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Rotaxanes with Fluorocarbon Blocking Groups

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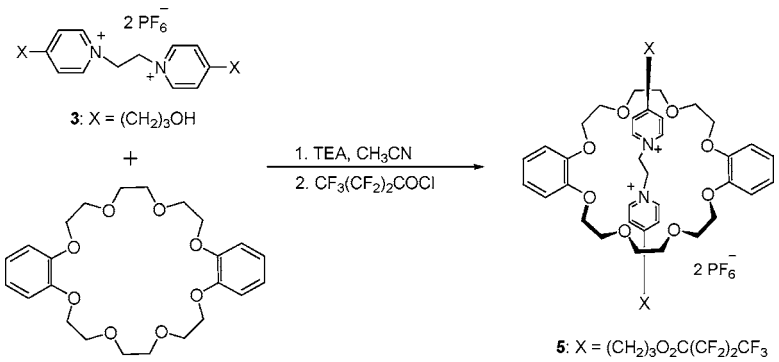
ABSTRACT



A novel [2]-rotaxane has been prepared in which perfluoropropyl stoppers have been utilized as electronic blocking groups. To further investigate this capability, a linear compound that was precapped with perfluoropropyl groups was also prepared. This compound did not demonstrate rotaxane formation when mixed with dibenzo-24-crown-8, providing further evidence that the perfluoropropyl groups were effective electronic stoppers for the macrocycle.

Since the initial experimental reports of rotaxanes nearly 40 years ago,[1] a number of methods utilizing a wide variety of cyclic and linear species have been used for their preparation.[2] A theme common to all of these syntheses is the placement of large blocking groups at the ends of the linear component to trap the cyclic species and prevent dissociation from occurring. For rotaxanes that employ dibenzo-24-crown-8 (DB24C8) as the cyclic component, bulky groups such as trityl, bis(cyclohexyl)methyl, and 4-*tert*-butylphenyl have all been employed as stoppers[2], although the effectiveness of the latter has recently been called into question.[3] As the field has evolved, a number of creative methods have been developed to introduce stoppers that possess unique functionality yet also prevent the loss of the DB24C8 macrocycle.[4] Like earlier rotaxane syntheses, these methods still utilize groups that are too large to pass through the cavity of DB24C8 and maintain the rotaxane structure via steric effects. The use of groups that would prevent dethreading by means of electronic interactions, meanwhile, has remained largely unexplored. Harada has employed this idea in a

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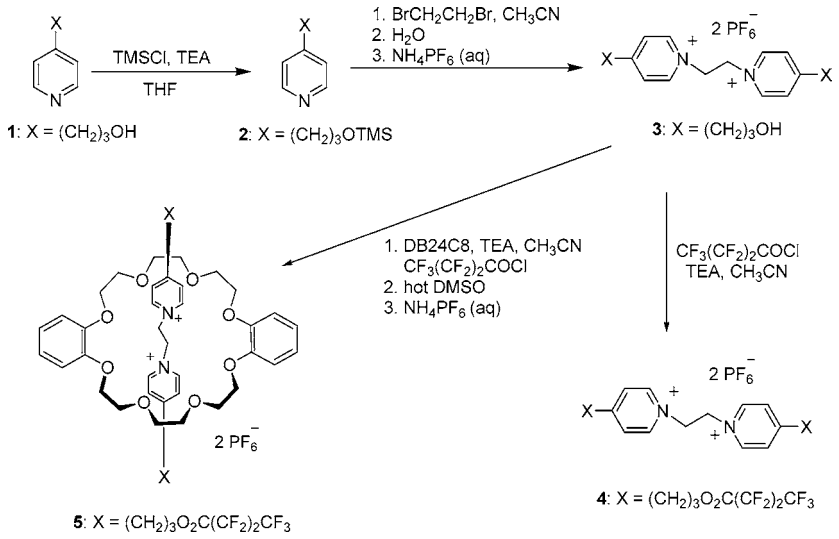
Scheme 1



cyclodextrin-based rotaxane,[5] but there are currently no examples of rotaxanes that use an electronic blocking group to trap DB24C8. Here, we report that a fluorocarbon stopper, specifically the perfluoropropyl ($CF_3CF_2CF_2-$) group, is able to act as a blocking group for DB24C8, resulting in a novel rotaxane that contains fluorocarbon moieties.

Fluorocarbons are well-known for their low surface energies and resistance to heat and oxidation.[6] Despite this, there are very few instances of rotaxanes that include fluorine atoms or fluorocarbon groups in either the cyclic or linear component. In devising a rotaxane-based molecular machine, Leigh included a short fluorocarbon segment in the linear component to introduce some hydrophobic character, but the cyclic component was an amide-functionalized macrocycle and not DB24C8.[7] Stoddart has also prepared linear components containing fluorine, but these were generally single fluorine atoms used for labeling purposes.[8]

While seeking to incorporate fluorocarbon segments into the linear species and prepare rotaxanes that might possess some of the their unique properties, we concluded that the fluorocarbon chains may also have the ability to act as a stopper for the cyclic component. The strongly electronegative fluorine atoms are high in electron density, and although they do not possess sufficient bulk to trap the macrocycle, they will not allow the electron-rich oxygen atoms of DB24C8 to pass over, thus preventing dissociation of the complex.

A derivative of a bis(pyridinium) ethane (BPE) axle, originally shown to complex with DB24C8 by Loeb,[9] was used as the linear component in this study. The hydroxy-functionalized BPE derivative **3**-2PF_6 was readily synthesized (Scheme 1) from commercially available 3(4-pyridine)-1-propanol **1**. Coupling of the TMS-protected derivative **2** to dibromoethane followed by counterion exchange (NH_4PF_6/H_2O) produced linear component **3**-2PF_6 in 29% overall yield. This linear precursor was then mixed with DB24C8 in acetonitrile to form the expected pseudorotaxane. Esterification of the terminal alcohol groups of the linear species using heptafluorobutyryl chloride attached perfluoropropyl stoppers that were of sufficient length to achieve the electronic blocking effect yet still maintain solubility for the rotaxane.[10] The product from this reaction was then dissolved in hot DMSO, a solvent known to disrupt pseudorotaxane formation, and reprecipitated from an aqueous solution of ammonium hexafluorophosphate to produce [2]-rotaxane **5**-2PF_6 in 16% overall yield. Because the uncomplexed linear compound was not observed after this process, this indicated that the perfluoropropyl groups were indeed acting as stoppers for the macrocycle.

Although the overall rotaxane yield was low, it can be improved through modifications to the linear compound that should result in a larger equilibrium constant for the pseudorotaxane precursor. Although the hydroxypropyl group of **1** increases the nucleophilicity of the pyridine nitrogen atom and leads to an improved yield during the synthesis of linear species **3**, it has a more detrimental effect on pseudorotaxane formation because the electron-donating capacity of the hydroxypropyl group decreases the electrophilicity of the protonated nitrogens and leads to a lower equilibrium constant for complexation. As a result, a significant amount (21%) of unthreaded linear compound **4**-2PF_6 was isolated as well. This was not an unexpected

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(10) Initial attempts to introduce stoppers using perfluorooctanoyl chloride had also been successful, but the resulting rotaxane had poor solubility. The uncomplexed linear species was also very limited in solubility when capped with fluorocarbon chains of this length.

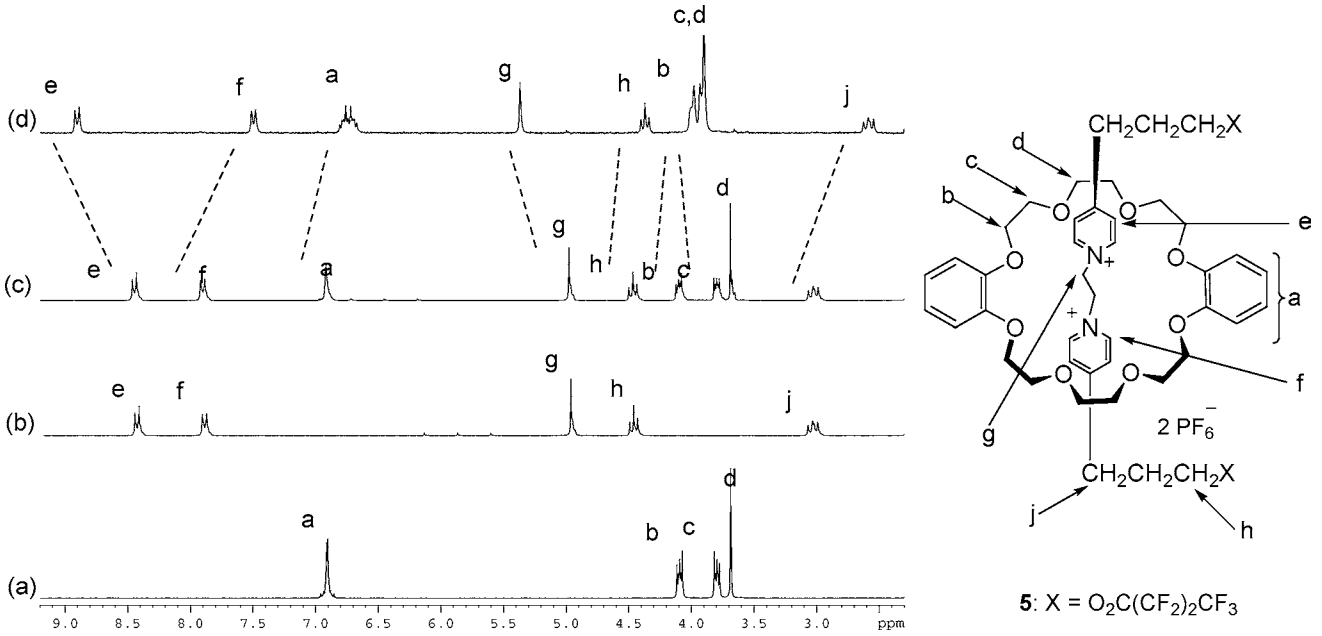

Figure 1. Partial ^{1}H NMR (200 MHz, CD_3CN) of (a) DB24C8, (b) **4**-2PF_6, (c) an equimolar mixture of **4**-2PF_6 and DB24C8 (0.01 M), and (d) [2]-rotaxane **5**-2PF_6.

result because Loeb had previously demonstrated that the presence of electron-donating groups on the BPE axle are less effective for complexation with DB24C8 whereas electron-withdrawing groups attached to the pyridine ring led to higher equilibrium constants for the pseudorotaxane.[9] The presence of an electron-withdrawing group directly on the pyridine ring, which could then ultimately be linked to a terminal hydroxy or amino group, would help to ensure that the formation of the pseudorotaxane would be maximized and lead to increased yields of the rotaxane.

Characterization by ^{1}H NMR spectroscopy and mass spectrometry confirmed that **5**-2PF_6 was a [2]-rotaxane. Even after treatment with hot DMSO, the ^{1}H NMR spectrum of **5**-2PF_6 in CD_3CN (Figure 1) was significantly different from the spectra for the individual cyclic (DB24C8) and linear (**4**-2PF_6) components. As expected for complexation, the β protons (e) of the pyridine rings and the methylene protons (g) of the ethane linkage between the two rings both experienced significant downfield shifts of 0.47 and 0.40 ppm, respectively, and the α protons (f) of the pyridine ring (0.41 ppm) and the aromatic protons (a) of DB24C8 (0.16 ppm) were shifted upfield. A significant upfield shift was also observed for the methylene protons (j) attached directly to the pyridine rings (0.44 ppm), whereas the methylene groups α to the terminal ester functionalities (h) also experienced a mild upfield shift of 0.10 ppm. Finally, the methylene groups of the crown ether experienced the upfield (b) or downfield (c,d) shifts of approximately 0.10−0.20 ppm that are typically observed during rotaxane formation.

Additionally, the fast-atom-bombardment (FAB) mass spectrum of **5**-2PF_6 gave a base peak at *m*/*z* 1287.1 for the rotaxane after the loss of a PF_6^- counterion. This corroborated the ^{1}H NMR results showing that the rotaxane was intact after reprecipitation from DMSO. Thus, the perfluoropropyl groups were acting as stoppers and preventing the dethreading of the cyclic component.

To fully demonstrate that the perfluoropropyl groups were acting as electronic blocking groups for DB24C8, characterization of a mixture of DB24C8 and the precapped linear speices **4**-2PF_6 was also performed. To obtain the desired linear compound, the esterification of **3**-2PF_6 (Scheme 1) with heptafluorobutyryl chloride was done in the absence of DB24C8. Counterion exchange (NH_4PF_6/H_2O) for the resulting product afforded **4**-2PF_6 in 57% yield.

In stark contrast to the spectrum for the rotaxane **5**-2PF_6, when equimolar amounts of **4**-2PF_6 and DB24C8 (0.01 M) were dissolved in CD_3CN, no changes (Figure 1) were observed relative to the individual ^{1}H NMR spectra of these species. Although the perfluoropropyl stoppers had prevented the loss of DB24C8 when introduced after pseudorotaxane formation, this result demonstrated that they also prohibit formation of the rotaxane if they are present prior to the addition of DB24C8.

This result was further reinforced by the observation that the ^{1}H NMR spectrum for an equimolar mixture of **3**-2PF_6 and DB24C8 in CD_3CN showed evidence of pseudorotaxane formation, producing chemical shift changes similar to those seen in the spectrum for **5**-2PF_6. Because the linear compound that was the precursor to **4**-2PF_6 was able to form a pseudorotaxane, it can be concluded that the presence of the perfluoropropyl stoppers was the factor that prevented the formation of the complex.

Likewise, FAB−mass spectrometry of an equimolar mixture of **4**-2PF_6 and DB24C8 did not show a molecular ion peak at the *m*/*z* of the complex and only the peaks for the individual components were significant. Again, the

mixture of **3**-2PF_6 and DB24C8 demonstrated signs of pseudorotaxane formation, indicating that the addition of the perfluoropropyl groups was the key to preventing complexation.

In summary, a [2]-rotaxane was prepared from DB24C8 and a bis(pyridinium) ethane linear compound capped with perfluoropropyl stoppers. Evidence of the rotaxane was seen through ^{1}H NMR spectroscopy and mass spectrometry even after reprecipitation of the product from hot DMSO. When perfluoropropyl stoppers were attached prior to the addition of DB24C8, however, no complexation was observed. These results demonstrate that the perfluoropropyl group is an effective blocking group for dibenzo-24-crown-8 due to an electronic effect in which the electron-rich crown ether is repelled by the highly electronegative fluorine atoms of the stoppers. These findings expand the repertoire of blocking groups possible for DB24C8 and allow for the creation of novel rotaxanes that may exhibit some of the unique properties of fluorocarbon materials. The concept of fluorocarbons as electronic blocking groups should also be applicable to polyrotaxanes, and work in this area has been initiated.

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Supporting Information Available: Experimental procedures and spectroscopic data for compounds **2**, **3**-2PF_6, **4**-2PF_6, and **5**-2PF_6; ^{1}H NMR spectra for **3**-2PF_6/DB24C8 and **4**-2PF_6/DB24C8; and mass spectrometry data for **3**-2PF_6, **4**-2PF_6, **5**-2PF_6, **3**-2PF_6/DB24C8, and **4**-2PF_6/DB24C8. This material is available free of charge via the Internet at http://pubs.acs.org.

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