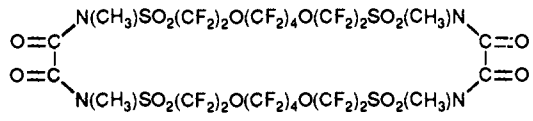
Although interest in fluorinated heterocycles is increasing,[4] reports of the synthesis and characterization of per- or polyfluorinated macrocycles are limited. The synthesis of perfluorinated 18-crown-6 has been achieved; however, its potential for formation of neutral complexes is expected to be poor.[23,24] A number of large perfluoroalkyl heterocycles (16-membered rings or smaller) containing the sulfamide functional group have been prepared and characterized.[25] The first successful host/guest relationship between a large polyfluorinated heterocyclic ether (an 18-membered ring) and fluoride ion has only recently been established by X-ray crystal structure analysis.[26]

We now report the synthesis and structure of a unique, polyfluorinated, 32-membered multifunctional heterocyclic ring, **1**. The ring contains four *N*-methyl sulfonamide, two α,β-diketone, and four ether functional groups. The starting material, I(C-



1

$F_2)_2O(CF_2)_2SO_2F$ (**2**), was prepared by the literature method.[27] Refluxing **2** in the presence of zinc in $CH_2Cl_2/(CH_3CO)_2O$ (1/1) for 8 h gave an 85% yield of $FO_2S(CF_2)_2O(CF_2)_4O(CF_2)_2SO_2F$ (**3**). The bis(*N*-methyl sulfonamide) $HN(CH_3)SO_2(CF_2)_2O(C-F_2)_4O(CF_2)_2SO_2(CH_3)NH$ (**4**) was obtained in 90% yield from the reaction of **3** with CH_3NH_2 at −40 °C over a period of 4 h.[28] Compound **4** was quantitatively converted to the bis(*N*-methyl sodium sulfonamide) **5** by reaction at 25 °C with sodium in anhydrous ethanol. The heterocycle **1** (mp 108 °C) is isolated in 60% yield when **5** (0.38 mmol in 5 mL of CH_3CN) is added dropwise to a solution of oxalyl chloride[29] (0.76 mmol in 3 mL of CH_3CN) with vigorous stirring at 0 °C, followed by the addition of 10 mL of water and filtration. The white solid thus obtained is recrystallized twice from a mixture of acetone and hexane (1/2) to give pure **1**. The ^{19}F NMR (ϕ −81.40, −82.99, −112.24, −125.56) and ^1H NMR (δ 3.48, 3.35) spectra and the elemental analytical data (Calcd: C, 21.43; F, 45.24; N, 4.16; S, 9.52. Found: C, 21.47; F, 45.1; N, 4.15; S, 9.62) are consistent with the structure of **1**.

The X-ray crystal structure of **1** (obtained with a $P2_1$ Syntex diffractometer system using the Nicolet SHELXTL (Version 5.1) structure solution package) is shown in Figure 1, along with selected bond lengths and angles. The crystal class is monoclinic with lattice constants of a = 11.836 (4) Å, b = 13.856 (5) Å, c = 14.658 (7) Å, β = 102.38 (3)°, and V = 2348 (2) Å^3 based on 25 reflections in the range $15 < 2\theta < 18$. A total of 3081 unique reflections were obtained with 1472 having $F > 3\sigma(F)$. Refinement of 251 parameters yielded R = 0.1073, R_w = 0.0683, and GOF = 1.717.

The observed bond angles and bond lengths are all as expected; however, a stereoview of this macroheterocycle provides some interesting observations. The gross symmetry of this molecule can best be described as a pair of bowls which are inverted with respect to each other. Each bowl is defined by 16 of the 32 atoms which make up the macrocyclic ring. The first bowl begins at N(1) and ends at S(1)′. The bottom of the bowl is confined by the methyl group bonded to N(2), the C(5) carbonyl, the di-

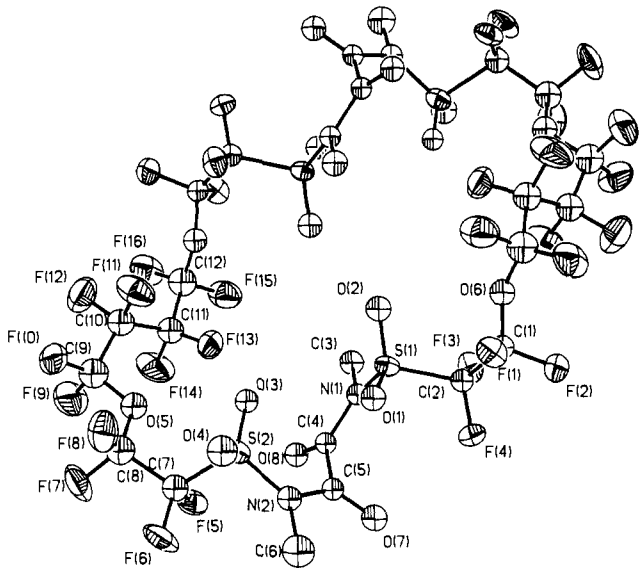


Figure 1. ORTEP diagram of **1** with hydrogen atoms removed. Selected bond lengths (Å): C(1)–C(2), 1.532 (17); C(1)–F(2), 1.341 (16); C(1)–O(6), 1.372 (16); S(1)–O(2), 1.400 (9); S(1)–C(2), 1.840 (13); S(1)–N(1), 1.646 (10); N(1)–C(3), 1.481 (15); N(1)–C(4), 1.398 (14); C(4)–O(8), 1.190 (15); C(4)–C(5), 1.576 (18). Selected bond angles (deg): C(2)–S(1)–N(1), 102.1 (5); O(1)–S(1)–O(2), 122.9 (5); O(1)–S(1)–C(2), 105.8 (5); O(1)–S(1)–N(1), 108.0 (5); C(3)–N(1)–S(1), 118.6 (7); C(4)–N(1)–S(1), 124.7 (8); C(3)–N(1)–C(4), 115.2 (9); N(1)–C(4)–O(8), 123.2 (11); C(5)–C(4)–N(1), 119.3 (10); C(5)–C(4)–O(8), 117.4 (10); C(4)–C(5)–N(2), 119.5 (11).

fluoromethylenes at C(11), C(12), C(1)′, and C(2)′, and the S(1)′ sulfone group. The remaining atoms form the sides and top of this bowl. For each bowl, a single oxygen of the sulfone is directed into the ring, as are one of the *N*-methyl moieties (N(2)) and the C(5) carbonyl group.

The crystal structures of such large, fluorinated multifunctional heterocycles have not been reported previously. We are continuing our exploration of the thermal and host/guest chemistry of this interesting and unusual molecule.

Acknowledgment. We thank the Air Force Office of Scientific Research (91-0189) and the National Science Foundation (CHE-9003509) for support of this work. We are also grateful to the National Science Foundation (Grant CHE-8408407) and the Boeing Company for the purchase of the X-ray diffractometer system and Dr. Roger Willet and Dr. Brian Scott for obtaining the crystal structure data.

Supplementary Material Available: Complete information on bond lengths and bond angles, atomic coordinates, and anisotropic and isotropic thermal parameters for **1** (4 pages); listing of observed and calculated structure factors for **1** (10 pages). Ordering information is given on any current masthead page.

Backside Displacement in the Unimolecular Gas-Phase Decarboxylation of Alkyl Phenyl Carbonate Radical Cations

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Received June 24, 1991

Expulsion of carbon dioxide in the course of unimolecular rearrangements is well-known throughout organic and biological

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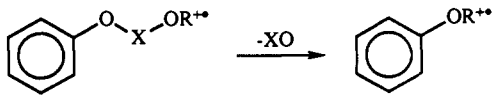
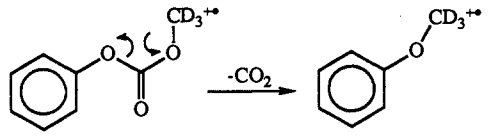
0002-7863/91/1513-9001$02.50/0

chemistry. We report here that the facile extrusion represented in eq 1, elimination of CO_2 (X = CO) from the molecular ions of carbonate esters in the gas phase,[1] inverts configuration when R is an alkyl group. This reaction was studied 25 years ago using



(1)

^{18}O labeling, which showed that the phenoxy oxygen is retained in the product ion.[2] At the time, several mechanisms were considered, none of which implies inversion of configuration. For example, the concerted interchange pictured in eq 2 has a four-center cyclic transition state whose geometrical constraints require retention of configuration at the migrating center. The exper-



(2)

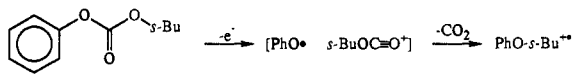
1 2

iments described herein exclude the previously suggested mechanisms and instead indicate that the reaction takes place via a bond fission followed by backside attack.

We first confirm that a new carbon–oxygen bond is indeed formed: methyl-d_3 phenyl carbonate radical cation (**1**) decomposes in the mass spectrometer to form the molecular ion of anisole-d_3 (**2**).[3] A stereochemical labeling experiment then demonstrates that the reaction proceeds with inversion of configuration when R = *sec*-butyl (**3**).

Mass spectrometry can distinguish the diastereomers of 3-deuterio-2-phenoxybutane as well as characterize the positional isomer 2-deuterio-2-phenoxybutane.[4] We have therefore prepared three monodeuterated analogues of **3** and have used collisionally activated decomposition[5] (CAD) to probe the structures of the butyl phenyl ether ions (m/z 151) formed by the decarboxylations of the *sec*-butyl-d_1 phenyl carbonate radical cations. Expulsion of butene dominates these CAD spectra, and Table I compares the results with the fragment ion ratios from CAD of authentic samples. The data summarized in Table I show that the erythro carbonate yields the threo ether ion and vice versa. The reaction inverts configuration at the migrating center.

We interpret these results in terms of an intermediate ion–neutral complex, as represented in eq 3. A C–O bond breaks,



(3)

3

but the two fragments attract each other strongly enough to remain close even in the absence of intermolecular collisions. Then the phenoxy radical displaces CO_2 from the ion in an S_N2-type reaction. This involves known chemistry. Ions of the form $ROC{\equiv}O^+$ have been prepared in solution.[6] Ion–neutral complexes containing phenoxy radical are well-known in the gas phase.[7]

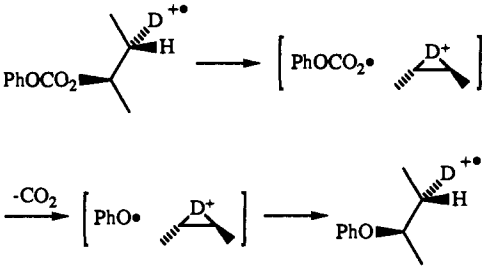
Table I. Fragment Ion Ratios ($PhOH^{+\bullet}$:$PhOD^{+\bullet}$) in the CAD of m/z 151 Ions from Specifically Monodeuterated Precursors

precursor (m/z 94):(m/z 95)	
$CH_3CH_2CD(CH_3)OPh$	$CH_3CH_2CD(CH_3)OCO_2Ph$
9.9 (0.8)[a]	8.4 (0.6)
$CH_3CHDCH(CH_3)OPh$ (erythro)	$CH_3CHDCH(CH_3)OCO_2Ph$ (threo)
3.43 (0.13)	3.44 (0.10)
$CH_3CHDCH(CH_3)OPh$ (threo)	$CH_3CHDCH(CH_3)OCO_2Ph$ (erythro)
3.00 (0.09)	2.95 (0.07)

[a] Values in parentheses correspond to standard deviations.

Nucleophilic displacement within ion–neutral complexes has precedent, since it is proposed in the decarbonylation of the molecular ion of acetamide.[8] While eq 3 does not necessarily imply backside displacement, S_N2 reactions at sp^3-hybridized carbon are well-known in the gas phase, both for nucleophilic anions attacking neutral molecules[9] and for neutral nucleophiles attacking cations. Where investigated, these have been shown to go via backside displacement.[10–12] Bimolecular substitution of water by alcohol in gaseous, protonated *sec*-butanol proceeds with inversion of configuration accompanied by a small amount of loss of configuration.[12] In the present case eq 3 gives the same sort of result: inversion of configuration with about 10% randomization (not detectable within experimental error for the 3-deuterio compounds but visible in 2-deuterio-*sec*-butyl carbonate).

A similar mechanism may operate for other leaving groups besides CO_2; e.g., acetal ions (X = CH_2) also decompose via eq 1 to give the same products for R = methyl and ethyl as seen from the corresponding carbonates. Stereochemistry rules out alternative complex-mediated pathways in the carbonate case. For instance, the ion–neutral complex might conceivably have been formed by fission of the sp^3 C–O bond to give *sec*-butyl cation with a phenoxycarbonyl radical, as drawn for the erythro d_1 isomer in eq 4. The prediction of this mechanism depends on the energy



(4)

content of the *sec*-butyl ion. One would expect it to have enough internal energy to scramble the non-methyl hydrogens completely[13] and give loss of configuration. But even if the ion were so cold that it remained in the bridged geometry calculated as the potential energy minimum,[14] the outcome would have been net retention of stereochemistry, as eq 4 portrays for a cation in which deuterium is the bridging atom. For the other diastereomeric starting material, half the product would have been formed with net retention and half with transposition of label.

Unimolecular expulsion of CO_2 is more sensitive to the identity of the alkyl group than are bimolecular S_N2 reactions in the gas

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phase. Fluoride reacts with neopentyl chloride to yield neopentyl fluoride.[9] However, neopentyl phenyl carbonate shows scarcely any extrusion of CO_2 in the mass spectrum (<0.05% of the phenol radical cation intensity). The labeled neopentyl phenyl carbonate ion **4** yields only $PhOH^{\bullet+}$ and $PhOD^{\bullet+}$ in the metastable ion mass spectrum (MIKES[5]), with no detectable M – CO_2 (m/z 166). In both MIKES and CAD, the $PhOH^{\bullet+}$:$PhOD^{\bullet+}$ ratios are the same as observed for $(CH_3)_3CCD_2OPh$.[15] We consider this result to be of special significance, for it implies that CO_2 expulsion for R = neopentyl yields the same [*tert*-amyl$^+$ PhO$^\bullet$] complex as does neopentyl phenyl ether,[16] as eq 5 depicts. The absence of any

$$(CH_3)_3CCD_2OC(=O)OPh^{\bullet+} \longrightarrow [(CH_3)_3CCD_2O\overset{+}{C}{\equiv}O \quad PhO^\bullet] \xrightarrow{-CO_2} PhOD^{\bullet+} \text{ or } PhOH^{\bullet+} \longleftarrow [(CH_3)_2\overset{+}{C}CD_2CH_3 \quad PhO^\bullet] \quad (5)$$

ion from recombination of these two fragments[17] suggests that proton transfer takes place at least 1000 times faster than reformation of a covalent bond for the low-energy ions in the MIKES.

In summary, the unimolecular decompositions of alkyl phenyl carbonate radical cations can be described using a familiar mechanistic vocabulary. For R = *sec*-butyl, expulsion of CO_2 occurs by means of bond fission and then backside displacement. We attribute the small amount of scrambling to a competing S_N1 pathway. For R = neopentyl, there is rearrangement followed by E1 elimination without any nucleophilic substitution. Viewed in this way, the pattern of gas-phase reactivity mirrors the trend seen in solution.

Acknowledgment. We are grateful to Prof. J. L. Holmes for providing a preprint of ref 18 prior to publication. This work was supported by the CNRS, the NSF (Grant CHE 88-02086), and a Fulbright travel grant to T.H.M.

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Elimination of Electrooxidizable Interferants in Glucose Electrodes

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Received June 13, 1991
Revised Manuscript Received September 25, 1991

Amperometric glucose electrodes, now in common use, are not as selective as they are intended to be, responding also to electrooxidizable interferants present in the analyzed medium.[1] A much studied assay is that of glucose in physiological fluids.

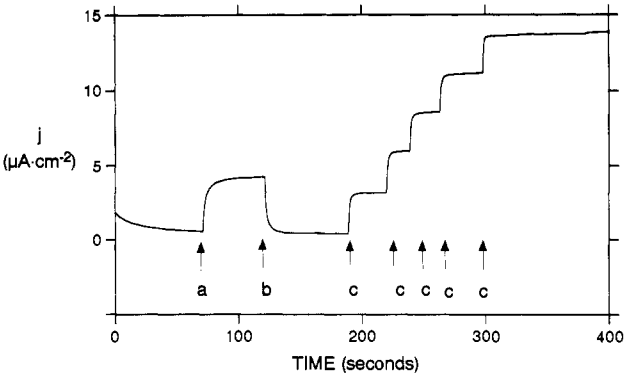

Figure 1. Oxidation currents measured with a bilayer electrode composed by an HRP film immobilized on top of an electrically "wired" GOD film. Ascorbate currents are eliminated by the HRP layer in the presence of hydrogen peroxide. The glucose concentration is unaffected and is measured by the "wired" GOD gel sensing layer: (a) ascorbate injection, 0.1 mM final concentration; (b) H_2O_2 injection, 0.1 mM final concentration; (c) glucose injections, 1.0 mM concentration steps. Three electrode stirred cell, glassy carbon working electrode poised at 0.5 V vs SCE, 0.1 M phosphate buffer pH 7.2, NaCl 0.1 M.

Glucose oxidase based electrodes respond also to ascorbate and urate ions and to *p*-acetamidophenol (Tylenol). These interferants may be oxidized both at the electrode surface or by a diffusing mediator or enzyme bound electron relay. Methods proposed to overcome their interference, based on size exclusion,[2] electrostatic repulsion,[3] electrochemical preoxidation,[4] or specific enzymatic reactions[5] partially solve but do not eliminate the problem of electrooxidizable interferants. Here we report on an enzymatic method that simplifies their combined elimination.

The enzyme horseradish peroxidase (HRP) catalyzes the oxidation of a range of compounds by hydrogen peroxide.[6] We find that urate, ascorbate, and *p*-acetamidophenol but not glucose are enzymatically oxidized. Interferants can thus be eliminated by their HRP-catalyzed oxidation by hydrogen peroxide (eq 1). Using electrodes covered by a thin layer of glutaraldehyde immobilized HRP (300 U·cm^{-2}) the electrooxidation currents for the different interferants in the presence or absence of H_2O_2 were measured and are shown for ascorbate in Figure 1. When ascorbate is injected in the cell, a substantial oxidation current is observed. This current is no longer measurable after addition of H_2O_2, implying that ascorbate is oxidized to an electrochemically inert species. Subsequent additions of ascorbate do not result in an oxidation current provided that the H_2O_2 is not exhausted. The oxidation current for ascorbate is decreased by a factor of more than 2500 in the presence of H_2O_2. Control experiments show that both H_2O_2 and HRP must be present for the elimination of ascorbate. The results for ascorbate, urate, or *p*-acetamidophenol or their various combinations are similar.

$$\text{interferant} + \text{glucose} + H_2O_2 \xrightarrow{\text{HRP}} \text{oxidized interferant} + \text{glucose} + 2H_2O \quad (1)$$

The observed elimination of interferants was implemented in "wired" glucose oxidase electrodes where an HRP layer covered

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