Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Convenient and Effective Synthesis of Tris-Bridged Tricationic Azolophanes

Yi Yuan [a] , Zong-Lin Jiang [b] , Jia-Ming Yan [a] , Ge Gao [a] , Albert S. C. Chan [c] & Ru-Gang Xie [a]

[a] Department of Chemistry , Sichuan University , Chengdu, 610064, P. R. China

[b] Department of Chemistry , Daxian Teacher's School , Dachuan, 635000, P. R. China

[c] Department of Applied Biology and Chemical Technology , The Hong Kong Polytechnic University , Hong Kong, P. R. China

Published online: 04 Dec 2007.

To cite this article: Yi Yuan , Zong-Lin Jiang , Jia-Ming Yan , Ge Gao , Albert S. C. Chan & Ru-Gang Xie (2000) A Convenient and Effective Synthesis of Tris-Bridged Tricationic Azolophanes, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 30:24, 4555-4561, DOI: 10.1080/00397910008087085

To link to this article: http://dx.doi.org/10.1080/00397910008087085

SYNTHETIC COMMUNICATIONS, 30(24), 4555–4561 (2000)

A CONVENIENT AND EFFECTIVE SYNTHESIS OF TRIS-BRIDGED TRICATIONIC AZOLOPHANES

Yi Yuan[a], Zong-Lin Jiang[b], Jia-Ming Yan[a], Ge Gao[a], Albert S. C. Chan*[c] and Ru-Gang Xie*[a]

[a]Department of Chemistry, Sichuan University, Chengdu 610064, P. R. China
[b]Department of Chemistry, Daxian Teacher's School, Dachuan 635000, P.R. China
[c]Department of Applied Biology and Chemical Technology,
The Hong Kong Polytechnic University, Hong Kong, P. R. China

Abstract Two new macrobicyclic imidazolium and benzimidazolium phanes were synthesized by direct quaternization of the corresponding tripodal azacycles with tribromide under high dilution condition in excellent yields. The cyclophanes were identified by ^{1}H-NMR, ^{13}C-NMR, FAB-MS, IR, elemental analysis and X-ray diffraction analysis.

In the field of supramolecular chemistry, cyclophanes play a very important role in molecular recognition, assembly, catalysis and transport processes.[1] In recent years, after the extensive studies on the host-guest chemistry of cationic molecules, the anion coordination chemistry, which is not less important than the cation one

* To whom correspondence should be addressed.

in chemistry and in biology, has received increasing interest.[2] Among the artificial receptors, the anion receptors bearing imidazolium as the interaction sites for anion binding through electrostatic effect, hydrogen bond and other second-order forces have attracted much attention. Some imidazolium-based open-chain and monocyclic receptors have been reported.[3] Although cyclophanes with large cavities can make important contribution to host-guest coordination, they are difficult to synthesize and a facile synthesis of three-dimensionally bridged macrobicyclic imidazolium phanes with suitable shape and binding sites for the cooperative binding of guests still lacks literature procedure.

Following our work on the design, synthesis and use of imidazole-containing macrocycles in enzyme mimic and selective catalysis,[4] we report herein the convenient and highly effective synthesis of novel water-soluble tris-bridged azolophanes containing imidazolium or benzimidazolium groups **4**, **5**.

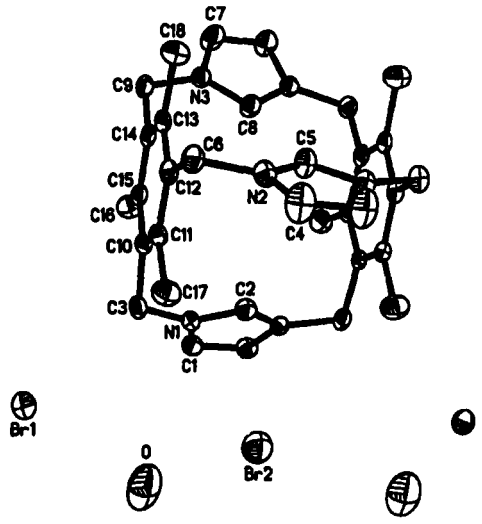


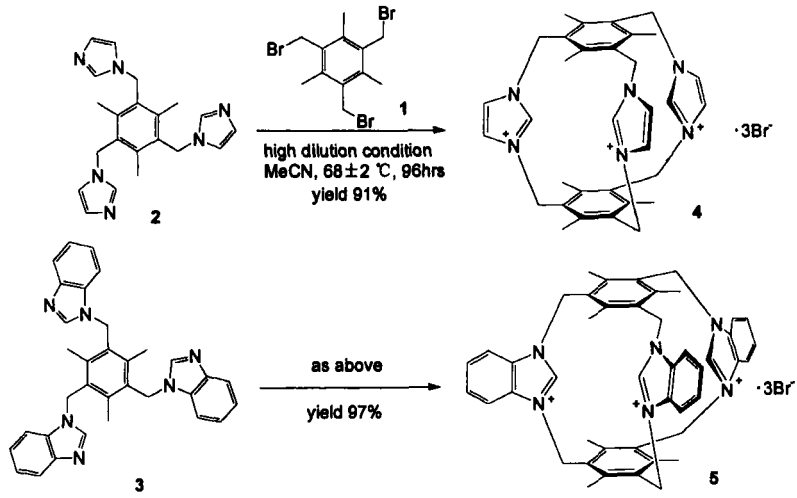
Fig. X-ray crystal structure of compound **4**

Analysis by X-ray showed that compound **4** has C_s symmetry (Fig.). The symmetry mirror is the plane of three 2-C of imidazolium rings. The parallel

capping benzene rings are about 0.52 nm apart. The distances of the three 2-C of the imidazolium are 0.45-0.47 nm. The shape, size and rigidity of cyclophanes **4** and **5** make them suitable to complex small anions exclusively or inclusively to form supramolecular system.

The synthesis of **4** and **5** is outlined in the scheme. 1, 3, 5-Tris(bromomethyl)-2, 4, 6-trimethylbenzene **1** was prepared according to the literature procedure.[5] Compounds **2** and **3** were prepared from **1** with imidazole or benzimidazole in the presence of NaH in DMF. The cyclization was performed by direct quaternization with tribromide **1** in highly diluted anhydrous acetonitrile at 68±2 ℃ for 4 days. After recrystallizaion from water, the pure products **4** and **5** were obtained in excellent yield (>91%).

Scheme



The reaction conditions may influence the quaternization-cyclization yield. Without the high dilution condition, the desired cyclophanes can not be obtained in high yield or in satisfactory purity, the open-chain compounds or polymers were formed instead. Acetonitrile was preferable to other solvents such as acetone, nitroethane, N, N-dimethylformamide and methanol-acetonitrile (1:1, v/v). In

acetonitrile, the cyclization was easily performed and the workup was quite simple and convenient.

The cyclophanes were characterized by ^{1}H-NMR, ^{13}C-NMR, FAB-MS, IR, elemental analysis and X-ray diffraction analysis. The imidazolium and benzimidazolium rings 2-H are between the two capping benzene rings, their high field shifts at 5.80, 6.37 ppm are caused by the shielding effects of benzene rings. The low field shifts of their 2-C at 177.72, 176.39 ppm result from the deshielding effect of the nitrogen cations.

Experimental

Melting points were determined on a micro-melting point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded on a Bruker DPX-300 or Bruker AC-E200 instrument, and chemical shifts are in δ scales relative to internal Me_4Si. ^{13}C-NMR were recorded at 75.42MHz. Mass spectra were recorded on a Finnigan MAT4510 or VG Autospec 3000 MS apparatus. IR spectra were obtained on a Nicolet FT-IR 170SX spectrometer. Elemental analyses were done on a Carlo Erba 1106 analyzer. X-ray crystallographic analysis was performed on a Siemens P4 diffractometer. Acetonitrile and N, N-dimethylformamide were purified according to the standard method. Compound **1** was prepared according to literature procedure.[5] All other chemicals or regents were obtained commercially and used without further purification.

General procedure for the synthesis of ***2, 3***

To a solution of imidazole (30 mmol, 2.04 g) or benzimidazole (30 mmol, 3.66 g) in 30 mL dry DMF under nitrogen, 31 mmol NaH (0.74 g) was added. After stirred at room temperature for 30 minutes, compound **1** (10 mmol, 3.99 g) in 30

mL DMF was added dropwise over 3 hours. The mixture was stirred for 20 hours, the solvent was removed *in vacuo* and the residue was purified by column chromatography on silica gel (50% CH_2Cl_2-EtOAc) to give **2** or **3**.

1, 3, 5-Tris(N-imidazolylmethyl)-2, 4, 6-trimethylbenzene **2** was obtained as colorless powder in 92% yield. m.p. 226-227℃. ^{1}H-NMR(200MHz, D_2O): 2.39(s, 9H, CH_3), 5.55(s, 6H, CH_2), 7.17(s, 6H, imidazolium ring 4, 5-H), 7.74(s, 3H, imidazolium ring 2-H). MS(m/z, RA%): 360(M^+, 12), 292(21), 225(100), 210(74), 69(71). Anal. calcd. for $C_{21}H_{24}N_6$: C, 69.97; H, 6.71; N, 23.32. Found: C, 69.59; H, 6.79; N, 23.39.

1, 3, 5-Tris(N-benzimidazolylmethyl)-2, 4, 6-trimethylbenzene **3** was obtained as white powder in 90% yield. m.p. >300 ℃. ^{1}H-NMR(200MHz, DMSO-d_6): 2.16(s, 9H, CH_3), 5.49(s, 6H, CH_2), 7.33-7.70(m, 12H, benzimidazolium ring 4, 5, 6, 7-H), 7.75(s, 3H, benzimidazolium ring 2-H). MS(m/z, RA%): 510(M^+, 100), 391(88), 276(58), 260(53), 119(23). Anal. calcd. for $C_{33}H_{30}N_6$: C,77.62; H, 5.92; N, 16.46. Found: C, 77.92; H, 5.65; N, 16.65.

General procedure for the synthesis of ***4, 5***

To 200 mL stirred acetonitrile, a solution of 1, 3, 5-tris(bromomethyl)-2, 4, 6-trimethyl-benzene **1**(1.0 mmol, 0.40 g) in 200 mL acetonitrile and a solution of 1, 3, 5-tris(N-imidazolylmethyl)-2, 4, 6-trimethylbenzene **2**(1.0 mmol, 0.36 g) or 1, 3, 5-tris (N-benzimidazolylmethyl)-2, 4, 6-trimethylbenzene **3**(1.0 mmol, 0.51 g) in 200 mL acetonitrile were added simultaneously drop by drop over 72 hours at 68±2 ℃. After complete reaction (monitored by TLC), the resulting mixture was stirred at the same temperature for additional 24 hours. The solution was then concentrated to half its volume, cooled and filtered. The filter cake was recrystallized from water affording pure product.

2, 11, 13, 21, 29, 31-Hexamethyl-5, 16, 24-triaza-8, 19, 27-triazanium heptacyclo [10. 10. 6. $1^{1,3}$. $1^{5,8}$. $1^{10,14}$. $1^{16,19}$. $1^{24,27}$] tritriaconta-1, 3(29), 6, 8(30), 10, 12, 14(31), 17, 19(32), 21, 25, 27(33)-dodecene tribromide·2H_2O 4 was obtained as colorless flake crystals in 91% yield. m.p. >300℃. ^{1}H-NMR(300MHz, D_2O): 2.21(s, 18H, CH_3), 5.61(s, 12H, CH_2), 5.80(s, 3H, imidazolium ring2-H), 7.97-7.98(d, 12H, imidazolium ring4, 5-H). ^{13}C-NMR(D_2O): 15.09(CH_3), 48.41 (CH_2), 125.18(*C*-CH_3), 130.17(*C*-CH_2), 141.89(imidazolium ring4, 5-C), 177.72 (imidazolium ring2-C). IR (KBr, cm^{-1}): 3455(br, s), 3075(s), 2994(m), 2834(w), 1635(s), 1566(s), 1454(m), 1394(m), 1135(vs), 811(s), 735(m), 615(s). Anal. calcd. for $C_{33}H_{39}N_6$·3Br· 2H_2O: C, 49.83; H, 5.46; N, 10.57. Found: C, 50.02; H, 5.27; N, 10.60. FAB-MS (m/z): 679(M^+-Br), 599(M^+-2Br), 517(M^+-2-3Br).

2, 15, 17, 29, 41,43-Hexamethyl-5, 20, 32-triaza-12, 27, 39-triazanium decacyclo [14. 14. 10. $1^{1,3}$. $1^{5,12}$.$0^{6,11}$.$1^{14,18}$. $1^{20,27}$. $0^{21,26}$. $1^{32,39}$. $0^{33,38}$] pentateraconta-1, 3(41), 6(11), 7, 9, 12(42), 14, 16, 18(43), 21(26), 22, 24, 27(44), 29, 33(38), 34, 36, 39(45)-octadecene tribromide 5 was obtained as colorless prismatic crystals in almost quantitative yield (97%). m.p. >300℃. ^{1}H-NMR(300MHz, D_2O): 2.29(s, 18H, CH_3), 5.89(s, 12H, CH_2), 6.37(s, 3H, benzimidazolium ring2-H), 7.93(m, 6H, benzimidazolium ring5, 6-H), 8.20(m, 6H, benzimidazolium ring4, 7-H). ^{13}C-NMR(D_2O): 13.93(CH_3), 44.82(CH_2), 112.49(benzimidazolium ring4, 7-C), 127.19, 128.25(*C*-CH_3 or benzimidazolium ring5, 6-C), 131.60(*C*-CH_2), 141.31 (benzimidazolium ring8, 9-C), 176.39(benzimidazolium ring2-C). IR(KBr, cm^{-1}): 3020(s), 2954(m), 2824(w), 1611(w), 1570(vs), 1471(s), 1390(m), 1162(s), 760(vs), 582(m). Anal. calcd. for $C_{45}H_{45}N_6$·3Br: C, 59.42; H, 4.99; N, 9.24. Found: C, 58.93; H, 5.05; N, 9.18. FAB-MS(m/z): 829(M^+-Br), 749(M^+-2Br), 667(M^+-2-3Br).

Acknowledgement: This work was supported by the National Natural Science

Foundation of China (*No.*29632004 and 29872028) and the Hong Kong Polytechnic University.

References

1. (a) Lehn, J.-M. "Supramolecular Chemistry: Concepts and Perspectives", Weinheim, VCH. **1995**. (b) Vögtle, F. "Cyclophane Chemistry", Wiley, Chichester, **1993**. (c) Seel, C. and Vögtle, F. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528. (d) Murakami, Y. Kikuchyi, J. I. Hisaeda, Y. and Hayashida, O. *Chem. Rev.* **1996**, *96*, 721.
2. Schmidtchen, F. P. and Berger, M. *Chem. Rev.* **1997**, *97*, 1609.
3. (a) Sato, K. Arai, S. and Yamagishi, T. *Tetrahedron Lett.* **1999**, *40*, 5219 and references cited therein. (b) Alcalde, E. Alvarez-Rúa, C. García-Granda, S. García-Rodriguez, E. Mesquida, N. and Pérez-García, L. *J. Chem. Soc., Chem. Commun.* **1999**, 295. (c) Zhou, C. Xie, R. and Zhao, H. *Org. Prep. Proced. Int.* **1996**, *28*, 345. (d) Alcalde, E. Alemany, M. and Gisbert, M. *Tetrahedron*, **1996**, *52*, 15171.
4. (a) Liu, Z. Zhou, C. Su, X. and Xie, R. *Synth. Commun.* **1999**, *29*, 2979. (b) Luo, M. Guo, S. Zhou, C. and Xie, R. *Heterocycles*. **1995**, *41*, 1421. (c) Yan, J. Xie, R. Zhao, H. Wu, D. and Xia, P. *Chin. J. Chem.* **1997**, *15*, 438.
5. Závada, J. Pánková, M. Holý, P. and Tichý, M. *Synthesis*. **1994**, 1132.

(Received in the USA 27 March 2000)