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Synthesis of new β-hydroxylated and β-carboxylated bisquaternary ammonium salts containing fluorinated spacer groups

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Abstract

The synthesis of new cationic bolaphiles in which the hydrophobic section is partially fluorinated, is described. These bisquaternary ammonium salts are obtained by quaternisation with methyl iodide of β-hydroxyamines and β-carboxyamines, synthesised from two sufficiently reactive intermediates, namely an ω–ω′ diepoxide and an ω–ω′ dibromoacetate which are the result of reaction with a diol, formula $HOCH_2(CF_2)_3CH_2OH$.

Keywords: Cationic bolaphiles

1. Introduction

The discovery of Archaebacteria, which thrive in harsh physical environments that are lethal to most other organisms, has stimulated research into the unique structural, biochemical, and physical properties of their membrane lipids [1–5]. The resistance of these bacteria has been attributed to the presence, in their outer membrane, of amphiphiles containing two polar heads separated by a hydrophobic body [6]. These amphiphiles are today known as bolaphiles.

Bolaphiles have possible applications in numerous domains. After treatment with the ultrasound these amphiphiles are able to form stable vesicles within which the bilayer is replaced by a single layer comprising amphiphiles arranged so that one head is on the inner face and other on the outer face [7]. Their properties are also potentially applicable in other fields, such as in the preparation of thermostable films [8], in mimetic membranes [9], artificial photosynthesis [10], detergents [11,12], stabilisation or destabilisation of vesicles transporting active substances [13], and sometimes even application as therapeutic agents [14]. Cationic bolaphile surfactants of the bisquaternary ammonium (bisQUAT) variety are those which posses the greatest potential applications. For example, they are often used for their fungicidal [15], herbicidal [16] and antimicrobial [17] activity.

What is more, it is known that the surfactants containing partially fluorinated hydrophobic chains and one polar head perform better than their hydrocarbon homologues [18] (higher stability, lower surface tension, etc.) and have extensive potential applications.

Because of the numerous potential applications of bolaphiles of the bisQUAT variety and the particular interest of fluorinated surfactants, we have considered the synthesis of new fluorinated bolaphiles of the bisquaternary variety. In this paper, we describe both the synthesis of these new surfactants and the comparison of their surfactants properties.

2. Results and discussion

The bolaphile **D**, β-hydroxylated, are obtained by quaternisation of the β-hydroxyamines **C** via route 1, and the bolaphiles **G**, β-carboxylated by the quaternisation of the β-carboxyamines **F** via route 2 (Fig. 1).

The preparation of the bolaphiles **D** and **G** requires three steps. The first step results in the synthesis of the intermediates **B** and **E**. These intermediates are subsequently reacted with hydrocarbon secondary amines. Opening of the diepoxide **B** and nucleophilic substitution of the bromide atoms of the intermediate **E** by amine groups leads respectively to the di-amines **C** and **F**. Finally in the last step, quaternisation of these di-amines by methyl iodide gives the cationic bolaphiles **D** and **G**.

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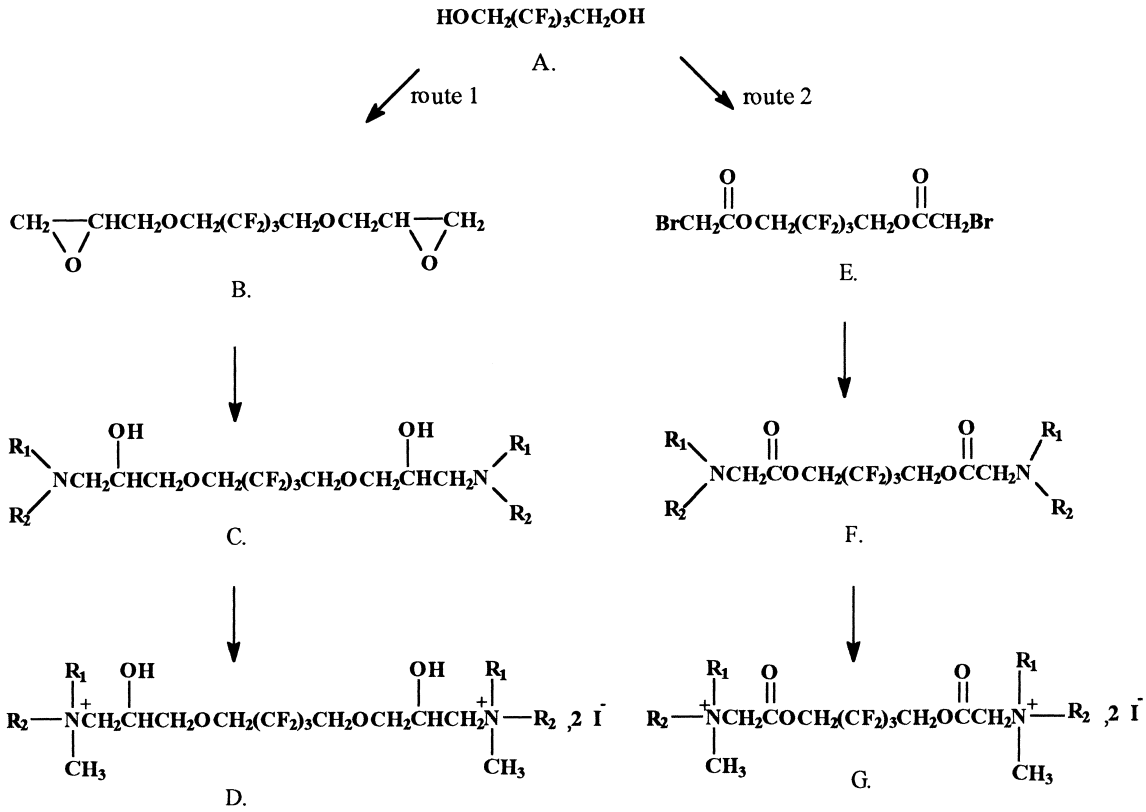

Fig. 1. Synthesis of the β-hydroxylated and β-carboxylated bisquaternary ammonium bolaphiles.

2.1. Synthesis of the bolaphiles **D**

It is well known that epoxides are generally very reactive with respect to various nucleophiles (thiols, amines, alcohols, etc) [19–21]. We therefore decided to synthesise the diepoxide B (a preceding paper describes this synthesis [22]). We were then interested in the opening of the epoxide rings by hydrocarbon amines [23] in the hope of obtaining the β-hydroxyamines **C** via route 1 (Fig. 1). The reaction involving the opening of the diepoxide takes place in an aprotic polar solvent, namely dimethyl sulphoxide, at a temperature of 70°C. The reaction takes place by an S_N2 mechanism to give the most substituted alcohol. The yields of the product vary with respect to the reactant used. For example, opening with short chain secondary amines results in higher yields than with those of longer hydrocarbon chain length. The use of bulky reactants such as di-isopropylamine considerably slows down the reaction and gives the desired product in poor yields (Table 1).

The tertiary amines C_1–C_5 were purified by distillation or rectification under high vacuum. The amine C_6 which is a solid was purified by recrystallisation from acetonitrile. The bisQUATS derived from the β-hydroxyamines **C** were subsequently quaternised by methyl iodide. The reaction takes place with ease, in acetone, at a temperature of 40°C. The cationic bolaphiles are obtained as gels which were purified by washing in diethyl ether, resulting in good yields (in the order of 95%) (Table 2).

Table 1
Yields and physical characteristics of the β-hydroxyamines obtained

No.	R_1	R_2	Yields (isolated products) (%)	Boiling Point (*B*) or melting point (*M*)
C_1	Et	Et	87	*B*: 150°C/10^{-2} mbar
C_2	Pr	Pr	72	*B*: 160°C/10^{-2} mbar
C_3	Bu	Bu	57	*B*>160°C/10^{-2} mbar
C_4	iBu	iBu	52	*B*>160°C/10^{-2} mbar
C_5	$(CH_2)_7CH_3$	$(CH_2)_7CH_3$	48	*B*>160°C/10^{-2} mbar
C_6	$(CH_2)_{17}CH_3$	CH_3	51	*M*: 46°C

Table 2
The yields of the bisQUATS obtained

No.	R_1	R_2	Yields (isolated products) (%)
D_1	Et	Et	98
D_2	Pr	Pr	97
D_3	Bu	Bu	97
D_4	iBu	iBu	96
D_5	$(CH_2)_6CH_3$	$(CH_2)_6CH_3$	94

2.2. Synthesis of the bolaphiles **G**

Recent work by our group has shown that compounds of formula $R_FC_2H_4OCOCH_2Br$ can act as the surfactant precursors, due to the strong polarisation of the C–Br bond

Table 3
Yields and physical characteristics of the β-carboxyamines obtained

No.	R_1	R_2	Yields (isolated products) (%)	Boiling Point (°C/mbar)
$\mathbf{F}_1$	Et	Et	55	$130/10^{-2}$
$\mathbf{F}_2$	Pr	Pr	51	$140/10^{-2}$
$\mathbf{F}_3$	Bu	Bu	45	$160/10^{-2}$
$\mathbf{F}_4$	$(CH_2)_7CH_3$	$(CH_2)_7CH_3$	40	$>160/10^{-2}$

which permits substitution of the bromine atom by a nucleophile [24,25]. We therefore decided to synthesise another reaction intermediate, the ω–ω′ dibromoacetate **E** (Fig. 1, route 2). This dibromoacetate is synthesised by reacting bromoacetyl bromide with the alcohol in the presence of dichloromethane. The yield of the product obtained is 75%, boiling point 90°C at 10^{-2} mbar.

The compound **E** was then reacted with various hydrocarbon secondary amines. Six equivalents of amine were added at 0°C to dibromoacetate and the reaction was then warmed to room temperature before heating to 40°C until the formation of the β-carboxyamine (the reaction was followed by vapour phase chromatography). The products, obtained with average yields, were purified by distillation or rectification in a kugelröhr under high vacuum (Table 3).

The bisQUATS derived from these β-carboxyamines **F**, were subsequently obtained by quaternisation by methyl iodide. The reaction takes place without difficulty, in acetone, at a temperature of 40°C. The cationic bolaphiles were obtained as gels which were purified by washing with diethyl ether in good yields in the order of 85% (Table 4).

2.3. Comparison of their surfactants properties

In both series the bisQUATS in which R_1=R_2=Et or R_1=R_2=Pr were soluble in water. We have therefore measured their surface tensions and critical micellar concentrations in the hope of studying firstly the influence of a hydroxylated spacer group $CH(OH)CH_2$ compared to a carboxylated spacer group C(O), and secondly, the influence of the chain lengths R_1 and R_2 attached to the polar heads. Table 5 presents both the surface tension and critical micellar concentration data corresponding to the compounds $\mathbf{D}_1$, $\mathbf{D}_2$ and $\mathbf{G}_1$, $\mathbf{G}_2$.

In the two series (Table 5), the critical micellar concentration (CMC) diminishes with the increase in hydrophobic chain length, in accordance with the literature [26,27]. Equally the surface tension diminishes with an increase in length of the hydrophobic chains R_1 and R_2, which is often the case for bolaphile surfactants as described in the literature [28,29].

Table 4
Yields of the bisQUATS **G**

No.	R_1	R_2	Yields (isolated products) (%)
$\mathbf{G}_1$	Et	Et	88
$\mathbf{G}_2$	Pr	Pr	89
$\mathbf{G}_3$	Bu	Bu	83

Table 5
CMC and γs data for the bisQUATS

No.	CMC ($\times 10^{-4}$ mol l^{-1})	γs (mN m^{-1})
$\mathbf{D}_1$	10.5	40.0
$\mathbf{D}_2$	9.40	34.0
$\mathbf{G}_1$	11.0	38.5
$\mathbf{G}_2$	5.00	36.0

What is more, if we compare the two series we find that the CMC for the compounds $\mathbf{D}_1$ and $\mathbf{G}_1$ are approximately equal, whereas compound $\mathbf{G}_2$ (Fig. 2) has a CMC lower than that of $\mathbf{G}_2$. The decrease of the CMC is found to be more significant in the case of the α-carboxylated bisQUATS. However, bolaphile $\mathbf{D}_2$ displays a surface tension value lower than that of $\mathbf{G}_2$.

These bisQUATS having a short fluorinated spacer group present the advantage of globally having lower critical micellar concentration (between 5 and 11×10^{-4} mol l^{-1}) in comparison to hydrocarbon bolaphiles described in the literature formula $R_1R_2R_3N^+(CH_2)_5N^+R_1R_2R_3$, 2 Br^- (CMC between 1.5×10^{-2} and 4.2×10^{-1} mol l^{-1} when R_1=R_2=CH_3 and R_3=hexyl, octyl or nonyl) [30]. What is more, the values for surface tension are relatively low for bolaphiles, in particular the surfactants $\mathbf{D}_2$ and $\mathbf{G}_2$ (in the order of 35 mN m^{-1}). We explain this lowering of both the CMC and surface tension in comparison to hydrocarbon bolaphile surfactants by the presence of atoms of fluorine in the centre of the hydrophobic body which, in bolaphiles, acts to confirm the exceptional properties of fluorinated surfactants.

3. Experimental

3.1. Synthesis of the β-hydroxyamines (compounds $\mathbf{C}_1$–$\mathbf{C}_6$)

Diepoxide (6.17 mmol) and secondary amine (13 mmol) in dimethyl sulphoxide (7 ml) are placed in a round bot-

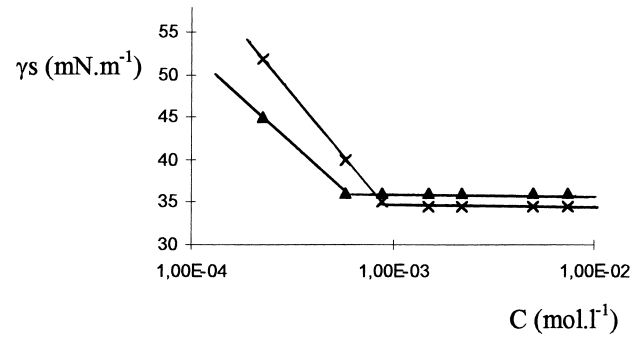

Fig. 2. γs vs f(C) for the compounds $\mathbf{D}_2$ (×) and $\mathbf{G}_2$ (▲) at 25°C.

Table 6
Spectroscopic characteristics of β- hydroxyamines $\mathbf{C_1}$–$\mathbf{C_6}$

No.	RMN ^{1}H	RMN ^{19}F
$\mathbf{C_1}$	1,1 ppm, t, $\mathbf{CH_3}CH_2N$; 2,5 ppm, m, $CH_3\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, CH2CH(OH)$\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{C_2}$	0,9 ppm, t, $\mathbf{CH_3}CH_2CH_2N$; 1,5 ppm, q, $CH_3\mathbf{CH_2}CH_2N$; 2,5 ppm, m, $CH_3CH_2\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, $CH_2CH(OH)\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{C_3}$	0,9 ppm, t, $\mathbf{CH_3}CH_2CH_2CH_2N$; 1,4 ppm, m, $CH_3\mathbf{CH_2}\mathbf{CH_2}CH_2N$; 2,5 ppm, m, $CH_3CH_2CH_2\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, $CH_2CH(OH)\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{C_4}$	0,9 ppm, dd, $(\mathbf{CH_3})_2CHCH_2N$; 1,7 ppm, m, $(CH_3)_2\mathbf{CH}CH_2N$; 2,2−2,4 ppm, dd, $(CH_3)_2CH\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, CH_2 $CH(OH)\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{C_5}$	0,9 ppm, t, $\mathbf{CH_3}(CH_2)_6CH_2N$; 1,4 ppm, s, $CH_3(\mathbf{CH_2})_5CH_2CH_2N$; 1,5 ppm, m, $CH_3(CH_2)_5\mathbf{CH_2}CH_2N$; 2,5 ppm, m, $CH_3(CH_2)_6\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, $CH_2CH(OH)\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{C_6}$	0,9 ppm, t, $\mathbf{CH_3}(CH_2)_{17}N$; 1,4 ppm, s, $CH_3(\mathbf{CH_2})_{15}(CH_2)_2N$; 1,5 ppm, m, $CH_3(CH_2)_{15}\mathbf{CH_2}CH_2N$; 2,4 ppm, s, $CH_3(CH_2)$ $_{16}CH_2N\mathbf{CH_3}$; 2,5 ppm, m, $CH_3(CH_2)_{16}\mathbf{CH_2}N\mathbf{CH_2}$; 3,6 ppm, m, $CH_2CH(OH)\mathbf{CH_2}O$; 3,7 ppm, m, **CH**(OH); 4,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$

Table 7
Spectroscopic characteristics of the bisQUATS $\mathbf{D}_1$–$\mathbf{D}_6$

No.	RMN ^{1}H	RMN ^{19}F
$\mathbf{D}_1$	1,3 ppm, t, $\mathbf{CH}_3CH_2N^+$; 2,9 ppm, s, $\mathbf{CH}_3N^+$; 3,4 ppm, m, $\mathbf{CH}_2N^+\mathbf{CH}_2CH(OH)$; 3,7 ppm, m, $CH_2CH(OH)\mathbf{CH}_2$; 4,15 ppm, t, $O\mathbf{CH}_2CF_2$; 4,4 ppm, m, **CH**(OH)	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{D}_2$	1,1 ppm, t, $\mathbf{CH}_3CH_2CH_2N^+$; 1,7 ppm, m, $CH_3\mathbf{CH}_2CH_2N^+$; 3,1 ppm, s, $\mathbf{CH}_3N^+$; 3,4 ppm, m, $\mathbf{CH}_2N^+\mathbf{CH}_2CH(OH)$; 3,7 ppm, m, $CH_2CH(OH)\mathbf{CH}_2$; 4,15 ppm, t, $O\mathbf{CH}_2CF_2$; 4,4 ppm, m, **CH**(OH)	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{D}_3$	1,0 ppm, t, $\mathbf{CH}_3CH_2CH_2CH_2N^+$; 1,4 ppm, m, $CH_3\mathbf{CH}_2CH_2CH_2N^+$; 1,8 ppm, m, $CH_3CH_2\mathbf{CH}_2CH_2N^+$; 3,3 ppm, s, $\mathbf{CH}_3N^+$; 3,7 ppm, m, $\mathbf{CH}_2N^+\mathbf{CH}_2CH(OH)$; 3,9 ppm, m, $CH_2CH(OH)\mathbf{CH}_2$;. 4,15 ppm, t, $O\mathbf{CH}_2CF_2$; 4,4 ppm, m, **CH**(OH); 5,1 ppm, d, $CH_2CH(\mathbf{OH})CH_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{D}_4$	1,1 ppm, dd, $(\mathbf{CH}_3)_2CHCH_2N^+$; 2,5 ppm, m, $(CH_3)_2\mathbf{CH}CH_2N^+$; $^+$; 3,5 ppm, s, $\mathbf{CH}_3N^+$; 3,7 ppm, m, $\mathbf{CH}_2N^+\mathbf{CH}_2CH(OH)$; 3,85 ppm, m, $CH_2CH(OH)\mathbf{CH}_2$; 4,15 ppm, t, $O\mathbf{CH}_2CF_2$; 4,7 ppm, m, **CH**(OH); 5,1 ppm, d, $CH_2CH(\mathbf{OH})CH_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{D}_5$	0,9 ppm, t, $\mathbf{CH}_3(CH_2)_6CH_2N^+$; 1,4 ppm, s, $CH_3(\mathbf{CH}_2)_5CH_2CH_2N^+$; 1,9 ppm, m, $CH_3(CH_2)_5\mathbf{CH}_2CH_2N^+$; 3,3 ppm, s, $\mathbf{CH}_3N^+$; 3,7 ppm, m, $\mathbf{CH}_2N^+\mathbf{CH}_2CH(OH)$; 3,8 ppm, m, $CH_2CH(OH)\mathbf{CH}_2$;. 4,15 ppm, t, $O\mathbf{CH}_2CF_2$; 4,4 ppm, m, **CH**(OH); 5,4 ppm, d, $CH_2CH(\mathbf{OH})CH_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$

Table 8
Spectroscopic characteristics of the β- carboxyamines $\mathbf{F}_1$–$\mathbf{F}_4$

No.	RMN ^{1}*funbcH*	RMN ^{19}F
$\mathbf{F}_1$	1 ppm, t, $\mathbf{CH}_3CH_2N$; 2,5 ppm, q, $CH_3\mathbf{CH}_2NCH_2C(O)$; 3,4 ppm, s, $CH_3CH_2N\mathbf{CH}_2C(O)$; 4,5 ppm, t, $O\mathbf{CH}_2CF_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{F}_2$	0,9 ppm, t, $\mathbf{CH}_3CH_2CH_2N$; 1,5 ppm, m, $CH_3\mathbf{CH}_2CH_2N$; 2,5 ppm, t, $CH_3CH_2\mathbf{CH}_2NCH_2C(O)$; 3,5 ppm, s, $CH_3CH_2CH_2N\mathbf{CH}_2C(O)$; 4,7 ppm, t, $O\mathbf{CH}_2CF_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{F}_3$	1,0 ppm, t, $\mathbf{CH}_3CH_2CH_2CH_2N$; 1,4 ppm, m, $CH_3\mathbf{CH}_2\mathbf{CH}_2CH_2N$; 2,5 ppm, t, $CH_3(CH_2)_2\mathbf{CH}_2NCH_2$; 3,6 ppm, s, $CH_3(CH_2)_3N\mathbf{CH}_2C(O)$; 4,6 ppm, t, $O\mathbf{CH}_2CF_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$
$\mathbf{F}_4$	0,9 ppm, t, $\mathbf{CH}_3(CH_2)_6CH_2N$; 1,4 ppm, s, $CH_3(\mathbf{CH}_2)_5CH_2CH_2N$; 1,5 ppm, m, $CH_3(CH_2)_5\mathbf{CH}_2CH_2N$; 2,5 ppm, t, $CH_3(CH_2)_6\mathbf{CH}_2NCH_2$; 3,6 ppm, s, $CH_3(CH_2)_7N\mathbf{CH}_2C(O)$; 4,6 ppm, t, $O\mathbf{CH}_2CF_2$	−126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2\mathbf{CF}_2$

Table 9
Spectroscopic characteristics of the bisQUATS $\mathbf{G_1}$–$\mathbf{G_3}$

No.	RMN ^{1}H	RMN ^{19}F
$\mathbf{G_1}$	1,3 ppm, t, $\mathbf{CH_3}CH_2N^+$; 3,2 ppm, s, $\mathbf{CH_3}N^+$; 3,6 ppm, q, $CH_3\mathbf{CH_2}N^+CH_2C(O)$; 4,4 ppm, s, $CH_3CH_2N^+\mathbf{CH_2}C(O)$; 5 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{G_2}$	1,1 ppm, t, $\mathbf{CH_3}CH_2CH_2N^+$; 1,7 ppm, m, $CH_3\mathbf{CH_2}CH_2N^+$; 3,3 ppm, s, $\mathbf{CH_3}N^+$; 3,6 ppm, t, $CH_3CH_2\mathbf{CH_2}N^+CH_2C(O)$; 4,5 ppm, s, $CH_3CH_2CH_2N^+\mathbf{CH_2}C(O)$; 5,1 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$
$\mathbf{G_3}$	1,0 ppm, t, $\mathbf{CH_3}CH_2CH_2CH_2N^+$; 1,4 ppm, m, $CH_3\mathbf{CH_2}CH_2CH_2N^+$; 1,8 ppm, m, $CH_3CH_2\mathbf{CH_2}CH_2N^+$; 3,7 ppm, t, $CH_3(CH_2)_2\mathbf{CH_2}N^+CH_2$; 4,7 ppm, s, $CH_3(CH_2)_3N^+\mathbf{CH_2}C(O)$; 5 ppm, t, $O\mathbf{CH_2}CF_2$	−126 ppm, $CF_2\mathbf{CF_2}CF_2$; −120 ppm, $\mathbf{CF_2}CF_2\mathbf{CF_2}$

tomed flask equipped with a condenser. The mixture is stirred vigorously at 70°C until the formation of the di-amine (the reaction was followed by vapour phase chromatography). The mixture is then extracted with diethyl ether, the ethereal phases were washed numerous times with water, and dried over sodium sulphate. Diethyl ether is then evaporated under vacuum. The crude di-amines obtained were then purified by distillation or rectification under high vacuum.

All these amines $\mathbf{C}_1$–$\mathbf{C}_6$ were characterised by ^{1}H (acetone d_6/TMS) and ^{19}F (acetone/$CFCl_3$) nuclear magnetic resonance and infra-red spectroscopy. The results of ^{1}H NMR and ^{19}F NMR are shown in Table 6.

The infra-red spectra for all compounds show: ν(O–H)=3418 cm^{-1}; ν(C–C)=2968 cm^{-1}; ν(C–O) and ν(C–F)=1150 cm^{-1}.

3.2. Synthesis of the bisQUATS (compounds $\mathbf{D}_1$–$\mathbf{D}_5$)

Di-amine (3.19 mmol) and methyl iodide (63.4 mmol) in a few ml of acetone are placed in a round bottomed flask equipped with a condenser. The mixture is heated to 40°C overnight. The excess methyl iodide and acetone is evaporated under vacuum, and the crude products obtained are purified by washing with diethyl ether.

These bisQUATS were characterised by ^{1}H (D_2O/TMS for D_1 and D_2 and acetone d_6 /TMS for D_3-D_5) and ^{19}F nuclear magnetic resonance (Table 7).

3.3. Synthesis of the dibromoacetate (compound **E**)

The diol $HOCH_2(CF_2)_3CH_2OH$ (9.43 mmol) was dissolved in a few ml of dichloromethane in a round bottomed flask equipped with stirrer, condenser and under an atmosphere of nitrogen. To this solution, bromo acetylbromide (56.5 mmol) was added dropwise from a dropping funnel at 0°C. The mixture was then left for 2 h at room temperature, before being heated to 60°C. The reaction was followed by vapour phase chromatography until the peak for the dibromoacetate (identified by GC/MS) appeared, upon which the reaction mixture was hydrolysed with water before being extracted with dichloromethane. The organic phase was washed with water and dried with anhydrous sodium sulphate. This was filtered over glass wool, followed by evaporation of the dichloromethane with a rotary evaporator. The dibromoacetate was purified by distillation in a kugelröhr.

The dibromoacetate **E** was characterised by ^{1}H (acetone d_6/TMS) and ^{19}F nuclear magnetic resonance and infrared spectroscopy:

- ^{1}H NMR: 4,2 ppm, t, $\mathbf{CH}_2CF_2$; 4,6 ppm, s, $Br\mathbf{CH}_2C(O)$.
- ^{19}F NMR: −126 ppm, $CF_2\mathbf{CF}_2CF_2$; −120 ppm, $\mathbf{CF}_2CF_2CF_2$.
- IR: ν(C–H)=2880–2950 cm^{-1}; ν(C=O)=1764 cm^{-1}; ν(C–F)=1158 cm^{-1}.

3.4. Synthesis of the β-carboxyamines (compounds $\mathbf{F}_1$–$\mathbf{F}_4$)

The secondary amine (6.60 mmol) was placed in a dropping funnel and added dropwise at 0°C to the fluorinated dibromoacetate (1.1 mmol), in a round bottomed flask, equipped with a condenser and stirring bead. The mixture was then allowed to reach room temperature, a few ml of diethyl ether added and then heated to 40°C for one night. The reaction progress was followed by vapour phase chromatography. On termination, a solution of 100 ml water saturated with NaCl was prepared. To this saline solution, NaOH 10% was added, and 20 ml of this mixture poured into the reaction vessel. The mixture was then extracted using diethyl ether, the organic layers washed with water and then dried over sodium sulphate. This was then filtered over glass wool, followed by evaporation of the ether with a rotary evaporator and the diamine obtained, purified by kugelröhr distillation.

The amines $\mathbf{F}_1$–$\mathbf{F}_4$ were characterised by ^{1}H (acetone d_6/TMS) and ^{19}F nuclear magnetic resonance (Table 8).

The infra-red spectra for all compounds show: ν(C–H)= 2972.8 cm^{-1}; ν(C=O)=1762 cm^{-1}; ν(C–F)=1152 cm^{-1}.

3.5. Synthesis of the bisQUATS (compounds $\mathbf{G}_1$–$\mathbf{G}_3$)

Di-amine (3.19 mmol) and methyl iodide (63.4 mmol) in a few ml of acetone were placed in a round bottomed flask equipped with a condenser. The mixture was heated to 40°C overnight. The excess of methyl iodide and acetone was evaporated under vacuum, and the crude products obtained are purified by washing with diethyl ether.

These bisQUATS were characterised by ^{1}H (D_2O/TMS for G_1 and G_2 and acetone d_6 /TMS for G_3) and ^{19}F NMR (Table 9).

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