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Synthesis and preliminary assessments of hybrid hydrocarbon–fluorocarbon anionic and non-ionic surfactants

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Abstract—We describe the synthesis and preliminary physico-chemical assessments of ionic and non-ionic hybrid hydrofluorocarbon amphiphiles. Monoreduction reaction of the symmetrical starting material 1,10-diiodo-3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecane provides the ethyl terminated fluorocarbon chains. These non-symmetrical hydrofluorocarbon surfactants contain an ethyl segment, a fluorocarbon core and either nonionic or anionic polar heads (sulfate, sulfonate, phosphate, carboxylate or glycosidic groups). The lactobionolactone can be reacted with hydrofluorocarbon amines to obtain the non-ionic hydrophilic moiety whereas the anionic heads come from monoiodo and/or hydroxyl hydrofluorocarbon substrates. The critical micellar concentration (CMC) values of these novel surfactants were determined by surface tension and conductivity measurements. The results are compared to those measured with fluorinated homologues previously described.

Fluorinated amphiphiles have attracted peculiar interest because of their remarkable characteristics. Such surface active molecules show much lower critical micellar concentration (CMC) and can reduce the surface tension of water more efficiently than their hydrocarbon counterparts. Furthermore, in addition to their unique chemical and thermal stability the fluorocarbon segments are known to be both hydrophobic and lipophobic. Thus, mixtures involving fluorinated and hydrocarbon surfactants exhibit limited miscibility. Among the fluorinated amphiphiles, hybrid single tail surfactants are of great interest especially for biological purposes. Indeed, highly fluorinated parts usually improve the amphiphiphile biocompatibility and consequently numerous applications could emerge.[1] Since the first synthesis of alkanoic acids bearing a perfluoroalkyl tail,[2] several articles have described the potentialities of hydrofluorocarbon compounds.[3] However, fluorinated amphiphiles with a hydrocarbon terminal part are less known.[4]

In previous studies, we explored the physicochemical and biological properties of highly fluorinated non-ionic amphiphiles derived from the trishydroxymethylacrylamidomethane (THAM).[5–8] We observed that the grafting of a hydrocarbon tip on the fluorocarbon tail seems to destabilize the micelle core organization because of the unfavorable interactions between hydrocarbon and fluorinated moieties. In the course of our work dealing with single tail hybrid amphiphiles, the modulation of the polar head allows better understanding of their micellar behavior.

The goal of the present work is to synthesize and examine the physicochemical properties of novel hydrofluorocarbon surfactants bearing either nonionic or anionic polar heads (sulfate, sulfonate, phosphate, carboxylate or glycosidic).

Basically, the synthetic work needed to carry out such hybrid structures can be divided into two steps. First, since the hybrid hydrophobic moiety is the main feature to achieve, we focused on preparing several hybrid building blocks bearing thiol, acid, hydroxyle and amine functions. Then, the anionic and/or non-ionic appropriate substrates are reacted with the functionalized hydrophobic tails to give the hybrid amphiphiles.

The hybrid hydrophobic architectures designed exhibit a distal ethyl radical, a fluorocarbon core and a proximal function. The synthetic pathway chosen is ramified into four ways leading to the thiol **7**, the carboxylic acid **4**, the alcohol **5** and the amines **13a** and **13b**, respectively. All these compounds come from either the symmetrical 1,10-diiodo-3,3,4,4,5,5,6,6,7,7,8,8-dodecafluorodecane **1a** or the unsymmetrical 1,12-diiodo-3,3,-4,4,5,5,6,6,7,7,8,8-dodecafluorododecane **1b** starting materials.[9]

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In the case of compounds **7**–**11**, the first reaction involves the selective reduction of only one iodine which is achieved by tri-*n*-butyltin hydride in the presence of azobisobutyronitrile (AIBN).[8] Since the unsymmetrical mono-iodo **2** is available, functionalized substrates can be prepared. The synthesis of thiol derivative **7** was previously described (Fig. 1).[8] Substitution of the iodine by sodium cyanide in a dimethyl sulfoxide/water mixture affords nitrile **3**. The hydrolysis reaction involving sulfuric and acetic acid of the nitrile function leads to carboxylic acid **4**. The latter is reduced by lithium aluminum hydride in diethyl ether. The resulting alcohol **5** is isolated in a yield of 99% (Fig. 1).

Amines **13a** and **13b** are obtained in two steps according to Fig. 2. Mono-substitution reactions of compounds **1a** or **1b** by sodium azide afford azido derivatives **12a** or **12b**. A simultaneous reduction in methanol of both iodo and azido groups is achieved in quantitative yield by hydrogenation in the presence of a catalytic amount of Pd/C.

Once the hydrophobic hybrid intermediates **4**, **5**, **7** and **13** are isolated, the synthetic work is completed to give the expected surfactants (Figs. 1 and 2). Thus, the oxidation of thiol **7** by performic acid leads to the sodium salt of sulfonate **8**. Carboxylate **9** comes from the neutralisation in methanol of acid **4**. Hydroxyle function

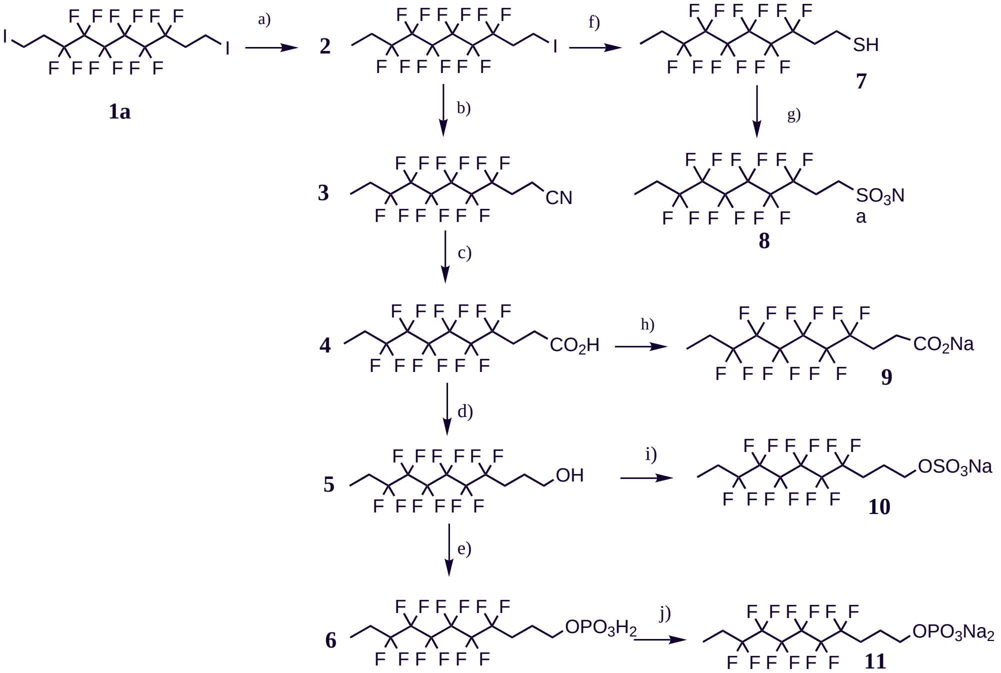

Figure 1. Synthesis of the hydrofluorocarbon non-ionic surfactants. (a) AIBN, tri-*n*-butyltin hydride, THF, Δ, 6 h, the residual diiodo is re-used. The yield rises to 60%. (b) NaCN, DMSO/H_2O 6/1, Δ, 48 h, yield: 74%. (c) H_2SO_4/AcOH/H_2O 2.5/3/2 (w/w), Δ, 24 h, yield: 82%. (d) 1/$AlLiH_4$, Et_2O, rt, 6 h; 2/H_2O/HCl 1/1, yield: 99%. (e) 1/$POCl_3$, TEA, Et_2O, rt, 2 h, 2/H_2O, yield: 60%. (f) Thiourea, THF/H_2O 20/1, Δ, 24 h followed by NH_4OH at rt, 6 h, yield: 95%. (g) 1/H_2O_2/HCOOH 1/1, Δ, 48 h; 2/$NaHSO_3$; 3/MeONa, MeOH, yield: 60%. (h) MeONa, MeOH, yield: 100%. (i) 1/SO_3/pyridine, DMF, Δ, 72 h; 2/ion exchange resin, yield: 96%. (j) MeONa, MeOH, yield: 100%.

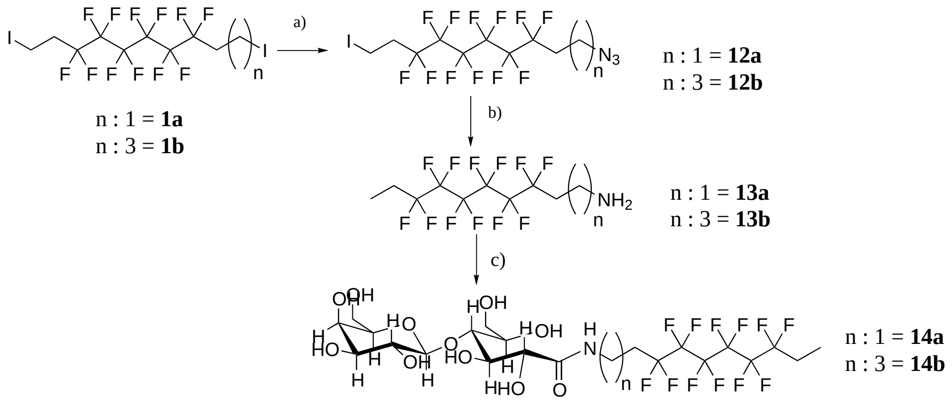

Figure 2. Synthesis of the hydrofluorocarbon anionic surfactants. (a) NaN_3, acetone/H_2O 50/1, rt, 24 h, yield: $n=1$: 39%, $n=3$: 72%. (b) H_2/Pd/C, MeOH, yield: $n=1$ or 3: 98%. (c) Lactobionolactone, MeOH, pH 9, Δ, 24 h, yield: $n=1$: 51%, $n=3$: 39%.

Table 1. Physico-chemical properties of hybrid surfactants

Polar head	Chain	Compounds	CMC in mM	γ (mN/m)
CO_2Na	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**9**	0.87	33.5
CO_2Na	C_6F_{13}-$(CH_2)_2$-	/	0.85	35
SO_3Na	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**8**	0.486	39
OSO_3Na	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**10**	0.308	25
OPO_3Na_2	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**11a**	0.09	24
OPO_3HNa	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**11b**	0.078	26
Lactobiono	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	**14a**	0.7	23.5
Lactobiono[a]	C_6F_{13}-$(CH_2)_2$-	/	1.04	19
Lactobiono	$C_2H_5C_6F_{13}$-$(CH_2)_4$-	**14b**	0.1	28
THAM-Trigal[b]	$C_2H_5C_6F_{13}$-$(CH_2)_2$-	/	0.5	25/26
THAM-Trigal[b]	C_6F_{13}-$(CH_2)_2$-	/	0.28	34

[a] Data from Ref. 11.

[b] Data from Ref. 8, γ=limit surface tension, CMC=critical micellar concentration.

of substrate **5** is reacted with the SO_3/pyridine complex following the usual procedure to give after neutralisation sulfate **10**.[10] Mono- and di-sodium salts of phosphorylated compounds **11a** and **11b** are obtained after hydrolysis by mixing in diethyl ether intermediate **5** with oxyphosphorus tri-chloride in the presence of triethylamine. Under basic conditions, amines **13a** and **13b** are condensed with lactobionolactone to lead to the non-ionic surfactants **14a** and **14b**, respectively.

In previous works we noticed that the short ethyl moiety located at the end of the chain has a significant impact on the micellization phenomenon. In the case of non-ionic hybrid THAM derivatives,[8] this hydrocarbon tip seems to induce a destabilization of micelles. Consequently, the CMC values measured are higher than expected.

The same behavior is observed with the hybrid molecules belonging to this work. Although the chain length of molecules is increased by the addition of an ethyl group (compared to the perfluorinated molecules bearing a $C_6F_{13}CH_2CH_2$- segment), their CMC values are quite similar to their perfluorinated analogues. For instance, the CMC of compound **9** is 0.87 mM, whereas this value should be much lower than the perfluorinated $C_6F_{13}CH_2CH_2$- carboxylate (0.85 mM, see Table 1). According to the hydrophobic character concept, our hybrid surfactants should exhibit lower CMC values. Usually, the addition of one methylene group must decrease more or less the CMC by a ratio of 1/2. Such a ratio seems to be not valid anymore in the case of our hybrid mono-chain amphiphiles.

Likewise, one can underline that the same behavior is noticed for our lactobionolactone derivatives (CMC of compound **14a** is in a similar range to the one of $C_6F_{13}CH_2CH_2$- non-ionic analogue, these CMCs are 0.7 and 1.04 mM, respectively).

Such behavior could be compared to the low miscibility of hydrocarbon and fluorocarbon surfactants: one short hydrocarbon tip seems to be sufficient to induce a great destabilization of the supramolecular assemblies usually formed by perfluorocarbon amphiphiles. Work is in progress to understand these curious aggregation phenomena.

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