doi:10.2533/chimia.2010.180 Chimia 64 (2010) 180–183

Oligoazobenzenes – Switching in a New Dimension

Raphael Reuter§, Nik Hostettler, Markus Neuburger, and Hermann A. Wegner*

§SCS–DSM Nutritional Products Award Winner (Poster Presentation)

Abstract: A new synthesis of cyclotrisazobenzene with different substituents was developed with yields of up to 30%. Solid-state structures of cyclotrisazobenzene as well as the *tert*-butyl derivative were obtained. Also, the photochromic properties and the complexation behaviour with alkali metal ions of this class of molecules were investigated.

Keywords: Azobenzenes · Macrocycles · Mills reaction · Molecular switches · Photochromic compounds

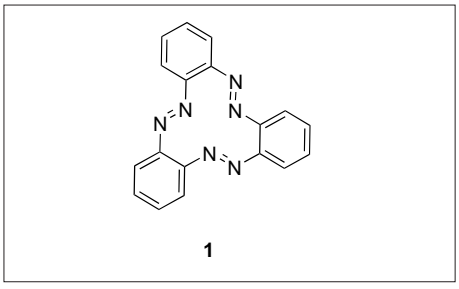
1. Introduction

Since their discovery in the mid 19th century, azo-compounds have always been important products as dyes and pigments for the chemical industry. In recent years, the scope of azo-compounds has widened beyond their traditional use.[1] Due to its *E*→*Z* photoisomerization the azo moiety has been applied in many examples to bring about structural changes in molecules and hence, to alter their physical and chemical properties reversibly by UV-irradiation.[2] However, in most cases only a photostationary state with mixtures of the *E*- and *Z*-isomer is obtained. Additionally, the thermodynamically unfavourable *Z*-isomer often has a short lifetime.

It has been shown that strain, which is induced when azo-bonds are incorporated into macrocyclic structures, can extend the lifetime of the unstable *Z*-isomer. This makes cyclic azobenzenes, or azobenzenophanes a particularly interesting class of compounds.[3] In a few cases, where a distorted geometry is present, the usual behaviour can be reversed, and the *Z*-isomer becomes the thermally more stable form.[4]

The cavity of macrocyclic azobenzenes also has the potential to act as a host for cations,[5] similar to crown ethers[6] or calixarenes.[7]

A special class of azobenzenophanes are cyclotrisazobenzenes **1** (Fig. 1), in which three aryl units are bridged in *ortho*-positions by azobenzene units to create a fully conjugated π-system. Dreiding and coworkers synthesized cyclotrisazobenzene in an overall yield of 2.6% from *N*-(1-pyridinio)-2-nitroanilide.[8] The synthesis of the precursor could be further improved by the work of Skrabal *et al*.[9] Because of its prospective photochromic behaviour and use as a molecular gripper (Fig. 2),[10] we initiated a research program to investigate the efficient preparation and the properties of such macrocycles.[11] Since the overall yield of the reported synthesis of cyclotrisazobenzene was low, a new and efficient synthetic strategy was developed. This approach also allows the introduction of functional groups.



1

Fig. 1. Structure of cyclotrisazobenzene.

2. Synthesis of Cyclotrisazobenzene

One of the oldest and probably still the most important protocol for preparing azo-compounds is the Mills reaction.[12] An important advantage of this method is that a large variety of substituted non-symmetric azobenzenes can be prepared under mild conditions by condensation of an aniline with a nitrosoarene. The major limitation consists in the accessibility and stability of the nitrosoarenes, which tend to dimerize or decompose. Recently, a two-step procedure based on Buchwald-Hartwig coupling of Boc-protected hydrazoaryls and halogenated arenes was reported, which is particularly efficient in the synthesis of azobenzenophanes.[13] For the synthesis of symmetrical azobenzenes, a larger variety of procedures is known, either by oxidation of anilines or reduction of nitrobenzenes.[14]

In our retrosynthetic analysis we envisioned that the last azo-bond to be formed had to be generated either by reductive

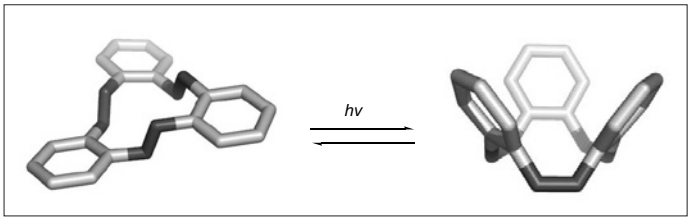
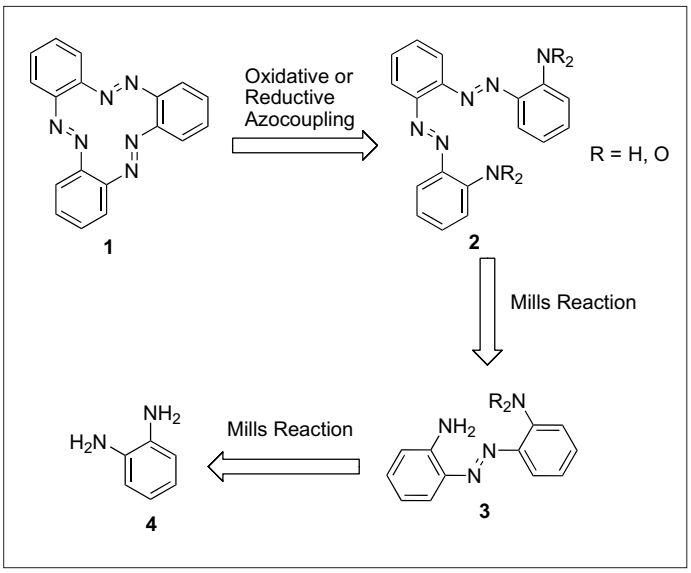


Fig. 2. Possible switching of cyclotrisazobenzene.

*Correspondence: Dr. H. A. Wegner
University of Basel
Department of Chemistry
St. Johanns-Ring 19
CH-4056 Basel
Tel.: +41 61 267 1147
Fax: +41 61 267 0976
E-mail: hermann.wegner@unibas.ch

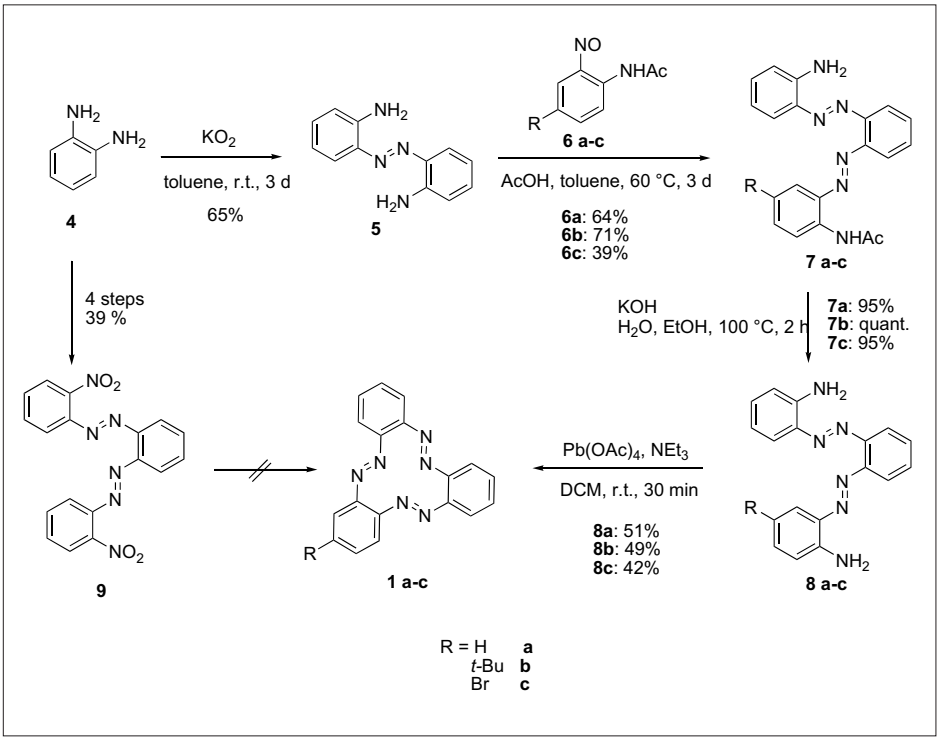


Scheme 1. Retrosynthetic analysis.

or oxidative azo-coupling. To favour the formation of a macrocycle, rather than an intermolecular reaction, the metal template effect could be of use. The bis-azo precursor could be prepared either by two sequential Mills coupling reactions, or in a one-pot reaction in which both azo-bonds would be formed in a single step. Cheap *ortho*-phenylenediamine (**4**) would be a suitable starting material (Scheme 1).

In our initial synthetic attempts, a route was established where the cyclization would be done reductively. An efficient route to dinitrobis-azo-compound **9** was prepared. However, no protocol could be found which was suitable for the last cyclization step. Therefore, we focused on generating the last azo-bond under oxidative conditions. Our first strategy starts with the preparation of 2,2'-diaminoazobenzene (**5**) from *ortho*-phenylenediamine (**4**) by oxidative coupling. The use of KO_2 instead of MnO_2 as an oxidant significantly increased the yield of the reaction.[15] The next azo-bond was installed by the Mills reaction with 2-nitrosoacetanilide (**6**). This reaction proceeds only in diluted conditions. A solvent screening showed that nonpolar solvents lead to an increased yield. Consequently, chloroform initially used as solvent was changed to toluene using only four equivalents of acetic acid. After deprotection of the acetyl protecting groups under basic conditions, the precursor **8** of cyclotrisazobenzene was obtained. Ring closure was achieved by treating the diamine **8** with $Pb(OAc)_4$ as a key step of the synthesis. A problem of this protocol was its low selectivity. When the method was employed according to Dreiding's original procedure, the corresponding bisbenzotriazol was obtained as the major product. It was found that the addition of NEt_3 prevented this unwanted side reaction, leading to an improvement of the yield from 26% to 51%. Two more derivatives, either with a bromide or a *tert*-butyl substituent were prepared, according to the same synthetic pathway (Scheme 2).

We also established a second procedure in which the first two azo-bonds can be created in a one-pot two-step strategy *via* Mills reaction, starting with *ortho*-phenylenediamine. The first coupling could only be achieved in toluene under the same conditions, as used in the first strategy. The second coupling, though, took place when the polarity of the solvent was enhanced by increasing the amount of acetic acid. After deprotection of the obtained bis-azo-compound **10** and oxidative coupling with $Pb(OAc)_4$ the unsubstituted macrocycle **1a** could be obtained in an overall yield of 30% (Scheme 3).



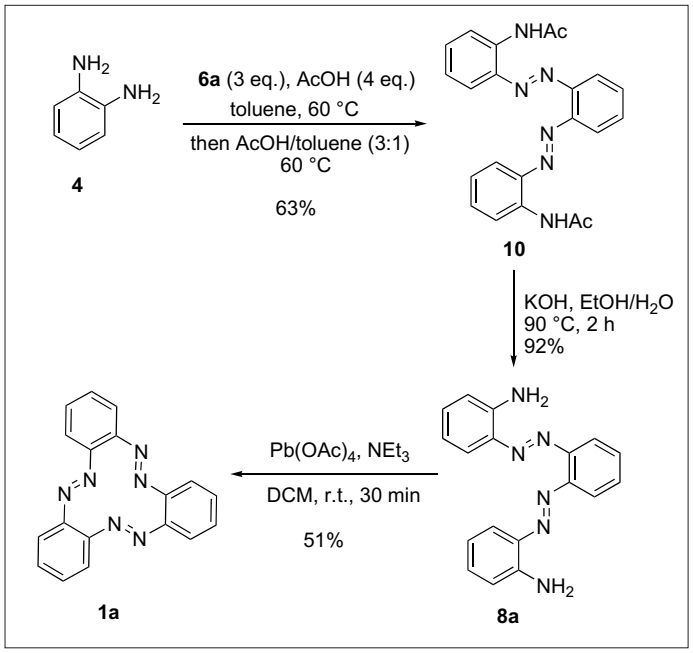
Scheme 2. Synthesis of cyclotrisazobenzene and derivatives.

3. Solid-State Structures

By slow evaporation of a solution of the *tert*-butyl substituted macrocycle (**1b**) in *tert*-butylmethylether, crystals could be obtained which were suitable for X-ray structural analysis. The structure of the unsubstituted derivative (**1a**) has already been discussed by Dreiding and co-workers earlier.[16] In both cases, for the *tert*-butyl substituted **1b** as well as the unsubstituted cyclotrisazobenzene **1a** the structure can only be described in pairs of molecules. For **1a**, two molecules are arranged in a face-to-face arrangement, caused by π–π-stacking interactions. These interactions are suppressed in *tert*-butylcyclotrisazobenzene (**1b**). The high steric demand of the *tert*-butyl group forces the two molecules to align in a different manner next to each other (Fig. 3).

4. Binding Studies

There are different heavy metal complexes of the Schiff's base macrocycles reported.[17] ESI-MS can be utilized to measure binding constants of alkali metal ion complexes of crown ethers.[18] Unfortunately, all attempts to detect first row transition metal complexes of **1a** failed. To investigate the gas phase binding properties of macrocycle **1a** with different alkali metal ions, an equimolar solution of



Scheme 3. Second generation synthesis of cyclotrisazobenzene.

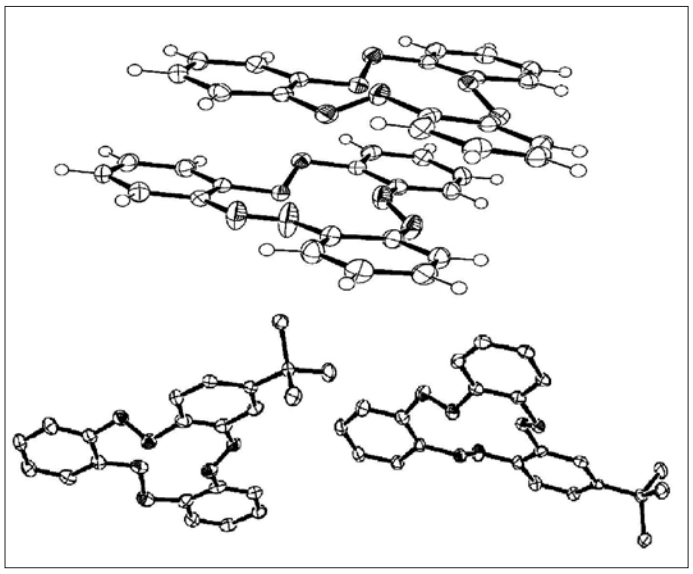


Fig. 3. Solid state structures of *tert*-butyl-cyclotrisazobenzene.

1a, and different alkali metal chlorides (LiCl, NaCl, KCl, RbCl) in methanol was analyzed by ESI-MS (Table 1). The mass spectrum of the solution showed all expected monomeric complexes [**1a** + M^+] as well as dimeric complexes [**2** * **1a** + M^+]. The signals for all metal complexes show intensities in the same order of magnitude. However, the two highest intensities for the 1:1 complexes could be seen with sodium and rubidium. Intensities of the signals, representing the 2:1 complexes, decline with decreasing cation size.

Apart from investigation of the complexation behaviour of cyclotrisazobenzene **1a** in the gas phase, ^{1}H-NMR titration experiments were performed to explore complexation properties in solution. Measurements of **1a** in DMSO-d_6 with increasing amounts of NaI from 0.5 equiv. to 10 equiv. did not show any change in chemical shifts of the aromatic protons, indicating that the host–guest interactions in solution are very weak.

Table 1. ESI-MS binding studies of cyclotrisazobenzene **1a** with different alkali cations.

Entry	m/z	Complex	Relativ ESI-MS intensity
1	313	[**1a** + H^+]	1
2	319	[**1a** + Li^+]	3.2
3	335	[**1a** + Na^+]	9.6
4	351	[**1a** + K^+]	9.2
5	397	[**1a** + Rb^+]	16.1
6	631	[2 * **1a** + Li^+]	30.4
7	647	[2 * **1a** + Na^+]	15.7
8	663	[2 * **1a** + K^+]	3.2
9	708	[2 * **1a** + Rb^+]	3.2

5. Isomerization Studies

The different azobenzenophanes were subjected to UV irradiation to investigate their photochromic properties. Cyclotrisazobenzene with one absorption band at 294 nm was irradiated at different wavelength ranging from 280 nm to 350 nm. Even after enduring irradiation, no change in the absorption spectrum was observed. A second experiment was done using laser flash photolysis. Again, no switching could be seen. We concluded that the strain in this small azobenzenophane is too high for the isomerization to occur, since the structure would become too distorted (Fig. 4).

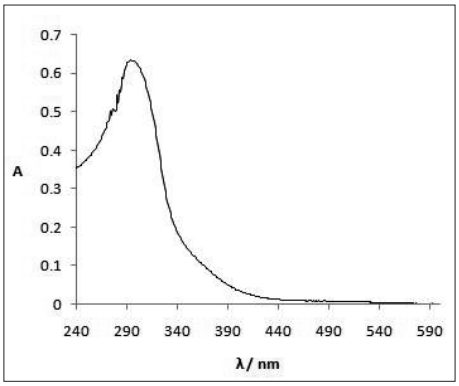


Fig. 4. Absorption spectrum of cyclotrisazobenzene (in chloroform).

6. Conclusion

An efficient synthesis of cyclotrisazobenzene was developed. Solid-state structures of two members of the family were obtained, which show a deviation of the molecules from planarity. The photochromic properties of this class of compounds were investigated. However, their strained structure prohibits isomerisation of the azo-bonds. First results on triscycloazobiphenyls, which are larger members of this family, indicate that these molecules do not possess this limitation and show isomerization. Further studies towards such macrocycles are ongoing.

Acknowledgements

We thank the Swiss National Science Foundation and the Fonds der chemischen Industrie for their financial support. The Swiss Chemical Society and DSM are thanked for awarding Raphael Reuter the SCS–DSM Nutritional Products Award.

Received: January 13, 2010

[1] a) J. Griffith, *Chem. Soc. Rev.* **1972**, *1*, 481; b) H. Rau, 'Photochromism: Molecules and Systems', Eds. H. Dürr, H. Bouas-Laurent, Elsevier, Amsterdam, **2003**.

[2] a) K. G. Yager, C. J. Barrett, *J. Photoch. Photobio. A* **2006**, *182*, 250; b) C. Dugave, L. Demange, *Chem. Rev.* **2003**, *103*, 2475; c) A. Natansohn, P. Rochon, *Chem. Rev.* **2002**, *102*, 4139; d) I. Willner, B. Willner, 'Bioorganic Photochemistry: Biological Applications of Photochemical Switches', Ed. H. Morrison, Wiley, New York, **1993**, Vol. 2, pp 1–110; e) K. Ichimura, 'Photochromism: Molecules and Systems', Eds. H. Dürr, H. Bouas-Laurent, Elsevier, Amsterdam, **1990**, 903; f) G. S. Kumar, D. C. Neckers, *Chem. Rev.* **1989**, *89*, 1915.

[3] For recent examples see a) H.-M. Kang, H.-Y. Kim, J.-W. Jung, C.-G. Cho, *J. Org. Chem.* **2007**, *72*, 679; b) P. Rajakumar, B. Senthilkumar, K. Srinivasan, *Aust. J. Chem.* **2006**, *59*, 75; c) N. Tamaoki, *J. Syn. Org. Chem. Jpn.* **2005**, *63*, 370; d) C. Ciminelli, G. Granucci, M. Persico, *J. Chem. Phys.* **2005**, *123*, 174317; e) Y. Norikane, K. Kitamoto, N. Tamaoki, *Org. Lett.* **2002**, *4*, 3907.

[4] Y. Norikane, R. Katoh, N. Tamaoki, *Chem. Comm.* **2008**, *16*, 1898.

[5] Y. Norikane, K. Kitamoto, N. Tamaoki, *J. Org. Chem.* **2003**, *68*, 8291.

[6] a) J. S. Ritch, T. Chivers, *Angew. Chem., Int. Ed.* **2007**, *46*, 4610; b) S. Jarosz, A. Listkowski, *Curr. Org. Chem.* **2006**, *10*, 643; c) G. W. Gokel, W. M. Leevy, M. E. Weber, *Chem. Rev.* **2004**, *104*, 2723; d) J. W. Steed, *Coord. Chem. Rev.* **2001**, *215*, 171; e) J. S. Bradshaw, R. M. Izatt, *Acc. Chem. Res.* **1997**, *30*, 338.

[7] C. D. Gutsche, 'Calixarenes', Cambridge, Royal Society of Chemistry, UK, **1989**.

[8] H. Hilpert, L. Hoesch, A. S. Dreiding, *Helv. Chim. Acta* **1985**, *2*, 325.

[9] P. Skrabal, M. Hohl-Blumer, *Helv. Chim. Acta* **1976**, *8*, 2906.

[10] V. A. Azov, A. Beeby, M. Cacciarini, A. G. Cheetham, F. Diederich, M. Frei, J. K. Gimzewski, V. Gramlich, B. Hecht, B. Jaun, T. Latychevskaia, A. Lieb, Y. Lill, F. Marotti, A. Schlegel, R. R. Schlittler, P. J. Skinner, P. Seiler, Y. Yamakoshi, *Adv. Funct. Mater.* **2006**, *16*, 147.

[11] R. Reuter, N. Hostettler, M. Neuburger, H. A. Wegner, *Eur. J. Org. Chem.* **2009**, *32*, 5647.

[12] a) C. J. Mills, *Chem. Soc.* **1895**, *67*, 925. For exemplary applications of the Mills reaction see b) P. Ruggli, W. Wüst, *Helv. Chim. Acta* **1945**, *28*, 781; c) P. Ruggli, L. Rohner, *Helv. Chim. Acta* **1942**, *25*, 1533.

[13] For a Pd-catalyzed two-step procedure see a) Ref. [3a]; b) Y.-K. Lim, K.-S. Lee, C.-G. Cho, *Org. Lett.* **2003**, *5*, 979.

[14] For diazocouplings see a) M. J. Jones, 'Organic Chemistry', 2nd ed., W. W. Norton & Company, New York, **2000**; b) A. F. Hegarty, 'The Chemistry of Diazonium and Diazo Groups', Wiley, New York, **1978**.

[15] G. Crank, M. I. H. Makin, *Tetrahedron Lett.* **1979**, *23*, 2169.

[16] A. S. Dreiding, J. H. Bieri, R. Prewo, A. Linden, H. Hilpert, L. Hoesch, *Private Communication to the CCDC* **1993**, Refcode: HACKEB.

[17] G. A. Melson, D. A. Busch, *J. Am. Chem. Soc.* **1965**, *87*, 1706.

[18] E. C. Kempen, J. S. Brodbelt, *Anal. Chem.* **2000**, *72*, 5411.