CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: A Nanosize Phenylene-Ethynylene-Butadiynylene [2]Catenane

Authors: Christopher Schweez and Sigurd Höger

To be cited as: *Chem. Eur. J.* 10.1002/chem.201802567

Link to VoR: http://dx.doi.org/10.1002/chem.201802567

Supported by
ACES

WILEY-VCH

10.1002/chem.201802567

WILEY-VCH

A Nanosize Phenylene-Ethynylene-Butadiynylene [2]Catenane

Christopher Schweez,[a] and Sigurd Höger*[a]

Dedicated to Professor Manfred T. Reetz on the occasion of his 75th birthday

Abstract: In a convergent, template-directed synthesis, an efficient route to a phenylene-ethynylene-butadiynylene based [2]catenane is described. The key step is performed by the aminolysis of the corresponding precatenane, which is obtained by a sequence of metal-catalyzed cross-coupling and desilylation reactions. The cyclization reaction leads besides the [2]precatenane to a variety of larger precatenanes and offers an attractive approach to mechanically interlocked structures of different size.

Introduction

Molecular nanotechnology has attracted considerable attention over the last years. Particularly, the design and assembly of artificial molecular architectures that mimic the function of biological systems[1] has drawn great interest. Mechanically interlocked molecules, e.g. catenanes and rotaxanes have proved appropriate to build these artificial devices, and significant developments have been made for the last years.[2]

Catenanes contain at least two macrocycles that are linked together. Their unique feature is the mechanical bond, a noncovalent linkage between the components. This special bonding situation offers unusual properties that make catenanes high potential materials for the construction of nanomachines. Especially the large amplitude motions and rotations of the components relatively to each other favor catenanes for utilization in artificial devices. Focus of the scientific efforts is the question how to exploit and to address the dynamics of such molecules and how to combine them with other structures or devices. There are numerous examples demonstrating the future applications, e.g. molecular motors, switches or shuttles.[2]

In the 1980's, the development of mechanically interlocked molecules was accelerated by the introduction of template methods.[3] Numerous synthetic approaches based on noncovalent interactions have been published during the last thirty years, whereas the covalent template approach was rejected, as it was regarded as less versatile and inefficient.[4] However, in the last 15 years some examples were published that illustrate the performance of this method.[5, 6] Recently we reported on the successful syntheses of [2]rotaxanes via this strategy.[7]

[a] C. Schweez, Prof. Dr. S. Höger*
Kekule-Institut für Organische Chemie und Biochemie
Rheinische Friedrich-Wilhelms-Universität Bonn
Gerhard-Domagk-Str. 1, 53121 Bonn, Germany
E-mail: hoeger@uni-bonn.de

Supporting information for this article is given via a link at the end of the document.

Results and Discussion

Here, we report on the synthesis of a [2]catenane consisting of shape-persistent phenylene-ethynylene-butadiynylene macrocycles. These macrocycles are highly attractive building blocks due to their structural and optical properties.[8] The emerging synthetic progress improved their availability in high yields, so that they are convenient building blocks for functional molecular nanoarchitectures with predictable structures in bulk, solution, or at interfaces.

Our approach toward the catenanes is based on a covalent template strategy, which we have already used successfully in the synthesis of two [2]rotaxanes.[7] The approach is very flexible and modular so that small variations led to the catenane synthesis as described here and in principle even more complex architectures can be obtained rather easily. Additionally, the [2]catenane can help to elucidate the rotaxane isomer hypothesis suggested by Morin et al.[6] and also discussed by ourselves (see below and Figure 1).[7]

The covalently bound template (Scheme 1a, blue) takes over two tasks in this strategy. First, it supports the cyclization reaction towards the first macrocycles (Scheme 1a, left) and second, it enables the further attachment of the building blocks for the second macrocycle by its two additional binding sites (Scheme 1a, middle). In the final step, the auxiliary bonds between both macrocycles are cleaved giving the mechanically interlocked molecule (Scheme 1a, right).

The synthesis of the precatenane (Scheme 1b) started with the coupling reaction of macrocycle **1** and the half-ring **2**. **1** was already used in our previous rotaxane synthesis and details on its synthesis can be found elsewhere.[7] It contains the *p*-terphenyl template, which is bound inside the ring via phenolic ester bonds and features two sterically non-congested aryl iodides. These allowed the transition-metal catalyzed coupling with the ethynylenes of the mono (3-cyanopropyl)diisopropylsilyl (CPDIPS)-protected "half-rings" **2** using the standard catalyst system $PdCl_2(PPh_3)_2$ and CuI in toluene and NEt_3 at 100 °C. The use of the CPDIPS group allowed a rather simple purification of **2** (see Supporting Information).[9] Removing of the CPDIPS groups of **3** with TBAF in THF in the presence of water gave **4**. Adding water to this reaction mixture is crucial to avoid the undesired cleavage of the phenolic ester bonds at this point of the synthesis.[10]

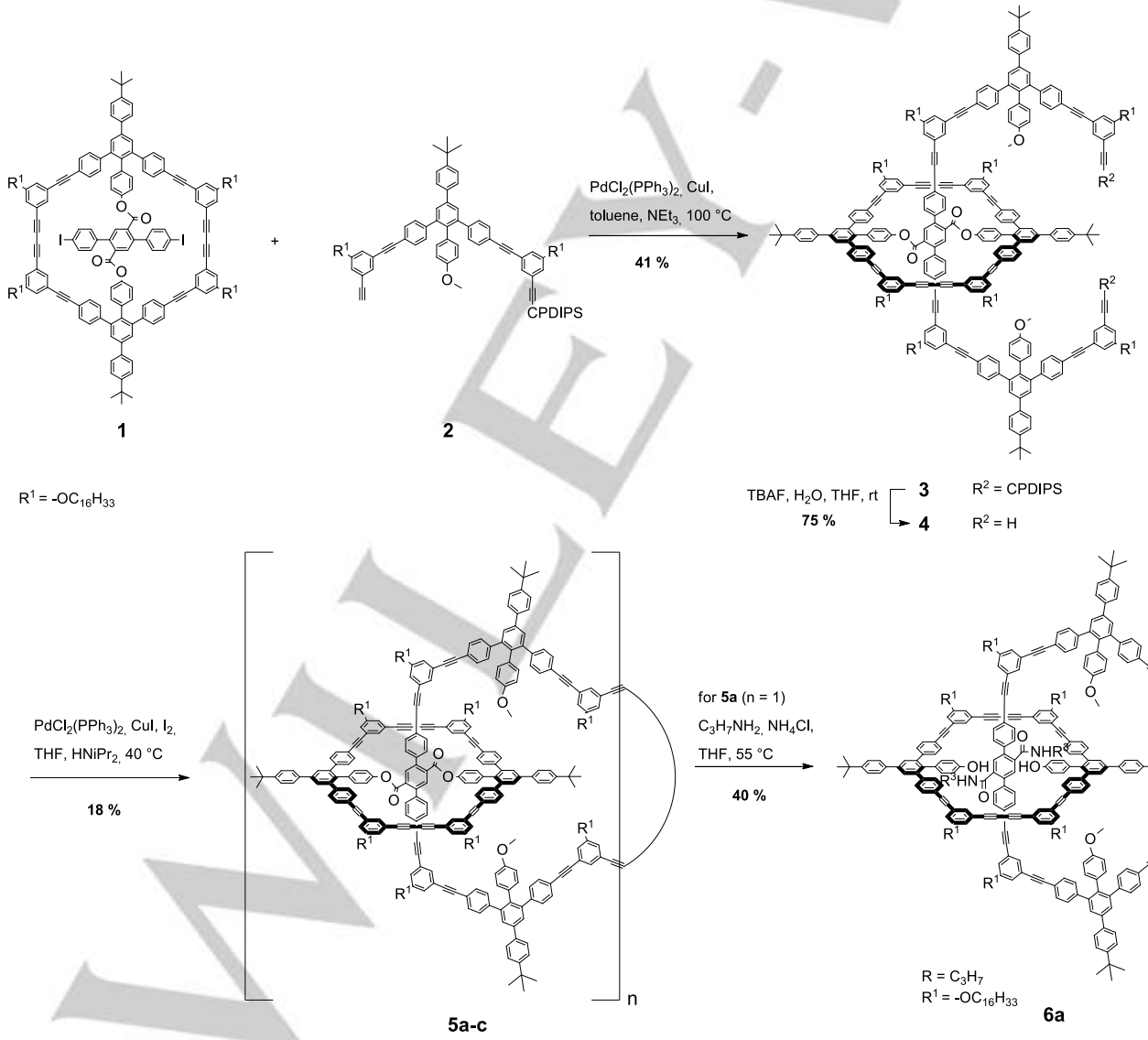
The precatenanes **5a-c** were formed by palladium catalyzed Glaser coupling[11] of **4** under pseudo high-dilution conditions. This step is similar to the synthetic pathway of Sauvage et al. and Anderson et al., respectively.[12, 13] High-dilution conditions should favor the formation of the [2]precatenane by an intramolecular coupling. However, according to the GPC analysis of the crude product a series of oligomeric precatenanes ([2]precatenane **5a**, [3]precatenane (**5b**),

[4]precatenane (**5c**)) were formed besides the desired product by intra- and intermolecular coupling reactions

Scheme 1. Schematic (a) and specific (b) synthesis of the [2]catenane.

a)

b)



(see Supporting Information). A successful separation of the products was performed by recycling GPC (recGPC) which allowed the isolation and characterization of the respective compounds.

Cleavage experiments with the higher precatenanes **5b** and **5c** have not yet been satisfactory and require larger product amounts than prepared here. These should be available by applying less diluted coupling conditions. However, those experiments were beyond the scope of this work. Anyhow, the [2]catenane **6a** was obtained by aminolysis of the corresponding [2]precatenane **5a** with n-propyl amine. After purification by recGPC, **6a** was fully characterized by ^{1}H NMR, mass spectrometry and GPC analysis.

Besides the exploration of this synthetic access to [2]catenanes and higher catenanes, the study of the so called isomer hypothesis, which was discussed by Morin et al.[6] and also by us,[7] was the impetus for our investigation. Specifically, during the rotaxane synthesis by using the covalent template approach under the usage of **1** arose the question if only the prerotaxane is formed or also a side product where the axis does not penetrate the wheel but touches the wheel tangentially. Aminolysis of the latter compound does not lead to the rotaxane but to the free wheel and axis. The free wheel and the free axis have been observed in those experiments, however, they can be also formed during the aminolysis by dethreading since it has been independently shown that dethreading occurs at elevated temperatures within the timescale of hours to days.[7] Transferred to the catenane syntheses described here, it means that in the synthesis of the precatenane (Scheme 1, steps 1 and 2) not only isomer **A** could be formed, which gives the desired catenane after the ester cleavage, but also isomer **B** (Figure 1). This topological isomer does not feature the topology of a precatenane, as the rings do not penetrate each other, so that cleavage of the auxiliary bonds leads to a separation of both rings (Figure 1).

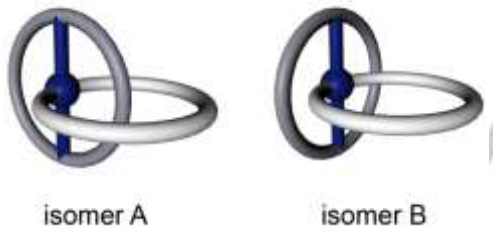


Figure 1. Both possible isomers of the precatenane synthesis.

The crude product of the aminolysis was carefully analyzed by GPC and MALDI-TOF mass spectrometry. The mass distribution of the GPC analysis reveals only a broadened signal at *m/z* = 6995 g/mol, which gives no hint for a separation of the catenane into its components. In addition, the mass spectrum of the crude product (see SI) also only shows two signals at *m/z* = 5153 and *m/z* = 5404.4 that result from the [2]catenane and its adduct with *E*-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB). This gives the evidence that a separation or fragmentation of the [2]precatenane during the course of the aminolysis does not take place. If both isomers had been formed, additional signals of the free macrocycles would have appeared in the spectrum at *m/z* = 2363.4 g/mol and at *m/z* = 2790 g/mol.

Thus, it seems that no second isomer is formed during the coupling of **1** and **2**. This selectivity can be attributed to the steric demand of the attached acetylenes. The Sonogashira coupling reaction proceeds consecutively, this means that initially one acetylene is coupled to the template followed by the second. The first one shields one face of the macrocycle and leads to a rotation of the template out of the plane of the macrocycles so that the second acetylene must attack the template from the other side of the ring. This geometry is fixed for the cyclization, because the molecule cannot flip its topological conformation, and therefore only one isomer is formed.

We are quite aware of the fact that the synthesis of a catenane via our covalent template can not be fully transferred to our previous rotaxane synthesis. However, it seems to be highly probable that the restricted yield in our rotaxane synthesis is rather a result of the deslipping reaction proceeding in parallel to the aminolysis of the bond to the template than the formation of a topological isomer of the prerotaxane.

Conclusions

In conclusion, we have successfully applied our covalent template approach to the synthesis of a phenylene-ethynylene-butadiynylene based [2]catenane. The synthetic pathway is convenient and benefits from the modular concept of our approach that has already been used for the rotaxane formation. The cleavage of the auxiliary template bonds of the precatenane leads selectively and exclusively to the [2]catenane. A separation of both rings is not observed, thus, we have no hint that another isomer (B) is formed during the reaction. The [2]catenane was fully characterized by ^{1}H NMR, MADLI-TOF mass spectrometry and GPC analysis. Additionally, the route easily opens access to larger catenanes (multicatenanes) via their corresponding precatenanes that are formed in intermolecular cyclization reactions.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

We gratefully acknowledge financial support by the Fonds der Chemischen Industrie.

Supporting Information

Supporting information and the ORCID number for the author of this article can be found under https://doi

Keywords: catenanes • rotaxanes • templates • macrocycles •

[1] (a) V. Balzani; A. Credi, F. M. Raymo, J. F. Stoddart, *Angew. Chem. Int. Ed*. **2000**, *39*, 3348–3391. (b) N. C. Seeman, *Mol. Biotechnol.* **2007**, *37*, 246–257. (c) N. C. Seeman, *Annu. Rev. Biochem*. **2010**, *79*, 65–87. (d) A. Coskun, M. Banaszak, R. D. Astumian, J. F. Stoddart, B. A. Grzybowski, *Chem. Soc. Rev.* **2012**, *41*, 19-30. (e) G. de Bo, S. Kuschel, D. A. Leigh, B. Lewandowski, M. Papmeyer, J. W. Ward, *J. Am. Chem. Soc.* **2014**, *136*, 5811–5814. (f) C. J. Bruns, J. F. Stoddart, *Acc. Chem. Res*. **2014**, *47*, 2186–2199. (g) S. F. M. van Dongen, S. Cantekin, J. A. A. W. Elemans, A. E. Rowan, R. J. M. Nolte, *Chem. Soc. Rev.* **2014**, *43*, 99-122. (h) E. R. Kay, D. A. Leigh, *Angew. Chem. Int. Ed.* **2015**, *54*, 10080–10088.

[2] (a) D. B. Amabilino, J. F. Stoddart, *Chem. Rev.* **1995**, *95*, 2725-2828. (b) J. P. Sauvage, C. Dietrich-Buchecker, (Eds.) *Molecular Catenanes, Rotaxanes and Knots*, Wiley-VCH, Weinheim, **1999**. (c) C. A. Schalley, K. Beizai, F. Vögtle, Acc. Chem. Res. **2001**, *34*, 465–476. (d) E. R. Kay, D. A. Leigh, F. Zerbetto, *Angew. Chem., Int. Ed.* **2007**, *46*, 72–191. (e) Z. Niu, H. W. Gibson, *Chem. Rev.* **2009**, *109*, 6024-6046. (f) E. A. Neal, S. M. Goldup, *Chem. Commun*. **2014**, *50*, 5128–5142. (g) G. Gil-Ramírez, D. A. Leigh, A. J. Stephens, *Angew. Chem. Int. Ed*. **2015**, *54*, 6110–6150. (h) M. Xue, Y. Yang, X. Chi, X. Yan, F. Huang, *Chem. Rev.* **2015**, *115*, 7398-7501. (i) H. Xing, Z. Li, Z. L. Wu, F. Huang, *Macromol. Rapid Commun.* **2018**, *39*, DOI: 10.1002/marc201700361.

[3] (a) F. Diederich, P. J. Stang, (Eds.) *Templated Organic Synthesis*, Wiley-VCH, Weinheim, **2000**. (b) C. A. Schalley, T. Weiland, J. Brüggemann, F. Vögtle, *Top. Curr. Chem.* **2005**, *248*, 141-200. (c) F. Arico, J. D. Badjic, S. J. Cantrill, A. H. Flood, K. C.-F. Leung, Y. Liu, J. F. Stoddart, *Top. Curr. Chem.* **2005**, *249*, 203-259.

[4] G. Schill, A. Lüttringhaus, *Angew Chem. Int. Ed*. **1964**, *3*, 546-547.

[5] (a) Ö. Ünsal, A. Godt, *Chem. Eur. J.* **1999**, *5*, 1728–1733. (b) N. Kameta, K. Hiratani, Y. Nagawa, *Chem. Commun.* **2004**, *4*, 466–467. (c) H. Kawai, T. Umehara, K. Fujiwara, T. Tsuji, T. Suzuki, *Angew. Chem. Int. Ed.* **2006**, *45*, 4281–4286. (d) K. Hirose, K. Nishihara, N. Harada, Y. Nakamura, D. Masuda, M. Araki, Y. Tobe, *Org. Lett.* **2007**, *9*, 2969–2972. (e) L. Steemers, M. J. Wanner, B. R. C van Leeuwen, H. Hiemstra, J. H. van Maarseveen, *Eur. J. Org. Chem*. **2018**, 874-878.

[6] K. Cantin, A. Lafleur-Lambert, P. Dufour, J.-F. Morin, *Eur. J. Org. Chem.* **2012**, 5335–5349.

[7] C. Schweez, P. Shushkov, S. Grimme, S. Höger, *Angew. Chem. Int. Ed.* **2016**, *55*, 3328-3333.

[8] (a) C. Grave, A. D. Schlüter, *Eur. J. Org. Chem.* **2002**, 3075-3098. (b) S. Höger, *Chem. Eur. J.* **2004**, *10*, 1320–1329. (c) W. Zhang, J. S. Moore, *Angew. Chem. Int. Ed.* **2006**, *45*, 4416–4439. (d) M. Iyoda, J. Yamakawa, M. J. Rahman, *Angew. Chem. Int. Ed.* **2011**, *50*, 10522–10553.

[9] (a) G. Gaefke, S. Höger, *Synthesis* **2008**, *14*, 2155-2157. (b) S. Höger, K. Bonrad, *J. Org. Chem*. **2000**, *65*, 2243-2245.

[10] S. Höger, A.-D. Meckenstock, *Chem Eur. J.* **1999**, *5*, 1686-1691.

[11] Q. Liu, D. J. Burton, *Tetrahedron Lett.* **1997**, *38*, 4371–4374.

[12] F. Bitsch, C. O. Dietrich-Buchecker, A. K. Khemiss, J. P. Sauvage, A. van Dorsselaer, *J. Am. Chem. Soc.* **1991**, *113*, 4023–4025.

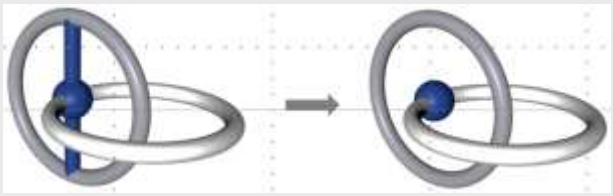
[13] M. J. Langton, J. D. Matichak, A. L. Thompson, H. L. Anderson, *Chem. Sci.* **2011**, *2*, 1897.

10.1002/chem.201802567

WILEY-VCH

Entry for the Table of Contents

FULL PAPER



*Christopher Schweez, Sigurd Höger**

Page No. – Page No.

A Nanosize Phenylene-Ethynylene-Butadiynylene [2]Catenane

Text for Table of Contents

A covalent template connected to the reactants by ester bonds supports the synthesis of both rings of the precatenane and subsequent aminolysis yields the corresponding catenane.