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Synthesis and surfactant properties of novel acrylic acid oligomers containing perfluoro-oxa-alkylene units: an approach to anti-human immunodeficiency virus type-1 agents

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Abstract

A new polymeric perfluoro-oxa-alkane diacyl peroxide has been prepared by the reaction of the corresponding perfluoro-oxa-alkane diacid fluoride and hydrogen peroxide under alkaline conditions. The decomposition behavior of this peroxide was quite similar to those of the fluoroalkanoyl peroxides [$(R_FCOO_2)_2$; R_F = perfluoroalkyl and perfluoro-oxa-alkyl groups]. This peroxide decomposed homolytically with decarboxylation to afford the $-R_F-$ unit and, in addition, was useful for the introduction of the perfluoro-oxa-alkylene ($-R_F-$) unit into acrylic acid homo- and co-oligomers via a radical process. These new acrylic acid oligomers containing the perfluoro-oxa-alkylene unit were shown to be soluble in water, methanol, ethanol, and tetrahydrofuran and were not only able to reduce the surface tension of water effectively but also to confer a good oil repellency. Furthermore, acrylic acid co-oligomers containing this perfluoro-oxa-alkylene unit were found to be potent and selective inhibitors of human immunodeficiency virus type 1 (HIV-1) in vitro.

Keywords: Synthesis; Surface properties; Acrylic acid oligomers; Perfluoro-oxa-alkylene units; NMR/IR spectroscopy; HIV-1

1. Introduction

In general, perfluoroalkylated compounds have various unique properties such as low surface tensions, high affinity for oxygen, high chemical and light resistance, excellent thermal properties and biological activities which cannot be achieved by the corresponding non-fluorinated materials [1]. Usually, perfluoroalkyl groups are introduced into these materials through the ester bond, since the usual methods for alkylation cannot be applied to perfluoroalkylation due to the strong electronegativity of fluorine atoms, and these organofluorine compounds are unstable under acid or alkaline conditions because of the ester moieties. For this reason, it is most desirable to explore novel synthetic methodology for direct fluoroalkylation.

Reactions with perfluoroalkyl iodides, in particular copper-induced Ullmann-type reactions, are a convenient strategy for the preparation of perfluoroalkylated compounds [2]. We have actively studied the reaction behavior of a series of fluoroalkanoyl peroxides ($R_FCO_2O_2CR_F$, R_F = perfluoroalkyl, perfluoro-oxa-alkyl groups), which are useful reagents for the introduction of the corresponding fluoroalkyl group into arenes and olefins via a single-electron-transfer or radical process. In particular, we have demonstrated that perfluoro-oxa-alkylated compounds cause a considerable decrease in surface tension and exhibit new biological activities which cannot be achieved by the corresponding perfluoroalkylated compounds [3]. However, developments for the direct introduction of perfluoro-oxa-alkyl or perfluoro-oxa-alkylene unit into various substrates have hitherto been limited, despite these novel fluorinated compounds being the subject of considerable research of both a fundamental and an applied nature. Very recently, an Ullmann-type perfluoro-oxa-alkylation with perfluoro-oxa-alkyl iodides has been reported by Eapen's group [4]. However, in contrast, there has been no report on the direct introduction of a perfluoro-oxa-alkylene

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unit into organic molecules with carbon–carbon bond formation.

Recently, much attention has been also focused on poly(anionic) derivatives such as dextran sulfate, heparin and pentosan polysulfate owing to their exhibiting antiviral activity, in particular anti-human immunodeficiency virus type-1 (anti-HIV-1) activity [5]. However, a clinical trial with dextran sulfate failed to demonstrate a therapeutic effect on acquired immunodeficiency syndrome (AIDS) patients due to its low oral bioavailability and rapid degradation of dextran sulfate in vivo because of the presence of ester moieties [6]. Hence, it is strongly desirable to explore novel polymeric inhibitors with high stability, potent antiviral activity and low toxicity.

In a preliminary account, we reported the synthesis of a new polymeric perfluoro-oxa-alkane diacyl peroxide, and this peroxide was shown to be useful for the introduction of a perfluoro-oxa-alkylene unit into acrylic acid oligomers [7]. Thus, numerous acrylic acid homo- and co-oligomers containing the perfluoro-oxa-alkylene unit with carbon–carbon bond formation derived from the corresponding polymeric perfluoro-oxa-alkane diacyl peroxide {$-[(O{:})CR_FC({:}O)OO]_p-$} are expected to be highly potent and selective poly(anionic) inhibitors of HIV-1 replication in vitro. In this paper, we describe the synthesis and surfactant properties of various novel acrylic acid homo- and co-oligomers containing a perfluoro-oxa-alkylene group using the polymeric perfluoro-oxa-alkane diacyl peroxide. Furthermore, we have examined these fluoroalkylated oligomers for their inhibitory effect on HIV-1 replication in vitro.

2. Results and discussion

The polymeric perfluoro-oxa-alkane diacyl peroxide (P-FPO) was prepared by the reactions of the corresponding perfluoro-oxa-alkane diacid fluoride and hydrogen peroxide in $CF_2ClCFCl_2$ under alkaline conditions as follows:

$$p\,F\text{–}\overset{O}{\overset{\|}{C}}R_F\overset{O}{\overset{\|}{C}}\text{–}F + pH_2O_2 \xrightarrow{OH^-} -[\overset{O}{\overset{\|}{C}}R_F\overset{O}{\overset{\|}{C}}OO]_p- \quad \text{(P-FPO)}$$

[$-R_F- = -(CF_3)CF[OCF_2(CF_3)CF]_n\text{–}O(CF_2)_5O\text{–}[CF(CF_3)CF_2O]_mCF(CF_3)-$, $(n+m=3)$]

The molecular mass of P-FPO could not be determined because of its thermal instability, but we succeeded in monitoring the thermal decomposition of P-FPO in $CF_2ClCFCl_2$ by iodometry at various temperatures from 26 °C to 35 °C. The rate of decomposition of P-FPO was found to conform very well to a first-order equation, and the results obtained are listed in Table 1.

The rate constants and activation parameters for the decomposition are quite similar to those for fluoroalkanoyl peroxides such as $[C_3F_7OCF(CF_3)CO_2]_2$ and $(C_7F_{15}CO_2)_2$,

Table 1
Thermal decomposition of polymeric perfluoro-oxa-alkane diacyl peroxide and fluoroalkanoyl peroxides in $CF_2ClCFCl_2$

Peroxide	Temp. (°C)	k_d (s^{-1}) × 10^5	ΔE_a (kcal mol^{-1})
$-[C({:}O)R_FC({:}O)OO]_p-$	26	8.33 ± 0.04	
	30	14.73 ± 0.52	21.9
	35	25.27 ± 0.85	
$(C_7F_{15}CO_2)_2$ [a]	30	11.8	23.5
$[C_3F_7OCF(CF_3)CO_2]_2$ [b]	30	19.6	23.9

[a] See Ref. [8].
[b] See Ref. [9].

suggesting a concerted dissociation with three-bond homolytic fission as previously reported [8,9].

$$R_F\overset{O}{\overset{\|}{C}}OO\overset{O}{\overset{\|}{C}}R_F \longrightarrow R_F\cdot + 2CO_2 + \cdot R_F$$

(R_F = perfluoroalkyl, perfluoro-oxa-alkyl group)

These results indicate that P-FPO decomposes with simultaneous homolysis of the C–C (carbonyl carbon–fluoroalkyl carbon) and O–O peroxy bonds in the same manner as the perfluoroalkanoyl and perfluoro-oxa-alkanoyl peroxides [$(R_FCO_2)_2$] which decompose homolytically with decarboxylation to afford $R_F\cdot$ radicals [8,9], and thereby provides a useful tool for the introduction of the perfluoro-oxa-alkylene unit ($-R_F-$) into oligomers via a radical process.

$$-(O\overset{O}{\overset{\|}{C}}R_F\overset{O}{\overset{\|}{C}}O)_p- \longrightarrow -(O\overset{O}{\overset{\|}{C}}\cdots R_F\cdots\overset{O}{\overset{\|}{C}}O\cdots)_p-$$

The reactions of P-FPO with acrylic acid were carried out for 5 h at 45 °C.

$$-[\overset{O}{\overset{\|}{C}}R_F\overset{O}{\overset{\|}{C}}OO]_p- + q\,pCH_2{=}CHCO_2H \xrightarrow{45\ °C/5\ h} -\{R_F\text{–}[CH_2\text{–}CH(CO_2H)]_q\}_p-$$

(P-FPO) (ACA)

The results are listed in Table 2.

As shown in Table 2, the reactions of P-FPO with acrylic acid proceeded smoothly to afford in good yield acrylic acid oligomers containing the perfluoro-oxo-alkylene unit. The molecular weights of the oligomers obtained were found to be sensitive to the molar ratio of acrylic acid/P-FPO, increasing with higher acrylic acid to P-FPO ratios as is usual for radical oligomerizations. Furthermore, it was found that as the proportion of acrylic acid increased, the content of $-R_F-$ units decreased from 8% to 2% (mol/mol). If each oligomerization listed in Table 2 proceeded with 100% yield, the corresponding theoretical $-R_F-$ unit content would decrease from 32% to 4% (mol/mol). Hence, the $-R_F-$ unit was introduced into the acrylic acid oligomers in only moderate yield. The reaction of P-FPO with acrylic acid is considered to be

Table 2
Reactions of polymeric perfluoro-oxa-alkane diacyl peroxide (P-FPO) with acrylic acid

ACA (mmol)	ACA/P-FPO (mol/mol)	Yield (%) [a]	$-\{R_F-[CH_2-CH(CO_2H)]_q\}_p-$	
			$\overline{M_n}$ ($\overline{M_w}/\overline{M_n}$)	Content of $-R_F-$ unit (wt.%) [b]
14	28	67	9900 (1.89)	8 (32) [c]
28	56	58	12000 (1.55)	7 (19)
35	117	77	13100 (1.51)	3 (10)
150	300	78	26300 (1.34)	2 (4)

[a] Yields based on the starting material (acrylic acid) and the decarboxylated peroxide unit ($-R_F-$).
[b] Content of $-R_F-$ unit in oligomer determined by ^{19}F NMR spectroscopy by comparing the peak area of the CF_3 groups of the oligomer with that of benzotrifluoride as the internal standard.
[c] Theoretical $-R_F-$ unit content.

initiated by the radical addition of $-[OC(:O)R_F(C:O)O]_r-OC(:O)R_F\cdot$ to acrylic acid. Perfluoro-oxa-alkylene unit-containing acrylic acid oligomers $\{-[R_F-(CH_2CHCO_2H_q]_p-\}$ are also useful for new fluorinated AB-type block co-oligomers since the molecular weight of the perfluoro-oxa-alkylene group is relatively high (MW of $-R_F-=980$).

Additionally, we have succeeded in preparing a series of acrylic acid co-oligomers containing this perfluoro-oxa-alkylene unit via the reactions of P-FPO with acrylic acid and trimethylvinylsilane or methyl methacrylate as shown below:

$$-[\overset{O}{\overset{\|}{C}}R_F\overset{O}{\overset{\|}{C}}OO]_p- + x\,pCH_2{=}CHCO_2H + y\,pCH_2{=}CR_1R_2$$
$$\text{(P-FPO)} \qquad \text{(ACA)}$$
$$\xrightarrow{45\ ^\circ C/5\ h} -[R_F-(CH_2-\underset{CO_2H}{\underset{|}{C}H})_x-(CH_2CR_1R_2)_y]_p-$$

($R_1=H$, $R_2=SiMe_3$; $R_1=Me$, $R_2=CO_2Me$)

Table 3 lists the results for the co-oligomerization of acrylic acid and trimethylvinylsilane (or methyl methacrylate) with P-FPO. Acrylic acid co-oligomers containing not only trimethylsilyl but also methyl ester moieties were obtained in 5% ~ 24% isolated yield. Co-oligomerization involving trimethylvinylsilane gave lower molecular weight oligomers. This may be due to trimethylvinylsilane being less capable of polymerization compared to methyl methacrylate. These novel fluoroalkylated oligomers, in particular fluoroalkylated silicon oligomers, should attract attention as useful functional materials in various fields since there has been a great need for the development of new functional materials possessing the excellent properties imparted by both fluorine and silicon [10].

Interestingly, the series of acrylic acid homo- and co-oligomers containing the perfluoro-oxa-alkylene unit thus obtained were found to be readily soluble not only in water but also in water-soluble organic solvents such as methanol, ethanol and tetrahydrofuran. Hence, these oligomers are also applicable as new fluorinated surfactants. The surfactant properties of the fluorinated oligomers were evaluated by surface tension measurements of their aqueous solutions using the Du Nöuy ring method at 25 °C. As shown in Table 4, both acrylic acid homo- and co-oligomers containing this perfluoro-oxa-alkylene unit were found to decrease the surface tension of water effectively compared with non-fluorinated poly(acrylic acid). On the other hand, an acrylic acid oligomer containing two perfluoro-oxa-alkylated end-groups [$R_F-(CH_2CHCO_2H)_n-R_F$; $R_F=CF(CF_3)OC_3F_7$], which was obtained by the oligomerization of acrylic acid with the

Table 3
Reactions of P-FPO with acrylic acid and trimethylvinylsilane (or methyl methacrylate)

$ACA/CH_2{=}CR_1R_2$/P-FPO (mol/mol/mol)	$-[R_F-(CH_2-CHCO_2H)_x-(CH_2CR_1R_2)_y]_p-$		
	Yield (%) [a]	$\overline{M_n}$ ($\overline{M_w}/\overline{M_n}$)	x/y [b]
$R_1=H$, $R_2=SiMe_3$			
70/100/1	9	2000 (1.36)	91:9
56/28/1	24	5980 (1.89)	98:2
272/56/1	16	4960 (1.68)	98:2
$R_1=Me$, $R_2=CO_2Me$			
56/56/1	9	16400 (3.02)	55:45
69/34/1	5	6060 (1.93)	90:10

[a] Yields based on starting materials (acrylic acid, trimethylvinylsilane and methyl methacrylate) and decarboxylated peroxide unit ($-R_F-$).
[b] Co-oligomerization ratio determined by ^1H NMR spectroscopy.

Table 4
Surface tensions ($mN\ m^{-1}$) of aqueous solutions of a series of acrylic acid oligomers containing the perfluoro-oxa-alkylene unit

Oligomer [$\overline{M}_n$ (x/y)]	Conc. of oligomer ($g\ dm^{-3}$)				
	10^{-3}	10^{-2}	10^{-1}	10^{0}	10^{1}
$-\{R_F-(CH_2CHCO_2H)_q\}_p-$ [9000]	72.6	72.4	67.0	43.9	32.0
$-\{R_F-(CH_2CHCO_2H)_x-(CH_2CHSiMe_3)_y\}_p-$ [2000 (91:9)]	72.6	72.4	59.2	44.8	–
$R_F-(CH_2CHCO_2H)_n-R_F$; [$R_F=CF(CF_3)OC_3F_7$] [12000 ($\overline{M}_w/\overline{M}_n$ = 1.54)]	72.6	71.6	29.8	17.8	17.6
$-(CH_2CHCO_2H)_n-$ [2000]	72.6	72.2	66.2	57.5	44.9

corresponding $(R_FCOO)_2$ [11], was capable of reducing the surface tension of water more effectively than the acrylic acid homo- and co-oligomers containing the perfluoro-oxa-alkylene unit. This finding indicates that since $-[R_F-(CH_2CHCO_2H)_q]_p-$ is an AB-type block oligomer, the perfluoro-oxa-alkylene chains in this oligomer are not likely to be arranged regularly above the water surface compared with the perfluoro-oxa-alkyl chains in $R_F-(CH_2CHCO_2H)_n-R_F$.

In addition, we have measured the contact angles for water and dodecane on glass treated with acrylic acid oligomers containing the perfluoro-oxa-alkylene unit at 25 °C and obtained the results listed in Table 5.

We were not able to measure the contact angle of water since these oligomer films are easily soluble in water; however, the contact angles for dodecane on the treated glass were found to increase strongly in comparison to the non-fluorinated acrylic acid oligomers, indicating that fluorinated oligomers possessing higher contents of the $-R_F-$ unit (or lower molecular weight oligomers) confer a good oil repellency. In contrast, acrylic acid oligomers containing two perfluoro-oxa-alkylated end-groups showed a high contact angle (60 °C), higher than those of the corresponding acrylic acid homo- and co-oligomers containing the perfluoro-oxa-alkylene unit. The contact angle measurements also strongly suggest that oligomer coatings containing the perfluoro-oxa-alkylene unit, which shows strong oleophobic properties, could not be oriented on the surface of glass slides, suggesting that the perfluoro-oxa-alkylene chains are approximately parallel to each other compared with $R_F-(CH_2CHCO_2H)_n-R_F$.

Acrylic acid oligomers thus obtained with the corresponding polymeric perfluoro-oxa-alkane diacyl peroxide are new compounds containing perfluoro-oxa-alkylene units and made via carbon–carbon bond formation. Furthermore, these compounds have been demonstrated to have excellent solubility in water and to reduce the surface tension of water effectively. Thus, these fluorinated oligomers are expected to become novel poly(anionic) inhibitors of HIV-1 with high

Table 5
Contact angles of dodecane on glass treated with $-\{R_F-[CH_2-CH(CO_2H)]_q\}_p-$ and $-[R_F-(CH_2-CHCO_2H)_x-(CH_2CR_1R_2)_y]_p-$

Oligomer	$\overline{M}_n$ ($\overline{M}_w/\overline{M}_n$) [x:y]	Contact angle (°)
$-\{R_F-[CH_2-CH(CO_2H)]_q\}_p-$	9900 (1.89)	54
	12000 (1.55)	52
	13100 (1.51)	51
	26300 (1.34)	46
$-[R_F-(CH_2-CHCO_2H)_x-(CH_2CR_1R_2)_y]_p-$ (R_1 = H, R_2 = $SiMe_3$)	2000 (1.36) [91:9]	52
	5980 (1.89) [98:2]	45
	4960 (1.68) [98:2]	48
(R_1 = Me, R_2 = CO_2Me)	16400 (3.02) [55:45]	54
	6060 (1.93) [90:10]	48
$R_F-[CH_2-CH(CO_2H)]_n-R_F$; [$R_F=CF(CF_3)OC_3F_7$]	12000 (1.54)	60
$-[CH_2-CH(CO_2H)]_n-$	2000	11

Table 6
Inhibitory effect of acrylic acid oligomers containing the perfluoro-oxa-alkylene unit on the replication of HIV-1 in MT-4 cells

Oligomer	$\overline{M_n}$ ($\overline{M_w}/\overline{M_n}$)	x:y	EC_{50} (μg ml^{-1}) [a]	CC_{50} (μg ml^{-1}) [b]
$-[R_F-(CH_2CHCO_2H)_q]_p-$	12000 (1.55)	-	> 100	> 100
$-[R_F-(CH_2CHCO_2H)_x-(CH_2CR_1R_2)_y]_p-$	2000 (1.36)	91:9	1.8	> 100
(R_1 = H, R_2 = $SiMe_3$)	5980 (1.89)	98:2	1.7	> 100
	4960 (1.68)	98:2	3.4	> 100
(R_1 = Me, R_2 = CO_2Me)	16400 (3.02)	55:45	5.5	> 100
	6060 (1.93)	91:9	18	> 100
$R_F-(CH_2CHCO_2H)_n-R_F$; [R_F = $CF(CF_3)[OCF_2CF(CF_3)]_3OC_3F_7$]	8800 (1.42)		6.2	> 100
Dextran sulfate (MW = 5000)			1.2	> 100

[a] 50% effective concentration, based on the inhibition of HIV-1-induced cytopathic effects in MT-4 cells.
[b] 50% cytotoxic concentration, based on the impairment of viability of mock-infected MT-4 cells.

stability and low toxicity. Such acrylic acid homo- and co-oligomers containing this perfluoro-oxa-alkylene unit have been evaluated for activity against HIV-1 replication in MT-4 cells (see Table 6).

As shown in Table 6, an acrylic acid homo-oligomer containing this perfluoro-oxa-alkylene unit was found to be inactive. However, acrylic acid–trimethylvinylsilane and acrylic acid–methyl methacrylate co-oligomers containing the perfluoro-oxa-alkylene unit were potent inhibitors of HIV-1 replication. These compounds showed a 50% effective concentration (EC_{50}) of 1.7–18 μg ml^{-1} whereas the 50% cytotoxic concentration (CC_{50}) was > 100 μg ml^{-1} in each case. Of these, $-[R_F-(CH_2CHCO_2H)_x-(CH_2CHSiMe_3)_y]_p-$ ($\overline{M_n}$ = 5980; x:y = 98:2) was the most active, with a 50% effective concentration (EC_{50}) of 1.7 μg ml^{-1}, a value similar to that of dextran sulfate, which has been considered to be a potent and selective polymeric inhibitor of HIV-1 replication in cell culture to date. We have recently reported that acrylic acid oligomers containing two perfluoro-oxa-alkylated end-groups proved to be effective against HIV-1 replication in MT-4 cells [12]. However, our present acrylic acid co-oligomers containing the perfluoro-oxa-alkylene unit as listed in Table 6 were shown to be more highly potent and selective inhibitors of HIV-1 replication in MT-4 cells compared to these oligomers. It is suggested that dextran sulfate is easily degraded into inactive fragments by glycosidic cleavage since it is a polysaccharide [6], and might be desulfated by sulfatase enzyme in vivo. In contrast, since our acrylic acid co-oligomers containing the fluoroalkylene unit are structurally stable, our new fluorinated oligomers are expected to show distinct advantages over dextran sulfate.

3. Experimental details

3.1. Measurements

NMR spectra were measured using a JEOL-EX-270 FT-NMR (270 MHz) spectrometer. IR spectra were recorded on a HORIBA FT-300 FT-IR spectrophotometer. Molecular weights were calculated by using a JASCO 830-RI gel permeation chromatograph fitted with Shodex KF-804 and KF-8025 columns (calibrations based on polystyrene standards). The surface tensions and contact angles were measured at 25 °C using the Du Nöuy ring method and the goniometer type contact angle meter (ERMA G-1-1000) respectively, according to our previously reported method [13].

3.2. Materials

Polymeric perfluoro-oxa-alkane diacyl peroxide {[$-(O{:})C(CF_3)CF[OCF_2(CF_3)CF]_n-O(CF_2)_5O-[CF(CF_3)CF_2O]_mCF(CF_3)C({:}O)OO]_p$} was prepared as follows. To a solution of potassium carbonate (2.7 g) in 16.2 g of water, 30% hydrogen peroxide (65.1 mmol) and then $CF_2ClCFCl_2$ (250 g) was added at 5 °C. The two-phase solution was cooled to −5 °C, stirred and the solution of the corresponding perfluoro-oxa-alkane diacyl fluoride (18.6 mmol) in $CF_2ClCFCl_2$ (100 g) added drop by drop. The reaction mixture was then kept at −5 °C for 1 h. The $CF_2ClCFCl_2$ layer was separated and the concentration of the peroxide determined iodometrically (yield, 52%). IR ν(cm^{-1}): 1857, 1828 (C=O). Because of its instability, the solution of the peroxide in $CF_2ClCFCl_2$ thus obtained was used without further purification.

The perfluoro-oxa-alkane diacyl fluoride [$F(O{:})C(CF_3)CF[OCF_2(CF_3)CF]_n-O(CF_2)_5O-[CF(CF_3)CF_2O]_mCF(CF_3)C({:}O)F$; $(n+m) = 3$] used in the synthesis was supplied by PCR Inc. (Gainesville, FL, USA).

3.3. General procedure for the synthesis of acrylic acid oligomers containing the perfluoro-oxa-alkylene unit

Polymeric perfluoro-oxa-alkane diacyl peroxide [0.5 mmol (calculated on the basis of the peroxidic monomer unit {$-C({:}O)R_FC({:}O)OO-$} from iodometric titration)] in $CF_2ClCFCl_2$ solution (51.8 g) was added to a mixture of acrylic acid (28 mmol) and $CF_2ClCFCl_2$ (30 g). The solution was stirred at 45 °C for 5 h under nitrogen. The white powder obtained was reprecipitated from methanol ethyl acetate to give the perfluoro-oxa-alkylene unit-containing acrylic acid oligomers $-[-R_F-(CH_2CHCO_2H)_q]_p-$ $[-R_F- = (CF_3)$-$CF[OCF_2(CF_3)CF]_n-O(CF_2)_5O-[CF(CF_3)CF_2O]_mCF$-$(CF_3)$, $n+m=3]$ (1.44 g).

This oligomer exhibited the following spectral characteristics. IR ν(cm^{-1}): 3080 (OH); 1724 (C=O); 1330 (CF_3); 1244 (CF_2). ^{1}H NMR (CD_3OD) δ: 1.41–2.11 ($-CH_2-$); 2.26–2.62 (=CH–) ppm. ^{19}F NMR (CD_3OD, ext. CF_3CO_2H) δ: −3.6 to 8.2 (21F); −46.3 (2F); −49.6 (10F); −69.0 (3F) ppm. ^{13}C NMR (CD_3OD) δ: 36.4; 42.9; 178.5 ppm. $\overline{M_n} = 12\,000$ ($\overline{M_w}/\overline{M_n} = 1.55$) (determined by gel permeation chromatography using standard polystyrenes for calibration).

The following spectral data were obtained for the other products studied.

$-[-R_F-(CH_2CHCO_2H)_x-(CH_2CHSiMe_3)_y]_p-$; IR ν(cm^{-1}): 3120 (OH); 1709 (C=O); 1300 (CF_3); 1246 (CF_2). ^{1}H NMR (CD_3OD) δ: 0.05–0.25 ($-CH_3$); 1.35–2.85 ($-CH_2-$, =CH–) ppm. ^{19}F NMR (CD_3OD, ext. CF_3CO_2H) δ: −3.5 to 8.5 (21F); −46.0 (2F); −49.0 (10F); −68.0 (3F) ppm.

$-[-R_F-(CH_2CHCO_2H)_x-(CH_2CMeCO_2Me)_y]-$: IR ν(cm^{-1}): 3120 (OH); 1734 (C=O); 1300 (CF_3); 1244 (CF_2). ^{1}H NMR (CD_3OD) δ: 1.00–2.85 ($-CH_3$, $-CH_2-$, =CH–); 3.60–3.85 ($-CH_3$) ppm. ^{19}F NMR (CD_3OD, ext. CF_3CO_2H) δ: −3.5 to 8.5 (21F); −46.0 (2F); −49.0 (10F); −68.5 (3F) ppm.

3.4. Antiviral assays

The antiviral activity of the compounds against HIV-1 (HTLV-III_B strain) replication was based on the inhibition of virus-induced cytopathic effect in MT-4 cells as described previously [12]. Briefly, MT-4 cells were suspended in a culture medium at 1×10^5 cells ml^{-1} and infected with HIV-1 at a multiplicity of infection of 0.2. Immediately after virus infection, the cell suspension (100 μl) was added to each well of a microtiter tray containing various concentrations of test compounds. After a 4-d incubation at 37 °C, the number of viable cells was determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) method [14].

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