Synthesis of the First Perfluoro-spiro-bis-crown Ethers

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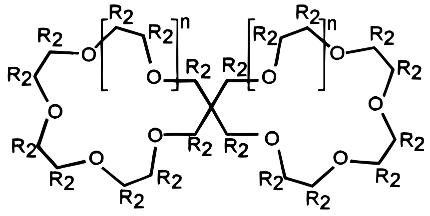
Introduction

Since the first perfluoro crown ethers were prepared by members of our research group,[1] many new perfluoro crown ethers have been synthesized,[2] and medical applications such as ^{19}F NMR imaging[3] and oxygen carrier applications[2b] as well as new chemistry[4] associated with these compounds are currently under study. Perfluoro crown ethers do not form extremely stable complexes with metal cations because the basicities of perfluoro crown ethers decrease as the amount of fluorine substitution increases.[5] On the contrary, perfluoro crown ethers form complexes with certain anions in the gas phase.[4] In order to explore the chemistry of theses new compounds, the preparation of new perfluoro crown ethers, such as multilooped perfluoro crown ethers, is very important. We report in this paper the syntheses of the first perfluoro-spiro-bis-crown ethers,[6] perfluoro-spiro-bis[19]crown-6 (**1**), perfluoro-spiro-bis[16]crown-5 (**2**), and perfluoro-spiro-bis[13]crown-4 (**3**), by elemental fluorine.



1: n=2, R=F **4**: n=2, R=H
2: n=1, R=F **5**: n=1, R=H
3: n=0, R=F **6**: n=0, R=H

Results and Discussion

The major side products of direct fluorination in the experiments are ring-opening and partially fluorinated compounds. The yields of **1**−**3** are low because of the steric hindrance between the eight fluorine atoms that are located next to the spiro carbon.

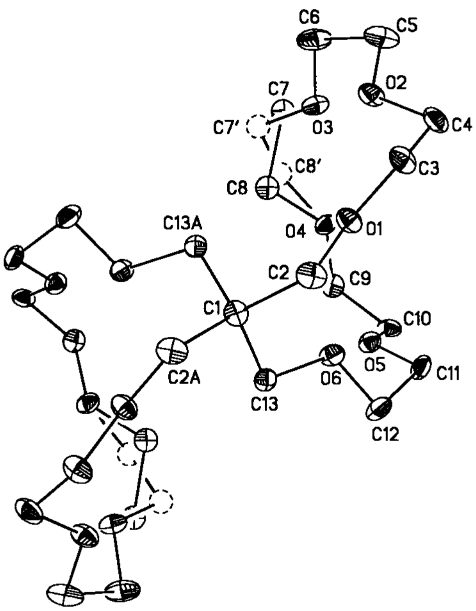


Figure 1. X-ray crystal structure of **1** (all fluorine atoms are omitted for clarity).

The ^{19}F NMR spectra of **1**−**3** exhibit distinct signals at two regions. One shows a singlet at approximately −66 ppm, which corresponds to the resonances of the eight fluorine atoms that are located next to the spiro carbon; the other one shows a singlet or a multisinglet at approximately −89 ppm, which corresponds to the resonances of fluorine atoms of the $-OCF_2CF_2O-$ units.

A crystal of **1** suitable for single-crystal structural determination was obtained by recrystallization from $CDCl_3/CFCl_3$ (1/1). The structure was solved by direct methods and refined on F^2 with anisotropic displacement parameters for all atoms. The molecule lies on a crystallographic 2-fold rotation axis that passes through the spiro carbon, C1. One of the ethylene groups was found to be disordered about two orientations representing two different conformations for that group. Final $R = 0.0451$, $R_w(F^2) = 0.1011$ for 2215 unique reflections. Experimental details, position parameters, and structural data including bond lengths and angles for **1** are available.[7] A graphical representation of **1** is given in Figure 1. The crystal structure of $\mathbf{4}\cdot 2LiI\cdot 4H_2O$ has been reported.[8] The hydrocarbon spiro crown ether (**4**) is coordinated by two Li^+ ions and four water molecules. Such coordinating species will distort the geometry of the parent hydrocarbon spiro crown ether. Figures 2 and 3 show this clearly to be the case.

The syntheses of the new types of perfluoro macrocyclic ethers, double-looped perfluoro crown ethers, is a new frontier for further studies of host−guest chemistry in the gas phase. Perfluro-spiro-bis-crown ethers **1**−**3** are currently being investigated to determine their binding abilities for oxygen and other molecules.

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[7] The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.

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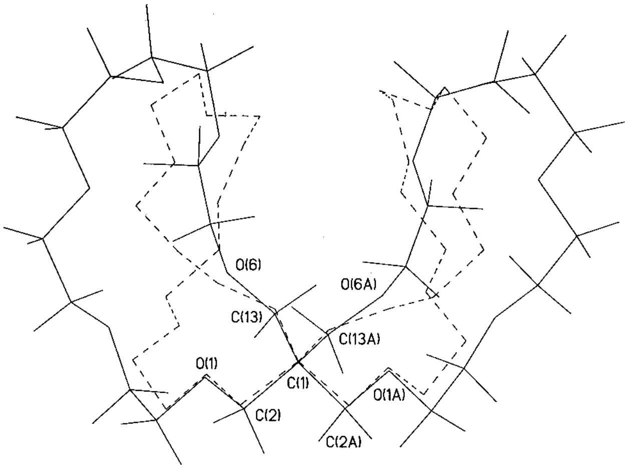

Figure 2. Superposition of **1** onto the equivalent atoms of the hydrocarbon. The atoms used in the fit are labeled. The dashed lines show the atoms of **1**. It is obvious that there are large conformational differences between the two molecules.

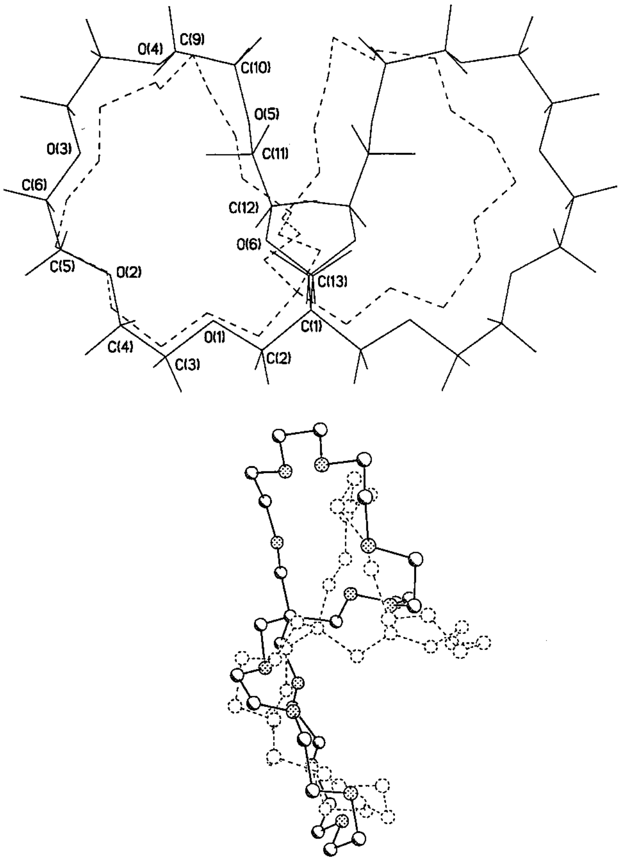

Figure 3. Superposition of **1** onto the equivalent atoms of the hydrocarbon. In this figure, the atoms of one half of the spiro compound are used in the comparison (less the disordered atoms in **1**). The dashed lines show the atoms of **1**.

Experimental Section

General Methods. Perfluorinated products were purified by preparative GC equipped with a 815Z column,[9] 10 ft × 0.25 in. 25% 815Z on chromosorb A 60/80. Helium flow rate was 45 mL/min, and column temperature was 200 °C. The purity of the perfluorinated products was monitored on a 815Z column. ^{19}F NMR were recorded at 282 MHz using $CDCl_3$ as the lock solvent and $CFCl_3$ as the internal standard ($CDCl_3/CFCl_3 = 1/1$). Chemical shifts are given in ppm with negative values indicating resonances at higher frequencies. Elemental compositions were studied by high-resolution mass spectroscopy employing chemical ionization in the positive mode.

Table 1. Direct Fluorination Conditions for 1−3

stage	He (mL/min)	F$_2$ (mL/min)	*T* (°C)	time (h)
1	400	0	−20	0.5
2	400	100	−20	6
3	10	10	0	12
4	10	10	ambient (~36)	24
5	0	10	ambient (~36)	24
6	0	10	ambient (~36)	24

Synthesis of 4−6. Hydrocarbon starting materials for direct fluorination were prepared by modification of the previous work.[10] In a typical reaction, pentaerythritol (6.1 g, 0.045 mol) and potassium metal (8 g, 0.2 mol) were dissolved in 1 L of *tert*-butyl alcohol, and then the solution was heated under argon atmosphere at reflux for 2 h. Pentaethylene glycol ditosylate (50 g, 0.09 mol) in 500 mL of dry dioxane was then added dropwise to the above solution over 8 h, and then the resultant mixture was stirred at reflux for 24 h. Workup and column chromatography using silica gel with dichloromethane/methanol (20/1) eluent gave **4** in 18% yield. Compounds **5** and **6** were prepared in the same manner by using sodium and lithium metal with tetraethylene glycol ditosylate and triethylene glycol ditosylate in 20 and 17% yields, respectively. The MS and ^{1}H NMR spectra of **4**−**6** were in agreement with published data.[11]

Direct Fluorination. The direct fluorination reactions were performed in a manner similar to the reactions that we have described previously.[12] Reaction details are summarized in Table 1. In a typical reaction, compound **4** (4.5 g) was dissolved in 1,1,2-trichlorotrifluoroethane (300 mL); subsequently, the solution was slowly introduced into a stainless steel reactor that contained 1,1,2-trichlorotrifluoroethane (600 mL), excess sodium fluoride, and a fluorine−helium mixture (stage 2; Table 1). During the next 84 h both the relative fluorine concentration and the reaction temperature were slowly raised.

Perfluoro-spiro-bis[19]crown-6 (1). Pure product (>99% purity) was collected by preparative GC as white solid in 19% yield. The retention time was 148.4 min: MS *m/z* (identification, intensity) 1385 ((M − F)$^+$, 100); HRMS calcd for $C_{25}F_{47}O_{12}$ (M − F)$^+$ 1384.8639; found 1384.8626; ^{19}F NMR δ −66.93 (s, 8F), −89.49 (s, 40F).

Pefluoro-spiro-bis[16]crown-5 (2). Pure product (>99% purity) was obtained as a colorless oil in 16% yield. The retention time was 66.2 min: MS *m/z* (identification, intensity) 1153 ((M − F)$^+$, 100); HRMS calcd for $C_{21}F_{39}O_{10}$ (M − F)$^+$ 1152.8869, found 1152.8881; ^{19}F NMR δ −66.47 (s, 8F), −89.59 (s, 16F), −89.94 (s, 8F), −90.10 (s, 8F).

Perfluoro-spiro-bis[13]crown-4 (3). Pure product (>98% purity) was obtained as colorless oil in 13% yield. The retention time was 30.8 min: MS *m/z* (identification, intensity) 921 ((M − F)$^+$, 100); HRMS calcd for $C_{17}F_{31}O_8$ (M − F)$^+$ 920.9098, found 920.9096; ^{19}F NMR δ −66.66 (s, 8F), −89.38 (s, 16F), −89.64 (s, 8F).

Acknowledgment. We are grateful for substantial support from the U.S. Department of Energy Division of Advanced Energy Projects (DE-FG05-91ER12119) and the Office of Naval Research.

Supporting Information Available: ^{19}F NMR spectra (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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