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13. ABSTRACT *(Maximum 200 words)*

As an approach to the preparation of organic molecules with very high thermooxidative stability, a study was carried out on the preparation of perfluorinated aromatic compounds by liquid-phase direct fluorination of aromatic hydrocarbon precursors followed by reductive defluorination. Diphenylether was converted to a perfluoro(dicyclohexylether) intermediate, however reductive defluorination afforded perfluoro(benzofuran) rather than perfluoro(diphenylether). By contrast, biphenyl was converted in high yield to perfluoro(dicyclohexyl) which, upon reductive defluorination afforded perfluoro(diphenyl). Diphenyl ketone was converted to perfluoro(dicyclohexyl) ketone, reductive defluorination of which is under investigation. Similarly, the o-, m-, and p- isomers of diphenoxybenzene were successfully fluorinated to the corresponding perfluoro(dicyclohexanoxylcyclohexanes), the reductive defluorination of which is under investigation.

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Final Technical Report

to

AIR FORCE OFFICE OF SCIENTIFIC RESEARCH

Washington, DC 20332

ELEMENTAL FLUORINE BASED SYNTHESES OF PENTAFLUORO PHENYL AND OTHER AROMATIC PERFLUOROPOLYETHER POLYMERS

Grant Number F49620-92-J-0104

February 1, 1994 - January 31, 1995

Presented by

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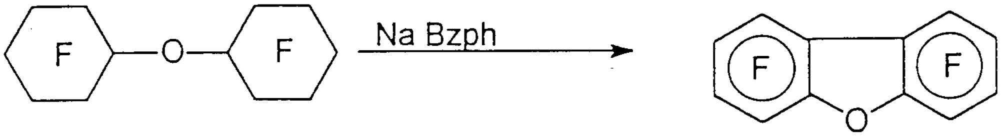
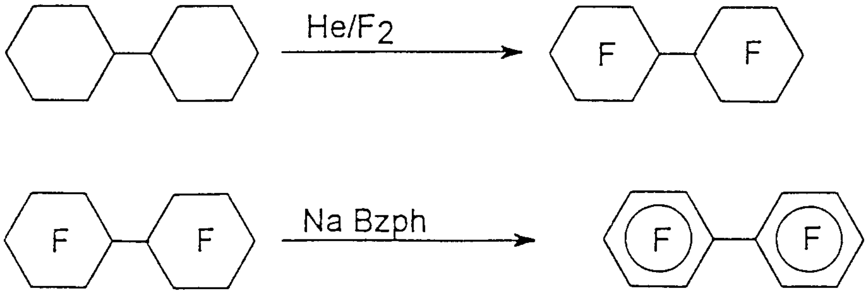
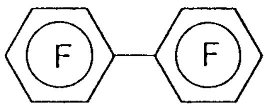
In last annual technical report, reductive defluorination of perfluoro(dicyclohexylether) was carried out with sodium benzophenone and the two perfluoro(cyclohexyl) groups were interestingly fused to form perfluoro(bezofuran). What about other perfluoro(dicyclohexyl) compounds ? Will they form fused products or other interesting compounds after the reductive defluorination ?

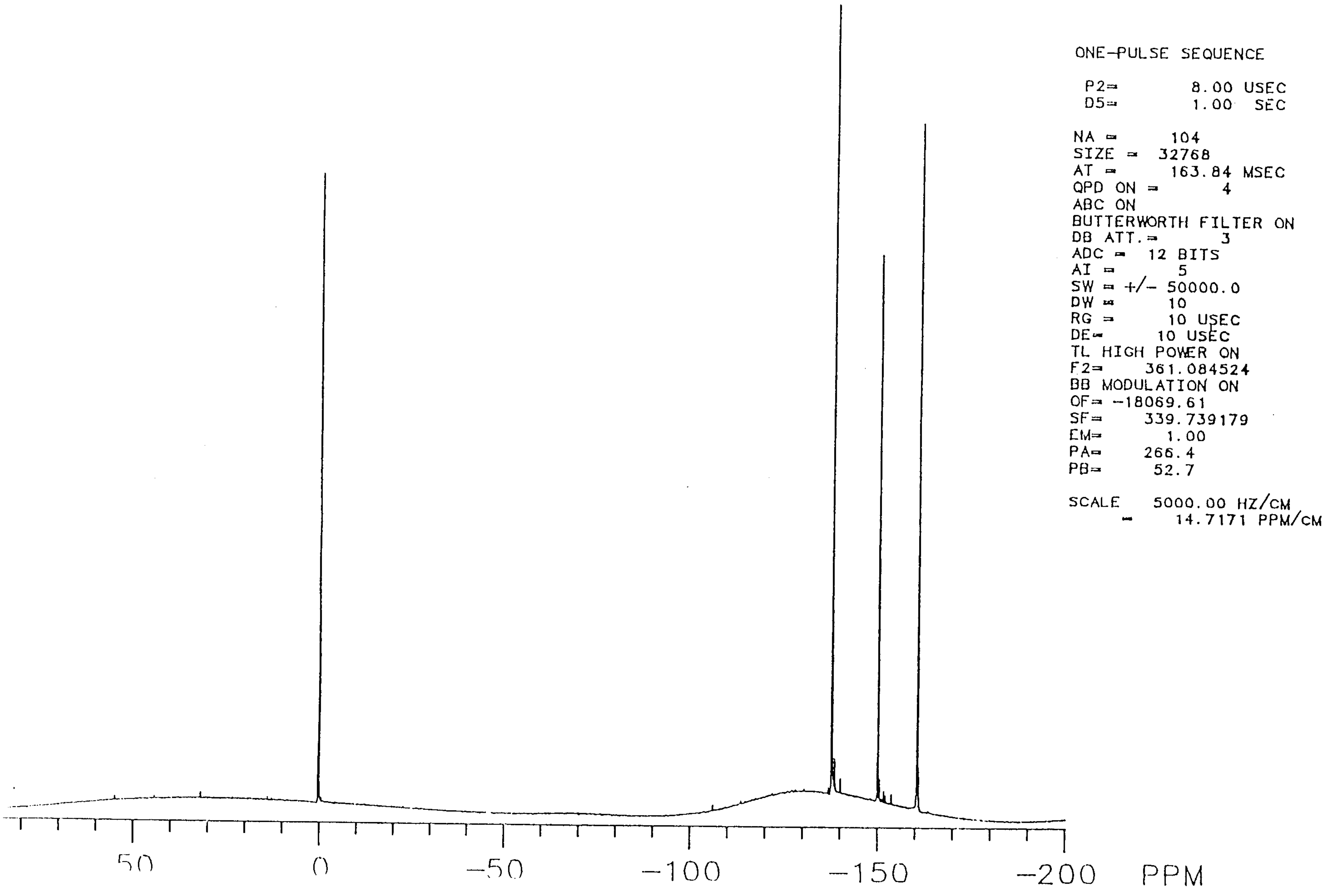


Perfluoro(dicyclohexyl) was prepared in 91% yield by liquid-phase direct fluorination of dicyclohexyl. Reductive defluorination of the perfluorinated compound produced a nonfused product, perfluoro(diphenyl), other than a fused product.



,311 . 002 MJB 06MAY94
!NG, CFCL3, CDCL3, F19





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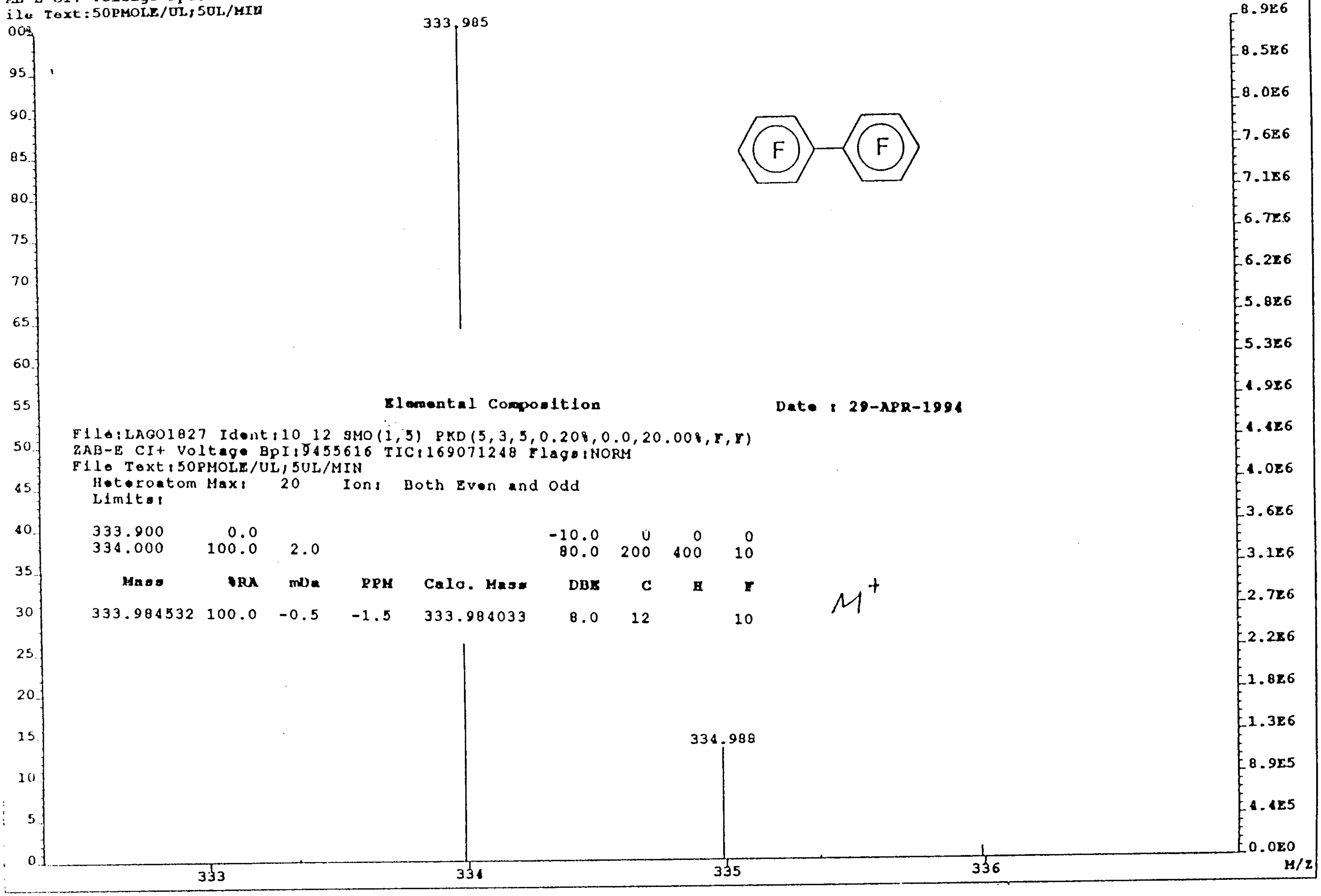

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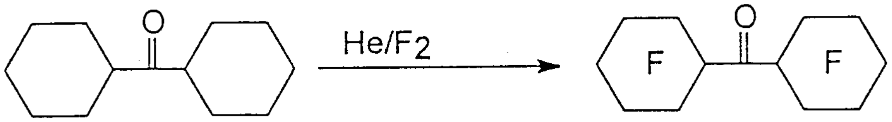
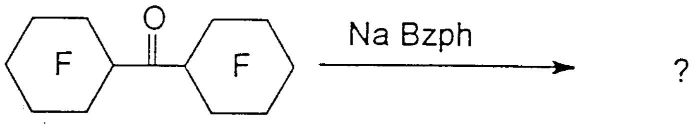
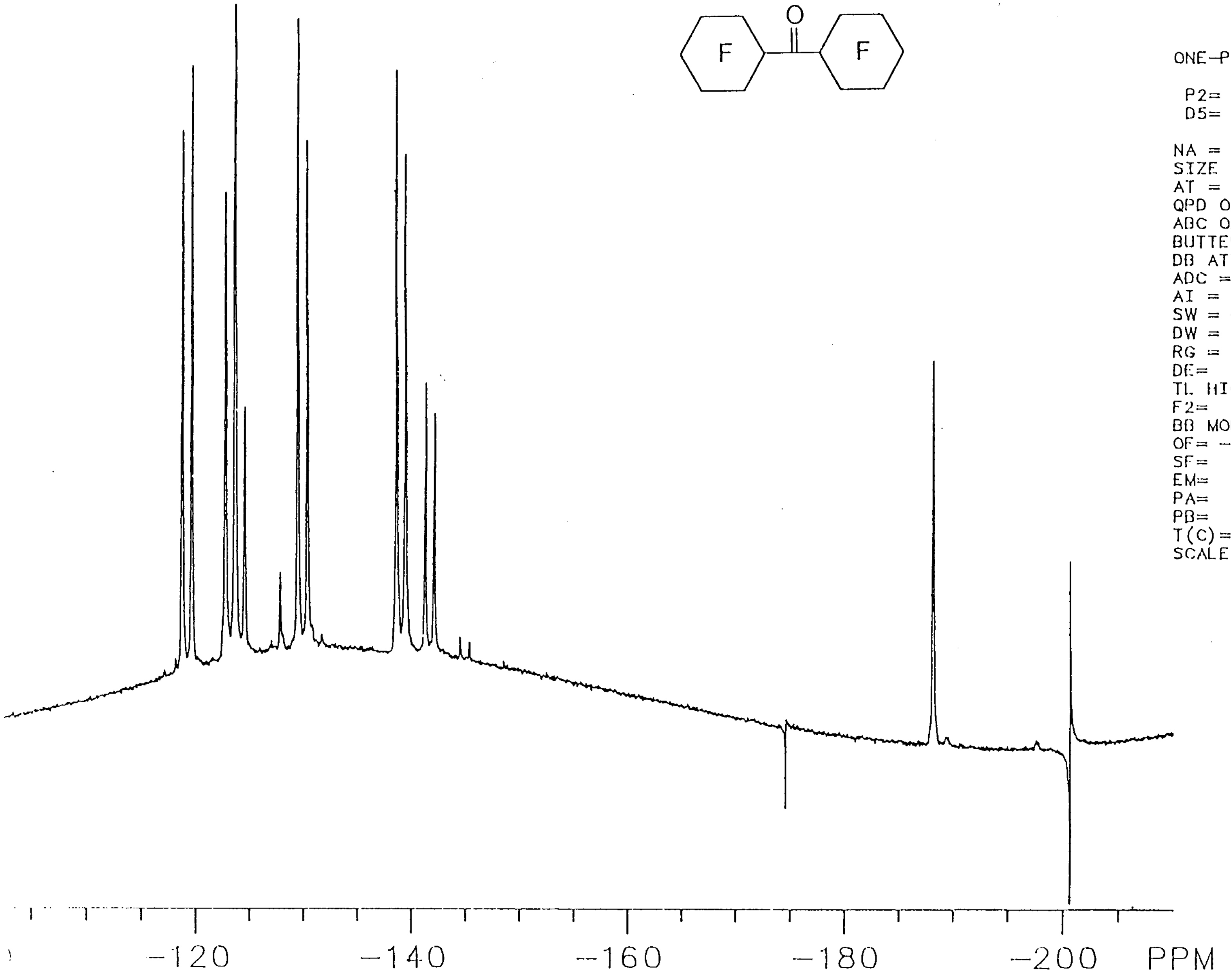
Perfluoro(dicyclohexyl) ketone was prepared in 82% yield by liquid-phase direct fluorination of dicyclohexyl ketone. Reductive defluorination of the perfluorinated ketone is under investigation.





111 . 002 MJB 13MAY94
ING, CFCL3, CDCL3, F19, 20C



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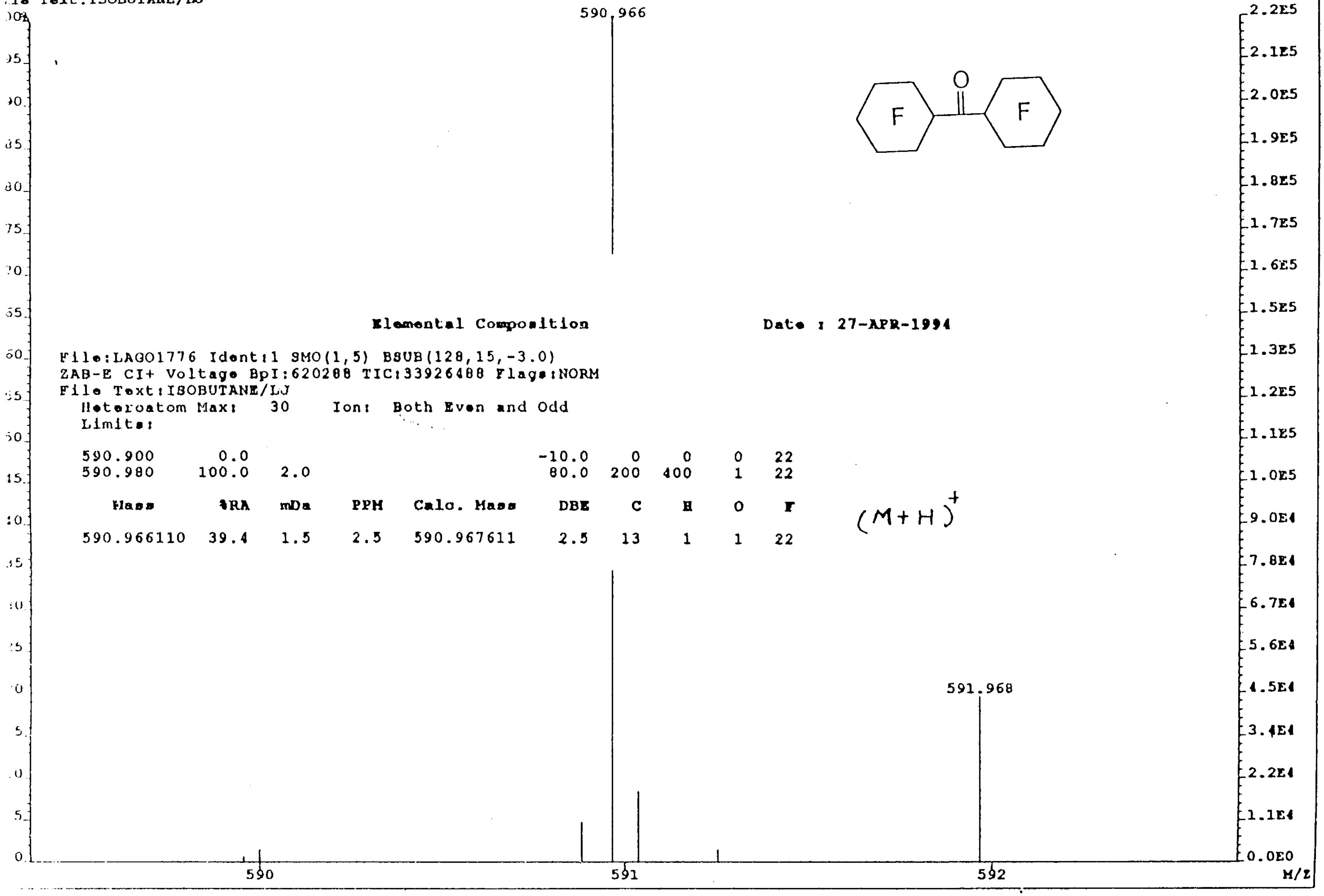

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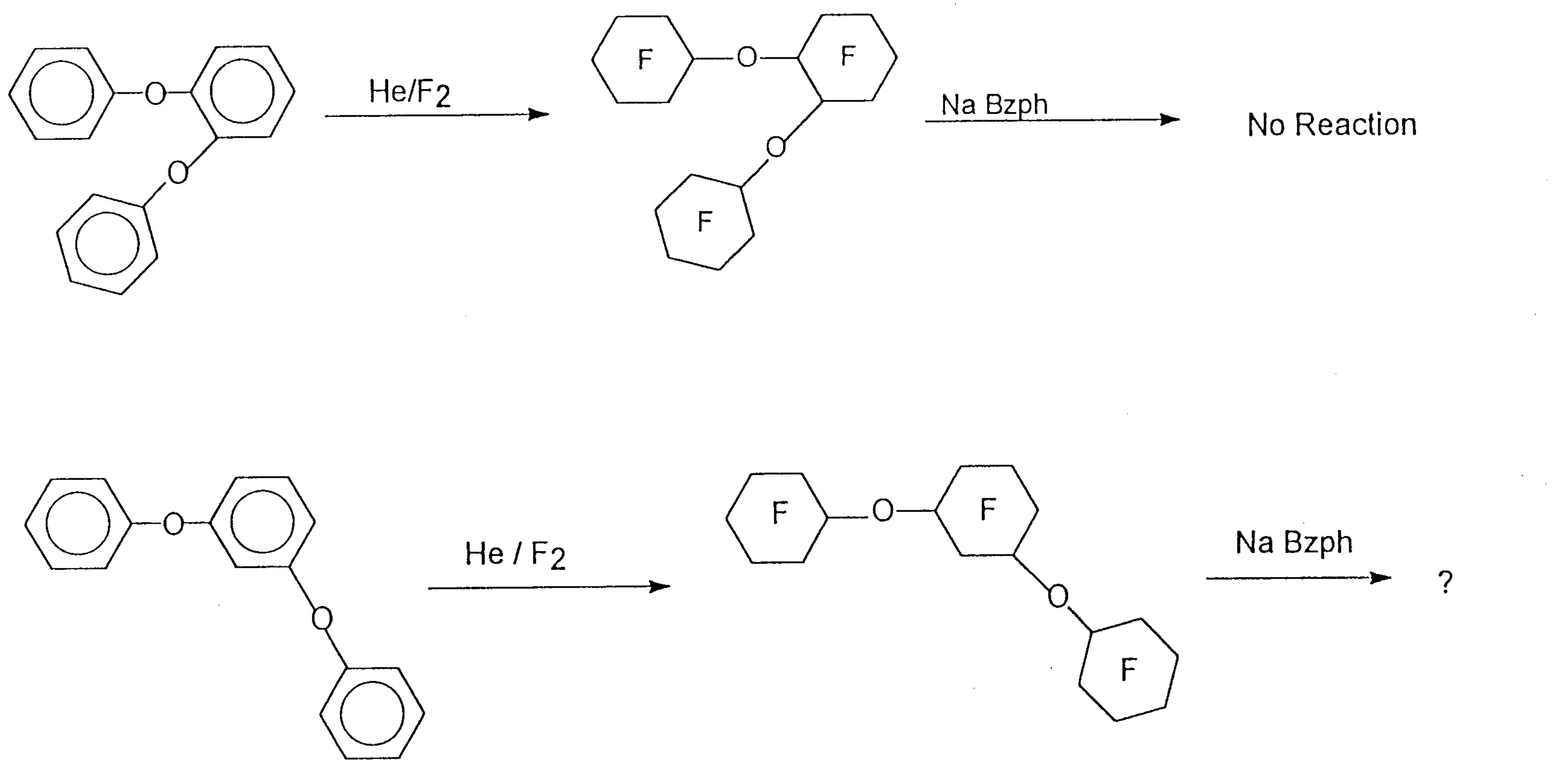
```

(M+H)+

Since we successfully obtained a fused perfluoro(benzofuran) from perfluoro(dicyclohexyl ether), reductive defluorination of the perfluorinated ethers containing three perfluoro(cyclohexyl) groups would be interesting. The three isomers of o-, m-, and p-perfluoro(dicyclohexanoxyl cyclohexane) were prepared by liquid-phase direct fluorination of o-, m-, and p- diphenoxyl benzene. After several run of liquid-phase direct fluorination, enough amount of o-perfluoro(dicyclohexanoxyl cyclohexane) was collected to carry out the following reductive defluorination. The reductive defluorination was carried out from -70 to 70 °C for 2 days, but the ortho-ether, however, kept unreacted. One of the reasons for that is perhaps steric hindrance. Reductive defluorination of the meta- and para- ethers are under investigation.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O
F
O
F
Na Bzph
No Reaction
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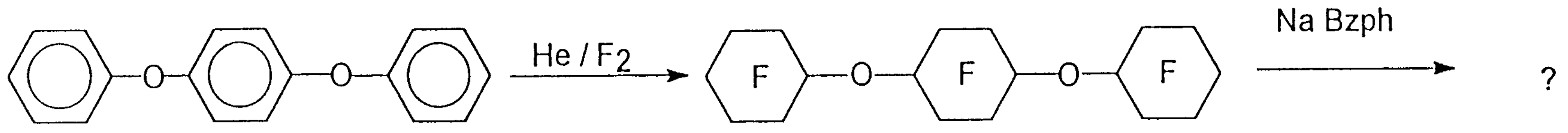
O
F
O
F
Na Bzph
?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Na Bzph
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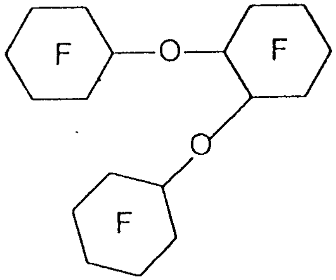
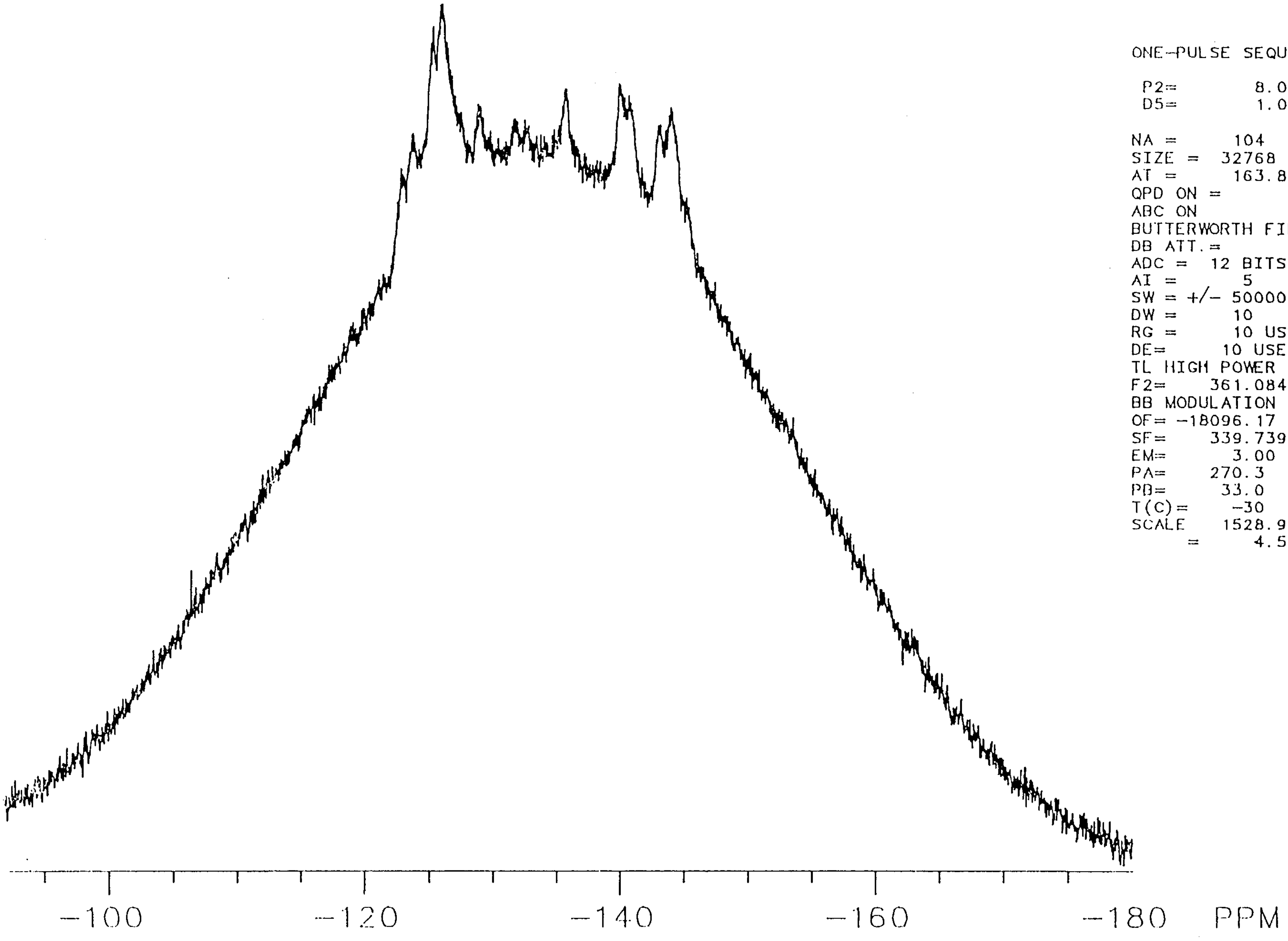
S222 004 MJB 11MAR94
UNG, CDCL3, CFCL3, F19, -30





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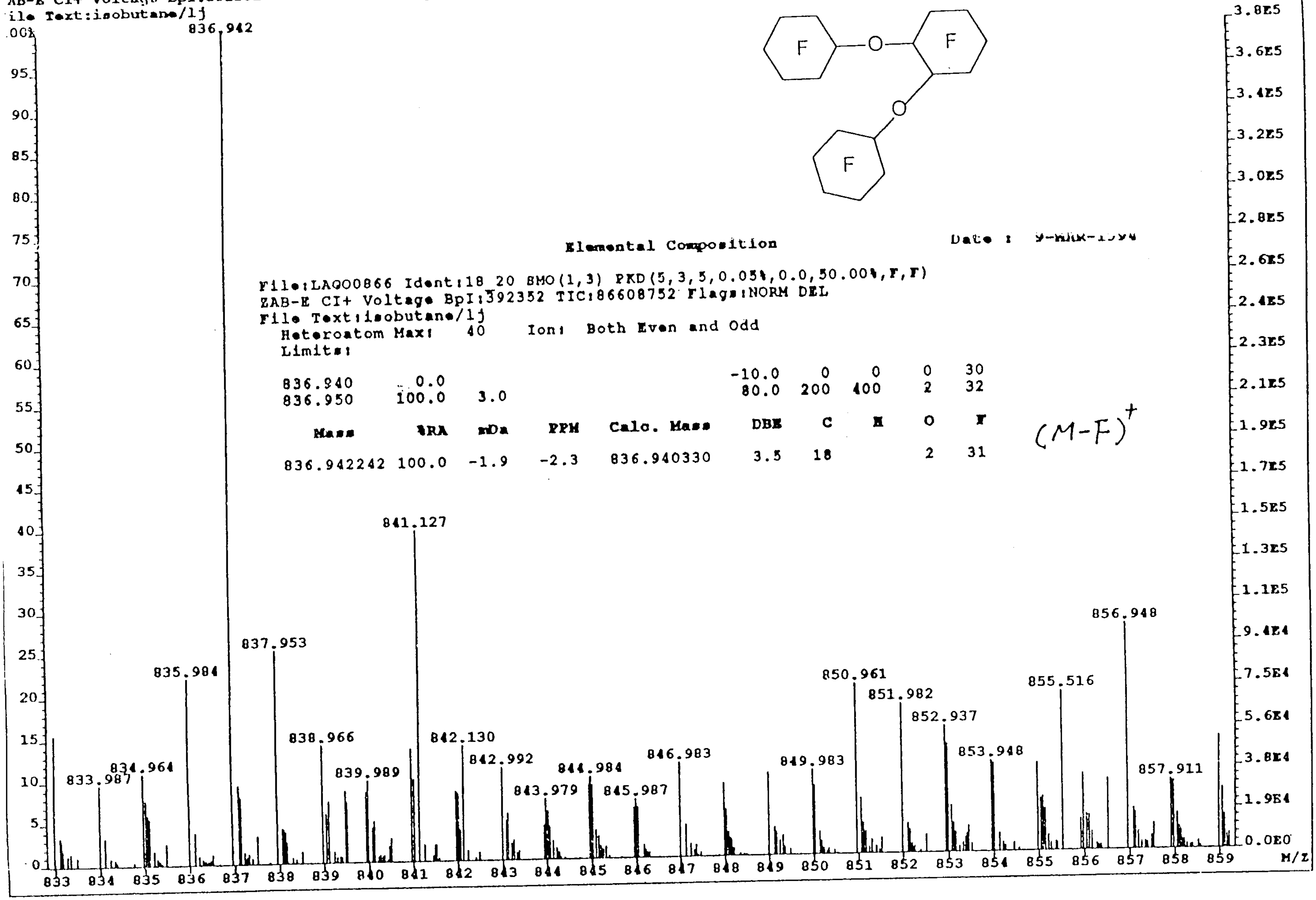

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  836.950     100.0    3.0

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$(M-F)^+$

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IG,  CDCL3,  CFCL3,  F19,  --30
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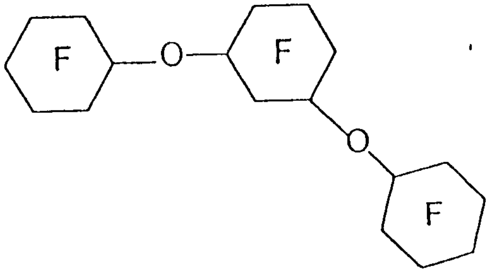

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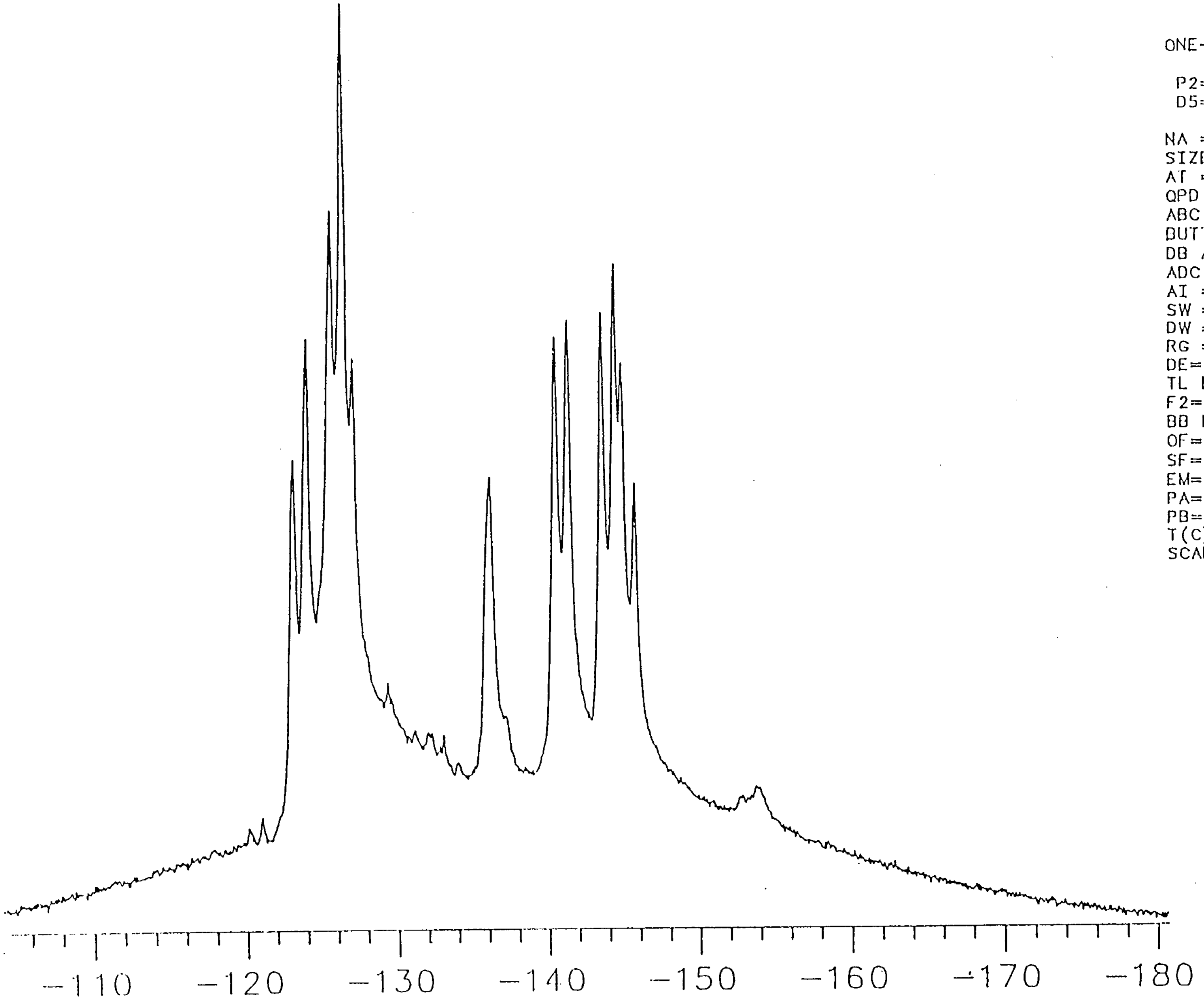

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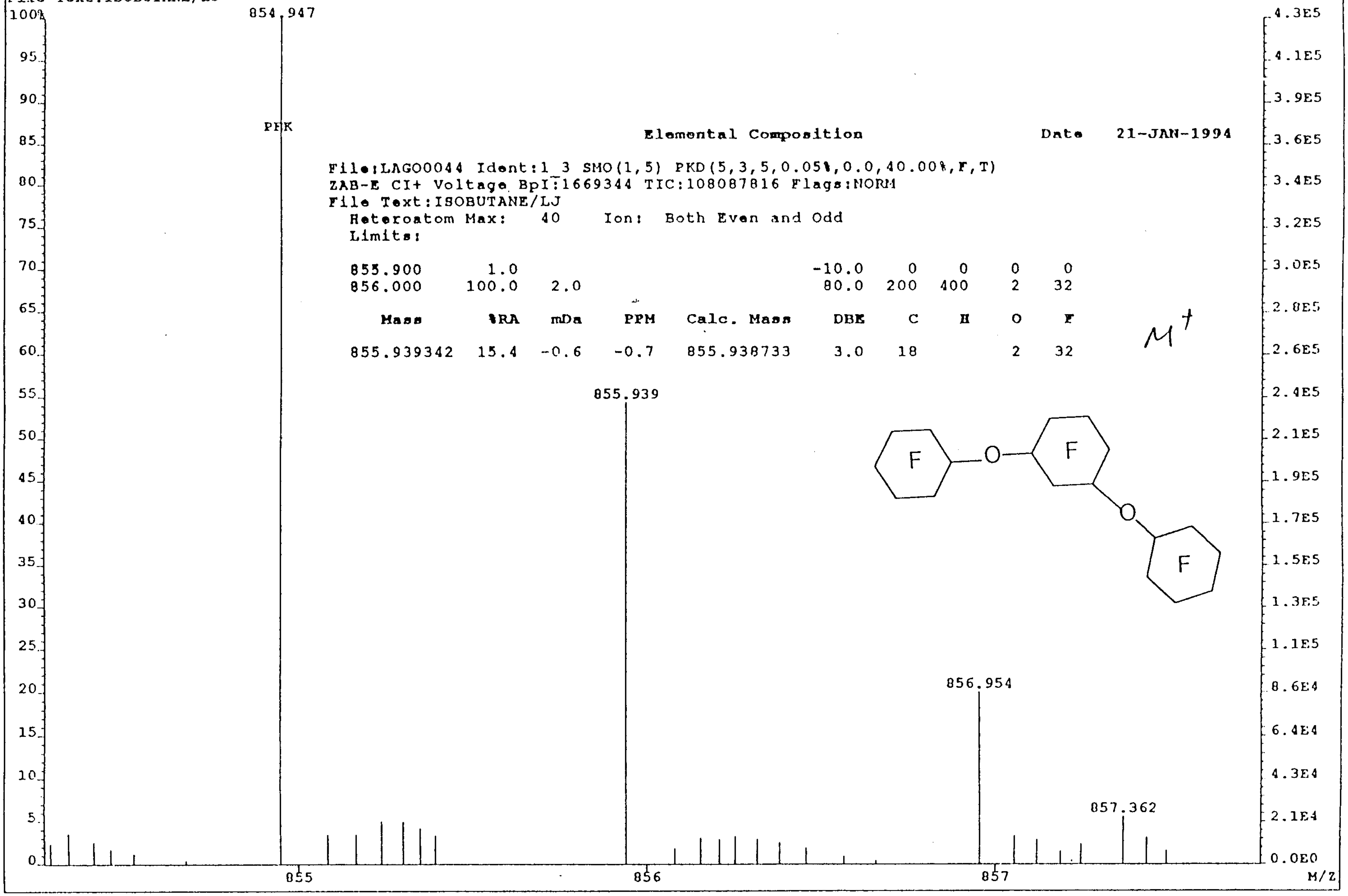

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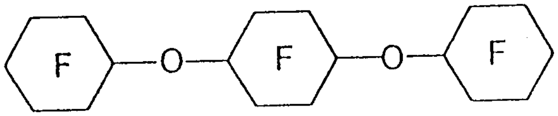
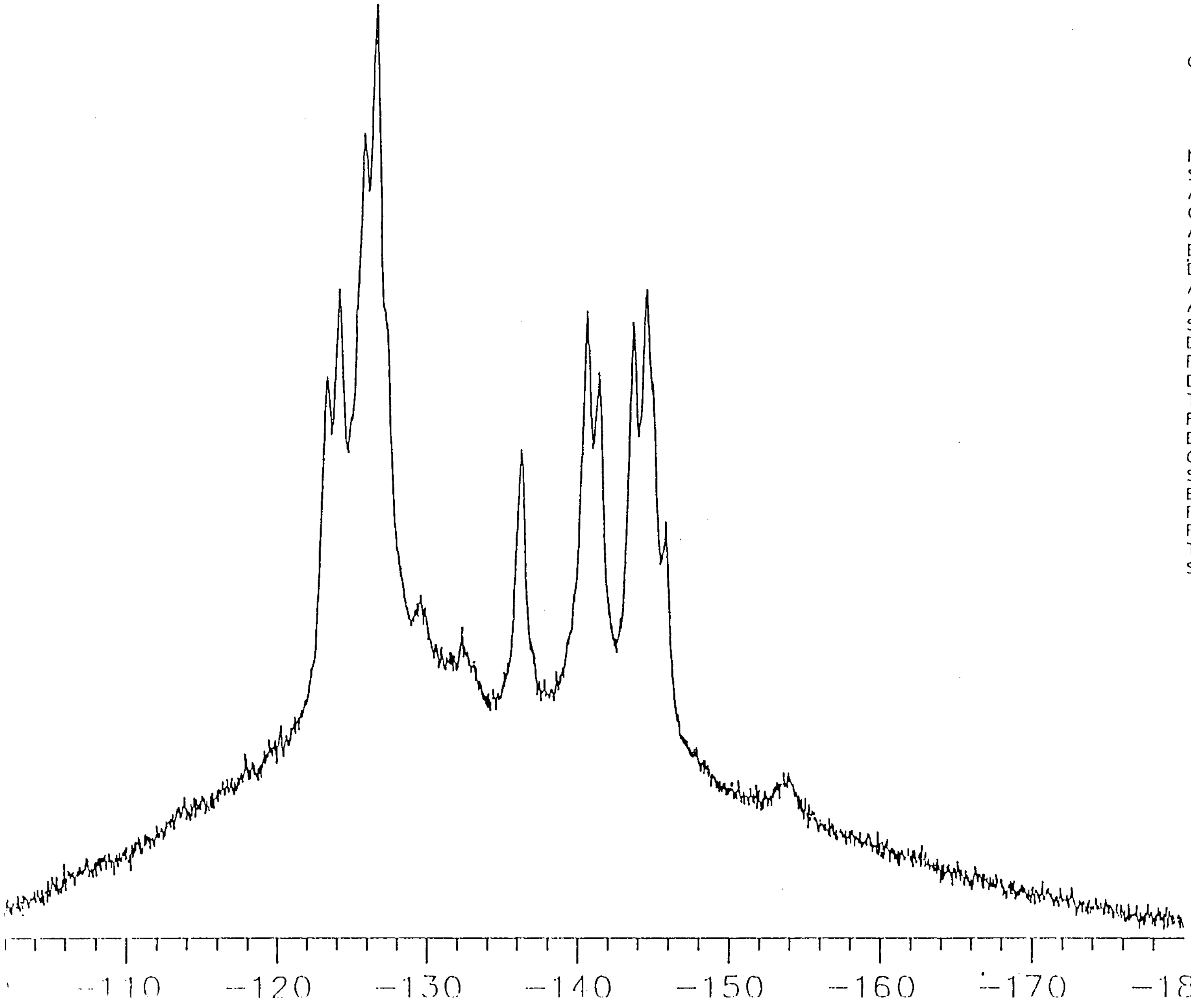
M+

200 . 002 MJB 06JAN94
ING, CDCL3, CFCL3, F19





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Synthesis of perfluoro(hexamethylcyclohexane-1,3,5-trione) was reported in last report. Now we want to show its unusual solid state conformation. The molecule is unusually flattened, as can be seen from the sum of the six ring torsion angles 31 + 18 + 14 + 32 + 18 + 12 = 125 °. By contrast, the sum of the ring torsional angles in cyclohexane and hexamethylcyclohexane-1,3,5-trione are 336 and 192 °, respectively. In comparison with boat conformation of hexamethylcyclohexane-1,3,5-trione, conformation of the perfluorinated analogue is a twisted boat in order to avoid the three axial trifluoromethyl groups, coming much too close and creating a serious strain.

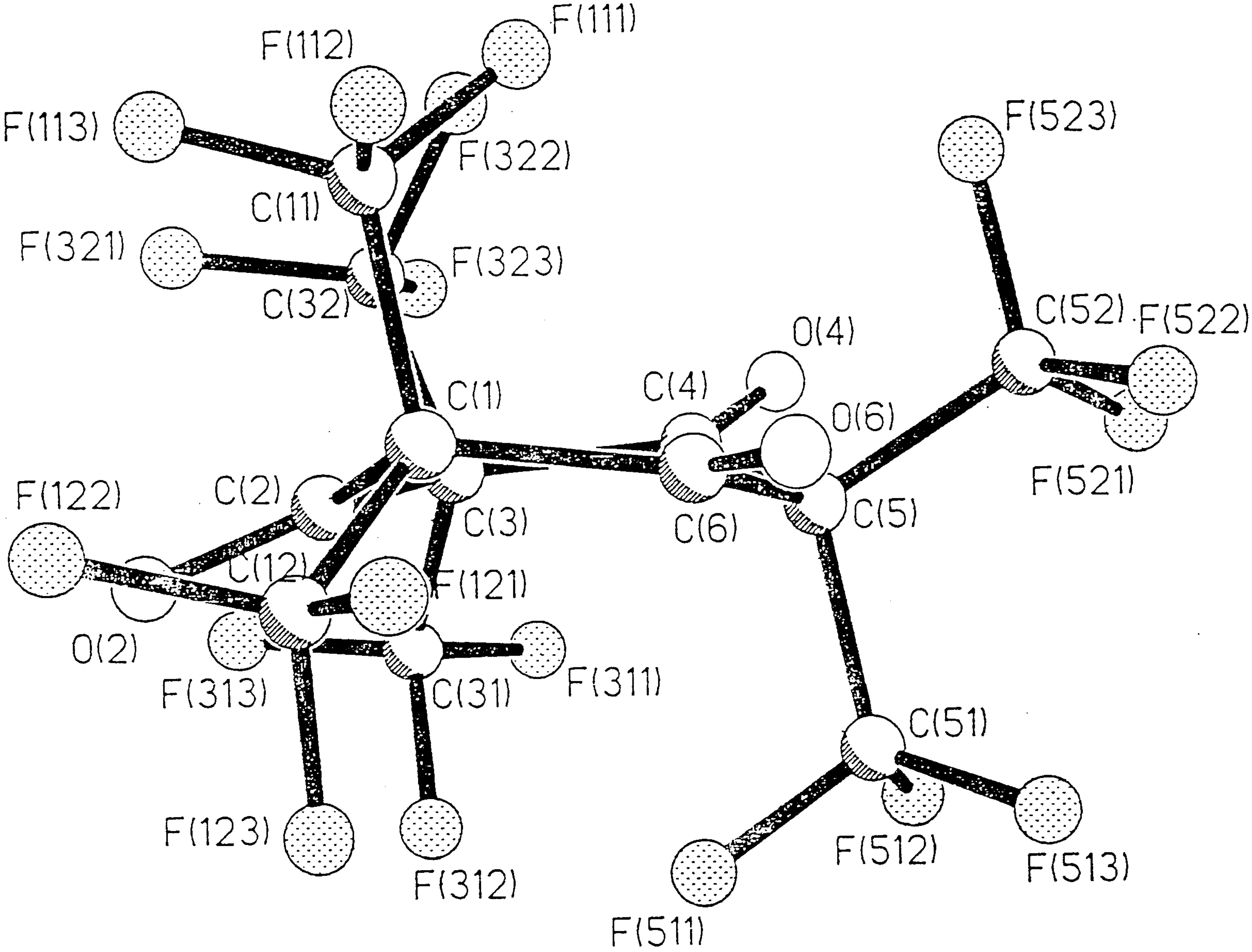
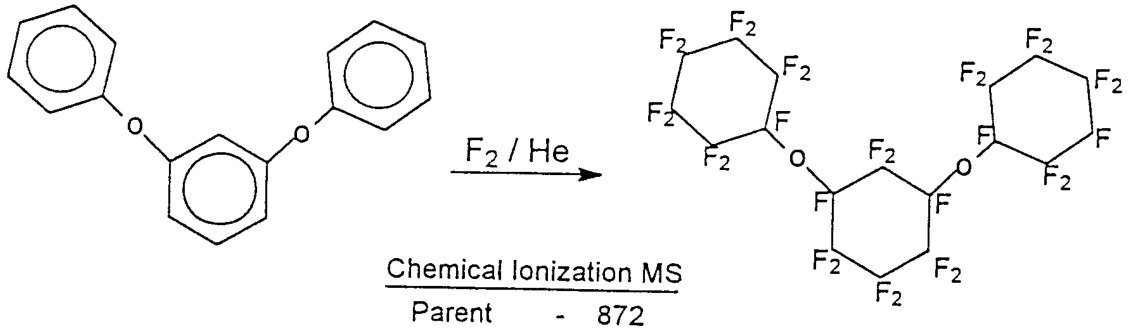


Fig.1. Molecular structure of ~~$C_{12}F_{18}O_3$~~ (1).;
Selected bond lengths (Å):C(2)-O(2) 1.188(5), C(4)-O(4) 1.179(5), C(6)-O(6) 1.178(5); bond angles (°): C(2)-C(1)-C(6) 115.7(4), C(2)-C(3)-C(4) 115.8(4), C(6)-C(5)-C(4) 116.0(4); torsion angles (°): C(6)-C(1)-C(2)-C(3) -30.8(6), C(1)-C(2)-C(3)-C(4) 17.9(6), C(2)-C(3)-C(4)-C(5) 14.4(6), C(3)-C(4)-C(5)-C(6) -32.3(6), C(4)-C(5)-C(6)-C(1) 18.3(6), C(2)-C(1)-C(6)-C(5) 11.8(6).

Other homologs of diphenyl ether such as 1,3-, and 1,4- diphenoxy benzene have also been perfluorinated for subsequent reductive defluorination.



Chemical Ionization MS

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P-F - 853
P- (C_6F_{11}) - 591
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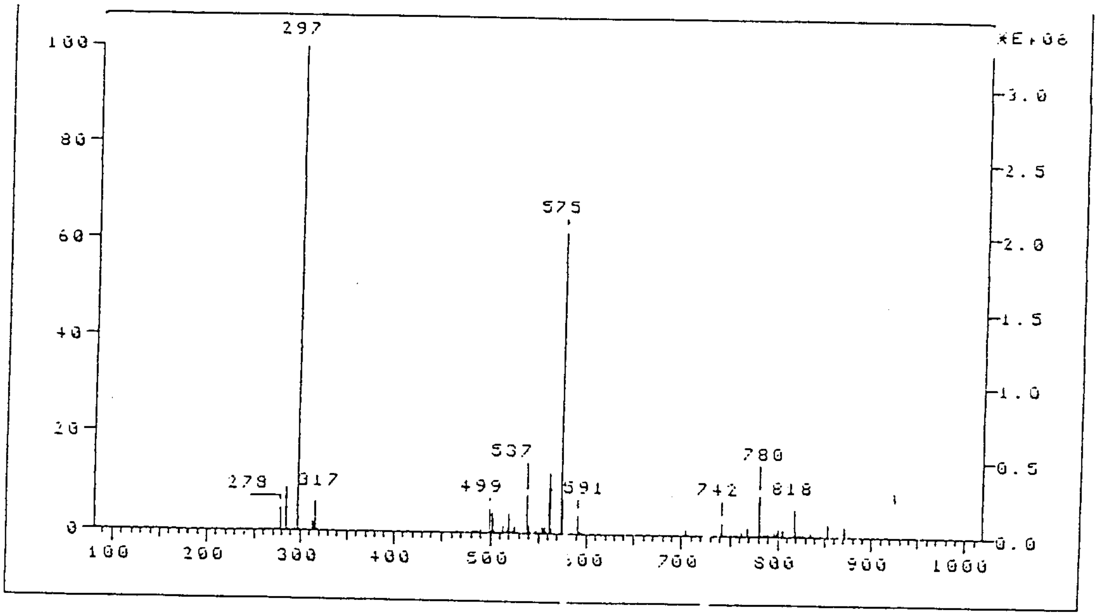
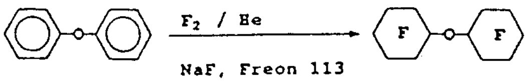
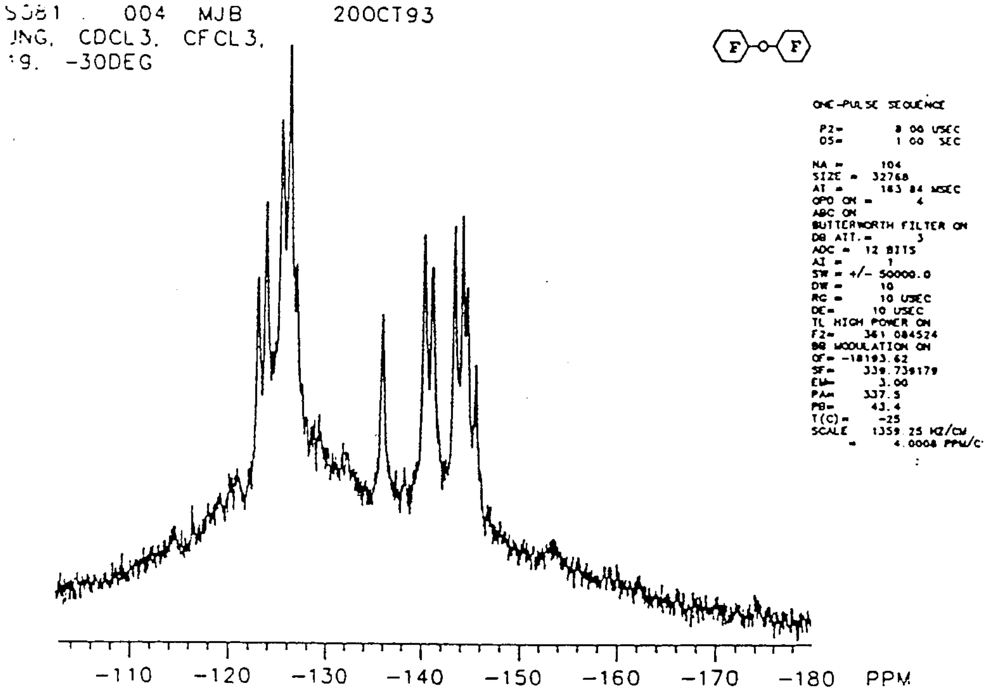
P- 2x ($C_6F_{11}O$) - 278



We have done considerable work on defluorination of cyclohexyl substituted fluorine compounds. This work is now becoming more and more successful and has been aided very considerably by the publication of a full manuscript by Dr. Guido Pez on methods using sodium benzophenone (J. Org. Chem. 1992, <u>57</u>, 2856-2860). Yet removing extra fluorines remains one of the problems that we are in the process of solving. There are a series of sodium substituted defluorination reagents. One of the mildest is sodium phenylthiolate by Professor David McNicol of Glasgow. The synthesis of perfluoro biscyclohexyl ether was accomplished in 83% yield.



The ^{19}F NMR Spectrum of Biscyclohexyl Ether



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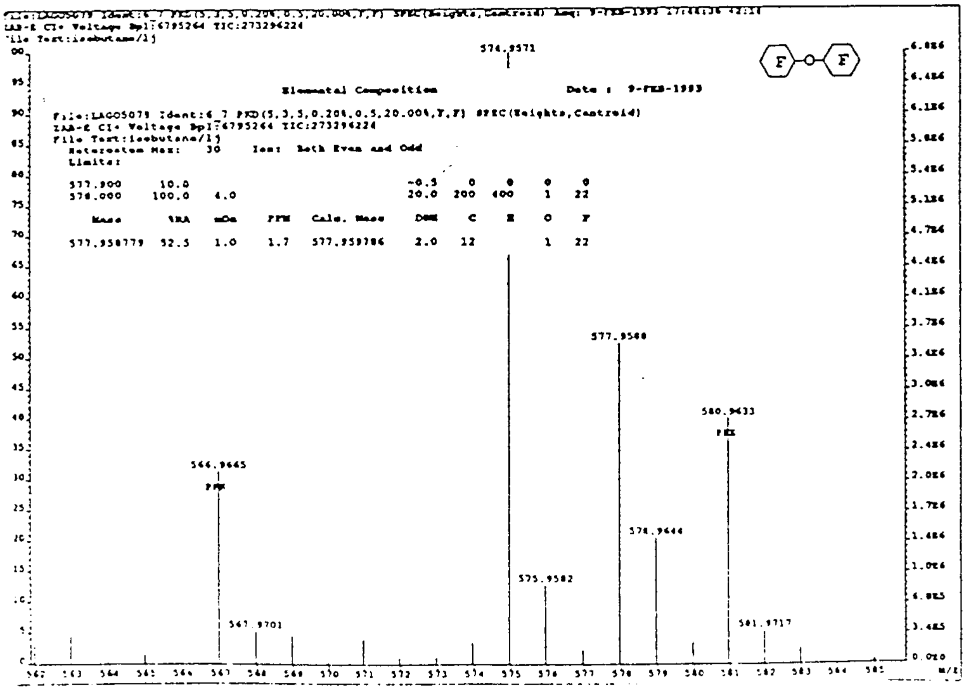
The high resolution mass spectrum of the final product contains a parent peak at 577.9588.



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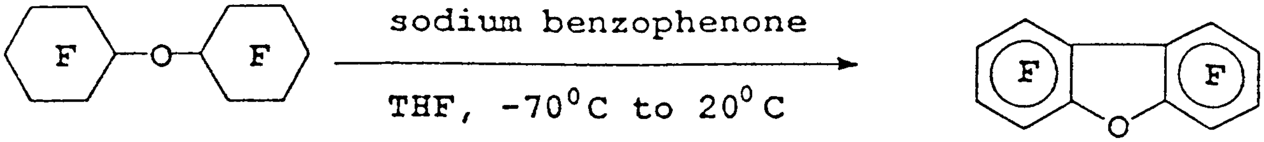
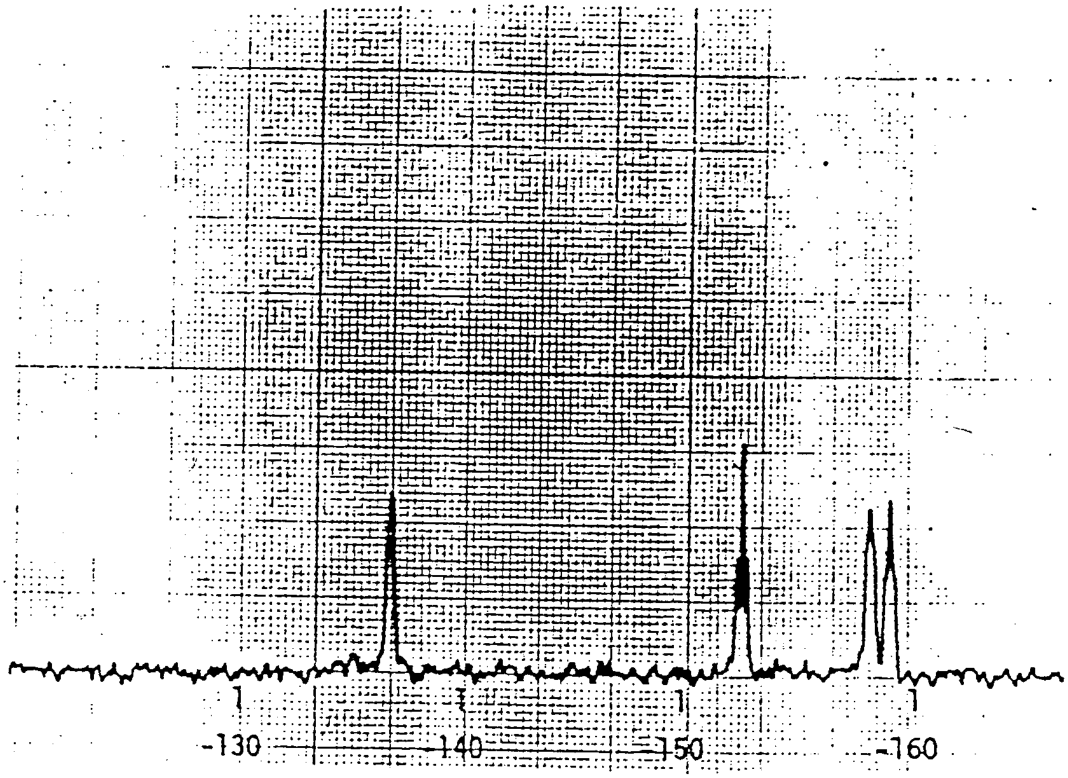
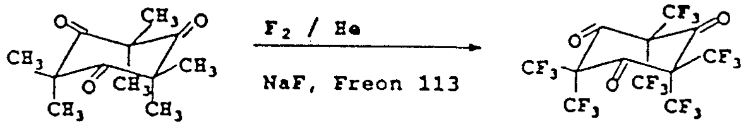


^{19}F NMR Spectrum of the Defluorinated Product

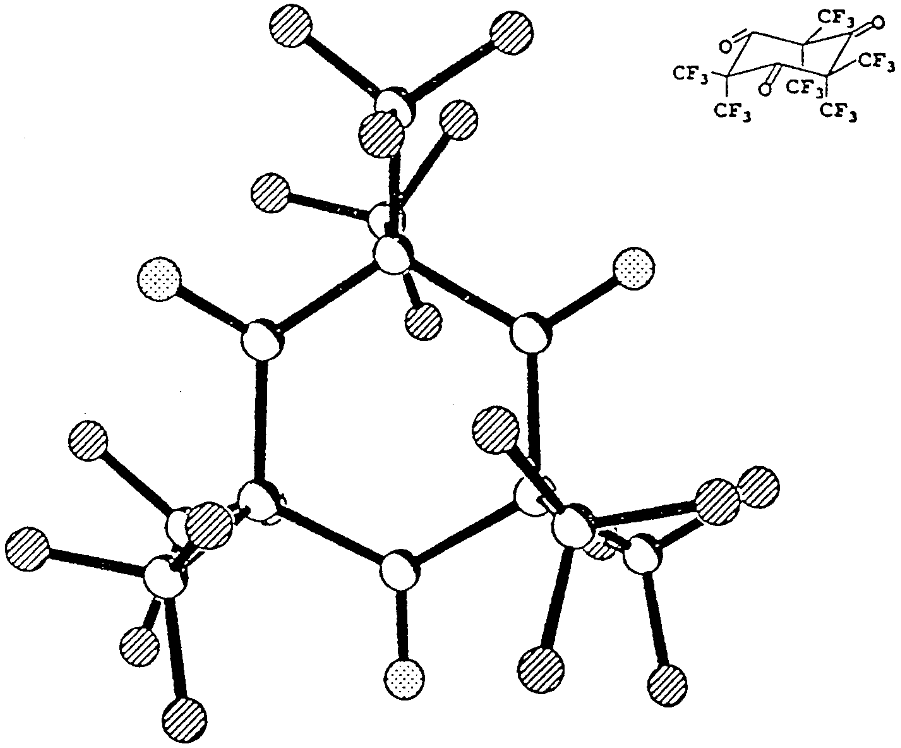


This is a very interesting case. Two extra fluorine were removed and we obtained the very interesting perfluoro furan compound shown above. We are now think we have been successful in applying it to a four-membered perfluoro cyclohexyl ether (page 7) (degree of polymerization four) and we shall see if we get the furan structure on that one as well. If successful it should produce an oligomer containing three furan units.

Very unusual perfluoro polyketone structures have been prepared by Dr. Kuangsen Sung. In particular, Dr. Sung has prepared a perfluorinated ketone from a hydrocarbon starting material in 72% yield.

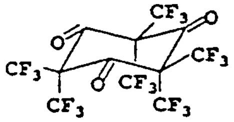


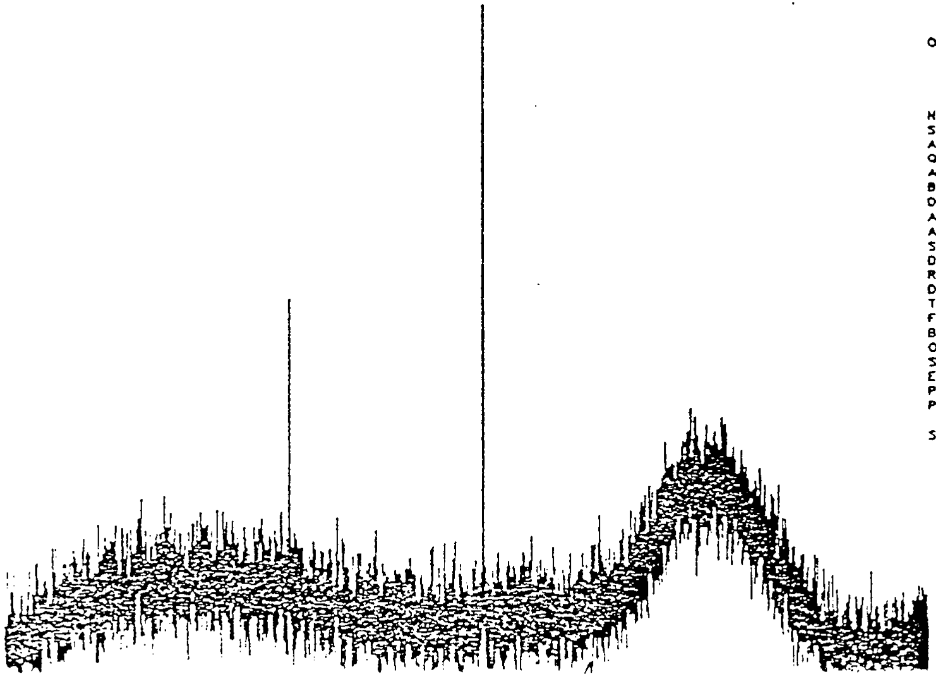
We have also obtained the crystal structure of this unusual new fluorocarbon material.



The ^{19}F NMR Spectrum of the Perfluorinated Ketone

```
3070A.   002   BAS        25AUG93
JNG.  ACETONE-D6,  CFCL3,  F19
```





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ONE-PULSE SEQUENCE

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 DS=        1.00  SEC

NA =      104
SIZE =  32768
AT =      163.84 MSEC
QPD ON =         4
ABC ON
BUTTERWORTH FILTER ON
DB ATT.=         3
ADC =  12 BITS
AI =            1
SW = +/- 50000.0
DW =        10
RC =        10 USEC
DE=       10 USEC
TL HIGH POWER ON
F2=     361.084524
BB MODULATION ON
OF= -17654.26
SF=.    339.739179
EW=       3.00
PA=     159.1
PB=      54.6

SCALE    5000.00 HZ/CM
     =      14.7171 PPM/CM
```
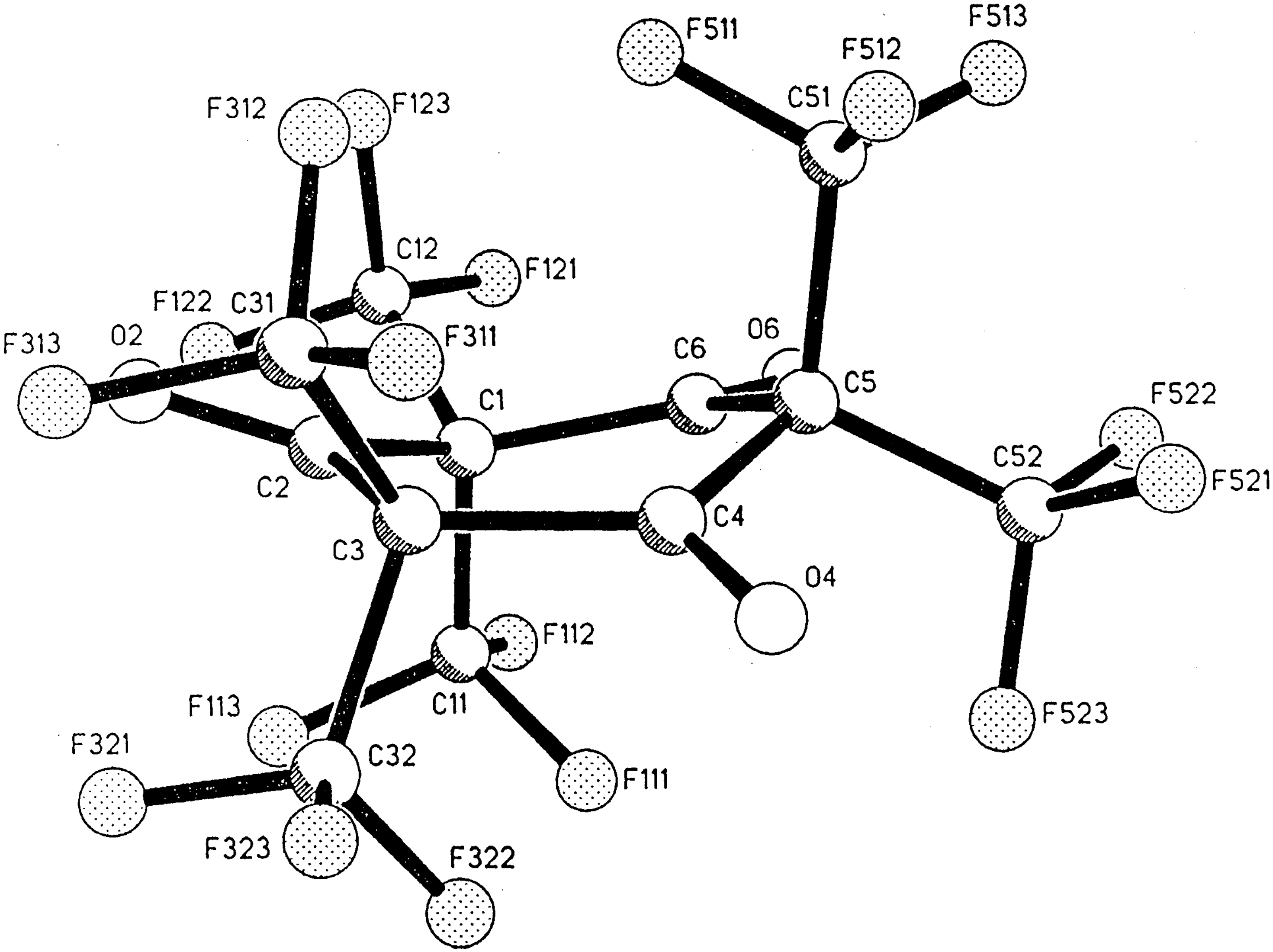
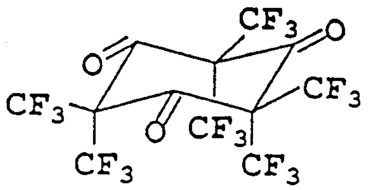
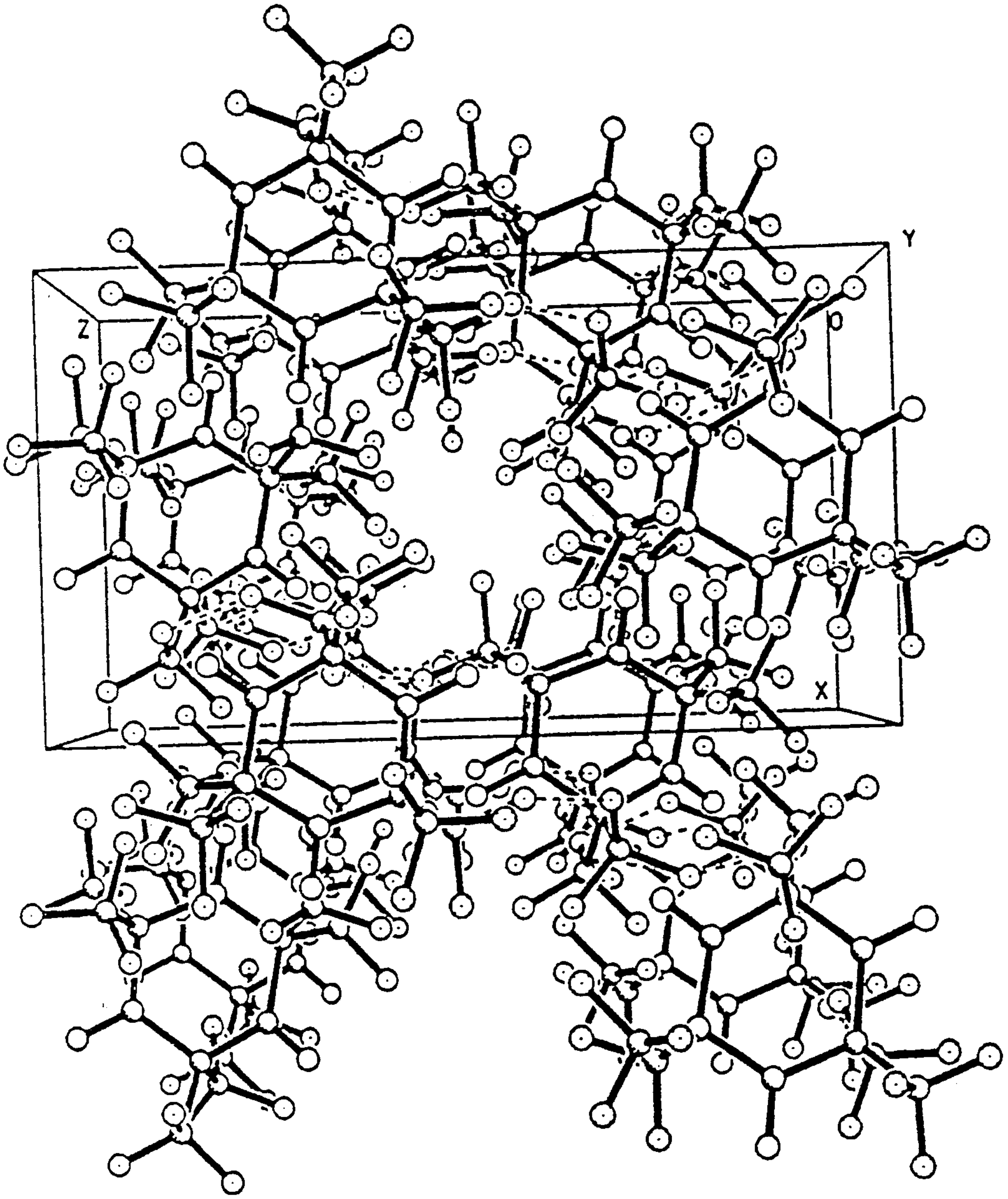

C12 F18 O3


F511
F513
F512
C51
F312
F123
C12
F121
F122
C31
F313
O2
F311
C6
O6
C5
F522
C1
C52
F521
C2
C4
C3
O4
F112
F113
C11
F523
F321
C32
F111
F323
F322

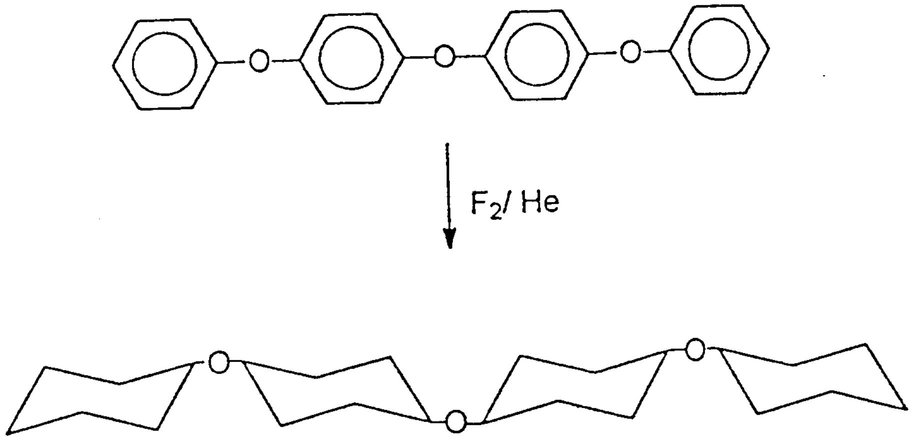
We think the zeolitic solid state structure of this very interesting perfluoro polyketone is most unusual and there may be interesting chemistry associated with the pockets of such a material.

Zeolitic Structure of





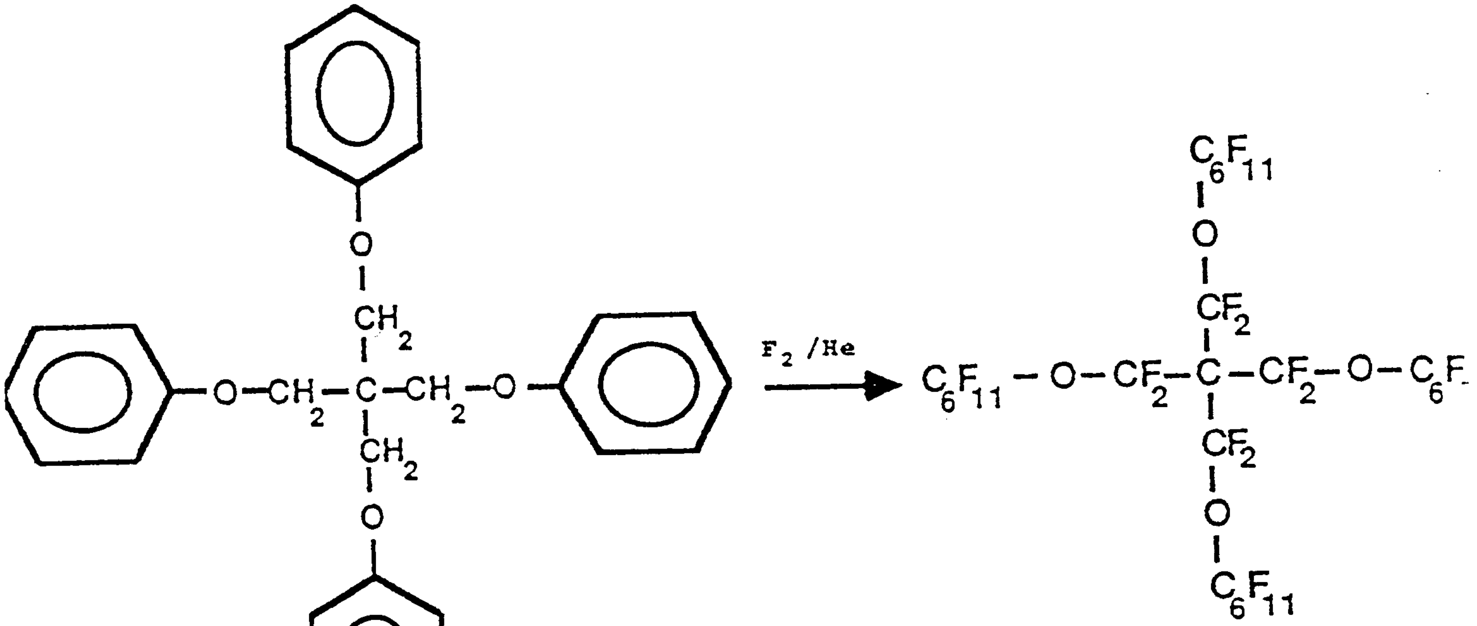
A number of other perfluoro organometallic compounds have been prepared for their conversion to perfluoro aromatic analogs.



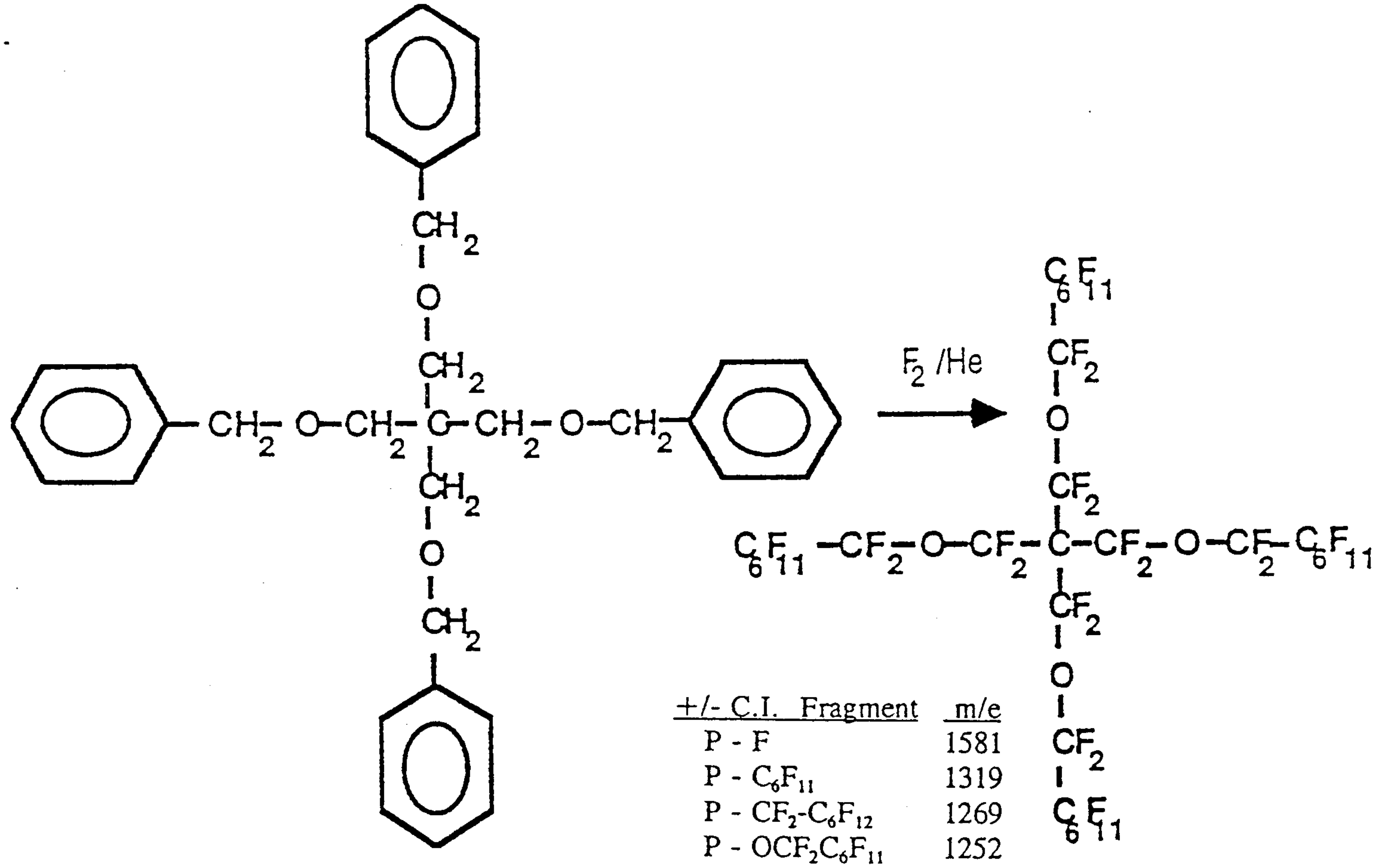
F

+/- C.I. Fragment	m/e
P - F	1115
P - C_6F_{11}	853
P - OC_6F_{11}	837
P - $C_6F_{10}OC_6F_{11}$	575
P - $OC_6F_{10}OC_6F_{11}$	559

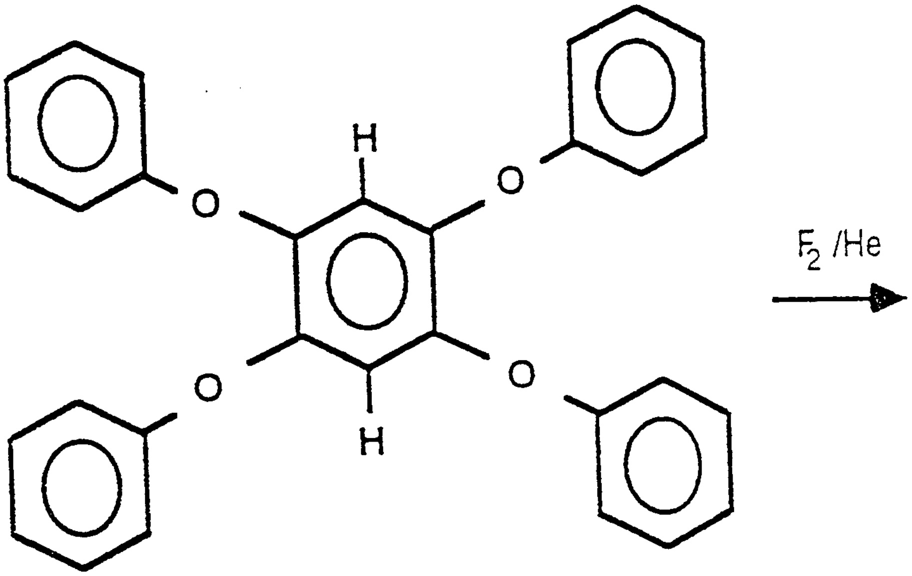
This structure is very interesting for under certain circumstances we hope to get the furan structure and with other reagents we hope to get the perfluorinated phenyl material. The perfluorinated cyclohexyl analog is already in hand.



+/- C.I. Fragment	m/e
Parent minus F	1381
P - C_6F_{11}	1119
P - OC_6F_{11}	1103
P - CF_2-O-C_6F_{11}	1053



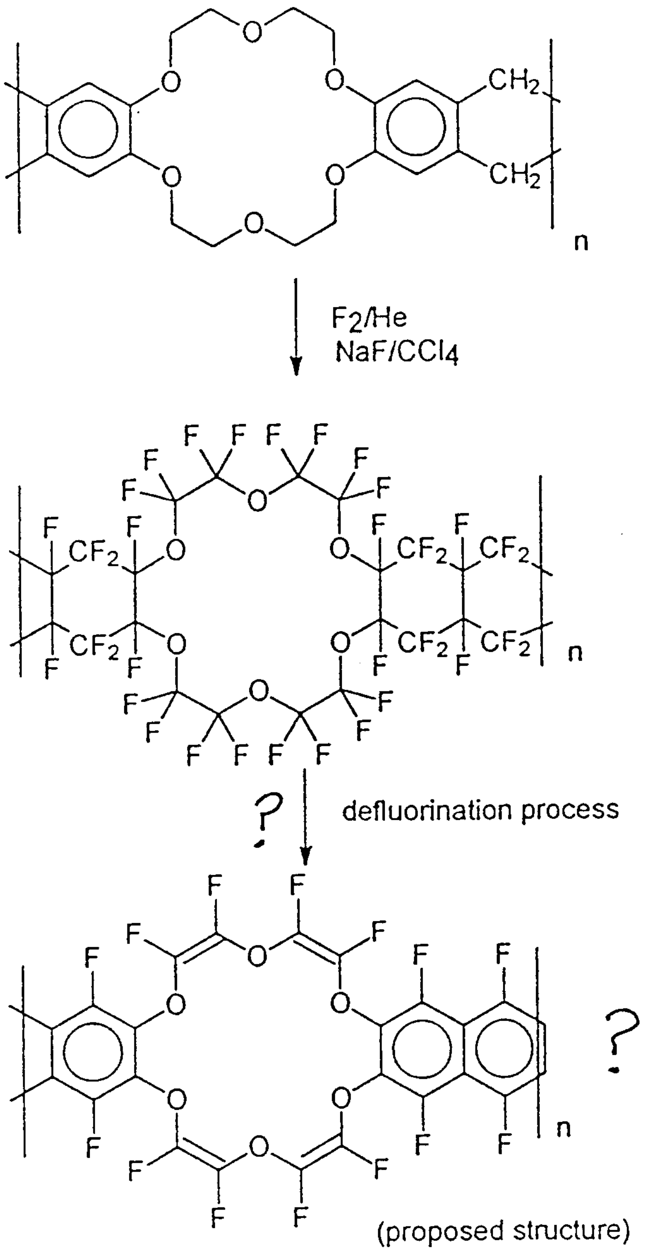
+/- C.I. Fragment	m/e
P - F	1581
P - C_6F_{11}	1319
P - CF_2-C_6F_{12}	1269
P - $OCF_2C_6F_{11}$	1252



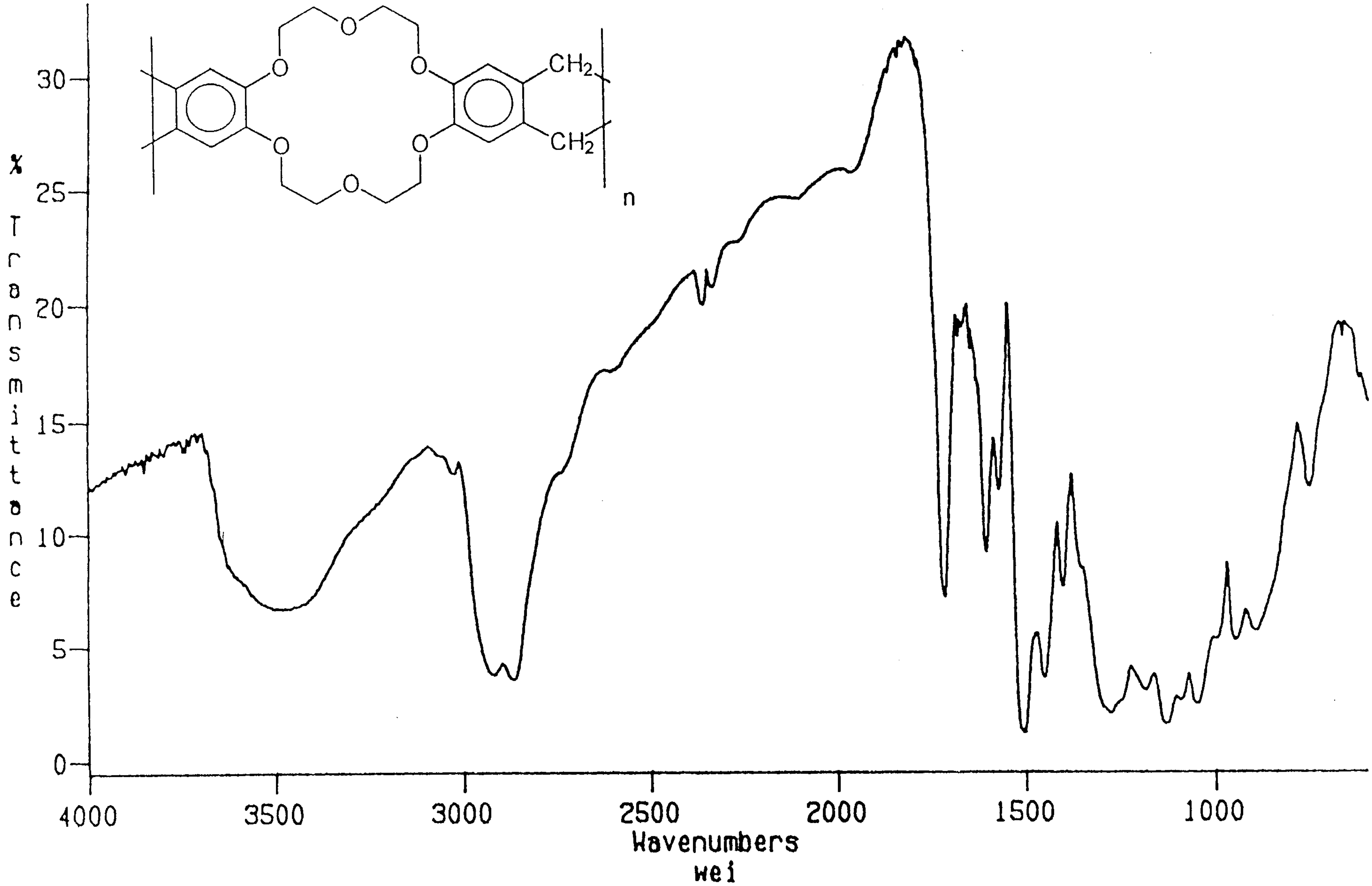
$C_6F_8(OC_6F_{11})_4$

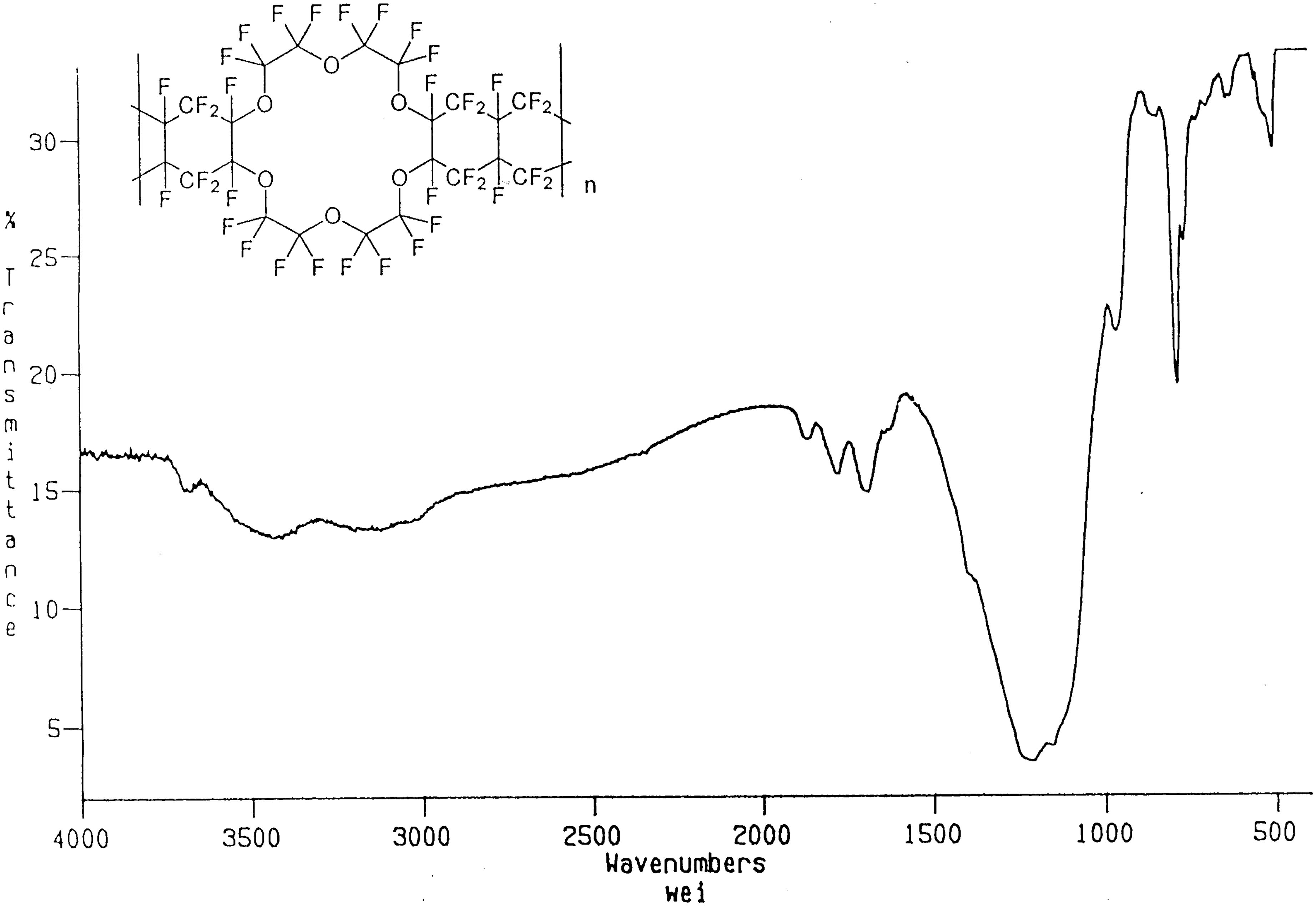
+/- C.I. Fragment	m/e
P - F	1393
P - C_6F_{11}	1131
P - OC_6F_{11}	1115

Mr. Han-Chao Wei of our research program has fluorinated this interesting crown ether polymer. We are very interested in exploring the defluorination process to see if we obtain the defluorinated material as indicated in the proposed structure.



He(cm^3/min.)	F$_2$(cm^3/min.)	Time(hr.)
50	0	0.5
50	2	24
25	2	24
10	3	24
3	3	24
0	3	24
25	0	0.5


% Transmittance
30
25
20
15
10
5
0
4000
3500
3000
2500
2000
1500
1000
Wavenumbers
wei
O
CH2
n


% Transmittance
30
25
20
15
10
5
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers
wei
F
CF2
O
n

Elemental analyses of the Perfluoro-crown ether-polymer

	Found	Calculated
Carbon ---	24.38% 24.34%	24.92%
Fluorine ---	64.68% 64.59%	65.11%
Oxygen ---	-----	9.97%

*Elemental analyses were done by **Schwarzkopf Microanalytical Laboratory** in New York

ACS SYMPOSIUM SERIES **555**

Inorganic Fluorine Chemistry

Toward the 21st Century

Joseph S. Thrasher, EDITOR
University of Alabama

Steven H. Strauss, EDITOR
Colorado State University

Developed from a symposium sponsored
by the Division of Fluorine Chemistry
at the 203rd National Meeting
of the American Chemical Society,
San Francisco, California,
April 5–10, 1992

American Chemical Society, Washington, DC 1994

Chapter 13

Synthesis and Chemistry of Perfluoro Macrocycles

Perfluoro Crown Ethers and Cryptands

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Wayne D. Clark, Wen-Huey Lin, Jennifer S. Brodbelt,
Simin D. Maleknia, and Chien Chung Liou

Department of Chemistry, The University of Texas at Austin,
Austin, TX 78712

Perfluoro macrocycles are a new development in organic and inorganic chemistry which has occurred in the last five years. The synthesis of perfluoro crown ethers and perfluorocryptands forecast the synthesis of many more perfluoro macrocycles in the next few years. The most surprising development to date with these new very chemically and thermally stable macrocycles has been the findings that they coordinate anions rather than cations and that they are extremely biocompatible materials. Perfluoro macrocycles have the potential for development as a new class of very thermally stable oxygen carriers which reversibly bind oxygen.

A recent breakthrough in our laboratory has involved the synthesis of perfluorinated crown ethers and cryptands. We have previously reported the synthesis of the first perfluoro crown ethers, perfluoro [18]crown-6, perfluoro [15]crown-5 and perfluoro [12]crown-4 *(1)*.

Perfluoro Crown Ethers

Perfluoro crown ethers have been synthetically inaccessible by conventional reactions of fluorocarbons and outside the capability of synthesis by fluorination using selective fluorination reagents. Examples of this potentially useful class of macrocycles have been prepared recently in our laboratory. These syntheses have been initially accomplished using the broadly applicable technique for controlling reactions of elemental fluorine (the La Mar process) developed in our laboratory. The reactions were conducted in the previously described cryogenic fluorination reactor *(2)*.

Perfluoro crown ethers are very thermally and chemically stable. The reactions to produce perfluoro macrocycles are all illustrated in Figure 1. There are potential applications of such perfluoro macrocycles in biomedical

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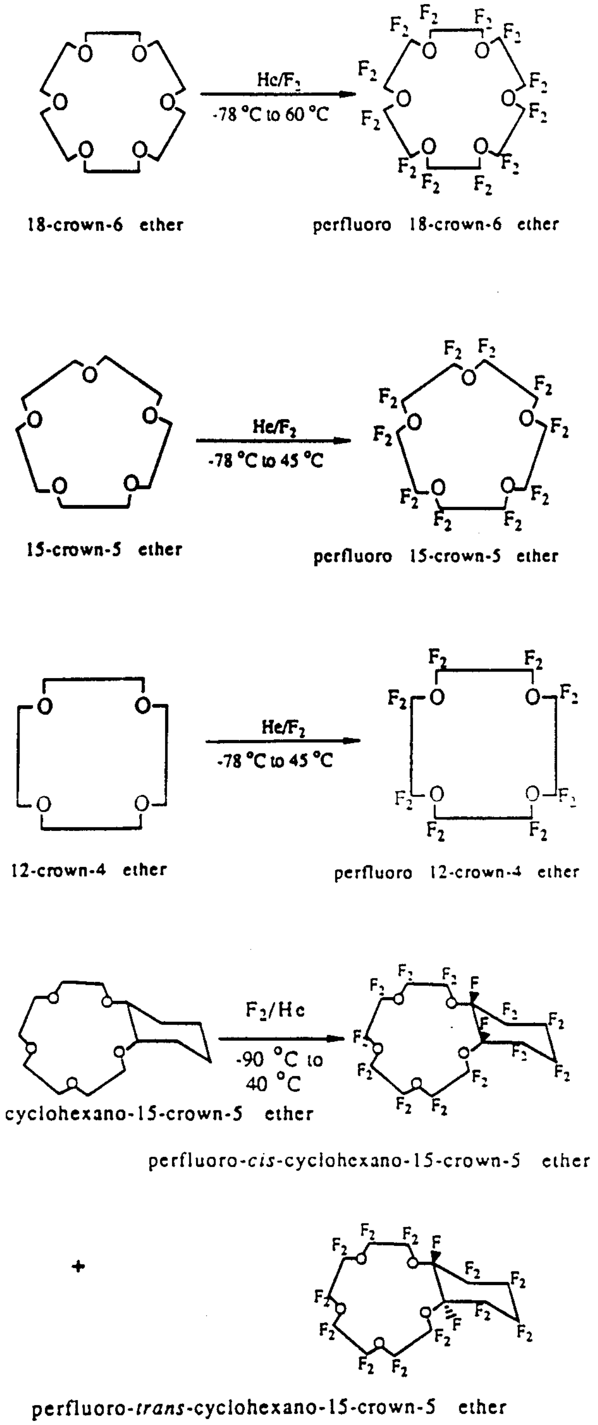

Figure 1. Reaction scheme for all compounds.

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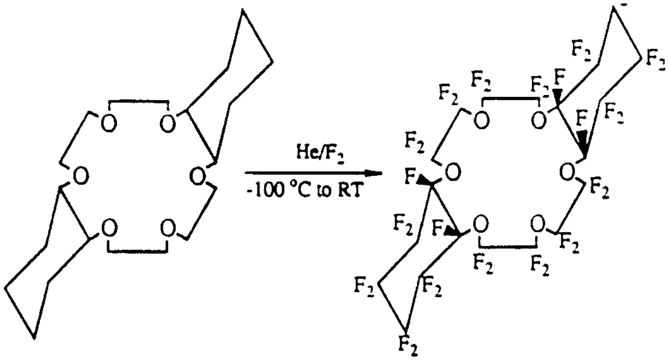
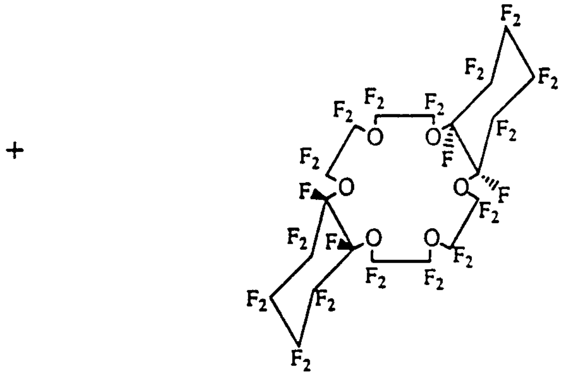
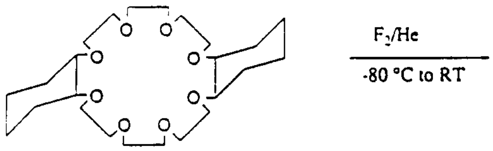


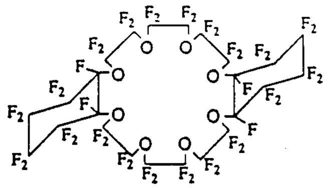
perfluoro-*cis-syn-cis*-dicyclohexano-18-crown-6 ether



perfluoro-*cis-anti-cis*-dicyclohexano-18-crown-6 ether



dicyclohexano-24-crown-8 ether



perfluorodicyclohexano-24-crown-8 ether

Figure 1. *Continued.*

and catalytic chemistry. Properties and characterization of perfluoro [15]crown-5 and perfluoro [12]crown-4 are shown in Table I.

Perfluoro [15]Crown-5 Ether. Perfluoro crown ethers *(1,3)* are becoming very important as the molecules of choice for many ^{19}F NMR imaging applications *(4)* in humans and is particularly effective in brain and spinal diagnostics when administered to the cerebrospinal fluid compartment. Synthesis scale up for perfluoro [15]crown-5 *(1-3)* and plans for commercialization are underway while research is being conducted on other biological applications of these new compounds *(5)*. In collaboration with Air Products, excellent brain imaging scans have been obtained by infusing perfluoro [15]crown-5 in the spinal fluids. Toxicology reports on these are very favorable; essentially no toxic effects physiologically were found in several studies involving different animals. There are some pharmaceutical companies actively negotiating to obtain licensing on perfluoro [15]crown-5 on which a composition of matter patent *(3)* has been obtained by our laboratory.

Perfluoro [18]Crown-6 Ether. The perfluoro [18]crown-6 ether analog has approximate C_2 symmetry, unlike [18]crown-6 which has C_i symmetry *(6)*, as illustrated with a view looking through the cavity of the molecule in Figure 2. The folding or puckering of the ring is seen in Figure 3.

The effects of perfluorinating [18]crown-6 show up very well in the shortened C-O bonds and lengthened C-C bonds. The average C-O bond length in perfluoro [18]crown-6 [1.376 (7) Å] is 0.034 Å shorter than the average C-O bond length in [18]crown-6 [1.411 (8) Å]. On the other hand, the perfluoro analog exhibits an average C-C bond length [1.539 (3) Å] that is 0.032 Å longer than the average value [1.507 (2) Å] in the nonfluorinated crown. The C-F bonds [average 1.334 (2) Å] are normal for disubstituted paraffinic C-F bonds *(7)*. Bond angles at O and C are also affected considerably by the H/F exchange. The COC angles change from an average 113.5° to 121.1 (5) ° and the OCC angles change from 109.8° to 107.1 (2) °.

The distances between O atoms across the cavity (and related by the pseudo-2-fold axis) range from 4.416 (2) - 5.528 (2) Å. This is considerably more circular than [18]crown-6 which has a range of 4.27-6.97 Å. In [18]crown-6, two H atoms project into the cavity, such that their interatomic distance is only 3.04 Å. Figure 2 illustrates that not just one pair of F atoms but two pairs project into the cavity resulting in F-F distances of 3.012 Å and 2.932 Å. Figure 3 illustrates the packing. The closest intermolecular contacts are between F atoms, the shortest of which is 2.845 (2) °.

Perfluoro cis-syn-cis- and cis-anti-cis-Dicyclohexyl[18]Crown-6 Ether. Very recently we have synthesized perfluoro crown ethers from the hydrocarbon dibenzo crown ether (see Figure 8) *(10)*. We have prepared two interesting isomers of perfluorodicyclohexyl[18]crown-6 ethers *(10)*, the cis-syn-cis and cis-anti-cis isomers. Their structures have also been established by X-ray crystallography.

Table I. Properties and Characterization of Perfluoro [15]Crown-5 and Perfluoro [12]Crown-4[a]

	[15]Crown 5	[12]Crown-4
Boiling Point (°C)	146	118
IR (vapor phase) (cm^{-1})	1250(s) 1228(vs) 1158(vs) 745(m)	1260(vs) 1188(vs) 1160(vs) 1080(m) 825(m) 745(br)
NMR (neat liquid)	^{19}F--91.8(s) ppm (ext. $CFCl_3$) ^{13}C δ114.9(s)	^{19}F--90.0(s) ppm (ext. $CFCl_3$) ^{13}C δ114.9(s)
Mass spectrum	580($C_{10}F_{20}O_5$, M^+)	445($C_8F_{15}O_4$, M^+--F)

[a] Satisfactory elemental analyses (C,F) were obtained.

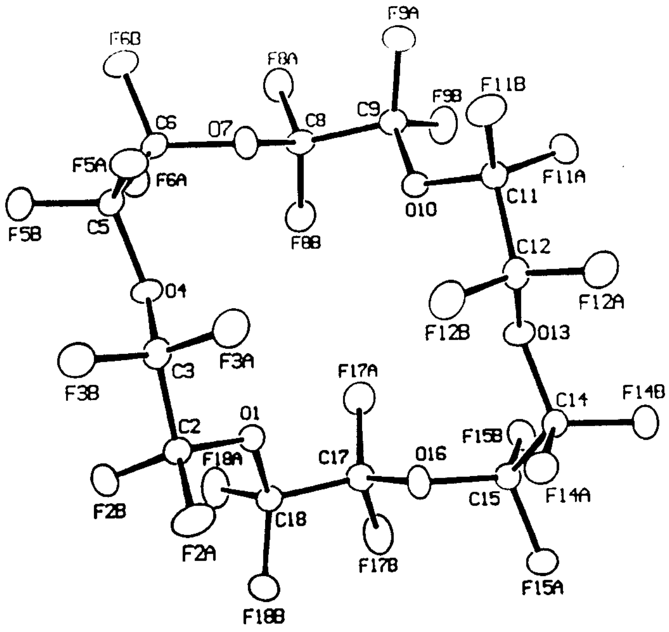


Figure 2. ORTEP drawing of perfluoro [18]crown-6 viewed through the cavity. Thermal ellipsoids are drawn at the 35% probability level.

The single crystals of each isomer were grown from the gas phase through condensation to a cold surface at 1 atm pressure *(8)*. X-ray structures *(9)* show that the isomers have distinctly different solid state structures. The syn- isomer has a twisted-bent elliptical ring structure with two cyclohexano groups located at two ends while the anti- isomer has an elliptical ring structure with two cyclohexano groups symmetrically distributed on two sides (see Figures 4-7 for X-ray structures).

Perfluorocryptands

We have also reported the first perfluorocryptand molecule, the perfluorocryptand[2.2.2] (see Figure 9) *(11)*. The perfluorocryptand is a very stable, inert, high boiling clear oil. While hydrocarbon crown ethers coordinate cations, both the perfluoro crown ethers and the new perfluorocryptand coordinate anions. Two manuscripts have recently appeared in collaboration with Professor Jennifer S. Brodbelt in which both perfluoro crown ethers and perfluorocryptands tenaciously encapsulate O_2 and F^- *(11-12)*.

The perfluorocryptand[2.2.2] compound is expected to have a number of interesting applications. Aside from the possibility of acting as a perfluoro "host " for certain types of "guest " species, perfluorocryptand[2.2.2] has shown potential as a very clean, high mass compound for use as a mass spectral marker material *(13)*. The compound is expected to be biologically inert (in contrast to the hydrocarbon analog), and as in the case of the perfluoro crown ether compounds, may be useful in fluorocarbon biological and medical applications where physiologically inert or oxygen carrying fluids are required. The ^{19}F NMR of the perfluorocryptand[2.2.2] is shown in Figure 10.

The basicities of the crown systems would be expected to decrease with an increased amount of fluorine substitution in the molecule. This trend is seen in the partially fluorinated cyclams *(14)* and is continued to the perfluoro crown ethers *(1,15)*. The coordination chemistry, organometallic chemistry, and reaction chemistry of perfluorocryptands are being explored in collaboration with Professor Jean-Marie Lehn. Lehn provided the original hydrocarbon samples and suggested this project to us many years before we had developed the direct fluorination capability to the extent required to effect this synthesis. In addition, we have underway a collaborative project with Professor Leland C. Clark, Jr., in which we are exploring the physiological and biological properties of the new perfluorocryptand. The physiological applications of perfluorocryptand[2.2.2] will be published elsewhere.

Gas-Phase Reactions of Perfluoro Macrocycles

The coordination capabilities of perfluorinated macrocycles have generated considerable interest based on the properties of crown ethers and related macrocycles as model hosts in the field of molecular recognition *(16-17)*. Numerous studies have described aspects of host-guest complexation of hydro crown ethers with a variety of model guests, including alkali metal ions and ammonium ions *(18)*. Thus, the perfluorinated macrocycles provide an

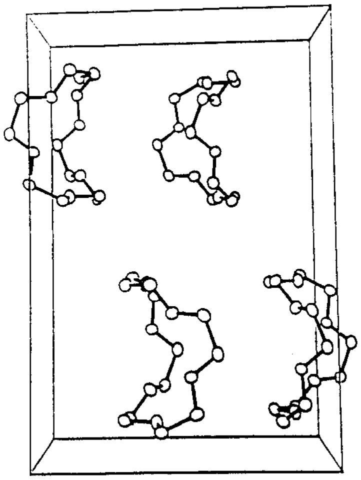


Figure 3. Packing diagram of perfluoro [18]crown-6 with F atoms removed as viewed along the a-axis. The c-axis is vertical and the b-axis is horizontal.

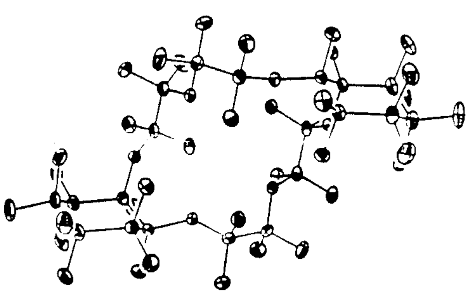


Figure 4. Single crystal X-ray structure of perfluoro -cis-syn-cis-dicyclohexyl[18]crown-6 ether.

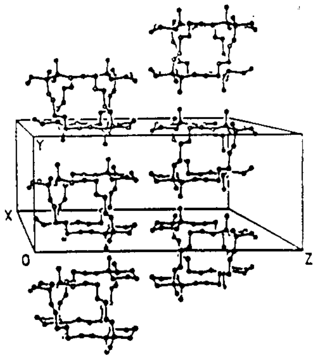


Figure 5. Unit cell packing of perfluoro-cis-syn-cis-dicyclohexyl-[18]crown-6 ether.

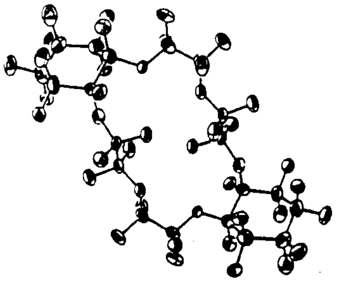


Figure 6. Single crystal X-ray structure of perfluoro-cis-anti-cis-dicyclohexyl[18]crown-6 ether.

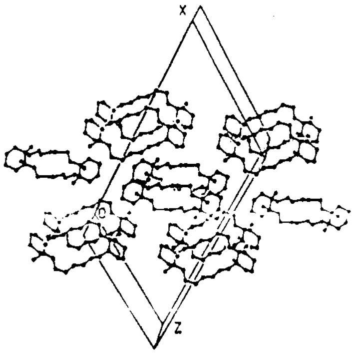


Figure 7. Unit cell packing of perfluoro-cis-anti-cis-dicyclohexyl-[18]crown-6 ether.

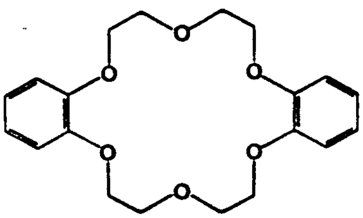


Figure 8. The dibenzo crown ether hydrocarbon starting material.

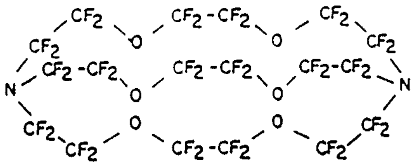
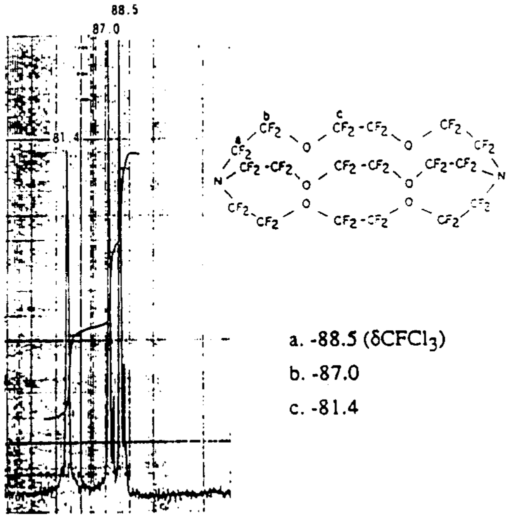


Figure 9. The perfluorocryptand[2.2.2].



a. -88.5 ($\delta CFCl_3$)

b. -87.0

c. -81.4

Figure 10. The ^{19}F NMR of the perfluorocryptand[2.2.2]

intriguing structural analog to the hydrogenated macrocycles. Studies of these novel model hosts may reveal new insight into the structural and thermodynamic factors which mediate selective complexation. Recently, studies of host-guest chemistry in the solvent-free environment of the gas phase has opened a new frontier for the investigation of molecular recognition *(11,12,19-22)*. Complexation may be evaluated in the absence of solvation effects, and thus the intrinsic binding properties of model hosts can be examined. Three studies of the gas-phase ion chemistry of perfluoro macrocycles are reviewed in the following section.

The high oxygen-carrying capacity of some perfluorocarbons makes them viable as artificial blood components *(23)*, and yet to date the mechanism of oxygen binding to fluoro ethers is not well understood. Thus, it was of considerable interest to probe the ability of perfluoro macrocycles to bind molecular oxygen and other small molecules in the gas phase in order to obtain new information about the binding affinities of these compounds *(11)*. For these studies, each perfluoro macrocycle was admitted into the source of a triple quadrupole mass spectrometer. Argon was introduced into the source manifold at 2-3 x 10^{-6} torr to aid in the production of thermal electrons for electron capture negative ionization. The desired reagent gas (CO, N_2, CO_2, air for O_2) was added to attain a total source pressure of 1-2 torr. The ethers examined included perfluoro [12]crown-4, perfluoro [15]crown-5, perfluoro [18]crown-6, perfluorinated 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (cryptand), their hydro crown analogs, and one acyclic perfluoro ether, perfluoro-triethylene glycol dimethyl ether.

Each perfluoro macrocycle was ionized to form $M^{-\cdot}$ then allowed to react with O_2 to successfully form $(M + O_2)^{-\cdot}$ adducts *(11)*. Ion/molecule reactions involving an acyclic perfluoro ether and hydrogenated crown ethers were also examined to determine whether the cyclic and/or perfluoro nature of the macrocycles played a role in the formation of the $(M + O_2)^{-\cdot}$ adducts. *Neither* the perfluoro acyclic analog nor hydrogenated crown ethers reacted with O_2 to form $(M + O_2)^{-\cdot}$ adduct ions. This result confirmed that the macrocyclic nature of the perfluoro crown ethers enhanced their ability to bind O_2.

Additionally, the ability of the perfluoro crown ethers to form complexes with CO, N_2, CO_2, and Ar, species with similar sizes and some similar chemical and physical properties as O_2, was examined. Adducts with these species were not observed *(11)*. Thus, the tendency of the perfluoro crown ethers to form adducts exhibited striking selectivity for O_2 only.

Structural details of the perfluoroether adduct ions, $(M + O_2)^-$, were probed via collisionally activated dissociation (CAD) of the mass-selected ions *(11)*. Figure 11 illustrates the 40 eV CAD spectra of the perfluoro 15-crown-5 $(M + O_2)^-$ adduct (m/z 612), showing two series of fragment ions. One is a series of losses of $(C_2F_4O)_n$, analogous to the series of losses observed from the $M^{-\cdot}$ ion, resulting in fragment ions at m/z 148, 264, 380, and 496. This trend indicates that the O_2 is bound to the perfluoro crown ether strongly enough to be retained after the adduct ion is activated and implies that the binding interaction must be at least as strong as the C-C and C-O bonds that are cleaved during the competing dissociation processes in which C_2F_4O units are expelled. The C-C and C-O bond energies for these perfluoro crown ethers have been estimated as 84 and 98 kcal/mole, respectively. Additionally, a series of fragment ions corresponding to loss of $[n(C_2F_4O) + O_2]$ units is seen as m/z 232, 348, and 464, where n = 3, 2, 1, the same fragment ions produced from CAD of the non-complexed molecular ion as shown in Figure 12.

Direct loss of O_2 is not a significant dissociation channel using any collisional activation conditions (for 10-120 eV kinetic energy collisions, the percentage of the total fragment ion abundance due to O_2 loss is 0 - 10%). This result suggests that the O_2-crown ether complex is not a loosely bound adduct, but instead a species in which stronger bonding forces are involved than those associated with a single weak ion/dipole electrostatic interaction. An adduct species in which O_2 is cradled by four electronegative fluorine atoms is feasible. In general, O-F bonds are not stronger than 50 kcal/mole, so a complex containing a single $F\text{-}O_2$ binding interaction is not supported.

It was also timely to examine the ability of perfluoro macrocycles to react with fluoride in the gas phase *(12)*. It has been shown recently from crystallographic studies that a fluoride ion may be held in the cavity of a fluorinated macrocyclic vinyl polymer *(24)*, and thus it was of interest to investigate the possibility of forming related fluoride complexes in the gas phase. Fluoride/macrocyclic adducts were successfully generated in the gas phase by ionization of a mixture of a macrocycle and a fluorinated reagent such as CHF_3 admitted simultaneously into the ion source. Moderately abundant $(M + F)^-$ adducts (relative abundance = 10% compared to $M^{-\cdot}$) are formed by reaction of F^- with the macrocyclic molecules. The CAD spectrum of the $(M + F)^-$ adduct of perfluoro [15]crown-5, shown in Figure 13, is similar to the CAD spectrum for the molecular anion $M^{-\cdot}$ of perfluoro [15]crown-5 shown in Figure 12, with the exception that each fragment ion is shifted to a higher mass by 19 amu (due to the fluorine addition). The series of ions incorporating the additional fluorine is the only type of fragment observed, indicating that the fluorine is *always* retained by the ionic portion during dissociation. The most abundant dissociation processes involve loss of two or three C_2F_4O units. The direct loss of $F\cdot$ from the $(M + F)^-$ adduct is not observed. This result suggests a very strong crown ether-fluoride binding interaction. For example, the fluoride ion may attack the least nucleophilic carbon position and promote ring opening, resulting in a branched monocyclic structure with a covalently bound fluorine. A mechanism depicting this proposed pathway is shown in Scheme 1.

In the third gas-phase study *(24)*, a new type of cluster ion consisting of a perfluorinated macrocycle (M) associated with multiple ether molecules was generated in the source of a triple quadrupole mass spectrometer. The clusters have the general formula $(M - F + nEther)^+$ where n = 1,2,3...depending on the type of ether. The ethers which promoted the most extensive clustering were highly strained cyclic ethers such as ethylene oxide and ethylene sulfide, whereas the perfluoro macrocycles attached only one unit of the acyclic ether analogs, such as dimethyl ether. Collisionally activated dissociation of the cluster ions revealed that the ether units were eliminated sequentially, indicating that the ether molecules are attached separately around the perfluoro

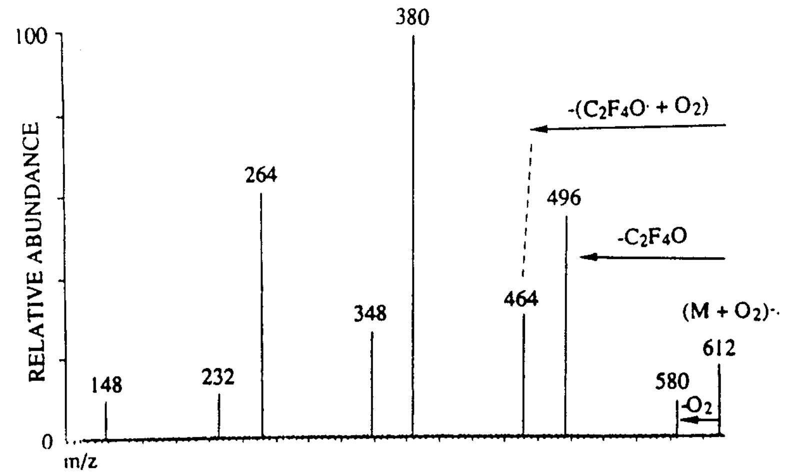


Figure 11. Collisionally activated dissociation mass spectra of the $(M + O_2)^{-\cdot}$ ion of perfluoro [15]crown-5 acquired with a triple quadrupole mass spectrometer.

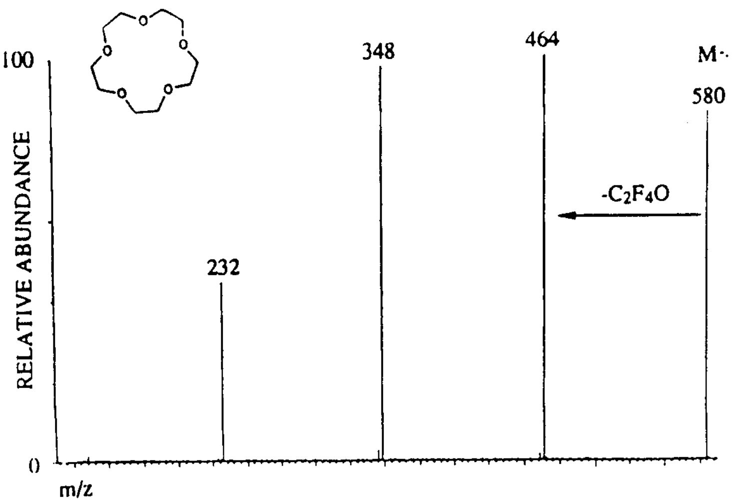


Figure 12. Collisionally activated dissociation mass spectra of the $M^{-\cdot}$ ion of perfluoro [15]crown-5 acquired with a triple quadrupole mass spectrometer.

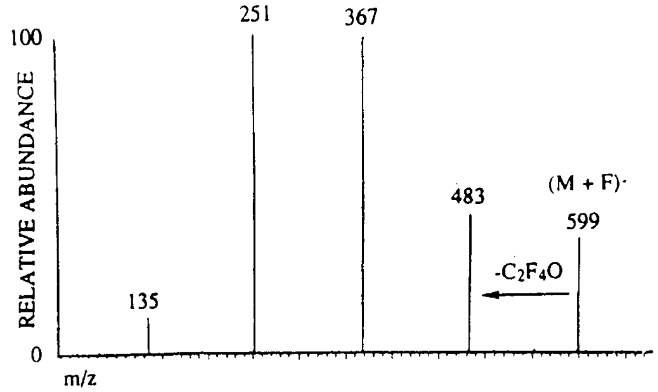
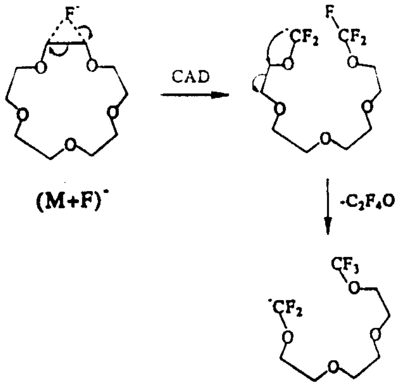


Figure 13. Collisionally activated dissociation mass spectra of the $(M + F)^-$ ion of perfluoro [15]crown-5 acquired with a triple quadrupole mass spectrometer.



Scheme 1. Proposed mechanism for dissociation of the $(M+F)^-$ adduct.

macrocyclic ion. The nature of the binding interactions in these novel types of cluster assemblies is still under investigation.

The ability to form and characterize new types of macrocyclic ion complexes involving perfluoro ethers holds great promise for future studies of host-guest complexation in the gas phase. Comparisons to the gas-phase chemistry of hydrogenated macrocycles may allow further insight into the influence of thermochemical and structural properties on the binding interactions of host molecules. All of the perfluoro crown ethers and perfluorocryptands to date have been found to coordinate O_2^- and F^- as well as some other anions *(24)*.

Mass Spectrometric Characterization by Collisionally Activated Dissociation

The structures of the perfluoro macrocycles were further characterized by CAD mass spectrometric techniques. CAD is a method in which a mass-selected ion undergoes energetic collisions with a neutral target gas, resulting in fragmentation of the ion by structurally diagnostic pathways *(25)*. The acquisition of characteristic CAD spectra is especially important for the interpretation of the gas-phase macrocyclic complexation studies described earlier. For the CAD spectra discussed in this section, a Finnigan MAT TSQ-70 triple stage quadrupole mass spectrometer was operated in both negative and positive ionization modes at a source temperature of 80 °C. For the negative ionization mode, methane or argon was introduced into the source at 1.2 torr to aid in the production of thermal electrons to promote electron capture negative ionization.

Each perfluorinated crown ether produced $(M - F)^+$ ions under positive chemical ionization conditions, likely as a result of elimination of HF from an initial $(M + H)^+$ ion *(26)*. These positive ions dissociate via two routes upon collisional activation. They may eliminate units of C_2F_4O or they may eliminate $(C_2F_2O_2 + nC_2F_4O)$ where n = 0,1,2... In the negative ion mode, the perfluoro crown ethers produce abundant anions, $M^{-\cdot}$, which dissociate by a characteristic series of losses *(26)*. For example, a typical CAD spectrum for perfluoro [15]crown-5 is shown in Figure 12. In general, the molecular radical anion of each perfluoro crown ether dissociates by loss of $n(C_2F_4O)$ units (n = 1,2,3).

The perfluorinated 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (cryptand) dissociates by several pathways that are analogous to those noted for the crown ethers: elimination of nC_2F_4O units are predominant, where n = 1,2,3,resulting in ions at m/z 908, 792, and 676 *(26)*. Additionally, losses of two or three C_2F_4O units in conjunction with C_4F_9N elimination are observed as fragment ions at m/z 559 and 443. These latter fragments are evidence of cleavage at the nitrogen bridge.

The CAD spectra of the molecular anions of two perfluoro dicyclohexyl crown ethers, the [18]crown-6 and [24]crown-8 ethers, also show characteristic fragmentation patterns *(26)*. The CAD spectrum for the first one is shown in Figure 14. For these substituted perfluoro crown ethers, the molecular anions do not dissociate via simple loss of C_2F_4O units as was observed for the other macrocycles. Instead, elimination of $C_6F_{11}^{\cdot}$ (cyclohexyl ring) is a predominant process and may then be coupled with losses of n(C_2F_4O). The first process may be rationalized as a radial-initiated ring cleavage, followed by a fluorine transfer to the cyclohexyl ring via a four-membered transition state. The resulting fragment ion is presumably acyclic. This fragment ion then proceeds to dissociate by consecutive losses of C_2F_4O units. For the [18]crown-6 ether shown in Figure 14, losses of up to three units of C_2F_4O are observed in conjunction with loss of C_6F_{11} (formation of m/z 391, 507, 623, 739). Additionally, loss of 3(C_2F_4O) is observed coupled to the loss of both C_6F_{11}, the first cyclohexyl ring, and C_4F_6, the second cyclohexyl ring, resulting in formation of m/z 229. For the analogous [24]crown-8 system, this latter pathway is coupled instead to the loss of 4(C_2F_4O) units.

Discussion

Two large scale syntheses using solvent reactors of a new design recently developed *(27)* by Lagow and associates at Exfluor Research Corporation have made possible the synthesis of kilogram quantities of perfluoro macrocycles in near quantitative yield. For example, two kilograms of the promising ^{19}F NMR agent perfluoro [15]crown-5 have been recently prepared for a biomedical industrial firm interested in NMR imaging.

Perfluorinated derivatives of hydrocarbon compound usually exhibit different properties than their hydrocarbon analogues. The perfluoro crown ethers are markedly more volatile than the hydrocarbon products. One would expect the dimensions of the pocket size to change and both modeling and crystal structures clearly establish that the pockets are smaller and the crown ether rings are slightly more bent. As observed in the gas phase studies, perfluoro crown ethers and cryptands all coordinate O_2^-, F^- and several other such anions. We have a collaboration with Jean-Marie Lehn at Louis Pasteur University in Strasbourg to explore this anion work on a macroscopic scale. Interestingly, sometime before this discovery, Jean-Marie Lehn had predicted during visits to the Lagow laboratory perhaps as early as 1975 that anions rather than cations would be the most favorable species to encapsulate in perfluorinated crown ethers *(28)*. Although a crystal structure of an encapsulated species is not yet in hand from Professor Lehn 's group, perfluoro crown ethers and cryptands are indeed very weak bases; if there is any base character at all. It would also appear that electron density from the anion is transferred to the binding sites in the crown ether. One would suspect that the binding occurs at the oxygen atoms. As indicated by the fragmentation thermodynamics, there is a 40-60 kcal interaction binding the anion to the macrocycle. Lehn 's insight at such an early date was indeed remarkable.

Whether the perfluoro macrocycles are also capable of binding cations is still not certain. Two talented collaborators on this project have not been successful in obtaining cationic complexes with the alkali metals. One complication was that the perfluoro macrocycles are not soluble in common organic solvents. On the other hand, both organometallic compounds and organic species as well as these perfluoro macrocycles are soluble in chlorofluoro solvents such as Freon 113, F_2ClC-CF_2Cl. It is also quite possible that the base character of such perfluoro macrocycles is nonexistent.

The single crystal X-ray diffraction studies of [18]crown-6 ether indicate that the ring is puckered in a manner so that the oxygen site are exposed and projected toward a metal coordinate site. In view of the possibility of a rigid conformation existing in the solution at lower temperature, the ^{19}F spectrum of perfluoro [18]crown-6 in $CFCl_3$ has been monitored at -85 °C. Only one singlet peak was observed. This fact reveals that the molecule is quite flexible in the solution. The energy barrier associated with the conformational change would be extremely low.

Three crystal structures of perfluoro crown ethers containing the [18]crown-6 ether skeleton are reported. Comparisons of these structures show that the perfluoro [18]crown-6 ether and the cis-syn-cis-dicyclohexyl-isomer have similar conformations of the ether ring skeleton *(29)*. Figure 15 shows the superposition of the carbon and oxygen atoms of the perfluoro -cis-syn-cis-dicyclohexyl[18]crown-6 ether (solid lines) onto the equivalent atoms of perfluoro [18]crown-6 ether (dashed lines) illustrating the similar configuration of the perfluoro ether rings of the two structures. The perfluorocyclohexyl groups may not be the dominating steric factor which controls the conformation of their ether ring skeleton. Distances between oxygen atoms and the center of the molecule, and between adjacent oxygen atoms in both isomer are given in Table II and Table III.

Although perfluoro [18]crown-6 has a melting point of 34 °C in a sealed capillary, the solid compound has a substantial vapor pressure; it can be sublimed easily and moves on a vacuum line. Perfluoro [18]crown-6 has a marked propensity to form large and beautiful single crystals. Crystals weighing at least one half gram which have the appearance of sparkling zircons are obtained routinely. Both the perfluoro [15]crown-5 and [12]crown-4 species are clear liquids with properties favorable for several biomedical applications.

As previously discussed, perfluoro [15]crown-5 has great potential as a ^{19}F NMR imaging agent *(4)*. This crown ether has only one fluorine resonance making very sharp pictures during brain scans and spinal scans of animals possible. Perfluoro [15]crown-5 is also used successfully as an oxygen carrier in collaborative studies between our group and Dr. Leland Clark 's laboratory. Work at Air Products has established that the perfluoro crown ethers are nontoxic in animals and are therefore very different from hydrocarbon crown ethers.

As previously indicated, a sample of over two kilograms in size of perfluoro [15]crown-5 has been made by new technology at Exfluor Research Corporation in Austin, Texas *(27)*. With new reaction technology the yields are on this substance are in the high ninety percent range and large quantities are possible. This opens the possibility of preparing any of the materials in this manuscript on a commercial scale.

The perfluorocryptand[2.2.2] compound is expected to have interesting applications, and we await with great interest further studies of its reaction chemistry.

The synthetic breakthroughs which have been responsible for these macrocycles open the possibility of preparation of many novel crown ether

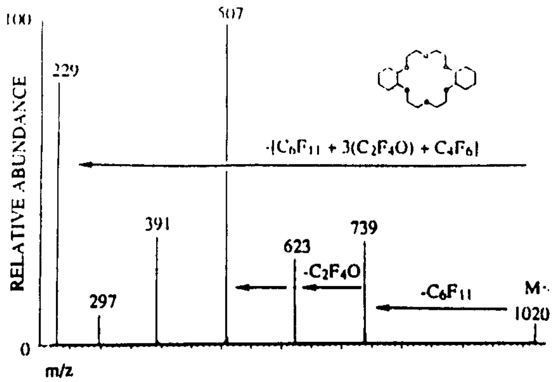


Figure 14. Collisionally activated dissociation mass spectra of the $M^{-\cdot}$ ion of perfluoro dicyclohexyl[18]crown-6 acquired with a triple quadrupole mass spectrometer.

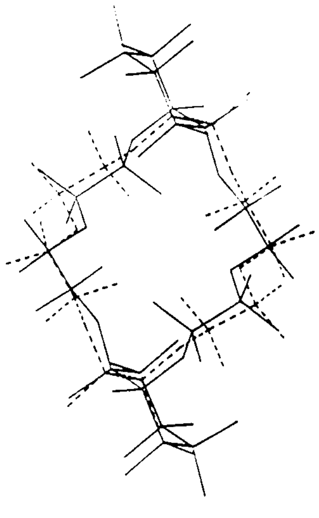
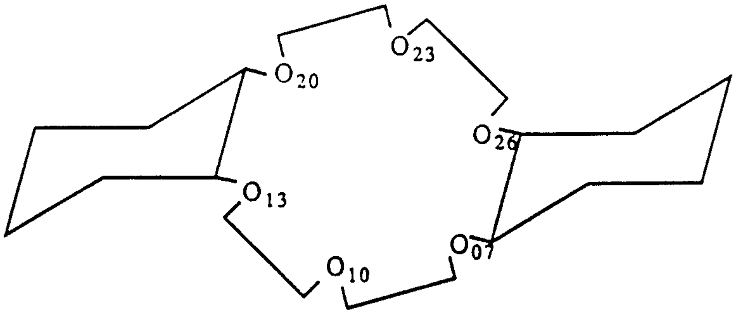


Figure 15. The superposition of the carbon and oxygen atoms of the perfluoro -cis-syn-cis-dicyclohexyl[18]crown-6 ether (solid lines) onto the equivalent atoms of perfluoro [18]crown-6 ether (dashed lines) illustrating the similar configuration of the perfluoro ether rings of the two structures.

Table II. Distances Between Oxygen Atoms and the Center of the Molecule, and Between Adjacent Oxygen Atoms in Perfluoro -cis-syn-cis-Dicyclohexyl-[18]Crown-6 Ether

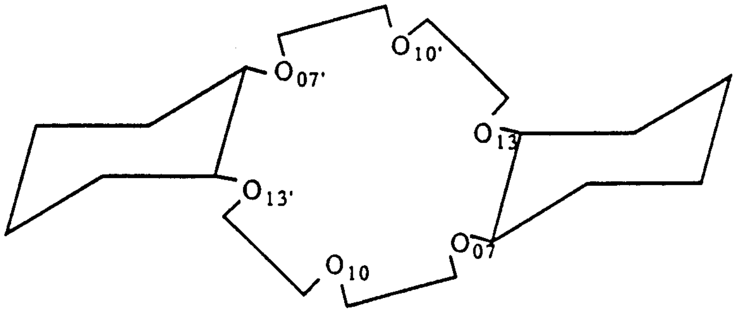


Perfluoro -cis-syn-cis-Dicyclohexyl[18]crown-6 ethers

Oxygen Atoms	Distance to center of molecule
O_{07}	2.536 Å
O_{10}	2.129 Å
O_{13}	3.177 Å
O_{20}	2.543 Å
O_{23}	2.141 Å
O_{26}	3.181 Å

Distances between adjacent oxygen atoms	
O_{13}-O_{20}	2.662 Å
O_{20}-O_{23}	2.713 Å
O_{23}-O_{26}	2.665 Å
O_{26}-O_{07}	2.667 Å
O_{07}-O_{10}	2.707 Å
O_{10}-O_{13}	2.667 Å

Table III. Distances Between Oxygen Atoms and the Center of the Molecule, and Between Adjacent Oxygen Atoms in Perfluoro-cis-anti-cis-Dicyclohexyl-[18]Crown-6 Ether



Perfluoro -cis-anti-cis-Dicyclohexyl[18]crown-6 ethers

Oxygen Atoms	Distance to center of molecule
O_{07}	3.156 Å
O_{10}	2.403 Å
O_{13}	3.332 Å

Distances between adjacent oxygen atoms	
O_{13}-O_{07}	2.702 Å
O_{07}-O_{10}	3.525 Å
O_{10}-O_{13}	2.727 Å

systems as well as the synthesis of the entire series of perfluorocryptands. Such high stability ligands will be much less subject to chemical attack, much less prone to thermal degradation, and as such offer unique properties as ligands.

Acknowledgment

We are grateful for support of this work by the Air Force Office of Scientific Research (F49620-92-J-O104), U.S. Department of Energy (DE-FG05-91ER12119), and NATO (Grant 87006). We also (RJL) acknowledge an Alexander von Humboldt Award (1992).

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(8) This was accomplished during the purification process using preparatory gas chromatography.

(9) Data for perfluoro cis-syn-cis- and cis-anti-cis-dicyclohexyl[18]crown-6 were collected at -75 °C on a Nicolet R3 diffractometer with Mo Kα radiation ($\lambda = 0.7107$ Å) using a graphite monochromator. Perfluoro cis-syn-cis-dicyclohexyl[18]crown-6 is monoclinic, space group C2/c, with a 27.051 (2), b = 10.087 (1), c = 23.526 (3) Å, β = 100.920 (8) °, V = 6303.5 (11) Å^3, with ρ(calc) = 2.15 g cm^{-3} for Z = 8. The structure was solved by direct methods and refined by full-matrix least-squares to R = 0.042, wR = 0.044 using 3959 reflections with Fo > 4(σ(Fo)). Perfluoro -cis-anti-cis-dicyclohexyl[18]crown-6 is also monoclinic, space group C2/c, with a = 32.211 (5), b = 6.0477 (6), c = 18.828 (3) Å, β = 124.782 (9) °, V = 3012.4 (8) Å^3, with ρ(calc) = 2.25 g cm^{-3} for Z = 4. The molecule lies around a crystallographic inversion center. The structure was solved by direct methods and refined by full-matrix least-squares to R = 0.096, wR = 0.11 using 1832 reflections with Fo > 4(σ(Fo)).

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THE SYNTHESIS OF PERFLUOROCYCLOHEXANO -15- CROWN-5 ETHER

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Abstract: Perfluorocyclohexano-15-crown-5 ether, *trans*- (**1**) and *cis*- (**2**) isomers have been prepared by direct fluorination using the LaMar fluorination technique[1]. They have several potential applications and are of special interest in a variety of fields[2].

The discovery of the complexing ability of crown ethers with metal cations by Pederson[3] has had a strong impact on modern chemistry. Since then, there has been a considerable amount of interest in the synthesis and chemistry of crown ethers[4] and cryptands[5]. However, only a few fluorinated macrocycles[6,7,8] and only one perfluoro-cryptand[222][9] have been prepared and studied. Our previous success in this field has led to our current research interest in preparation of perfluoro-crown ethers. An extraordinarily significant application of direct fluorination is in the synthesis of oxygen-containing fluorocarbons that are inaccessible by other techniques.

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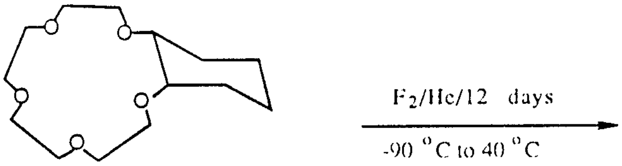
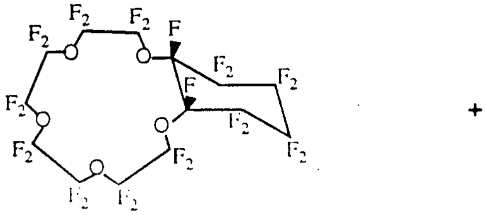
In 1985, W. H. Lin and Lagow[7] reported the first perfluoro-crown ethers and showed strong applications as NMR imaging agents[10]. Recently T. Y. Lin and Lagow[8] reported crystal structures of perfluorodicyclohexano-18-crown-6 ether, the *cis-syn-cis*-(**3**) and *cis-anti-cis*-(**4**) isomers. Three crystal structures of perfluoro-crown ethers, containing the 18-crown-6 ether skeleton, were reported in the publications mentioned above. A comparison of these structures shows that the perfluoro-18-crown-6 ether and (**3**) have similar ether ring skeletons[11]. All cyclohexano groups in both isomers (**3**, **4**) are of the chair form in solid state, but in solution both isomers are fluxional and the assignment of the ^{19}F resonance of the ether rings and cyclohexano groups are very difficult. The isomers of perfluorocyclohexano-15-crown-5 ether reported here are lower in molecular weight and are clear, volatile oils. We have been able to assign the ^{19}F resonance of the cyclohexano groups.

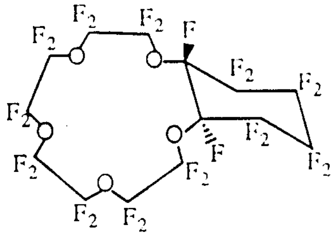
Perfluorocyclohexano-15-crown-5 ether, (**1**) and (**2**) were analyzed by mass spectrometry, ^{19}F NMR and IR. Both isomers show strong *m/e* of 742 and m-C_6F_{11} = 461 with similar ion fragmentation patterns. There are two tertiary fluorines in the expected perfluoro-structure which we inferred that these were two isomers [i.e. (**1**) and (**2**)]. The ^{19}F NMR of these isomers show similar chemical shifts pattern to that of *trans*- and *cis*- perfluorodecalin[12] which clearly establishes the stereochemistry of (**1**) and (**2**). The first major peak collected from the GC is compound (**2**) and the second is (**1**). All cyclohexano groups are in the chair conformation in solution. The perfluoro-cyclohexano structure associated with the perfluoro crown ether ring leads to a complex spectrum and positive assignment of ^{19}F signals of the ether ring is difficult. The ^{19}F NMR chemical shift ($\delta CFCl_3$) for (**1**): -86.7 to -93 ppm (complex), -121.35 ppm (d, 2F), -125.61 ppm (d, 2F), -135.23 ppm (s, 2F), -136.82 ppm (d, 2F), -143.64 ppm (d, 2F), for (**2**) : -87 to -95 ppm (complex), -131.3 ppm (br, 4F), -134.0 ppm (br, 4F), -150.07 ppm (br, 2F). The latter has a fluxional cyclohexano group on the NMR time scale. The infrared spectra has typical perfluoro-ether's absorptions below 1500 cm^{-1}, data for (**1**): 633 (w), 647 (w), 692 (w), 722 (w), 751 (w), 969 (s), 984 (m), 1048 (m), 1189 (s, br), 1193 (s, br), 1317 (m) cm^{-1}; for (**2**) : 633 (w), 661 (w), 714 (w), 720 (w), 762 (w), 972 (s), 1046 (m), 1146 (s, br), 1193 (s, br), 1266 (m, br), 1314 (m) cm^{-1}. The elemental composition was studied with high resolution mass spectroscopy: Chemical ionization negative mode : Calcd. 741.9330, (**1**) found : 741.9306, ppm = 3.3; (**2**) found : 741.9336, ppm = -0.9.



cyclohexano-15-crown-5 ether *trans*- and *cis*- isomers



perfluoro-*cis*-cyclohexano-15-crown-5 ether



perfluoro-*trans*-cyclohexano-15-crown-5 ether

The isomer ratio of the starting material were not available from the manufacturer[13]. The yield ratio of (**1**) to (**2**) is 1 to 0.8. Their boiling points are the same within error limit. Bp. of (**1**) is 199-200 °C and (**2**) is 200-201 °C without calibration. The melting

Table 1

Reaction Parameters for Perfluorocyclohexano-15-crown-5 ether.

Time days	F_2 ml/min	He ml/min	Temp. °C
.5	0	100	-90
1	1	100	-90
1	1	50	-90
1	2	20	-90
1	2	10	-90
1	4	10	-90
1	4	0	-90
1	4	0	-80
1	4	0	-60
1	4	0	-40
1	4	0	-10
1	4	0	RT[a]
1	4	0	40
.5	0	100	40

[a] room temperature

points of (**1**) to (**2**) are between -44 to -46 °C. The melting point of the starting material (mixture of isomers) is below 26 °C[3b], and the boiling point is 110 °C (.001 torr; molecular distillation)[14]. The total yield of (**1**) and (**2**) is 18.5 % but the yields were not optimized.

Experimental

In a typical reaction, 1 gram of the starting material was mixed with 10 grams of dried NaF powder with enough CH_2Cl_2 to make a slush. The solvent was then removed under vacuum and the white powder was evenly dispersed through a 20 mesh screen over copper turning into a disk reactor, a previously described direct fluorination reactor[15]. The system was purged with a 100 ml/min He gas flow overnight at -90 °C. A liquid nitrogen cryogenic device was used to control the temperature. The reaction then proceeded following the reaction conditions in Table 1. After the 12 days of fluorination. Fluorine gas in the system was swept out by He gas. A white powder collected from the disk reactor was placed under vacuum and the volatiles collected into a acetone/dry ice trap. The GC assay of this volatile liquid on a Kel-F column (15% Chromosorb A 60/80, 10 feet x .25 in.) at 100 °C, (isothermal) gave two major peaks with a ratio of 1:0.8. The retention times are 13.45 min. and 15.07 min. for the *cis* (**2**) and *trans* (**1**) isomer, respectively. The hydrocarbon starting material, 15-crown-5 ether, purchased from PCR Chemicals, was dried over 4 Å molecular sieve (Aldrich Chemical Co.) before use. Fluorine gas was technical grade, ordered from Air Products. NaF powder and CH_2Cl_2 were from Fisher Scientific.

Acknowledgment

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Reactions of Perfluorinated Compounds with Ethers: Evidence for Gas-Phase Cationic Polymerization

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Abstract: Evidence for a novel type of gas-phase cationic polymerization process is described. Gas-phase ions consisting of a perfluorinated ion attached to an assembly of cyclic ether or thioether molecules, such as ethylene oxide, ethylene sulfide, and tetrahydrofuran, are formed in the chemical ionization source of a mass spectrometer. The ions contain up to five ether molecules depending on the size of the perfluorinated compound and the nature of the ether involved in the reaction. The highly strained ethylene oxide forms product ions containing the most ether molecules bound to a perfluorinated substrate, whereas the unstrained acyclic dimethyl ether results in product ions containing only a single ether molecule. The experimental results suggest that the cyclic ethers attach to a perfluorinated substrate ion and then undergo ring-opening gas-phase polymerization in the gas phase to form an extended polyether chain which is covalently bound to the perfluorinated substrate. Collisionally activated dissociation techniques were used to further characterize the structures of the ions.

Introduction

The variety of types of gas-phase clusters reported over the past decade has increased as new methods of forming and characterizing clusters have been developed.[1-11] Although much attention has recently focused on the evaluation of carbon cluster chemistry,[10] there also has been growing interest in the loosely-bound organic clusters typified by van der Waals and other molecular aggregates.[1-19] Such clusters, bound by dispersive (induced dipole) and electrostatic interactions, represent an intriguing class of chemical species which may undergo internal reactions that can result in covalently bound ions.[11-19] or may possess properties unlike those of the individual subunits. In this report, the formation and characterization of an unusual array of gas-phase ions consisting of perfluorinated ions bound to multiple ether molecules are described. The polymeric ions are generated through ion–molecule association and condensation reactions in the chemical ionization source of a triple-quadrupole mass spectrometer. As shown herein, examination of the nature of the ethers that form product ions with the perfluorinated substrates supports the proposal that these ions are formed by a new gas-phase ring-opening cationic polymerization process. Cationic polymerization has been reported previously in the gas phase,[11-19] especially for unsaturated molecular substrates such as acetylene, 1,1-difluoroethylene, propene, ethene, isoprene, and benzylacetate, and is a common mechanistic route in solution to produce polymers,[20-27] especially of epoxides and other cyclic ethers. Gas-phase studies of cationic polymerization have provided new insight and a solvent-free perspective of the mechanisms and kinetics of ionic chain growth processes.[11-19]

Perfluorocarbons afford an intriguing yet little studied class of compounds in gas-phase ion chemistry. The synthesis[28] and characterization of perfluorocarbons[29] have developed rapidly over the past two decades because of their unique properties as artificial blood substitutes.[30] Clearly perfluorinated compounds have very different reactive properties than their hydrocarbon counterparts because of the substitution of highly electronegative fluorine atoms for hydrogen atoms. The comparison of gas-phase reactions of perfluorocarbons to those of hydrocarbons provides an illustration of the types of distinctive association reactions that these two related classes of compounds undergo, and may provide insight into new ways to evaluate their novel binding

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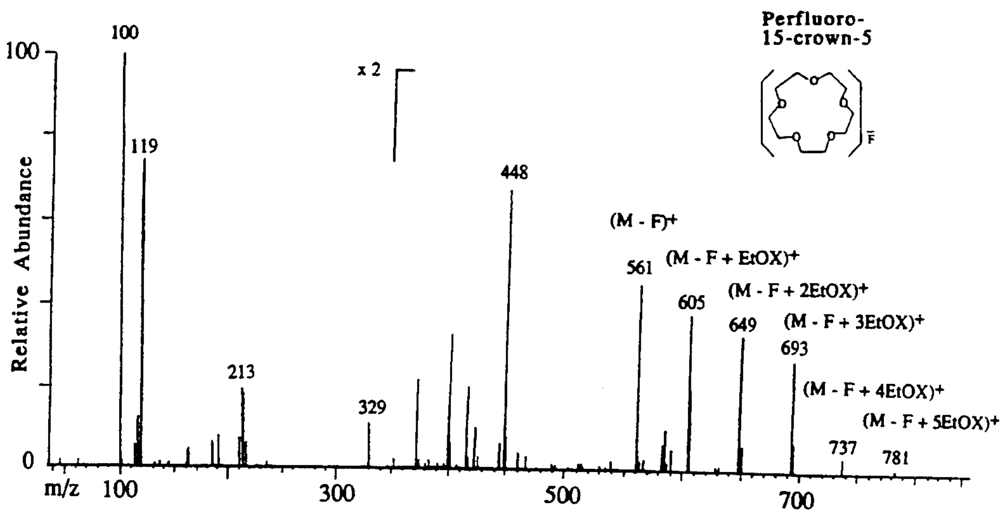

Figure 1. Positive ionization mass spectrum of a mixture of ethylene oxide and perfluoro-15-crown-5.

properties. In this study, collisionally activated dissociation[31] (CAD) techniques are used to characterize the nature of the binding interactions of the ions, although the CAD spectra provide ambiguous information regarding the actual structures of the ions.

Experimental Section

Gas-phase product ions composed of perfluorinated ions condensed with various ether neutrals were formed via ion–molecule reactions in the chemical ionization source of a Finnigan TSQ-70 triple-quadrupole mass spectrometer. The ether neutrals were introduced into the source through a gas chromatographic inlet, and the pressure was varied from 2×10^{-6} to 1×10^{-5} Torr in the manifold, corresponding to 2–6 Torr in the chemical ionization ion volume, for optimal product formation. Perfluoro compounds were admitted via a variable leak value to attain a manifold pressure of about 3×10^{-6} Torr. The source temperature was 50 °C. Higher source temperatures were avoided to prevent thermal decomposition of the perfluoro compounds. Under these conditions, the typical abundances of the product ions, $(M-F + n\text{Ether})^+$ relative to the $(M-F)^+$ ions were 5–40% or more depending on the number and type of ether reagent used.

The structures of the product ions were characterized by using low-energy collisionally activated dissociation techniques.[31] A product ion was mass-selected with the first quadrupole, then accelerated into the second quadrupole, which was filled with an inert collision gas. The collision energy in the laboratory frame was 10 eV, and argon was used as the collision gas at 2 mTorr in the second quadrupole. The fragment ions resulting from the collisional activation process were mass-analyzed in the third quadrupole.

The perfluorinated ethers examined included perfluoro-12-crown-4, perfluoro-15-crown-5, perfluorotriethylene glycol monomethyl ether (perfluorotriglyme), and perfluoro-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane(perfluorocryptand). These compounds were synthesized by the LaMar direct fluorination procedure.[28] Perfluorodecalin, 15-crown-5, and the ether reagents were obtained from Aldrich Chemical Co. (Milwaukee, WI) and used without further purification. Dimethyl ether was obtained from MG Industries. Ethylene oxide was obtained from Wilson Supplies.

Results and Discussion

Formation of Cluster Ions. In the positive ionization mode, perfluoro compounds by themselves typically form abundant $(M-F)^+$ ions and related fragment ions,[32] but not molecular ions $M^{\bullet+}$. Upon addition of various ether neutrals to the ion source, product ions identified as $(M-F + n\text{Ether})^+$ are formed. For each pair of perfluorinated compounds and ether reagents, the total relative contribution of these unusual product ions is 5–15% compared to the sum of the molecular-type ions and fragment ions of the perfluorinated substrate. A representative spectrum of the products formed from reactions of one perfluorinated compound, perfluoro-15-crown-5, and ethylene oxide (EtOx) is shown in Figure 1. A series of product ions assigned as $(M-F + n\text{EtOx})^+$ extends from $n = 0$ to $n = 5$ units. The ions at *m/z* 100, 119, 213, and 329 are common fragments of the perfluorinated ether $(M-F)^+$ molecular ion. The ions at *m/z* 329 and 213 are attributed to loss of one or two C_2F_4O units, respectively, whereas the ions at *m/z* 100 and 119 likely involve loss of $C_2O_2F_3$ or $C_2O_2F_2$ in conjunction with C_2F_4O units. The results obtained for the formation of ethylene oxide products with other perfluorinated substrates, including both perfluorinated cyclic and acyclic ethers and one perfluorinated alkane (decalin) are summarized in Table I. All of the perfluoro compounds form products with multiple units of ethylene oxide, and in each case, the products may be assigned as $(M-F + n\text{EtOx})^+$. One nonfluorinated substrate (hydro-15-crown-5) was also examined but formed no products with the ethers.

Table I. Formation of Ethylene Oxide Product Ions[a]

	percent of product ion current: $(M-F + n\text{EtOx})^+$					
substrate	$n = 0$	$n = 1$	$n = 2$	$n = 3$	$n = 4$	$n = 5$
perfluoro-12-C-4	50	25	10	10	5	0
perfluoro-15-C-5	30	25	20	20	<5	<2
perfluoro-18-C-6	35	20	25	10	5	5
perfluorotriglyme	65	20	10	<5	<2	<2
perfluorocryptand	40	15	10	25	5	5
perfluorodecalin	75	15	5	5	0	0

[a] Values rounded to the nearest 5%.

Reactions of the perfluoro compounds with a variety of other ether or thioether neutrals, such as ethylene sulfide, tetrahydrofuran, cyclohexene oxide, diethyl ether, dimethyl ether, and butadiene monoxide, were also evaluated to compare the product formation properties of these ethers. The results are summarized in Table II for reactions with perfluoro-15-crown-5. In each case, the pressure of the reactive ether was varied to promote optimal product formation in the ion source. Of all the ethers examined, the small cyclic ether ethylene oxide forms the most extensive array of products with the perfluorinated compounds, whereas its thioether analog, ethylene sulfide, demonstrates the second most abundant product formation. Reactions with ethylene sulfide result in addition of one, two, or three units, but not four or five units as observed for the ethylene oxide products. A larger cyclic ether, tetrahydrofuran (THF), shows a strong

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Table II. Extent of Cluster Formation with Perfluoro-15-crown-5

ether	number of ether molecules attached
ethylene oxide	$n = 1, 2, 3, 4, 5$
ethylene sulfide	$n = 1, 2, 3$
tetrahydrofuran	$n = 1, 2$
cyclohexene oxide	$n = 1, 2$
diethyl ether	$n = 1$
dimethyl ether	$n = 1$
butadiene monoxide	$n = 1, 2$
NH_3	$n = 1$
2-methylaziridine	$n = 1$
CH_4	$n = 0$
H_2O	$n = 1$

preference for attachment of two ether units to the perfluorinated compounds (*i.e.* typically the ratio $(M-F + 2THF)^+:(M-F + THF)^+$ is 20:1), but in fact does not promote formation of products containing more than two THF units. Butadiene monoxide shows limited product formation, such that the products containing one butadiene monoxide unit appear to be 5–20 times more abundant than those products containing two units, but products with three or more butadiene monoxide units are not observed. The acyclic ethers, diethyl ether (DEE) and dimethyl ether (DME), attach once to the perfluorinated ions, but larger products are not observed.

Further experiments indicated that products are only formed when the ether unit contains an electronegative sulfur or oxygen heteroatom because simple hydrocarbon molecules, such as methane, do not associate with the perfluorinated ions (see Table II). Additionally, certain amines are not effective in the ion–molecule association reactions with the perfluorinated ions. The perfluorinated substrates may attach a single unit of ammonia, forming $(M-F + NH_3)^+$, but further association is not observed. Likewise, reactions with the strained cyclic amine 2-methylaziridine, a nitrogen-containing analog to ethylene oxide, result in attachment of only one amine molecule, producing $(M-F + \text{2-methylaziridine})^+$. The latter result suggests that these amines are in some way chemically nonreactive toward product formation.

Cyclohexene oxide is unusual in that it forms products with one or two cyclohexene oxide units in conjunction with losses of 26 amu (apparently loss of C_2H_2). The results for cyclohexene oxide formation are summarized in Table III.

In all cases, the reactions of the reactive ethers with nonfluorinated analogs to the perfluorocarbons, such as hydro-15-crown-5 and decalin, fail to produce product ions. This contrasting result highlights the importance of the highly electronegative nature of the perfluorinated substrates in selectively promoting the reactions.

With respect to the structures of the products, these initial results may be interpreted in two ways. First, each ether unit may be attached separately to the perfluoro substrate, such that there is a "cloud" of ether units surrounding each $(M-F)^+$ ion. This description is consistent with the model that the products consist of a loose electrostatically-bound van der Waals assembly of ether molecules around a central perfluorinated ion.

Altenatively, the spectra may suggest a growing polymer chain of ether units anchored to the perfluorinated substrate. A mechanism is shown in Scheme I which may conceptually represent the gas-phase cationic polymerization process. As shown, ethylene oxide attaches to the electropositive carbonium ion site of the perfluorinated substrate. This product ion presumably may rearrange to a more stable secondary carbonium ion or may continue to propagate via attack of a second ethylene oxide molecule via an S_N2-type reaction. Two conjectures regarding the limit of polymerization are offered. Eventually the cationic terminus may be stabilized by interaction with the electron-rich perfluorinated substrate, by a type of "self-solvation", resulting in termination of polymerization. Alternatively, the polymerization may terminate when the cationic tail becomes too spatially distant from the activating fluorocarbon substrate. For this latter reason, the larger perfluorinated compounds would thus tend to promote a correspondingly longer polymerization sequence due to their greater electrostatic polarizability. Because the ether molecules by themselves do not undergo spontaneous ring opening and polymerization in the gas phase (as shown later experimentally), we speculate that interaction with an $(M-F)^+$ ion provides an *activating catalytic site* to initiate the polymerization process. The following sections explore in greater detail rationalizations for each of the two hypotheses.

Evidence for Gas-Phase Cationic Polymerization vs van der Waals Cluster Formation. The dipole moments of the various ethers were examined to correlate the electrostatic properties of the ethers with product formation (see Table IV). Presumably the ethers with the highest dipole moments may result in the most extensive van der Waals-type clusters due to their enhanced electrostatic interactions with the electropositive $(M-F)^+$ ions. This hypothesis appears to be a reasonable explanation for the great clustering abilities of ethylene oxide and ethylene sulfide, each of which have dipole moments larger than 1.8 D.[18] However, it fails to explain the absence of products for H_2O (dipole moment 1.85 D) or NH_3 (dipole moment 1.47 D). This lack of correlation erodes support for the hypothesis that the products are van der Waals clusters.

From the preliminary results involving different ether units, the most highly strained cyclic ethers, such as ethylene oxide, result in the most extensive formation of products containing multiple ether units. Conversely, the acyclic ethers do not participate in these types of reactions. It is difficult to formulate a reason why this factor would affect the formation of van der Waals clusters, but an explanation related to polymerization processes is obvious. This effect may be related to the fact that the cyclic structures possess ring strain which specifically promotes ring-opening polymerization. This idea clearly explains the failure of NH_3 and H_2O, both of which have high dipole moments but lack sufficient covalent backbone structure, to react with the $(M-F)^+$ ions. None of the acyclic ethers would polymerize, and the larger cyclic ethers which are less strained would be correspondingly less reactive compared to ethylene oxide. Steric factors which would tend to inhibit polymerization are also suggested by the reduced cluster formation for the bulkier ethers, such as cyclohexene oxide and tetrahydrofuran.

Some of the most convincing evidence in support of the cationic polymerization hypothesis is obtained from examination of the product spectra for the reactions of cyclohexene oxide (CxO) with the perfluorinated substrate ions. These reactions result in formation of the unusual ions identified as $(M-F + CxO - n26)^+$ products (Table III) where 26 Da must represent C_2H_2, suggesting that the association reactions are sufficiently exothermic to cause covalent bond rupture within the cyclohexene oxide units. This behavior is incompatible with that expected for formation of van der Waals clusters held by only weak electrostatic interactions, but is consistent for ions formed through a gas-phase eliminative polymerization process[12-13] in which new covalent bonds are formed as the polymer chain is propagated.

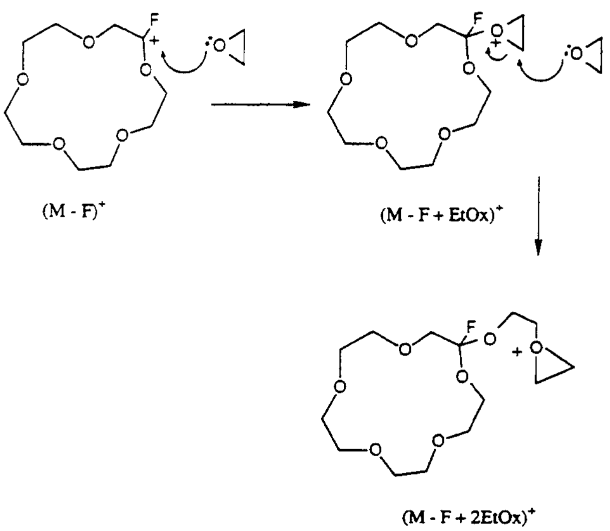
The observations described above lend greater support to the proposal that the product ions are formed by gas-phase cationic polymerization rather than by van der Waals clustering. Several more experiments described in the following sections were done to further elucidate the nature of the reactions.

Pressure Dependence of Product Formation. The selectivity of product formation was evaluated by the examination of product distributions at variable ether reagent pressure. Shown in Table V are the product distributions for the ethylene oxide/perfluorotriethylene glycol dimethyl ether system at two different ethylene oxide pressures. The products containing more ethylene oxide units are favored at the higher ethylene oxide pressure, but even at the higher ethylene oxide pressure, addition of six or more

Table III. Formation of Cyclohexene Oxide (CxO) Product Ions

	percent of product ion current: cluster formula					
substrate	$(M-F)^+$	$(M-F + CxO)^+$	$(M-F + CxO - 26)^+$	$(M-F + CxO - 26 - 26)^+$	$(M-F + 2CxO)^+$	$(M-F + 2CxO - 26)^+$
perfluoro-15-C-5	50	10	5	30	5	0
perfluoro-18-C-6	55	5	10	30	0	0
perfluorotriglyme	65	10	5	15	0	5

Scheme I. Proposed Mechanism for Gas-Phase Polymerization of Perfluoro-15-crown-5[a]



[a] The multiple fluorine atoms attached to the polyether skeleton are omitted.

Table IV. Dipole Moments of Ethers[a]

ether	dipole moment (D)
ethylene oxide	1.89
ethylene sulfide	1.85
tetrahydrofuran	1.63
diethyl ether	1.15
dimethyl ether	1.30
NH_3	1.47
CH_4	0
H_2O	1.85

[a] From ref 33.

Table V. Cluster Formation of Perfluorotriglyme at Variable Ethylene Oxide Pressure

pressure of EtOx (Torr)[a]	percent of ion current of major ions formed: $(M-F + n\text{EtOx})^+$					
	$n = 0$	$n = 1$	$n = 2$	$n = 3$	$n = 4$	$n = 5$
0.5	65	20	10	3	2	0
1.1	15	4	40	30	5	4

[a] Nominal pressure measured in the ion source.

ethylene oxide units is not observed. This suggests that polymeric product formation is not merely a pressure-dependent function but also has a limit dependent on the size or geometry of the perfluoro substrate and/or the kinetics of competing chain termination reactions. For example, as shown in Table I, perfluoro-12-crown-4 can accommodate no more than four ethylene oxide molecules, and perfluorodecalin can accommodate only three ethylene oxide molecules. In fact, the perfluorinated ions may act as size-selective catalysts for cationic polymerization.

Intrinsic Clustering Capabilities of Ethers. The ion–molecule reactions of each ether alone were also examined to determine whether the ethers will polymerize spontaneously in the gas phase or whether they require an activating catalyst (such as a fluorocarbon) in order to polymerize. These results are summarized in Table VI. Most of the ethers form proton-bound dimers at 1 Torr in the chemical ionization source, but none show the extensive association observed in the presence of the perfluoro ions. Proton-bound dimers are commonly observed at high pressures in an ion source; the unusual perfluoro/ether polymer-type ions described in this report, however, involve no proton interactions and thus are of a very different nature than any simple proton-bound adduct. These results suggest that the perfluoro substrates indeed *selectively* promote the polymerization process.

Table VI. Mass Spectra of Ethers in a Chemical Ionization Source[a]

	percent of ion current of major ions observed				
ether	$M^{\cdot+}$	$(M + H)^+$	$(2M + H)^+$	$(3M + H)^+$	related fragments
butadiene monoxide	0	50	0	0	50
ethylene sulfide	30	40	5	0	25
tetrahydrofuran	0	50	40	0	5
cyclohexene oxide	10	20	20	5	50
ethylene oxide	10	80	<5	0	5

[a] At 1 torr of ether pressure; nominal pressure measured in the ion source.

Collisionally Activated Dissociation of Polymeric Product Ions. Collisionally activated dissociation techniques were used to characterize the structures of the polymeric product ions. A representative CAD spectrum is illustrated in Figure 2, and Table VII summarizes the CAD spectra obtained for the $(M-F)^+$ ion of perfluoro-15-crown-5 and its various ethylene oxide products $(M-F + n\text{EtOx})^+$. The bare $(M-F)^+$ ion dissociates by loss of one or two C_2F_4O units (formation of 329^+ and 213^+, respectively) or by elimination of $C_6O_2F_{14}$, resulting in a dicarbonyl fluoroether fragment ion at *m/z* 191. In contrast, the $(M-F + n\text{EtOx})^+$ product ions predominantly fragment by loss of one of more ethylene oxide units, with low abundances of fragment ions analogous to dissociation of the bare $(M-F)^+$ ion also observed. For each product ion, the loss of one ethylene oxide unit is favored over the loss of two or more units. Apparently fragmentation of the polymer chain is kinetically favored over the disruption of the macrocyclic structure. It is well-recognized that many types of polymer ions dissociate by elimination of a sequence of monomer units,[34] in many respects analogous to the series of ethylene oxide units observed in the CAD spectra shown herein. Thus, the CAD spectra are consistent with the behavior expected for dissociation of polymeric structures. However, electrostatically-bound cluster ions also tend to dissociate by elimination of a series of monomer units, so the CAD spectra are rather ambiguous in distinguishing the nature of the ion structures. CAD spectra could not be acquired for all of the product ions due to the relatively low abundance of some of the ions.

Cationic Polymerization in Solution. A comparison between cationic polymerization in solution and the present gas-phase results provides insight into their similarities and thus potentially gives many feasible explanations for some of the features observed in these gas-phase results. Ring-opening polymerization processes based on cationic mechanisms have been studied for years in solution[24-27] and are routinely used in industrial processes. The generally accepted initiation and propagation steps for polymerization of epoxides, cyclic ethers, lactones, lactams, and other cyclic monomers containing heteroatoms involve S_N2 processes

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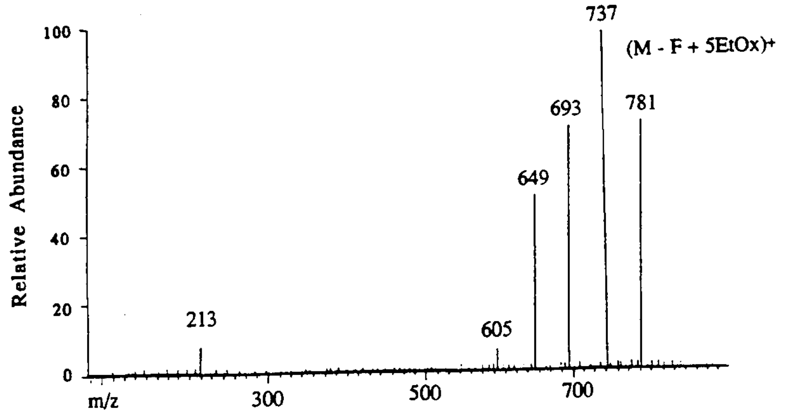


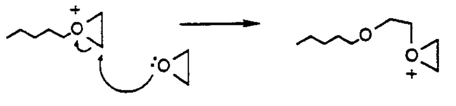
Figure 2. CAD spectrum of the (perfluoro-15-crown-5–F + 5EtOx)$^+$ product, *m/z* 781.

Table VII. CAD Spectra of the Perfluoro-15-crown-5 Product Ions

	percent of ion current of major fragment ions							
precursor ion	191^+	213^+	329^+	$-C_2H_4O$	$-2C_2H_4O$	$-3C_2H_4O$	$-4C_2H_4O$	others
$(M-F)^+$	20	45	15	na[a]	na	na	na	20
$(M-F+2C_2H_4O)^+$	20	40	10	30	0	na	na	10
$(M-F+3C_2H_4O)^+$	5	35	10	30	5	0	na	5
$(M-F+4C_2H_4O)^+$	<2	5	<2	50	30	10	0	5
$(M-F+5C_2H_4O)^+$	0	<2	0	45	30	20	5	<2

[a] na: not applicable because a sufficient number of C_2H_4O units are not available in the ion to allow this loss.

in which a heteroatom of a monomer molecule promotes nucleophilic attack on an electron deficient α-methylene group of the polymeric ion,[26–27] as illustrated here for an oxonium ion.



The addition causes ring opening and concomitant chain growth. Often cationic initiators, such as boron trifluoride, tin tetrachloride, or various other Lewis acids, are used.[26] Termination of the process is typically attributed to an intramolecular reaction, for example, forming a stable macrocyclic ion.[26–27] The mechanism proposed in Scheme I seems feasible in light of the accepted mechanism in solution. Moreover, the same type of self-termination may be reasonable, although not provable, for the gas-phase reactions.

It is known that the ring strain of the monomer is the single most influential factor and thus the driving force for determining the extent of polymer chain growth in solution.[25–27] For instance, tetrahydropyran does not polymerize, tetrahydrofuran shows limited polymerization, and ethylene oxide polymerizes extensively. This reactivity trend agrees with the gas-phase results described in Table III (*i.e.* compare ethylene oxide to tetrahydrofuran). Accurate quantitation of the trend is not possible due to the difficulty in monitoring the gas-phase concentrations of the extremely volatile ethers in the ionization source.

The presence of methyl or other alkyl groups on the cyclic monomers is also unfavorable for polymerization in solution because they restrict the rotation of the polymer and thus reduce its entropy.[26] Moreover, substitution of sulfur heteroatoms for oxygen heteroatoms in the monomer units reduces the strain energy of the ring system and thus decreases polymerizability.[26] Although nitrogen heterocycles have strain energies and thus polymerizabilities similar to their oxygenated counterparts,[26] methyl substitution at one of the ring carbon atoms greatly disrupts polymerization. Each of these factors observed in solution is mimicked in the gas-phase results. Ethylene sulfide and 2-methylaziridine are less reactive than ethylene oxide, likely due to the sulfur heteroatom and methyl-substituent effects, respectively.

Temperature studies of polymerization have shown two predominant effects. As the temperature is raised, the rate of polymerization generally increases, but the degree of polymerization and overall conversion efficiency typically decrease due to the faster rates of competing termination reactions.[25] Temperature studies are not possible for the gas-phase experiments; however, the pressure study described in an earlier section tends to parallel the general effect seen in solution because the collision frequencies and therefore rates are greater at higher pressures in the gas phase. The contributions due to the competing polymerization and termination processes on the product distributions cannot be distinguished, yet this combined effect may explain the failure of the fluorocarbon ions to promote unlimited polymerization, even at higher pressures.

Conclusions. In summary, evidence suggests that a novel class of polymeric products consisting of a perfluorinated ion $(M-F)^+$ and multiple ether molecules has been identified. The highly electronegative nature of the fully fluorinated substrate promotes the cationic polymerization process. A reasonable proposal for the mechanism of formation of the product ions is that they result from initial addition of a neutral ether unit to a $(M-F)^+$ ion which has an activating electropositive carbonium ion site surrounded by many electronegative fluorine atoms. The subsequent mechanism of propagation of the larger ions represents a case of gas-phase ring-opening cationic polymerization, in which each ether unit is added to the growing polyether chain anchored to the perfluorinated substrate.

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Synthesis and Chemistry of Perfluoro Macrocycles

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Abstract: The perfluoro macrocycles perfluoro-18-crown-6, perfluoro-12-crown-4, perfluoro-15-crown-5, perfluorocyclohexano-15-crown-5, perfluorodicyclohexano-18-crown-6, perfluorodicyclohexano-24-crown-8, and perfluoro-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane (perfluorocryptand [222]) have been prepared by carefully controlled elemental fluorination. Although they are much weaker bases than their hydrocarbon analogues, these perfluoromacrocycles are very stable materials which should have a number of applications. The crystal structures of perfluoro-18-crown-6 and of a perfluorodicyclohexano-18-crown-6 isomer are reported. Gas-phase studies with several perfluoro crown ethers and with the perfluorocryptand [222] have shown that such macrocycles tenaciously bind O_2^- and F^-. Perfluoro crown ethers and cryptands coordinate anions preferentially over cations. The collisionally activated mass spectra of several perfluoro macrocyclic ions are described.

Introduction

Since Pederson[1] first discovered the complexing power of crown ethers, the role of macrocycles has become more important in understanding the principles of host–guest chemistry in molecular recognition.[2,3] Cryptands were prepared by Lehn and co-workers[4] and have been studied extensively by Lehn and others. As is well-known, these are a very useful class of ligands which form very stable complexes with numerous metal cations. The preparation of new crown ethers is important because crown ethers have many applications in research laboratories and industry. Crown ethers not only complex with cations but also complex with neutral molecules.[5] Many important applications derive from their complexing ability with alkali metals[6] and their catalytic effect on chemical reactions.[7-9] Lehn first reported the coordination of a fluoride ion in a macrocycle.[10] Recently, Farnham and co-workers prepared a fluorinated macrocyclic compound complexed with a fluoride anion.[11] The fluoride ion is held within the chiral cavity and interacts with four ethylene (CH_2) groups. In both cases the fluoride ions are held in place by hydrogen bonding and coordinate the hydrogen atoms bound to the central ring.

Perfluoro crown ethers have been synthetically inaccessible by conventional reactions of fluorocarbons and outside the capability of synthesis using selective fluorination reagents. The first examples of this potentially useful class of macrocycles have been prepared in our laboratory. These syntheses have been accomplished using the La Mar process, a broadly applicable technique for controlling reactions of elemental fluorine.[12] All reactions were conducted in the previously described cryogenic fluorination reactor.[12,13] Perfluoro crown ethers were expected to be unusually stable. The reactions to produce perfluoro macrocycles are illustrated in Figure 1. Perfluoro crown ethers have applications in biomedical technology and may have applications in catalytic chemistry and perhaps as oxygen carriers.

Experimental Section

The starting hydrocarbon crown ethers were dried using a molecular sieve (4 Å) or purified by distillation or recrystallization before use. In a typical experiment of 18-crown-6, 15-crown-5, and 12-crown-4, 0.81 g of 18-crown-6 and 2.09 g of NaF were ground to a fine powder and mixed well in a drybox. We found for these experiments that several factors influenced the yield obtained: the surface area exposed to fluorine, the reaction temperatures, the reaction time, and the fluorination conditions. The surface area variable was particularly important. To increase the surface area, sodium fluoride was used as solid support upon which the starting crown ether was coated. A second function of this sodium fluoride was to react with the hydrogen fluoride produced as the reaction proceeds. It is also important to dry carefully the crown ether starting materials. If this is not done or the sodium fluoride support is not provided, the yields are drastically reduced.

The mixture was placed in a nickel boat inside a bucket reactor[12] and loaded into a fluorination system. A trap was placed after the reactor which was used to collect the volatile products. After a He purge was maintained for at least several hours, the reactor and trap were cooled to –78 °C. The fluorination reaction was started and followed conditions similar to those shown in Table 1. After the reaction, He was passed through the reactor to sweep fluorine from the system.

Volatile products or by-products produced were transferred from the –78 °C trap to a vacuum line for fractionation. Fractions were obtained that stopped in traps at –23 and –78 °C. The –23 °C fraction was further separated into three components using a gas chromatograph with a 25-ft × 0.25-in., 10% QF-1, chromosorb P column. Mass spectra of 18-crown-6, 15-crown-5, and 12-crown-4 were taken with a Bell & Howell Model 21–491 low-resolution spectrometer at 70 eV at 250 °C, unless otherwise specified.

Perfluoro-18-crown-6. The major component was identified as perfluoro-18-crown-6 ether. Perfluoro-18-crown-6 was a volatile colorless crystalline solid with a melting point of 34 °C, obtained in 33% yield (0.71 g based on starting 18-crown-6). Elemental analyses were consistent with $C_{12}F_{24}O_6$. Calcd: C, 20.71; F, 65.60. Found: C, 20.90; F, 65.35. The vapor-phase IR spectrum exhibited bands at 1240 (vs), 1220 (vs), 1140 (vs), and 730 (m) cm^{-1}. The ^{19}F NMR (C_6F_6 solution) contained a singlet at –91.0 ppm from external $CFCl_3$. The ^{13}C NMR (C_6F_6 solution) also contained a singlet which was observed at 114.9 ppm from

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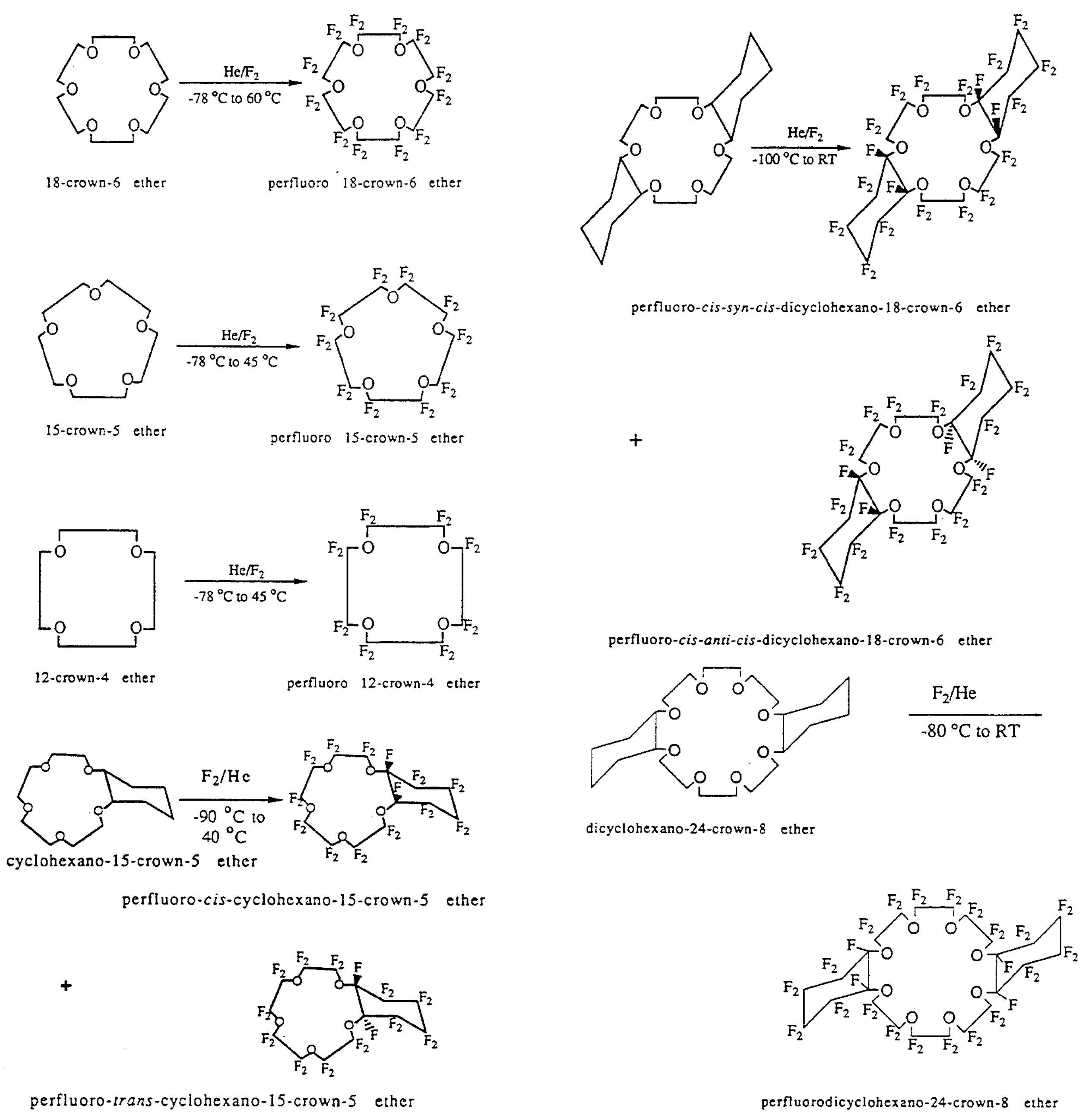

Figure 1. Reaction scheme for all compounds.

Table 1. Fluorination Parameters for 18-Crown-6

t, h	He, cm^3/min	F_2, cm^3/min	T, °C
16	60	0	−78
23	40	1.0	−78
24	20	1.0	−78
24	10	1.0	−78
24	10	3.0	−78
24	0	1.0	−78
36	0	2.0	−78
29	0	2.0	RT[a]
24	0	2.0	45
47	0	2.0	60
24	60	0	60

[a] RT = room temperature.

external TMS. The mass spectrum (with the spectrometer cooled to ambient temperature) gave no parent peak, but instead, a peak at m/e 677 was observed which corresponded to the molecular ion minus one fluorine. Other prominent peaks included m/e 630 ($C_{11}F_{22}O_5^+$), 564 ($C_{10}F_{20}O_4^+$), 445 ($C_8F_{15}O_4^+$), 332 ($C_6F_{12}O_2^+$), 313 ($C_6F_{11}O_2^+$), 213 ($C_4F_7O_2^+$), 185 ($C_3F_7O^+$), 119 ($C_2F_5^+$, base peak), 100 ($C_2F_4^+$), 69 (CF_3^+), and 50 (CF_2^+). The remaining two fractions from the GC separation were identified as $CF_3O(CF_2CF_2O)_4CF_3$ (40 mg) and $CF_3CF_2O(CF_2CF_2O)_4CF_3$ (22 mg) (see Table 2). These are reaction by-products, straight chain perfluoropolyethers, resulting from the ring system cleavage. The separations of 15-crown-5 and 12-crown-4 were performed in a similar manner.

Perfluoro-15-crown-5 Ether. A 17.9% yield (0.503 g) of perfluoro-15-crown-5 was obtained from the reaction of 1.06 g of 15-crown-5, accompanied by three major fragment products (see Table 2). Perfluoro-15-crown-5 has a boiling point of 146 °C and a freezing point of −11.5 C (Calcd for $C_{10}F_{20}O_5$: C, 20.71; F, 65.50. Found: C, 20.90; F, 65.04). The IR spectrum gave bands at 1250 (s, sh), 1228 (vs, sh), 1158 (vs, sh), and 745 (m) cm^{-1}. The ^{19}F NMR showed a singlet at −91.8 ppm from $CFCl_3$. The ^{13}C NMR consisted of a singlet at 114.9 ppm from TMS. The mass spectrum contained the following peaks: m/e 580 ($C_{10}F_{20}O_5^+$, P), 561 ($C_{10}F_{19}O_5^+$, P − F), 448 ($C_8F_{16}O_3^+$), 329 ($C_6F_{11}O_3^+$), 215 ($C_4F_8O^+$), 213 ($C_4F_7O_2^+$), 185 ($C_3F_7O^+$), 119 ($C_2F_5^+$, base peak), 100 ($C_2F_4^+$), 97 ($C_3F_7O^+$), 85 (CF_3O^+), 69 (CF_3^+), 50 (CF_2^+), 47 (CFO^+).

Perfluoro-12-crown-4 Ether. A 0.93 g of 12-crown-4 reacting with elemental fluorine yielded 0.88 g of perfluoro-12-crown-4. The reaction yield was 35%. The principal by-products isolated were $CF_3O(CF_2CF_2O)_2CF_3$ and $CF_3CF_2O(CF_2CF_2O)_2CF_3$ (see Table 2). Perfluoro-12-crown-4 has a boiling point of 118 °C, and the freezing point is −64

Table 2. Characterizations of Straight Chain Perfluoropolyethers

compound (highest m/e in mass spectrum)	assigned ^{19}F chemical shift, ppm (vs ext. $CFCl_3$)	relative intensities	
		obsd	theor
1. $CF_3OCF_2CF_2OCF_2CF_2OCF_3$			
a b c c b a	a = –58.5	1.5	1.5
367 ($C_6F_{13}O_3$, P-F)	b = –93.2	1.1	1.0
	c = –91.1	1.0	1.0
2. $CF_3CF_2OCF_2CF_2OCF_2CF_2OCF_3$			
a b c c c c d	a = –58.3	1.4	1.5
417 ($C_7F_{15}O_3$, P-F)	b = –93.0	1.0	1.0
	c = –91.0	4.4	4.0
	d = –89.7	1.5	1.5
3. $CF_3CF_2OCF_2CF_2OCF_2CF_2OCF_2CF_3$			
a b b b b b b a	a = –89.9	1.0	1.0
467 ($C_8F_{17}O_3$, P-F)	b = –91.0	2.1	2.0
4. $CF_3O[CF_2CF_2OCF_2CF_2OCF_2CF_2O]CF_3$			
a b c c c c b a	a = –58.1	1.5	1.5
483 ($C_8F_{17}O_4$, P-F)	b = –92.0	1.0	1.0
	c = –90.9	2.2	2.0
5. $CF_3CF_2O[CF_2CF_2OCF_2CF_2OCF_2CF_2O]CF_3$			
a b c c c c c c d	a = –58.0	1.2	1.5
(533 ($C_9F_{19}O_3$, P-F)	b = –92.7	1.0	1.0
	c = –90.8	5.2	6.0
	d = –89.6	1.2	1.5
6. $CF_3O[CF_2CF_2OCF_2CF_2OCF_2CF_2OCF_2CF_2O]CF_3$			
a b c c c c c c b a	a = –58.3	1.5	1.5
599 ($C_{10}F_{21}O_5$, P-F)	b = –93.0	1.0	1.0
	c = –91.0	2.9	3.0
7. $CF_3CF_2O[CF_2CF_2OCF_2CF_2OCF_2CF_2OCF_2CF_2O]CF_3$			
a b c c c c c c c c d	a = –58.0	1.4	1.5
599 ($C_{10}F_{21}O_5$, P-CF_3)	b = –92.7	1.0	1.0
	c = –90.6	8.0	8.0
	d = –89.4	1.3	1.5

°C (Calcd for $C_8F_{16}O_4$: C, 20.71; F, 65.50. Found: C, 20.99; F, 65.18). The IR spectrum showed bands at 1260 (vs, sh), 1212 (vs, sh), 1188 (vs, sh), 1160 (vs, sh), 1080 (m), 825 (w), and 745 (w, br) cm^{-1}. The ^{19}F NMR gave a singlet at –90.0 ppm from external $CFCl_3$, and ^{13}C NMR gave a singlet at 114.9 ppm from TMS. The mass spectrum consisted of the following peaks: m/e 445 ($C_8F_{15}O_4^+$, P – F), 213 ($C_4F_7O_2^+$), 185 ($C_3F_7O^+$), 2131 ($C_3F_5^+$), 119 ($C_2F_5^+$, base peak), 100 ($C_2F_4^+$), 97 ($C_2F_3O^+$), 85 (CF_3O^+), 69 (CF_3^+), 50 (CF_2^+), 47 (CFO^+).

Perfluorocyclohexano-15-crown-5 Ether, Trans- and Cis-Isomers. After the fluorination was finished, the white powder containing products and sodium fluoride from the disk reactor[13] was collected and placed under vacuum. The volatiles were transferred into an acetone/dry ice trap. The GC assay of the volatile liquid on a 15% Kel-F column (Chromosorb A 60/80, 10 ft × 0.25 in., isothermal at 120 °C, helium carrier gas flow at 45 mL/min) gave two major peaks with a ratio of 1.0:0.82, based on peak area integration. The retention times were 13.4 and 15.0 min for cis- and trans-isomers, respectively. The hydrocarbon starting material, 15-crown-5 ether, purchased from PCR Inc., was dried over a 4-Å molecular sieve (Aldrich Chemical Co.) before use. The trans- and cis-isomers were analyzed by mass spectra, ^{19}F NMR, high-resolution mass spectra, and IR. Both isomers gave strong m/e of 742 and M – C_6F_{11} = 461 with similar ion fragmentation patterns. There are two tertiary fluorines in the expected perfluoro structure which lead to two possible isomers: trans and cis. The ^{19}F NMR clearly established the structure differences between the two isomers. The first major peak collected from GC was the cis-isomer and the second was the trans. All cyclohexano groups are in chair form in solution. Due to the fluxional character of the perfluorocyclohexyl groups bound to the ether ring, positive assignments of ^{19}F signals of ether ring fluorines are difficult. However, assignment of their configuration was based on the chemical shifts of perfluorodecalin published in the literature.[14]

^{19}F NMR chemical shift (δ $CFCl_3$) for the trans-isomer: –86.7 to –93 ppm (complex), –121.35 ppm (d, $J_{f\text{-}f}$ = 309.17 Hz, 2F), –125.61 ppm (d, $J_{f\text{-}f}$ = 290.48 Hz, 2F), –135.23 ppm (s, 2F), –136.82 ppm (d, $J_{f\text{-}f}$ = 309.17 Hz, 2F), –143.64 ppm (d, $J_{f\text{-}f}$ = 290.48 Hz, 2F). ^{19}F NMR chemical shift for the cis-isomer: –87 to –95 ppm (complex), –131.3 ppm (br, 4F), –134.0 ppm (br, 4F), –150.07 ppm (br, 2F). This illustrates the fluxional character of the cyclohexyl group on the NMR time scale. The infrared spectrum shows typical perfluoro ether absorptions below 1500 cm^{-1}. Data for the trans-isomer: 633 (w), 647 (w), 692 (w), 722 (w), 751 (w), 969 (s), 984 (m), 1048 (m), 1189 (s, br), 1193 (s, br), 1317 (m) cm^{-1}. Data for the cis-isomer: 633 (w), 661 (w), 714 (w), 720 (w), 762 (w), 972 (s), 1046 (m), 1146 (s, br), 1193 (s, br), 1266 (m, br), 1314 (m) cm^{-1}. Elemental compositions were studied with high-resolution mass spectroscopy, chemical ionization negative mode. Calcd: 741.9330. Found (trans): 741.9306, mDa = 2.4; the Found (cis): 741.9336, mDa = –0.6. Both isomers are clear, volatile oils. The boiling point of the trans-isomer is 199–200 °C, and that of the cis-isomer is 200–201 °C. The melting points for both isomers are between –44 and –46 °C. The melting point of the starting material is below 26 °C.[15] The boiling point of the trans-isomer starting material is 110 °C (0.001 Torr, molecular distillation).[16] The total yield of trans- and cis-isomers is 18.5% for 1 g of starting material. The yields are not optimized.

Perfluorodicyclohexano-18-crown-6 Ether, Cis-Syn-Cis- and Cis-Anti-Cis-Isomers. After the fluorination was finished, a white powder was collected from the disk reactor and extracted with a 100 mL of Freon 113 (1,1,2-trichlorotrifluoroethane) twice. This solution was washed with 100 mL of 0.5 M sodium hydroxide solution three times. The Freon 113 was removed by distillation, leaving a viscous oil. This oil was distilled under vacuum (0.5 mm, 125 °C). The distillate was further separated using gas chromatography (25% Fomblin Z, 0.25-in. × 10-ft column, isothermal at 200 °C, helium flow rate of 45 mL/min). The retention times were 31.2 and 34.5 min for the cis-syn-cis- and cis-anti-cis-isomers, respectively.

The two perfluoro isomers were identified primarily by GC/CIMS. Both isomers gave intense parent peaks at m/e = 1020. All cyclohexano groups in both isomers are in the chair form in the solid state, but in solution, both isomers are fluxional. Therefore, the assignments of the ^{19}F resonances of the ether rings and cyclohexano groups are difficult. Infrared spectra of both isomers were taken as neat liquids, and they were virtually identical. The infrared spectra exhibited bands at 1192 (vs, br), 1042 (m), 974 (vs), 709 (w), 632 (w), and 485 cm^{-1} (w). The ^{19}F NMR spectra of both isomers show complex patterns at –80 to –95 ppm (δ $CFCl_3$), which correspond to the resonances of fluorine atoms of the ether ring, and –120 to –150 ppm (δ $CFCl_3$), which correspond to fluorines attached to the cyclohexano groups. The low-temperature ^{19}F NMR spectra were studied and were not helpful in assigning the structures. Both isomers are colorless crystalline solids obtained in a total of 8.2–12.3% yield based on 1 g of starting material. The approximate ratio of

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the syn-isomer to the anti-isomer is 53.54% based on GC assay. The syn-isomer has a melting point of 54–55 °C, and the anti-isomer, 49–50 °C.

Perfluorodicyclohexano-24-crown-8 Ether. This reaction was run on 1-g scale. After 8 days following conditions similar to those shown in Table 1, the disk reactor was purged again with helium at 150 °C and fluorocarbon liquids were collected in a room temperature trap and in a –78 °C trap. The room temperature liquid contains most of the desired product. Final purification was performed using gas chromatography (15% SE-30, $^3/_8$-in. × 10-ft column, isothermal at 180 °C, helium flow rate of 45 mL/min). The retention time was 24.1 min. The desired product was identified primarily by the mass spectrum and high-resolution mass spectrum. Mass spectrum, chemical ionization negative mode (methane, 2 × 10^{-5} Torr, 130 °C): *m/e* 1252 (M^-), 1214 $(M - 2F)^-$, 1020 $(M - C_4F_8O_2)^-$, 971 $(M - C_6F_{11})^-$, 959 $(M - C_7F_{11})^-$, 877 $(M - C_8F_{13}O_2)^-$, 827 $(M - C_9F_{15}O_2)^-$, 761 $(M - C_{10}F_{17}O_3)^-$, 711 $(M - C_{12}F_{21}O_3)^-$, 645 $(M - C_{12}F_{21}O_4)^-$, 633 $(M - C_{13}F_{21}O_4)^-$, 595 $(M - C_{13}F_{23}O_4)^-$, 529 $(M - C_{14}F_{25}O_5)^-$, 479 $(M - C_{15}F_{27}O_5)^-$, 367 $(M - C_{18}F_{31}O_5)^-$, 317 $(M - C_{19}F_{33}O_5)^-$, 251 $(M - C_{20}F_{35}O_6)^-$, 201 $(M - C_{21}F_{37}O_6)^-$. The elemental composition was studied by high-resolution mass spectrometry using a chemical ionization negative mode. Calcd: 1251.8891. Found: 1251.8874, mDa = 1.6. The infrared spectrum was taken as a neat liquid. The infrared spectrum exhibits bands at 1220 (vs, br), 1150 (m), 950 (vs), 900 (w), 750 (m), 740 (m), 730 (m), 560 (w), and 475 cm^{-1} (w). In solution, fluxional structures, as expected, and again the assignments of ^{19}F resonances of the ether rings and cyclohexyl groups are difficult. The ^{19}F NMR data gave a complex pattern at –80 to –93 ppm (δ $CFCl_3$), which corresponds to the resonances of fluorine atoms of the ether ring, and at –120 to –150 ppm (δ $CFCl_3$), which corresponds to fluorines of the cyclohexyl ring. The low-temperature ^{19}F NMR spectra were studied and were not very useful in assigning the structure. The yield was 3% based on 1 g of starting material. Attempts to separate the isomers were not successful. It is probable that the large ring structure decreases the polar character expected from the tertiary fluorines.

Perfluoro-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane. A 0.99-g sample of the cryptand was dissolved in 25 mL of methylene chloride and added to 10 g of dry sodium fluoride powder. The mixture was slurried to coat the starting material on sodium fluoride particles. The solvent was removed under vacuum, and the dry material was finely ground and dispersed over the copper turnings in the reactor chamber. The disk reactor system has been previously described.[13] The reactor was connected to the fluorination system and purged with helium to remove any air from the system. The reactor was cooled to –100 °C, and the fluorination sequence was begun.

Upon completion of the reaction sequence, the reactor was removed and the contents extracted with $CFCl_2CF_2Cl$. The solvent was removed using a rotovap. The crude product was isolated as ca. 2 mL of a cloudy light yellow oil. Purification of the material was performed by preparative gas chromatography using a 0.25-in. × 10-ft stainless steel column packed with 25% OV-101 on Chromosorb A, 60/80 mesh. With the column temperature at 150 °C and the helium carrier gas flow at 45 mL/min, the compound was eluted in 5.4 min.

Preparative gas chromatography of the crude material was used to isolate 0.75 g of a clear colorless oil for a yield of 28%. The compound was identified using ^{19}F NMR, mass spectral analysis, and elemental analysis. The ^{19}F NMR spectrum ($CFCl_3$) consisted of three signals at –81.4 (s), –87.0 (t, $J_{f-f} \sim 1$ Hz), and –88.5 ppm (t, $J_{f-f} \sim 1$ Hz). The $^{13}C\{^{19}F\}$ NMR spectrum (TMS) also shows three peaks at 113.5, 115.3, and 116.8. The melting point of perfluorocryptand [222] is 32.7 °C. The infrared analysis was performed as a thin film on KBr, showing peaks at 1276 (vs, br), 1229 (vs, br), 1211 (vs, br), 1256 (vs, br), 1131 (vs, br), 1049 (m, sh), 984 (w), 893 (m), 878 (m), 840 (w), 769 (m), 744 (m, sh), 715 (m), and 704 (m) cm^{-1}. Elemental analysis was performed by Schwarzkopf Microanalytical Laboratories, Woodside, NY. The elemental analysis agreed well with $C_{18}F_{36}N_2O_6$. Calcd: C, 21.10; F, 66.80; N, 2.74. Found: C, 21.41; F, 66.50; N, 2.39. Electron-impact mass spectral analysis of the compound, performed on a Bell and Howell Model 491 spectrometer at 70 eV, provided little structural information. The molecular ion was observed at *m/e* 1024 as a small peak (<1% relative abundance (R.A.), allowing confirmation of the expected molecular weight. Electron capture negative ion (ECNI) mass spectrometry combined with collisionally induced dissociation (CID) provided more structural information and contained a large (100%) parent ion at 1024.[17]

Table 3. Crystallographic Data[a] for $C_{12}F_{24}O_6$ (I) and $C_{20}F_{36}O_6$ (II)

	I	II
fw	696.09	1020.16
a, Å	9.8203(10)	27.0514(15)
b, Å	11.8778(20)	10.0876(10)
c, Å	17.8395(21)	23.5261(26)
β, deg	95.162(15)	100.920(8)
V, Å^3	2072.4(5)	6303.5(11)
Z	4	8
$F(000)$	1344	3936
cryst syst	monoclinic	monoclinic
space group	$P2_1/n$	$C2/c$
T, °C	–110	–75
radiation	graphite monochromatized, Mo Kα (λ = 0.710 73 Å)	
2θ range, deg	4–50	4–55
scan speed, deg/min	6	6–12
ρ_{calcd}, g/cm^3	2.23	2.15
no. of reflns measd	3 855	13 623
no. of unique reflns	0	7 649
R_{int}	0	0.025
μ, cm^{-1}	2.916	2.787
transmn factor[b] range	not applied	not applied
cryst size, mm	.5	0.25 × 0.44 × 0.44
no. of reflns used	2 991	3 959
no. of reflns rejected[c]	864	3 278
$R(F)$[d]	0.0330	0.0425
$R_w(F)$	0.0456	0.0449
goodness of fit	1.71	1.288
parameters	380	559
max $\|\Delta/\sigma\|$	<0.1	<0.1
min, max peaks, e/Å^3	–0.35, 0.27	–0.28, 0.22

[a] Data were collected on a Nicolet P3 diffractometer. Data for I and II were collected at reduced temperature using a Nicolet low-temperature delivery system. Lattice parameters were obtained from the least-squares refinement of 15 reflections with $28.0 < 2\theta < 29.8°$ for I and 40 reflections with $22.5 < 2\theta < 29.6°$ for II. [b] Absorption correction was based on measured crystal faces. [c] Unobserved reflections have $F < 4(\sigma(F))$ for II and $F < 5(\sigma(F))$ for I. [d] The function, $\sum w(|F_o| - |F_c|)^2$, was minimized, where $w = 1/(\sigma(F_o)^2 + (0.02F)^2)$.

The GC/ECNI spectrum of the compound had a base peak attributed to the molecular ion at *m/e* 1024. No reagent gas adducts were observed under any conditions investigated due to the high electron affinity of the compound. Ions observed at *m/e* 986, 908, and 792 were attributed to the loss of F_2, C_2F_4O, and $C_4F_8O_2$, respectively. The other ions at *m/e* 496, 346, and 296 were the result of further ionization in the source and are not major features of the CID spectra. Stepwise or concerted multiple extrusion of neutral perfluoroethylene oxide was observed and produces the ions at *m/e* 908, 792, and 560. Further loss of the C_2F_4O or C_3F_6N fragment yields ions at *m/e* 428, 444, and 676. CID studies suggest that the cyclic structure of the perfluorinated cryptand is preserved as the fragmentation proceeds.

X-ray Experimental Studies on Perfluoro-18-crown-6, $C_{12}F_{24}O_6$ (I), and Perfluoro-*cis-syn-cis*-dicyclohexyl-18-crown-6, $C_{20}F_{36}O_6$ (II). Large, colorless, blocklike crystals were grown by sublimation. These materials sublimed readily at room temperature and at atmospheric pressure. The data were collected at reduced temperatures on a Nicolet $P2_1$ diffractometer for I and a P3 diffractometer for II using graphite monochromatized, Mo Kα radiation (λ = 0.7107 Å). A Nicolet low-temperature delivery system was used to control the temperature of the data crystals. Details of the crystal data, data collection, and structure refinement are listed in Table 3. Check reflections of moderate intensity were remeasured periodically during the data collection to monitor instrument and crystal stability. A smoothed curve of the intensities of these check reflections was used to scale the data. The data were also corrected for *Lp* effects. A 1° scan range in ω was used for I and II. The molecule in II lies around a crystallographic inversion center at 0, $^1/_2$, 0. The structures were solved by direct methods using MULTAN78 for I[18] and SHELXTL-*Plus* for II.[19] The structures were refined by full-matrix least-squares procedures with anisotropic thermal parameters using SHELX76 for I[20] and

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[18] Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; DeClercq, J.-P.; Woolfson, M. M. *MULTAN78. A system of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*; Universities of York, England, and Louvain, Belgium, 1978.

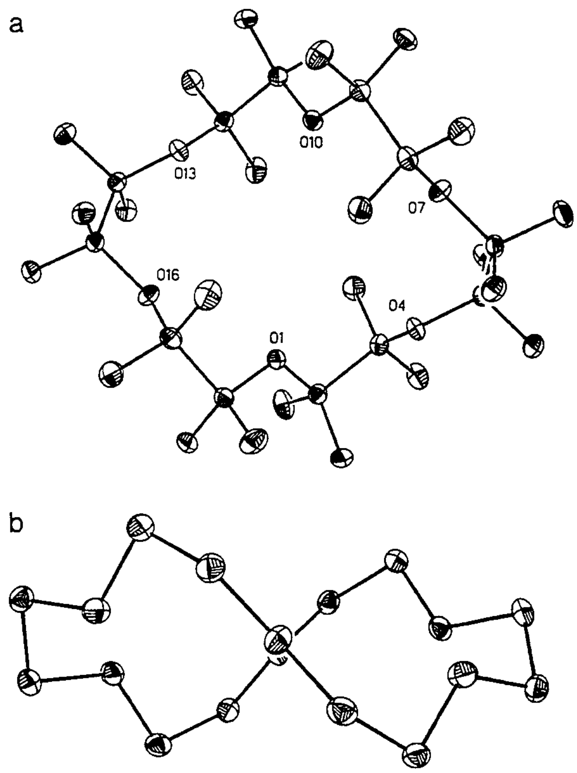

Figure 2. View of the thermal ellipsoid representations of perfluoro-18-crown-6 (I). Ellipsoids are scaled to the 30% probability level. (a) View approximately normal to the plane through the six oxygen atoms (O_6 plane). All atoms are shown. (b) Side view of the crown illustrating a twisted conformation. The F atoms are omitted for clarity.

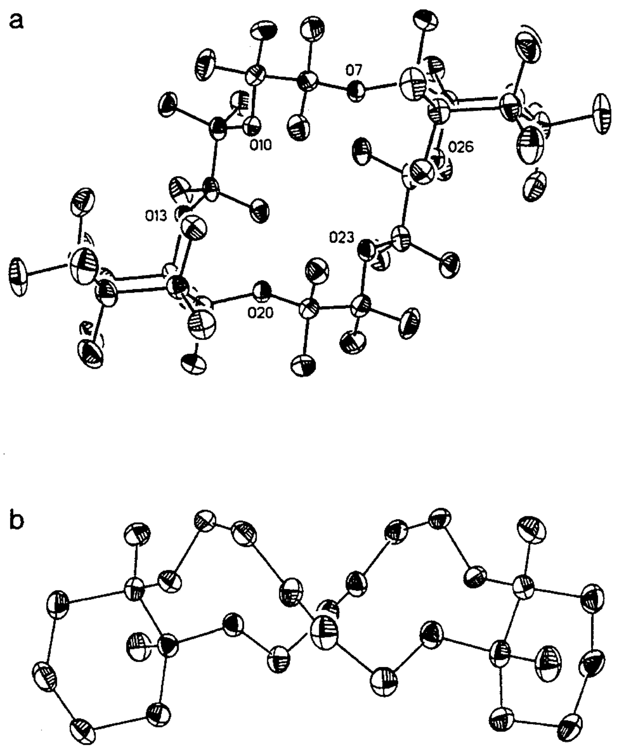

Figure 3. View of the thermal ellipsoid representations of perfluoro-*cis-syn-cis*-dicyclohexyl-18-crown-6 (II). Ellipsoids are scaled to the 30% probability level. (a) Usual chair conformation of the cyclohexyl ring. All atoms are shown. (b) Twisted conformation of the crown. Only F atoms at the bridgehead carbons are shown. This conformation is similar to that found for I.

SHELXTL-*Plus* for II[19] (see Figures 2 and 3). The function, $\Sigma w(|F_o| - |F_c|)^2$, was minimized, where $w = 1/(\sigma(F_o))^2$ and $\sigma(F_o) = 0.5kI^{-1/2}[(\sigma(I))^2 + (0.02I)^2]^{1/2}$. The intensity, I, is given by $(I_{peak} - I_{background})$(scan rate), 0.2 is a factor to downweigh intense reflections and to account for instrument instability, and k is the correction due to *Lp* effects, absorption (where applied), and decay. $\sigma(I)$ was estimated from counting statistics: $\sigma(I) = [(I_{peak} + I_{background})^{1/2}$(scan rate)]. The scattering factors for the non-H atoms were taken from Cromer and Mann,[21] with anomalous-dispersion corrections taken from Cromer and Liberman.[22] The linear absorption coefficient was obtained from values found in the *International Tables for X-ray Crystallography*.[23] Other computer programs are listed in ref 11 of Gadol and Davis.[24]

Mass Spectrometric Characterization by Collisionally Activated Dissociation. The perfluoro macrocycles were further characterized by collisionally activated dissociation (CAD) mass spectrometric techniques. CAD is a method in which a mass-selected ion undergoes energetic collisions with a neutral target gas, resulting in fragmentation of the ion by structurally diagnostic pathways.[25] The acquisition of characteristic CAD spectra is especially important for the interpretation of the gas-phase macrocyclic complexation studies described later. For the CAD spectra discussed in this section, a Finnigan MAT TSQ-70 triple-stage quadrupole mass spectrometer was operated in both negative and positive ionization modes at a source temperature of 80 °C. For the negative ionization mode, methane or argon was introduced into the source at 1.2 Torr to aid in the production of thermal electrons to promote electron capture negative ionization.

Each of the perfluorinated crown ethers produced $(M - F)^+$ ions under positive chemical ionization conditions, likely as a result of elimination of FH from an initial $(M + H)^+$ ion.[26] These positive ions dissociate via two routes upon collisional activation. They may eliminate units of C_2F_4O, or they may eliminate ($C_2F_2O_2$ + nC_2F_4O) where n = 0, 1, 2.... In the negative ion mode, the perfluoro crown ethers produce abundant anions, $M^{\bullet-}$, which dissociate by a characteristic series of losses.[26] For example, a typical CAD spectrum for perfluoro-15-crown-5 is shown in Figure 4. In general, the molecular radical anion of each perfluoro crown ether dissociates by loss of nC_2F_4O units (n = 1, 2, 3).

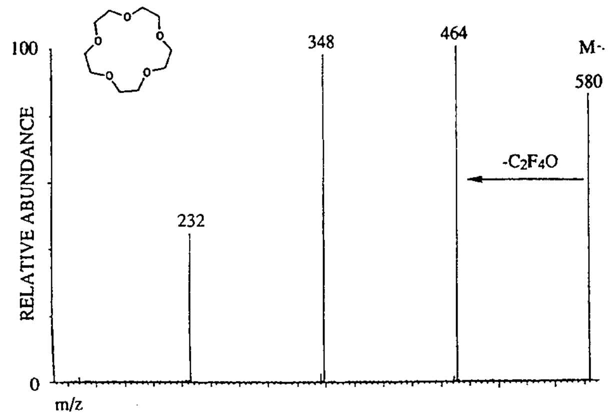

Figure 4. Collisionally activated dissociation mass spectra of the $M^{\bullet-}$ ion of perfluoro-15-crown-5 acquired with a triple-quadrupole mass spectrometer.

The perfluorinated 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (cryptand) dissociated by several pathways that are analogous to those noted for the crown ethers: elimination of nC_2F_4O units is predominant, where n = 1, 2, 3, resulting in ions at *m/e* 908, 792, and 676.[26] Additionally, losses of two or three C_2F_4O units in conjunction with C_4F_9N elimination are observed as fragment ions at *m/e* 559 and 443. These latter fragments are evidence of cleavage at the nitrogen bridge.

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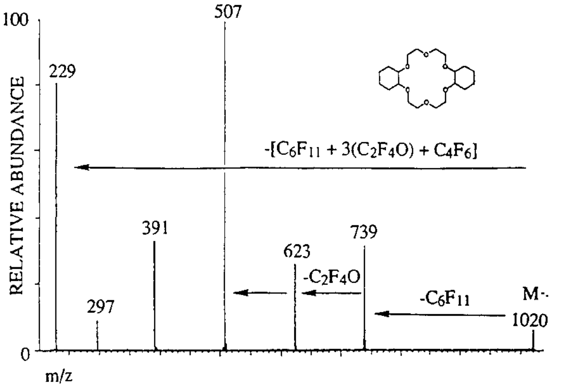

Figure 5. Collisionally activated dissociation mass spectra of the $M^{\bullet -}$ ion of perfluorodicyclohexano-18-crown-6 acquired with a triple-quadrupole mass spectrometer.

The CAD spectra of the molecular anions of two perfluorodicyclohexano crown ethers, the 18-crown-6 and 24-crown-8 ethers, also show characteristic fragmentation patterns.[26] The CAD spectrum for the first isomer is shown in Figure 5. For these substituted perfluoro crown ethers, the molecular anions do not dissociate via simple loss of C_2F_4O units as was observed for the other macrocycles. Instead, elimination of C_6F_{11} (cyclohexyl ring) is a predominant process and may then be coupled with losses of nC_2F_4O. The first process may be rationalized as a radical-initiated ring cleavage, followed by a fluorine transfer to the cyclohexyl ring via a four-membered transition state. The resulting fragment ion is presumably acyclic. This fragment ion then proceeds to dissociate by consecutive losses of C_2F_4O units. For the 18-crown-6 ether shown in Figure 5, losses of up to three units of C_2F_4O are observed in conjunction with loss of C_6F_{11} (formation of m/e 391, 507, 623, 739). Additionally, loss of three C_2F_4O units is observed, coupled to the loss of both C_6F_{11}, the first cyclohexyl ring, and C_4F_6, the second cyclohexyl ring, resulting in formation of m/e 229. For the analogous 24-crown-8 system, this latter pathway (elimination of both cyclohexyl rings) is coupled instead to the loss of four C_2F_4O units.

Discussion

Perfluorinated derivatives of hydrocarbon compounds usually exhibit different properties than their hydrocarbon analogues. The perfluoro crown ethers are markedly more volatile than the hydrocarbon products. One would expect the dimensions of the pocket size to change, and both modeling and crystal structures clearly establish that the pockets are smaller and that the crown ether rings are slightly more bent. As observed in the gas-phase studies, perfluoro crown ethers and cryptands all coordinate O_2^-, F^-, and several other such anions. Although a crystal structure of an encapsulated anionic species is not yet in hand, the possibility of obtaining the formation of such a structure is being studied.

Perfluoro crown ethers and cryptands are indeed very weak bases if there is any base character at all. For the gas-phase complexes of O_2^- and F^-, it would also appear that electron density from the anion is transferred to the binding sites in the crown ether. One would suspect that the binding occurs at the oxygen. As indicated by the fragmentation thermodynamics, there is a 40–60-kcal interaction binding the anion to the macrocycle.

Whether the perfluoro macrocycles are also capable of binding cations is still not certain. Two talented collaborators on this project have not been successful in obtaining cationic complexes with the alkaline metals. One reason was that the perfluoro macrocycles are not soluble in common organic solvents. On the other hand, both organometallic compounds and organic species as well as these perfluoro macrocycles are soluble in chlorofluoro solvents such as Freon 113, $F_2ClC–CF_2Cl$. It is also quite possible that the base character in such perfluoro macrocycles is nonexistent.

The single crystal X-ray diffraction studies of 18-crown-6 ether indicate that the guest-free ring is puckered in a manner so that the oxygen sites are exposed and projected toward a possible metal coordination site. In view of the possibility of a rigid conformation existing in the solution at lower temperature, the ^{19}F spectrum of 18-crown-6 in $CFCl_3$ has been monitored at –85 °C. Only one singlet peak was observed. This observation establishes that the molecule is quite flexible in the solution. The energy barrier associated with the conformational change should be extremely low.

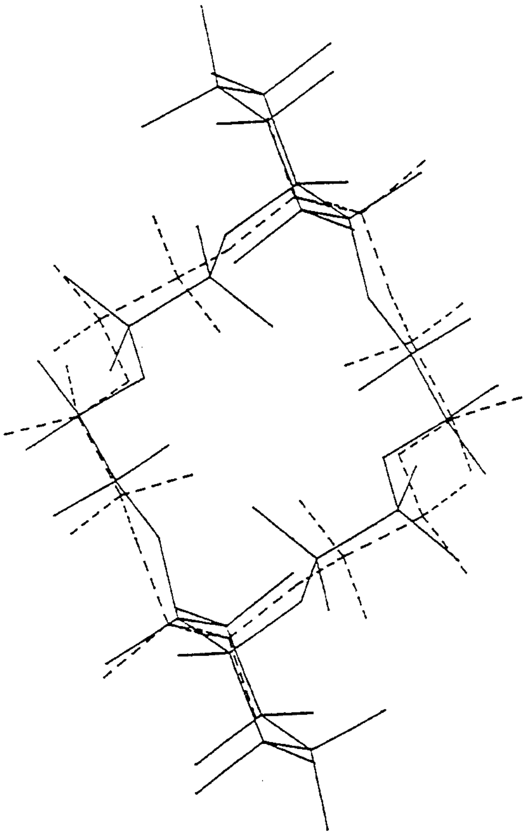

Figure 6. Superposition of the carbon and oxygen atoms of the perfluoro-*cis-syn-cis*-dicyclohexano-18-crown-6 ether (solid lines) onto the equivalent atoms of perfluoro-18-crown-6 ether (dashed lines) illustrating the similar configurations of the perfluoro ether rings of the two structures.

Two crystal structures of perfluoro crown ethers, containing the 18-crown-6 ether skeleton, are reported. Comparisons of these structures show that the perfluoro-18-crown-6 ether and the cis-syn-cis-isomer have similar conformations of the ether ring skeleton.[27] Figure 6 shows the superposition of the carbon and oxygen atoms of the perfluoro-*cis-syn-cis*-dicyclohexano-18- crown-6 ether (solid lines) onto the equivalent atoms of perfluoro-18-crown-6 ether (dashed lines). This illustrates the similar configurations of the perfluoro ether rings of the two structures. The perfluorocyclohexyl groups may not be the dominating steric factor which controls the conformation of the ether ring skeleton. Distances between oxygen atoms and the center of the molecule and between adjacent oxygen atoms in the cis-syn-cis-isomer are given in Tables 4. Previously, preliminary data on the structure of the cis-anti-cis-isomer have been reported,[28] but the problem of disorder in crystals grown by sublimation has not been solved.

Although perfluoro-18-crown-6 has a melting point of 34 °C in a sealed capillary, the solid compound has a substantial vapor pressure; it can be sublimed easily and moves on a vacuum line. Perfluoro-18-crown-6 has a marked propensity to form large and beautiful single crystals. Crystals weighing at least 0.5 g which have the appearance of sparkling zircons are obtained routinely. Both perfluoro-15-crown-5 and -12-crown-4 species are clear liquids with properties favorable for several biomedical applications.

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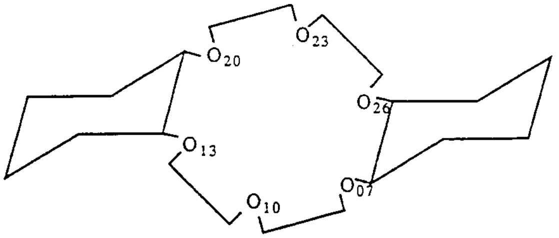
Table 4. Distances between Oxygen Atoms and the Center of the Molecule, and between Adjacent Oxygen Atoms in Perfluoro-*cis-syn-cis*-dicyclohexano-18-crown-6 Ether



atom(s)	distance (Å)
From Atom to Center of Molecule	
O_7	2.536
O_{10}	2.129
O_{13}	3.177
O_{20}	2.543
O_{23}	2.141
O_{26}	3.181
Between Adjacent Oxygen Atoms	
O_{13}–O_{20}	2.662
O_{20}–O_{23}	2.713
O_{23}–O_{26}	2.665
O_{26}–O_{07}	2.667
O_{07}–O_{10}	2.707
O_{10}–O_{13}	2.667

Perfluoro-15-crown-5 has great potential as a ^{19}F NMR imaging agent.[29] This crown ether has only one fluorine resonance, making very sharp pictures during brain scans and spinal scans of animals possible. Perfluoro-15-crown-5 has also been used successfully as an oxygen carrier in collaborative studies between our group and Dr. Leland Clark's laboratory. Toxicology work at Air Products has established that the perfluoro crown ethers are nontoxic in animals and therefore very different from hydrocarbon crown ethers. Recently over 2 kg of perfluoro-15-crown-5 has been made in very high yield by new technology.[30]

The perfluorocryptand [222] compound is expected to have interesting applications. Aside from the possibility of acting as a perfluoro "host" for certain types of "guest" species, the perfluorocryptand [222] has shown potential as a very clean, high-mass compound for use as a mass spectral marker material.[17] The compound is expected to be biologically inert (in contrast to the hydrocarbon analogue) and, as in the case of the perfluoro crown ether compounds, may be useful in fluorocarbon biological and medical applications where physiologically inert or oxygen-carrying fluids are required.

The synthetic work reported here coupled with new technology[30] opens the possibility of preparation of many novel crown ether systems as well as the synthesis of a series of perfluoro cryptands. Such ligands should be much less subject to chemical attack or thermal degradation.

Gas-Phase Reactions of Perfluoro Macrocycles. The coordination capabilities of perfluorinated macrocycles have generated considerable interest because of the importance of crown ethers and related macrocycles as model hosts in the field of molecular recognition.[2-3] Numerous studies have described aspects of host–guest complexation of hydro crown ethers with a variety of model guests, including alkali metal ions and ammonium ions.[6] Thus, the perfluorinated macrocycles provide an intriguing structural analog to the hydrogenated macrocycles. Studies of these novel model hosts may reveal new insight into the structural and thermodynamic factors which mediate selective complexation. Recently, studies of host–guest chemistry in the solvent-free environment of the gas phase have opened a new frontier for the investigation of molecular recognition.[31-36] Complexation may be evaluated in the absence of solvation effects, and thus the intrinsic binding properties of model hosts can be examined. Three studies of the gas-phase ion chemistry of perfluoro macrocycles are reviewed in the following section.

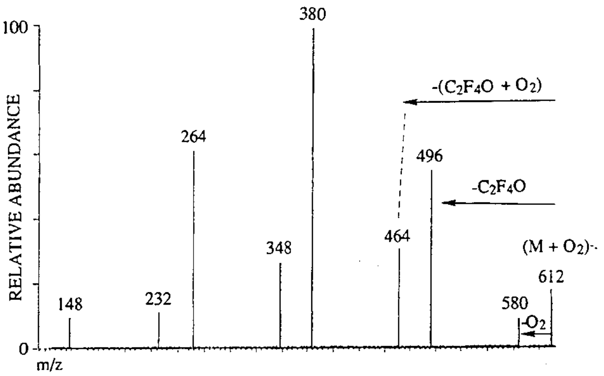


Figure 7. Collisionally activated dissociation mass spectra of the $(M + O_2)^{\bullet-}$ ion of perfluoro-15-crown-5 acquired with a triple-quadrupole mass spectrometer.

The high oxygen-carrying capacity of some perfluorocarbons makes them viable as artificial blood components,[37] and yet to date the mechanism of oxygen binding to fluoro ethers is not well understood. Thus, it was of considerable interest to probe the ability of perfluoro macrocycles to bind molecular oxygen and other small molecules in the gas phase in order to obtain new information about the binding affinities of these compounds.[31] For these studies, each perfluoro macrocycle was admitted into the source of a triple-quadrupole mass spectrometer. Argon was introduced into the source manifold at 2–3 × 10^{-6} Torr to aid in the production of thermal electrons for electron capture negative ionization. The desired reagent gas (CO, N_2, CO_2, or air for O_2) was added to attain a total source pressure of 1–2 Torr. The ethers examined included perfluoro-12-crown-4, perfluoro-15-crown-5, perfluoro-18-crown-6, perfluorinated 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8,8,8]hexacosane (cryptand), their hydro crown analogs, and one acyclic perfluoro ether, perfluorotriethylene glycol dimethyl ether.

Each perfluoro macrocycle was ionized to form $M^{\bullet-}$ then allowed to react with O_2 to successfully form $(M + O_2)^{\bullet-}$ adducts.[31] Ion/molecule reactions involving *acyclic* perfluoro ethers and *hydrogenated* crown ethers were also examined to determine whether the cyclic and/or perfluoro natures of the macrocycles played a role in the formation of the $(M + O_2)^{\bullet-}$ adducts. *Neither* the perfluoro acyclic analogs nor any hydrogenated crown ether reacted with O_2 to form $[M + O_2]^{\bullet-}$ adduct ions. This result confirmed that the macrocyclic nature of the perfluoro crown ethers enhanced their ability to bind O_2.

Additionally, the abilities of the perfluoro crown ethers to form complexes with CO, N_2, CO_2, and Ar, species with sizes and some chemical and physical properties similar to those of O_2, were examined. Adducts with these species were *not* observed.[31] Thus, the tendencies of the perfluoro crown ethers to form adducts exhibited striking selectivity for O_2 only.

Structural details of the perfluoroether adduct ions, $(M + O_2)^-$, were probed via collisionally activated dissociation of the mass-selected ions.[31] Figure 7 illustrates the 40-eV CAD spectra of the perfluoro-15-crown-5 $(M + O_2)^-$ adduct (m/e 612), showing two series of fragment ions. One is a series of losses of $(C_2F_4O)_n$,

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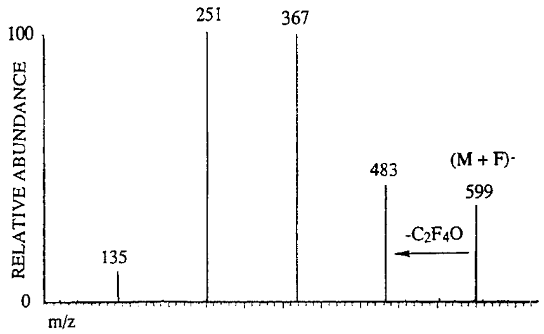


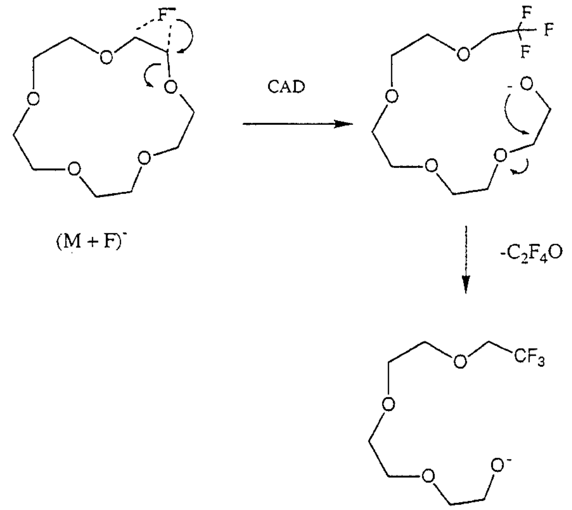
Figure 8. Collisionally activated dissociation mass spectra of the (M + F)$^-$ ion of perfluoro-15-crown-5 acquired with a triple-quadrupole mass spectrometer.

analogous to the series of losses observed from the M$^{\bullet-}$ ion, resulting in fragment ions at m/e 148, 264, 380, and 496. This trend indicates that the O_2 is bound to the perfluoro crown ether strongly enough to be retained after the adduct ion is activated and implies that the binding interaction must be at least as strong as the C–C and C–O bonds that are cleaved during the competing dissociation processes in which C_2F_4O units are expelled. The C–C and C–O bond energies for these perfluoro crown ethers have been estimated as 84 and 98 kcal/mol, respectively. Additionally, a series of fragment ions corresponding to loss of ($nC_2F_4O + O_2$) units is seen at m/e 232, 348, and 464, where $n = 3, 2, 1$, the same fragment ions produced from CAD of the noncomplexed molecular ion shown in Figure 4.

Direct loss of O_2 is not a significant dissociation channel using any collisional activation conditions (for 10–120-eV kinetic energy collisions, the percentage of the total fragment ion abundance due to O_2 loss is 0–10%). This result suggests that the O_2–crown ether complex is not a loosely bound adduct but, instead, a species in which stronger bonding forces are involved than those associated with a single weak ion/dipole electrostatic interaction. An adduct species in which O_2 fits in the pocket of the crown ether anion is possible (enhancing multiple bonding interactions), or a structure in which the O_2 is cradled by four electronegative fluorine atoms is feasible. In general, O–F bonds are not stronger than 50 kcal/mol, so a complex containing a single F–O_2 binding interaction is not supported.

It was also timely to examine the ability of perfluoro macrocycles to react with fluoride in the gas phase.[32] It has been shown recently from crystallographic studies that a fluoride ion may be held in the cavity of a fluorinated macrocyclic ether,[11] and thus it was of interest to investigate the possibility of forming related fluoride complexes in the gas phase. Fluoride/macrocyclic adducts were successfully generated in the gas phase by ionization of a mixture of a macrocycle and a fluorinated reagent such as CHF_3 admitted simultaneously into the ion source. Moderately abundant (M + F)$^-$ adducts (relative abundance = 10% compared to M$^{\bullet-}$) are formed by reaction of F$^-$ with the macrocyclic molecules. The CAD spectrum of the (M + F)$^-$ adduct of perfluoro-15-crown-5, shown in Figure 8, is similar to the CAD spectrum for the molecular anion M$^{\bullet-}$ of perfluoro-15-crown-5, shown above in Figure 4, with the exception that each fragment ion is shifted to a higher mass by 19 amu (due to the fluorine addition). The series of ions incorporating the additional fluorine is the only type of fragment observed, indicating that the fluorine is *always* retained by the ionic portion during dissociation. The most abundant dissociation processes involve loss of two or three C_2F_4O units. The direct loss of F$^\bullet$ from the (M + F)$^-$ adduct is not observed. This result suggests a very strong crown ether–fluoride binding interaction. For example, the fluoride ion may attack any carbon position and promote ring opening, resulting in an acyclic structure with a covalently bound fluorine. A mechanism depicting this proposed pathway is shown in Scheme 1.

Scheme 1. Proposed Mechanism for Dissociation of the (M + F)$^-$ Adduct



In the third gas-phase study,[38] a new type of polymer ion consisting of a perfluorinated macrocycle (M) associated with multiple ether molecules was generated in the source of a triple-quadrupole mass spectrometer by a novel gas-phase cationic polymerization process. The polymer ions have the general formula (M – F + nEther)$^+$, where $n = 1, 2, 3....$ depending on the type of ether. The ethers which promoted the most extensive polymerization were highly strained cyclic ethers such as ethylene oxide and ethylene sulfide, whereas the perfluoro macrocycles attached only one unit of the acyclic ether analogues, such as dimethyl ether. It is proposed that the strained cyclic ethers attach to the perfluorinated ion and then undergo sequential ring-opening polymerization to form an extended polyether chain which is covalently anchored to the perfluorinated substrate. The nature of the binding interactions in these novel types of polymer assemblies is still under investigation.

The ability to form and characterize new types of macrocyclic ion complexes involving perfluoro ethers holds great promise for future studies of host–guest complexation in the gas phase. Comparisons to the gas-phase chemistry of hydrogenated macrocycles may allow further insight into the influence of thermochemical and structural properties on the binding interactions of host molecules.

Acknowledgment. We are grateful for support of this work by the Air Force Office of Scientific Research (F49620-92-J-0104) and the U.S. Department of Energy (DE-FG05-91ER12119).

Supplementary Material Available: Tables listing fractional atomic coordinates and equivalent isotropic thermal parameters, anisotropic thermal parameters, bond lengths and angles, and torsion angles, and drawings showing the atom labeling schemes and the unit cell packings for I and II (22 pages); observed and calculated structure factors (65 pages). This material is contained in many 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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The First Cyclic Perfluoropolyketone: The Synthesis and Solid State Conformation of Perfluoro(hexamethylcyclohexane-1,3,5-trione)

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A novel perfluorinated cyclic polyketone **1** was synthesized by liquid-phase direct fluorination; its crystal structure and solid state conformation were determined by X-ray crystallography.

Perfluoroketones are useful intermediates for several classes of compounds.[1,2] They can be prepared by several indirect methods, such as rearrangement of perfluoroepoxides over SbF_5 or KF, halogen exchange reactions between chlorinated ketones and hydrogen fluoride using a Cr^{III} catalyst, sulfuric acid hydrolysis of alkyl perfluorocycloalkyl ethers, reactions of perfluoroalkyl carboxylates with perfluoroalkyl lithium or perfluorinated Grignard reagents and fluoride-induced substitution of perfluoroacyl fluorides with perfluoroalkenes.[1] Because starting materials are difficult to prepare or the yields of these reactions are low, these methods are seldom used to prepare novel perfluoroketones. Other direct methods such as CoF_3 and $KCoF_4$ have been used to fluorinate ketones but the major reaction of the fluorination was cleavage of the C–CO bond.[3] Elemental fluorine also has been used to fluorinate monoketones by using several special methods and reactors, such as jet reactor,[4] aerosol direct fluorination[5] and cryogenically controlled direct fluorination,[6] but these methods often give lower yields or cleavage of the C–CO bond. The target of the present synthesis was the polyketone **1** which was obtained in 72% yield.

We report here the first example of liquid-phase direct fluorination of a cyclic polyketone and the crystal structure of its perfluorinated analogue **1**. The liquid-phase direct fluorination of hexamethylcyclohexane-1,3,5-trione was carried out by slowly injecting a trichlorotrifluoroethane solution of the compound into a reactor containing trichlorotrifluoroethane saturated with fluorine and sodium fluoride. The reactor design of the liquid-phase direct fluorination was described previously.[7] The fluorination conditions are shown in Table 1. After fluorination, the solvent was distilled off and the residue was distilled under high vacuum to give pure corresponding perfluoro(hexamethylcyclohexane-1,3,5-trione) **1** in 72% isolated yield. Its melting point is 40 °C.

The byproducts were lower molecular weight fluorinated alcohols produced by hydrolysis. Straight chain products were absent from the byproducts indicating that cleavage of the C–CO bond did not occur in this reaction. Sodium fluoride as a hydrogen fluoride scavenger is essential for the reaction since addition of hydrogen fluoride to fluorinated ketones followed by fluorination, gives hypofluorites.[8]

The ^{19}F NMR signal of **1** is a singlet at $\delta(CDCl_3, CFCl_3)$ −59.5. The carbonyl absorption in its IR spectrum is shifted to 5.7 μm from the value of 5.9 μm for the hydrocarbon analogue.[9] Single crystals of **1** were obtained by sublimation and its molecular structure (Fig. 1) was determined by X-ray structure analysis.†

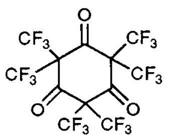

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Table 1 Fluorination conditions for **1**

Temp./°C	He/ml min^{-1}	F_2/ml min^{-1}	Time/h
−28	500	0	0.5
−28	500	60	5[a]
0	80	10	12
25	80	10	24

[a] Slowly adding sample into reactor during this time.

The molecule is unusually flat, as can be seen from the sum of the six ring torsion angles 31° + 18° + 14° + 32° + 18° + 12° = 125°. By comparison, the sum of the torsional angles in the cyclohexane ring and for hexamethylcyclohexane-1,3,5-trione are 336° and 192°, respectively.[9] In comparison to the boat conformation of hexamethylcyclohexane-1,3,5-trione,[9] the conformation of **1** is a twisted boat. The three axial trifluoromethyl groups, which are larger than methyl groups, create steric bulk and possibly strained and hindered rotation. The atoms C(1), C(3), C(4), and C(6) are 0.08 Å out of the best plane through these atoms. The atoms C(2) and C(5) are 0.3 Å out of this plane in the same direction. The shortest intramolecular CF_3---CF_3 contact of **1** is 3.7 Å [C(11)---C(32)].

The average C–O bond length of **1**, 1.18 Å, is significantly shorter than the average C–O bond length (1.21 Å) of hexamethylcyclohexane-1,3,5-trione.[9] This causes the carbonyl absorption in the IR spectrum of **1** to shift to a shorter wavelength. The three ring angles other than carbonyl angles in **1** are close to 115.8°, which is far from an ideal tetrahedral angle 109.28° and even larger than those of hexamethylcyclohexane-1,3,5-trione (107.2, 111.6 and 112.4°).[9]

We are currently investigating liquid-phase direct fluorination of other polyketones.

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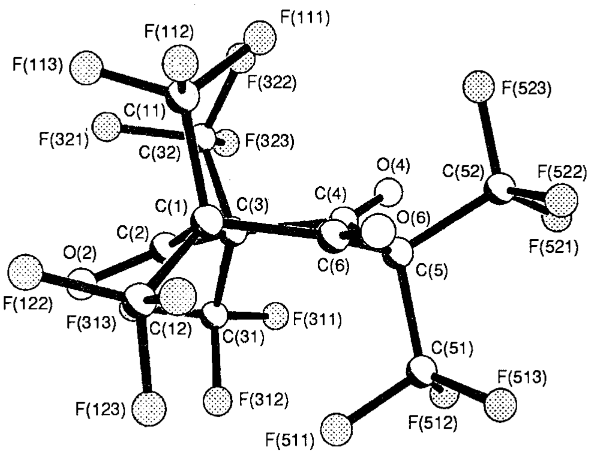

Fig. 1 Molecular structure of $C_{12}F_{18}O_3$ **1**; a twisted boat conformation. Selected bond lengths (Å): C(2)–O(2) 1.188(5), C(4)–O(4) 1.179(5), C(6)–O(6) 1.178(5); selected bond angles(°): C(2)–C(1)–C(6) 115.7(4), C(2)–C(3)–C(4) 115.8(4), C(6)–C(5)–C(4) 116.0(4); selected torsional angles(°): C(6)–C(1)–C(2)–C(3) −30.8(6), C(1)–C(2)–C(3)–C(4) 17.9(6), C(2)–C(3)–C(4)–C(5) 14.4(6), C(3)–C(4)–C(5)–C(6) −32.3(6), C(4)–C(5)–C(6)–C(1) 18.3(6), C(2)–C(1)–C(6)–C(5) 11.8(6).

Footnote

† *Crystal data* for **1**: $C_{12}F_{18}O_3$, crystal size $0.1 \times 0.2 \times 0.2$ mm, $M = 534.12$ g mol^{-1}, monoclinic, space group $P2_1/n$ (No. 14, Internat. Tab.) $a = 8.6493(1)$, $b = 11.9106(1)$, $c = 15.239(2)$ Å, $\beta = 90.044(1)°$, $V = 1569.9(4)$ Å^3 (from 25 reflections with 2θ range 6 to 27°), $Z = 4$, $D_c = 2.260$ g cm^{-3}, $F(000)$ 1032, $\mu = 0.296$ mm^{-1}. 3212 data were collected on a Siemens *P*4 diffractometer [graphite monochromator, $\lambda = 0.71073$ Å (Mo-Kα), $T = 173$ K, 2θ range 5–50°, $\theta/2\theta$ scans, program system XSCANS].[10] Three standard reflections were measured periodically for intensity calibration. The number of unique reflections is 2762 ($R_{\text{int.}} = 0.0254$). Intensity data were corrected for Lorentz and polarisation effects. The structure was solved by direct methods (SHELXTL PLUS)[11] and refined by full-matrix least-squares methods on F^2 using program system SHELXL-93.[12] The final *R* value was $wR2 = 0.067$ for 2753 data and 298 parameters [$R1 = 0.0452$ for 1209 data, $I > 2\sigma(I)$]. The final maximum shift/esd was -0.003 and the final $\rho_{(\max)}/\rho_{(\min)}$ values (e Å^{-3}) were $+0.26$ and -0.33, respectively. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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