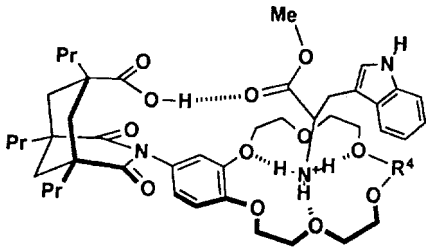
benzo-naphtho receptor **6**, having two dialkyl and four alkyl aryl oxygens. The dibenzo receptor **5** shows slightly higher extractabilities than benzo-naphtho receptor **6** does. This might indicate that a phenolic oxygen is more efficient acceptor in the hydrogen bond than a naphtholic oxygen. Additionally, a contribution of π-stacking interactions in these receptors is too small compared with the hydrogen-bonding interactions to notice it.

The receptor **3** extracts both Tyr-OMe and Trp-OMe hydrochlorides much more efficiently than its methyl ester derivative **4** does. As shown in complex **9**, this could be rationalized by an additional hydrogen bond between the carboxylic acid of the receptor **3** and the carbonyl oxygen of amino esters. This hydrogen bond greatly enhances extractabilities of our receptors, though an ester group has been hardly utilized as a hydrogen-bonding acceptor in artificial receptors.[6]



9

The imide receptor **3** and amidine receptor **8** are same two binding sites, crown ether and carboxylic acid. Small difference in geometrical position of two binding sites caused to decrease considerably extractability of the receptor **8**, in which it might not be possible to achieve an optimum hydrogen bond between the carboxylic acid of the receptor **8** and the carbonyl oxygen of amino esters. Another possible explanation for different extractabilities of **3** and **8** is that the N-C bond (imide-phenyl) in the receptor **3** is freely rotatable to form simultaneous hydrogen bonds in two binding sites. Quantitative analysis of this hydrogen bond has been determined by liquid-liquid extraction method described by Cram.[7] The extraction experiments have been performed employing 0.15 M of the receptor, **3** or **4**, in CH_2Cl_2 and 0.015 M of amino ester hydrochloride in 1.0 N aqueous HCl. Under these conditions receptors **3** and **4** extract, respectively, 60± 2% and 10± 2% of Trp-OMe hydrochloride from aqueous into organic layer, while the extraction of more hydrophilic Tyr-OMe hydrochloride[8] by both of the receptors are negligible. The amount extracted has been determined by measuring changes in absorbances of Trp-OMe hydrochloride in aqueous 1 N HCl layer at 279 nm (ε=5250 M^{-1} cm^{-1}). The difference of 50% extraction is corresponding to 30 times differences of binding constant (K_a),[7] and thus an additional hydrogen bond between the carboxylic acid and the carbonyl oxygen is estimated to be ΔG°=2.0 kcal/mol.

In conclusion, we synthesized geometrically well-defined receptors which recognize amino esters through multiple hydrogen bonds. Our system can be further utilized as a model of the protease enzyme;[9] the crown ether part in our receptors may function as a binding site and the carboxylic acid as a catalytic site. The efforts to elucidate this possibility are underway in our laboratory.

Acknowledgment. This work was financially supported by the Yonsei University and the Organic Chemistry Research Center.

References

1. (a) Atwood, J. L.; Orr, G. W.; Juneja, R. K.; Bott, S. G.; Hamada, F. *Pure Appl. Chem.* **1993** *65*, 1471. (b) Branda, N; Wyler, R.; Rebek, J., Jr. *Science* **1994**, *263*, 1267.
2. (a) Behr, J.-P.; Lehn, J.-M.; Vierling, P. *Helv. Chim. Acta* **1982**, *65*, 1853. (b) Rebek, J., Jr.; Askew, B.; Nemeth, D.; Parris, K. *J. Am. Chem. Soc.* **1987**, *109*, 2432. (c) Galan, A.; Andreu, D.; Echavarren, A. M.; Prados, P.; de Mendoza, J. *J. Am. Chem. Soc.* **1992**, *114*, 1511.
3. Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. M. *Chem. Rev.* **1991**, *91*, 1721, and references are therein.
4. We used the tripropyl triacid **2** instead of commecially available Kemp triacid to increase solubilities of receptors in organic solvents. For a preparation of **2**, see: Jeong K. S.; Tjivikua, T.; Muehldorf, A.; Deslongchamps, G.; Famulok, M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 201.
5. (a) van Keulen, B. J.; Kellogg, R. M.; Piepers, O. *J. Chem. Soc., Chem. Comm.* **1979**, 285. (b) Weber, E.; Josel, H.-P.; Puff, H.; Franken, S. *J. Org. Chem.* **1985**, *50*, 3125.
6. For the hydrogen bond between amino esters and aromatic hydroxyl groups, see: (a) Aoyama, Y.; Yamagishi, A.; Asagawa, M.; Toi, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1988**, *110*, 4076. (b) Mizutani, T.; Ema, T.; Tomita, T.; Kuroda, Y.; Ogoshi, H. *J. Am. Chem. Soc.* **1994**, *116*, 4240.
7. (a) Moore, S. S.; Tarnowski, T. T.; Newcomb, M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6398. (b) Koenig, K. E.; Lein, G. M.; Stuckler, P.; Kaneda, T.; Cram, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 3553.
8. Wolfenden, R.; Andersson, L.; Cullis, R. M.; Southgate, C. C. B. *Biochemistry* **1981**, *20*, 849.
9. Sasaki, S.; Koga, K. In *Crown Ethers and Analogous Compound*; Studies in Organic Chemistry 45; Hiraoka, M., Ed.; Elsevier: Amsterdam, 1992; p 265-310.

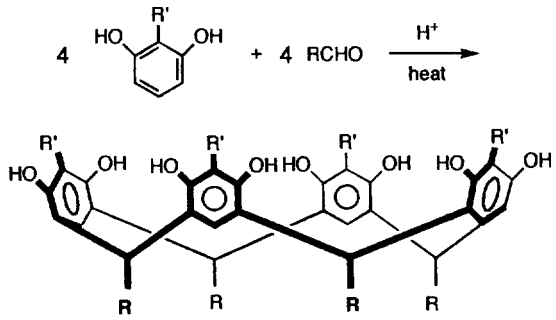
Hexadecols. New Bisfunctional Molecular Vessels from Condensation Reaction among Resorcinol, Monoaldehyde, and Dialdehyde

Kyungsoo Paek

Department of Chemistry, Soong-Sil University, Seoul 156-743
Center for Biofunctional Molecules, P.O. Box 125, Pohang 790-600, Korea

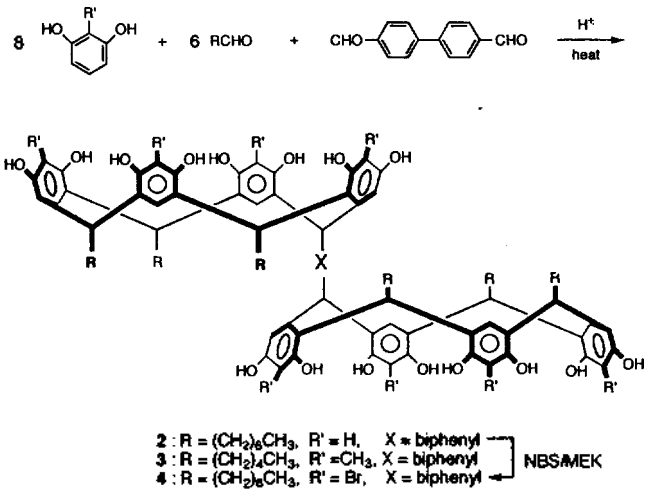
Received June 22, 1994

Octols **1** are cyclotetramers from the fourfold homogeneous condensations of various aldehydes with resorcinol or 2-substituted resorcinols as shown in Scheme 1.[1] With aliphatic aldehydes and resorcinol or 2-methylresorcinol, only C_{4v}-octols are yielded, whose crystal structures exhibit bowl-shaped



1 (R = Alkyl or aryl, R' = H, CH_3, OH etc.)

Scheme 1.

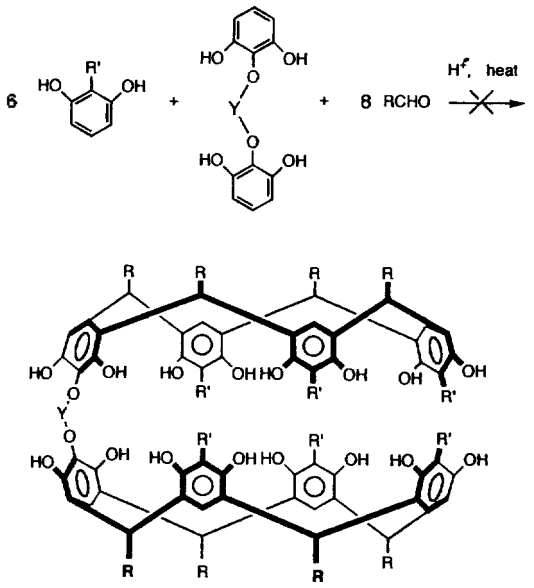


2 : R = $(CH_2)_6CH_3$, R' = H, X = biphenyl
3 : R = $(CH_2)_4CH_3$, R' = CH_3, X = biphenyl
4 : R = $(CH_2)_6CH_3$, R' = Br, X = biphenyl
NBS/MEK

Scheme 2.

conformations. The inside hydrophobic cavity of octols is surrounded by 8-hydroxyl groups on the rim.[1b] Octols are studied as hosts for ammonium ions,[2] dicarboxylic acids,[3] sugars,[4] and nucleosides.[5] Also they are used as important starting vessels for the syntheses of cavitands,[6] carcerands,[7] and hemicarcerands,[8] as well as monolayer materials.[9] The facile functionalizations of octols make them more attractive intermediates toward designed organic hosts having defined dimension and stability.[10]

The heterogeneous condensation among resorcinol (or 2-methylresorcinol), octanal (or hexanal), and 4,4'-bisformylbiphenyl gave hexadecol 2[11] (or 3[12]) in 14.6 (or 22.8%) yield (Scheme 2) together with the major octols. Hexadecols were crudely separated by fractional crystallyzation from the major homo-condensed octols and then finely by reversed-phase flash chromatography. The rather high yield from 2-methylresorcinol and hexanal can be ascribed to the better crystallinity of the corresponding hexadecol 3. Hexadecols consist of two octols connected by biphenyl unit in back-to-back fashion, which could enable independent recognition by the two divergent binding sites. Flexible dialdehyde such as glutaric aldehyde does'nt give separable hexadecols presumably due to the tangle of two condensing sites. The pac-man type hexadecol 5 which consists of two octols connected in front-to-front fashion forming a convergent three dimensional binding site was designed. But the heterogeneous condensation among resorcinol, bispyrogallol, and monoaldehyde gave only insoluble mixture (Scheme 3). It also seems that structually rigid bispyrogallol or bisresorcinol should be used to inhibit random polymerization.



5 (Y = ethylene or propylene)

Scheme 3.

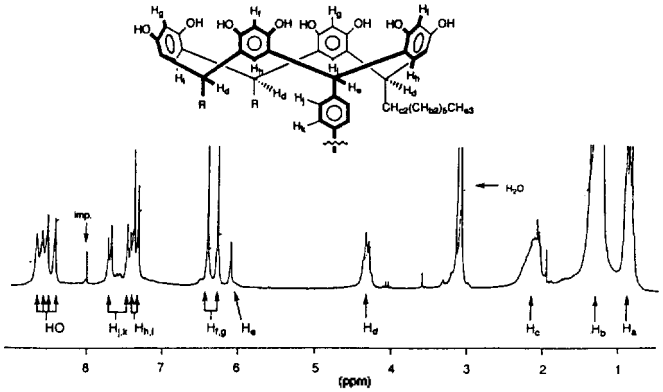


Figure 1. ^{1}H NMR spectrum (200 MHz, acetone-d_6) of hexadecol 2 and its peak assignment.

Hexadecols have C_{2v} symmetry and their ^{1}H NMR spectra distinctively illustrate their stereochemistries. Figure 1 shows ^{1}H NMR spectrum of hexadecol 2 in acetone-d_6 and its peak assignments. Alkyl protons H_a, H_b, H_c, and methine protons H_d and H_e can be easily assigned. H_j and H_k on bridging biphenyl unit can be clearly distinguished from other proton peaks due to its unique two doublets at 7.42 (J=8 Hz) and 7.67 ppm (J=8 Hz). Aryl protons H_f and H_g at 6.26 and 6.38 ppm were also differenciated from H_k and H_i because the peaks for H_f and H_g were disappeared when hexadecol 2 were treated with NBS in MEK to give a octabromide 4.[7] Hydroxy protons at 8.40-8.70 ppm were exchanged with D_2O and also disappeared when hydroxys were

bridged to give a cavitand using CH_2BrCl/K_2CO_3.[7] The crystal structure of a hexadecol derivative was resolved and will be reported elsewhere.

The representative synthetic procedure of hexadecol 2 is as follows: Resorcinol (4.2 g, 38.1 mmol), octanal (4.5 mL, 28.8 mmol), and 4,4'-bisformylbiphenyl (1.0 g, 4.7 mmol) were dissolved in 95% EtOH (50 mL) at 80℃. Through the condenser, conc. HCl (12.5 mL) was slowly added, and then the mixture was stirred for 18 h at 80℃ under argon. After cooling to room temperature, the solution was poured into 500 mL of water with shaking. The precipitation was filtered, washed with 200 mL of water 3 times, and then dissolved in minimum amount of hot MeOH. After standing overnight, octol was filtered off and the filtrate was concentrated. The concentrate was loaded on C-18 capped reversed phase flash column (5×15 cm, 25% H_2O in acetone and then 5 to 3% H_2O in MeOH).[13] The best portions were collected and the solvent was evaporated to give precipitates. The precipitates were filtered through medium fritted glass funnel and dried under high vacuum to give 1.2 g (14.6%) of hexadecol 2.

Conclusively we observed that the hetero condensation procedure described above is an efficient method to get hexadecols which could be valuable starting vessels for multifunctional hosts only if structually rigid bridging units (dialdehyde or bisresorcinol) were applied. The back-to-back connected hexadecol 2 and 3 could be derivatized to biscavitands and biscarcerands as well as monomers leading to a new kind of polymers formed not by covalent bonds but by π-π stacking interactions.[14] Unfortunately pure hexadecols 2 and 3 are too insoluble in CH_2Cl_2 or $CHCl_3$ to be useful for guest recognition studies in nonpolar solvents. Preparation of more soluble hexadecols and their molecular recognition studies are in progress.

Acknowledgement. The financial supports from Korea Science and Engineering Foundation and Korea Institute of Science and Technology are gratefully acknowledged.

References

1. (a) Högberg, A. G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6046. (b) Tunstad, L. M.; Tucker, J. A.; Dalcanale, E.; Weiser, J.; Bryant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram. D. J. *J. Org. Chem.* **1989**, *54*, 1305.
2. Schneider, H. J. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 647.
3. Tanaka, Y.; Kato, Y.; Aoyama, Y. *J. Am. Chem. Soc.* **1990**, *112*, 2807.
4. (a) Aoyama, Y.; Tanaka, Y.; Sugahara, S. *J. Am. Chem. Soc.* **1989**, *111*, 5397. (b) Kurihara, K.; Ohto, K.; Tanaka, Y.; Aoyama, Y.; Kunitake, T. *J. Am. Chem. Soc.* **1991**, *113*, 444. (c) Kikuchi, Y.; Tanaka, Y.; Sutarto, S.; Kobayashi, K.; Toi, H.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10302.
5. Kobayashi, K.; Asakawa, Y.; Kato, Y.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 10307.
6. (a) Cram, D. J.; Stewart, K. D.; Goldgerg, I.; Trueblood, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2574. (b) Moran, J. R.; Ericson, J. L.; Dalcanale, E.; Bryant, J. A.; Knobler, C. B.; Cram, D. J. *J. Am Chem. Soc.* **1991**, *113*, 5707.
7. (a) Bryant, J. A.; Blanda, M. T.; Vincenti, M.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2167. (b) Sherman, J. C.; Knobler, C. B.; Cram, D. J. *J. Am. Chem. Soc.* **1991**, *113*, 2194.
8. (a) Cram, D. J.; Blanda, M. T.; Paek, K.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7765. (b) Robbins, T. A.; Konbler, C. B.; Bellew, D. R.; Cram, D. J. *J. Am. Chem. Soc.* **1994**, *116*, 111.
9. van Velzen, E. U. T.; Engbersen, J. F. J.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 3597.
10. Kim, K.; Paek, K. *Bull. Korean Chem. Soc.* **1993**, *14*, 658.
11. 2: mp>290℃ (decompose): ^{1}H NMR (200 MHz, Acetone-d_6) 0.85-0.91 (m, 18H, CH_3×6), 1.20-1.35 (m, 60H, CH_2×30), 1.97-2.13 (m, 12H, CH_2×6), 4.30-4.34 (m, 6H, methine), 6.09 (s, 2H, methine), 6.26 (s, 4H, Ar-H), 6.38 (s, 4H, Ar-H), 7.29 (s, 4H, ArH), 7.35 (s, 4H, Ar-H), 7.40, 7.44, 7.65, 7.69 (AB quartet, 8H, biphenyl), 8.39, 8.50, 8.56, 8.63 (four s, each 4H, OH, exchange with D_2O); FAB$^+$ MS (Xenon, NOBA) m/z 1714 (M^+, 27%). 1614 (M^+-$(CH_2)_6CH_3$+1, 100%); Anal. Calcd for $C_{110}H_{138}O_{16}+2H_2O$ (dried at 80℃ ×10^{-5}×5 hr): C, 75.40; H, 8.18. Found: C, 75.32; H, 8.03.
12. 3: mp>220℃ (decompose); ^{1}H NMR (200 MHz, Acetone-d_6) 0.80-1.00 (m, 18H, CH_3×6), 1.13-1.50 (m, 36H, CH_2×18), 1.95-2.25 (m, 30H, CH_3×6+CH_2×6), 4.36 (m, 6H, methine×6), 6.11 (s, 2H, methine×2), 7.11, 7.14 (s, 8H, Ar-H), 7.39, 7.43, 7.67, 7.71 (AB quartet, 8H, biphenyl), 7.86, 7.94, 7.98, 8.11 (four s, each 4H, OH); FAB$^+$ MS (Xenon, NOBA) m/z 1659 (M^++1, 50%), 1587 (M^+-$(CH_2)_4CH_3$, 50%); Anal. Calcd for $C_{106}H_{130}O_{16}+2H_2O$ (dried at 80℃ ×10^{-5}×5 hr): C, 75.06; H, 7.96. Found: C, 75.12; H, 7.97.
13. Küher, T.; Lindstern, G. R. *J. Org. Chem.* **1983**, *48*, 3589.
14. Cram, D. J.; Choi, H. J.; Bryant, J. A.; Knobler, C. B. *J. Am. Chem. Soc.* **1992**, *114*, 7748.

Transformation of Primary Carboxamides to Aldehydes by Sodium Tris(dialkylamino)aluminum Hydrides

Jin Soon Cha*, Jong Mi Kim, and Min Kyoo Jeoung

Department of chemistry, Yeungnam University, Kyongsan 712-749, Korea

Received June 30, 1994

A new class of reducing agents, dialkylamino-substituted derivatives of lithium aluminum hydride have appeared useful reagents for the selective transformation of organic functionalities.[1] Especially, the successful conversion of primary carboxamides to the corresponding aldehydes by lithium tris (diethylamino)aluminum hydride (LTDEA)[1a,c] and lithium tripiperidinoaluminum hydride (LTPDA)[1c] provides a new methodology in organic synthesis.

Very recently, we have synthesized various dialkylamino-substituted derivatives of sodium aluminum hydride, and applied them for selective reduction of organic functionalities.[2] In the course of this study, we found that the sodium deriva-