ORGANIC LETTERS

2001
Vol. 3, No. 25
4031−4034

Synthesis and Ring-Expanding Oligomerization of an Extremely Strained Macrocyclic Aromatic Ether–Sulfone

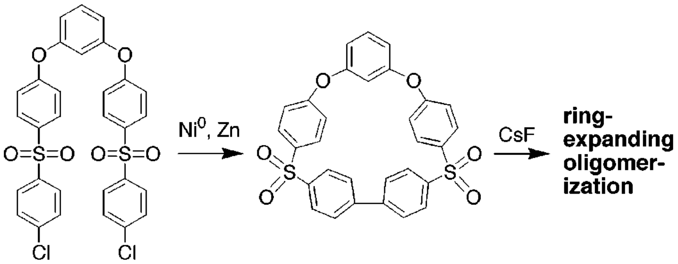
Howard M. Colquhoun,*,† Zhixue Zhu,† and David J. Williams*,‡

Department of Chemistry, University of Reading, Whiteknights,
Reading, RG6 6AD, U.K., and Chemical Crystallography Laboratory, Department of
Chemistry, Imperial College, South Kensington, London, SW7 2AY, U.K.

h.m.colquhoun@rdg.ac.uk

Received September 12, 2001

ABSTRACT



An extremely strained, 5-ring, macrocyclic aromatic ether–sulfone, [-1,4-$C_6H_4SO_2$-1,4-C_6H_4O-1,3-C_6H_4O-1,4-$C_6H_4SO_2$-1,4-C_6H_4-], synthesized by nickel-catalyzed intramolecular coupling of a bis-chlorophenylene-terminated precursor, undergoes fluoride-promoted ring expansion in dilute solution, giving a series of higher macrocyclic oligomers including cyclic dimer, trimer, and tetramer. The latter contains 20 aromatic residues in a 92-atom ring and is one of the largest synthetic organic macrocycles to be crystallographically characterized. The synthesis, structure, and ring expansion of a related macrocyclic ether–ketone are also reported.

Ring−chain interconversion between macrocyclic aromatic ethers and linear, high molar-mass polymers has been intensively investigated in recent years as a potential technique for recycling high-performance polymers.[1] Conversion of aromatic poly(ether−sulfones) and poly(ether−ketones) to macrocycles has been shown to occur at low polymer concentration, in the presence of catalysts such as fluoride ion which reversibly cleave the activated-ether linkages,[2] and theoretical work on the general principles of ring−chain interconversion in fact suggests that under equilibrium conditions there should exist a threshold concentration below which *only* cyclic species should be present.[3] This being so, it seemed possible that ring-opening polymerization of a small, strained macrocyclic aromatic ether in dilute solution would lead not to linear polymer but instead to a series of higher-order macrocycles. Such reactions are well-known for strained *aliphatic* ethers such as oxirane (resulting in the formation of crown ethers)[4] but do not seem to have previously been considered in the context of aromatic ether chemistry. We now describe the synthesis and characterization of an extremely strained

---

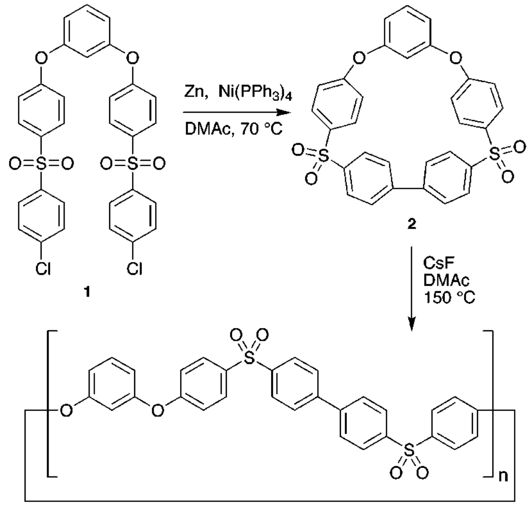
† University of Reading.
‡ Imperial College, London.
(1) Reviews: Wang, Y. F.; Chan, K. P.; Hay, A. S. *React. Funct. Polym.* **1996**, *30*, 205−227. Brunelle, D. J. In *New Methods of Polymer Synthesis*; Ebdon, J. R., Eastmond, G. C., Eds.; Blackie: London, 1995; pp 197−235.
(2) Ben-Haida, A.; Baxter, I.; Colquhoun, H. M.; Hodge, P.; Kohnke, F. H.; Williams, D. J. *Chem. Commun.* **1997**, 1533−1534. Ben-Haida, A.; Baxter, I.; Colquhoun, H. M.; Hodge, P.; Kohnke, F. H.; Williams, D. J. *Chem. Commun.* **1998**, 2213−2214.
(3) Ercolani, G.; Mandolini, L.; Mencarelli, P.; Roelens, S. *J. Am. Chem. Soc.* **1993**, *115*, 3901−3908.
(4) Dale J.; Daasvatn, K. *J. Chem. Soc., Chem. Commun.* **1976**, 295−296.

10.1021/ol010201n CCC: $20.00

macrocyclic aromatic ether–sulfone, an investigation of its potential for ring-expanding oligomerization, and the structural characterization of an extraordinarily large macrocyclic ether–sulfone oligomer derived from this reaction.

Reaction of resorcinol with excess 4,4′-dichlorodiphenyl sulfone afforded the linear oligomer **1**, and this, after purification by column chromatography, was found to undergo nickel-catalyzed dehalogenative coupling[5] in the presence of zinc powder to give the cyclic "monomer" **2** in ca. 25% yield (Scheme 1). The X-ray structure of this compound shows the molecule to have crystallographic C_2 symmetry and to be *highly* strained, even more so than the biarylene-ketone macrocycles obtained previously by this type of chemistry.[6] Very large strain-induced distortions occur within the biphenylene unit, the terminal S–C bonds of which deviate from collinearity by no less than 70°. This extreme level of distortion is reflected both in boatlike deformations of the rings comprising the biaryl unit and in pyramidalization at carbon atoms C(3) and C(6), which lie 0.09 and 0.11 Å, respectively, out of the planes of their substituent atoms. The internal angles at sulfone are strongly compressed, from a conventional value[7] of 105° to ca. 100°, and a number of other bond-angle distortions are noted in Figure 1. Despite the relatively small size of the macroring—comprising only five aromatic units—there is still a free pathway through its center (defined by van der Waals radii) some 3.6 Å in diameter.

Scheme 1. Synthesis and Ring-Expanding Oligomerization Reaction of **2**



3 (n = 2), **4** (n = 3), **5** (n = 4)

On heating a dilute solution (0.0189 M) of **2** in dimethylacetamide (DMAc) with 1 molar equiv of cesium fluoride at 150 °C for 48 h, ring-expanding oligomerization did indeed occur (Scheme 1) to give a series of higher cyclic oligomers, including the cyclic dimer **3** (45% yield), cyclic trimer **4** (12%), and cyclic tetramer **5** (4%), as evidenced by ^{1}H NMR, HPLC, and MALDI-TOF MS. Other products still remain to be identified, but MALDI-TOF analysis suggests that these may include even larger macrocyclic oligomers.

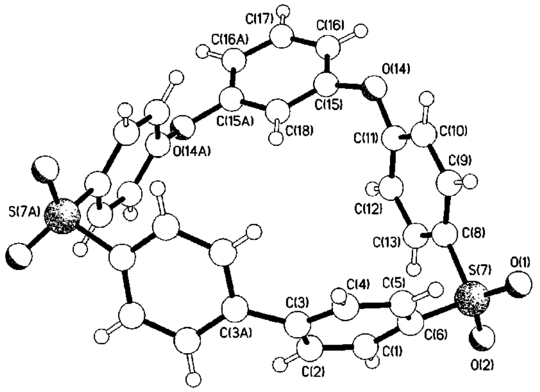


Figure 1. Molecular structure of **2**. Selected bond angles: C(6)–S(7)–C(8) 100.0(1), C(10)–C(11)–O(14) 114.6(3), C(11)–O(14)–C(15) 123.2(2), O(14)–C(15)–C(16) 115.5°.

Macrocycles **3**, **4**, and **5** (though *not* the strained cyclic monomer **2**) were also obtained [in analytical (HPLC) yields of 38%, 21%, and 19%, respectively] from nucleophilic cyclo-polycondensation of resorcinol with 4,4′-bis(4-chlorobenzenesulfonyl)biphenyl in DMAc. Column chromatography of the product mixture afforded isolated yields of 15%, 7%, and 3%, respectively. Cyclic dimer **3** crystallizes with two independent molecules in the asymmetric unit, both of which have crystallographic inversion symmetry.[8] However, in one conformer, **3a**, the resorcinol residues are folded in toward the center of the macrocycle whereas in the other

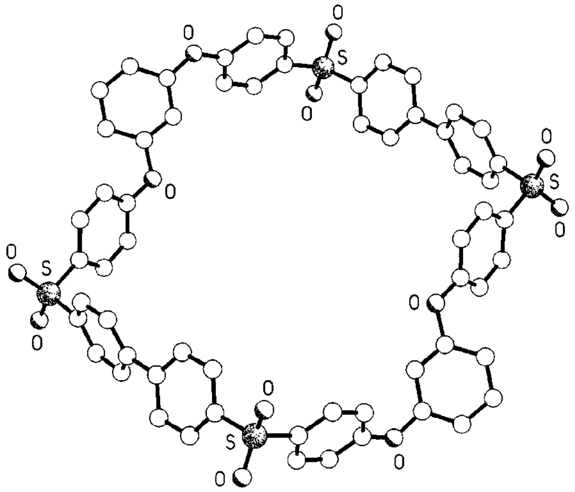


Figure 2. Molecular structure of **3b** (hydrogens omitted). Internal bond angles at sulfur and oxygen are in the ranges 102.9(4)–105.0(4)° and 121.1(7)–121.8(7)°, respectively.

---

(5) Colon, I.; Kelsey, A. *J. Org. Chem.* **1986**, *51*, 2627–2637.

(6) Colquhoun, H. M.; Dudman, C. C.; Thomas, M.; O'Mahoney, C. A.; Williams; D. J. *J. Chem. Soc., Chem. Commun.* **1990**, 336–339.

(7) Sime J. G.; Woodhouse, D. I. *J. Cryst. Mol. Struct.* **1974**, *4*, 269–285, 287–303.

(**3b**, Figure 2) they are directed outward. In both conformers the transannular separation between the two biaryl units is ca. 1.49 nm.

Cyclic tetramer **5** contains no fewer than 20 aromatic residues and includes a 92-atom ring.[9] This is one of the largest synthetic organic macrocycles so far characterized by X-ray crystallography,[10] although a number of much larger macrocyclic species have been synthesized.[11] The molecule has crystallographic inversion symmetry and a highly elongated conformation with overall dimensions ca. 1.1 × 3.9 nm (Figure 3). The central region, where opposite sides of the macrocycle come into contact, appears to be stabilized by the cooperative effects of four C−H···π interactions (H···π distances of 2.67 and 2.87 Å). The two more open regions have free pathways of a size potentially capable of including for example aromatic guest molecules, but in the current structure these voids are occupied by molecules of solvent.

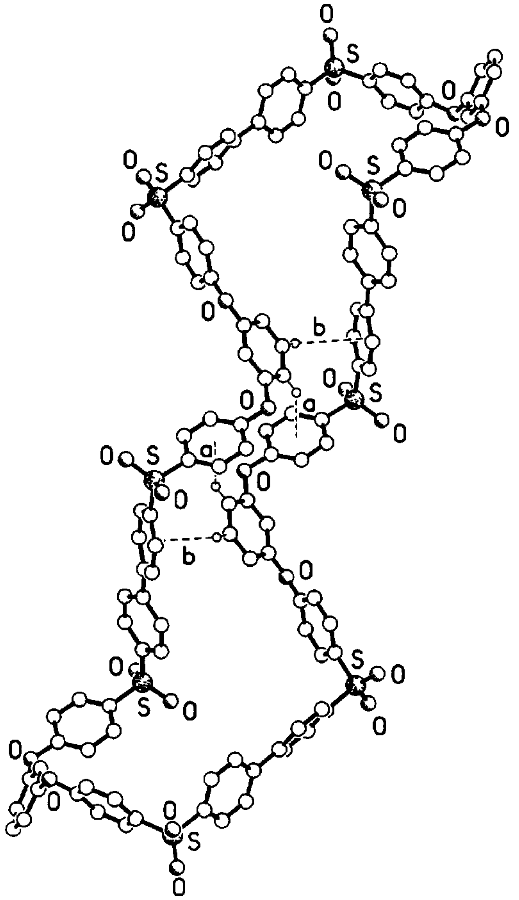
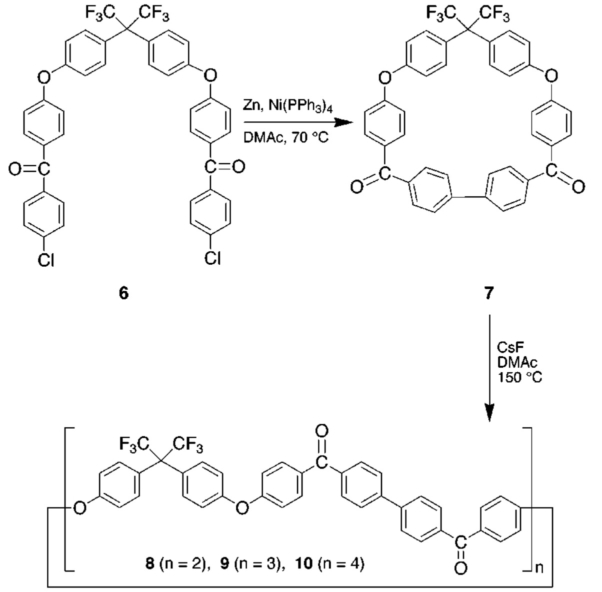


Figure 3. Molecular structure of **5** (hydrogens omitted for clarity). Internal bond angles are in the ranges C−S−C 103.9(3)−105.7(3)°, C−O−C 116.5(6)−122.0(5)°. Dashed lines indicate intramolecular C−H···π contacts (H···π distance in Å, C−H···π angle in deg, (a) 2.67, 139; (b) 2.87 127).

Macrocycle **5** has conformational features in common with those of **2** and **4**, in particular: (i) open-book conformations for the diaryl sulfone fragments (maximum deviation from orthogonality with the bridging C−S−C plane of 22°); (ii) twisted conformations for the biphenylene units (26 and 34° from coplanarity); and (iii) skewing between the resorcinol residue and its neighboring aromatic rings. In **5** the internal angles at sulfone (range 103.9−105.8°) are very close to the unstrained value of ca. 105°. These observations of consistent conformational preferences in large macrocyclic aromatic ether−sulfones strongly suggest that nanoscale, crystalline oligomers of this type provide very realistic models for chain conformation and folding in (amorphous) high molar mass poly(ether−sulfones).

Preliminary studies of related ether−*ketone* macrcoycles focused on compound **7**, also synthesized by nickel(0)-catalyzed coupling (Scheme 2). This compound crystallizes with two independent molecules in the asymmetric unit, both of which have essentially the same conformation (Figure 4). The hexafluoroisopropylidene and diaryl ether units, and one of the diaryl ketone fragments, have skewed conformations; the other diaryl ketone has a geometry that more closely

Scheme 2. Synthesis and Ring-Expanding Oligomerization Reaction of **7**



---

(8) **Crystal data for 3:** $C_{60}H_{40}O_{12}S_4 \cdot 3.125CH_2Cl_2$, M = 1346.55, triclinic, space group $P\bar{1}$, a = 13.855(2), b = 15.246(4), and c = 15.631 (4) Å, α = 92.71(2), β = 109.49(2), and γ = 90.02(1)°, V = 3108.7(12) Å^3, T = 193 K, Z = 2, D_c = 1.439 g cm^{-3}, μ(Cu Kα) = 4.39 mm^{-1}, F(000) = 1383; 9134 independent reflections, R_1 = 0.110, wR$_2$ = 0.206 for 4389 independent observed reflections [$2\theta \leq 120°$, $I > 2\sigma(I)$].

(9) **Crystal data for 5:** $C_{120}H_{80}O_{24}S_8 \cdot Et_2O \cdot 6.8CH_2Cl_2$, M = 2813.94, triclinic, space group $P\bar{1}$, a = 10.991(1), b = 14.921(2), and c = 20.600 (2) Å, α = 96.55(1), β = 93.30(1), and γ = 104.43(1)°, V = 3237.4(5) Å^3, T = 203 K, Z = 1, D_c = 1.443 g cm^{-3}, μ(Cu Kα) = 4.45 mm^{-1}, F(000) = 1448; 8893 independent reflections, R_1 = 0.084, wR$_2$ = 0.183 for 5099 independent observed reflections [$2\theta \leq 120°$, $I > 2\sigma(I)$].

(10) The crystal structure of a 96-membered macrocyclic polyamide, in the form of a trefoil knot, was reported very recently. See: Safarowsky, O.; Nieger, M.; Fröhlich, R.; Vögtle, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 1616−1618.

(11) For a recent review of very large synthetic macrocycles, see: Prautzsch, V.; Ibach, S.; Vögtle, F. *J. Incl. Phenom.* **1999**, *33*, 427−458.

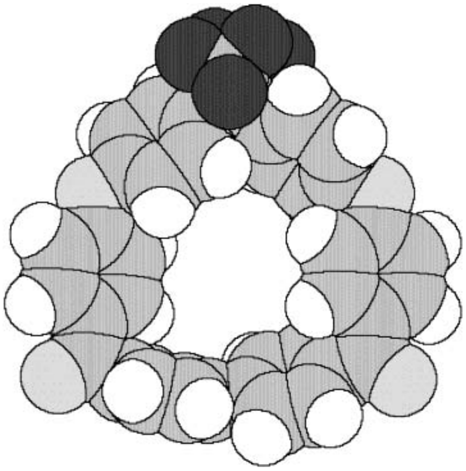


Figure 4. Space-filing representation of one of the two independent molecules in the structure of **7**. Internal bond angles at carbonyl carbons and ether-oxygens are 114.9(2), 115.4(2)° and 118.5(2), 119.7(2)°, respectively.

approaches orthogonal.[12] In both molecules the biphenylene unit is both twisted (ca. 30° torsonal twist) and bowed, the terminal C−aryl bonds subtending an angle of ca. 126°. As can be seen from Figure 4, the macrocycle has a free pathway through the ring center (of ca. 4.5 Å) that has been shown by molecular modeling to be of sufficient size to accommodate the threading of, for example, a poly(ethylene oxide) chain. Ring-expanding oligomerization was observed for **7** under very similar conditions to those used for macrocycle **1**, giving mainly the cyclic dimer **8** but also a number of higher macrocycles, indicating that ring expansion is in fact a quite general reaction of strained macrocyclic aromatic ethers in which the ether linkages are activated toward nucleophilic attack.

Acknowledgment. We thank the University of Reading for grants in support of this work and the Overseas Research Student Scheme for an award to Z.Z.

Supporting Information Available: Experimental procedures and characterization data for **2**, **3**, **4**, **5**, **7**, and **8**. Full crystallographic data for macrocycles **2**, **3**, **5**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL010201N

---

(12) **Crystal data for 7:** $2(C_{41}H_{24}O_4F_6)\cdot Et_2O\cdot MeOH$, $M = 1495.37$, monoclinic, space group $P2_1/c$, $a = 26.873(1)$, $b = 12.652(1)$, and $c = 20.611(1)$ Å, $\beta = 98.84(1)°$, $V = 6924.7(6)$ Å^3, $T = 173$ K, $Z = 4$, $D_c = 1.434$ g cm^{-3}, μ(Cu Kα) = 0.975 mm^{-1}, $F(000) = 3088$; 10905 independent reflections, $R_1 = 0.053$, wR$_2$ = 0.129 for 8259 independent observed reflections [$2\theta \leq 124°$, $I > 2\sigma(I)$]. Data for all four compounds were measured on a Siemens P4/RA diffractometer with graphite-monochromated Cu Kα radiation using ω-scans. The structures were solved by direct methods, and non-hydrogen atoms were refined anisotropically using F^2 and the SHELXTL program package, version 5.03. The relatively high values for the residuals, R_1, in **4** and **5** are a consequence of poor crystal quality and severe disorder of the included solvent.