A diastereoselective process induced in a curved aromatic molecule: oxidation of thioether-substituted subphthalocyanines

David González-Rodríguez, Tomás Torres *

Universidad Autónoma de Madrid, Departamento de Química Orgánica (C-I), Facultad de Ciencias, Cantoblanco, 28049-Madrid, Spain

ABSTRACT

Different sulfoxide-substituted subphthalocyanines have been synthesized by oxidation reaction of the corresponding thioether precursors. We have observed for the first time that when the oxidation takes place close to the macrocyclic core, the intrinsically chiral subphthalocyanine can induce a high degree of diastereoselectivity in this process.

Subphthalocyanines (SubPcs, Fig. 1a)[1] are 14 π-electron aromatic boron macrocycles that mainly differ from their higher homologues, the phthalocyanines (Pcs),[2] in that they present three isoindole units arranged in a cone-shaped structure. These singular three-dimensional chromophores are continuously finding potential uses in applied fields, such as nonlinear optics,[3] energy and electron transfer systems,[4] light-emitting diodes,[5] anion sensing,[6] and supramolecular chemistry.[7]

SubPcs are generated by cyclotrimerization reaction of phthalonitriles in the presence of a boron halide.[8] When the precursor phthalonitrile does not have a C_{2v} symmetry, a mixture of C_3- and C_1-symmetric regioisomers is formed.[9] Due to their curved, rigid structure, each of these SubPc regioisomers is actually constituted by a racemic mixture of enantiomers, which have been described by means of the helical descriptors M and P, regarding the SubPc macrocycle as a superimposition of three chiral helices going along the key X–B–N–C dihedral angles (Fig. 1b).

Despite the great interest in intrinsically chiral, π-conjugated molecules in the areas of materials science and supramolecular chemistry,[10] the resolution and application of SubPcs in a pure chiral form have not been developed to a great extent so far. SubPc enantiomers have been separated in an analytical scale by chiral HPLC[11] and their circular dichroic response, having a mirror symmetry with respect to the baseline, has been recorded.[12] In addition, chiral self-discrimination effects in racemic mixtures have been recently observed. Concretely, in the presence of a palladium complex, a tripyridyl-substituted SubPc enantiomer only recognizes its opposite upon the formation of supramolecular M_3L_2 cages under thermodynamic control.[7b] There is still a lot of excitement, however, in exploiting other aspects of SubPc chirality. For instance, it would be very interesting to organize chiral SubPcs in helical columns of a preferred handedness, which may show very

interesting chiroptical and liquid-crystalline properties, or to use them as sensors for chiral substrates.

As part of an ongoing research project aimed at obtaining high amounts of enantiomerically pure SubPc products via diastereomeric resolution, we have studied the functionalization of these macrocycles with chiral sulfoxide groups, widely employed in asymmetric synthesis,[13] at the peripheral positions of the macrocycle. To date, the incorporation of sulfoxide functionalities on the SubPc macrocycle has not been reported. A probable reason is that, quite often, the main problem encountered in the functionalization of these singular molecules is their chemical instability, which usually leads to decomposition via ring-opening. In addition, the harsh conditions required for their synthesis limit to a great extent the kind of functional groups that can be introduced in the precursor phthalonitriles.

And in fact, our initial attempts to directly introduce sulfoxide groups into the SubPc skeleton by condensation of 4-(p-tolylsulfinyl)-phthalonitrile in the presence of BCl_3 were, as expected, unsuccessful. The reaction yielded, in contrast, the corresponding
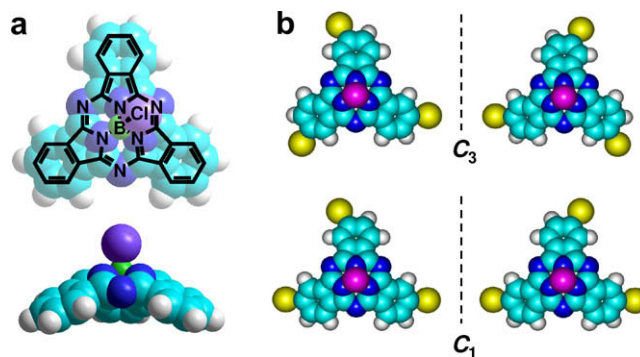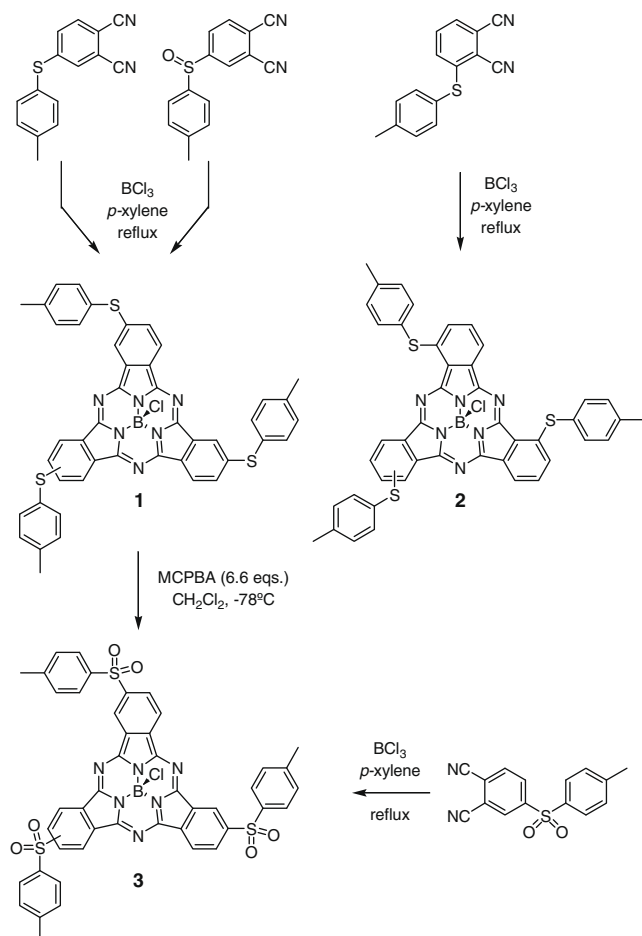

Figure 1. (a) Top and side view of the SubPc molecular structure. (b) SubPc regio- and stereoisomers formed in the condensation of a 4-substituted phthalonitrile.

* Corresponding author. Tel.: +34 91 497 4151; fax: +34 91 497 3966.
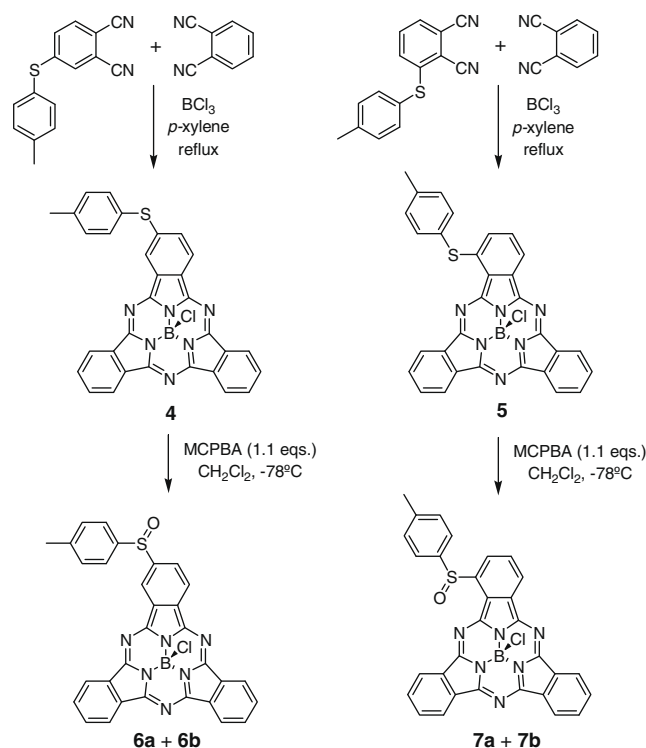*E-mail address:* tomas.torres@uam.es (T. Torres).

Scheme 1. Synthesis of SubPcs **1**, **2**, and **3**.

Scheme 2. Synthesis of SubPcs **6** and **7** as a mixture of diastereoisomers (**a** and **b**).

in which the main component is the unsubstituted SubPc, followed by compound **4** or **5**. As a result, chromatographic separation of the mixture is greatly facilitated at the expense of a higher loading of phthalonitrile.[15]

The oxidation reaction of **4** and **5** in the presence of 1.1 equiv of MCPBA led now to sulfoxide-SubPcs **6** and **7**, respectively, in good yields (~80%). A small amount of the corresponding sulfone-Sub-Pcs was as well obtained. All compounds were purified and characterized by NMR, LSI-MS, HR-MS, UV–vis, and IR techniques.

Figure 2 shows the aromatic region of the ^{1}H NMR spectrum of compounds **4** and **6**. The formation of a new chiral center in the molecule led to a 1:1 mixture of SubPc diastereoisomers (**6a** and

trithioether-substituted SubPc (**1**, Scheme 1), the boron halide playing the role of condensation template and reducing agent at once.

Since alkyl- and aryl-thioether SubPcs can be easily obtained by direct condensation of the respective phthalonitriles, we then looked for efficient methods to carry out the oxidation of the sulfur atoms that preserved the structure of the macrocycle. We found that the use of *m*-chloroperbenzoic acid (MCPBA) in CH$_2$Cl$_2$ at low temperatures was a good option. Oxidation was fast and virtually quantitative, while SubPc decomposition was not significant providing the temperature was kept at −78 °C.

SubPcs **1** and **2** were thus synthesized from 4-(*p*-tolylthio)pht-halonitrile or 3-(*p*-tolylthio)phthalonitrile, respectively.[14] The oxidation of compound **1**, having three thioether groups, in the presence of 3 equiv of MCPBA was, however, quite difficult to stop at the level of the trisulfoxide product. The reaction instead led to a complex mixture of unsymmetrical SubPcs substituted with thioether, sulfoxide, and sulfone groups. On the other hand, complete oxidation in the presence of an excess of MCPBA led to compound **3** in 59% yield (Scheme 1). This product can also be accessed by direct condensation of 4-(*p*-tolylsulfonyl)-phthalonitrile in the presence of BCl$_3$.[3b]
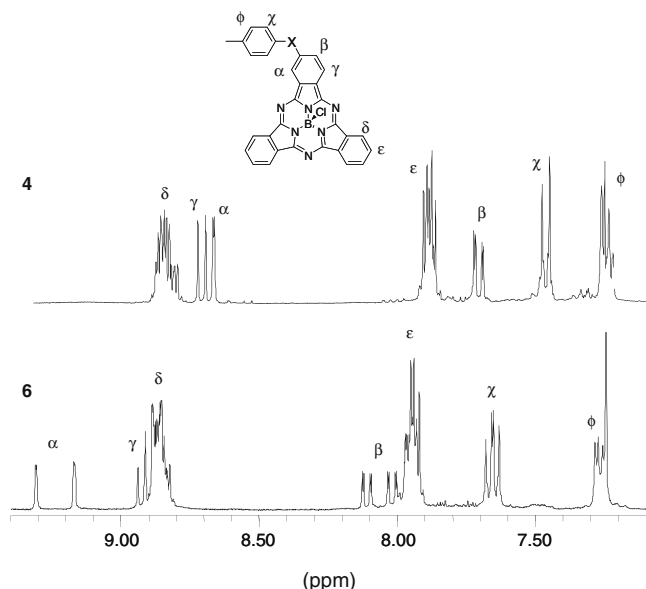
Therefore, the oxidation of unsymmetrically substituted SubPcs **4** and **5**, equipped with a single thioether unit at the β- or α-positions of the macrocycle, respectively, was next examined (Scheme 2). These products were obtained by the mixed condensation reaction of 4-(*p*-tolylthio)-phthalonitrile (for **4**) or 3-(*p*-tolylthio)-pht-halonitrile (for **5**) and phthalonitrile in the presence of BCl$_3$. The use of a high excess (9 equiv) of phthalonitrile generated a mixture

Figure 2. Aromatic region of the ^{1}H NMR spectra in CDCl$_3$ of SubPcs **4** and the 1:1 mixture of diastereoisomers of SubPc **6** (**6a** and **6b**).

6b), manifested by a clear splitting of some of the aromatic proton signals. This is specially evident in the protons that are in *ortho*-position to the sulfoxide group (α, β, and χ in Fig. 2). Such a splitting in SubPc diastereoisomers has also been observed in SubPc-fulleropyrrolidine dyads.[4a] Although we could separate these two diastereoisomers by HPLC in an analytical scale, any attempt to isolate them by column chromatography in higher amounts was fruitless.

On the other hand, when we carried out the oxidation reaction of compound **5**, bearing the sulfoxide group at the SubPc α position, we observed a totally different behavior. In contrast to compound **4**, the reaction of **5** led to a 95:5 mixture of diastereoisomers, as determined by ^{1}H NMR and HPLC analysis. Moreover, in this case, the two diastereoisomers could be separated by standard column chromatography, yielding compounds **7a** and **7b** in 76% and 4% yields, respectively. Figure 3 shows the aromatic region of the ^{1}H NMR spectra of the mixture of sulfoxide-SubPcs formed in the oxidation reaction of **5**, as well as of the isolated diastereomeric products **7a** and **7b**.

The proximity of the thioether group to the core of the chiral macrocycle in **5**, when compared to SubPc **4**, is likely to be responsible for the diastereoselectivity observed in this oxidation process. Molecular models, however, did not help in establishing a preferential attack mode of the oxidizing agent that could account for such selectivity. It may be that at such low temperatures, the phenylsulfide moiety in **5** adopts a well-defined conformation that is then subject to attack from only one of the sides of the macrocycle. Another possible explanation for this effect would be the existence of specific interactions between the MCPBA reagent and one of the sides of the SubPc ring in the transition state.

This is one of the few cases of diastereoselective reactions induced by a curved aromatic substrate,[16] and certainly the first one in SubPc chemistry. The preliminary results obtained from these experiments are encouraging for the utilization of asymmetric oxidation procedures[13] on peripherally or axially thioether-substituted SubPcs. The separation of SubPc diastereoisomers bearing an enantiomerically pure sulfoxide group would lead, after elimination of the stereogenic center, to the desired enantiomeric macrocycles. These optically active chromophores may show very valuable properties to be applied in supramolecular chemistry and molecular materials science.

Supplementary data

Supplementary data (synthetic procedures and characterization data of compounds C_3-**1**, C_1-**1**, C_3-**2**, C_1-**2**, **3**, **4**, **5**, **6**, **7a**, and **7b**) associated with this paper can be found, in the online version, at doi:10.1016/j.tetlet.2008.11.126.

References and notes

1. (a) Claessens, C. G.; González-Rodríguez, D.; Torres, T. *Chem. Rev.* **2002**, *102*, 835–853; (b) Torres, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 2834–2837.
2. (a)*The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 2003; Vols. 15–20, (b) de la Torre, G.; Claessens, C. G.; Torres, T. *Chem. Commun.* **2007**, 2000–2015.
3. (a) Sastre, A.; Torres, T.; Díaz-García, M. A.; Agulló-López, F.; Dhenaut, C.; Brasselet, S.; Ledoux, I.; Zyss, J. *J. Am. Chem. Soc.* **1996**, *118*, 2746–2747; (b) del Rey, B.; Keller, U.; Torres, T.; Rojo, G.; Agulló-López, F.; Nonell, S.; Marti, C.; Brasselet, S.; Ledoux, I.; Zyss, J. *J. Am. Chem. Soc.* **1998**, *120*, 12808–12817; (c) Claessens, C. G.; González-Rodríguez, D.; Torres, T.; Martín, G.; Agulló-López, F.; Ledoux, I.; Zyss, J.; Ferro, V. R.; García de la Vega, J. M. *J. Phys. Chem. B* **2005**, *109*, 3800–3806.
4. SubPcs have been employed as electron donors: (a) González-Rodríguez, D.; Torres, T.; Guldi, D. M.; Rivera, J.; Herranz, M. A.; Echegoyen, L. *J. Am. Chem. Soc.* **2004**, *126*, 6301–6313; as energy donors: (b) González-Rodríguez, D.; Claessens, C. G.; Torres, T.; Liu, S.; Echegoyen, L.; Vila, N.; Nonell, S. *Chem. Eur. J.* **2005**, *11*, 3881–3893; or as electron acceptors: (c) González-Rodríguez, D.; Torres, T.; Olmstead, M. M.; Rivera, J.; Herranz, M. A.; Echegoyen, L.; Atienza-Castellanos, C.; Guldi, D. M. *J. Am. Chem. Soc.* **2006**, *128*, 10680–10681.
5. Díaz, D. D.; Bolink, H. J.; Cappelli, L.; Claessens, C. G.; Coronado, E.; Torres, T. *Tetrahedron Lett.* **2007**, *48*, 4657–4660.
6. (a) Xu, S.; Chen, K.; Tian, K. *J. Mater. Chem.* **2005**, *15*, 2676–2680; (b) Palomares, E.; Martínez-Díaz, M. V.; Torres, T.; Coronado, E. *Adv. Funct. Mater.* **2006**, *16*, 1166–1170.
7. (a) Kang, S. H.; Kim, K.; Kang, Y.-S.; Zin, W.-C.; Olbrechts, G.; Wostyn, K.; Clays, K.; Persoons, A. *Chem. Commun.* **1999**, *17*, 1661–1662; (b) Claessens, C. G.; Torres, T. *J. Am. Chem. Soc.* **2002**, *124*, 14522–14533; (c) Rodríguez-Morgade, M. S.; Claessens, C. G.; Medina, A.; González-Rodríguez, D.; Gutiérrez-Puebla, E.; Monge, A.; Alkorta, I.; Elguero, J.; Torres, T. *Chem. Eur. J.* **2008**, *14*, 1342–1350.
8. (a) Meller, A.; Ossko, A. *Monatsh. Chem.* **1972**, *103*, 150–155; (b) Claessens, C. G.; González-Rodríguez, D.; del Rey, B.; Torres, T.; Mark, G.; Schuchmann, H.-P.; von Sonntag, C.; MacDonald, J. G.; Nohr, R. S. *Eur. J. Org. Chem.* **2003**, 2547–2551.
9. (a) Hanack, M.; Geyer, M. *J. Chem. Soc., Chem. Commun.* **1994**, 2253–2254; (b) Claessens, C. G.; Torres, T. *Eur. J. Org. Chem.* **2000**, 1603–1607.
10. Palmans, A. R. A.; Meijer, E. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 8948–8968.
11. Claessens, C. G.; Torres, T. *Tetrahedron Lett.* **2000**, *41*, 6361–6365.
12. Kobayashi, N.; Nonomura, T. *Tetrahedron Lett.* **2002**, *43*, 4253–4255.
13. (a) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717–1760; (b) Procter, D. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 835–871.
14. The C_3 and C_1 regioisomers of **1** and **2** (C_3-**1**, C_1-**1**, C_3-**2** and C_1-**2**), could be isolated and were characterized independently (see the Supplementary data).
15. González-Rodríguez, D.; Claessens, C. G.; Torres, T. *J. Porphyrins Phthalocyanines.*, in press.
16. More is known, however, on stereoselecitve processes in helicene chemistry: Urbano, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3986–3989.
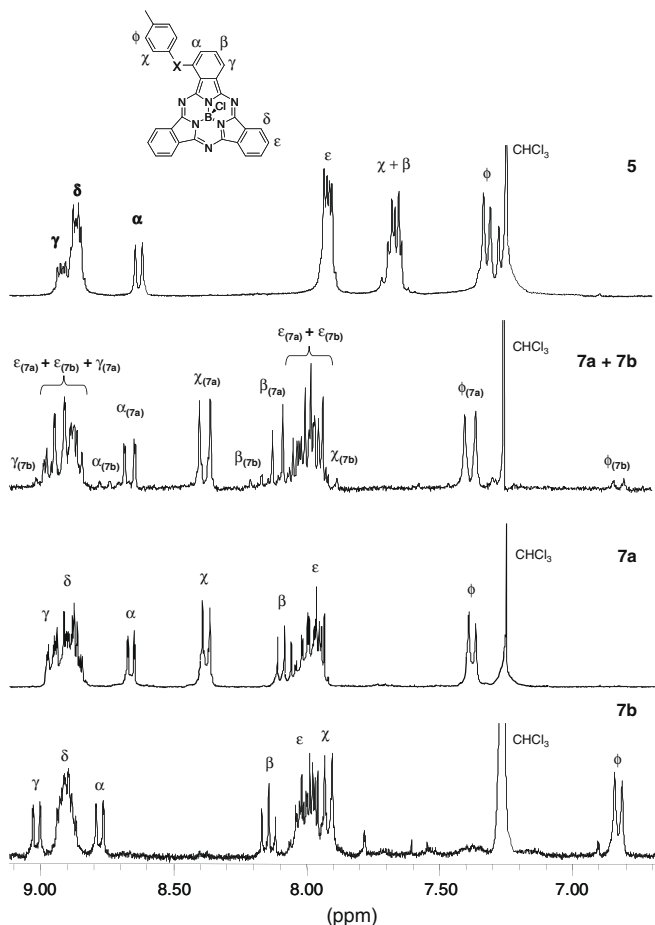

Figure 3. Aromatic region of the ^{1}H NMR spectra in CDCl$_3$ of SubPcs **5**, the 95:5 mixture of diastereoisomers of SubPc **7** (**7a + 7b**) as isolated from the reaction mixture, and compounds **7a** and **7b** after separation by column chromatography.