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A structure–function study of the surface tension changes of *m*-xylene in the presence of fluorous 1H-1,2,3-triazoles and tetrazoles

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ABSTRACT

A study of surface tension measurements in *m*-xylene has shown that new hybrid 1H-1,2,3-triazoles and tetrazoles bearing perfluoroalkylethyl and -methyl substituents in combination with *n*-alkyl (lipophilic), *n*-alkoxymethyl (mildly hydrophilic), or methoxy(triethylenoxy)methyl (hydrophilic) substituents do have considerable surfactant properties. The properties of those with lipophilic substituents, especially those with alkyl chains of 8 carbons (or possibly more) border on erratic, while those with mildly hydrophilic or hydrophilic substituents exhibit highly predictable behaviour that is consistent with current understanding of surfactants. The change from two methylene spacer groups (perfluoroalkylethyl) to one methylene spacer group (perfluoroalkylmethyl) [equal to increasing the fluorine content], and the change from triazole to tetrazole nucleus, impart very significant increases on surface activity, whereas increases in the chain length of *n*-alkyl or perfluoroalkyl substituents have incremental effects.

1. Introduction

Some of the first hybrid fluorous surfactants [1] comprised semifluorinated alkanes [2,3] and molecules with a perfluorocarbon chain and a hydrocarbon chain attached through a common carbon to a sulfate [4], or other, polar headgroup. Numerous others have emerged bearing perfluoroalkyl chains and either lipophilic or hydrophilic groups, or in some cases both, but almost invariably the groups have been joined by a saturated carbon, single heteroatom or flexible, simple functional group [5,6], sometimes in combination with a benzene ring [7–10]. Highly fluorinated amphiphiles, with a more formal, modular design and systematic variations within the components of the molecules [11,12], have been investigated for use as drug carriers and delivery systems [8]. More recent designs have yielded organised assemblies of detergent-solubilised membrane proteins, guided by two-dimensional arrays of free standing fluorous surfactants [13], and have foundations in membrane protein extraction using fluorosurfactants [14,15].

In the absence of a polar headgroup there can be other novel and intriguing possibilities for aggregation in different solvents [9,16,17]. We have established an interest in the design of hybrid fluorous surfactants that are based on relatively small, planar heterocycles [18]. One motivation for constructing hybrid fluorous surfactants around heterocycles was to provide modularity to the synthesis, but another was to impose added constraints and order to the surfactant system. Potential benefits of this order on the resulting architectures of any fluorous aggregates, was likely to come from formation of stable, disk-like assemblies brought about by ring stacking and self associated polyfluoroalkyl side chains (see Fig. 1) [19]. These differ somewhat from related porphyrin [20] and other larger organometallic ring systems. Ultimately, these secondary structures have the potential to organise into attractive aggregates such as micelles and liposomal structures with obvious applications in transport as functional materials. There are only isolated examples of simple, hybrid fluorous molecules in which the central element is heterocyclic [21–27], and few have been studied for their surfactant or self-assembly properties.

This paper describes the influence of fluorous 1,2,3-triazoles and tetrazoles on surface tension as a means of probing surfactant properties of the molecules.

We have had some experience in the use of fluorous tagging methods through acetal formation [28], and have recently reported on the synthesis of fluorous triazoles [19,29] and on an improved method of alkylation of fluorous tetrazoles [30]. Elsewhere, only a few examples of fluorous surfactant-like modals based on 1H-1,2,3-triazoles have been described, although none have highlighted the potential of the materials as surfactants. Thus, perfluorooctylethyl azide and 3,5-di(perfluorooctyl)phenylmethyl azide have been used to react with a range of alkyne substrates, including a modified cinchonidine molecule, as part of a general tagging methodology [31]. Of more relevance, a 1-(perfluoroocty-

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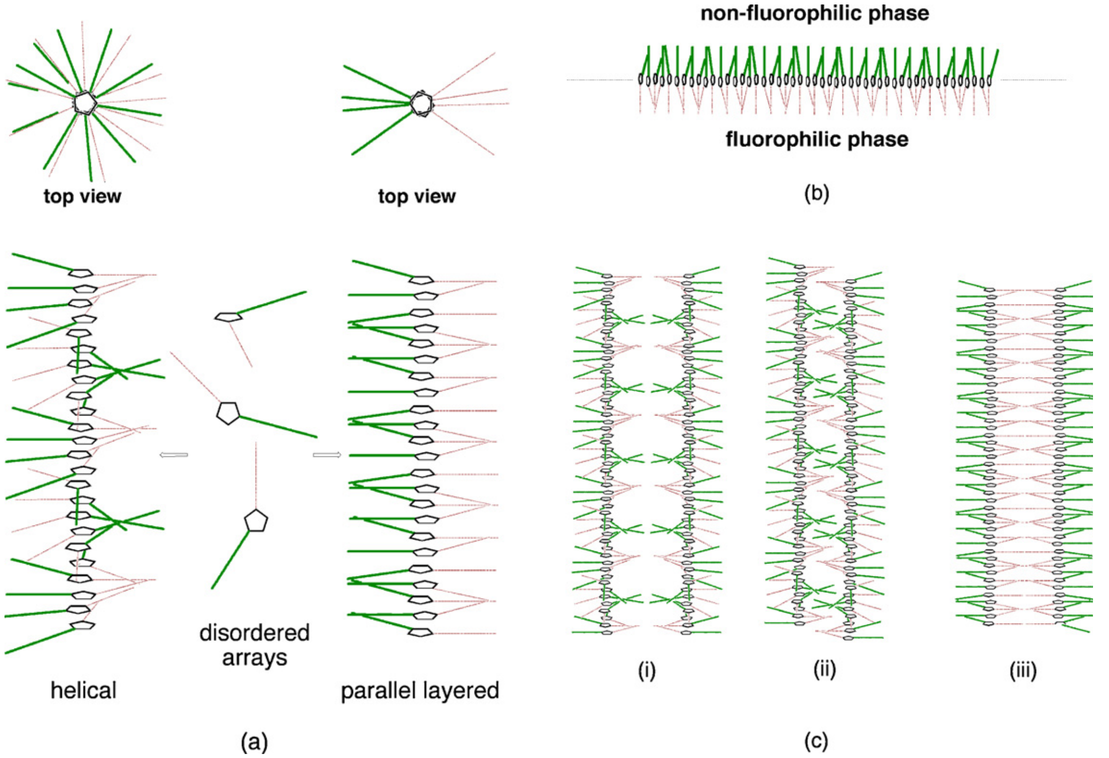
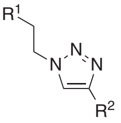


Fig. 1. Potential (a) secondary structures with disordered, helical or layered self assembly, (b) orientation of parallel mono-layered structure in a biphasic system, and (c) bilayer tertiary structures with (i) matching and (ii) intercalated helices or (iii) in parallel bilayers derived from self assembly of hybrid surfactants.

lethyl)-1,2,3-triazolyl)-TEMPO derivative was described as a recyclable catalyst for aerobic oxidation of alcohols to carbonyl derivatives [26a] and slower oxidation of sulfides to sulfoxides [26b]; very recently, 4-phenyl-1-(perfluorooctylethyl)-1,2,3-triazole was demonstrated to be recyclable as an organocatalyst for the aldol reaction [27]. A related cycloaddition approach has been described towards 5-polyfluoroalkylated 1,2,3-triazoles, especially those with α,α-difluoroalkyl substituents [22], and more recently, the copper(I) promoted cycloaddition between a limited range of polyfluoroalkyl azides ($R_fCH_2N_3$, where $R_f = CF_3$, CF_2CF_2H, and $(CF_2)_5CF_3$) and terminal alkynes (RCCH, where R = Ph, C_4H_9, C_6H_{13}, CH_2OTHP, CH_2OAc) was used to generate polyfunctional, 1,4-disubstituted 1,1-dihydro-perfluoroalkylated triazoles in a highly regioselective manner [23]. Again, this latter work was not directed towards surfactants, although the report of compounds in which $R_f = (CF_2)_5CF_3$ and R = C_4H_9 and C_6H_{13} were of relevance to the current paper.

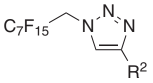
There has been one systematic study of surfactant properties of fluorous amphiphiles derived from triazoles [25]. It examined water-soluble 4- and 5-monocarboxylic acid and 4,5-dicarboxylate 1-(2-perfluoroalkylethyl)-1,2,3-triazole derivatives whose surfactant properties, surface tension in particular, were measured at the air-water interface. Surface tension, γ, was reduced by 30–35 mN m^{-1} at concentrations of 1.2–10.0 × 10^{-3} mol dm^{-3}. This is typical of classical fluorous surfactants [3,32,33]. Elsewhere, the physicochemical properties of neutral perfluoroalkylated acrylic acid/alkyl methyacrylate/trimethylamine co-oligomers have been measured [34]. Surface tension of these substances was measured at air–organic interfaces, and reductions of 30 mN m^{-1} at concentrations of 10–150 × 10^{-3} mol dm^{-3} were measured in *m*-xylene. Proprietary vaseline oil had much earlier been used to measure surface activity of hybrid polyfluorocarbon–hydrocarbon substances that were immiscible in water, but anomalies were recognized that were suggested to be due to viscosity issues with the compounds [35]. *m*-Xylene has advantages as a solvent for measurements as it has a relatively high surface tension amongst organic solvents, yet can dissolve fluorinated materials, and has been used very successfully in measuring critical micelle concentrations and surface activity of perfluoroalkylbenzenes [36]. Notably, in neither of the carboxylic nor acrylic acid cases above were critical micelle concentrations achieved, probably due to solubility issues, rather than the absence of aggregation phenomena.

These studies provided background for the studies of surfactant properties in this paper.



	R¹	R²	m.p. °C (ref)
1	C_4F_9	*n*-C_4H_9	48-51 (18)
2	C_4F_9	*n*-C_6H_{13}	54-57 (18)
3	C_4F_9	*n*-C_8H_{17}	69-70 (18)
4	C_6F_{13}	*n*-C_4H_9	79-81^a (18)
5	C_6F_{13}	*n*-C_6H_{13}	84-85^a (18)
6	C_6F_{13}	*n*-C_8H_{17}	91-93^a (18)
7	C_8F_{17}	*n*-C_4H_9	110-111 (18)
8	C_8F_{17}	*n*-C_6H_{13}	113-115 (18)
9	C_8F_{17}	*n*-C_8H_{17}	119-120 (18)

[a] Incorrectly reported in ref. 18



	R²	m.p. °C (ref)
10	*n*-C_4H_9	102-103 (42)
11	*n*-C_6H_{13}	101-102 (42)
12	*n*-C_8H_{17}	107-108 (42)

2. Methods and procedures

2.1. Materials

It was decided to measure changes induced in surface tension by a range of fluorous triazoles and tetrazoles as an indicator of surface activity. The preparation of fluorous triazoles 1–9 [18] and tetrazoles 13–20 and 37, 38 [30] has been reported. The synthesis of fluorous triazolyl ethers 21–36, amongst other related compounds, has been described in the accompanying paper [29], and fluorous triazoles 10–12 [37] were prepared by a published alkylative procedure [30]. Non-fluorous triazolyl triethyleneglycol ethers 27 and 28 were synthesized under modified Meldal-Sharpless conditions from 1-azidohexane and

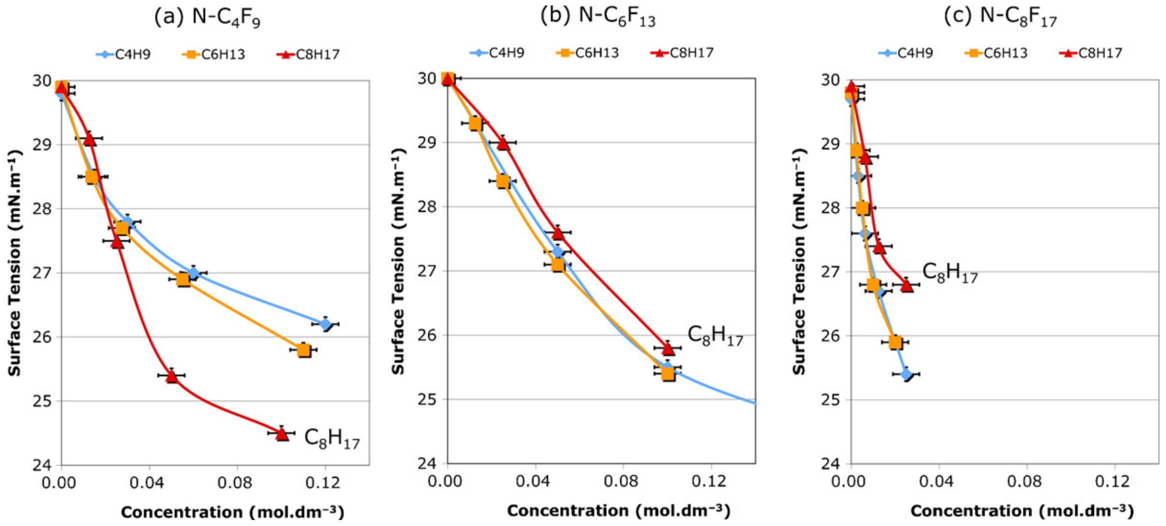


Fig. 2. Changes in surface tension of compounds (a) 1–3, (b) 4–6, (c) 7–9 in *m*-xylene.

1-azidooctane, respectively, by treatment in equimolar amounts with methoxy(triethyleneoxy)propyne (3.00 mmol), $CuSO_4 \cdot 5H_2O$ (0.15 mmol) and sodium ascorbate (0.30 mmol) in DMSO (1.0 cm^3) under microwave irradiation at 70 °C and 150 W power for 2 h, followed by chromatography on silica gel.

Triazole 27 an oil (73% yield). ^1H NMR (300 MHz; $CDCl_3$) δ: 0.87 (t, 3H), 1.31 (m, 6H), 1.92 (m, 2H), 3.37 (s, 3H), 3.65 (m, 2H), 3.60–3.72 (m, 10H), 4.34 (t, 2H), 4.71 (s, 2H), 7.62 (s, 1H). ESI-MS found *m*/*z*: 352.2197 (15%), calcd for $[M+Na]^+$ *m*/*z*: 352.2214; found *m*/*z*: 331.2407 (18) calcd for $[M+2H]^+$ *m*/*z*: 331.2472; found *m*/*z*: 330.2378 (100) calcd for $[M+H]^+$ *m*/*z*: 330.2394.

Triazole 28 an oil (83% yield). ^1H NMR (300 MHz; $CDCl_3$) δ: 0.87 (t, 3H), 1.20–1.35 (m, 6H), 1.90 (m, 2H), 3.36 (s, 3H), 3.53 (m, 2H), 3.65 (s, 2H), 3.60–3.72 (m, 10H), 4.35 (t, 2H), 4.72 (s, 2H), 7.67 (s, 1H). ESI-MS found *m*/*z*: 738.5737 (13%), calcd for $[2M+H+Na]^+$ *m*/*z*: 738.5235; found *m*/*z*: 594.3498 (14); found *m*/*z*: 381.2537 (20) calcd for $[M+H+Na]^+$ *m*/*z*: 381.2605; found *m*/*z*: 380.2509 (100), calcd for $[M+Na]^+$ *m*/*z*: 380.2527; found *m*/*z*: 358.2693 (30) calcd for $[M+H]^+$ *m*/*z*: 358.2707.

2.2. Surface tension measurement

Surface tension was measured in *m*-xylene at the solvent-air interface by the du Noüy ring method using a Krüss T53E Interfacial-Tensiometer K8600 with a thermostat vessel 8600T set at 25 °C and 0.37 mm wire diameter, 60 mm circumference platinum–iridium ring [38]. The instrument was calibrated daily and before each set of experiments against freshly drawn samples of Milli-Q water and triply glass distilled *m*-xylene. Samples of 0.1199–0.9425 ± 0.0005 g were prepared in most cases in a 10 ± 0.05 cm^3 (in three cases in 20 cm^3) volumetric flask as *m*-xylene solutions whose concentrations were systematically decreased by dilution to within the range 0.0100–0.1500 ± 0.005 mol dm^{-3}. Surface tension data were recorded as the average values of three measurements on solutions of polyfluoroalkylated 1,2,3-triazoles and tetrazoles. Systematic and standard errors were considered to give a measurement uncertainty in surface tension of ±0.11 mN m^{-1}. Surface tension was plotted against concentration in Figs. 2–7 (see additional charts in Supplementary Data), but in all cases, as in the literature [25,34], the critical micelle concentration (CMC)

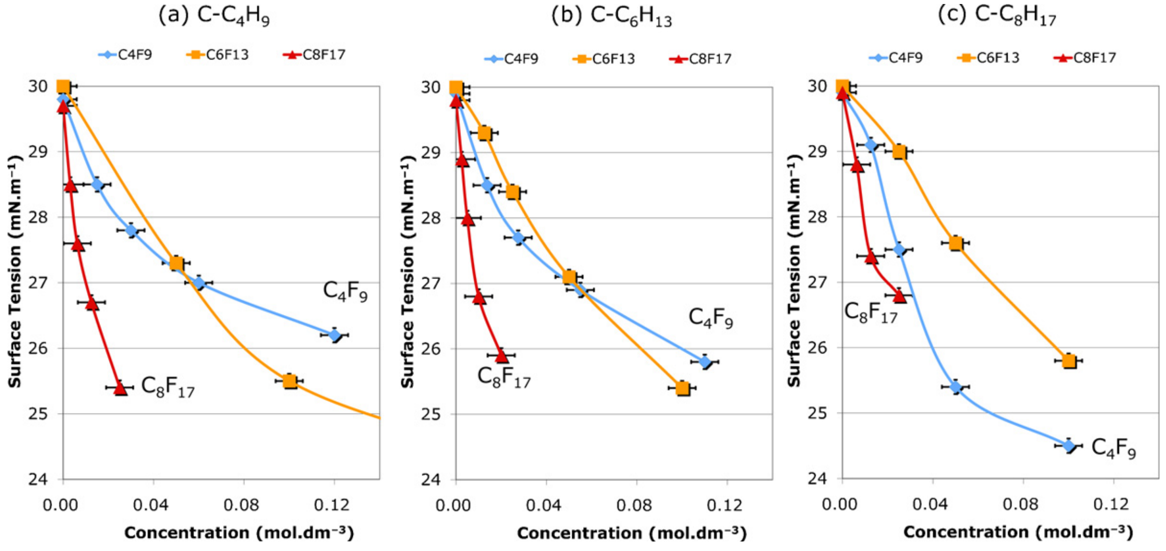


Fig. 3. Changes in surface tension of solutions of compounds (a) 1,4,7 ($R^2 = C_4H_9$), (b) 2,5,8 ($R^2 = C_6H_{13}$), and (c) 3,6,9 ($R^2 = C_8H_{17}$), in *m*-xylene.

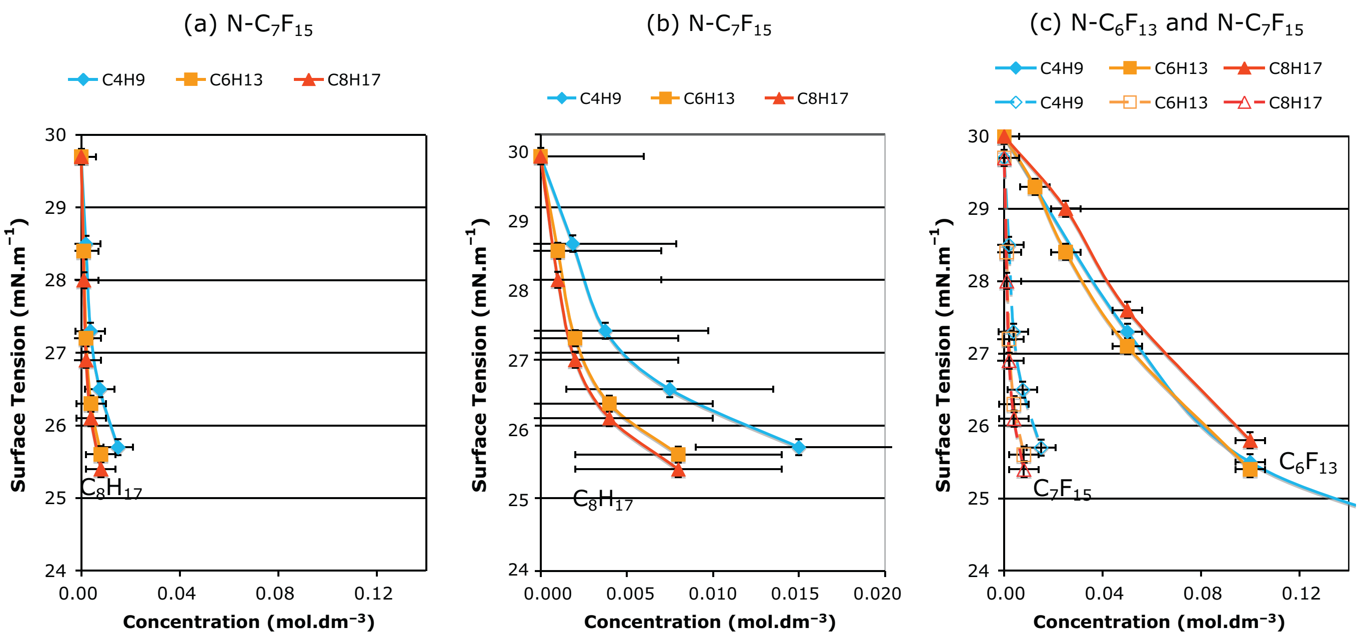


Fig. 4. Changes in surface tension of solutions of compounds 10–12 in *m*-xylene (a) on the scale in Figs. 2 and 3, (b) showing detail on an expanded horizontal scale, (c) on the original horizontal scale and compared with data in Fig. 2b.

could not be attained because the samples became insoluble before the cloud point was achieved. In a few cases, as for example in Figs. 2a and 3c, there were sufficient changes in the curvature of the surface tension plot to indicate some form of aggregation had taken place, although characterization of these aggregates was beyond the scope of the current paper.

3. Results and discussion

3.1. Fluorophilic–lipophilic combinations

Initial studies were directed towards the properties of a small library of 1H-1,2,3-triazole derivatives 1–12. Compounds 1–9 [18] comprised a matrix of compounds with one of three 2-(perfluoroalkyl)ethyl substituents at position 1 and one of three *n*-alkyl substituents at position 4. Meanwhile, triazoles 10–12 [30], contained a perfluoroheptylmethyl substituent at position 1 and the same range of *n*-alkyl groups at position 4. Selection of these compounds was designed to measure the effect of added fluorine or replacement of the ethylene spacer group with a methylene spacer [39]. The compounds were prepared by the copper(I) promoted Meldal-Sharpless 1,3-dipolar cycloaddition chemistry [40] of azides and alkynes and so were obtained with high regiochemical purity.

In practice, triazoles 1–12, especially 1–9, exhibited surprisingly erratic surface active behaviour (see Figs. 2–4), reminiscent of that reported for polyfluorocarbon–hydrocarbon substances in vaseline oil [35].

Within the first matrix of substituent types, 1–9, if one considers, for example, triazoles 1–3 (Fig. 2a), these molecules contain a fixed perfluoroalkyl chain of four carbons, C_4F_9, attached through an ethylene bridge to nitrogen at position-1. They also contain linear hydrocarbon chains of increasing length, C_4H_9, C_6H_{13} and C_8H_{17}, at position-4. Beyond this were similar sets of derivatives, 4–6 (Fig. 2b and c) with perfluorohexylethyl and 7–9, with perfluorooctylethyl *N*-1 substituents, respectively, each with hydrocarbon chains of increasing length at position-4. The higher solubility of triazoles 1–3, with their short fluorocarbon chains, C_4F_9, meant that measurements could be extended to higher concentrations with these molecules, more than for the other heterocycles in this series (Fig. 2).

In each series (Fig. 2a–c), the 4-*n*-butyl and 4-*n*-hexyl derivatives showed nearly identical behaviour for each of the fixed fluorous chain lengths, while the 4-*n*-octyl derivative gave distinctly higher, lower or equal, changes in surface tension to the changes with the shorter alkyl chains. Within the C_4F_9 and C_8F_{17} series the *n*-octyl derivatives showed inflections in the surface tension curves that indicated aggregation phenomena at concentration values of 0.045 mol dm^{-3} and 0.015 mol dm^{-3}, respectively.

An inverse plot (Fig. 3) showed increasingly larger decreases in surface tension with increasing length of the fluorous chain, *albeit* with an interesting crossover from *n*-perfluorobutylethyl to *n*-perfluorohexylethyl (Fig. 3a and b), respectively, although the perfluorooctylethyl derivatives showed significantly higher reductions, and more rapid reductions than the former. Again, with the molecules with fixed *n*-octyl hydrocarbon chain but variable chain length of the fluoroalkyl substituent (Fig. 3c), the behaviour was erratic. Indeed, the perfluorobutylethyl derivative showed higher activity than its perfluorohexyl counterpart and the most significant decrease in surface tension of any of the derivatives. Thus, there was an unexpected disconnection in the properties of the *n*-octyl derivatives when compared with the lower homologues.

3.2. Fluorophilic–lipophilic combinations with increased fluorine content

The effect of fluorine content or, expressed differently, the influence of one instead of two methylene spacer groups, was enlightening. Hence, the equivalent series of 4-*n*-alkyl substituted 1-perfluoroheptylmethyl-triazoles, 10–12 proved much more surface active than their counterparts, compounds 4–6 (compare results in Fig. 4 with those in Fig. 2b); the reduction in surface tension to below 26 mN m^{-1} for 10–12 was effected at concentrations 10–20 times less than for triazoles 4–6. Interestingly, they gave the anticipated reduction in surface tension with increasing concentration (Fig. 4b), but the expected decrease in surface tension with increasing hydrocarbon chain length occurred at almost the same rate for the *n*-hexyl and *n*-octyl derivatives but much more slowly for the *n*-butyl derivative. In this case it was not

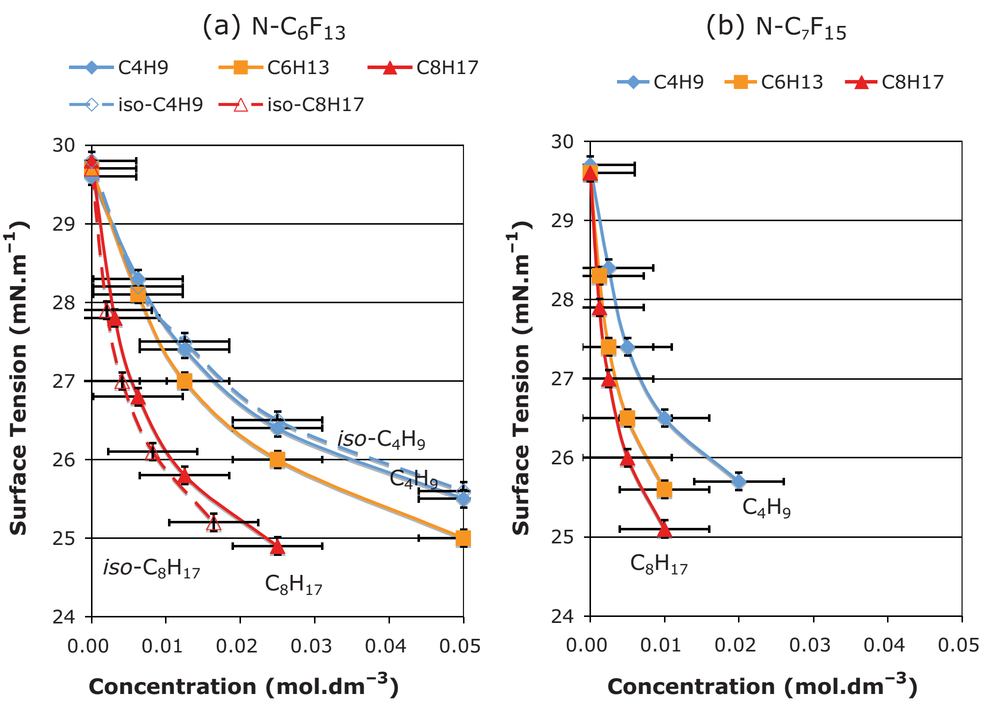
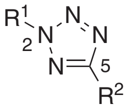


Fig. 5. Surface tension measurements for solutions of tetrazoles (a) 13–15 and 19–20, and (b) 16–18, in *m*-xylene.

possible to determine if the *n*-butyl or the *n*-octyl derivative was the culprit, nor indeed, especially from Fig. 4a–c, if the behaviour of the *n*-hexyl derivative was anomalous. Although such behaviour is difficult to explain, it may have important consequences. For example, it has been reported and highlighted that the excretion rates of fluorous surfactant-like molecules, perfluorohexyl-sulfonic and -carboxylic acids from humans are variable, but lower than for the corresponding perfluoro-*n*-pentanoic and *n*-nonanoic acids [41,42]. Specificity of fluorous chain lengths might therefore be worth further investigation.

3.3. Fluorophilic–lipophilic combinations with tetrazole nuclei

A parallel series of fluorous tetrazoles with 1-perfluorohexylethyl 13–15 and 1-perfluoroheptylmethyl 16–18 substituents, and *n*-alkyl groups of increasing chain length at position 4, were next evaluated by the same technique (Fig. 5). In addition, two representative examples, 19 and 20, of positional isomers were studied. Tetrazoles 19 and 20 contained identical substituents at position 5 to those in tetrazoles 13 and 15, respectively, but their perfluorohexylethyl substituent resided at position 1 rather than at position 2.



	R^1	R^2	m.p. °C (ref)
13	$CH_2CH_2C_6F_{13}$	*n*-C_4H_9	oil (30)
14	$CH_2CH_2C_6F_{13}$	*n*-C_6H_{13}	oil (30)
15	$CH_2CH_2C_6F_{13}$	*n*-C_8H_{17}	oil (30)
16	$CH_2C_7F_{15}$	*n*-C_4H_9	35-36[a] (30)
17	$CH_2C_7F_{15}$	*n*-C_6H_{13}	34-35 (30)
18	$CH_2C_7F_{15}$	*n*-C_8H_{17}	31-32 (30)
19	$CH_2CH_2C_6F_{13}$	iso-*n*-C_4H_9[b]	40.5-42 (30)
20	$CH_2CH_2C_6F_{13}$	iso-*n*-C_8H_{17}[b]	65-67 (30)

[a] Incorrectly reported as m.p. 35-46°C in ref. 30.
[b] 1,5-isomer *versus* 2,5-isomer for all others.

In all these cases, there was highly consistent behaviour.

In both cases, Fig. 5a and b, increasing the hydrocarbon chain length gave increasing surface activity, reflected in a steady decrease in surface tension. The molecules with the higher fluorine content, tetrazoles 16–18, had lower solubility than 13–15, but showed very normal trends, and much increased surface activity (Fig. 5b versus a solid lines). Decreases in surface tension from the normal value of 29.7 mN m^{-1} to less than 26 mN m^{-1} required concentrations of the 1-perfluoroheptylmethyl tetrazoles of far less than 0.02 mol dm^{-3} compared with at least 0.04 mol dm^{-3} and up to 0.05 mol dm^{-3} for the corresponding triazoles and tetrazoles with perfluorohexylethyl substituents.

Tetrazoles 16–18 were also direct analogues of the perfluoroheptylmethyl substituted triazoles 10–12, and careful comparison of Figs. 4b and 5b revealed both sets of surface tension measurements were similar. This was unlike the situation of perfluorohexylethyl substituted tetrazoles, 13–15, in which the tetrazoles were significantly more surface active than their equivalents, the corresponding triazoles, 4–6.

Finally in this series, displacement of the perfluoroalkylethyl group from the more remote position-2 on the tetrazole ring to position-1, as in the 1,5-substituted tetrazoles 19 and 20, revealed near parallel surface tension modifying behaviour to that of their 2,5-substituted analogues 13 and 15. This was somewhat remarkable given the altered geometry, but must have had its basis in the types of sidechain interactions.

The tetrazole ring system therefore appeared to be beneficial in the design of fluorous surfactants, but more complete fluorination of the alkyl groups could have a more dominant effect. Unexpectedly, placement of alkyl and perfluoroalkylethyl substituents on adjacent positions on the tetrazole ring induced little change in surfactant behaviour.

3.4. Mild lipophobicity a potential cause for erratic behaviour

While one of the features of fluorous materials is that they are hydrophobic and lipophobic, the inconsistent surface tension behaviour in *m*-xylene of hybrid molecules with changing hydrocarbon and fluorophilic substituent combinations, observed in Figs. 2–4 for triazoles 1–12 and Fig. 5 for tetrazoles 13–18, raised the possibility that, at least in these small molecule, heterocyclic systems examined here, the lipophobicity might not be as severe as

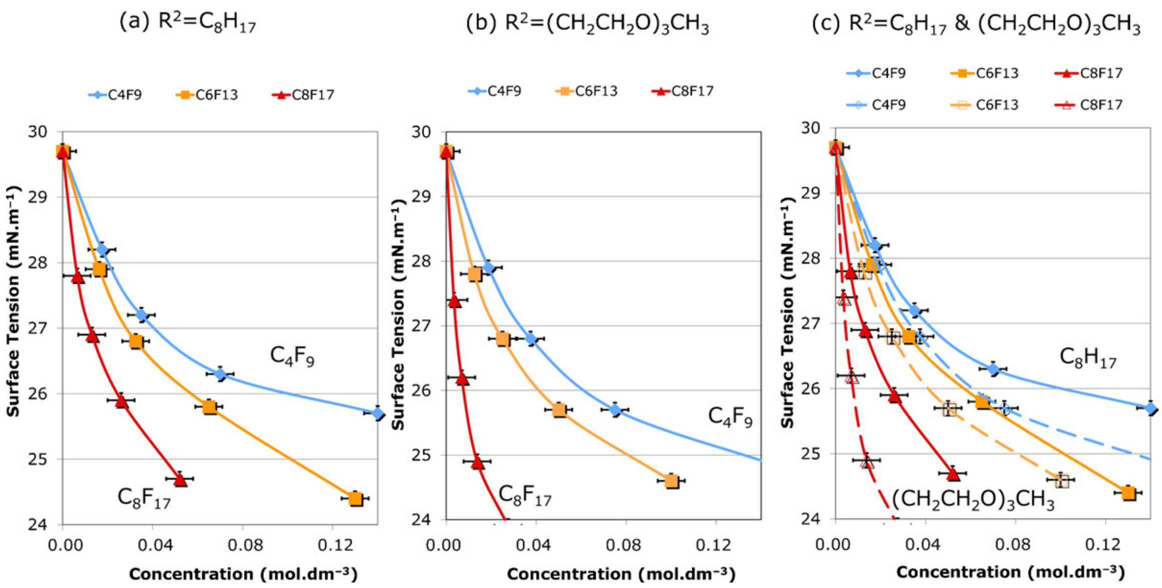


Fig. 6. Changes in surface tension measurements for solutions of compounds (a) 21–23 and (b) 24–26 in *m*-xylene, and (c) a comparison of (a) and (b).

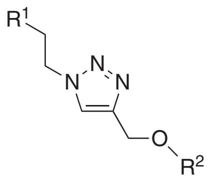
had been first imagined. Efforts were therefore made to prepare equivalent structures in which the hydrocarbon chain was replaced with a more hydrophilic element [22].

3.5. *Fluorophilic–hydrophilic combinations*

Firstly, the effect of inserting a single oxygen atom in the hydrocarbon chain was examined for convenience. Triazoles 21–23 with perfluoroalkylethyl substituents on position 1 and *n*-octyloxymethyl substituents at position 4 were tested (Fig. 6a). Equivalent triazoles 24–26 with the same range of fluorous groups at position 1 and a triethyleneglycol methyl ether substituent at position 4 were also examined (Fig. 6b).

Measurement of the surfactant properties of the ether substituted triazoles 21–23 (Fig. 6a) and the polyether substituted triazoles 24–26 (Fig. 6b) revealed highly consistent surfactant behaviour and similarities between the two series. As the length of the fluorous chain increased, so there was a marginal increase in the degree of decrease in surface tension. Curiously, there was a more dramatic decrease in moving from perfluorohexyl to perfluorooctyl than was shown in moving from perfluorobutyl to perfluorohexyl, and this raises a similar question to the one above over the impact of chain lengths of eight carbons or more.

Comparisons between each of the pairs of results for triazoles with like polyfluoroalkyl groups and single ether versus polyether substituents, i.e., 21/24, 22/25 and 23/26 (Fig. 6c, solid versus dashed lines), revealed significantly more rapid decrease in surface tension by the polyether than the single ether derivative. This is entirely consistent with the proposed benefit of having a more hydrophilic group in combination with the fluorophilic group for optimum surface activity behaviour. In other words, this outcome further supported the concept that hydrophilic groups were better than lipophilic groups as partners for any fluorophilic groups if predictable surfactant properties were to be achieved.



	R^1	R^2	m.p. °C (ref)
21	C_4F_9	C_8H_{17}	40-42 (29)
22	C_6F_{13}	C_8H_{17}	52-54 (29)
23	C_8F_{17}	C_8H_{17}	80-82 (29)
24	C_4F_9	$(CH_2CH_2O)_3CH_3$	wax (29)
25	C_6F_{13}	$(CH_2CH_2O)_3CH_3$	wax (29)
26	C_8F_{17}	$(CH_2CH_2O)_3CH_3$	47-49 (29)

3.6. *Benefits of fluorophilic–hydrophilic rather than lipophilic–hydrophilic combinations*

With the previous results in mind, the actual benefit of the presence of fluorine was also assessed. A direct comparison between fluorous hydrophilic triazoles, 24 and 25, and their hydrocarbon analogues, 27 and 28, respectively, did demonstrate a

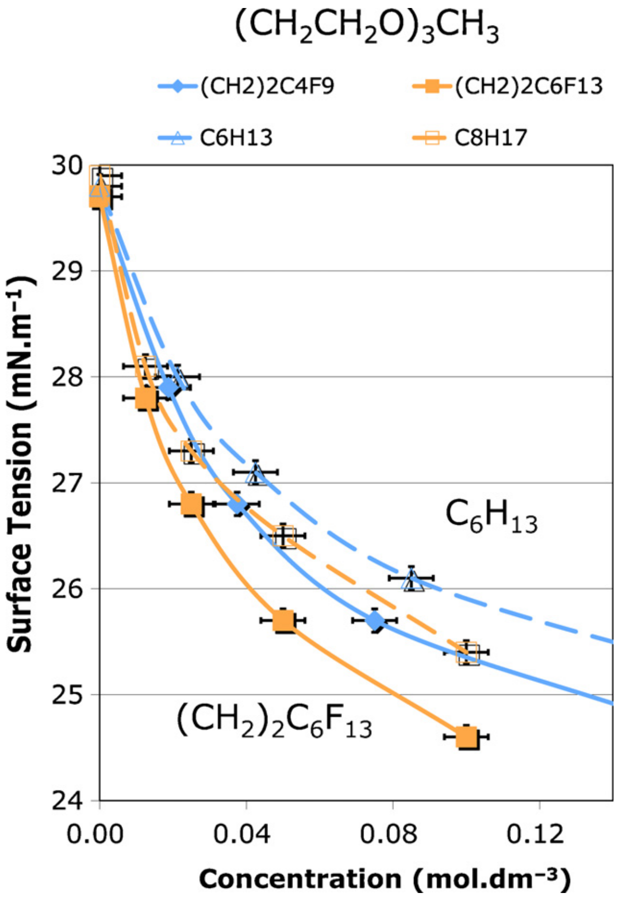
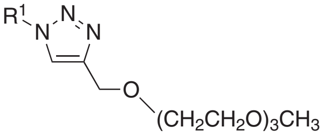


Fig. 7. Surface tension measurements in *m*-xylene for the matrix of fluorous triazoles 24 and 25 and non-fluorous triazoles 27 and 28, with the same chain length but fluorous and non-fluorous substituents.

higher surface activity for the fluorous molecules (Fig. 7). The results showed that for triazole molecules with alkyl substituents of differing chain length (C_6 and C_8) at position 1, the presence of fluorine led to a more rapid decrease in surface tension than without.



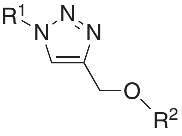
	R^1	m.p. °C (ref)
24	$CH_2CH_2C_4F_9$	wax (29)
25	$CH_2CH_2C_6F_{13}$	wax (29)
27	C_6H_{13}	oil (43)
28	C_8H_{17}	oil (43)

In partial summary, these various experiments demonstrated that surface activity was definitely enhanced by the presence of polyfluorination and that surface tension was most influenced by the chain length of the ether or hydrocarbon side-chains, and could be made more effective by incorporation of central tetrazole rather than triazole rings. They also revealed that triethyleneglycol substituted heterocycles would reach their critical micelle concentration values at much lower concentration than their less oxygenated counterparts, and were more effective in their surfactant power. The disconnection between hydrocarbon side-chains of between 6 and 8 carbons in length was noted although probably the result of the strong hydrophobic nature of both lipophilic and fluorophilic groups.

3.7. Switching the fluorophilic substituent from N(1) to C(4)

The effect of switching the point of attachment of fluorous and non-fluorous substituents, rather than merely moving substituents to adjacent positions, was next examined. In doing so, it was decided to retain one oxygen in the substituent at position 4.

Triazoles 29–36, with various *n*-alkyl groups at position 1 and perfluorohexylethoxymethyl, 29–32, or perfluoroheptylmethoxymethyl, 33–36, substituents at position 4 were studied. In contrast to the earlier groups, all the compounds showed high solubility in *m*-xylene.



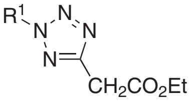
	R^1	R^2	m.p. °C (ref)
29	C_4H_9	$CH_2CH_2C_6F_{13}$	oil (29)
30	C_6H_{13}	$CH_2CH_2C_6F_{13}$	wax, 31-32 (29)
31	C_8H_{17}	$CH_2CH_2C_6F_{13}$	34-35 (29)
32	C_9H_{19}	$CH_2CH_2C_6F_{13}$	41-43 (29)
33	C_4H_9	$CH_2C_7F_{15}$	oil (29)
34	C_6H_{13}	$CH_2C_7F_{15}$	29-31 (29)
35	C_8H_{17}	$CH_2C_7F_{15}$	39-40 (29)
36	C_9H_{19}	$CH_2C_7F_{15}$	55-56 (29)

Interestingly, these alternatively substituted, fluorous ether substituted triazoles behaved with remarkable consistency as surfactants, as measured by expected smooth and gradual changes in surface tension (see charts in Supplementary Data).

Comparison of the data then for the same molecules, but considering fixed hydrocarbon substituents and varying perfluoroalkyl chains, i.e., perfluorohexylethyl versus perfluoroheptylmethyl, showed consistently lower surface tension for the chains with higher fluorine content. These results suggested that the molecules in this series behaved as normal surfactants and followed traditional understanding of surfactant behaviour.

The substitution pattern found in triazoles 29–36 therefore appeared to provide materials with near ideal surface activity behaviour.

A direct comparison of this latter triazole system with the analogous tetrazole system was not made, but a pair of tetrazoles, 37 and 38, with 1-polyfluoroalkyl substituents and ethyl acetic ester substituents at position 4, analogous to tetrazoles 13–18, were available and assessed.



	R^1	m.p. °C (ref)
37	$CH_2CH_2C_6F_{13}$	oil (30)
38	$CH_2C_7F_{15}$	52-53 (30)

As with triazoles 29–36, tetrazoles 37 and 38 proved to be very highly active in reducing surface tension in *m*-xylene, with performance equivalent to or better than that of the 4-*n*-octyloxymethyl substituted derivatives (see Supplementary Data). Given that the ethyl acetic ester substituent is five atoms in length, the additional surface activity of these ester molecules must have arisen from the added hydrophilicity of the ester group. This result will point to further studies.

3.8. Correlation between surface activity and physical properties of molecular tensides

It was instructive to compare the physical state of the molecular tensides examined in this study with the surface activity findings that have now been described in an effort to understand something of the self-assembly of the molecules. The melting points of lipophilic triazoles 1–12 followed very clear trends that belied their somewhat chaotic effect on surface tension. For example, within each set of 1-perfluoralkylethyl- (1–3, 4–6, 7–9) and 1-perfluoroheptylmethyl-substituted (10–12) triazoles, melting points increased with increasing 4-alkyl substituent chain length. Such increases could be ascribed to increases in formula weight. However, it was noticed that for the 1-perfluorooctylethyl- (7–9) and 1-perfluoroheptylmethyl-substituted (10–12) substances, the melting points increased marginally from 4-*n*-butyl- to 4-*n*-hexyl-substituted derivatives, but more significantly from 4-*n*-hexyl- to 4-*n*-octyl-substituted derivatives. At the lower formula weight homologue level, the melting point rose by about 6 °C for each iteration, or 3 °C for each CH_2 group. In contrast, melting points increased by approximately 25 °C for each step increase in fluorous chain length, or 12–13 °C for each CF_2 group. Incorporation of more fluorine into molecules of the same size, e.g., 1-perfluoroheptylmethyl- derivatives (10–12) compared with 1-perfluorohexyethyl- derivatives (4–6), induced very significant increases in melting point (15–30 °C). These were consistent with increased rigidity of the saturated carbon chain, but the level of increase became less as the hydrocarbon chain length increased.

Similar, but generally smaller, changes in melting points were observed, where relevant, throughout each series of triazolyl tensides 21–38. The observations for tetrazoles 13–20 differed from those of the triazoles in some respects. Molecules with the 1-perfluoroheptylmethyl-substituent 16–18 certainly had higher (though indeterminably higher) melting points than those with 1-perfluorohexylethyl-substituent 13–15, but subsequent increases in 4-alkyl substituent chain length led to very small but significant decreases in melting point. This observation possibly arose from a more dominant effect of the tetrazole over the triazole nucleus in defining melting points. Importantly, the isomerically substituted 1-perfluorohexylethyl 5-alkyl-substituted tetrazoles, had significantly higher melting points than their corresponding 2-perfluorohexylethyl-5-substituted tetrazole analogues. This observation was entirely consistent with the earlier proposal that in the 1,5-disubstituted tetrazoles the perfluoroalkyl and the *n*-alkyl substituents both behave as hydrophobic groups and probably self associate, either intramolecularly causing relatively rigid, possibly rod-like, monomeric species, or intermolecularly causing networks of cross-associated monomeric species. Commensurate with this suggestion, the higher homologue of this pair, 19 and 20, namely tetrazole 20, melted at approximately 15 °C higher in temperature than did its shorter homologue 19. This is what might be expected for longer substituent sidechains that could better interact.

4. Conclusion

Overall, these studies reveal very positive surfactant behaviour for fluorous triazole and tetrazole derivatives in which there is at least one ether oxygen in the substituent at position 4. The evidence suggests that this position may contain a polyfluoroalkyl substituent or a plain *n*-alkyl substituent. Key to the normal surfactant behaviour is a hydrophilic group to counteract the powerful hydrophobic properties of fluorophilic substituents. This insight into small molecule fluorous surfactants is perhaps understandable, but has not been demonstrated before with such clarity and convincing evidence that highlights the major influencing factors.

A determination of the structural form of aggregates will now be pursued and applications of fluorous heterocycles will be examined based on the findings in the present study.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jfluchem.2011.07.030.

References

[1] E. Kissa, Fluorinated surfactants and repellants, second ed., Surfactant Science Series, vol. 97, Marcel Dekker, New York, 2001, pp. 615.
[2] G.L. Gaines, Langmuir 7 (1991) 3054–3056.
[3] M.P. Krafft, J.G. Riess, Chem. Rev. 109 (2009) 1714–1792.
[4] W. Guo, Z. Li, B.M. Fung, E.A. O'Rear, J.H. Harwell, J. Phys. Chem. 96 (1992) 6738–6742.
[5] M. Allouch, C. Selve, J. Fluorine Chem. 66 (1994) 31–38.
[6] P. LoNostro, S.–M. Choi, C.–Y. Ku, S.–H. Chen, J. Phys. Chem. B 103 (1999) 5347–5352.
[7] K. Kratzat, F. Guittard, E. Taffin de Givenchy, A. Cambon, Langmuir 12 (1996) 6346–6350.
[8] P. Vierling, C. Santaella, J. Greiner, J. Fluorine Chem. 107 (2001) 337–354.
[9] K. Matsuoka, Y. Moroi, Curr. Opin. Colloid Interface Sci. 8 (2003) 227–235.
[10] N. Yoshino, Y. Kondo, Curr. Opin. Colloid Interface Sci. 10 (2005) 88–93.
[11] J.G. Riess, M.P. Krafft, Biomaterials 19 (1998) 1529–1539.
[12] J.G. Riess, Curr. Opin. Colloid Interface Sci. 14 (2009) 294–304.
[13] V. Petkova, J.–J. Benattar, M. Zoonens, F. Zito, J.–L. Popot, A. Polidori, S. Jasseron, B. Pucci, Langmuir 23 (2007) 4303–4309.
[14] S. Nuss, C. Mioskowski, L. Lebeau, Chem. Phys. Lipids 103 (1999) 21–35.
[15] L. Lebeau, F. Lach, C. Vénien-Bryan, A. Renault, J. Dietrich, T. Jahn, M.G. Palmgren, W. Kühlbrandt, C. Mioskowski, J. Mol. Biol. 308 (2001) 639–647.
[16] J.G. Riess, Tetrahedron 58 (2002) 4113–4131.
[17] M.P. Krafft, M. Goldmann, Curr. Opin. Colloid Interface Sci. 8 (2003) 243–250.
[18] R.W. Read, X.B. Wang, Chiang Mai, J. Sci. 36 (2009) 247–257.
[19] Inspiration for this notion has come from reviews by Nolte (J.A.A.W. Elemans, A.E. Rowan, R.J.M. Nolte, J. Mater. Chem. 13 (2003) 2661–2670); Moore (D.J. Hill, M.J. Mio, R.B. Prince, T.S. Hughes, J.S. Moore, Chem. Rev. 101 (2001) 3893–4011); Percec (V. Percec, C.-H. Ahn, G. Ungar, D.J.P. Yeardley, M. Möller, S.S. Sheiko, Nature 391 (2001) 161–164; V. Percec, C.-H. Ahn, W.-D. Cho, A.M. Jamieson, J. Kim, T. Leman, M. Schmidt, M. Gerle, M. Müller, S.A. Prokhorova, S.S. Sheiko, S.Z.D. Cheng, A. Zhang, G. Ungar, D.J.P. Yeardley, J. Am. Chem. Soc. 120 (1998) 8619–8631), and others. Such behaviour has also recently been invoked to explain the extreme stabilization against oxidation of silicon surfaces that have alkyl-1,2,3-triazole appendages (S. Ciampi, P.K. Eggers, G.L. Le Saux, M. James, J.B. Harper, J.J. Gooding, Langmuir 25 (2009) 2530–2539).
[20] J. Leroy, A. Bondon, Eur. J. Org. Chem. (2008) 417–433.
[21] A.R. Katritzky, T.L. Davis, G.W. Rewcastle, G.O. Rubel, M.T. Pike, Langmuir 4 (1988) 732–735.
[22] S.A. Lermontov, S.V. Shkavrov, A.N. Pushin, J. Fluorine Chem. 105 (2000) 141–147.
[23] W. Peng, S. Zhu, Tetrahedron 59 (2003) 4395–4404.
[24] Y.M. Wu, J. Deng, X. Fang, Q.Y. Chen, J. Fluorine Chem. 125 (2004) 1415–1423.
[25] E. Mayot, C. Gérardin-Charbonnier, C. Selve, J. Fluorine Chem. 126 (2005) 715–720.
[26] (a) A. Gheorghe, E. Cuevas-Yañez, J. Horn, W. Bannwarth, B. Narsaiah, O. Reiser, Synlett (2006) 2767–2770;
(b) T. Chinnusamy, O. Reiser, ChemSusChem 3 (2010) 1040–1042.
[27] Y.W. Zhu, W.B. Yi, C. Cai, J. Fluorine Chem. 132 (2011) 71–74.
[28] (a) R.W. Read, C. Zhang, Tetrahedron Lett. 44 (2003) 7045–7048;
(b) C. Zhang, R.W. Read, in: J. Gladysz, E. Horváth, D.P. Curran (Eds.), The Handbook on Fluorous Chemistry, Wiley-VCH, New York, 2004, pp. 471–473.
[29] D.V. Francis, D.H. Miles, A.I. Mohammed, R.W. Read, X. Wang, J. Fluorine Chem., in press.
[30] Y. Huang, R.W. Read, X. Wang, Aust. J. Chem. 63 (2010) 802–807.
[31] Z. Kaleta, O. Egyed, T. Soós, Org. Biomol. Chem. 3 (2005) 2228–2230.
[32] S. Cosgun, M. Özer, F. Hamdoune, C. Gerardin, S. Thiebaut, B. Henry, J. Amos, L. Rodehüser, C. Selve, J. Fluorine Chem. 107 (2001) 375–386.
[33] D. Papadopolous, S. Auberger, C. Gérardin, J. Amos, M. Maugras, M.J. Stébé, C. Selve, N. J. Chem. 23 (1999) 657–663.
[34] H. Sawada, K. Tanba, N. Itoh, C. Hosoi, M. Oue, M. Baba, T. Kawase, M. Mitani, H. Nakajima, J. Fluorine Chem. 77 (1996) 51–64.
[35] M. Napoli, C. Fraccaro, A. Scipioni, J. Fluorine Chem. 51 (1991) 103–115.
[36] M. Abe, K. Morikawa, K. Ogino, H. Sawada, T. Matsumoto, M. Nakayama, Langmuir 8 (1992) 763–764.
[37] Y. Huang, unpublished results, private communication.
[38] P.L. du Noüy, J. Gen. Physiol. 7 (1925) 625–631, Surface tension measured by the ring method: www.kruss.de/en/theory/measurements/surface-tension/ring-method.html.
[39] V.M. Sadtler, F. Giulieri, M.P. Krafft, J.G. Riess, Chem. Eur. J. 4 (1998) 1952–1956.
[40] (a) C.W. Tornøe, C. Christensen, M. Meldal, J. Org. Chem. 67 (2002) 3057–3064;
(b) V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, Angew. Chem. Int. Ed. Engl. 41 (2002) 2596–2599.
[41] K.S. Betts, Environ. Health Perspect. 15 (2007) A250–A256.
[42] G.W. Olsen, J.M. Burris, D.J. Ehresman, J.W. Froelich, A.M. Seacat, J.L. Butenhoff, L.R. Zobel, Environ. Health Perspect. 15 (2007) 1298–1305.