Chiang Mai J. Sci. 2009; 36(2) : 247-257
www.science.cmu.ac.th/journal-science/josci.html
Invited Paper

A Conceptual Design of Fluorous Surfactants Based on a Heterocyclic Core, Put into Practice Through Synthesis of Fluorous 1,2,3-Triazoles

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ABSTRACT

The concept of a design of fluorous surfactants based on a heterocyclic core molecule is introduced and illustrated through the synthesis of polyfluoroalkyl-substituted 1,2,3-triazoles. A two step, one-pot process is described in which a small range of perfluoroalkylethyl azides is prepared *in situ* and made to undergo Huisgen 1,3-dipolar cycloaddition with terminal alkynes. Measurement of the changes in surface tension of the library of fluorous triazoles at different concentrations in *m*-xylene reveals unusual behaviour in molecules with a secondary, C8 alkyl substituent.

Keywords: organic synthesis, heterocycles, fluorous chemistry, surfactants, click chemistry, polyfluoroalkyl-1,2,3-triazoles.

1. INTRODUCTION

Fluorous surfactants have been studied widely, not least for their interest in combination with perfluorocarbons, as emergency blood replacements.[1] Highly fluorinated amphiphiles and colloid systems are chemically stable and can carry high concentrations of oxygen and carbon dioxide, and therefore have many applications in the biomedical field [2,3]. Fluorous surfactants have also been studied in combination with non-fluorous surfactants, where they can influence the properties of the surfactants. The unique solubility properties of highly fluorous materials also mean that they self associate more readily than non-fluorous surfactants, and readily form multi-layered architectures rather than normal bi-layered structures [3-7].

This latter feature attracted our interest because it indicated that fluorous surfactants might have applications in the design of new drug delivery systems and, through self-assembly, unique molecular devices. Considerable literature exists in the area of fluorous block polymers with localised crystalline segments and fluorous liposomes and vesicles for drug delivery, but, with a few exceptions [8-11], most fluorous components have been relatively unsophisticated or difficult to synthesise [12-20].

We describe in this paper the concept of fluorous surfactants based on a heterocyclic core. While a number of molecules of this type have been described, very few have been examined for their self assembly or surfactant properties and there has been no systematic study to our knowledge of surfactants of this type. The concept will be illustrated with the synthesis of a small library of structurally

5related fluorous 1,2,3-triazoles and their evaluation as surface active agents. There have been three reports of fluoroalkylated 1,2,3-triazoles[14,21,22] but only one in which they have been considered as surfactants.[14] This describes a single family of molecules that are carboxylic acid derivatives and there has been no more recent development of the work.

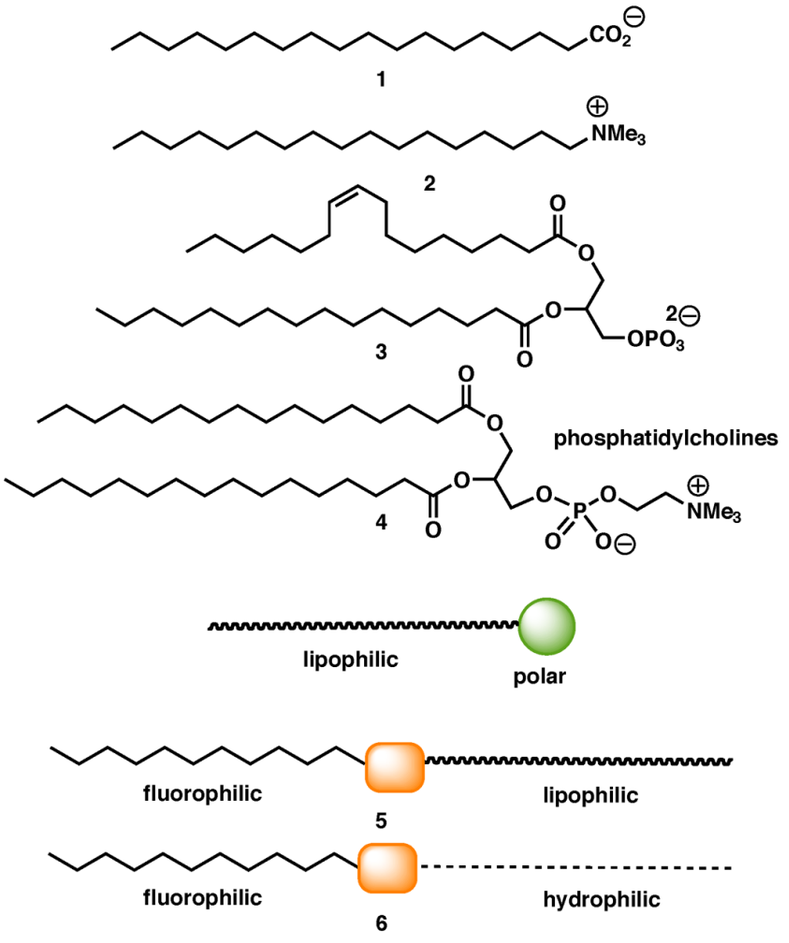


Figure 1

Traditional surfactants (Figure 1) comprise one or more lipophilic groups (tails) attached to a polar (neutral or charged) head group. The two moieties are often directly attached to each other, as in long chain, saturated or unsaturated alkanoate salts **1**, long chain alkyl-substituted quaternary ammonium salts **2**, or glycolipids (ester conjugates of fatty acids. and short polyalcohols and sugars). In Nature, the two moieties are sometimes held together by an intermediate group, such as in the phospholipids, where often two of the hydroxyl groups of glycerol are esterified by saturated or unsaturated fatty acids while the third forms a half phosphate ester, *e.g.* **3**. Indeed, acetylcholine **4** is just one such molecule in which the phosphate group is further esterified.

Fluorous analogues of each of these types have been reported, especially in the context of drug transport in materials related to blood substitutes, but all have been prepared by relatively linear synthetic approaches. The fluorous species that are conceived of here are of a distinct modular design. They have any one of an array of heterocycles as the core of the molecule, including aromatic and non-aromatic nitrogen, oxygen and sulfur containing species. These might provide two, three or more points of attachment of substituents. A few isolated examples of fluorous pyridine derivatives have been reported.[23-24]

Fluorous materials generally repel aqueous and many common organic solvents, therefore one could imagine many interesting situations with heterocycles bearing combinations of fluorophilic and lipophilic, **5**, or fluorophilic and hydrophilic substituents, **6**. Homogenous materials made up of either of these combinations might form regular or inverted multilayers or micelles, or even liposomes, in single fluorous, organic or aqueous solvents. Similarly, heterogenous mixtures of two different types of candidate surfactants, say **5** and **6**, might form relatively complex, complementary multilayers in biphasic solvent systems.

An added dimension to the concept of the heterocycle as the core molecule is the practical consideration that the heterocycle might be constructed from fragments that are fluorophilic and either lipophilic or hydrophilic, or it might be prepared as an intermediate with one type of substituent possibly already attached, and a second type of substituent added in a subsequent process. The concept is also open in some cases to the use of an heterocycle to which a third substituent, perhaps one with a reporting function, could be attached, and to multi heterocyclic core modifications, *i.e.* situations in which the heterocyclic core comprises two or more heterocyclic subunits. The nearest surfactant examples to these in the literature are referred to as gemini surfactants.[25] The latter molecules might serve as useful molecular inclusion species in which the two or more heterocycles could serve as ligands. A second generation of the core conceptual molecules might also have heterocycles that are dynamic in their formation and fragmentation. This could lead to valuable dynamic covalent chemistry outcomes, and even more sophisticated self-assembly possibilities.

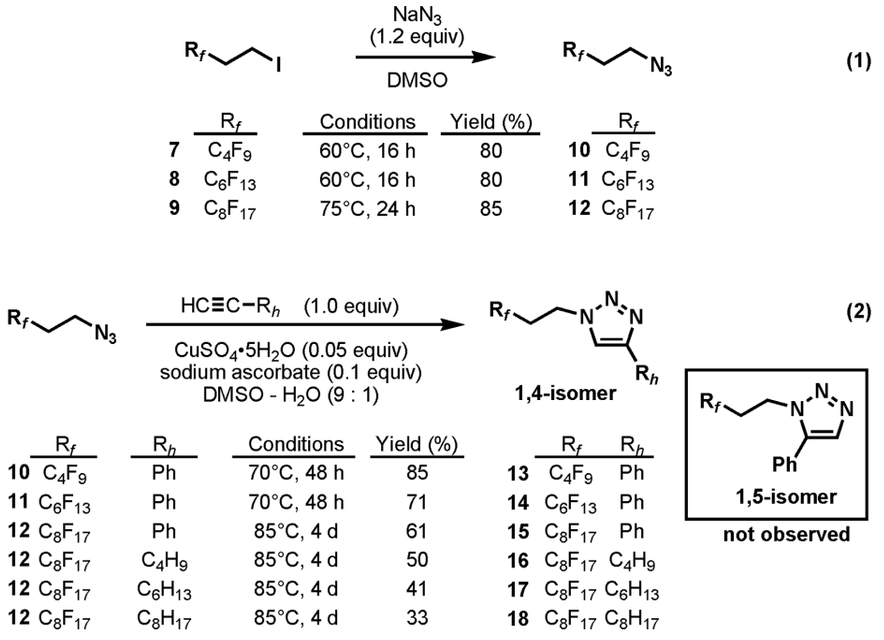
As a preliminary study to evaluate the concept, a series of *n*-alkyl and *n*-polyfluoroalkyl substituted 1,2,3-triazoles was synthesised. Advantage was taken of the very reliable 1,3-dipolar cycloaddition of organic azides with alkynes, as a means of constructing the molecules.

A range of perfluoroalkyl iodides **7-9** are commercially available and were found to readily undergo conversion to perfluoroalkyl azides in DMSO. Thus, iodides **7**-**8** were treated with a small excess of sodium azide in DMSO at 60°C to give the corresponding perfluoroalkyl azides **10** and **11** in 80% yield, in each case (Scheme 1, eq. 1). The higher analogue, perfluorooctylethyl iodide **9**, appeared to give little or no product under these conditions, but when the reaction was repeated under more forcing conditions, at 75°C for 24 h, the desired azide **12** was isolated in 85% yield.

The Huisgen 1,3-dipolar cycloaddition approach to 1,2,3-triazoles,[26] popularised as an example of 'click' chemistry[27] by Sharpless in recent years, can, in its copper(I) catalyzed form,[28-30] provide a highly regioselective outcome. In this case it would provide the desired 1,4-disubsituted derivatives in which the *n*-polyfluoroalkyl and *n*-alkyl groups would be distal in their disposition around the ring. In practice,

treatment of each of the fluorous azides **10**-**12** with phenylethyne under relatively standard copper-catalyzed click conditions ($CuSO_4$, sodium ascorbate, 1:9 water-DMSO, ambient temperature) gave no reaction at all. Fortunately, repetition without the addition of added water and at elevated temperatures (Scheme 1, eq. 2) eventually gave satisfactory to good, isolated yields of triazoles **13**-**15**, respectively. Notably, the higher homologue again required a slightly higher reaction temperature and significantly longer reaction time for complete reaction. The reactions were highly regioselective with only one isomer detected by ^{1}H NMR spectroscopy in each of the crude products (as determined by the absence of isomeric heteroaromatic proton signals).

With this success in hand, the most difficult fluorous azide to make react, namely **12**, was subjected to parallel reactions with 1-hexyne, 1-octyne and 1-decyne, under the same conditions that had given product with phenylethyne. The desired triazoles, **16**-**18**, were isolated in equally acceptable though somewhat lower yields (Scheme 1).



	R_f	Conditions	Yield (%)		R_f
7	C_4F_9	60°C, 16 h	80	**10**	C_4F_9
8	C_6F_{13}	60°C, 16 h	80	**11**	C_6F_{13}
9	C_8F_{17}	75°C, 24 h	85	**12**	C_8F_{17}

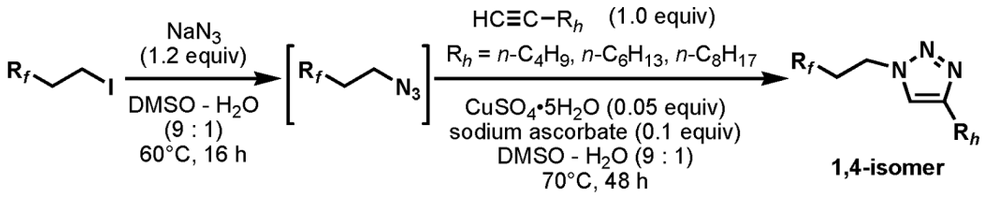
	R_f	R_h	Conditions	Yield (%)		R_f	R_h
10	C_4F_9	Ph	70°C, 48 h	85	**13**	C_4F_9	Ph
11	C_6F_{13}	Ph	70°C, 48 h	71	**14**	C_6F_{13}	Ph
12	C_8F_{17}	Ph	85°C, 4 d	61	**15**	C_8F_{17}	Ph
12	C_8F_{17}	C_4H_9	85°C, 4 d	50	**16**	C_8F_{17}	C_4H_9
12	C_8F_{17}	C_6H_{13}	85°C, 4 d	41	**17**	C_8F_{17}	C_6H_{13}
12	C_8F_{17}	C_8H_{17}	85°C, 4 d	33	**18**	C_8F_{17}	C_8H_{17}

Scheme 1

Consideration of the recommended dipolar cycloaddition reaction conditions, indicated that they were entirely compatible with those of the previous substitution reaction, except perhaps for the addition of water. On this point, it seemed most likely that the initial reactions had failed because they were not heated rather than because there were issues with solubility. There has also been one report of the two processes being combined.[31]

A set of one pot, parallel reactions was therefore carried out in which triplicate solutions of the iodides **7** and **8**, in 1:9 water-DMSO, were again treated with sodium azide (1.1 equivalent) at 60°C for 16 h. The flasks were cooled to room temperature and the three replicates treated with one of 1-hexyne, 1-octyne or 1-decyne, then $CuSO_4$ and sodium ascorbate. The mixtures were again allowed

to react at 70°C for 48 h. The resulting crude products were then analysed by ^{1}H NMR spectroscopy and finally separated by chromatography and recrystallized. The triazoles **19**-**24** were isolated in the yields summarised in Scheme 2.



	R_f	R_f	Yield (%)		R_f	R_h
7	C_4F_9	**10** C_4F_9	32	**19**	C_4F_9	C_4H_9
8	C_6F_{13}	**11** C_6F_{13}	36	**20**	C_4F_9	C_6H_{13}
			34	**21**	C_4F_9	C_8H_{17}
			61	**22**	C_6F_{13}	C_4H_9
			31	**23**	C_6F_{13}	C_6H_{13}
			68	**24**	C_6F_{13}	C_8H_{17}

Scheme 2

^{1}H NMR analysis indicated that the reactions had proceeded again with perfect regiocontrol, as evidenced by the appearance of only one triazolyl proton signal at δ 7.31-7.33 in $CDCl_3$. Assignment as the 1,4-disubstituted derivatives followed from nuclear Overhauser enhancement experiments. For example, the NOESY experiment on a $CDCl_3$ solution of triazole **18** showed a strong correlation between the heteroaromatic proton signal, at δ 7.34, and the multiplet methylene signals for the CF_2CH_2 group, at δ 2.80, and for the 4-CH_2 group at δ 2.71. These results would be inconsistent with the 1,5-disubstituted isomer.

2. CONCLUSIONS

Overall, the new one-pot synthesis had proven successful in yielding a small range of molecules for evaluation as surfactants. It is likely that this approach would be successful for the higher fluorous homologues although the second part of the one-pot process might require higher temperatures and longer reaction times.

The surface tension of solutions of known concentration of fluorous triazoles **16**-**24** in *m*-xylene was measured using an interfacial tensiometer. Changes in the surface tension with concentration were plotted for all samples. Details will be reported elsewhere, but all samples caused reduction in the surface tension of the solutions with increasing concentration, which was as expected for a surfactant. Curiously, the 4-*n*-octyl derivatives all behaved differently to the *n*-butyl and *n*-hexyl derivatives, in some cases with higher and in other cases lower surface activity. This unexpected behaviour will be the subject of future research.

3. MATERIALS AND METHODS

3.1 Synthesis of Azides 10-12 [32]

Exemplified by the synthesis of 2-perfluorohexylethyl azide **11.** Sodium azide (0.52 g, 8 mmol) was added to a solution of 2-perfluorohexylethyl iodide **8** (0.95 g, 2 mmol) in dry DMSO (3.5 mL). The mixture was stirred vigorously in an oil bath at 60°C for 16 h, then cooled, poured into H_2O

(30 mL) and extracted with Et_2O (4×20 mL). The combined organic phases were washed with brine (2×10 mL), water (2×10 mL), and finally brine (10 mL), then dried over $MgSO_4$, and the solvent evaporated to dryness under reduced pressure to give 2-perfluorohexylethyl azide **11** as a pale yellow liquid (0.62 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.61 (t, 2H), 2.39 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -81.2 (m, 3F), -114.3 (m, 2F), -122.3 (δ, 2F), -123.2 (t, 2F), -123.9 (m, 2F), -126.5 (m, 2F).

The yield for azide **10** under the same conditions was 80%.

The reaction mixture of 2-perfluorooctylethyl iodide **9** and NaN_3 was heated in a bath at 75°C for 24 h to give azide **12** in 85% yield. The spectroscopic data for azides **10** and **12** were virtually identical to those for azide **11**.

3.2 Reaction of Polyfluoroalkyl Azides 10-11 with Phenylethyne to Give Triazoles 13-14

General procedure: Polyfluoroalkyl azide (2.0 mmol) was dissolved in DMSO (9.0 mL) and H_2O (1.0 mL) was added. Alkyne (2.0 mmol), sodium ascorbate (0.040 g, 0.2 mmol), and $CuSO_4 \cdot 5H_2O$ (0.025 g, 0.1 mmol) were added sequentially, the mixture immersed in a bath at 70°C and stirred rapidly for 48 h. The resultant mixture was diluted with, extracted with Et_2O, the extracts dried over $MgSO_4$ and evaporated to dryness. The residue was analysed by ^{1}H NMR spectroscopy then chromatographed on silica gel and the major fraction recrystallized from Et_2O or $CHCl_3$.

(a) Perfluorobutylethyl azide **10** and phenylethyne afforded *4-phenyl-1-(perfluorobutylethyl)-1H-[1,2,3]triazole* **13** as colourless needles (0.66 g, 85%) m.p. 129-131°C (Found: C, 43.22; H, 2.73; N, 10.88.$C_{14}H_{10}F_9N_3$ requires: C, 42.98; H, 2.58; N, 10.74%). IR (KBr) ν_{max} 3444, 3130, 2959, 2360, 1557, 1227, 1210, 1133, 991, 765 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.85 (d, *J* = 8.0 Hz, 2H, H2" and H6"), 7.81 (s, 1H, H5), 7.46 (t, *J* = 7.5 Hz, 2H, H3" and H5"), 7.32 (t, *J* = 7.5 Hz, H4"), 4.73 (t, *J* = 7.4 Hz, 2H, NCH_2), 2.87 (m, 2H, CF_2CH_2); ^{13}C NMR ($CDCl_3$): δ 130.1, 128.8 (2 x C), 128.3, 125.7 (2 x C), 120.0, 117.1, 115.3, 42.3 (C1′), 31.7 (C2′). MS (ESI, *m/z*) 430.25 (M+K), 414.29 (M+Na), 392.29 (M+1).

(b) Perfluorohexylethyl azide **11** and phenylethyne afforded *4-phenyl-1-(perfluorohexylethyl)-1H-[1,2,3]triazole* **14** as colourless needles (0.70 g, 71%) m.p. 130-135°C (Found: C, 39.11; H, 2.06; N, 8.51. $C_{16}H_{10}F_{13}N_3$ requires: C, 39.12; H, 2.05; N, 8.55%). IR (KBr) ν_{max} 3456, 3130, 2364, 1470, 1240, 1201, 1139, 1080, 986, 768 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.84 (d, *J* = 8 Hz, 2H, H2" and H6"), 7.81 (s, 1H, H5), 7.45 (t, *J* = 7.5 Hz, 2H, H3" and H5"), 7.35 (t, *J* = 7.5 Hz, 1H, H4"), 4.74 (t, *J* = 7.3 Hz, 2H, NCH_2), 2.88 (m, 2H, CF_2CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.5, 128.8 (2×C), 128.4, 125.7 (2×C), 84.2, 59.5, 50.5. MS (ESI, *m/z*): 530.31 (M+K), 514.35 (M+Na), 492.35 (M+1).

(c) Perfluorooctylethyl azide **12** and phenylethyne afforded *1-(perfluorooctylethyl)-4-phenyl-1H-[1,2,3]-triazole* **15** as colourless needles (0.72 g, 61%) m.p. 145-148°C (Found: C, 36.29; H, 1.80; N, 7.00. $C_{18}H_{10}F_{17}N_3$ requires: C, 36.56; H, 1.70; N, 7.11%). IR (KBr) ν_{max} 3832, 3733, 3500, 2361, 1654, 1469, 1400, 1203, 1146, 1115, 986 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.85 (d, *J* = 8 Hz, 2H, H2" and H6"), 7.46 (t, *J* 7.5 Hz, 2H, H3" and H5"), 7.33 (t, *J* = 7.5 Hz, 1H, H4"), 4.74 (t, *J* = 7.3 Hz, 2H, NCH_2), 2.88 (m, 2H, CF_2CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 187.2, 154.2, 128.8 (2×C), 128.4, 125.7 (2×C), 92.8, 36.1 (C2′). MS (ESI, *m/z*): 630.40 (M+K), 614.38 (M+Na), 592.39 (M+1).

3.3 Reaction of Perfluorooctylethyl Azide 12 with 1-Hexyne, 1-Octyne and 1-Decyne to Give Triazoles 16-18

*General procedure:*A mixture of 1-alkyne (2 mmol), perfluorooctylethyl azide **12** (2 mmol), sodium ascorbate (0.0396 g, 0.20 mmol) and $CuSO_4 \bullet 5H_2O$ (0.025 g, 0.10 mmol) in DMSO (3.6 mL) and H_2O (0.4 mL), was stirred rapidly at 85°C for 4 d. The resultant mixture was diluted with H_2O (50 mL) and extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and evaporated to dryness under reduced pressure. The residue was chromatographed a silica gel and the major product recrystallized from $CHCl_3$ to afford the desired triazoles as white or pale yellow powder.

(a) Phenylethyne and perfluorooctylethyl azide **12** afforded *1-(perfluorooctylethyl)-4-phenyl-1H-[1,2,3]-triazole* **15** as colourless needles (0.72 g, 61%) m.p. 145-148°C (Found: C, 36.29; H, 1.80; N, 7.00. $C_{18}H_{10}F_{17}N_3$ requires: C, 36.56; H, 1.70; N, 7.11%). IR (KBr) ν_{max} 3832, 3733, 3500, 2361, 1654, 1469, 1400, 1203, 1146, 1115, 986 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.85 (d, J = 8 Hz, 2H, H2" and H6"), 7.46 (t, J = 7.5 Hz, 2H, H3" and H5"), 7.33 (t, J = 7.5 Hz, 1H, H4"), 4.74 (t, J = 7.3 Hz, 2H, NCH_2), 2.88 (m, 2H, CF_2CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 187.2, 154.2, 128.8 (2×C), 128.4, 125.7 (2×C), 92.8, 36.1 (C2′). MS (ESI, m/z): 630.40 (M^++K), 614.38 (M^++Na), 592.39 (M+1).

(b) 1-Hexyne and perfluorooctylethyl azide **12** afforded *4-butyl-1-(perfluorooctylethyl)-[1,2,3]-triazole* **16** as white powder (0.57 g, 50%) m.p. 110-111°C (Found: C, 33.58; H, 2.47; N, 7.08. $C_{16}H_{14}F_{17}N_3$ requires: C, 33.64; H, 2.47; N, 7.36 %). IR (KBr) ν_{max}: 3426, 2960 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.31 (br s, 1H, H5), 4.62 (t, J = 7.3 Hz, 2H, NCH_2), 2.81 (m, 2H, CF_2CH_2), 2.73 (t, 2H, J = 7.5 Hz, 4-CH_2), 1.64 (m, 2H, 4-CH_2CH_2), 1.37 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 148.8 (C4), 121.0 (C5), 41.9 (C1′), 31.8 (C2′), 31.3 (C2"), 25.1 (C1"), 22.1 (C3"), 13.6 (C4"). MS (ESI) m/z: 610.42 ($M+K^+$), 594.46 ($M+Na^+$), 572.47 (M+1).

(c) 1-Octyne and perfluorooctylethyl azide **12** gave *1-(perfluorooctylethyl)-4-hexyl-[1,2,3]-triazole* **17** as pale yellow powder (0.49 g, 41%) m.p. 113-115°C (Found: C, 35.42; H, 3.12; N, 6.72. $C_{18}H_{18}F_{17}N_3$ requires: C, 36.07; H, 3.03; N, 7.01 %). IR (KBr) ν_{max}: 3433, 3066, 2957, 2928, 2855 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.35 (br s, 1H, H5), 4.63 (t, J = 7.3 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.71 (m, 2H, J = 7.5 Hz, 4-CH_2), 1.66 (m, 2H, 4-CH_2CH_2), 1.31 (m, 6H) 0.87 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 132.4, 42.1 (C1′), 40.9, 32.1 (C2′), 31.4 (C3"), 29.2 (C2"), 28.7 (C4"), 25.5 (C1"), 22.4 (C5"), 13.9 (C6"). MS (ESI) m/z: 638.50 ($M+K^+$), 622.48 ($M+Na^+$), 600.49 (M+1).

(d) 1-Decyne and perfluorooctylethyl azide **12** gave *1-(perfluorooctylethyl)-4-octyl-[1,2,3]-triazole* **18** as white powder (0.41 g, 33%) m.p. 119-120°C (Found: C, 37.37; H, 3.53; N, 6.35. $C_{20}H_{22}F_{17}N_3$ requires: C, 38.29; H, 3.53; N, 6.70 %). IR (KBr) ν_{max}: 3422, 3065, 2920, 2851 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ: 7.36 (br s, 1H, H5), 4.63 (t, J = 7.4 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.73 (m, 2H, 4-CH_2),1.66 (m, 2H, -CH_2CH_2), 1.26 (m, 10H), 0.86 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 121.0, 53.3, 43.2, 40.8, 31.8 (C3"), 29.2 (C2"), 29.1 (C4"), 25.4 (C1"), 22.5 (C5"), 13.9 (C6"). MS (ESI) m/z: 666.49 ($M+K^+$), 650.53 ($M+Na^+$), 628.54 (M+1).

3.4 Single Pot Synthesis of Triazoles 19-24

General procedure:[28] A mixture of NaN_3 (0.156 g, 2.4 mmol) and 2-perfluoroalkylethyl

iodide (2.0 mmol) in DMSO and H_2O (9:1, 4.0 mL) was stirred at 60°C overnight, then 1-alkyne (2.0 mmol), sodium ascorbate (0.040 g, 0.1 mmol) and $CuSO_4 \cdot 5H_2O$ (0.025 g, 0.05 mmol) were added and the mixture stirred rapidly at 70°C for 48 h. The resultant mixture was poured into H_2O (30 mL) and extracted with Et_2O (315 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was column chromatographed (silica gel, LP:Et_2O / 80:20) and the major component recrystallized from Et_2O to afford the major product.

(a) Perfluorobutylethyl iodide **7** and 1-hexyne afforded *4-butyl-1-(perfluorobutylethyl) -1H-[1,2,3]triazole* **19** as off white powder (0.24 g, 32%) m.p. 48-51°C (Found: C, 38.91; H, 3.88; N 11.07. $C_{12}H_{14}F_9N_3$ requires: C, 38.82; H, 3.80; N, 11.32%). IR (KBr) ν_{max} 3485, 3117, 3065, 2936, 1560, 1223, 1138 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.31 (s, 1H, H5), 4.63 (t, *J* 7.5 Hz, 2H, NCH_2,), 2.82 (m, 2H, CF_2CH_2,), 2.69 (m, 2H, 4-CH_2), 1.65 (t, *J* = 3.0 Hz, 2H, 4-CH_2CH_2), 1.38 (m, 2H, CH_2CH_3), 0.93 (t, *J* = 6.2 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149 and 121 (C4 and C5, too broad to be visible), 42.0 (C1′), 31.7 (C2′), 31.4 (C2″), 25.7 (C1″), 22.1 (C3″), 13.6 (C4″). MS (ESI, *m/z*) 410.33 (M+K), 394.36 (M+Na), 372.36 (M+1).

(b) Perfluorobutylethyl iodide **7** and 1-octyne afforded *4-hexyl-1-(perfluorobutylethyl) -1H-[1,2,3]triazole* **20** as colourless needles (0.29 g, 36%) m.p. 54-57°C (Found: C, 41.65; H, 4.53; N, 10.03. $C_{14}H_{18}F_9N_3$ requires: C, 42.11; H, 4.54; N, 10.52%). IR (KBr) ν_{max} 3116, 3064, 2958, 2929, 2854, 1469, 1234, 1215, 1134, 986 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.31 (s, 1H, H5), 4.63 (t, *J* = 7.5 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.72 (t, *J* = 7.5 Hz, 2H, 4-CH_2), 1.67 (m, 2H, 4-CH_2CH_2), 1.31 (m, 6H), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 128.2, 65.7, 44.7, 31.4 (C2′), 29.2, 25.5 (C1″), 22.4 (C3″), 13.9 (C4″). MS (ESI, *m/z*) 438.36 (M+K), 422.33 (M+Na), 400.33 (M+1).

(c) Perfluorobutylethyl iodide **7** and 1-decyne afforded *1-(perfluorobutylethyl)-4-octyl -1H-[1,2,3]triazole* **21** as colourless needles (0.29 g, 34%) m.p. 69-70°C (Found: C, 44.66; H, 5.39; N, 9.58. $C_{16}H_{22}F_9N_3$ requires: C, 44.97; H, 5.19; N, 9.83%). IR (KBr) ν_{max} 3115, 3063, 2957, 2920, 2850, 1556, 1215, 1135, 986 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.34 (s, 1H, H5), 4.63 (t, *J* = 7.4 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.71 (t, *J* = 7.5 Hz, 2H, 4-CH_2), 1.68 (m, 2H, 4-CH_2CH_2), 1.31 (m, 10H, $(CH_2)_5CH_3$), 0.87 (t, *J* = 6.8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) d: 148 (not visible), 120.9, 42.0, 31.7 (2 X C), 29.1 (4 X C), 25.5, 22.5, 13.9. ^1H NMR (300 MHz, $(CD_3)_2CO$) d: 7.79 (s, 1H, H5), 4.76 (t, *J* = 7.2 Hz, 2H, NCH_2), 2.97 (tt, *J* = 17.7 Hz, 7.2 Hz, 2H, CF_2CH_2), 2.65 (t, *J* = 7.5 Hz, 2H, 4-CH_2), 1.64 (m, 2H, 4-CH_2CH_2), 1.30 (br s, 10H, $(CH_2)_5CH_3$), 0.87 (t, *J* = 7.8 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ: 147.8 (C4), 121.4 (C5), 41.5 (C1′), 31.6 (C6″), 30.9 (C2′), 29.2 (C2″), 28.9 (C3″-C5″), 25.2 (C1″), 22.3 (C7″), 13.3 (C8″). MS (ESI, *m/z*) 468.50 (M+K), 450.46 (M+Na), 428.46 (M+1).

(d) Perfluorohexylethyl iodide **8** and 1-hexyne afforded *4-butyl-1-(perfluorohexylethyl) -1H-[1,2,3]triazole* **22** as pale yellow needles (0.57 g, 61%) m.p. 82-84°C (Found: C, 35.92; H, 3.28; N, 8.63. $C_{14}H_{14}F_{13}N_3$ requires: C, 35.68; H, 2.99; N, 8.92%). IR (KBr) ν_{max} 2959, 1465, 1235, 1194, 1143, 1124, 986, 704 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.33 (s, 1H, H5), 4.64 (t, *J* = 7.5 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.72 (t, *J* = 7.5 Hz, 2H, 4-CH_2), 1.66 (m, 2H, 4-CH_2CH_2), 1.40 (m, 2H, CH_2CH_3), 0.93 (t, *J* = 7.4 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149 (C4), 121.0 (C5), 42.0 (C1′), 31.8 (C2′), 31.5 (C2″), 25.2

(C1''), 22.1 (C3''), 13.6 (C4''). MS (ESI, *m/z*) 510.45 (M+K), 494.42 (M+Na), 472.49 (M+1).

(e) Perfluorohexylethyl iodide **8** and 1-octyne afforded *4-hexyl-1-(perfluorohexylethyl) -1H-[1,2,3]triazole* **23** as pale yellow needles (0.31 g, 31%) m.p. 70-74°C (Found: C, 38.30; H, 3.54; N, 8.34. $C_{16}H_{18}F_{13}N_3$ requires: C, 38.49; H, 3.63; N, 8.42%). IR (KBr) ν_{max} 3065, 2959, 2928, 2855, 1556, 1466, 1236, 1215, 1142, 1124, 987, 706 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.31 (s, 1H, H5), 4.64 (t, J = 7.3 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.72 (t, J = 7.7 Hz, 2H, 4-CH_2), 1.64 (t, J = 6.9 Hz, 2H, 4-CH_2CH_2), 1.35 (m, 6H, $(CH_2)_3CH_3$), 0.88 (t, J = 6.2 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 114.1, 42.0 (C1′), 31.4 (C3''), 29.2 (C2''), 28.7 (C4''), 25.5 (C1''), 22.4 (C5''), 13.9 (C6'') MS (ESI, *m/z*) 538.29 (M+K), 522.33 (M+Na), 500.33 (M+1).

(f) Perfluorohexylethyl iodide **8** and 1-decyne afforded *4-octyl-1-(perfluorohexylethyl) -1H-[1,2,3]triazole* **24** as colourless needles (0.72 g, 68%) m.p. 95-97°C (Found: C, 41.03; H, 4.26; N, 7.91. $C_{18}H_{22}F_{13}N_3$ requires: C, 40.99; H, 4.20; N, 7.97%). IR (KBr) ν_{max} 3116, 3064, 2956, 2919, 2850, 1556, 1468, 1235, 1194, 1142, 1084, 986, 706 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.33 (s, 1H, H5), 4.63 (t, J = 7.4 Hz, 2H, NCH_2), 2.80 (m, 2H, CF_2CH_2), 2.71 (m, 2H, 4-CH_2), 1.67 (t, J = 7.5 Hz, 2H, 4-CH_2CH_2), 1.31 (m, 10H, $(CH_2)_5CH_3$), 0.87 (t, J = 6.6 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 121.3 (C5), 42.0 (C1′), 31.8 (2×C), 29.2 (4×C), 25.5 (C1''), 22.5 (C5''), 13.9 (C6''). MS (ESI, *m/z*): 566.34 (M+K), 550.32 (M+Na), 528.39 (M+1).

ACKNOWLEDGEMENTS

This work was supported in its preliminary form by the Australian Research Council through its Discovery Project and by a UNSW Science Faculty Research Grant. The authors are grateful to Dr Hua Zhang for initial training and assistance with the surface tension measurements.

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