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Synthesis of perfluoro-oxa-alkylated compounds by the use of perfluoro-oxa-alkanoyl peroxides and their applications

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Abstract

A series of perfluoro-oxa-alkanoyl peroxides [$(R_FCO_2)_2$; $R_F = C_3F_7O\{CF(CF_3)CF_2O\}_mCF(CF_3)$; $m = 0, 1, 2$] has been prepared by the reactions of the corresponding acyl fluorides and hydrogen peroxide under alkaline conditions. It has been demonstrated that perfluoro-oxa-alkanoyl peroxides are convenient tools for the introduction of perfluoro-oxa-alkyl groups into organic molecules with carbon–carbon bond formation. Such perfluoro-oxa-alkylated compounds possess unique properties such as extremely low surface tensions and new biological activities not demonstrated by the corresponding perfluoroalkylated materials.

Introduction

Incorporation of fluorine, trifluoromethyl or perfluoroalkyl groups into organic molecules leads to changes in the chemical and physical properties which yield products which have applications in various fields such as pharmaceuticals, agricultural chemicals and material science [1]. Hydrogen fluoride [2], potassium fluoride [3], DAST (diethylaminosulfur trifluoride) [4], cesium fluoroxy sulfate [5], *N*-fluoropyridinium salts [6] and *N*-fluorosulfonamides [7] are used for the preparation of selectively fluorinated compounds. Acrylic or methacrylic polymers containing perfluoroalkyl groups have been widely used in various fields, but the perfluoroalkyl groups are introduced into such polymers through the ester bond and so these materials are in general unstable under acid or alkaline conditions. Hence, the development of more efficient synthetic methodology for the direct introduction of perfluoroalkyl groups is especially desirable and has been actively studied. In general, perfluoroalkylations with perfluoroalkyl iodides provide convenient methods [8] for introducing perfluoroalkyl groups, since these starting materials can be handled easily and are commercially available. Copper-induced Ullmann-type reactions with perfluoroalkyl iodides [$CF_3(CF_2)_nI$; $n = 0, 1, 2,$

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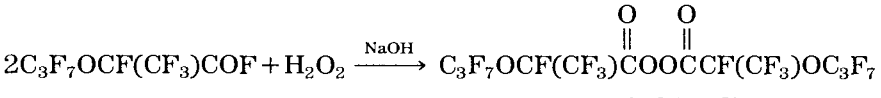
3, ... etc.] are a well-known strategy [9] for the preparation of perfluoroalkylated compounds with carbon–carbon bond formation. However, there are difficulties for the introduction of perfluoro-oxa-alkyl groups into molecules, although this is of considerable interest from both the synthetic and applications point of view. Thus, the chemistry of perfluoro-oxa-alkylated molecules has not yet been studied extensively.

Yoshida *et al.* have demonstrated that perfluoroalkanoyl peroxides [$(R_FCO_2)_2$; $R_F = CF_3, C_3F_7, C_6F_{13}, C_7F_{15}$] are useful reagents for the introduction of the corresponding perfluoroalkyl group into aromatic [10] and heteroaromatic compounds [11], and into electron-rich olefins such as styrene and ethyl vinyl ether [12]. We have also studied the synthesis and reaction behaviors of a series of perfluoro-oxa-alkanoyl peroxides [$(R_FCO_2)_2$; $R_F = C_3F_7O\{CF(CF_3)CF_2O\}_mCF(CF_3)$; $m = 0, 1, 2$]. Perfluoro-oxa-alkanoyl peroxides were found to be effective reagents for the introduction of the perfluoro-oxa-alkyl groups into organic molecules via single electron-transfer reactions analogous to the perfluoroalkanoyl peroxides. The perfluoro-oxa-alkanoyl peroxides are excellent precursors for the generation of perfluoro-oxa-alkyl radicals and are thus convenient tools for the synthesis of new functional materials containing perfluoro-oxa-alkyl groups with carbon–carbon bond formation. We have shown that perfluoro-oxa-alkylated compounds have various unique properties such as extremely low surface tensions, and new biological activities which cannot be achieved by the corresponding perfluoroalkylated materials. Here, we would like to describe our results, with particular emphasis on the synthesis and surface nature of these new compounds.

Synthesis and thermal decomposition of perfluoro-oxa-alkanoyl peroxides

In 1982, Zhao *et al.* reported that perfluoro-2-methyl-3-oxa-hexanoyl fluoride reacts with hydrogen peroxide under alkaline conditions to afford perfluoro-2-methyl-3-oxa-hexanoyl peroxide (POAP 2) [13].



$$2C_3F_7OCF(CF_3)COF + H_2O_2 \xrightarrow{NaOH} C_3F_7OCF(CF_3)\overset{\overset{O}{\|}}{C}OO\overset{\overset{O}{\|}}{C}CF(CF_3)OC_3F_7$$

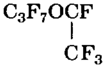
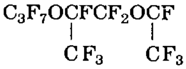
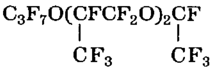
(POAP 2)

Scheme 1.

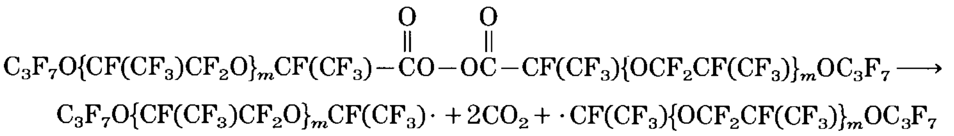
We have similarly succeeded in preparing a series of perfluoro-oxa-alkanoyl peroxides [$C_3F_7O\{CF(CF_3)CF_2O\}_mCF(CF_3)CO_2O_2CCF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$; $m = 1$ (POAP 3), 2 (POAP 4)] by using the corresponding acyl fluorides [14]. The infrared spectra of POAP 2, 3 and 4 all showed the characteristic diacyl peroxide carbonyl bands at 1825–1860 cm^{-1}. Thermal decomposition of these peroxides in $CF_2ClCFCl_2$ was found to occur readily in comparison with the perfluoroalkanoyl peroxides; see, for example, $(C_7F_{15}CO_2)_2$ listed in Table 1.

TABLE 1

Thermal decomposition and IR spectra of perfluoro-oxa-alkanoyl peroxides ($R_FCO_2O_2CR_F$) in $CF_2ClCFCl_2$

R_F	ΔE_a (kcal mol^{-1})	τ (min, 20 °C)	$\nu_{C=O}$ (cm^{-1})
 $C_3F_7O\underset{CF_3}{\underset{\mid}{C}}F$	24.3 [13]	240 [13]	1825, 1860
 $C_3F_7O\underset{CF_3}{\underset{\mid}{C}}FCF_2O\underset{CF_3}{\underset{\mid}{C}}F$	21.0	433	1830, 1860
 $C_3F_7O(\underset{CF_3}{\underset{\mid}{C}}FCF_2O)_2\underset{CF_3}{\underset{\mid}{C}}F$	22.1	261	1835, 1860
C_7F_{15}	25.2	614	1835, 1860

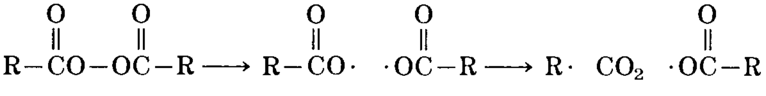
The half-life values and activation energies for POAP 2, 3 and 4 [22.1–24.3 kcal mol^{-1}) indicate that these peroxides decompose homolytically with fission of three bonds and are useful precursors for the generation of perfluoro-oxa-alkyl radicals.



$$C_3F_7O\{CF(CF_3)CF_2O\}_mCF(CF_3)-\overset{O}{\overset{\|}{C}}O-O\overset{O}{\overset{\|}{C}}-CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7 \longrightarrow$$
$$C_3F_7O\{CF(CF_3)CF_2O\}_mCF(CF_3)\cdot + 2CO_2 + \cdot CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$$

Scheme 2.

In contrast, the activation energy values for the decomposition of non-fluorinated alkanoyl peroxides are higher than those of the corresponding perfluoroalkanoyl peroxides by 5–8 kcal mol^{-1} and these peroxides are known to decompose by stepwise homolytic fission [15].



$$R-\overset{O}{\overset{\|}{C}}O-O\overset{O}{\overset{\|}{C}}-R \longrightarrow R-\overset{O}{\overset{\|}{C}}O\cdot \quad \cdot O\overset{O}{\overset{\|}{C}}-R \longrightarrow R\cdot \quad CO_2 \quad \cdot O\overset{O}{\overset{\|}{C}}-R$$

Scheme 3.

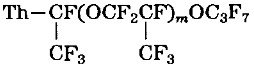
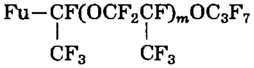
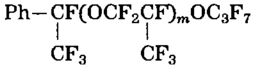
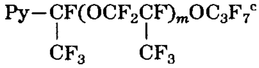
Introduction of perfluoro-oxa-alkyl groups into aromatic compounds

POAP 2, 3 and 4 were treated with benzene, furan, thiophene and pyrrole to give perfluoro-oxa-alkyl benzenes, -furans, -thiophenes and -pyrroles in moderate to high yield under mild conditions as shown in Table 2 [14].

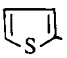
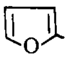
The orbital energy level of the unoccupied σ^*(O—O) orbital in POAP 2 (−1.507 eV) [16] was calculated by the MNDO molecular orbital method and shown to have a similar value to those of perfluorobutyryl peroxide

TABLE 2

Perfluoro-oxa-alkylations of aromatic compounds with peroxides: $[\text{C}_3\text{F}_7\text{O}\{\text{CF}(\text{CF}_3)\text{CF}_2\text{O}\}_m\text{-CF}(\text{CF}_3)\text{CO}_2]_2$

ArH	Peroxide	Temp. (°C)	Time (h)	Product (% yield)[a]
ThH[b]				 $\text{Th}-\underset{\text{CF}_3}{\text{CF}}(\text{OCF}_2\underset{\text{CF}_3}{\text{CF}})_m\text{OC}_3\text{F}_7$
	$m=0$	40	5	62
	$m=1$	40	5	65
	$m=2$	40	5	94
FuH[b]				 $\text{Fu}-\underset{\text{CF}_3}{\text{CF}}(\text{OCF}_2\underset{\text{CF}_3}{\text{CF}})_m\text{OC}_3\text{F}_7$
	$m=0$	40	5	62
	$m=1$	40	5	71
	$m=2$	40	5	96
PhH[b]				 $\text{Ph}-\underset{\text{CF}_3}{\text{CF}}(\text{OCF}_2\underset{\text{CF}_3}{\text{CF}})_m\text{OC}_3\text{F}_7$
	$m=0$	40	5	59
	$m=1$	40	5	30
	$m=2$	40	5	42
Pyrrole				 $\text{Py}-\underset{\text{CF}_3}{\text{CF}}(\text{OCF}_2\underset{\text{CF}_3}{\text{CF}})_m\text{OC}_3\text{F}_7$[c]
	$m=0$	r.t.	1	33
	$m=1$	r.t.	1	36
	$m=2$	r.t.	1	67
ThH[b]				
	$(\text{CF}_3\text{CO}_2)_2$	60	5	Th-CF_3 72 [10]
	$(\text{C}_3\text{F}_7\text{CO}_2)_2$	40	3	$\text{Th-C}_3\text{F}_7$ 98 [10]
	$(\text{C}_7\text{F}_{15}\text{CO}_2)_2$	40	3	$\text{Th-C}_7\text{F}_{15}$ 97 [10]

[a] Yields were determined by GC methods.

[b] Th- =  , Fu- = 

[c] Py indicates the pyrrolyl group.

(−1.614 eV) [17] and perfluoropropionyl peroxide (−1.385 eV) [17]. Thus, perfluoro-oxa-alkylation of the aromatic compounds with POAP 2–4 may be explained by the following scheme involving a single electron-transfer reaction from the substrates to the antibonding (2pσ*) O—O bond of the peroxide as was proposed for perfluoroalkylations with perfluoroalkanoyl peroxides [10].

$$
\begin{aligned}
(R_FCO_2)_2 + Ar{-}H &\longrightarrow [(Ar{-}H)^{\cdot +} + (R_FCO_2)_2^{\cdot -}] \\
&\longrightarrow [(Ar{-}H)^{\cdot +} + R_F\cdot + CO_2 + R_FCO_2^{-}] \\
&\longrightarrow Ar{-}R_F + R_FCO_2H + CO_2
\end{aligned}
$$

$R_F = CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$; Ar = Th, Fu, Ph, 2-pyrrolyl; $m = 0, 1, 2$

Scheme 4.

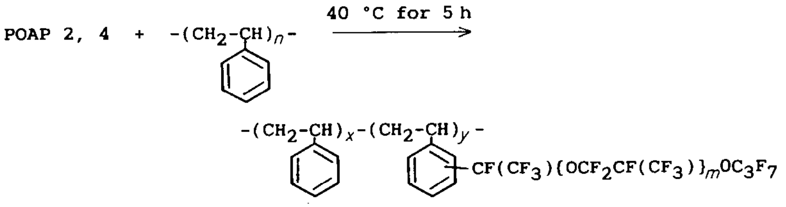
Furthermore, in the reactions of polystyrene with POAP 2 and 3, direct aromatic perfluoro-oxa-alkylations of polystyrene were found to proceed smoothly in moderate to high perfluoro-oxa-alkylated ratios (R_F ratios) under mild conditions, even though the reactions were carried out in heterogeneous systems [14] as for perfluoroalkanoyl peroxides (R_F ratios = *c.* 69%) [18].

Syuyama [19] and Pearce *et al.* [20] have individually reported that FITS (perfluoroalkyl phenyliodonium trifluoromethane sulfonate) and hexafluoroacetone, respectively, are useful reagents for the direct aromatic fluoroalkylation of polystyrene. However, these reagents give the corresponding fluoroalkylated compounds in low fluoroalkylated ratios.

Direct aromatic perfluoroalkylation ($R_F = C_3F_7$, C_6F_{13}, $(CF_2)_6H$, C_7F_{15}) of a polyimide (6FDA-BAPF) proceeded by using perfluoroalkanoyl peroxides under mild conditions; the T_g value of a perfluoroalkylated polyimide decreased whereas its dielectric constant was increased by the perfluoroalkylation [21].

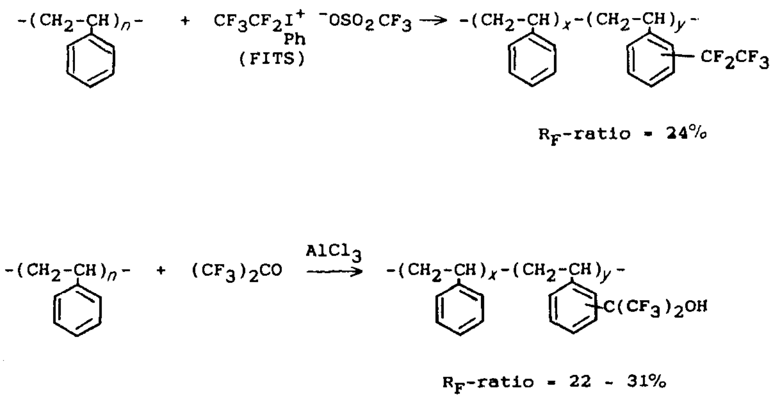
Perfluoroalkanoyl peroxides have been used for the synthesis of perfluoroalkylated styrene monomer. Thus, perfluoroalkylation of ethylbenzene derivatives occurred smoothly and the products were converted into perfluoroalkylated styrenes [22] (Scheme 9).

Perfluoroalkylated styrene monomers are very useful since the polymers which may be obtained by polymerization of these monomers are expected to be water- and oil-repellent, and applicable as optical materials in various fields.

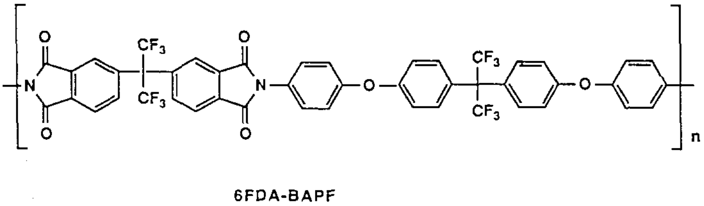


m	R_F ratio $[y/(x+y)]$ (%)	M_n	M_w/M_n
0	10	1.5×10^5	1.59
1	43	1.7×10^5	1.89
–	0	1.0×10^5	2.18

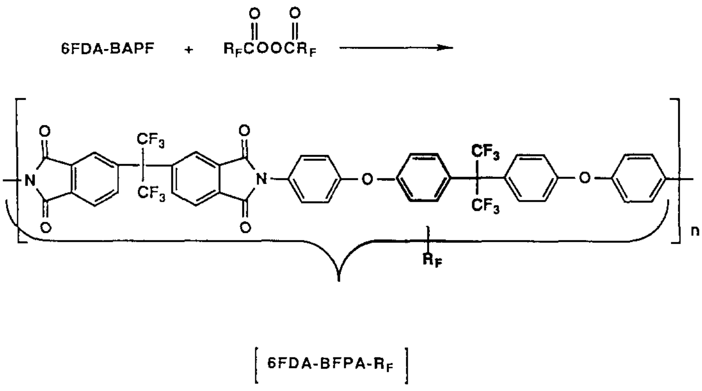
Scheme 5.



Scheme 6.



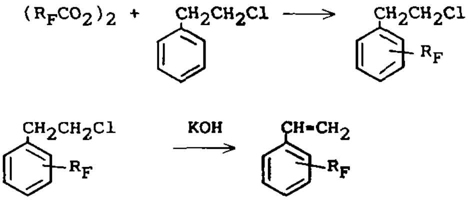
Scheme 7.



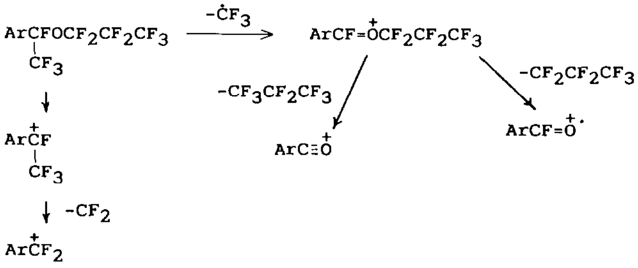
Scheme 8.

EI mass spectra of perfluoro-oxa-alkylated aromatic compounds

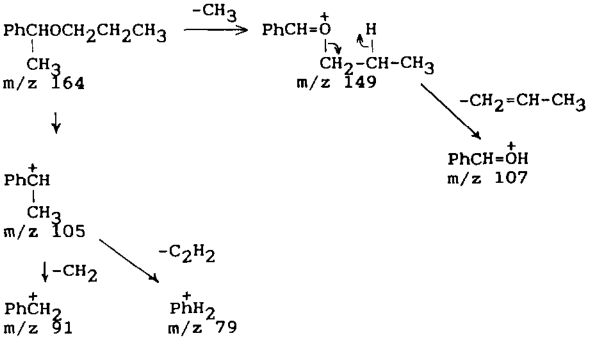
The EI mass spectral fragmentations of a series of perfluoro-oxa-alkylated aromatic compounds, [$ArCF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$; $m=0$, 1, 2; Ar = phenyl, 2-furyl, 2-thienyl, 2-pyrrolyl] have been studied relative to those of a non-fluorinated compound {$PhCH(CH_3)OC_3H_7$} and of fluoroalkylated benzenes [$Ph(CF_2)_nCF_3$; $n=2$, 6] [23].



Scheme 9.



Scheme 10.



Scheme 11.

Perfluoro-oxa-alkylated aromatic compounds exhibit the characteristic fragmentation pathways which result from α-fission of the parent ion and dissociation of an oxygen–carbon bond in a perfluoro-oxa-alkyl group on the basis of accurate mass measurements and *B*/*Z* constant-linked scannings (Scheme 10).

In the case of the non-fluorinated compound, we observed the usual rearrangement of a hydrogen atom associated with the alkyl group in an unsymmetrical ether (Scheme 11).

Perfluoroalkylated benzenes exhibit a mass fragmentation pathway involving loss of perfluoroalkyl groups to afford the difluorobenzyl ion.

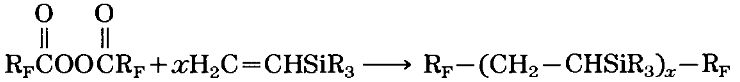
$$[Ph(CF_2)_nCF_3]^{\cdot +} \longrightarrow PhCF_2^+ \longrightarrow Ph^+$$

Synthesis of fluoroalkyl-containing organosilicon compounds by the use of fluoroalkanoyl peroxides

Considerable work has been devoted in recent years to the study of organosilicon compounds, due to their synthetic utilities and unique physical properties [24]. Particular effort has been focused on the synthesis of new functional organosilicon materials possessing the excellent properties imparted by fluorine.

Hydrosilylation of fluorine-containing alkenes promoted by organotransition metal catalysts such as platinum [25], ruthenium [26], rhodium [26] and palladium [26] complexes provides a convenient synthetic tool for the introduction of perfluoroalkyl groups. Hydrosilylation with a platinum catalyst has been commercially available for the production of 'fluorosilicone'. However, preparative methods for these compounds have hitherto been limited.

We were interested in preparing fluorine-containing organosilicon compounds by the use of fluoroalkanoyl peroxides. We found that new organosilicon oligomers not only perfluoroalkyl groups but also perfluoro-oxa-alkyl groups, $R_F-(CH_2CHSiR_3)_x-R_F$, may be obtained in excellent to moderate yields by the reaction of fluoroalkanoyl peroxides with the corresponding vinylsilanes under mild conditions as shown in Scheme 12 and Table 3 [27].

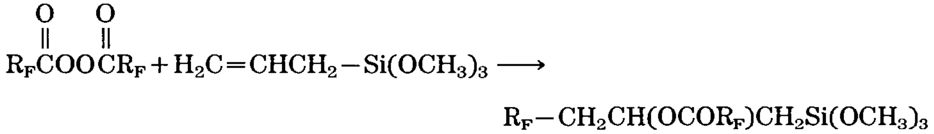


$$R_F\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}R_F + xH_2C{=}CHSiR_3 \longrightarrow R_F-(CH_2-CHSiR_3)_x-R_F$$

$(R_F = CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7,\ C_3F_7;\ m = 0,\ 1;\ R = OCH_3,\ CH_3)$

Scheme 12.

In contrast, allyltrimethoxysilane (AL-Si) was found to react with fluoroalkanoyl peroxides to give 1:1 adducts $[R_F-CH_2CH(OCOR_F)CH_2Si(OCH_3)_3]$ in good yields without oligomer formation [28] (Scheme 13).

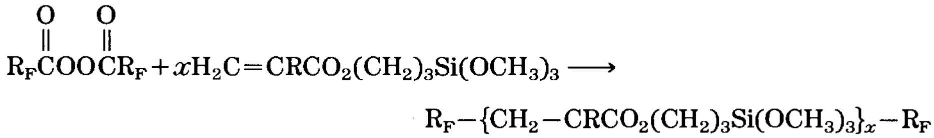


$$R_F\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}R_F + H_2C{=}CHCH_2-Si(OCH_3)_3 \longrightarrow R_F-CH_2CH(OCOR_F)CH_2Si(OCH_3)_3$$

$(R_F = CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7,\ C_3F_7,\ C_6F_{13};\ m = 0,\ 1)$

Scheme 13.

3-Methacryloxypropyltrimethoxysilane (MMA-Si) and 3-acryloxypropyltrimethoxysilane (AC-Si) were shown to react smoothly with the peroxides under mild condition to give fluorine-containing silicon oligomers in good yield [29] (Scheme 14).



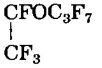
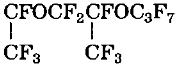
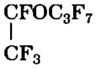
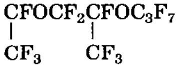
$$R_F\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}R_F + xH_2C{=}CRCO_2(CH_2)_3Si(OCH_3)_3 \longrightarrow R_F-\{CH_2-CRCO_2(CH_2)_3Si(OCH_3)_3\}_x-R_F$$

$(R_F = CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7,\ C_3F_7,\ C_6F_{13};\ m = 0,\ 1;\ R = CH_3,\ H)$

Scheme 14.

TABLE 3

Reactions of vinylsilanes with peroxides

Run No.	R in $R_3SiCH{=}CH_2$	R_F in $(R_FCO_2)_2$	$R_F{-}(CH_2{-}CHSiR_3)_{n_1}{-}R_F$	
			Isolated yield (%)	Product ratio $(n_1=2)/(n_1=3)$
1	OCH_3	C_3F_7	34	74:26
2	OCH_3	 $\underset{CF_3}{CF}OC_3F_7$	65	86:14
3	OCH_3	 $\underset{CF_3}{CF}OCF_2\underset{CF_3}{CF}OC_3F_7$	46	72:28
4	CH_3	 $\underset{CF_3}{CF}OC_3F_7$	93[a]	–
5	CH_3	 $\underset{CF_3}{CF}OCF_2\underset{CF_3}{CF}OC_3F_7$	95[a]	–

[a]Determined by GC methods. A trace amount of trimer was also detected.

The reactions of fluoroalkanoyl peroxides with vinylsilanes (including MMA-Si and AC-Si) and AL-Si gave quite different reaction products. It has been suggested that the different reactivities with the vinylsilanes and AL-Si are dependent upon the different HOMO energy levels and HOMO electron densities between these silicon compounds. In fact, both the HOMO electron densities and the HOMO energy levels of these substrates and styrene have been calculated using the MNDO-PM3 semiempirical MO method with the MOPAC 5.0 program [30], the results obtained being listed in Fig. 1.

Yoshida *et al.* have already reported that styrene reacts with perfluorobutyryl peroxide to give a 1:1 adduct [$PhCH(OCOC_3F_7)CH_2C_3F_7$] via single-electron transfer from styrene to the peroxide [31]. A strong interaction between HOMO and LUMO (peroxide) should assist electron transfer from AL-Si to the peroxide as shown in Scheme 15 since AL-Si has a similar HOMO energy level to styrene.

$$H_2C{=}CHCH_2Si(OMe)_3 + (R_FCO_2)_2 \longrightarrow H_2C\overset{+}{\overset{\cdot}{=}}CHCH_2Si(OMe)_3 + (R_FCO_2)_2^{\cdot-}$$

$$\longrightarrow H_2C\overset{+}{\overset{\cdot}{=}}CHCH_2Si(OMe)_3 + R_F\cdot + R_FCO_2^- + CO_2$$

$$\longrightarrow R_F{-}CH_2{-}\overset{+}{C}HCH_2Si(OMe)_3 + R_FCO_2^- + CO_2$$

$$\longrightarrow R_F{-}CH_2CH(OCOR_F)CH_2Si(OMe)_3 + CO_2$$

Scheme 15.

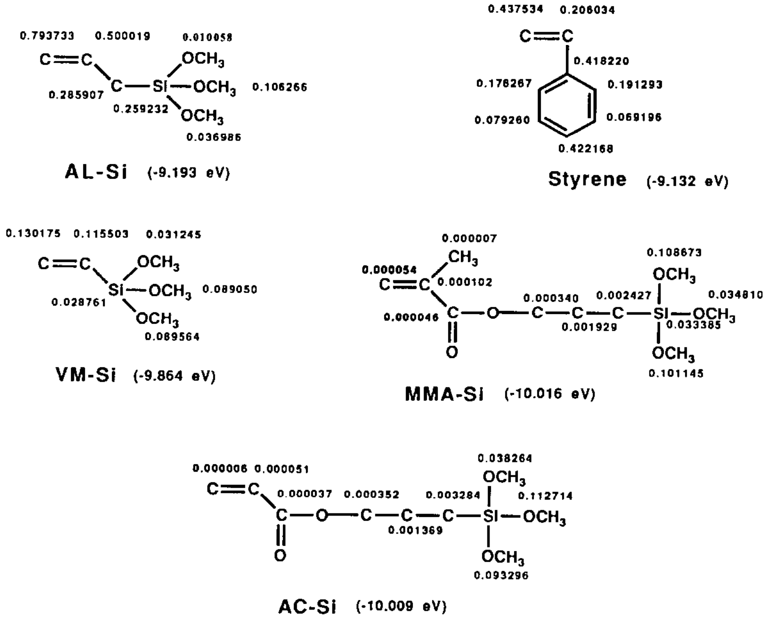


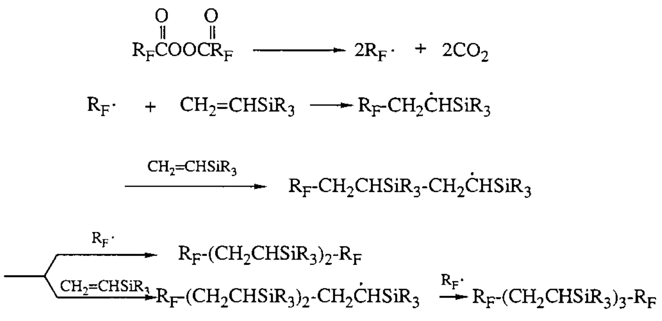
Fig. 1. HOMO energy levels and HOMO electron densities of AL-Si, styrene, VM-Si, MMA-Si and AC-Si calculated using the MNDO-PM3 semiempirical MO method with the MOPAC 5.0 program.

As shown in Fig. 1, the site where the higher electron density in the HOMO orbital of AL-Si was found would be preferentially fluoroalkylated via electron transfer in the same manner as with styrene. In particular, the carbonium ion in the β position relative to a silicon atom in Scheme 15 should be stabilized by σ–π conjugation which is shown as a very large resonance effect [32], so that an electron-transfer reaction from AL-Si to the peroxide would proceed more smoothly.

Vinyltrimethoxysilane (VM-Si), MMA-Si or AC-Si have considerably lower HOMO energy levels than that shown in Fig. 1 for AL-Si. In general, fluoroalkyl radicals are electrophilic due to the high electronegativity of fluorine. Hence, an interaction between SOMO (fluoroalkyl radical) and HOMO (VM-Si, MMA-Si or AC-Si) should determine radical addition to VM-Si, MMA-Si or AC-Si of a fluoroalkyl radical ($R_F\cdot$) produced by the thermal decomposition of the peroxide, thus affording the corresponding oligomers in good yield as in the reaction of VM-Si shown in Scheme 16.

Synthesis of fluoroalkylated oligomers with carbon–carbon bond formation via radical processes

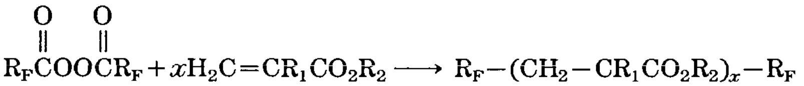
Acrylic or methacrylic polymers containing perfluoroalkyl groups exhibit excellent physical, thermal, and surface properties. Usually, perfluoroalkyl groups are introduced into polymers through the ester bonds, and these



Scheme 16.

materials are in general unstable owing to the ester moieties. A novel synthetic method for the direct fluoroalkylation of these compounds is provided by a radical process using fluoroalkanoyl peroxides to promote carbon–carbon bond formation. Particularly in the case of a substrate such as methyl methacrylate (MMA, -10.522 eV) or acrylic acid (ACA, -11.134 eV), possessing a lower HOMO energy level than styrene (-9.132 eV), it can be suggested that a radical addition reaction of the type shown in Scheme 16 would occur easily to afford a fluoroalkylated oligomer.

Reactions of MMA and ACA with peroxides have been found to proceed smoothly to afford the corresponding perfluoroalkylated and also perfluoro-oxa-alkylated oligomers in excellent to moderate yields under very mild conditions (Scheme 17) [33, 34]. Table 4 lists some fluoroalkylated acrylic acid oligomers prepared from fluoroalkanoyl peroxides.



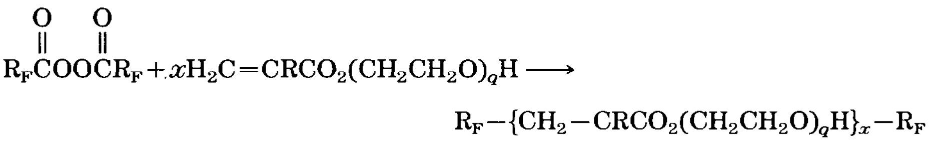
$$R_F\overset{\overset{O}{\|}}{C}OO\overset{\overset{O}{\|}}{C}R_F + xH_2C{=}CR_1CO_2R_2 \longrightarrow R_F{-}(CH_2{-}CR_1CO_2R_2)_x{-}R_F$$

($R_1 = H$, CH_3; $R_2 = H$, CH_3; $R_F = CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$, C_3F_7, C_6F_{13}; $m = 0, 1, 2$)

Scheme 17.

Some of the oligomeric products obtained ($M_w/M_n > 1.0$) can only contain one fluorinated end-group per molecule, since these reactions were considered to proceed by the usual addition to MMA or ACA of fluoroalkyl radicals produced by the thermal decomposition of the peroxides.

In the case of methacrylate or acrylate monomers containing hydroxy ethylene oxide units, oligomers containing such units linked to perfluoro-oxa-alkylated were obtained under similar conditions [33, 39] (Scheme 18).



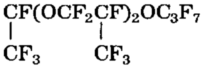
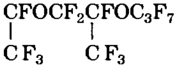
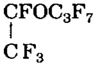
$$R_F\overset{\overset{O}{\|}}{C}OO\overset{\overset{O}{\|}}{C}R_F + xH_2C{=}CRCO_2(CH_2CH_2O)_qH \longrightarrow R_F{-}\{CH_2{-}CRCO_2(CH_2CH_2O)_qH\}_x{-}R_F$$

($R = CH_3$, H; $q = 1$–9)

Scheme 18.

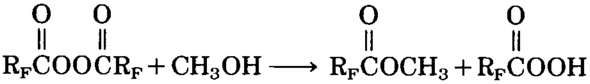
TABLE 4.

Reactions of acrylic acid with fluoroalkanoyl peroxides

Run No.	Acrylic acid (mmol)	R_F in $(R_FCO_2)_2$ (mmol)	Isolated yield (%)[a]	M_n (M_w/M_n)
1	17	 $\underset{CF_3}{C}F(OCF_2\underset{CF_3}{C}F)_2OC_3F_7$ (6.8)	29	12800 (1.72)
2	120	 $\underset{CF_3}{C}FOCF_2\underset{CF_3}{C}FOC_3F_7$ (50)	34	11200 (1.54)
3	566	 $\underset{CF_3}{C}FOC_3F_7$ (236)	45	12000 (1.54)
4	204	C_3F_7 (95)	39	5100 (1.47)
5	69	C_6F_{13} (29)	26	4600 (1.43)

[a] Yields based on the starting materials {acrylic acid and the decarboxylated peroxide unit (R_F-R_F)}.

Perfluoroalkanoyl peroxides react with substrates containing hydroxy groups such as methyl alcohol via transesterification, as shown in Scheme 19 [35].



$$R_F\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}R_F + CH_3OH \longrightarrow R_F\overset{O}{\overset{\|}{C}}OCH_3 + R_F\overset{O}{\overset{\|}{C}}OOH$$

Scheme 19.

However, in reactions with monomers containing hydroxylated ethylene oxide units, oligomerization to afford perfluoro-oxa-alkylated oligomers containing hydroxy groups was observed rather than transesterification.

The different reactivities between these monomers and methyl alcohol may be correlated with the sites of the HOMO electron densities in these compounds. The higher electron density in the HOMO orbital of hydroxyethyl methacrylate (HEMA) was not found at the same hydroxy position as in methyl alcohol but rather at the vinyl position. Hence, interaction between SOMO ($R_F\cdot$) and HOMO (HEMA) should determine the radical addition of $R_F\cdot$ to the vinyl group in HEMA.

Surfactive properties of perfluoro-oxa-alkylated aromatic compounds

It is well known that surfactive compounds bearing perfluoroalkyl chains as hydrophobic and oleophobic moieties exhibit much lower surface tensions in their solutions than those bearing non-fluorinated alkyl chains. Usually, long-chain ($C > 5$) perfluoroalkanoic and perfluoroalkanesulfonic acids, and perfluoroalkyl acrylate polymers, are widely used as fluorinated surfactants. These surfactants, however, possess straight perfluorinated carbon chains and these structures are known to be hard and inflexible giving a low solubility in various solvents. Hence, it is desirable to develop surfactants bearing other fluoroalkyl groups such as perfluoro-oxa-alkyl.

We have measured the reduction of surface tension by fluorinated surfactants possessing perfluoroalkyl and perfluoro-oxa-alkyl groups [36]. Those having perfluoro-oxa-alkyl groups were capable of reducing the surface tension of *m*-xylene to *c.* 10 dyn cm^{-1} (see Fig. 2).

The behavior of surfactants possessing perfluoro-oxa-alkyl groups is of particular interest because they exhibit a surface activity not shown either by ordinary hydrocarbon surfactants or other fluoroalkylated surfactants. This unique surface tension reduction is associated with a surfactant having a particular number of trifluoromethyl groups and ether linkages.

Similarly, the critical surface tension of the perfluoro-oxa-alkylated polystyrene (Pst-R_F, prepared by the reaction of polystyrene with perfluoro-oxa-alkanoyl peroxides) films is diminished dramatically in comparison with those of perfluoroalkylated polystyrene as shown in Table 5 [37].

The critical surface tension (γ_c) of both perfluoro-oxa-alkylated and perfluoroalkylated polystyrene films decreased with an increase in the R_F

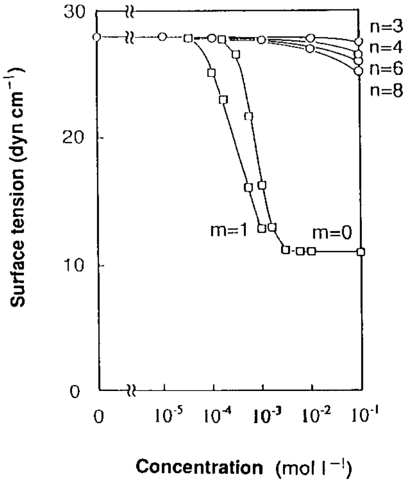


Fig. 2. Plot of surface tension versus concentration for Ph−RF/*m*-xylene solutions (at 30 °C): (○) $R_F=C_nF_{2n+1}$; (□) $R_F=CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$ ($m=0$, 1).

TABLE 5

Critical surface tension [γ_c (dyn cm^{-1})] of Pst-$CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$ and Pst-$(CF_2)_nCF_3$ films

Polymer	R_F ratio (%)	γ_c (dyn cm^{-1})
Pst-$CF(CF_3)\{OCF_2CF(CF_3)\}_mOC_3F_7$		
$m=0$	0	35.7
	2	27.2
	5	24.6
	10	22.7
$m=1$	4	25.4
	6	24.0
	13	16.2
	43	16.2
Pst-$(CF_2)_nCF_3$		
$n=2$	4	28.7
	12	26.4
	26	25.2
	40	24.7
	69	24.6
$n=5$	2	27.0
	3	26.2
	7	25.5
	16	23.5
	30	23.4
	60	23.4
$n=6$	67	23.3

ratio, but remained constant above a specific R_F ratio value [for example, 13% when $R_F = CF(CF_3)OCF_2CF(CF_3)OC_3F_7$].

Surfactive properties of organosilicon compounds containing fluoroalkyl groups

Organosilicon compounds containing fluoroalkyl groups obtained by the reaction of VM-Si, AL-Si, MMA-Si and AC-Si with fluoroalkanoyl peroxides are useful as surface-active substances. These compounds have been evaluated for their surface activity as new types of fluorine-containing silane-coupling agents [28, 29].

As Table 6 shows, the contact angles of water and dodecane on treated glass were found to increase significantly, indicating that these compounds possess good water- and oil-repellency.

The surface tensions (especially, the oil-repellency) on glass treated with these fluorine-containing silane-coupling agents showed a greater decrease

TABLE 6

Contact angles of water and dodecane on glass treated with fluorine-containing organosilicon compounds

Fluorine-containing organosilicon compound		Contact angle (°)	
		Water	Dodecane
$R_F-\{CH_2CHSi(OMe)_3\}_x-R_F$			
$R_F=$			
C_3F_7		96	50
$CF(CF_3)OC_3F_7$		111	67
$CF(CF_3)OCF_2CF(CF_3)OC_3F_7$		112	67
$R_FCH_2CH(OCOR_F)CH_2Si(OEt)_3$			
$R_F=$			
C_3F_7		106	60
C_6F_{13}		110	61
$CF(CF_3)OC_3F_7$		110	71
$R_F-\{CH_2CRCO_2(CH_2)_3Si(OMe)_3\}_x-R_F$			
$R_F=CF(CF_3)OC_3F_7$			
R=	M_n (M_w/M_n)		
Me	1200 (1.03)	107	61
Me	4000 (1.82)	100	48
H	820 (1.02)	107	45
Untreated glass		49	0

for the perfluoro-oxa-alkylated compounds in comparison to the perfluoroalkylated materials, as has been observed for fluoroalkylated aromatic compounds.

Properties of fluorinated amphiphiles prepared by perfluoro-oxa-alkanoyl peroxides

Recently, much effort has been focused on the synthesis and surfactant properties of long-chain fluorinated amphiphiles such as perfluoroalkyl-polyoxyethylenes, in which the hydrophobic tail is a perfluoroalkyl chain and the hydrophilic head is a polyoxyethylene unit [38]. A Williamson-type condensation between a fluoroalcohol ($C_mF_{2m+1}OH$) and ethylene oxide has been used for the synthesis of these compounds.

Various fluorinated amphiphiles can now be prepared readily by the use of fluoroalkanoyl peroxides (e.g. Schemes 17 and 18).

The surfactant properties of the new fluorinated amphiphiles containing carboxy groups [$R_F-\{CH_2-CH(CO_2H)\}_x-R_F$] have been evaluated from surface tension measurements of their aqueous solutions at 25 °C. The results obtained are illustrated in Fig. 3 [34, 39].

A decrease in the surface tension of water was found for both perfluoro-oxa-alkylated and perfluoroalkylated acrylic acid oligomers. In particular, the oligomer bearing the perfluoro-oxa-alkyl group provides a novel high molecular

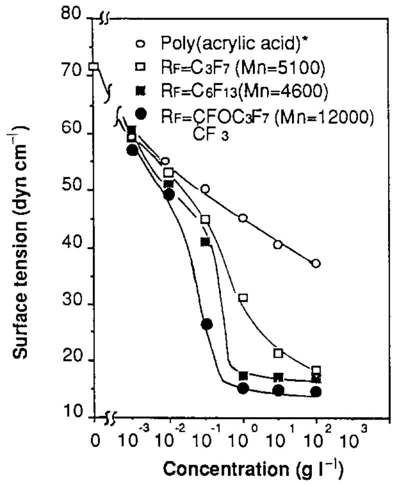


Fig. 3. Surface tensions of aqueous solutions of fluoroalkylated oligomers [R_F–{CH_2–$CH(CO_2H)$}$_x$$R_F$]. * Commercially available polyacrylic acid was used.

TABLE 7

Contact angles of water and dodecane on glass treated with perfluoro-oxa-alkylated oligomers [$R_F = CF(CF_3)OC_3F_7$]

Oligomer	M_n (M_w/M_n)	Contact angle (°)	
		Water	Dodecane
R_F–{CH_2–$CMe(CO_2Me)$}$_x$–R_F	1300 (1.13) 52100 (1.66)^a	98 (72)^a	49 (7)^a
R_F–[CH_2–CMe{$CO_2(CH_2CH_2HO)_2$}]$_x$–R_F	1500 (1.09)	55	47
R_F–[CH_2–CMe{$CO_2(CH_2CH_2O)_{4,5}H$}]$_x$–R_F	1400 (1.04)	5	46
R_F–[CH_2–CMe{$CO_2(CH_2CH_2O)_{7\text{–}9}H$}]$_x$–$R_F$	7130 (1.37)	0	46
R_F–[CH_2–CH{$CO_2(CH_2CH_2O)_{7\text{–}9}H$}]$_x$–$R_F$	4050 (1.73)	0	48

^{a}Commercially available methyl methacrylate polymer was used.

mass surfactant capable of greatly reducing the surface tension of water. This property could be dependent both upon the flexibility of the perfluoro-oxa-alkyl groups as a result of the ether linkage and the particular number of trifluoromethyl groups in these moieties. In addition, perfluoro-oxa-alkylated oligomers containing hydroxylated ethylene oxide units [R_F–{CH_2–$CRCO_2(CH_2CH_2O)_qH$}$_x$–R_F] were found to show surface properties typical of amphipathic compounds [33, 39].

The surface behavior of perfluoro-oxa-alkylated oligomers containing hydroxy ethylene oxide units (Table 7) is of considerable interest because the contact angles of these oligomers, especially those of oligomers bearing long ethylene oxide chains, exhibit strong hydrophilic properties despite the fact that these oligomers possess perfluoro-oxa-alkyl groups. These new fluorinated amphipathic compounds await exploitation in the medicinal and material fields.

Biological activity of 5-(perfluoro-1-methyl-2-oxa-pentyl)-1,3-dimethyluracil

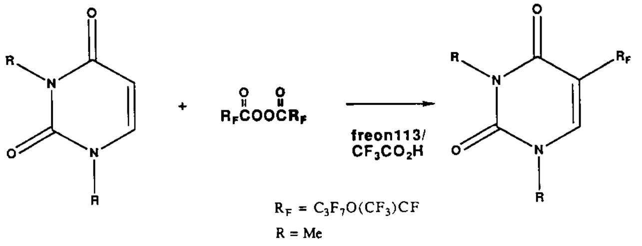
Fluorine-containing molecules such as 5-fluorouracil (5-FU) have attracted increasing attention because of their unique biological activities [1]. Various fluorinated [40], trifluoromethylated [41] and perfluoroalkylated [42] uracil derivatives have been synthesized and tested for their biological properties.

We have found that a new 5-(perfluoro-1-methyl-2-oxa-pentyl)-1,3-dimethyluracil (5-PFDU) may be prepared by the reaction of the corresponding peroxide with 1,3-dimethyluracil in $CF_2ClCFCl_2$ under mild conditions in the presence of trifluoroacetic acid as a cosolvent [43] (Scheme 20).

Interestingly, 5-PFDU displayed cytotoxicities as potent as 5-FU for both MT-4 cells and KB cells [43]. A different pharmacological mechanism from that for 5-FU would be expected since 5-PFDU has a perfluoro-1-methyl-2-oxa-pentyl group at C-5 instead of a fluorine atom.

Conclusions

This account shows that perfluoro-oxa-alkylated derivatives prepared by using perfluoro-oxa-alkanoyl peroxides exhibit unique properties which are not shown by the corresponding perfluoroalkylated compounds. The drastic decrease in the surface tension results from the flexibility of the perfluoro-oxa-alkyl groups due to the presence of ether linkages as well as the particular numbers of trifluoromethyl groups present. Useful biological activities are also exhibited. The reactivities of fluoroalkanoyl peroxides arise from two unique reaction pathways based on the HOMO energy levels of substrates: one is a single electron transfer from the substrate possessing the higher HOMO energy level such as styrene, allyltrimethoxysilane, ethyl vinyl ether or benzene to the peroxides; the other is an addition to the substrate (which possesses a lower HOMO energy level than that of benzene) of fluoroalkyl



Scheme 20.

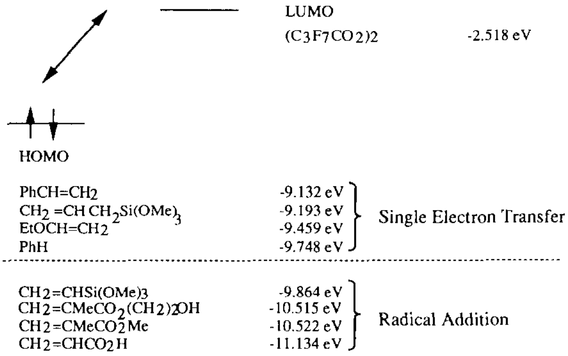


Fig. 4. HOMO energy levels of various substrates, the LUMO energy level of perfluorobutyryl peroxide and HOMO–LUMO interactions.

radicals produced by the thermal decomposition of the peroxides as shown in Fig. 4.

In particular, radical processes involving fluoroalkanoyl peroxides have been shown to be essential to the synthesis not only of perfluoro-oxa-alkylated but also of perfluoroalkylated oligomers containing functional groups such as carboxy and hydroxylated ethylene oxide with carbon–carbon bond formation. This method is widely applicable for the direct synthesis of fluoroalkylated, especially perfluoro-oxa-alkylated, oligomers as no convenient alternative exists at present.

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