bond in **1** decreases. Initially the resulting decrease in energy is not compensated by the nascent interaction between the AO (b) of the rotating methylene and the 2p AO (c in **4**) of the adjacent olefinic carbon atom. As the reaction proceeds, the latter interaction becomes progressively more important and so at some point the effect of bond formation outweighs that of bond breaking. The energy of the system would therefore be expected to rise to a maximum in the vicinity of a twist angle of 45° and then to decrease again. This is exactly what we find.

These results stress once more the categorical need for complete geometry optimization in calculations of reaction paths. Calculations in which assumptions are made concerning the geometries of the intermediate phases are worthless and can be very misleading.

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Michael J. S. Dewar,\* Steven Kirschner

Department of Chemistry, The University of Texas at Austin  
Austin, Texas 78712

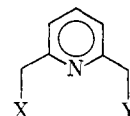
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## The Pyridyl Unit in Host Compounds<sup>1</sup>

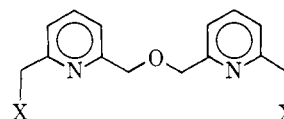
Sir:

Multiheteromacrocycles that contain as part of the major ring 2,6-disubstituted pyridine units have been reported combined with just CH<sub>2</sub>CH<sub>2</sub> units,<sup>2a,b</sup> just CH<sub>2</sub>SCH<sub>2</sub> units,<sup>2c</sup> just CH<sub>2</sub>SCH<sub>2</sub> combined with CH<sub>2</sub>O-CH<sub>2</sub> units,<sup>2d</sup> and just CH<sub>2</sub>OCH<sub>2</sub> combined with *o*-CH<sub>2</sub>-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub> units.<sup>2e</sup> The ability of crown ethers to bind cations<sup>3</sup> stimulated the design of cyclic polyethers that as host compounds formed highly structured molecular complexes with appropriate guest compounds.<sup>4</sup> We report here the feasibility of introducing into host compounds pyridyl units, which act as binding and shaping sites for specific guest compounds.

Treatment of **1**<sup>5</sup> with hydrobromic acid at 120° (1 hr) gave, after neutralization, extraction, and chromatography, 39% recovered **1**, 16% of **2**,<sup>2a</sup> and 41% of



**1**, X = Y = OH; **2**, X = Y = Br; **3**, X = Br, Y = OH;  
**4**, X = OH, Y = H; **5**, X = Cl, Y = H; **6**, X = Y = Cl



**7**, X = H; **8**, X = OAc; **9**, X = OH

**3**,<sup>6a,b,c,e</sup> mp 74–78° (dec). In tetrahydrofuran at 25°, **4**<sup>2a</sup> was metalated with sodium hydride, and then treated with **5**<sup>2a</sup> to give (74%) **7**,<sup>6a,b,c,d</sup> mp 77–78°. Ether **7** in glacial acetic acid–30% hydrogen peroxide at 80° (14 hr) gave (85%) crude bis(*N*-oxide),<sup>6b</sup> mp 161–173°, which was heated in acetic anhydride<sup>5</sup> at 100° (9 hr) to give (17%) after chromatography and crystallization, **8**,<sup>6a,b,d</sup> mp 97–98.5°. Hydrolysis of **8** with sodium hydroxide gave (90%) crude **9**.<sup>6b</sup>

Treatment of **1** with tetraethylene glycol ditosylate in refluxing tetrahydrofuran, potassium *tert*-butoxide, and 2.5% water gave (29%) after chromatography and

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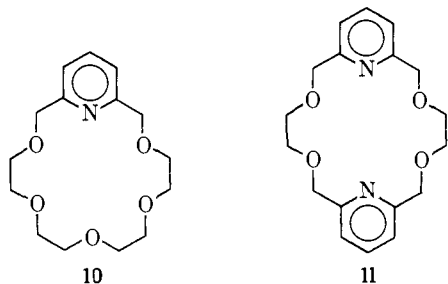
(2) (a) W. Baker, K. M. Buggle, J. F. W. McOmie, and D. A. M. Watkins, *J. Chem. Soc.*, 3594 (1958); (b) W. Jenny and H. Holzrichter, *Chimia*, **22**, 306 (1968); (c) F. Vögtle and L. Schunder, *Chem. Ber.*, **102**, 2677 (1969); (d) F. Vögtle and E. Weber, *Angew. Chem.*, **86**, 126 (1974); (e) G. R. Newkome and J. M. Robinson, *J. Chem. Soc., Chem. Commun.*, 831 (1973).

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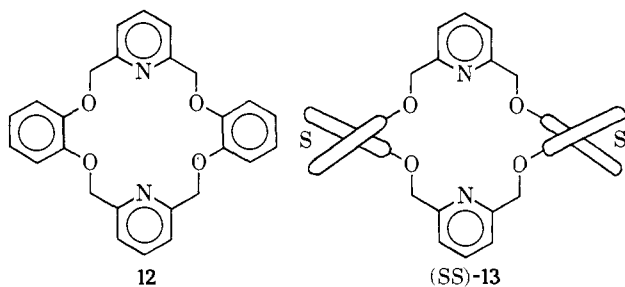
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(6) (a) Carbon and hydrogen analyses were within 0.30 of theory; (b) pmr spectra were consistent with structure; (c) mass spectra gave molecular ion; (d) osmotic molecular weights in CHCl<sub>3</sub> were within 4% of theory; (e) compound is lachrymatory.

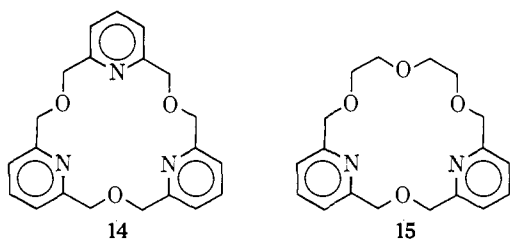


crystallization (dichloromethane-pentane) **10**:<sup>6a,c</sup> mp 40–41°; pmr spectrum (60 MHz, CDCl<sub>3</sub>),  $\delta$  3.55 and 3.65 (s, s, OCH<sub>2</sub>CH<sub>2</sub>O, 18 H), 4.70 (s, ArCH<sub>2</sub>, 4 H), 6.0–7.7 (six lines, A<sub>2</sub>B, ArH, 3 H). To ethylene glycol in tetrahydrofuran was added sodium hydride, then **2** (dropwise in tetrahydrofuran). From the mixture after 70 hr at 25°, **11**<sup>6a,b,c</sup> was isolated (18%) by extraction, sublimation, and crystallization, mp 147–148°. From catechol and **6**<sup>2a</sup> (tetrahydrofuran and potassium *tert*-butoxide at reflux, 24 hr), **12**<sup>6a-c</sup> was produced



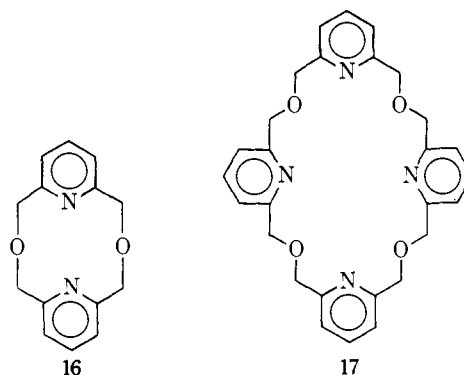
(9%), mp 184–186°. Similarly with optically pure (*S*)-(–)-2,2'-dihydroxy-1,1'-binaphthyl,<sup>4b</sup> (*SS*)-**13**<sup>6a,c</sup> was prepared (26%) as a bistetrahydrofuran clathrate: mp 288–292° (dec),  $[\alpha]_D^{25}$  –302° (*c* –0.3, CHCl<sub>3</sub>); pmr spectrum (100 MHz, CDCl<sub>3</sub>)  $\delta$  1.76 and 3.66 (m, m, (CH<sub>2</sub>)<sub>4</sub>O, 16 H), 4.82 (s, ArCH<sub>2</sub>, 8 H), 6.32 and 6.40 (s, s, pyridine- $\beta$ -H's, 4 H), 6.8–7.9 (m, naphthalene ArH and pyridine- $\gamma$ -H's, 26 H). As molecular models suggest should be the case, the two sets of  $\beta$ -hydrogens of the pyridine rings of (*SS*)-**13** are in different magnetic environments.

Diol **9** was metalated with sodium hydride in tetrahydrofuran and mixed with **2** at 25° for 100 hr. Gel permeation (Bio Beads SX-8) chromatographic separation of the products gave 32% of **14**:<sup>6a,d</sup> mp 125–128°

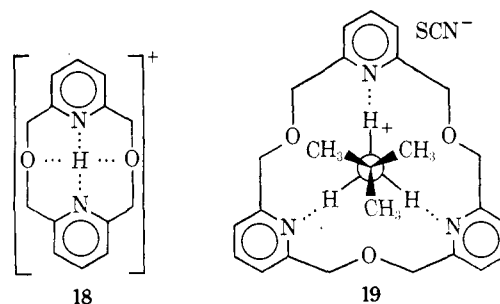


(dec); pmr spectrum (60 MHz in CDCl<sub>3</sub>)  $\delta$  4.6 (s, ArCH<sub>2</sub>, 12 H), 7.1–7.7 (m, ArH, 9 H). Similarly, **9** and diethylene glycol ditosylate gave **15**<sup>6b</sup> mixed with about 10% of an unremoved impurity (pmr). Similarly, **1** and **2** gave 1% of **16**,<sup>6a,d</sup> mp 172–175° (dec), and 20% of **17**,<sup>6a,d</sup> mp 173–176°. The pmr spectra (60 MHz in CDCl<sub>3</sub>) of **16** and **17** gave respectively:  $\delta$  4.6 (s, ArCH<sub>2</sub>, 8 H) and 6.7–7.4 (m, ArH, 6 H); 4.6 (s,

ArCH<sub>2</sub>, 16 H) and 7.1–7.7 (m, ArH, 12 H). Reaction of **3** with sodium hydride in tetrahydrofuran (25°, 100 hr) gave, after gel permeation chromatography, 1% of **14**, 6% of **16**, and 6% of **17**.



The pK<sub>a</sub>'s at 25° in water of the monoprotinated (diprotonated) cycles were the following: **10**, 4.8; **11**, 5.3 (3.6); **14**, 5.3 (3.7); **16**, 7.9 (<3); **17**, 4.8 (>3); pyridine,<sup>7</sup> 5.1; 2,4,6-trimethylpyridine,<sup>7</sup> 7.4. Monoprotinated **16** is ~4 kcal/mol more stable than monoprotinated **10** or **17**, but diprotonated **16** is less stable than diprotonated **11**, **14**, or **17**. Molecular models (Corey, Pauling, Koltun) of monoprotinated **16** suggest structure **18**.



Cycle **14** strongly complexes *tert*-butylammonium thiocyanate<sup>8</sup> and forms a crystalline one-to-one complex<sup>6a,b</sup> (from chloroform, 83%), mp 198–201° (dec). Molecular models suggest the complex possesses structure **19**. Cycle (*SS*)-**13** complexes and shows chiral recognition (EDC ~ 2) toward (*S*)-phenylglycine methyl ester hexafluorophosphate (distribution experiments at –13° between water-salt and chloroform),<sup>4e</sup> comparable to its oxygen analog.<sup>9</sup>

These experiments demonstrate that 2,6-pyridinedimethyl units can be substituted for CH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub> units in the design and synthesis of host molecules for forming highly structured molecular complexes. The reactions and properties of these and other pyridine-containing multiheteromacrocycles are under active investigation.

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Martin Newcomb, George W. Gokel, Donald J. Cram\*

Contribution No. 3345, Department of Chemistry  
University of California at Los Angeles  
Los Angeles, California 90024

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