Pergamon

Tetrahedron Letters, Vol. 37, No. 18, pp. 3141-3144, 1996

0040-4039/96 $15.00 + 0.00

S0040-4039(96)00511-4

Synthesis and Structure of a Novel Molecular Bowl with an All-carbon and Acyclic Framework

Kei Goto, Michel Holler, and Renji Okazaki*

Department of Chemistry, Graduate School of Science, The University of Tokyo,
7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan

Abstract: A novel all-carbon molecular bowl **2** where the central functionality is surrounded by two rigid tetramethyl-*m*-terphenyl units was designed. Bromide **3** was readily synthesized by copper (I)-catalyzed coupling reaction between **4** and **5**. X-ray crystallographic analysis established that **3** has a bowl-shaped structure although it is an acyclic molecule. Butyl sulfide **6** and thiol **8** were synthesized via lithiation of **3**. Copyright © 1996 Elsevier Science Ltd

The design of a reaction environment which can specifically regulate the reactivity of a functional group is a major area of current interest and importance. We have been investigating the development of a reaction environment based on a molecular cavity (Figure 1), to which we refer as a *reaction bowl*,[1] and recently reported the synthesis of a stable arenesulfenic acid **1** bearing a bimacrocyclic cyclophane skeleton.[1b] The high stability of **1** indicated that a *reaction bowl* type environment, which surrounds a functional group *from all sides* and *from a distance*, is quite effective for the inhibition of the approach of functional groups on molecules of the same kind without diminution of their reactivities towards a different kind of molecules. The construction of a macrocyclic structure, however, usually requires a multistep synthesis and tend to be accompanied by polycondensation. Although the aryl benzyl ether framework is suitable for the construction of a cyclic structure, it increases the conformational flexibility of the molecule as well as causes the side reactions with some reagents such as alkyllithiums. Furthermore, the interaction between the heteroatoms present in the skeleton and the functional group embedded in the cavity is sometimes undesirable, especially when it is applied to the kinetic stabilization of reactive species. The development of a molecular bowl with higher accessibility and a more inert framework will lead to the wide application of this type of reaction environment. We report here the synthesis and structure of a novel molecular bowl **2** (denoted as ArX hereafter in this paper) with an all-

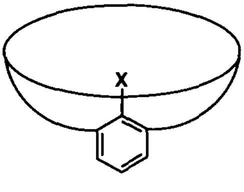
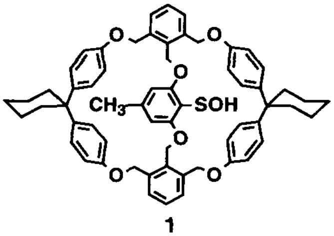


Figure 1. Schematic drawing of a *"reaction bowl"*.



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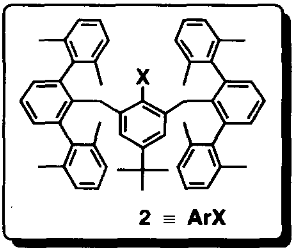


2 ≡ **ArX**

carbon and acyclic framework.

Before we started experiments, we carried out a molecular mechanics calculation (MM2* force field)[2] of ArBr **3** as a model of such a molecular skeleton, the result of which is shown in Figure 2. Inspection of the results of the calculation as well as of the CPK model of **3** suggested that the rigid tetramethyl-*m*-terphenyl units in the side arms would serve as elliptic "shields" and the conformational mobility of the skeleton of **3** would be considerably low for an acyclic molecule. Thus, the skeleton of **2** was expected to fulfill the requirements for a *reaction bowl* useful for the protection of the functional group X.

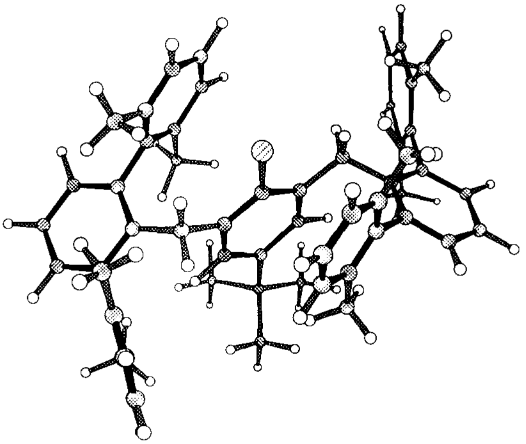
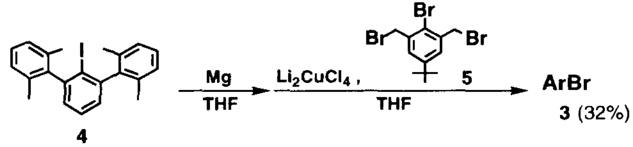


Figure 2. Energy-minimized structure of **3**

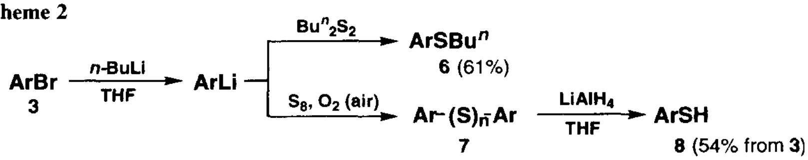
Bromide **3** was readily synthesized by a cross-coupling reaction[3] between Grignard reagent of *m*-terphenyl-2'-iodide **4**[4] and tribromide **5**[5] in the presence of a copper (I) catalyst (Scheme 1).[6] The structure of **3** was determined by X-ray crystallography as shown in Figure 3.[7] The figure clearly shows that **3** is a bowl-shaped molecule, its diameter being about 13 Å. As expected, two *m*-terphenyl units surround the bromide functionality from a distance like two shields and the *tert*-butyl group on the central unit blocks the bottomside of the molecule to construct a bowl-shaped framework. The wide opening on the upper side of the molecule forms a cavity which looks large enough to work as a reaction field for the central functionality.[9] These results are in good agreement with those of the molecular mechanics calculation. The ^{1}H NMR spectrum of **3** at room temperature shows the equivalence of all methyl groups on the *m*-terphenyl units. Since the rotational barrier around the biphenyl bonds of the tetramethyl-*m*-terphenyl unit is considered to be fairly high at room temperature, this result is most reasonably explained in terms of the rapid rotation around the Ar-CH_2-Ar' linkage.

Lithiation of bromide **3** with butyllithium followed by quenching with electrophiles enables the introduction of new functionalities into the cavity. Thus, butyl sulfide **6** was obtained by quenching with dibutyl disulfide in 61% yield (Scheme 2). The reaction of the lithiated compound with S_8

Scheme 1



Scheme 2



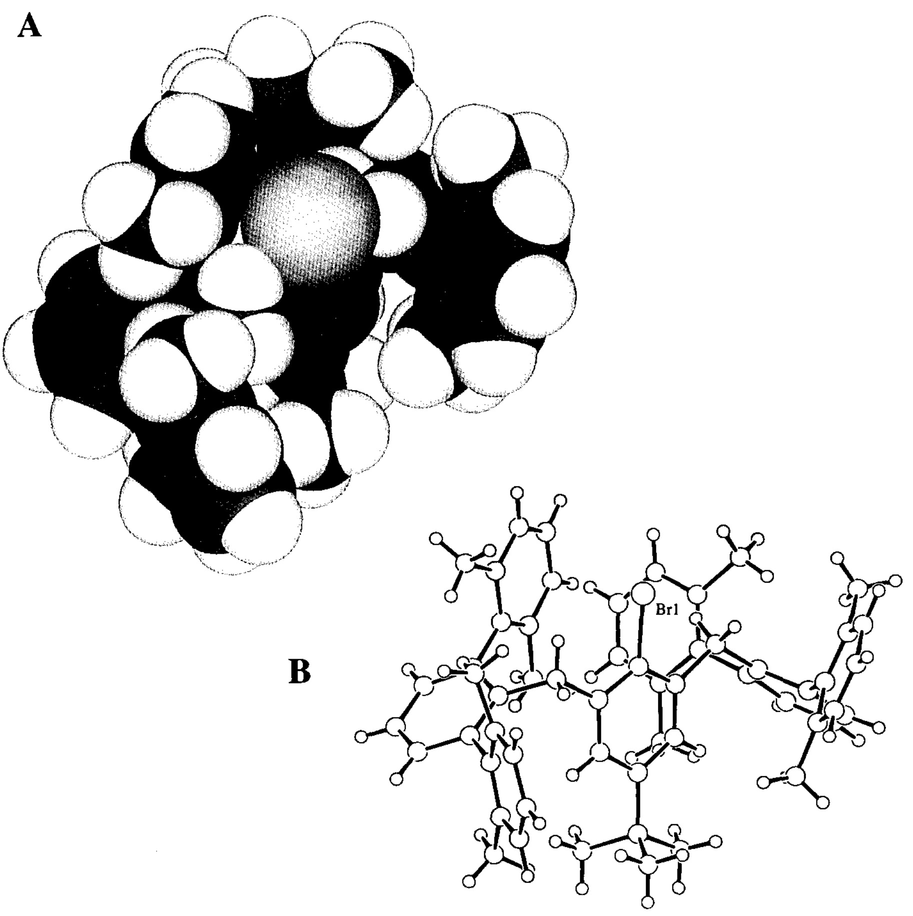


Figure 3. Molecular structure of **3**. (A) Space-filling model of the top view. (B) The side view.

followed by air oxidation afforded the mixture of polysulfide **7**.[12] The average number of sulfur atoms of **7** was found to be 7.8 by elemental analysis.[13] Thiol **8** was obtained by the treatment of **7** with $LiAlH_4$ (54% from **3**). The ^1H NMR spectrum of **8** showed the signal of the SH proton at $\delta = 1.14$, indicating that it is shielded by the xylyl rings of the *m*-terphenyl units.

The results presented here demonstrate that a bowl-shaped environment can be realized even by using an acyclic framework if the rigid units are employed and the conformational mobility of the molecule is sufficiently reduced. The application of this novel molecular bowl to the synthesis of compounds having highly reactive functional groups is currently in progress.

Acknowledgments: This work was supported by Grants-in-aid for Scientific Research (No. 07854035 and 94187) from the Ministry of Education, Science and Culture, Japan. We also thank Tosoh Akzo Co., Ltd. for the generous gift of alkyllithium compounds. M. H. is grateful to the Japan Society for the Promotion of Science for the Postdoctoral Fellowship for Foreign Researchers.

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2. A 10000-step Monte Carlo multiple-minimum conformational search was performed with MacroModel 4.5X program: Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440-467.
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6. **3:** colorless crystals (from CH_2Cl_2-acetonitrile), mp 258-260 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 0.97 (s, 9H), 1.93 (s, 24H), 3.49 (s, 4H), 6.38 (s, 2H), 6.87 (d, J = 7.5 Hz, 8H), 6.99 (t, J = 7.5 Hz, 4H), 7.04 (d, J = 7.5 Hz, 4H), 7.34 (t, J = 7.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9 (q), 31.0 (q), 34.3 (s), 36.8 (t), 124.6 (d), 125.6 (s), 126.7 (d), 126.9 (d), 127.4 (d), 129.2 (d), 135.9 (s), 137.2 (s), 138.6 (s), 140.5 (s), 142.1 (s), 146.1 (s); HRMS (FAB) *m/z* 810.3617, calcd for $C_{56}H_{57}{}^{81}Br$ 810.3638.
7. Crystallographic data for **3**: $C_{56}H_{57}Br$, FW = 809.97, *monoclinic*, space group C2/c, a = 26.416(7) Å, b = 21.478(6) Å, c = 20.532(6) Å, β = 128.72(1) °, V = 9089(4) Å^3, Z = 8, D_{calcd} = 1.184 g/cm^3, μ = 9.43 cm^{-1}. The intensity data were collected on a Rigaku AFC7R diffractometer with graphite monochromated MoKα radiation (λ = 0.71069 Å), and the structure was solved by direct methods using SHELXS-86[8] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 2605 observed reflections [$I > 3.00\sigma(I)$] and 514 variable parameters with R (Rw) = 0.100 (0.116). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
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13. **7**: Anal. Calcd for $C_{112}H_{114}S_{7.8}\cdot 4\ H_2O$: C, 75.48; H, 6.90; S, 14.03. Found: C, 75.38; H, 6.92; S, 13.62. Molecular weight (vapor pressure osmometry in $CHCl_3$) 1800, calcd for $C_{112}H_{114}S_{7.8}$ 1710.

(*Received in Japan* 7 *February* 1996; *revised* 12 *March* 1996; *accepted* 15 *March* 1996)