

A Polyaromatic Receptor with an Etheral Fence that Directs K^+ for Effective Cation– π Interaction

Ruchi Shukla, Sergey V. Lindeman, and Rajendra Rathore*

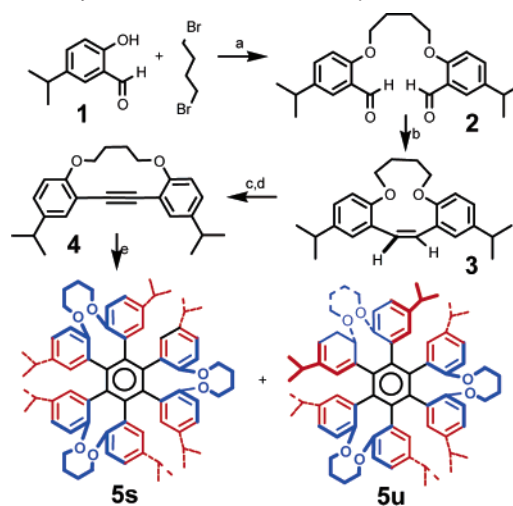
Department of Chemistry, Marquette University, P.O. Box 1881, Milwaukee, Wisconsin 53201-1881

Received January 28, 2006; E-mail: rajendra.rathore@marquette.edu

The hexaphenylbenzene core has gained considerable attention due to its unique propeller-shaped structure and its usage for the preparation of modern graphitic materials for the applications in the emerging area of molecular electronics and nanotechnology.¹ Numerous possibilities exist for future development and use of novel architectures based on hexaarylbenzene (HAB) derivatives in sensor applications and host–guest chemistry, in general, if a controlled synthesis can be developed which will allow the positioning of all the *ortho* substituents (such as etheral oxygens on the peripheral aryl rings) on one face of the central benzene ring. Interestingly, however, the *ortho*-substituted HAB derivatives exist as a mixture of rotamers due to the restricted rotation around the C–C bonds between the six peripheral aryl rings and the central benzene ring. For instance, it has been established² that trimerization of bis(2-methoxyphenyl)acetylene leads to the formation of only eight rotamers (i.e., six achiral and one pair of enantiomeric rotamers) of hexakis(2-methoxyphenyl)benzene out of the possible nine rotamers. The only missing rotamer from this synthesis is the one which contains all the etheral oxygens on one face of the propeller. Such a symmetrical isomer can be potentially useful for directing a metal cation to the central benzene ring with the aid of six etheral oxygens that are prearranged in a manner akin to an 18-crown-6 geometry.³ Accordingly, in this paper, we now report a new strategy to access this elusive rotamer containing all the etheral oxygens on one face of the HAB and delineate by NMR spectroscopy and X-ray crystallography that it binds a single potassium cation to the central benzene ring via a synergistic interaction with the hydrophilic etheral fence and the hydrophobic π -cloud of the central benzene ring⁴ as follows.

It was conceived that preparation of the HAB derivative with oxygens on one face can be accomplished by a trimerization of a diarylacetylene in which the etheral oxygens are tied together with a polymethylene bridge (see structure **4** in Scheme 1). Unfortunately, the synthesis of such bridged acetylenic derivatives from existing procedures was possible only in very poor yields.⁵ Therefore, we first developed a practical route to access the bridged diarylacetylene **4** in which the etheral oxygens are tied with a tetramethylene bridge (see Scheme 1).⁶ For example, a reaction of 2 equiv of isopropylsalicylaldehyde (**1**) with 1,4-dibromobutane in the presence of NaOH in refluxing ethanol afforded dialdehyde **2** in 95% yield. The McMurry coupling under mild dilution produced a mixture of *cis/trans* stilbenes **3** in >85% yield on a 20 g scale reaction, which were readily converted to the corresponding acetylene **4** (in >80% yield) by a simple bromination and dehydrobromination reaction sequence (see Supporting Information).

A $\text{Co}_2(\text{CO})_8$ -catalyzed trimerization of **4** in refluxing dioxane for 12 h produced a mixture which contained roughly 25% trimer and ~75% of the starting acetylene **4**. A quick chromatographic separation on silica gel (using hexanes and ethyl acetate mixture as eluent) afforded pure symmetrical isomer **5s** and the unsymmetrical isomer **5u** in ~1:2 ratio in >95% yield based on the

Scheme 1. Synthesis of HAB-based Receptor **5s**^a

^a Conditions: (a) NaOH, EtOH, reflux; (b) TiCl_4 , Zn, Py, THF, reflux; (c) Br_2 , AcOH; (d) KOtBu , THF, 22 °C; (e) $\text{Co}_2(\text{CO})_8$, dioxane, reflux.

recovered **4**. The identity of **5s** was readily established by the simplicity of its $^1\text{H}/^{13}\text{C}$ NMR spectra in comparison to that of **5u** and was further confirmed by FAB mass spectrometry (see Supporting Information).

The binding of K^+ cation to **5s** was monitored by ^1H NMR spectroscopy. Thus, an incremental addition of potassium perfluorotetraphenylborate solution (0.08 M) to a solution of **5s** in acetone- d_6 (0.02 M) showed the appearance of a new set of signals in addition to the initial signals due to the uncomplexed **5s**. The ^1H NMR signals due to the **5s** were completely replaced by the new signals upon addition of 1 equiv of K^+ , as shown in Figure 1. It is noteworthy that the ^1H NMR spectrum remained unchanged upon further addition of K^+ solution (i.e., beyond 1 equiv). Such a spectral change is readily reconciled as arising from the complexation of K^+ to **5s**. Moreover, it is noted that the potassium cation is held strongly in the [**5s**, K^+] complex because of the fact that it does not undergo an exchange reaction with the uncomplexed **5s** on the NMR time scale (at 22 °C). Unfortunately, an accurate binding constant for the formation of [**5s**, K^+] could not be determined by NMR method as it simply showed complete capture of the K^+ and suggested that the binding constant is too large to be measured by NMR spectroscopy.⁷

To ascertain the structure of the [**5s**, K^+] complex, we attempted the crystallization of [**5s**, K^+] $\text{B}(\text{C}_6\text{F}_5)_4$ by a slow diffusion of hexanes in an acetonitrile solution of the complex that resulted in poor quality crystals. However, by changing the counteranion from $\text{B}(\text{C}_6\text{F}_5)_4^-$ to BPh_4^- , the formation of an excellent crop of single crystals of the [**5s**, K^+] BPh_4 from an acetonitrile– CH_2Cl_2 mixture at 22 °C resulted. The structure of the complex [**5s**, K^+ CH_3CN] BPh_4 is shown in Figure 2.

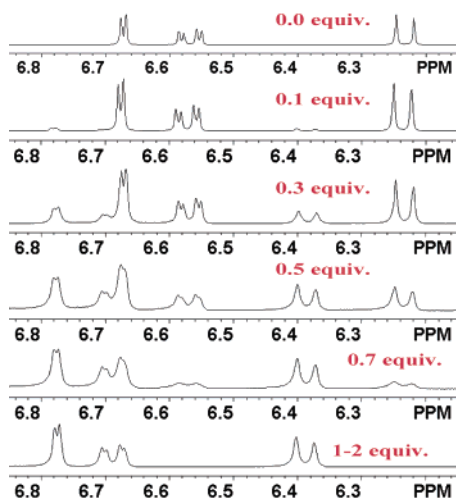


Figure 1. Partial ^1H NMR spectra obtained upon the incremental addition of $\text{KB}(\text{C}_6\text{F}_5)_4$ to **5s** in acetonitrile– CH_2Cl_2 at 22 $^\circ\text{C}$.

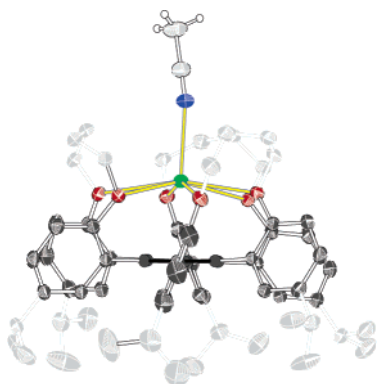


Figure 2. Structure of $[\mathbf{5s}, \text{K}^+] \cdot \text{BPh}_4$ with a single CH_3CN molecule complexed to K^+ . The hydrogens and the anion are omitted.

The X-ray structure in Figure 2 reveals that a single potassium cation sits in a shallow cavity with an (hydrophobic) aromatic bottom (i.e., the central benzene ring) while effectively interacting with the (hydrophilic) polar fence formed by six etheral oxygens. The depth (i.e., the distance between the mean planes of the central benzene ring carbons and the etheral fence) and the radius of the cavity are 2.22 and 2.97 Å, respectively. Such a bipolar nature of the cavity in **5s** allows a tight van der Waals fit for a single K^+ cation as discussed below.

The most striking feature of the structure in Figure 2 is the symmetrical η^6 -coordination of the K^+ by the central benzene ring of **5s**. The distance between the mean plane of the benzene ring and the K^+ is 2.742 Å, a distance that is much shorter than the sum of van der Waals/ionic radii of carbon and K^+ (i.e., 3.22 Å) and surpasses any of the previous experimental observations of the cation–arene contacts.⁸ One of the main factors favoring such a close $\text{K}^+ \cdots \text{Ar}$ coordination is the synergistic coordination of potassium cation by the all six etheral oxygens prearranged in a geometry similar to that of the 18-crown-6. Another feature of the structure is that the K^+ sits slightly (i.e., ~ 0.52 Å) above the coordination plane of the etheral fence, as pictured below in Figure 3. A simple geometrical consideration showed that the possible perpendicular orientation of the peripheral aryl rings in **5s** could provide a more coplanar coordination of potassium cation with the etheral fence with an almost normal $\text{K}^+ \cdots \text{O}$ separation of ~ 2.84 Å (as opposed to the observed $\text{K}^+ \cdots \text{O}$ separation of 2.83–3.21 Å or av. 3.02 Å). However, such a structural alteration of the **HAB**

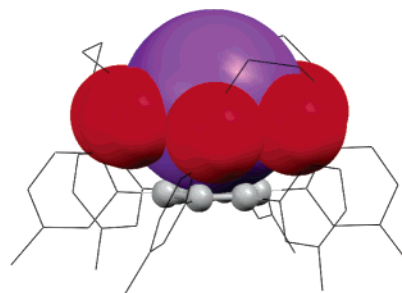


Figure 3. Molecular structure of $[\mathbf{5s}, \text{K}^+]$ showing the effective overlap of the polar etheral fence with K^+ while it rests on the aromatic bottom via cation– π interactions. The methyls of isopropyl groups and CH_3CN are omitted.

propeller may only occur at the expense of substantial repulsive interaction among the peripheral aryl rings.⁹

In summary, we have designed and synthesized a **HAB**-based receptor that contains a bipolar receptor site that allows a remarkably efficient binding of a single potassium cation because it synergistically interacts with the polar etheral fence and with the central benzene ring via cation– π interaction—a phenomenon that is well established in gas phase¹⁰ and in solid state⁸ and is known to play an important role in the stabilization of tertiary structures of various proteins.¹¹ We believe that the development of this unique receptor with an amphiphilic binding pocket and the electronically coupled peripheral aryl groups¹² will allow its usage for the development of practical sensors for various metal ions. We are currently exploring the selectivity of the binding of various metal cations to receptor **5s** as well as its usage for sensing devices.

Acknowledgment. We thank the National Science Foundation (Career Award) and Marquette University for financial support. This paper is dedicated to Prof. S. Chandrasekaran (I. I. Sc., Bangalore, India) on the occasion of his 60th birthday.

Supporting Information Available: Preparation, spectral data for **1–5**, and the X-ray data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References

- (a) *Introduction to Molecular Electronics*; Petty, M. C.; Bryce, M. R., Bloor, D., Eds.; Oxford University Press: New York, 1995. (b) Watson, M. D.; Fechtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267.
- Pepermans, H.; Willem, R.; Gielen, M.; Hoogzand, C. *J. Org. Chem.* **1986**, *51*, 301.
- Compare: Trueblood, K. N.; Knobler, C. B.; Maverick, E.; Helgeson, R. C.; Brown, S. B.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 5594.
- Via a cation– π interaction, for example, see: (a) Gokel, G. W.; De Wall, S. L.; Meadows, E. S. *Eur. J. Org. Chem.* **2000**, 2967. (b) Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303 and references therein.
- Brizius, G.; Billingsley, K.; Smith, M. D.; Bunz, U. H. F. *Org. Lett.* **2003**, *5*, 3951 and references therein.
- Complete synthetic details for the preparation of various bridged diaryl-acetylenes will be presented separately.
- Competition experiments indicated that **5s** and 18-crown-6 have a comparable affinity for K^+ .
- (a) Atwood, J. L.; Crissinger, K. D.; Rogers, R. D. *J. Organomet. Chem.* **1978**, *155*, 1. (b) King, B. T.; Noll, B. C.; Michl, J. *Collect. Czech. Chem. Commun.* **1999**, *64*, 1001. (c) Compare: Hu, J.; Barbour, Gokel, G. W. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5121 and references therein.
- Note that dihedral angles between peripheral aryl rings and central benzene ring vary between 55 and 70°; see CCD Database.
- Guo, B. C.; Purnell, J. W.; Castlman, A. W., Jr. *Chem. Phys. Lett.* **1990**, *168*, 155 and references therein.
- (a) Burley, S. K.; Petsko, G. A. *FEBS Lett.* **1986**, *203*, 139. (b) Sakurai, Y.; Mizuno, T.; Hiroaki, H.; Gohda, K.; Oku, J.; Tanaka, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 6180 and references therein.
- Rathore, R.; Burns, C. L.; Abdelwahed, S. H. *Org. Lett.* **2004**, *6*, 1689.

JA060502Y