One-Pot Syntheses of a Carceplex, a Hemicarceplex, and a Gate-Functionalized Hemicarceplex

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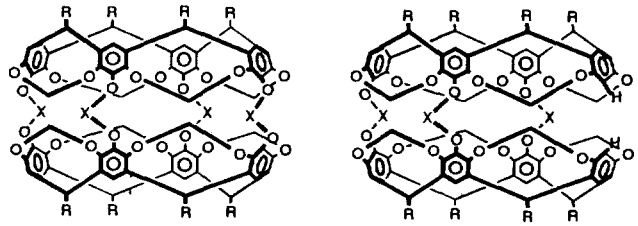
Cram and co-workwer's carcerands and hemicarcerands are based on cavitands derived from octols which are obtained by cyclotetramerization of resorcinol and aldehydes.[1] Carcerands are host molecules having spherical cavity for the inclusion of small guests, but once the guest is captured inside it cannot escape the cavity even at high temperature unless some chemical bonds of host shell are broken.[2] Usually the guests are captured during the formation of carcerands so it exists as carceplex from the beginning. Hemicarcerands are similar to carcerands except that the guests can enter or exit the hosts interior through the shell's gate.[3] The constrictive binding energy of hemicarcerands is defined as the steric repulsions that must be overcome for dissociation of a hemicarceplex. The steric constraints are imposed by the size and shape of the guest, and those of the portal and attractions of the inner phase. Many interesting properties of hemicarcerands are reported such as shell's roll as chemical reactor,[4] control of guest's in-and-out kinetics,[5] molecular container[6] etc., which implies the tremendous applicabilities of hemicarcerands in various fields from material sciences to medicinal chemistry.

Basically the physicochemical properties of hemicarcerands have been controlled by variation of gate size using different number or length of bridging units between two polar caps (hemispheres) as shown in Figure 1. The four-methylene bridged host **1** is a carcerand and the hosts having longer four-bridging units **2**, **3**, **4** are hemicarcerands. But the three methylene bridged host **5** is a hemicarcerand. At this point it might be very interesting if other functional groups could be added around the gate of a hemicarcerand. They could trigger the entrance or the escape of a guest through the gate, which should be another useful way to manipulate the physicochemical properties of hemicarceplexes.[7] Also the functional group(s) could be used to tie-up hemicarcerands together or graft to polymer back-bone, which might result in unprecedented supramolecular properties such as intratransport of guest, intra-redox switching molecule, multi-cellar polymer, etc.

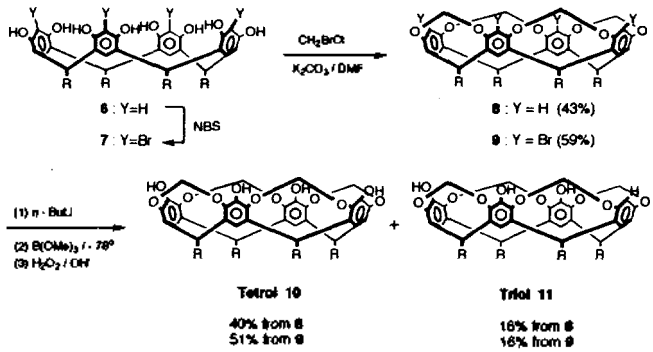
Here we report the first efficient one-pot synthesis of a carcerand **1**, a hemicarcerand **5**, and a gate-hydroxylated hemicarcerand **12**, all of which contain DMA (dimethylacetamide) inside and have undecyl groups as legs (R=$(CH_2)_{10}CH_3$). The first two are similar to those[2b,3] reported except they



1 : X = CH_2[2b]
2 : X = $(CH_2)_4$[4]
3 : X = 1,2-$(CH_2)_2C_6H_4$[5]
4 : X = CH_2COCH_2[6]

5 : X = CH_2[3]

Figure 1. Reported Carcerands and Hemicarcerands.



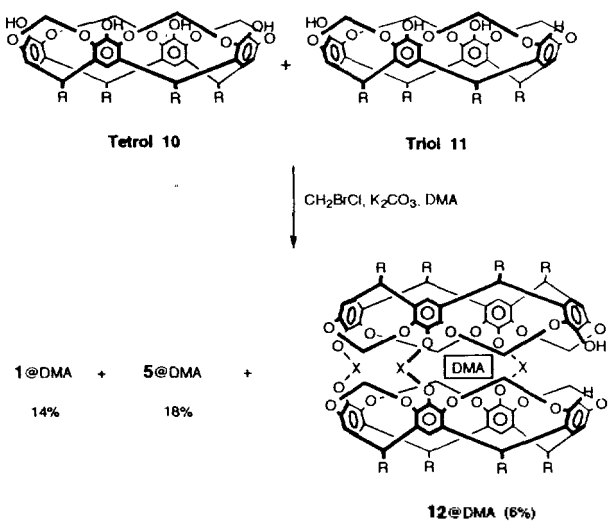
Scheme 1. Synthetic Routes of Tetrol **10** and Triol **11** (R=$(CH_2)_{10}CH_3$).

have the longer legs which give much higher solubilities in various organic solvents.

The semifinal intermediates tetrol **10** and triol **11** were obtained by two routes. The known procedure[2b] from octol **6** *via* tetrabromide **7** and cavitand **9** was well reproduced in good yields (Scheme 1). When cavitand **8**, obtained directly from octol **6**, was treated with *n*-BuLi at RT, quenched with borate at −78 ℃, and then oxidized with H_2O_2/NaOH tetrol **10** and triol **11** were obtained in 40% and 16% yields respectively. Even the latter route reduces one step, the former procedure is preferred overall in the aspect of convenience.

Using the same procedure for converting cavitand **8** to hydroxycavitands **10** and **11**, the attempt to obtain gate-hydroxylated hemicarcerand **12** from hemicarcerand **5** (R=$(CH_2)_{10}CH_3$) which was independently obtained from triol **11**[3] was unsuccessful. It might be attributable to the extreme steric hindrance in the crowded gate of **5** even the process is adaptable to 1,3-dimethoxybenzene or the cavitand **8**.

The extraordinary high yields of carcerands due to the solvent-templation[8] made it possible to design one-pot trial as shown in Scheme 2. One-pot shell-closing reaction between tetrol **10** and triol **11** gave carceplex 1@DMA, hemicarceplex 5@DMA, and hydroxyhemicarceplex 12@DMA in 14%, 18%, and 6% yields respectively. Their distinct R_f values on SiO_2 in a 2 : 1 mixture of hexane and CH_2Cl_2 are 0.4, 0.5, and 0.2 respectively, which make the chromatographic separation easy. ^{1}H NMR, IR, and FAB$^+$ mass spectral data of carceplex 1@DMA and hemicarceplex 5@DMA are exactly those anticipated. IR spectrum of hydro-



Scheme 2. One-Pot Synthesis of Three Hosts **1**, **5**, and **12** Containing DMA ($R=(CH_2)_mCH_3$).

xyhemicarceplex 12@DMA (KBr) shows the stretching band of hydroxy group at 3,447 cm^{-1} and that of DMA's carbonyl group at 1,643 cm^{-1}. Due to its low C_s symmetry ^1H NMR spectrum (300 MHz) of 12@DMA is much more complex compared to that of 5@DMA (C_{2v} symmetry), but the characteristic peaks of guest (DMA) protons were appeared at −2.40 for acetyl, −1.50 and −0.85 ppm for two *N*-methyl hydrogens. The DMA hydrogens are shielded strongly by two polar caps of host. The three singlets of DMA implies the rotation of DMA at ambient temperature along the long axis through the two polar caps is rapid on 300 MHz NMR time scale, which might be hindered at low temperature.[39] FAB^+ mass spectrum (in nitrobenzylalcohol matrix) shows host **12** peak (calcd for $C_{155}H_{224}O_{23}+H_2O+H^+$) at m/z 2,472.8 (12%).

Currently the longer bridged functionalized hemicarcerands are being synthesized using one-pot as well as stepwise trials. But for the three methylene-bridged species it seems that one-pot trial is the only choice. The thermodynamic properties as well as multifunctionalization of hydroxyhemicarcerand **12** are also under investigation.

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