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SPONTANEOUS REACTIONS OF POTASSIUM PHENOXIDE WITH DIBROMOPERFLUOROALKANES. FIRST EVIDENCE FOR BROMOPHILIC ATTACK ON C-Br BONDS BY THE PHENOXIDE ION.[1]

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Summary: In contrast to earlier reports, It has been found that dibromoperfluoroalkanes actually can react spontaneously with PhOK, yielding fluoroalkyl phenyl ethers as products. Evidence for an anionic chain mechanism involving a bromophilic attack by the phenoxide ion is presented.

The recent years have witnessed a growing interest in the reactions involving nucleophilic attacks on the halogen atoms of C-X bonds.[2] Dibromoperfluoroalkanes, such as CF_2Br_2 and CF_2BrCF_2Br, were found to be susceptible to such attacks by a variety of nucleophiles.[3-5] Notably, however, there is as yet no definitive evidence for a bromophilic attack on C-Br bond by oxygen nucleophiles,[6] one of the most common families of nucleophilic species. In fact, Rico and Wakselman have very recently communicated that phenoxides do not react spontaneously with CF_2BrX (X = Cl, Br and CF_2Br), although the reactions can be initiated by thiophenoxides and mercaptans.[4] These authors stated that a mercaptan was necessary to perform the reaction because ArO^- was probably too "hard" to attack $BrCF_2X$ in the first step of the reaction,[4] or because of the weakness of phenoxides in capability of transferring an electron to the substrates,[7] Furthermore, the spontaneity of the reaction of 2-allylphenol with CF_2Br_2 was attributed to the participation of small amounts of carbanions formed in this system.[5]

In contradiction to these allegations, we have found that PhOK can actually react spontaneously with 1,2-dibromo-2-chlorotrifluoroethane (1) in various solvents to afford phenyl ethers of the type $PhOCF_2CFXY$ (X,Y = Cl, Br, H) in good total yields. Thus, potassium phenoxide and 1, carefully purified and dried, were stirred in diglyme under argon for 2 h. The reaction was slightly exothermic and could be carried out either at room temperature or below. After work-up, distillation gave the main product 2. Yields of the minor products were determined by GC analysis calibrated with pure authentic samples. The results are shown in Table I.[8]

Formation of all the products can be best rationalized by an anionic chain mechanism (Scheme I). This scheme differs from those previously proposed in the initiation step (eq. 1), which is now postulated to be a nucleophilic attack on bromine by an oxygen nucleophile, the phenoxide ion.

$PhOCF_2CFBrCl$	$PhOCF_2CFClH$	$PhOCF_2CFCl_2$	$PhOCF_2CFBr_2$	$PhOCF_2CFBrH$
$\underline{2}$	$\underline{3}$	$\underline{4}$	$\underline{5}$	$\underline{6}$

Table I. Product Yields of the Reaction of PhOK with $\underline{1}$ at Room Temperature.

solvent	reaction time h.	Yield % (based on PhOK) $\underline{2}$	$\underline{3}$	$\underline{4}$	$\underline{5}$	$\underline{6}$	total
Benz.+ crown[a]	19	80	1	1	7	1	88
Diglyme	2	65	3	2	15	1	86
Tetraglyme	2	67	2	5	18	1	92
DMF	2	59	2	8	18	1	88
DMSO	2	59	2	5	16	1	82
HMPA	2	65	1	10	12	1	88

a. Dicyclohexo-[18]crown-6.

Scheme I

$$PhO^- + Br\text{-}CFClCF_2Br \longrightarrow PhOBr + \underset{\underline{7}}{{}^-CFClCF_2Br} \text{ (and } \underset{\underline{8}}{{}^-CF_2CFClBr}) \qquad (1)$$

$$\underline{7} \text{ (and } \underline{8}) \longrightarrow CF_2{=}CFCl + Br^- \qquad (2)$$

$$PhO^- + CF_2{=}CFCl \longrightarrow PhOCF_2CFCl^- \;\; \underline{9} \qquad (3)$$

$$\underline{9} + CF_2BrCFBrCl \longrightarrow \underline{2} + \underline{7} \text{ (and } \underline{8}) \qquad (4)$$

$$\underline{9} + PhOBr \longrightarrow \underline{2} + PhO^- \qquad (5)$$

$$\underline{9} + H^+\text{-donor} \longrightarrow \underline{3} \qquad (6)$$

$$\underline{9} + Cl\text{-}CFBrCF_2Br \longrightarrow \underline{4} + \underset{\underline{10}}{{}^-CFBrCF_2Br} \qquad (7)$$

$$PhO^- + ClCFBrCF_2Br \longrightarrow PhOCl + \underline{10} \qquad (8)$$

$$\underline{10} \longrightarrow CF_2{=}CFBr + Br^- \qquad (9)$$

$$PhO^- + CF_2{=}CFBr \longrightarrow \underset{\underline{11}}{PhOCF_2CFBr^-} \qquad (10)$$

$$\underline{11} + CF_2BrCFBrCl \longrightarrow \underline{5} + \underline{7} \text{ (and } \underline{8}) \qquad (11)$$

$$\underline{11} + H^+\text{-donor} \longrightarrow \underline{6} \qquad (12)$$

It is noteworthy that using 1 as a substrate provides an additional piece of evidence, i.e., the lack of symmetry of 1 leads to the formation of an unsymmetrical olefin CF_2=CFCl, and only nucleophiles are known with certainty to add regiospecifically to the CF_2-end of such an alkene.[9] Furthermore, in accordance with an anionic chain mechanism, the use of PhOH/KOH instead of PhOK resulted in significant retardation of this reaction, whereas the absolute yields of 3 (23%) and 6 (6%) were increased.

Apparently as minor reaction pathways, "positive"-chlorine abstraction reactions, eq.(7) and (8), were also involved, as implicated by the formation of the products 4, 5 and 6. In fact, considerable amounts of 5 suggest that an initiation step involving a chlorophilic attack by PhO^- (eq. 8) is rather likely.

This complication would no longer exist in the reactions of PhOK with CF_2Br_2 and CF_2BrCF_2Br. In fact, we soon found in a reexamination that they also reacted smoothly at room temperature without initiating reagent. With CF_2BrCF_2Br, although the reaction was somewhat slower, the yield (up to 83%) of the main product $PhOCF_2CF_2Br$ was actually better than that from the reaction with $CF_2BrCFBrCl$. Similar results were obtained with $CF_2BrCFBrCF_3$ as the substrate, and again, the entering PhO group ended up on CF_2. Finally, the reaction with CF_2Br_2 under similar conditions likewise gave the expected product, $PhOCF_2Br$ (23%). The similarity in product distributions suggests that similar mechanistic pathways are involved throughout our reaction series.

Table 2. Reactions of PhOK with Dibromoperfluoroalkanes at room temperature

Substrate	Solvent	Reaction time h.	Products and Yields (%)[8]	
CF_2BrCF_2Br			$PhOCF_2CF_2Br$ 12,	$PhOCF_2CF_2H$ 13
	Benzene + crown	96	14	1
	Diglyme	36	66	1
	HMPA	6	83	2
$CF_2BrCFBrCF_3$			$PhOCF_2CFBrCF_3$ 14,	$PhOCF_2CFHCF_3$ 15
	DMF	8	80	2
CF_2Br_2			$PhOCF_2Br$ 16,	$PhOCF_2H$ 17
	Diglyme	8	23	5

With the objective of eliminating a remote possibility that these reactions were initiated by bromophilic attacks by carbanions derived from deprotonation of the solvents, we made use of the nonpolar aprotic solvent benzene containing a catalytic amount of dicyclohexo-[18]crown-6. Data in Tables 1 and 2 clearly demonstrate that these reactions proceed successfully, and obviously, solvent-derived carbanions can not be involved.

Finally, additional proof for the bromophilic attack by the phenoxide ion is provided by the mass-spectral indentification of ring-brominated products $Br-C_6H_4OCF_2CF_2Br$ (18) and $Br-C_6H_4-OCF_2CF_2H$ (19) in the PhOH/KOH/diglyme system, which are most likely derived from the electrophilic attack of PhOBr on phenyl rings.

In separate experiments, potassium benzyloxide and isopropoxide have also been shown to react spontaneously with $CF_2BrCFBrCl$, CF_2BrCF_2Br and $CF_2BrCFBrCF_3$, furnishing products analogous to those from phenoxide in fair to good yields. Thus, the bromophilic attack on the C-Br bond may well be a general reaction of oxygen nucleophiles.

References and Notes

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4. I. Rico, C. Wakselman, *Tetrahedron Lett.* 22, 323 (1981); *Tetrahedron,* 37, 4209 (1981); *J. Fluorine Chem.*, 20 (1982), 759.
5. I. Rico, C. Wakselman, *J. Fluorine Chem.* 20 (1982), 764.
6. The formation of $PhOCF_2H$ in the reaction of PhONa with CF_2Br_2 in acetone (see: ref. 3e) is most probably a consequence of an enolate ion initiated process, as we recently proved in a separate work.
7. I. Rico, D. Cantacuzene, C. Wakselman, *J. Org. Chem.* 48, 1979 (1983).
8. Satisfactory ^{1}H-NMR, ^{19}F-NMR and Mass spectra were obtained for all products. Selected Data:

    2, ^{19}F-nmr (neat), δ_{TFA} -4.1 (t, J = 9.7 Hz, 1 F), 5.7(d, J = 9.7 Hz, 2F); MS, m/e (%), 292 (3.5, $M^+ + 4$), 290 (13, $M^+ + 2$), 288 (9.3, M^+), 143 (33, $PhOCF_2^+$), 77 (100, $C_6H_5^+$).

    4, ^{19}F-nmr δ -3.3 (t, J = 8.4 Hz, 1F), 6.8(d, J = 8.4 Hz, 2F); MS, 248 (1.7, $M^+ + 4$), 246 (9.0, $M^+ + 2$), 244 (13, M^+), 143 (30, $PhOCF_2^+$), 77 (100).

    5, ^{19}F-nmr δ -3.5 (t, J = 12Hz, 1F), 5.0 (d, J = 12 Hz, 2F); MS, 336 (2.8, $M^+ + 4$), 334 (6.1, $M^+ + 2$), 332 (2.7, M^+), 143 (48, $PhOCF_2^+$), 77 (100).

    6, ^{1}H-nmr δ 6.18 (dt, J = 48 Hz, J = 4.9 Hz, 1H), 7.02 (s, 5H); ^{19}F-nmr δ 3.4 (dd, J = 15 Hz, J = 4.9 Hz, 2F), 79.2 (dt, J = 48 Hz, J = 15 Hz, 1F); MS, 256 (80, $M^+ + 2$), 254 (80, M^+), 175 (29, $M^+ - Br$), 143 (49, $PhOCF_2^+$), 94 (83, $PhOH^+$), 77 (100).

    14, ^{19}F-nmr δ -0.5 (m, 3F), 1.5 (m, 2F), 64.5 (m, 1F); MS, 324 (37, $M^+ + 2$), 322 (35, M^+), 243 (3.9, $M^+ - Br$), 143 (31, $PhOCF_2^+$), 93 (13.6, PhO^+), 77 (100).

    18, MS, 354 (29, $M^+ + 4$), 352 (56, $M^+ + 2$), 350 (29, M^+), 223 (13, $BrC_6H_4OCF_2^+ + 2$), 222 (14, $BrC_6H_4OCF_2^+$), 181 (5.1), 179 (5.2, $CF_2CF_2Br^+$), 173 (27), 171 (24, $BrC_6H_4O^+$), 157 (66), 155 (68, $BrC_6H_4^+$), 63 (100, $C_5H_3^+$).
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