ChemComm

COMMUNICATION

View Article Online
View Journal

Cite this: DOI: 10.1039/c5cc09088a

Received 2nd November 2015,
Accepted 24th November 2015

DOI: 10.1039/c5cc09088a

www.rsc.org/chemcomm

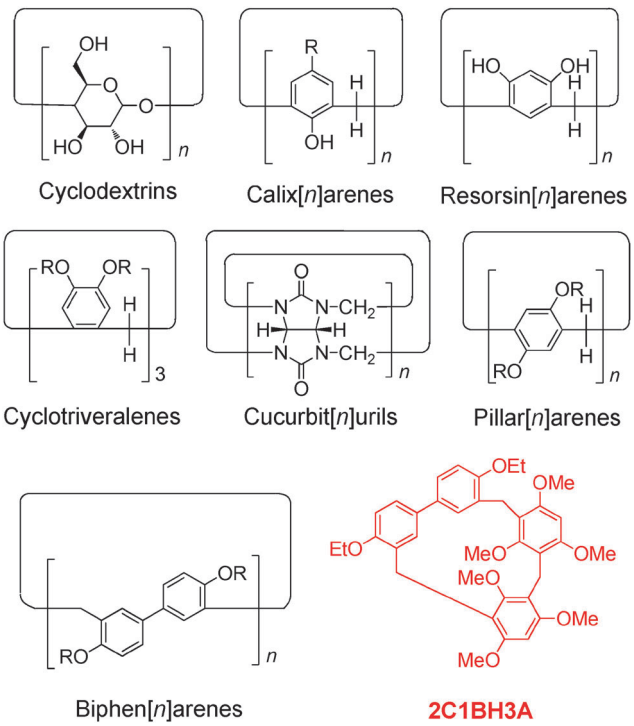
The synthesis, structure, and molecular recognition properties of a [2]calix[1]biphenyl-type hybrid[3]arene†

Jiong Zhou, Jie Yang, Bin Hua, Li Shao, Zhihua Zhang and Guocan Yu*

The first [2]calix[1]biphenyl-type hybrid[3]arene was synthesized. Its molecular recognition was investigated by using 1-dihexylammonium hexafluorophosphate as a guest.

The design and synthesis of novel macrocyclic receptors which display remarkable affinity and high selectivity have been a challenging issue for supramolecular chemists.[1] These supramolecular hosts not only contribute to the basic understanding of the molecular recognition properties and self-assembly behaviors, but also possess many prospective applications in the construction of various supramolecular systems, such as molecular machines and devices,[2] drug-delivery systems,[3] supramolecular polymers,[4] artificial transmembrane channels,[5] chemosensors,[6] and stimuli-responsive materials.[7] Synthetic macrocycles including crown ethers,[8] cyclodextrins,[9] calixarenes,[10] cucurbiturils,[11] pillararenes,[12] biphenarenes,[13] coronarenes,[14] cyclophanes[15] and others,[16] continue to be the focus of substantial research attention due to their interesting conformational characteristics and abundant host–guest properties.

However, most of the current supramolecular scaffolds are composed of identical building units (Scheme 1), limiting their further application in various fields. Typical supramolecular macrocycles include cyclodextrins from D-galactose, calixarenes from phenol, resorcinarenes from resorcinol, cyclotriveratrylenes from veratrole, cucurbiturils from glycoluril, pillararenes from hydroquinone, and biphenarenes from 4,4′-biphenol. The integration of two or more different types of units in one macrocycle enables the selective introduction of orthogonal or multiple functional groups and undoubtedly promotes the development of macrocyclic host molecules possessing different shapes, cavity sizes and flexibilities. Recently, Szumna and coworkers constructed a series of cyclic phenolic oligomeric compounds consisting of different alkoxybenzene units and named them "hybrid[*n*]arenes".[17] The obtained products expand the pool of relatively easy accessible macrocycles for multifarious applications in supramolecular chemistry.

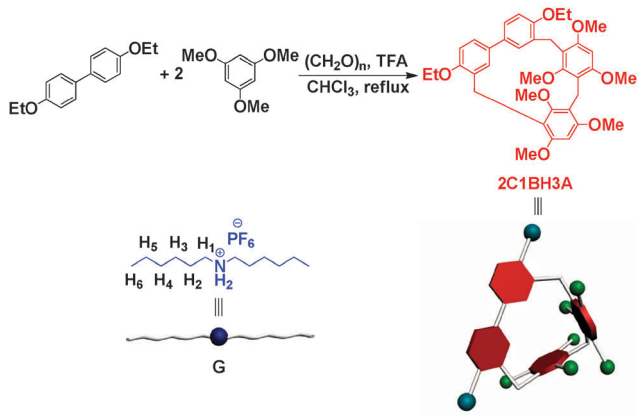


Scheme 1 Structures of some typical supramolecular macrocycles.

Herein, we report the synthesis, structure, and molecular recognition properties of the first [2]calix[1]biphenyl-type hybrid[3]arene (**2C1BH3A**), which is made of two 1,3,5-trimethoxybenzene units and one 4,4′-biphenol diethyl ether unit linked by methylene bridges (Scheme 2). To prepare **2C1BH3A**, a mixture of 1 equiv. of 4,4′-biphenol diethyl ether, 2 equiv. of 1,3,5-trimethoxybenzene,

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China. E-mail: guocanyu@zju.edu.cn; Fax: +86-571-8795-3189; Tel: +86-571-8795-3189

† Electronic supplementary information (ESI) available: Synthetic procedures, characterization, the X-ray crystallographic file (CIF) for **2C1BH3A**, association constant and stoichiometry determination, and other materials. CCDC 1431824. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5cc09088a



Scheme 2 Synthesis of [2]calix[1]biphenyl-type hybrid[3]arene (**2C1BH3A**) and chemical structure of **G**.

3 equiv. of paraformaldehyde, and a catalytic amount of trifluoroacetic acid (TFA) was refluxed in chloroform for 30 min. The reaction mixture was cooled to room temperature, and an excess of saturated aqueous Na_2CO_3 was added to neutralize TFA. After purification by column chromatography, **2C1BH3A** was isolated in 25% yield as a white solid. Furthermore, mass fragments with *m*/*z* values corresponding to [2+3] and [4+2] hybrid macrocycles[18] were also detected in the low-resolution electrospray ionization mass spectrometric (LRESI-MS) characterization of the separated products with a prolonged reaction time. However, when it came to characterizing these larger hybrid macrocycles, the corresponding ^{1}H NMR spectra quickly became complicated to the extent that, with limited information, assigning constitutions became challenging. The structure of **2C1BH3A** was characterized by ^{1}H NMR, ^{13}C NMR and ESI-MS. Assignment of the proton resonances of **2C1BH3A** was aided by the observation of its solid-state crystal structure (Fig. 1).

Single crystal X-ray analysis of **2C1BH3A** confirmed the formation and the structure of **2C1BH3A** in the solid state (Fig. 1). A single crystal of **2C1BH3A** suitable for X-ray crystallography was grown by slow diffusion of isopropyl ether into a chloroform solution at room temperature. As shown in Fig. 1, **2C1BH3A** is made of two 1,3,5-trimethoxybenzene units and one 4,4′-biphenol diethyl ether unit linked by methylene bridges. **2C1BH3A** exhibits a distorted triangular-prismatic structure. The 1,3,5-trimethoxybenzene units locate at different planes and are perpendicular to each other. The two benzene rings of the 4,4′-biphenol diethyl ether unit are not coplanar with a dihedral angle of 27.49°. In addition, it can be noticed that the biphenyl unit in **2C1BH3A** is in the *cis*-conformation according to the relative positions of the two methylene linkers.[13a]

The host–guest complexation properties of **2C1BH3A** towards an appropriate guest were investigated by ^{1}H NMR spectroscopic experiments in solution. Herein, we employed 1-dihexylammonium hexafluorophosphate (**G**) as a guest molecule. As shown in Fig. 2b, the ^{1}H NMR spectrum of a solution of **2C1BH3A** and **G** in chloroform-*d* shows only one group of resonance peaks, demonstrating fast-exchange complexation between **2C1BH3A** and **G** on the ^{1}H NMR time scale.[12a] In the presence of **2C1BH3A**, chemical shift changes related to the protons of **G** occurred (Fig. 2a and b), suggesting the formation of host–guest interactions between **2C1BH3A** and **G**. In comparison with free **G**, the peaks related to the protons of **G** exhibited upfield shifts ($\Delta\delta$ = −0.07, −0.04 ppm for H_1 and H_2, respectively). These chemical shift changes verified the complexation between **2C1BH3A** and **G** in solution. Considering that **2C1BH3A** possesses a distorted triangular-prism structure and has neither a large nor an effective cavity, the possible binding mode related to such NMR changes is that the guest lies at the entrance of **2C1BH3A** in a latitudinal orientation.[13c]

To determine the association constant and stoichiometry of the complexation between **2C1BH3A** and **G**, ^{1}H NMR titration experiments were carried out in $CDCl_3$. On the basis of chemical shift changes of H_1 on **G** (Fig. S6, ESI†), the association constant (K_a) for the complex **2C1BH3A**⊃**G** was determined to be 59 ± 1 M^{-1} by employing a non-linear fitting method (Fig. S7, ESI†). Moreover, the binding stoichiometry was found to be 1 : 1 from a molar ratio plot (Fig. S8, ESI†).

Additionally, the complexation properties of **2C1BH3A** towards **G** were verified by electrospray ionization mass spectroscopy (ESI-MS) (Fig. 3).[12a,13a] The ESI-MS spectrum of an equimolar mixture of **2C1BH3A** and **G** exhibited a peak at

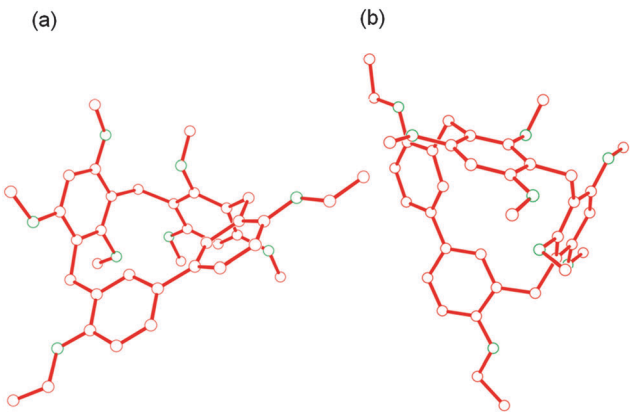


Fig. 1 Two views of the crystal structure of **2C1BH3A**. Hydrogens and solvent molecules were omitted for clarity. Carbon atoms are red and oxygen atoms are green.

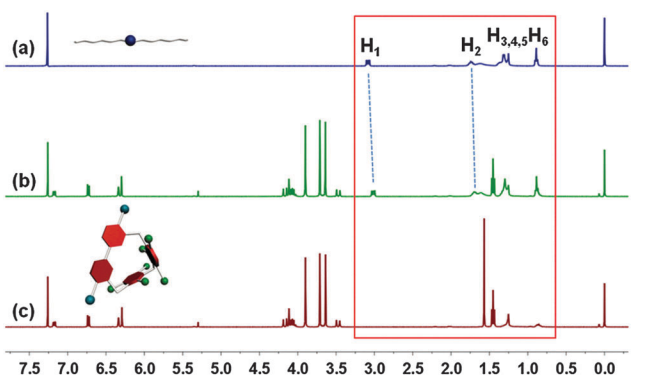


Fig. 2 ^{1}H NMR spectra (400 MHz, chloroform-*d*, 293 K) of (a) 5.00 mM **G**; (b) 5.00 mM **G** and 10.0 mM **2C1BH3A**; (c) 10.0 mM **2C1BH3A**.

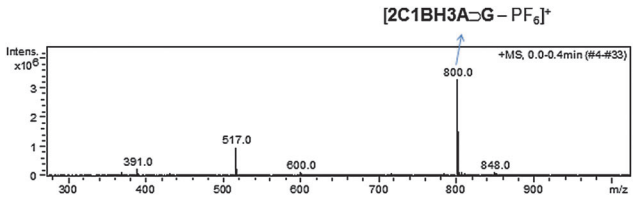


Fig. 3 Electrospray ionization mass spectrum of an equimolar mixture of **2C1BH3A** and **G**.

m/*z* 800.0 (100%), corresponding to $[\mathbf{2C1BH3A}\supset\mathbf{G}–PF_6]^+$, which confirmed the formation of the 1 : 1 complex of **2C1BH3A** with **G**, in good agreement with the results obtained from ^{1}H NMR titrations.

In conclusion, we reported a new macrocyclic receptor, [2]calix[1]biphenyl-type hybrid[3]arene (**2C1BH3A**). It is made of two 1,3,5-trimethoxybenzene units and one 4,4′-biphenol diethyl ether unit linked by methylene bridges. The macrocyclic product offers a simple and effective method to synthesize supramolecular scaffolds with different types of building units by a hybrid approach. We can forecast that the integration of other types of building units, such as phenol, hydroquinone, biphenol, dinaphthalene, or the introduction of diverse functional groups, such as alkoxy, propargyl, ester, and amino, will endow the resultant synthetic macrocycles with rich topological structures and prosperous host–guest properties. Furthermore, their functionalized derivatives can be made by modifying selectively, making them promising candidates for applications in the construction of chemosensors, transmembrane channels, supramolecular polymers, liquid crystals and drug delivery systems. Currently, relevant efforts are underway in our laboratory.

This work was supported by the Fundamental Research Funds for the Central Universities.

Notes and references

1 (*a*) E. R. Kay, D. A. Leigh and F. Zerbetto, *Angew. Chem., Int. Ed.*, 2007, **46**, 72–191; (*b*) Z. Niu and H. W. Gibson, *Chem. Rev.*, 2009, **109**, 6024–6046; (*c*) J. Hu and S. Liu, *Acc. Chem. Res.*, 2014, **47**, 2084–2095; (*d*) M. Arunachalam and H. W. Gibson, *Prog. Polym. Sci.*, 2014, **39**, 1043–1073; (*e*) S. Li, J. Huang, F. Zhou, T. R. Cook, X. Yan, Y. Ye, B. Zhu, B. Zheng and P. J. Stang, *J. Am. Chem. Soc.*, 2014, **136**, 5908–5911; (*f*) Z.-Y. Li, Y. Zhang, C.-W. Zhang, L.-J. Chen, C. Wang, H. Tan, Y. Yu, X. Li and H.-B. Yang, *J. Am. Chem. Soc.*, 2014, **136**, 8577–8589.

2 (*a*) A. Harada, *Acc. Chem. Res.*, 2001, **34**, 456–464; (*b*) H. Li, J.-N. Zhang, W. Zhou, H. Zhang, Q. Zhang, D.-H. Qu and H. Tian, *Org. Lett.*, 2013, **15**, 3070–3073; (*c*) A. C. Fahrenbach, C. J. Bruns, H. Li, A. Trabolsi, A. Coskun and J. F. Stoddart, *Acc. Chem. Res.*, 2014, **47**, 482–493; (*d*) H. Liu, X.-Y. Li, X.-L. Zhao, Y. A. Liu, J.-S. Li, B. Jiang and K. Wen, *Org. Lett.*, 2014, **16**, 5894–5897.

3 (*a*) Q. Duan, Y. Cao, Y. Li, X. Hu, T. Xiao, C. Lin, Y. Pan and L. Wang, *J. Am. Chem. Soc.*, 2013, **135**, 10542–10549; (*b*) H. Zhang, X. Ma, K. T. Nguyen and Y. Zhao, *ACS Nano*, 2013, **7**, 7853–7863; (*c*) G. Yu, W. Yu, Z. Mao, C. Gao and F. Huang, *Small*, 2015, **11**, 919–925.

4 (*a*) Z. Zhang, Y. Luo, J. Chen, S. Dong, Y. Yu, Z. Ma and F. Huang, *Angew. Chem., Int. Ed.*, 2011, **50**, 1397–1401; (*b*) Z. Niu, F. Huang and H. W. Gibson, *J. Am. Chem. Soc.*, 2011, **133**, 2836–2839; (*c*) X. Ji, S. Dong, P. Wei, D. Xia and F. Huang, *Adv. Mater.*, 2013, **25**, 5725–5729; (*d*) X. Wang, K. Han, J. Li, X. Jia and C. Li, *Polym. Chem.*, 2013, **4**, 3998–4003; (*e*) J. Zhan, Q. Li, Q. Hu, Q. Wu, C. Li, H. Qiu, M. Zhang and S. Yin, *Chem. Commun.*, 2014, **50**, 722–724; (*f*) Y.-K. Tian, Z.-S. Yang, X.-Q. Lv, R.-S. Yao and F. Wang, *Chem. Commun.*, 2014, **50**, 9477–9480; (*g*) Y. Zhang, B. Shi, H. Li, W. Qu, G. Gao, Q. Lin, H. Yao and T. Wei, *Polym. Chem.*, 2014, **5**, 4722–4725; (*h*) Y.-K. Tian, Y.-G. Shi, Z.-S. Yang and F. Wang, *Angew. Chem., Int. Ed.*, 2014, **53**, 6090–6094; (*i*) N. Sun, X. Xiao and J. Jiang, *Polym. Chem.*, 2015, **6**, 5015–5020; (*j*) L.-B. Meng, D. Li, S. Xiong, X.-Y. Hu, L. Wang and G. Li, *Chem. Commun.*, 2015, **51**, 4643–4646.

5 (*a*) J. L. Seganish, P. V. Santacroce, K. J. Salimian, J. C. Fettinger, P. Zavalij and J. T. Davis, *Angew. Chem., Int. Ed.*, 2006, **45**, 3334–3338; (*b*) W. Si, L. Chen, X.-B. Hu, G. Tang, Z. Chen, J.-L. Hou and Z.-T. Li, *Angew. Chem., Int. Ed.*, 2011, **50**, 12564–12568; (*c*) X.-B. Hu, Z. Chen, G. Tang, J.-L. Hou and Z.-T. Li, *J. Am. Chem. Soc.*, 2012, **134**, 8384–8387.

6 (*a*) N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2011, **133**, 5668–5671; (*b*) G. Yu, Z. Zhang, C. Han, M. Xue, Q. Zhou and F. Huang, *Chem. Commun.*, 2012, **48**, 2958–2960.

7 (*a*) S. Dong, B. Zheng, F. Wang and F. Huang, *Acc. Chem. Res.*, 2014, **47**, 1982–1994; (*b*) X.-Y. Hu, T. Xiao, C. Lin, F. Huang and L. Wang, *Acc. Chem. Res.*, 2014, **47**, 2041–2051; (*c*) Z. Qi and C. A. Schalley, *Acc. Chem. Res.*, 2014, **47**, 2222–2233; (*d*) Q. Lin, X. Zhu, Y.-P. Fu, Y.-M. Zhang, R. Fang, L.-Z. Yang and T.-B. Wei, *Soft Matter*, 2014, **10**, 5715–5723.

8 (*a*) L. Chen, Y.-K. Tian, Y. Ding, Y.-J. Tian and F. Wang, *Macromolecules*, 2012, **45**, 8412–8419; (*b*) S. Li, G.-H. Weng, W. Lin, Z.-B. Sun, M. Zhou, B. Zhu, Y. Ye and J. Wu, *Polym. Chem.*, 2014, **5**, 3994–4001; (*c*) M. Zhang, X. Yan, F. Huang, Z. Niu and H. W. Gibson, *Acc. Chem. Res.*, 2014, **47**, 1995–2005.

9 (*a*) Y. Wang, N. Ma, Z. Wang and X. Zhang, *Angew. Chem., Int. Ed.*, 2007, **46**, 2823–2826; (*b*) A. Harada, Y. Takashima and H. Yamaguchi, *Chem. Soc. Rev.*, 2009, **38**, 875–882.

10 (*a*) M. Song, Z. Sun, C. Han, D. Tian, H. Li and J. S. Kim, *Chem. – Asian J.*, 2014, **9**, 2344–2357; (*b*) X. Zeng, J. Ma, L. Luo, L. Yang, X. Cao, D. Tian and H. Li, *Org. Lett.*, 2015, **17**, 2976–2979; (*c*) G. Nie, Y. Sun, F. Zhang, M. Song, D. Tian, L. Jiang and H. Li, *Chem. Sci.*, 2015, **6**, 5859–5865; (*d*) Y. Chen and Y. Liu, *Adv. Mater.*, 2015, **27**, 5403–5409.

11 (*a*) J. W. Lee, S. Samal, N. Selvapalam, H.-J. Kim and K. Kim, *Acc. Chem. Res.*, 2003, **36**, 621–630; (*b*) J. Lagona, P. Mukhopadhyay, S. Chakrabarti and L. Isaacs, *Angew. Chem., Int. Ed.*, 2005, **44**, 4844–4870; (*c*) W. Jiang, Q. Wang, I. Linder, F. Klautzsch and C. A. Schalley, *Chem. – Eur. J.*, 2011, **17**, 2344–2348; (*d*) E. A. Appel, J. Barrio, X. J. Loh and O. A. Scherman, *Chem. Soc. Rev.*, 2012, **41**, 6195–6214.

12 (*a*) C. Han, F. Ma, Z. Zhang, B. Xia, Y. Yu and F. Huang, *Org. Lett.*, 2010, **12**, 4360–4363; (*b*) X.-Y. Hu, X. Wu, Q. Duan, T. Xiao, C. Lin and L. Wang, *Org. Lett.*, 2012, **14**, 4826–4829; (*c*) M. Xue, Y. Yang, X. Chi, Z. Zhang and F. Huang, *Acc. Chem. Res.*, 2012, **45**, 1294–1308; (*d*) T. Ogoshi and T.-A. Yamagishi, *Eur. J. Org. Chem.*, 2013, 2961–2975; (*e*) H. Li, D.-X. Chen, Y.-L. Sun, Y. B. Zheng, L.-L. Tan, P. S. Weiss and Y.-W. Yang, *J. Am. Chem. Soc.*, 2013, **135**, 1570–1576; (*f*) D. Cao and H. Meier, *Asian J. Org. Chem.*, 2014, **3**, 244–262; (*g*) Y. Wang, J.-F. Xu, Y.-Z. Chen, L.-Y. Niu, L.-Z. Wu, C.-H. Tung and Q.-Z. Yang, *Chem. Commun.*, 2014, **50**, 7001–7003; (*h*) J. Zhou, M. Chen and G. Diao, *ACS Appl. Mater. Interfaces*, 2014, **6**, 18538–18542; (*i*) Y. Fang, X. Yuan, L. Wu, Z. Peng, W. Feng, N. Liu, D. Xu, S. Li, A. Sengupta, P. K. Mohapatra and L. Yuan, *Chem. Commun.*, 2015, **51**, 4263–4266; (*j*) W.-B. Hu, W.-J. Hu, Y. A. Liu, J.-S. Li, B. Jiang and K. Wen, *Org. Lett.*, 2015, **17**, 2940–2943.

13 (*a*) H. Chen, J. Fan, X. Hu, J. Ma, S. Wang, J. Li, Y. Yu, X. Jia and C. Li, *Chem. Sci.*, 2015, **6**, 197–202; (*b*) J. Zhou, G. Yu, L. Shao, B. Hua and F. Huang, *Chem. Commun.*, 2015, **51**, 4188–4191; (*c*) J. Ma, H. Deng, S. Ma, J. Li, X. Jia and C. Li, *Chem. Commun.*, 2015, **51**, 6621–6624.

14 Q.-H. Guo, Z.-D. Fu, L. Zhao and M.-X. Wang, *Angew. Chem., Int. Ed.*, 2014, **53**, 13548–13552.

15 (*a*) V. Balzani, M. Gómez-López and J. F. Stoddart, *Acc. Chem. Res.*, 1998, **31**, 405–414; (*b*) S. T. J. Ryan, J. Del Barrio, I. Ghosh, F. Biedermann, A. I. Lazar, Y. Lan, R. J. Coulston, W. M. Nau and O. A. Scherman, *J. Am. Chem. Soc.*, 2014, **136**, 9053–9060.

16 (*a*) H. Zhou, Y. Zhao, G. Gao, S. Li, J. Lan and J. You, *J. Am. Chem. Soc.*, 2013, **135**, 14908–14911; (*b*) Y. Han, Z. Meng, Y.-X. Ma and C.-F. Chen, *Acc. Chem. Res.*, 2014, **47**, 2026–2040; (*c*) Z. He, X. Yang and W. Jiang, *Org. Lett.*, 2015, **17**, 3880–3883.

17 T. Boinski, A. Cieszkowski, B. Rosa and A. Szumna, *J. Org. Chem.*, 2015, **80**, 3488–3495.

18 The former number corresponds to the number of biphenyl unit, and the latter number corresponds to the number of phenyl unit. For example, [2+3] hybrid macrocycle corresponds to two 4,4′-biphenol diethyl ether units and three 1,3,5-trimethoxybenzene units.