ORGANIC LETTERS

2011
Vol. 13, No. 21
5908–5911

A Chiral Cyclotrisazobiphenyl: Synthesis and Photochemical Properties

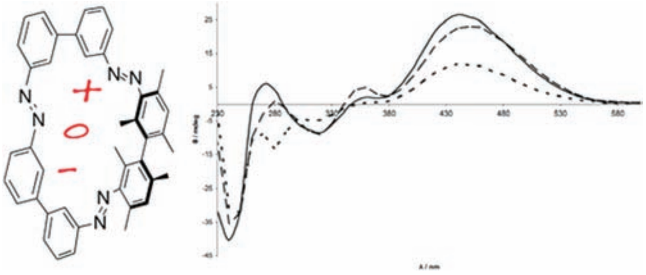
Raphael Reuter and Hermann A. Wegner*

Department of Chemistry, University of Basel, St. Johanns-Ring 19, CH-4056 Basel, Switzerland

Hermann.wegner@unibas.ch

Received September 21, 2011

ABSTRACT



A chiral cyclotrisazobiphenyl macrocycle was synthesized conveniently in three steps from the literature known 3,3′-diaminobimesityl in 37–38% overall yield. Irradiation with 302 nm, 365 nm or visible light allows access to different photostationary states (PSSs). These PSSs can be conveniently read out by CD-spectroscopy as each of them exhibits a positive, a negative, or no signal, respectively, at 275 nm.

Azobenzenes have been known for over 170 years.[1] Especially, their characteristic colorant properties led to their fame as dyes for various applications to the present day.[2] Later, it was recognized that azobenzenes can be switched reversibly from the usually thermodynamically more stable *E*-isomer to the *Z*-isomer upon irradiation or heating.[3,4] This dramatic structural change has led to numerous applications[5] such as photoresponsive host–guest systems,[6] controlling the activity of catalysts,[7] influencing the orientation and folding of peptides in biochemistry[8] or neuronal activity[9] as well as in materials chemistry and on surfaces.[10]

However, in most of these cases only one azobenzene moiety is incorporated into the system giving access to two distinct stages. The construction of compounds consisting of two or more azobenzene units offers the possibility to access multiple different states.[11,12] In order to do so, it must be possible to access these states selectively and, even more challenging, to conveniently read out the actual status. We recently showed that the construction of an azobenzene macrocycle,[13] a cyclotrisazobiphenyl, in which

---

(1) Mitscherlich, E. *Ann. Phys. Chem.* **1834**, *32*, 224.

(2) Rau, H. In *Photochromism: Molecules and Systems*; Dürr, H., Bouas-Laurent, H., Eds.; Elsevier: Amsterdam, 2003.

(3) Bouas-Laurent, H.; Dürr, H. *Pure Appl. Chem.* **2001**, *73*, 639.

(4) (a) Rau, H. In *Photochemistry and Photophysics*, Vol. 2; Rabek, J. F., Ed.; CRC Press: Boca Raton, FL, 1990; p 119. (b) For specific applications of azobenzene switches, see refs 5–10.

(5) (a) Balzani, V.; Venturi, M.; Credi, A. *Molecular Devices and Machines - A Journey into the Nanoworld*; Wiley-VCH: Weinheim, 2003. (b) Yager, K. G.; Barrett, C. J. *J. Photochem. Photobiol. A* **2006**, *182*, 250. (c) Russew, M.-M.; Hecht, S. *Adv. Mater.* **2010**, *22*, 3348.

(6) (a) An, H.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1992**, *92*, 543. (b) Vögtle, F. *Supramolecular Chemistry: An Introduction*; Wiley: Chichester, 1993. (c) An, H.; Bradshaw, J. S.; Izatt, R. M.; Yan, Z. *Chem. Rev.* **1994**, *94*, 939. (d) Losensky, H. W.; Spelthann, H.; Ehlen, A.; Vögtle, F.; Bargon, J. *Angew. Chem.* **1988**, *100*, 1225. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1189. (d) Vögtle, F.; Müller, W. M.; Müller, U.; Bauer, M.; Rissanen, K. *Angew. Chem.* **1993**, *105*, 1356. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1295.

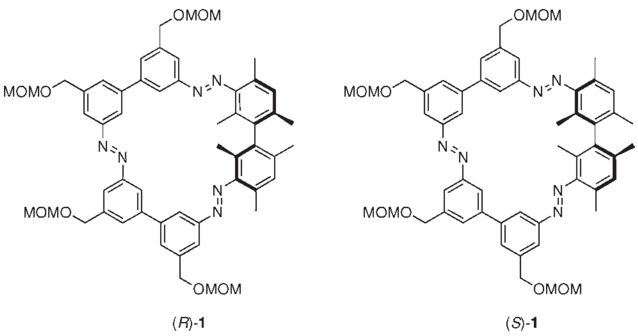
(7) (a) Peters, M. V.; Stoll, R. S.; Kuehn, A.; Hecht, S. *Angew. Chem.* **2008**, *120*, 6056. *Angew. Chem., Int. Ed.* **2008**, *47*, 5968. (b) Stoll, R. S.; Peters, M. V.; Kuhn, A.; Heiles, S.; Goddard, R.; Bühl, M.; Thiele, C. M.; Hecht, S. *J. Am. Chem. Soc.* **2009**, *131*, 357.

(8) (a) For a selected example, see: Hoppmann, C.; Seedorff, S.; Richter, A.; Fabian, H.; Schmieder, P.; Rück-Braun, K.; Beyermann, M. *Angew. Chem.* **2009**, *121*, 6763. *Angew. Chem., Int. Ed.* **2009**, *48*, 6636. (b) Renner, C.; Moroder, L. *ChemBioChem* **2006**, *7*, 868. (c) Rück-Braun, K.; Kempa, S.; Priewisch, B.; Richter, A.; Seedorff, S.; Wallach, L. *Synthesis* **2009**, *24*, 4256.

(9) (a) Janovjak, H.; Szobota, S.; Wyart, C.; Trauner, D.; Isacoff, E. Y. *Nat. Neurosci.* **2010**, *13*, 1027. (b) Kramer, R. H.; Fortin, D. L.; Trauner, D. *Curr. Opin. Neurobiol.* **2009**, *19*, 544. (c) Banghart, M.; Borges, K.; Isacoff, E.; Trauner, D.; Kramer, R. H. *Nat. Neurosci.* **2004**, *7*, 1381.

10.1021/ol202556z

each of the possible isomers [(*E*,*E*,*E*), (*E*,*E*,*Z*), (*E*,*E*,*Z*), (*Z*,*Z*,*Z*)] can be accessed as the major component in a photostationary state (PSS) selectively by choosing the right conditions.[14] Although all isomers can be distinguished and analyzed by NMR, the similarity in the absorption property rules out an easy analysis by UV-spectroscopy. Therefore, an additional source of information enabling an easy readout has to be introduced in the macrocycle. If a chiral entity would be placed in the cyclotrisazobenzene, this information should be highly dependent on the conformation of the different azobenzenes allowing a facile analysis via circular dichroism (CD) spectroscopy. There have been reports on the combination of a monomeric azobenzene unit with chiral molecules and the photochromic behavior of such a system.[15] In these cases, though, only two states could be addressed. To validate the concept a chiral biphenyl was chosen as a chiral source leading to the target compound **1** (Figure 1).

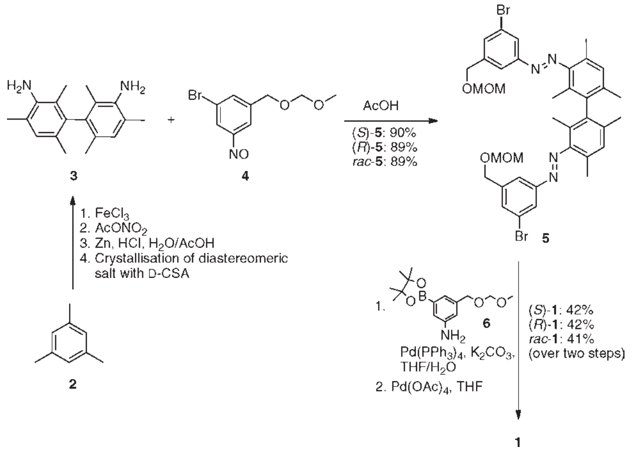


(*R*)-**1** (*S*)-**1**

Figure 1. (*R*) and (*S*) enantiomer of bimesitylcyclotrisazobiphenyl macrocycle **1**.

Chiral macrocycle **1** was prepared in three steps starting with the literature known 3,3′-diaminobimesityl (**3**) (Scheme 1), which was first synthesized by Moyer and Adams from iodomesitylene.[16] Their procedure included an Ullmann coupling of iodomesitylene followed by nitration with acetylnitrate and reduction of the nitro groups with zinc powder. We replaced the Ullmann coupling by a Scholl reaction of mesitylene (**2**) with ferric chloride, according to a procedure described by Rossnagel and co-workers.[17] Instead of using explosive acetyl nitrate, the nitrating reagent was prepared in situ from fuming nitric acid and acetic anhydride. Chiral resolution was also done as described in the procedure from Moyer and Adams by a recrystallization of the diastereomeric D-camphorsulfonic acid salt. The absolute configuration of 3,3′-diaminobimesityl (**3**) was already assigned by Bloch et al.[18] Both enantiomeric forms and the racemic mixture were transformed to the corresponding macrocycle **1** in three convenient steps. The Mills reaction with 1-bromo-3-[(methoxymethoxy)methyl]-5-nitrosobenzene (**4**) produced bisazocompund **5** in a high yield of 90% (for *rac*-**5**; 90% for (*S*)-**5** and 89% for (*R*)-**5**). After Suzuki reaction with boronic acid pinacolate **6**, the obtained diamine was oxidatively cyclized using $Pb(OAc)_4$ to furnish macrocycle **1** (41−42%).

Scheme 1. Synthesis of Both Enantiomers and the Racemic Mixture of Macrocycle **1**



The absorption spectrum of **1** showed the characteristic features observed for azobenzenes with three maxima: one at 444 nm, corresponding to the n−π* transition; one at

---

(10) (a) Natansohn, A.; Rochon, P. *Chem. Rev.* **2002**, *102*, 4139. (b) Barrett, C. J.; Mamiya, J.; Yager, K. G.; Ikeda, T. *Soft Matter* **2007**, *3*, 1249. (c) For an azobenzene-containing foldamer, see: Khan, A.; Kaiser, C.; Hecht, S. *Angew. Chem.* **2006**, *118*, 1912. *Angew. Chem., Int. Ed.* **2006**, *45*, 1878. (d) Yu, Z.; Hecht, S. *Angew. Chem.* **2011**, *123*, 1678. *Angew. Chem., Int. Ed.* **2011**, *50*, 1640. (e) Browne, W. R.; Feringa, B. L. *Annu. Rev. Phys. Chem.* **2009**, *60*, 407. (f) Wang, S.; Song, Y.; Jiang, L. *J. Photochem. Photobiol. C* **2007**, *8*, 18. (g) Wang, Y.; Ge, X.; Schull, G.; Berndt, R.; Bornholdt, C.; Koehler, F.; Herges, R. *J. Am. Chem. Soc.* **2008**, *130*, 4218. (h) Iwicki, J.; Ludwig, E.; Kalläne, M.; Buck, J.; Köhler, F.; Herges, R.; Kipp, L.; Roßnagel, K. *Appl. Phys. Lett.* **2010**, *97*, 063112.

(11) Cisnetti, F.; Ballardini, R.; Credi, A.; Gandolfi, M. T.; Masiero, S.; Negri, F.; Pieraccini, S.; Spada, G. P. *Chem.—Eur. J.* **2004**, *10*, 2011.

(12) (a) Bléger, D.; Dokić, J.; Peters, M.; Grubert, L.; Saalfrank, P.; Hecht, S. *J. Phys. Chem. B* **2011**, *115*, 9930. (b) For a recent example of peptides controlled by two isolated azobenzene units, see: Samanta, S.; Woolley, G. A. *ChemBioChem* **2011**, *12*, 1712.

(13) (a) Rau, H.; Lueddecke, E. *J. Am. Chem. Soc.* **1982**, *104*, 1616. (b) Tamaoki, N.; Koseki, K.; Yamaoka, T. *Angew. Chem.* **1990**, *102*, 66. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 105. (c) Tamaoki, N.; Yamaoka, T. *J. Chem. Soc., Perkin Trans. 2* **1991**, 873. (d) Norikane, Y.; Kitamoto, K.; Tamaoki, N. *J. Org. Chem.* **2003**, *68*, 8291. (e) Norikane, Y.; Tamaoki, N. *Org. Lett.* **2004**, *6*, 2595. (f) Norikane, Y.; Katoh, R.; Tamaoki, N. *Chem. Commun.* **2008**, 1898. (g) Mathews, M.; Tamaoki, N. *J. Am. Chem. Soc.* **2008**, *130*, 11409. (h) Müri, M.; Schuermann, K. C.; De Cola, L.; Mayor, M. *Eur. J. Org. Chem.* **2009**, 2562. (i) Reuter, R.; Hostettler, N.; Neuenburg, M.; WegnerH. A. *Eur. J. Org. Chem.* **2009**, 5647. (j) Reuter, R.; Hostettler, N.; Neuenburg, M.; Wegner, H. A. *Chimia* **2010**, *64*, 180. (i) For a recent review, see: Reuter R.; Wegner, H. A. *Chem. Commun.* **2011**, *Advance Article*, DOI: 10.1039/C1CC13773E.

(14) Reuter, R.; Wegner, H. A. *Chem.—Eur. J.* **2011**, *17*, 2987.

(15) (a) Haberhauer, G.; Kallweit, C. *Angew. Chem.* **2010**, *122*, 2468. *Angew. Chem., Int. Ed.* **2010**, *49*, 2418. (b) Kawamoto, M.; Shiga, N.; Takaishi, K.; Yamashita, T. *Chem. Commun.* **2010**, *46*, 8344. (c) Takaishi, K.; Kawamoto, M.; Tsubaki, K.; Furuyama, T.; Muranaka, A.; Uchiyama, M. *Chem.—Eur. J.* **2011**, *17*, 1778.

(16) Moyer, W. W.; Adams, R. *J. Am. Chem. Soc.* **1929**, *51*, 630.

(17) Fischer, E.; Hess, H.; Lorenz, T.; Musso, H.; Rossnagel, I. *Chem. Ber.* **1991**, *124*, 783.

(18) Bloch, M.; Lau, N.; Musso, H.; Záhorszky, U.-I. *Chem. Ber* **1972**, *105*, 1790.

326 nm representing the $\pi-\pi^*$ transition; and the third absorption of the $\sigma-\pi^*$ transition at 256 nm. Upon irradiation with UV light, a slight increase and a hypsochromic shift of the $n-\pi^*$ absorption to 437 nm was observed. This was combined with the typical sharp decrease of the $\pi-\pi^*$ transition maximum. An interesting feature was the splitting of the absorption maximum at 256 nm into two distinct bands at 248 and 270 nm. This is probably the result of a bathochromic shift of the $\sigma-\pi^*$ transition in the *Z*-azobenzene moieties, whereas the absorption at 248 nm can be attributed to the biphenyl units. Comparing the optical rotation of 3,3′-diaminobimesityls (**3**) and chiral macrocycle **1**, a large increase in the angle is observed (for (*S*)-**1**: $[\alpha]^{20}_{D} = 2128°$, for (*R*)-**1**: $[\alpha]^{20}_{D} = -2077°$). This behavior corresponds to a helical shape of the macrocyclic species. For the measurement of the CD spectra of chiral macrocycles (*S*)-**1** and (*R*)-**1**, the samples were heated at 45 °C overnight to effect thermal *Z*→*E* isomerization; in this case only the all-*E* isomer was present in the solutions. The CD spectra of the two enantiomers are mirror images with four different absorption maxima (Figure 2).

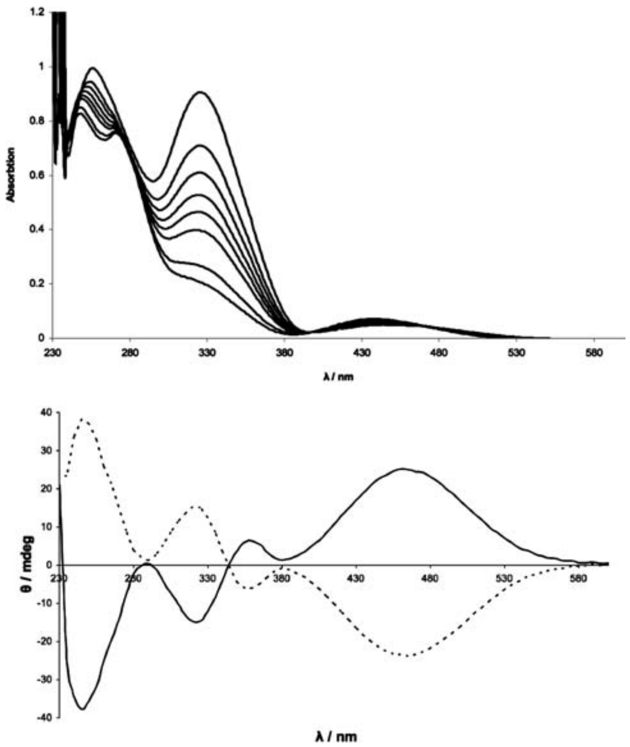


Figure 2. Absorption spectrum of (*rac*)-**1** with change upon irradiation at 365 nm from 0 to 3 min (2.0×10^{-5} M) and CD spectra of (*S*)-**1** (solid line) and (*R*)-**1** (dashed line) after both enantiomers were heated in the dark for 20 h at 45 °C (5.9×10^{-5} M).

We irradiated a CD sample of (*S*)-**1** with three light sources of different wavelength (302 nm, 365 nm, and visible light from a halogen floodlight).[19] In every irradiation experiment a photostationary state was obtained after approximately 15 min. ^{1}H NMR experiments revealed that (*S*)-**1** could adopt seven different isomeric species. Six of these isomers could be assigned to the different *E*/*Z* isomers [one (*E*,*E*,*E*), two (*E*,*E*,*Z*), two (*E*,*Z*,*Z*), and one (*Z*,*Z*,*Z*)], whereas one of them is thought to be a stable conformer of the (*E*,*E*,*Z*)-isomer where a diazobond next to the bimesityl unit has isomerized to its *Z*-form.[20]

In every investigated PSS a different ratio of these isomers is obtained. This fact was also expressed in the CD spectra of the irradiated mixtures. Upon comparison of the three different states, it was observed that they mostly vary in intensity with a similar overall shape (Figure 3). However, a significant difference can be seen for the values at about 275 nm. The sample which was irradiated at 302 nm shows a positive value, while the one irradiated with visible light shows almost no circular dichroism, and the one irradiated at 365 nm shows a negative value (Figure 3, inset). This observation opens the possibility of a ternary switch with three very distinct outputs with a convenient readout +, −, and 0.[21] Although such behavior is in principle not unique, it is essential to be able to access three metastable states, which display different chirality and hence CD spectra at a given wavelength. A sample of (*S*)-**1** can be irradiated with 302 nm, 365 nm, or visible light to set the molecule to the desired state. Since the switching of azobenzenes is known to be fully reversible, several cycles were done, switching between the different PSSs without any sign of fatigue (Figure 4). It does not matter from which starting state the switching is done; in every case reliable CD signals were obtained.

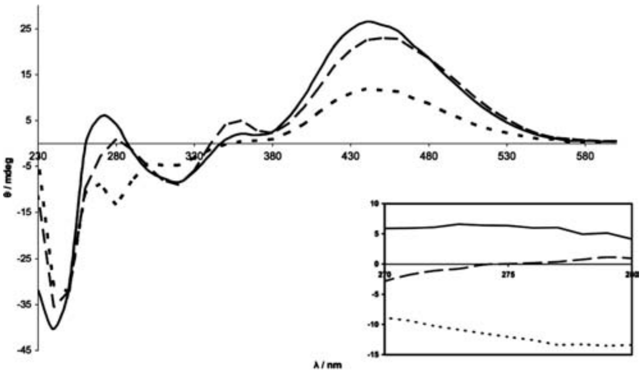


Figure 3. CD spectra at different PSSs at 302 nm (solid line), visible light (dashed line), and 365 nm (pointed line) (5.9 × 10−5 m), with an enlarged graph for the region 270−280 nm (inset).

Irradiated samples of macrocycle (*S*)-**1** were also tested for thermal *Z*→*E* isomerization. The samples were stored

---

[19] The time required to reach the PSS is dependent on the irradiation source as well as the concentration. Irradiations with 302 and 365 nm were done with a 8 W hand-held UV lamp. Irradiation with visible light was done with a tungsten-halogen lamp with 500 W. For the UV-isomerization experiments the PSS was obtained after 3 min as the concentration was three times lower than that for the CD measurements.

[20] For a detailed NMR analysis, see Supporting Information.

[21] For a recent example of a tristable fluorescent switch, see: Ferreira, R.; Remón, P.; Pischel, U. *J. Phys. Chem. C* **2009**, *113*, 5805.

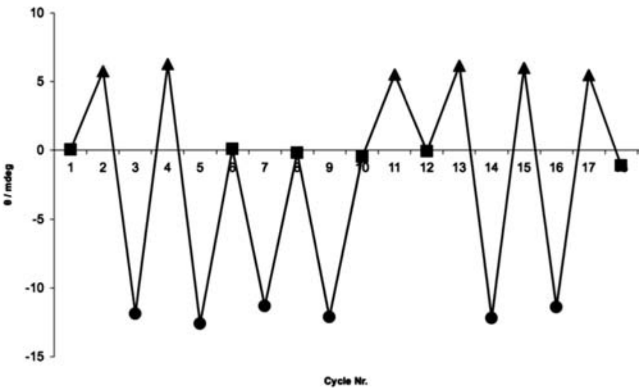


Figure 4. Switching between different PSSs with the value taken at 275 nm starting with a heated sample. 302 nm (▲), 365 nm (●), and vis (■) (5.9×10^{-5} m; 15 min irradiation time).

at 4 °C in the dark, and all of them showed a small decrease in θ of about 1 mdeg per day. The characteristic shape of the different PSSs was still clearly visible after four days of irradiation. Therefore, it can be said that the thermal isomerization is negligibly low, compared to the irradiation times needed to reach a certain photostationary state.

In summary, we presented the synthesis of two enantiomers as well as the racemic form of a chiral cyclotrisazobenzene macrocyle incorporating a chiral bismesityl unit into the molecule. In this manner the compound can be set to three different PSSs by irradiation with 302 nm, 365 nm, or visible light. The actual status of the system can be conveniently read out by CD spectroscopy as the CD signal of each of the PSSs shows a different sign at 275 nm. The concept will be applied in the future to control molecular function by incorporating this macrocycle into materials.

Acknowledgment. The authors thank the Swiss National Science Foundation for project funding. H.A.W. is indebted to the Fonds der Chemischen Industrie for a Liebig Fellowship.

Supporting Information Available. Experimental procedures, characterization data, assignment of different photoisomers, isomer ratio at different PSSs and thermal stability charts. This material is available free of charge via the Internet at http://pubs.acs.org.