Synthesis and structural characterization of cyclic aryl ethers

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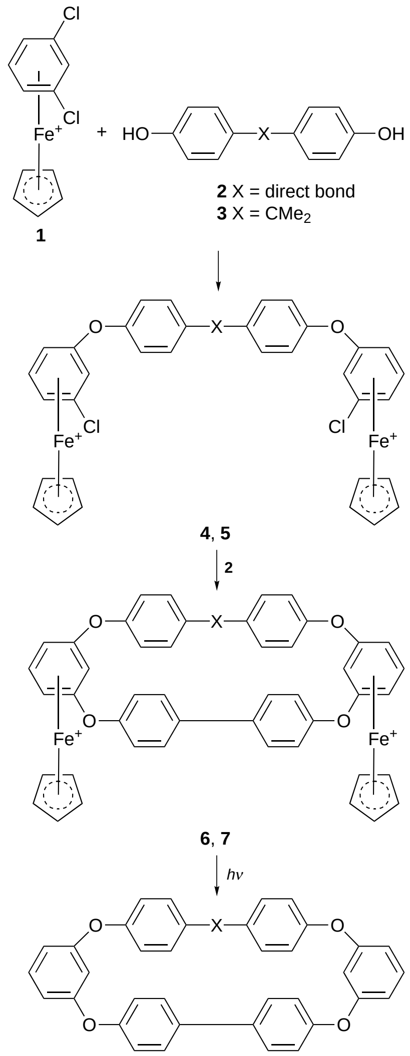
The facile preparation of macrocyclic ethers is achieved using $\mathrm{S_NAr}$ reactions of (dichlorobenzene)CpFe$^+$ complexes with various dinucleophiles, followed by photolytic demetallation; X-ray crystallography gives unequivocal structural proof for one of these macrocycles.

Cyclic polyethers are important synthetic targets owing to their selective complexation and chiral recognition.[1–3] Interest in these materials originates from the size and nature of their cavity, which dictates whether or not such materials are capable of binding with other compounds.[2] Although a great deal of attention has been directed toward the encapsulation abilities of supramolecules, there is a growing interest in the synthesis of cyclic aryl ethers.[3–5] These compounds are appealing since the rigidity and stability of their structures greatly reduces conformational freedom which may allow chiral recognition or catalysis at high temperature or in hostile environments.[4a] Mullins *et al.* reported that cyclic aryl ethers may be subjected to ring-opening polymerization to produce linear polyethers without the release of side-products.[4b] Here, we report the synthesis of four new cyclic aryl ethers, and the crystal structure of **8** utilizing temporary complexation to the cyclopentadienyliron (CpFe$^+$) moiety.

The molecular design and controlled synthesis of aromatic polyethers with pendant CpFe$^+$ moieties has been a focus of our recent research. The complexation of chloroarenes to the CpFe$^+$ moiety has allowed nucleophilic aromatic substitution ($\mathrm{S_NAr}$) reactions to take place with a large number of dinucleophiles.[6] This methodology has enabled us to prepare a number of oligomeric ethers, thioethers and amines under very mild experimental conditions. Owing to the paucity of existing methods for the preparation of cyclic aryl ethers, we have been exploring new routes for the synthesis of such materials. A drawback of the existing methods is the need for electron withdrawing substitutents on the haloarene ring to promote the substitution reactions.[5] The ease of complexation and decomplexation of the CpFe$^+$ to the arene systems shows the advantages of our methodology. The stepwise displacement of both chloro groups in [(η^6-1,2-dichlorobenzene)(η^5-cyclopentadienyl)]iron(II) hexafluorophosphate **10** or [(η^6-1,3-dichlorobenzene)(η^5-cyclopentadienyl]iron(II)hexafluorophosphate **1** with a variety of dinucleophiles has allowed for the facile preparation of macrocycles **8**, **9**, **17**, and **18**. To our knowledge there are few reports which outline the preparation of macrocyclic materials using $\mathrm{S_NAr}$ reactions of substituted chlorobenzenes activated by temporary complexation to a metal moiety.[7] The preparation of dibenzo crown ethers was achieved *via* the $\mathrm{S_NAr}$ reactions of (*o*-dichlorobenzene)-Cr(CO)$_3$ with diethylene glycol and bis(2-mercaptoethyl) ether.[7a] A disadvantage of this particular synthetic method is the implementation of harsh reaction conditions in order to obtain the desired products in rather modest yields.

Scheme 1 outlines the reaction sequence employed for the preparation of cyclic aryl ethers **8** and **9**. The initial reaction of complex **1** and dinucleophile **2** or **3** in a 2 : 1 molar ratio was carried out in order to obtain the bimetallic complex (**4** or **5**) in high yield. The reaction of **4** or **5** with **2** in an equimolar ratio led to the formation of complexed cyclic aryl ethers **6** and **7** in yields of 86 and 89%, respectively. The rigid nature of these complexed macrocycles introduces both *cis*- and *trans*-orientations of the CpFe$^+$ moieties attached to the arene ring.[8] The presence of two different cyclopentadienyl (Cp) resonances as well as a complex aromatic region in the ^{1}H NMR spectra indicated that there was a mixture of both *cis* and *trans* products present. Based on the integration of the respective Cp resonances, it was determined that for complex **6** the ratio was 3 : 1 while it was 1 : 1 for complex **7**. The major structure was predicted to be *trans* based on previous findings.[8]

Photolytic demetallation was implemented to allow for the recovery of the free organic macrocycles **8** or **9** in yields of 64 and 58%, respectively, which may be attributed to the poor solubility of these macrocyclic materials in most organic



Scheme 1

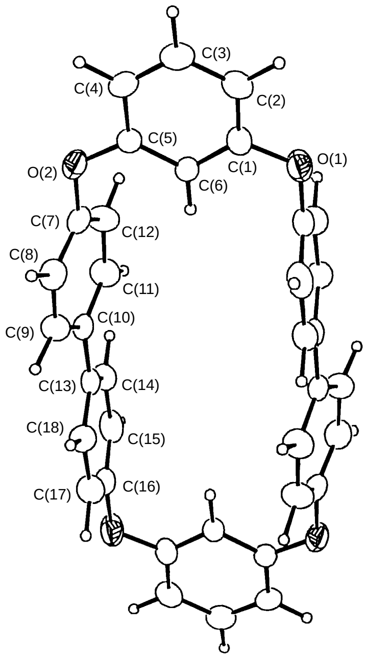


Fig. 1 ORTEP plot of cyclic aryl ether **8**. Selected bond lengths (Å) and angles (°): O(2)–C(5) 1.384(10), O(2)–C(7) 1.416(9), O(1)–C(1) 1.396(9), O(1)–C(16) 1.417(10), C(10)–C(13) 1.504(11); C(5)–O(1)–C(7) 117.7(5), C(1)–O(1)–C(16) 118.0(6), C(10)–C(13)–C(14) 121.0(7), C(10)–C(13)–C(18) 120.3(7).

solvents. The ^{1}H NMR spectra indicated the symmetric nature of these materials. It was noted that a triplet was present at a rather high field chemical shift of δ 5.6 (**8**) or 6.2 (**9**) which was attributed to the inner-ring protons of the benzene ring. This shift is explained by the large diamagnetic shielding caused by the two adjacent biphenyl rings on the inner-ring protons. Our observation is in accordance with similar cyclic aryl ether NMR shifts.[5] Unequivocal proof of the structure of **8** was obtained by an X-ray crystallographic study.† Single crystals suitable for X-ray analysis were obtained by slow evaporation of a chloroform solution of the cyclic aryl ether at room temp. Fig. 1 illustrates the rigidity imparted in the structure by the biphenyl and benzene rings, respectively. The biphenyl groups of the macrocycle are separated by 5.2 Å while the diagonal distance of oxygen atoms was found to be 10.9 Å.

Scheme 2 illustrates that an analogous sequence of reactions may be employed with the (*o*-dichlorobenzene)CpFe$^+$ complex (**10**) and dinucleophiles containing both aliphatic and aromatic bridges. In this fashion, macrocyclic compounds **17** and **18** with both oxygen and sulfur bridges were prepared. Once again NMR spectroscopy and elemental analyses were used to confirm the structure of all new materials. Unlike the rigid macrocycles prepared in Scheme 1, these structures have no inner ring protons and as a result no high field chemical shifts were observed.

This is the first example of iron cyclopentadienyl mediated cyclic aryl ether synthesis. The presented methodology will enable us to prepare a variety of these cyclic compounds under mild experimental conditions and in very high yields. An additional benefit of this process is the ability to isolate the intermediate bimetallic complex prior to ring closure. It has been demonstrated that it is possible to prepare both symmetric and asymmetric cyclic aryl ethers depending on the nucleophile used to close the macrocycle. Further investigations aimed at increasing the cavity size and varying the nature of the substituents are in progress and will be reported in due course.

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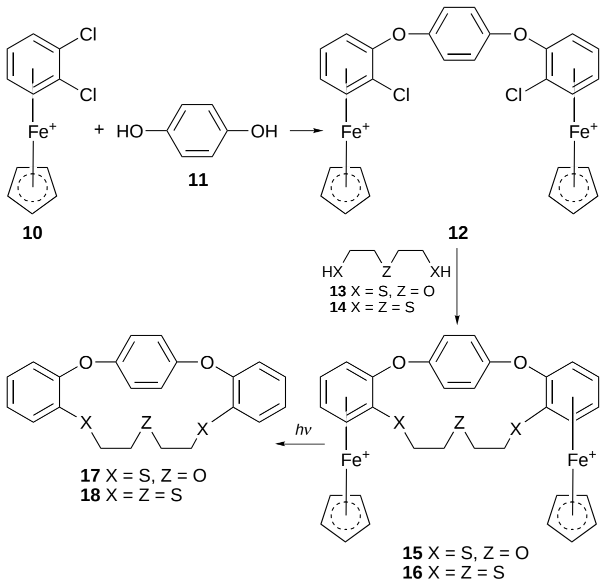

Scheme 2

Footnotes and References

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† *Crystal data* for **8**. Colourless crystals from $CHCl_3$, crystal dimensions 0.40 × 0.20 × 0.20 mm, monoclinic, space group $P2_1/c$, a = 6.0546(16), b = 16.093(2), c = 13.514(4) Å, V = 1314.7(6) Å^3, Z = 4, μ = 0.07 mm^{-1}, 1814 reflections measured, 1736 unique, R = 0.058, R_w = 0.050. CCDC 182/696.

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