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Synthesis of triphilic, Y-shaped molecular surfactants

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Abstract

Novel multiphilic molecules comprising three chains with antagonistic affinities have been synthesized. These 'triphilic' surfactants (*FnHmEOy*) contain a perfluorinated arm (*Fn*=C_nF_{2n+1}), a hydrocarbon arm (*Hm*=C_mH_{2m+1}), and a methyl-caped, poly(ethylene glycol) arm (*EOy*=$CH_3(OC_2H_4)_yO$). These moieties have variable lengths (n=5 or 7, m=8, 10, or 14, and y=2–7) and are interconnected in a Y shape; hence, each unit is directly connected to the other two. The key intermediates in the synthetic route are 3-*F*-alkyl-3-alkyloxypropanoic acids, on which the polar *EOy* chain is subsequently grafted. Monodisperse methyl-caped diethylene glycol (*EO*2) and triethylene glycol (*EO*3) led to the corresponding monodisperse triaffine surfactants. In parallel, a library of five *F5H*10*EOy* triaffines (y=3–7) has been obtained simultaneously when starting from the polydisperse methyl-caped poly(ethylene glycol) MPEG 350. Separation of pure individual compounds was achieved through column chromatography on silica gel. The relative concentration of the *Z* and *E* isomers has been quantified in the reaction mixtures of the intermediates and final products by ^{1}H NMR (*Z* largely predominant). Several products have been obtained in their isomerically pure form. Chemical characterization (^{1}H, ^{13}C, and ^{19}F NMR, elemental analysis) was consistent with the expected structures.

1. Introduction

The design and synthesis of building blocks with multiple affinities (philicities) are prerequisites for the development of novel nanostructures based on surfactant self-assembly. Two main driving forces can be used to promote self-assembly and determine the architecture and properties of the resulting aggregates. One is the differential affinities and repulsions that exist between the diverse moieties that are combined within the surfactant molecule. Fluorinated chains, because of their exceptional aptitude at developing both hydrophobic and lipophobic effects, are highly effective in generating compartmentation of molecular systems into segregated nano- to meso-scale phases.[1–3] Another driving force involves the architecture of the building block. Classically, only two segments with antinomic affinities are connected within an amphiphilic molecule, namely a hydrophilic moiety and a lipophilic moiety.[4] When a third protagonist, i.e., a fluorinated chain, is present, the three moieties are usually not directly connected to each other through a same junction point. In the case of single-chain surfactants, they are arranged in a linear configuration.[5] In double- or multi-chain surfactants, an ethyl segment[5] or a phenyl ring[6] is systematically inserted between the fluorinated moiety and the junction between the three arms. Likewise, polymeric structures such as linear ABC triblock copolymers, and statistical and block copolymer soaps have been reported,[7] in which the three antagonist arms are not directly connected to each other. An exception to these configurations is an ABC 'miktoarm' star block terpolymer bearing a perfluorinated polyether arm, a poly(ethylene oxide) arm, and a hydrocarbon polymer arm.[8] This triphilic polymer was found to self-assemble into micelles having three different types of compartments (one hydrophilic, one lipophilic, and one fluorophilic, the latter being both hydrophobic and lipophobic).[9]

We develop fluorinated amphiphiles designed for the elaboration of self-assemblies with original structures, including monodisperse surface micelles,[10–12] tubules,[13] polyhedral

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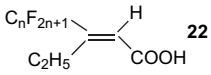
vesicles,[14] and direct and reverse fluorocarbon emulsions,[15] with potential as templates in materials sciences and as drug carriers in medicine.[2,16] We report here the synthesis of a family of triphilic molecular amphiphiles (*FnHmEOy*, n=5 or 7, m=8, 10, or 14, and y=2–7) comprising a perfluorinated arm (*Fn*=C_nF_{2n+1}), a hydrocarbon arm (*Hm*=C_mH_{2m+1}), and a methyl-caped poly(ethylene oxide) arm (*EOy*=$CH_3(OC_2H_4)_yO$), the three units being connected in a Y shape via a double bond. This feature should eliminate the uncertainties that have been introduced by the previous multiaffine products in physical and structural studies because of, for example, the presence of an alkyl spacer or a phenyl ring, usually in the fluorophilic arm, resulting in the presence of two fragments of distinct affinities and steric requirements within one same arm. It is well known that such 'spacers' can profoundly modify the properties and, in particular, the self-association behavior of surfactants.

2. Results and discussion

The synthesis of monomethyl ether poly(ethylene glycol) (MPEG) 3-*F*-alkyl-3-alkyloxypropenoate triphilic compounds, **a**, (Scheme 1) is based on the preparation of 3-*F*-alkyl-3-alkyloxypropenoic acid intermediates, **b**. The carboxylic function is subsequently used to graft the polar MPEG arm.

2-*F*-Hexyl ethanoic acid, **2**, and 2-*F*-octyl ethanoic acid, **15**, were synthesized by oxidation of the commercially available corresponding 2-*F*-alkylethanols, **1** and **14**.[17]

The synthesis of 3-*F*-alkyl-3-ethoxypropenoic acids, **22**, has been reported.[18] It involved treatment of *F*-alkylethanoic acids with an excess of alcoholic potassium hydroxide, which gave the corresponding enol ethers by elimination of HF. In the presence of *F*-chain, the protons in α position to the carboxylate function were sufficiently acidic to undergo deprotonation under mild conditions. The mechanism was reported to be similar to that described for the attack of alcoholates on ethyl 3-*F*-heptyl-3-fluoropropenoates, **23**.[19] In a first step, the small amount of alcoholate formed initiated the elimination of HF at the carboxylate group level. In a second step, the Michael-type addition of a second molecule of alcoholate led to the target product.



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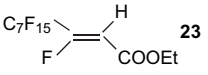
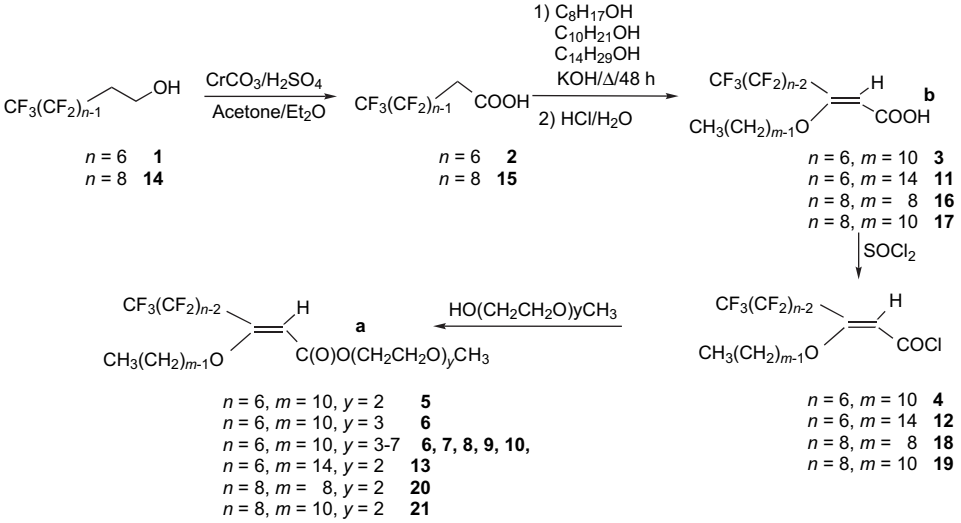


23

However, owing to the difficulties encountered in eliminating the excess alcohol at the end of the reaction, this method was limited to ethanol and to the water-soluble diethylene glycol. As a consequence, the propenoic acids were substituted either with a short lipophilic ethyl moiety or with a hydrophilic diethylene glycol moiety. Two series of surfactants were derived from these propenoic acids that comprise a fluorinated chain (5, 7, and 9 carbon atoms) and an ethyl or a diethylene glycol chain. They were obtained by reduction of the acid function or aminolysis of the corresponding esters. These surfactants were classical surfactants with two distinct affinities only.

Our aim was to graft a long hydrophobic, fluorophobic arm, capable of introducing by itself effective interfacial activity, onto 2-*F*-alkylethanoic acids, and thus to generate triphilic surfactants. We have therefore adapted the protocol of Ref. 18 to use 1-octanol, 1-decanol, and 1-tetradecanol inthe second step of Scheme 1. Therefore, an excess of alcohol was used so that the alcohol played the role of both reactant and solvent during the synthesis. 3-*F*-Alkyl-3-alkyloxypropenoic acids **3**, **11**, **16**, and **17** were obtained with the following yields: **3** (28%), **11** (8%), **16** (15%), and **17** (34%). These yields are lower than those obtained with ethanol (65–95%, depending on the length of the fluorinated chain). It is likely that the higher temperature required for the larger alcohols (130 °C) induced partial decomposition of the enol ether function during the reaction. This was in particular the case for tetradecane, for which 4 days at 130 °C were required. Attempts at dissolving the long-chain alcohols in a solvent (1,4-dioxane or acetonitrile) did not improve the yields.



Scheme 1. Synthesis of the fluorophilic/lipophilic/hydrophilic triaffine star-shaped molecular surfactants.

Acidification performed to recover the acid could also produce hydrolysis.

The relative proportions of *Z* and *E* configurations were determined in the reaction mixtures by ^{1}H NMR by comparison with the chemical shifts of similar compounds.[19,20] For all propenoic acids, the *Z* isomers were obtained quasi-exclusively (**3**: *Z*/*E* molar ratio=96/4; **11**, **16**, and **17**: *Z*/*E*=100/0), as reported for 3-*F*-alkyl-3-ethoxypropenoic acids.[18] This stereoselectivity was explained by the strong tendency to minimize interactions between fluorinated chain and carboxylic group.

Reaction of thionyl chloride with the intermediates **3**, **11**, **16**, and **17**, without solvent and under N_2, led to the corresponding chlorides **4**, **12**, **18**, and **19** in good yields (60%, 89%, 98%, and 95%, respectively). As for the acid precursors, *Z* isomers were obtained quasi-exclusively.

Addition of methyl-caped di-, tri-, and poly(ethylene glycol) was conducted in anhydrous CH_2Cl_2, at room temperature and under N_2. Di- and triethylene glycol gave the corresponding surfactants **5**, **6**, **13**, **20**, and **21**, with yields ranging from 32% to 52% (Table 1). Formation of both *Z* and *E* isomers was detected by ^{1}H NMR for all compounds. The two isomers have been isolated and characterized in the case of compounds **5**, **20**, and **21**. It can be seen that, for a constant number of *EO* groups (y=2), the amount of *E* isomer increased (from 15% to 21%) when increasing the hydrocarbon chain length from *H*10 to *H*14, for a constant length of the fluorinated chain *F*5, while it decreased (from 15% to 5%) when increasing the fluorinated chain length from *F*5 to *F*7, for a constant hydrogenated chain length *H*10.

A library of five surfactants, **6**–**10**, each with a different *EOy* polar head (y=3–7) was obtained by adding MPEG 350 to acid chloride **4**. Column chromatography on silica allowed separation of the individual triaffines with a total yield of 36% (Table 1). Compounds **7**–**10** were obtained in over 99% purity after two columns (a first crude chromatography to remove MPEG 350 and polar compounds and a second chromatography allows separation of the various components of the library); the purity of **6** was then only 80%. The *Z*/*E* molar ratio was determined (Table 1). It can be seen that the amount of *E* isomer decreased as the EO moiety became longer, likely reflecting the increasingly unfavorable interaction with the fluorinated chain.

Table 1
Yields and *Z*/*E* ratios of the triaffine molecules

Compound	Code	Yield (%)	*Z*/*E*
5	*F5H10EO2*	33	85/15*
6	*F5H10EO3*	52	85/15**
6	*F5H10EO3*	36	85/15**
7	*F5H10EO4*		86/14**
8	*F5H10EO5*		89/11**
9	*F5H10EO6*		92/8**
10	*F5H10EO7*		94/6**
13	*F5H14EO2*	40	79/21**
20	*F7H8EO2*	27	87/13*
21	*F7H10EO2*	32	95/5*

* Isolated isomers.
** Non-isolated isomers.

Preliminary results showed that this series of triaffine surfactants formed highly stable Langmuir monolayers and surface hemimicelles with a hitherto unreported, facetted structure.

3. Experimental part

3.1. General

2-*F*-Alkyl ethanols were provided by Elf Atochem. 2-*F*-Hexyl ethanol $C_6F_{13}(CH_2)_2OH$ (Foralkyl EOH 6) was purified by distillation (47 °C/0.05 mm Hg) and 2-*F*-octyl ethanol $C_8F_{17}(CH_2)_2OH$ (Foralkyl EOH 8) was recrystallized from $CHCl_3$ prior to use. Jones' reagent was prepared as reported:[17] chromium(VI) oxide (25 g, 0.25 mol) was dissolved in water (70 mL); the solution was cooled in an water/ice bath and concentrated H_2SO_4 (25 mL) was slowly added. Thionyl chloride was distilled prior to use (bp 76 °C). Diethylene glycol monomethyl ether and triethylene glycol monomethyl ether (Fluka, >98%) were used without further purification. Commercial monomethyl ether poly(ethylene glycol) (MPEG 350, Fluka) was dried by co-evaporation of trace water with toluene prior to use. MPEG 350 presented a distribution of ethylene oxide units ranging from 2 to 7, as evidenced by size exclusion chromatography. 1-Octanol, 1-decanol, and 1-tetradecanol (Sigma) were distilled before use. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ or CD_3COCD_3 with a Bruker AM 400 spectrometer. Chemical shifts are reported in parts per million (δ in ppm) relative to Me_4Si (^{1}H, ^{13}C) and $CFCl_3$ (^{19}F).

3.2. 2-F-Hexyl ethanoic acid 2

Compound **2** was prepared according to Ref. 17. 2-*F*-Hexyl ethanol (12 g, 33 mmol), acetone (60 mL), and diethyl ether (20 mL) were placed in a round-bottomed flask equipped with an addition funnel and a condenser. Freshly prepared Jones' reagent (23 mL, ~2 equiv) was added dropwise until a persistent red-brown dispersion was obtained. The blue precipitate was decanted; 25 mL of water was added in order to dissolve any of the remaining blue crystals. The solution was extracted with diethyl ether (4×100 mL) and the combined ether extracts were washed with water (2×100 mL). The organic phase was dried over Na_2SO_4, the drying agent was filtered off, and the solvent removed on a rotary evaporator. The crude product was recrystallized from CCl_4 (30 mL). It was dried under vacuum to yield white crystals (9.1 g, 73%, mp 55 °C). ^{1}H NMR ($CDCl_3$): δ_H/ppm 3.22 (2H, t, CF_2CH_2COOH, $^3J_{H-F}$=17.2 Hz).

3.3. 2-F-Octyl ethanoic acid 15

The above protocol was used with the following quantities: 2-*F*-octyl ethanol (50.38 g, 109 mmol), acetone (240 mL), diethyl ether (80 mL), and Jones' reagent (150 mL). After recrystallization in CCl_4 (30 mL), the crude product was dried under vacuum to yield white crystals (26.04 g, 50.2%, mp 82 °C). ^{1}H NMR ($CDCl_3$): δ_H/ppm 3.22 (2H, t, CF_2CH_2COOH, $^3J_{H-F}$=17.2 Hz).

3.4. 3-F-Pentyl-3-decyloxypropenoic acid **3**

The method described in Ref. 18 was modified to use 1-decanol instead of ethanol. 2-*F*-Hexyl ethanoic acid **2** (1.9 g, 5 mmol) and KOH (1.7 g, crushed) were dispersed in 1-decanol (120 mL) under stirring and the mixture was heated at 130 °C for 48 h. The reaction medium was allowed to cool down to room temperature and most of the unreacted decanol was removed by distillation under vacuum. The resulting residue was acidified with 1 N HCl (100 mL) and stirred until no solid was left and a yellow oil was formed. The reaction medium was extracted with ethyl acetate (4×100 mL) and the extracts washed with water (2×100 mL). The organic phase was dried over Na_2SO_4, the drying agent was filtered off, and the solvent was removed on a rotary evaporator. ^{1}H NMR ($CDCl_3$) of the crude oil revealed the presence of decanol, which was eliminated by a second distillation under vacuum. Purification of the crude oil was done by flash column chromatography using silica gel and elution with ethyl acetate/$CHCl_3$/ethanol 20/1/1 (R_f 0.25). The product was dried under vacuum to yield **3** as a pale transparent yellow oil (0.7 g, 28%). ^{1}H NMR ($CDCl_3$): δ_H/ppm 0.90 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.29 (14H, m, $CH_3(CH_2)_7CH_2$), 1.74 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.31 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.0 Hz), 5.80 (1H, s, C=*CH*).

3.5. 3-F-Pentyl-3-tetradecyloxypropenoic acid **11**

The protocol used for the synthesis of **3** was employed with 1-tetradecanol instead of 1-decanol. The following quantities were utilized: 2-*F*-hexyl ethanoic acid (2.14 g, 5.6 mmol), 1-tetradecanol (83 g), and KOH (1.94 g, crushed). The reaction mixture was heated at 130 °C for 100 h. Most of the unreacted tetradecanol was removed by vacuum distillation. The resulting residue was acidified with 1 N HCl (100 mL) and the mixture was stirred until no solid was left and a crude yellow oil was formed. After extraction, washing, drying, filtration, and solvent evaporation, ^{1}H NMR ($CDCl_3$) revealed the presence of tetradecanol. Purification was achieved on two silica gel chromatographic columns (first column: ethyl acetate/acetonitrile 100/1 (R_f 0.3); second column: first elution with $CHCl_3$ and second elution with ethyl acetate). The product was dried under vacuum, yielding **11** as a pale brown viscous oil (0.24 g, 7.6%). ^{1}H NMR (CD_3COCD_3): δ_H/ppm 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.29 (22H, m, $CH_3(CH_2)_{11}CH_2$), 1.61 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.31 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.0 Hz), 5.83 (1H, s, C=*CH*).

3.6. 3-F-Heptyl-3-octyloxypropenoic acid **16**

The above protocol was applied to 1-octanol. The following quantities were utilized: 2-*F*-octyl ethanoic acid **15** (5.18 g, 12 mmol), 1-octanol (200 mL), and KOH (2.3 g, crushed). The mixture was heated at 130 °C for 72 h. Vacuum distillation removed most of the unreacted octanol. The residue was acidified with 1 N HCl (100 mL) and the mixture was stirred until a viscous pale brown oil was obtained. After extraction, washing, drying, filtering, solvent evaporation, and vacuum drying, the crude oil was purified by flash column chromatography using silica gel, and eluted first with $CHCl_3$ and then with ethyl acetate (R_f 0.18). After vacuum drying, **16** was obtained as a pale yellow oil (1.05 g, 15.3%). ^{1}H NMR (CD_3COCD_3): δ_H/ppm 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.30 (10H, m, $CH_3(CH_2)_5CH_2$), 1.73 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.33 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.1 Hz), 5.88 (1H, s, C=*CH*).

3.7. 3-F-Heptyl-3-decyloxypropenoic acid **17**

The above protocol was implemented with the following reactants: 2-*F*-octyl ethanoic acid **15** (2.4 g, 5 mmol), 1-decanol (200 mL), and KOH (2.08 g, crushed). The reaction medium was heated at 130 °C for 72 h. Most of the unreacted decanol was removed by vacuum distillation. The resulting residue was acidified with 1 N HCl (100 mL) and the mixture was stirred until a pale brown viscous oil was obtained. After extraction, washing, drying, filtering, solvent evaporation, and vacuum drying, the crude oil was purified by flash column chromatography using silica gel, and eluted first with chloroform and then ethyl acetate (R_f 0.07). The product was dried under vacuum to yield **17** as a pale yellow oil (2.9 g, 34.3%). ^{1}H NMR ($CDCl_3$): δ_H/ppm 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.25 (14H, m, $CH_3(CH_2)_7CH_2$), 1.6 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.17 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.1 Hz), 5.70 (1H, s, C=*CH*).

3.8. 3-F-Pentyl-3-decyloxypropenoyl chloride **4**

3-*F*-Pentyl-3-decyloxypropenoic acid **3** (0.67 g, 1.35 mmol) and $SOCl_2$ (15 mL) were stirred at room temperature under N_2 for 8 h. Excess $SOCl_2$ was removed with a rotary evaporator and residual $SOCl_2$ was removed by co-evaporation with cyclohexane (6×20 mL). The product was dried under vacuum to yield **4** as a yellow oil (0.41 g, 60%). ^{1}H NMR ($CDCl_3$): δ_H/ppm 0.90 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.29 (14H, m, $CH_3(CH_2)_7CH_2$), 1.74 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.1 Hz), 4.28 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.1 Hz), 6.05 (1H, s, C=*CH*).

3.9. 3-F-Pentyl-3-tetradecyloxypropenoyl chloride **12**

The above protocol was implemented with the following reactants: 3-*F*-pentyl-3-tetradecyloxypropenoic acid **11** (0.24 g, 0.44 mmol) and $SOCl_2$ (15 mL). The product was dried under vacuum to yield **12** as an opaque yellow oil (0.22 g, 89%). ^{1}H NMR ($CDCl_3$): δ_H/ppm 0.90 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.45 (22H, m, $CH_3(CH_2)_{11}CH_2$), 1.74 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.28 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.0 Hz), 6.05 (1H, s, C=*CH*).

3.10. 3-F-Heptyl-3-octyloxypropenoyl chloride **18**

The above protocol was implemented with 3-*F*-heptyl-3-octyloxypropenoic acid **16** (1.05 g, 1.85 mmol) and $SOCl_2$

(35 mL). The product was dried under vacuum to yield **18** as a yellow oil (1.05 g, 100%). ^{1}H NMR (CD_3COCD_3): δ_H/ppm 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.1 Hz), 1.32 (10H, m, $CH_3(CH_2)_5CH_2$), 1.77 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.38 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.0 Hz), 6.33 (1H, s, C=*CH*).

3.11. 3-F-Heptyl-3-decyloxypropenoyl chloride **19**

The same protocol was implemented with 3-*F*-heptyl-3-decyloxypropenoic acid **17** (2.9 g, 4.9 mmol) and $SOCl_2$ (35 mL). The product was dried under vacuum to yield **19** as an opaque yellow oil (1.16 g, 1.9 mmol). ^{1}H NMR ($CDCl_3$): δ_H/ppm 0.90 (3H, t, CH_2CH_3, $^3J_{H-H}$=8.0 Hz), 1.28 (14H, m, $CH_3(CH_2)_7CH_2$), 1.75 (2H, q, $CH_2CH_2CH_2O$, $^3J_{H-H}$=8.0 Hz), 4.28 (2H, t, CH_2CH_2O, $^3J_{H-H}$=8.1 Hz), 6.05 (1H, s, C=*CH*).

3.12. Monomethyl ether diethylene glycol 3-F-pentyl-3-decyloxypropenoate F5H10EO2 **5**

3-*F*-Pentyl-3-decyloxypropenoyl chloride **4** (0.70 g, 1.35 mmol), anhydrous CH_2Cl_2 (20 mL), and diethylene glycol monomethyl ether (0.17 g, 1.41 mmol) were stirred at room temperature under N_2 for 72 h. CH_2Cl_2 was removed on a rotary evaporator. The crude product was purified by flash column chromatography using silica gel and elution with $CHCl_3$, which also allowed for the separation of the *Z* and *E* isomers. The R_f values in $CHCl_3$ were 0.32 for the *Z* isomer and 0.20 for the *E* isomer. The isomers were recovered in an isomerically pure form, both of them as colorless transparent oils. The overall yield was 33%; 0.24 and 0.04 g of *Z* and *E* isomers were recovered, respectively. The *Z*/*E* ratio was 85/15. ^{1}H NMR: δ_H/ppm, *Z* isomer: 0.87 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.25 (14H, br, $CH_3(CH_2)_7CH_2$), 1.69 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.38 (3H, s, $CH_2CH_2OCH_3$), 3.55 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.5 Hz), 3.65 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.6 Hz), 3.73 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.25 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.6 Hz), 4.31 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.78 (1H, s, C=*CH*); *E* isomer: 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.26 (14H, br, $CH_3(CH_2)_7CH_2$), 1.74 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.38 (3H, s, $CH_2CH_2OCH_3$), 3.55 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.5 Hz), 3.64 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.5 Hz), 3.71 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 3.79 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.4 Hz), 4.30 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.50 (1H, s, C=*CH*). ^{13}C NMR ($CDCl_3$): δ_C/ppm, *Z* isomer: 14.04 (CH_3CH_2), 22.64, 25.36, 29.16, 29.27, 29.45, 29.63, 31.86 (7s, $CH_3(CH_2)_8CH_2O$), 59.04 (OCH_3), 64.01, 68.98, 70.56, 71.89 (4s, $OCH_2CH_2OCH_2$-CH_2OCH_3), 76.69, 77.00, 77.32 (t, CH_2CH_2OC=C), 102.12 (C=C(H)*C*OO), 154.5 (*C*=C(H)COO), 163.46 (*C*=C(H)*C*OO). ^{19}F NMR ($CDCl_3$): δ_F/ppm, *Z* isomer: −80.8 (CF_3, 3F), −115.9 (CF_2C=C, 2F), −121.8 ($CF_3CF_2CF_2$, 2F), −122.8 ($CF_3CF_2CF_2$, 2F), −126.2 (CF_3CF_2, 2F). Element. Anal. Calcd: *Z* isomer: C 46.16%, H 5.56%, F 34.92%; found: C 46.23%, H 5.59%, F 35.48%.

3.13. Monomethyl ether triethylene glycol 3-F-pentyl-3-decyloxypropenoate F5H10EO3 **6**

3-*F*-Pentyl-3-decyloxypropenoyl chloride **4** (0.84 g, 1.62 mmol), anhydrous CH_2Cl_2 (20 mL), and triethylene glycol monomethyl ether (0.27 g, 1.63 mmol) were stirred at room temperature under N_2 for 72 h. CH_2Cl_2 was removed on a rotary evaporator. The crude product was purified by flash column chromatography using silica gel and elution with $CHCl_3$ (R_f 0.12). Compound **6** was obtained as a transparent colorless oil (0.54 g, 52%). Although it was not possible to separate the *Z* and *E* isomers, the *Z*/*E* molar ratio was determined by NMR to be 85/15. ^{1}H NMR: δ_H/ppm, *Z* isomer: 0.86 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.25 (14H, br, $CH_3(CH_2)_7CH_2$), 1.68 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.36 (3H, s, $CH_2CH_2OCH_3$), 3.53 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.7 Hz), 3.65 (6H, m, $CH_2CH_2OCH_2CH_2OCH_3$), 3.72 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.24 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.29 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.77 (1H, s, C=*CH*); *E* isomer: 3.79 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.3 Hz), 5.49 (1H, s, C=*CH*). Element. Anal. Calcd: C 46.73%, H 5.80%, F 32.52%; found: C 46.90%, H 5.81%, F 31.97%.

3.14. Monomethyl ether diethylene glycol 3-F-pentyl-3-tetradecyloxypropenoate F5H14EO2 **13**

3-*F*-Pentyl-3-tetradecyloxypropenoyl chloride **12** (0.22 g, 0.39 mmol), anhydrous CH_2Cl_2 (20 mL), and diethylene glycol monomethyl ether 98% (0.052 g, 0.43 mmol) were stirred at room temperature under N_2 for 100 h. CH_2Cl_2 was removed on a rotary evaporator. The crude viscous pale brown oil was purified by flash column chromatography using silica gel and eluted first with chloroform and then with ethyl acetate to yield **13** as a pale yellow oil (0.100 g, 40%). Although it was not possible to separate the *Z* and *E* isomers, the *Z*/*E* molar ratio was determined by NMR to be 79/21. ^{1}H NMR ($CDCl_3$): δ_H/ppm, *Z* isomer: 0.90 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.39 (22H, br, $CH_3(CH_2)_{11}CH_2$), 1.73 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.40 (3H, s, $CH_2CH_2OCH_3$), 3.56 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.7 Hz), 3.66 (2H, t, $CH_2CH_2OCH_3$, J_{H-H}=4.5 Hz), 3.75 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.27 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.33 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.77 (1H, s, C=*CH*); *E* isomer: 3.81 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.3 Hz), 5.51 (1H, s, C=*CH*). Element. Anal. Calcd: C 49.54%, H 6.31%, F 31.93%; found: C 49.48%, H 6.35%, F 32.41%.

3.15. Monomethyl ether diethylene glycol 3-F-octyl-3-octyloxypropenoate F7H8EO2 **20**

3-*F*-Heptyl-3-octyloxypropenoyl chloride **18** (1.05 g, 1.8 mmol), anhydrous CH_2Cl_2 (20 mL), and diethylene glycol monomethyl ether (98%) (0.24 g, 2.0 mmol) were stirred under N_2 at room temperature for 9 days and 40 °C for 7 days. CH_2Cl_2 was removed on a rotary evaporator. The crude viscous pale brown oil was purified by flash column chromatography

using silica gel and eluted, first with $CHCl_3$ and then with ethyl acetate to yield 0.204 g of the *Z* isomer of **20** as a colorless transparent oil and 0.127 g of unseparated *Z* and *E* isomers (total yield 0.331 g, 27%). The *Z*/*E* molar ratio was 87/13. ^{1}H NMR ($CDCl_3$): δ_H/ppm, *Z* isomer: 0.89 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.29 (10H, br, $CH_3(CH_2)_5CH_2$), 1.71 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.40 (3H, s, $CH_2CH_2OCH_3$), 3.57 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.7 Hz), 3.67 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.5 Hz), 3.75 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.27 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.33 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.80 (1H, s, C=*CH*); *E* isomer: 3.81 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.3 Hz), 5.51 (1H, s, C=*CH*). Element. Anal. Calcd: *Z* isomer: C 41.20%, H 4.36%, F 42.50%; found: C 41.33%, H 4.33%, F 42.03%.

3.16. Monomethyl ether diethylene glycol 3-F-octyl-3-decyloxypropenoate F7H10EO2 **21**

3-*F*-Heptyl-3-decyloxypropenoyl chloride **19** (1.16 g, 1.9 mmol), anhydrous CH_2Cl_2 (20 mL), and diethylene glycol monomethyl ether (98%) (0.250 g, 0.2 mmol) were stirred under N_2 at room temperature for 48 h. CH_2Cl_2 was removed on a rotary evaporator. The crude viscous pale brown oil was purified by flash column chromatography using silica gel and elution first with chloroform and then with ethyl acetate to yield the *Z* isomer of **21** as a pale yellow oil (0.38 g, 29%) and 0.04 g of unseparated *Z* and *E* isomers (total yield 0.42 g, 32%). ^{1}H NMR ($CDCl_3$): δ_H/ppm, *Z* isomer: 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.27 (14H, br, $CH_3(CH_2)_7CH_2$), 1.71 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.39 (3H, s, $CH_2CH_2OCH_3$), 3.56 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.7 Hz), 3.65 (2H, t, $CH_2CH_2OCH_3$, J_{H-H}=4.6 Hz), 3.75 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.27 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.32 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.79 (1H, s, C=*CH*); *E* isomer: 3.80 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 5.51 (1H, s, C=*CH*). Element. Anal. Calcd: *Z* isomer: C 42.98%, H 4.76%, F 40.80%; found: C 43.37%, H 4.90%, F 40.41%.

3.17. Library of five triaffine surfactants (F5H10EOy, y=3–7) **6–10**

3-*F*-Pentyl-3-decyloxypropenoyl chloride **4** (1.4 g, 2.7 mmol), anhydrous CH_2Cl_2 (20 mL), and MPEG 350 (0.95 g, 2.7 mmol) were stirred together at room temperature under N_2 for 30 h. CH_2Cl_2 was removed on a rotary evaporator. The crude brown oil was purified first by flash column chromatography using silica gel and elution with acetone to eliminate the remaining MPEG 350. Fractions with R_f<0.40 were discarded. Fractions with $R_f \geq 0.40$ were purified by flash column chromatography using silica gel and elution with ethyl acetate/$CHCl_3$/EtOH (20/1/1), which allowed separation of five compounds with EO units varying from 3 to 7. The total yield was 36%. All products were obtained as colorless transparent oils. The amount of each one and their R_f values in ethyl acetate/$CHCl_3$/EtOH (20/1/1) were: *F5H10EO3* 0.06 g, R_f 0.62; *F5H10EO4* 0.11 g, R_f 0.55; *F5H10EO5* 0.18 g, R_f 0.43; *F5H10EO6* 0.25 g, R_f 0.31; and *F5H10EO7* 0.21 g, R_f 0.19. It was not possible to separate the isomers, but the *Z*/*E* ratio was determined. ^{1}H NMR ($CDCl_3$) δ_H/ppm: *F5H10EO3*, δ values were identical for *Z* and *E* isomers to those of compound **6** obtained by using triethylene glycol monomethyl ether. *Z*/*E* molar ratio=85/15. *F5H10EO4*: *Z* isomer: 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.26 (14H, br, $CH_3(CH_2)_7CH_2$), 1.70 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.38 (3H, s, $CH_2CH_2OCH_3$), 3.55 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.6 Hz), 3.64 (10H, m, $(CH_2CH_2O)_2CH_2CH_2OCH_3$), 3.73 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.25 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.6 Hz), 4.30 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 5.78 (1H, s, C=*CH*); *E* isomer: 3.80 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.4 Hz), 5.50 (1H, s, C=*CH*); *Z*/*E* molar ratio=86/14. *F5H10EO5*: *Z* isomer: 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.26 (14H, br, $CH_3(CH_2)_7CH_2$), 1.70 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.38 (3H, s, $CH_2CH_2OCH_3$), 3.54 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.7 Hz), 3.65 (14H, m, $(CH_2CH_2O)_3CH_2CH_2OCH_3$), 3.73 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.25 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.30 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.7 Hz), 5.78 (1H, s, C=*CH*); *E* isomer: 3.80 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.4 Hz), 5.50 (1H, s, C=*CH*); *Z*/*E* molar ratio=89/11. *F5H10EO6*: *Z* isomer: 0.88 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.26 (14H, br, $CH_3(CH_2)_7CH_2$), 1.70 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.38 (3H, s, $CH_2CH_2OCH_3$), 3.54 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.6 Hz), 3.65 (18H, m, $(CH_2CH_2O)_4CH_2CH_2OCH_3$), 3.73 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.25 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.30 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.7 Hz), 5.78 (1H, s, C=*CH*); *E* isomer: 3.80 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.3 Hz), 5.50 (1H, s, C=*CH*); *Z*/*E* molar ratio=92/8. *F5H10EO7*: *Z* isomer: 0.87 (3H, t, CH_2CH_3, $^3J_{H-H}$=6.8 Hz), 1.26 (14H, br, $CH_3(CH_2)_7CH_2$), 1.69 (2H, q, $CH_2CH_2CH_2O$, $^5J_{H-H}$=6.9 Hz), 3.37 (3H, s, $CH_2CH_2OCH_3$), 3.54 (2H, t, $CH_2CH_2OCH_3$, $^3J_{H-H}$=4.6 Hz), 3.65 (22H, m, $(CH_2CH_2O)_5CH_2CH_2OCH_3$), 3.73 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=4.8 Hz), 4.25 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.5 Hz), 4.29 (2H, t, $CH_2CH_2CH_2O$, $^3J_{H-H}$=4.7 Hz), 5.78 (1H, s, C=*CH*); *E* isomer: 3.80 (2H, t, $COOCH_2CH_2O$, $^3J_{H-H}$=6.4 Hz), 5.50 (1H, s, C=*CH*); *Z*/*E* molar ratio=94/6. Element. Anal. *F5H10EO4* Calcd: C 47.23%, H 6.02%; found: C 47.42%, H 6.04%; *F5H10EO5* Calcd: C 47.67%, H 6.21%; found: C 48.11%, H 6.42%; *F5H10EO6* Calcd: C 48.06%, H 6.38%, F 26.97%; found: C 48.78%, H 6.47%, F 26.68%; *F5H10EO7* Calcd: C 48.41%, H 6.52%; found: C 49.10%, H 6.83%.

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