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Aust. J. Chem.
http://dx.doi.org/10.1071/CH14458

Full Paper

Fluorous 1,2,3-Triazol-4-ylmethyl Amines and Amine Derivatives for Novel Surfactant Applications

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A series of fluorous surfactants with additional functionality were generated through the attachment of substituents at the amino nitrogen atom of the surfactant moiety. Examples of molecules containing one and two triazole ring systems were synthesized through *N*-alkylation and *N*-acylation strategies.

Manuscript received: 19 July 2014.
Manuscript accepted: 30 August 2014.
Published online: 7 October 2014.

Introduction

Polyfluorinated molecules have received widespread attention as a result of the unusual surface activity they exhibit, in addition to other interesting physical and biological properties.[1–4] Compared with their non-fluorinated counterparts, fluorous molecules are more efficient self-aggregators and are inherently capable of self-aggregating to form stable, well-organised three-dimensional supramolecular assemblies such as multilayered structures, micelles, and tubules.[1,5–10] These characteristics have made traditional fluorous surfactants highly suitable for biomedical use as adjuvants in blood substitutes, as diagnostic agents and carriers in drug delivery, and in industrial applications as firefighting foams and antifogging agents.[1–3,8,9,11–13]

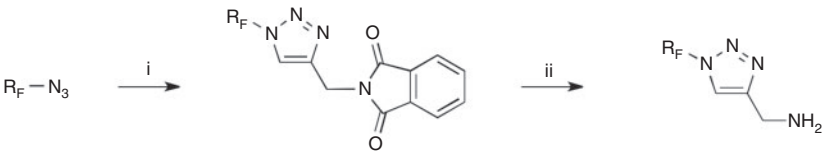
The small size of fluorine atoms, their extreme electronegativity, and the rigidity of perfluorinated segments of polyfluoroalkyl chains endow molecules that contain them with exceptional aggregation properties in water and segregation ability from hydrocarbon chains from the same or nearby molecules. The physicochemical properties of perfluoroalkyl-substituted compounds have been reviewed,[14–17] and pioneering work on the ability of fluorinated surfactants to form unusual structures, including stable vesicles using single-chain surfactants[18] and tubules with various morphologies and characteristics[19,20] is noteworthy.

Recently, we have reported the potential of heterocycles with attached fluorous chains as surfactants and participants in self-assembly,[12] and have described the synthesis of 1,2,3-triazoles[2,12,21] and tetrazoles[2] with one perfluoroalkyl substituent and either one *n*-alkyl, one *n*-alkoxymethyl, or one methoxytriethylenoxymethyl substituent. Surface tension measurements of the various substituent combinations revealed that surfactants bearing fluorophilic and hydrophilic partner substituents exhibit the greatest surface activity.[22] However, we wish to extend the capabilities of these surfactants through the addition of functionality. One way to achieve this involves changing the molecular design from the previously used ether-linked systems[2,12,21] to those that are capable of accommodating the necessary fluorophilic and hydrophilic substituents, plus additional functionality. In this paper, we describe the synthesis of a new generation of fluorous 1,2,3-triazole analogues, in which the linking ether oxygen is replaced with a nitrogen atom in the form of either an amine or an amide. The nitrogen atom is used as an anchor for the attachment of additional functional substituents with either potential bioactive, reporter, shape-filling, or shape-matching roles, and the molecules are expected to take on the features of so-called ABC miktoarm star motifs.[16]

Results and Discussion

As a first approach to constructing nitrogen-bearing surfactant systems, *N*-propargylphthalimide **1**[23] was treated with each of the azides **2**–**5**[12] under standardized copper-catalyzed azide-alkyne cycloaddition (CuAAC) conditions.[12] Phthalimide derivatives **6**–**9** were obtained in acceptable yields, though these yields decreased with increasing fluorous chain length after workup (Scheme 1). Although yields declined, it was noted that there was no apparent correlation between the length of the perfluoroalkyl chain, or fluorine content (defined as percentage fluorine by weight vs formula weight), and the melting points of the homologous phthalimides **6**–**9**. This suggested that the packing density in the polyfluoroalkyl triazolyl phthalimide series was not related to the CF_2 chain length.

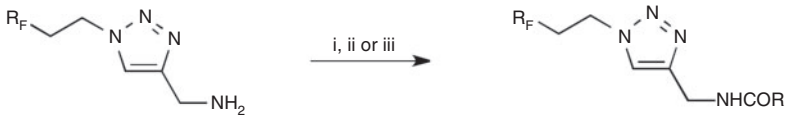
Treatment of phthalimides **6**–**9** with hydrazine hydrate in ethanol at reflux for a standard 16 h gave the desired amines **10**–**12**, but not amine **13**. Again, yields were inversely proportional to CF_2 chain length and fluorine content, but in this case, there was also a correlation with melting point (Scheme 1). Despite several attempts at different temperatures (0°C to reflux) and reaction times (16 to 72 h), the hydrazinolysis of phthalimide **9** did not give the corresponding amine **13** in practical quantities (<10% conversion to the desired amine **13** in each case), presumably owing to poor solubility of the starting material. Despite the disappointing result for amine **13**, the new phthalimide **6**–**9** and amine **10**–**12** derivatives represented valuable additions to a small library of readily available synthetic



	R_F	Yield [%]		R_F	mp [°C]	F [%]	Yield [%]		R_F	mp [°C]	F [%]
2	$C_4F_9CH_2CH_2$	80	**6**	$C_4F_9CH_2CH_2$	136–38	36.1	76	**10**	$C_4F_9CH_2CH_2$	94–96	49.7
3	$C_6F_{13}CH_2CH_2$	68	**7**	$C_6F_{13}CH_2CH_2$	148–50	43.0	58	**11**	$C_6F_{13}CH_2CH_2$	103–05	55.6
4	$C_7F_{15}CH_2$	61	**8**	$C_7F_{15}CH_2$	142–44	46.7	27	**12**	$C_7F_{15}CH_2$	118–20	59.3
5	$C_8F_{17}CH_2CH_2$	46	**9**	$C_8F_{17}CH_2CH_2$	131–33	47.9	<10	**13**	$C_8F_{17}CH_2CH_2$	–	59.3

Reagents & conditions: i. *N*-propargylphthalimide **1**, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, DMSO, 80°C, 16 h; ii. $NH_2NH_2{\cdot}H_2O$, EtOH, reflux, 16 h.

Scheme 1.



	R_F	Yield [%]		R_F	COR
10	C_4F_9	40	**14**	C_4F_9	$COCH_2Cl$
11	C_6F_{13}	67	**15**	C_4F_9	$COCH_2CH_2Cl$
		56	**16**	C_6F_{13}	$COCF_3$

Reagents & conditions: i. $ClCOCH_2Cl$, $PhNMe_2$, THF, reflux, 16 h; ii. $ClCOCH_2CH_2Cl$, $PhNMe_2$, THF, reflux, 16 h; iii. $(CF_3CO)_2O$, no solvent, N_2, rt, 16 h.

Scheme 2.

building blocks from which to elaborate the desired surfactant-like molecules.

Utilization of Amide Derivatives

As a next step in this first approach to desired aza-analogues of the previously prepared ether systems, three amide derivatives **14**–**16** were synthesized by conventional methods (Scheme 2).[24] Amides themselves can serve as a linker to other groups or they can be reduced to alkylamines to retain amine character in either secondary or tertiary form in the linker. Secondary amides can also be useful as intermediates for electrophilic attachment of groups to generate tertiary amides.

Reaction of chloroalkanamides **14** and **15** with commercially available methoxydiethylenoxyethanol **17** (Chart 1) in the presence of base was investigated as a route to hydrophilic monotriazoles **18** and **19** (Chart 1) respectively. Amide **14** with alcohol **17** and excess potassium bis(trimethyldisilyl)amide (KHMDS) gave what appeared from ^{1}H NMR spectroscopy and mass spectrometry to be the anticipated derivative **18** in 43 % yield from reaction at room temperature, but only 28 % yield from reaction at reflux. In contrast, near-identical treatment of amide **15** at room temperature with equimolar or two-fold equivalents of KHMDS each gave 48 % yield of acrylate **20** (Chart 1), rather than of the homologous amide **19**. This result suggested that the conditions were too basic and led to competing elimination. Use of a two-fold equivalent of the alcohol **17** and *N*,*N*-dimethylaminopyridine (DMAP) in place of KHMDS at room temperature afforded only traces of the elimination product **20** but 55 % yield of what was deduced from ^{1}H NMR spectroscopy to be the desired amide **19**. Repetition of the reaction at reflux gave again only traces of the acrylamide **20**, but a much decreased yield of the desired amide **19**.

Thus, indications had been obtained that potentially useful amide analogues of hybrid fluorous–hydrophilic monotriazolylmethyl-based surfactant molecules could be generated, and a pathway to a useful acrylamide intermediate **20** had been revealed.

N-Alkylation of trifluoroacetamide **16** using mesylate **21** was investigated, but without success. Several methods using combinations of base and solvent at different temperatures gave only recovery of the starting amide **16** or, in a few cases, loss of material. This outcome was attributed to a lack of nucleophilicity of the anion derived from amide **16**. As a consequence, this approach to nitrogen analogues was abandoned in favour of direct amine *N*-alkylation (see below).

Direct N*-Alkylation Strategy*

As an alternative to preparation of amide derivatives and the use of amide **16** as an intermediate for *N*-alkylation, direct *N*-alkylation of the primary amine **10** was examined. Treatment of amine **10** with an equimolar quantity of mesylate **21** in combinations of potassium carbonate in either dry DMF at 40°C or acetonitrile at reflux for 16 h gave inseparable mixtures of the secondary and tertiary amine products **22** and **23** (Chart 1), based on ^{1}H NMR spectroscopic analyses. Normally, excess amine reactant would be used in such circumstances when monoalkylation was sought, but in this case, the fluorous amine was precious and of limited supply. An attempt was therefore made to use a fluorous solvent, perfluorohexane, to increase the availability of fluorous amine **10** reactant in the presence of the hydrophilic mesylate **21**, and triethylamine was employed in

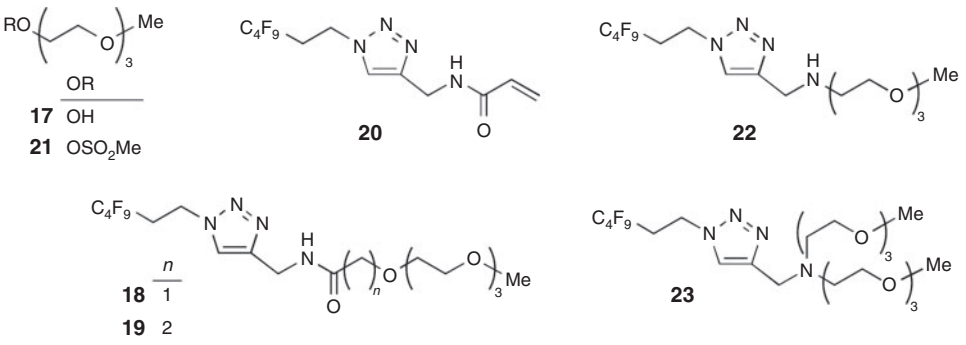


Chart 1.

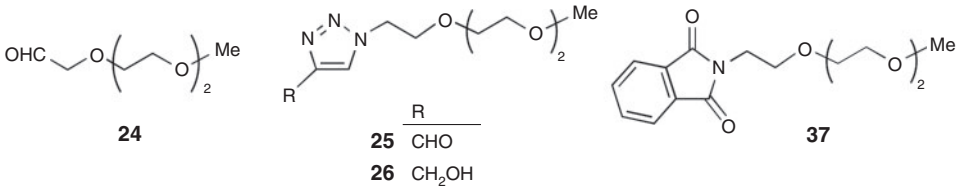


Chart 2.

place of the highly insoluble carbonate base; this arrangement might have limited the supply of the alkylating agent. In practice, vigorous stirring for 16 h gave a similar mixture of the same products, **22** and **23**, with 82 % mass recovery. This approach was also abandoned.

Reductive Amination Strategy

Yet another approach to mono- and bis-triazolylmethyl amines was envisaged through reductive amination. This would be most efficient if achieved in one pot, but could also proceed in two steps through isolation of intermediate imines from combination of aldehyde and amine partners. With the availability of the fluorous triazolylmethyl amines **10** and **12**, and potentially **13**, attention turned to hydrophilic aldehyde partner **24** (Chart 2),[25–27] and eventually aldehyde **25** through alcohol **26** (Chart 2). In our hands, none of the literature Swern oxidation methods[25–27] gave useful quantities of aldehyde **24** from alcohol **17**. Each of these methods gave mixtures of aldehyde **24** and alcohol **17**, of which 5–30 % was aldehyde **24**, and varying reactant proportions did not improve the yield of aldehyde **24**.

It was decided to swap the character of the reductive amination components. This required (i) the preparation of fluorous triazolylmethyl alcohols and selective oxidation to their corresponding aldehydes, and (ii) synthesis of complementary, hydrophilic amine partners.

Commercial fluorous iodides **27**–**29** were transformed in situ to the corresponding azides and subsequently via CuAAC with propargyl alcohol into alcohols **30**–**32**. In addition, preformed fluorous azide **5** was transformed by a near-identical CuAAC process into alcohol **33**.

A variety of oxidizing agents and conditions were tested with the representative alcohol **31**. Optimum yields and minimum technical difficulties were obtained using commercially available manganese dioxide. Under these conditions, aldehyde **34** was obtained as a white powder in 89 % yield at full conversion (Scheme 3), whereas Jones reagent and Dess–Martin periodinane conditions gave 58 and 53 % respectively of what was believed to be the corresponding acid **35**, and pyridinium dichromate gave no reaction at all.

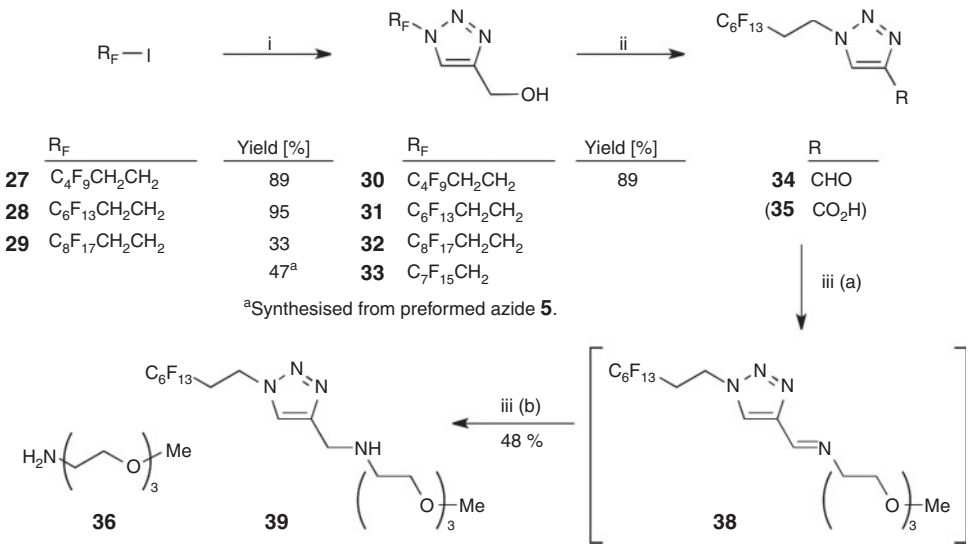
It was concluded from these positive results that there were significant issues with the oxidation of the previous hydrophilic alcohols **17** and **26**, or the stability of the aldehydes **24** and **25**, that had not been resolved, but these issues were not evident in the fluorous triazolylmethyl alcohols and their corresponding aldehydes.

Meanwhile, known amine **36**[28] was successfully synthesized from methoxydiethylenoxyethanol **17** via its phthalimide derivative **37** (Chart 2), which was prepared through a Mitsunobu reaction,[29] and subsequent hydrazinolysis.[30] It was isolated but used in subsequent reactions without purification.

Initial attempts to reductively aminate aldehyde **34** with amine **36** in THF via imine **38** in the presence of excess sodium triacetoxyborohydride under a variety of conditions of temperature, time, pre- and post-formed reagent, and sequential addition of reactants failed to give any of the desired secondary amine **39**. Utilization of two mole equivalents of the more vigorous reagent sodium borohydride in THF also failed. However, identical treatment with sodium borohydride in ethanol rather than THF gave complete conversion to the desired amine **39**. Further optimization showed the need for one full mole equivalent of sodium borohydride for complete conversion, whereupon the product **39** was isolated in 48 % yield (Scheme 3).

With a successful strategy to the desired hybrid fluorous–hydrophilic monotriazolylmethyl amines in place, efforts were made to extend it to equivalent bis(triazolylmethyl)amines.

Thus, as an example, the known hydrophilic azide **40**[31] was treated with *N*-propargylphthalimide **1** under the previously described CuAAC conditions in DMSO and the resultant *N*-(4-triazolylmethyl)phthalimide **41** was converted using hydrazinolysis into hydrophilic triazolylmethylamine **42** as an orange oil in 45 % overall yield. Unfortunately, amine **42** could not be purified using chromatography; however, a portion was characterized as its crystalline oxalate salt **43**. The remaining amine **42** reacted with fluorous triazolylcarboxaldehyde **34** under CuAAC



	R_F	Yield [%]
27	$C_4F_9CH_2CH_2$	89
28	$C_6F_{13}CH_2CH_2$	95
29	$C_8F_{17}CH_2CH_2$	33
		47[a]

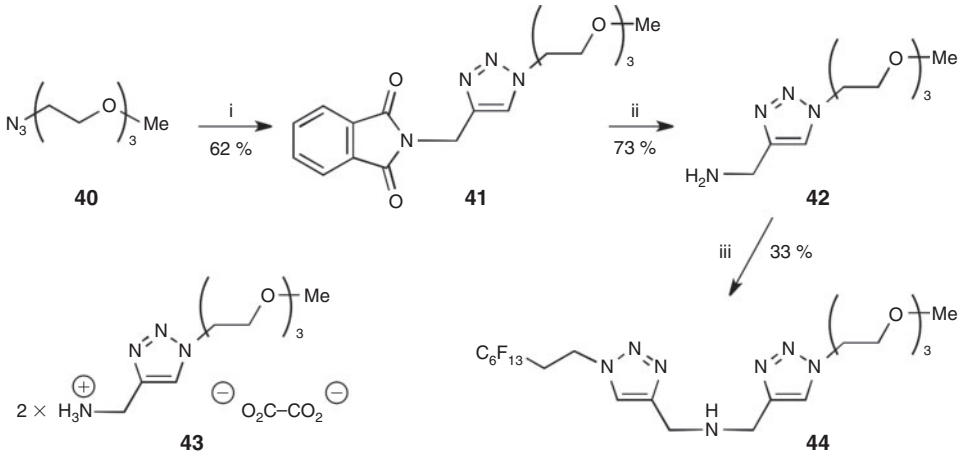
	R_F	Yield [%]
30	$C_4F_9CH_2CH_2$	89
31	$C_6F_{13}CH_2CH_2$	
32	$C_8F_{17}CH_2CH_2$	
33	$C_7F_{15}CH_2$	

	R
34	CHO
(**35**	CO_2H)

[a]Synthesised from preformed azide **5**.

Reagents & conditions: i. propargyl alcohol, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, DMSO, 65–85°C, 16 h; ii. MnO_2, benzotrifluoride, reflux, 16 h; iii. (a) **34** and **36**, EtOH, reflux, 1 h, then cool to 0°C; (b) $NaBH_4$, warm to rt, 16 h.

Scheme 3.



Reagents & conditions: i. *N*-propargylphthalimide **1**, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, DMSO, 65°C, 16 h; ii. $NH_2NH_2{\cdot}H_2O$, EtOH, reflux, 16 h; iii. (a) **34**, EtOH, reflux, 1 h, then cool to 0°C; (b) $NaBH_4$, warm to rt, 16 h.

Scheme 4.

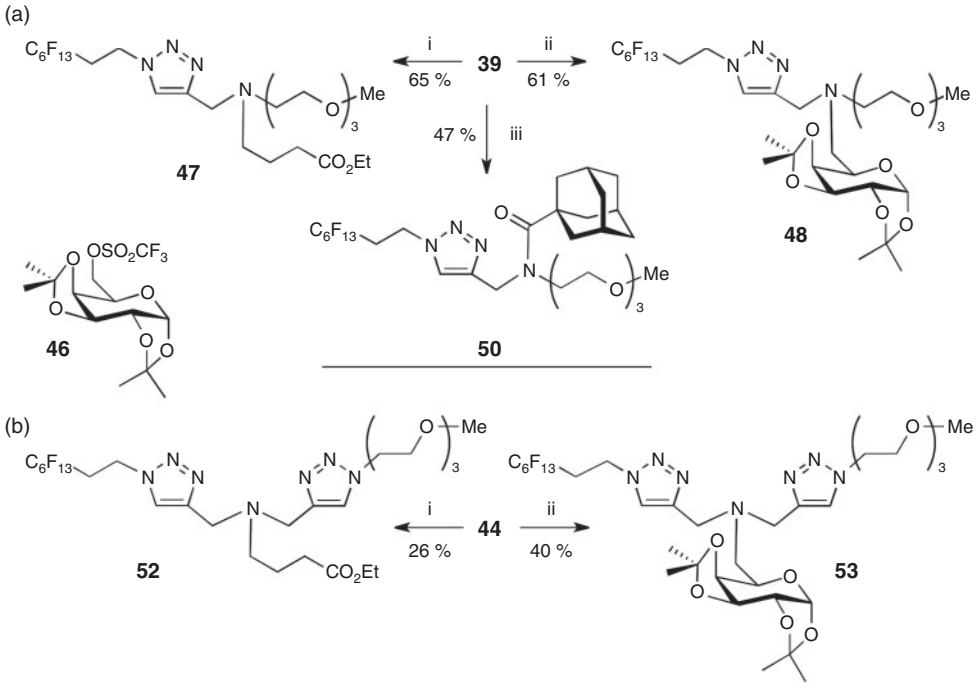
conditions in DMSO to afford the bis(triazolylmethyl)amine **44** in 48 % yield as a pale white powder after chromatography and recrystallization (Scheme 4).

*Functionalization of Hybrid Triazolylmethyl Amines **39** and **44***

A small variety of representative functional substituents classified as neutral (ethoxy carbonylpropanyl and 1-adamantanoyl) and or bioactive (α-D-pyranogalactosyl) groups were selected for attachment to amines **39** and **44**. Although bioactive groups have obvious applications, neutral groups were also an attractive option because they could serve in either a space-filling or a shape-matching role, or generate a face on a self-assembled aggregate that might be either attractive or repellent to the surroundings.

N-Alkylation provided a relatively direct method of linear derivatization. Monotriazolylmethylamine **39** was treated separately with commercially sourced ethyl 4-bromobutyrate **45** and readily prepared 6-galactosyl triflate **46** under identical conditions, in acetonitrile at reflux in the presence of triethylamine. The anticipated tertiary amines **47** and **48** were isolated in 65 and 61 % yields respectively (Scheme 5).

Linear acylation was also a means of attaching substituents to amines. Other studies have shown that the secondary amine function of molecules like amines **39** and **44** can participate in preferential protonation.[32–34] Here, the generation of an amide product would provide a less basic nitrogen linker group, and one that might behave differently to changes in the pH of the medium. In this situation, they might adopt a different geometry to the amines already prepared, thereby introducing another



Reagents & conditions: i. $BrCH_2CH_2CH_2CO_2Et$ **45**, Et_3N, CH_3CN, reflux, 16 h; ii. **46**, Et_3N, CH_3CN, reflux, 16 h; iii. 1-adamantoyl chloride **49**, Et_3N, CH_3CN, reflux, 16 h.

Scheme 5.

source of controlled variability in unimolecular species or self-assembled aggregates. With these thoughts in mind, the 1-adamantoyl group, known for use in certain specialist antiviral and anti-Parkinsonian drugs,[35] was introduced.

1-Adamantane carbonyl chloride **49**[36] was prepared in situ, volatiles removed through distillation, and the reagent combined with amine **39** in acetonitrile in the presence of 1.1 molar equivalents of triethylamine. Reflux for 16 h, then aqueous quenching and extractive workup gave a mixture of amide derivative **50** and an unknown compound (**51**), which was detected using thin-layer chromatography. After chromatography, amide **50** was isolated in 47 % yield as a yellow oil, while a slower-moving compound, deduced to be the original amine hydrochloride salt **51**, was recovered in 23 % yield. Although identification of compound **51** was never confirmed, evidence from the ^{1}H NMR spectrum suggested that the compound did not contain an adamantane moiety. The spectrum appeared very similar to the ^{1}H NMR spectrum for the starting material amine **39**, except that the signal for the proton in the triazole ring had shifted downfield dramatically from δ 7.57 in amine **39** to δ 8.55 in compound **51**. Considering that the chemical shift for the equivalent site in amide **50** was δ 7.61, the significant downfield shift of the triazole proton in compound **51** was likely to involve charge on the triazole ring, possibly involving a shared proton from the saturated linking amine group, rather than the presence of a stronger electron-withdrawing group on the bridging nitrogen (see also ref. 14). Meanwhile, the high-resolution (HR) electrospray ionization (ESI) mass spectrometric peak of compound **51** *m*/*z* 591.1632 was almost identical to that of amine **39** *m*/*z* 591.1641 ($[M+H]^+$) and elemental microanalysis was consistent with the hydrochloride salt of amine **39**.

Extrapolation of the *N*-alkylation process with bis(triazolylmethyl)amine **44** under identical conditions to those used for the preparation of compounds **47** and **48** afforded the 4-aminobutyrate **52**, as a white powder, and galactopyranosyl amine derivative **53**, as a highly viscous, colourless gum, in 26 and 40 % yields respectively (Scheme 5).

Conclusion

Satisfactory methods have been developed to new classes of hybrid fluorous-polyether mono- and bis-(triazolylmethyl) amine surfactant candidates. *N*-Alkylation of both and *N*-adamantanoylation of the monotriazolylmethylamine have provided a small library of novel surfactant-like molecules with potential orthogonal functionality. Ultimately, one of the challenges will be to design such ABC miktoarm star molecules with dominant self-assembly characteristics in the original A and B arms of the star.[16,17] The surfactant properties and demonstrated functionality of these novel compounds will be explored in future work.

Experimental

General

All reagents used in synthetic procedures were purchased from either Sigma–Aldrich or Alfa Aesar and were used without further purification. Quantities reported in the procedures involving sodium hydride and/or propargyl bromide are based on 60 % sodium hydride in mineral oil and 80 % propargyl bromide in toluene respectively. KHMDS was used as a 0.5 M solution in toluene. Hexane refers to *n*-hexane, whereas brine refers to a saturated aqueous solution of sodium chloride. Organic solvents were either used as received from Ajax Finechem or collected from a PureSolv MD solvent purification system.

Thin-layer chromatographic analyses were conducted using Merck TLC silica gel 60 F_{254} (0.2-mm) aluminium plates. Visualization was performed using a UVP UVGL-58 ultraviolet lamp at 254 nm where chromophores were available; otherwise,

either basic potassium permanganate stain[37] or ninhydrin in ethanol[37] were used to develop TLC plates for analysis. Flash column chromatography was performed on Merck silica gel 60 (0.040–0.063 mm), whereas flash column reverse-phase fluorous chromatography was performed on FluoroFlash® silica gel (0.040 mm).

Melting points were measured on a Mel-Temp II melting point apparatus and are uncorrected. Microanalyses were carried out by the Microanalytical Unit, Australian National University. Infrared spectra were recorded using either a Nicolet 380 Fourier-transform (FT)IR instrument as either a Nujol mull or as a neat film, or on a Cary 630 attenuated total reflectance Fourier-transform infrared (ATR-FTIR) spectrometer as a neat sample.

^{1}H and ^{13}C NMR spectroscopic characterization was performed on either a Bruker DPX 300 MHz spectrometer (^{1}H, 300 MHz; ^{13}C, 75 MHz; ^{19}F, 282 MHz) equipped with an autosampler, a Bruker Avance III 400 MHz spectrometer (^{1}H, 400 MHz; ^{13}C, 100 MHz), or a Bruker Avance III 600 MHz spectrometer (^{1}H, 600 MHz; ^{13}C, 150 MHz) equipped with an autosampler. All chemical shifts are reported relative to tetramethylsilane. Mutiplicities are reported as either singlet (s), doublet (d), doublet of doublets (dd), triplet (t), triplet of triplets (tt), quartet (qr), quintet (q), or multiplet (m). Broad signals are reported as br. Coupling constants (J, Hz) are reported for both H–H and H–F coupling (where applicable); where not specified, coupling constants refer to H–H coupling. Carbon atoms in the perfluoroalkyl chains are not reported for any compounds, as the low signal-to-noise ratio of these signals made it difficult to accurately identify the relevant peaks.

Mass spectra were measured using the ESI technique, at low resolution on a Waters Micromass ZQ2000 LC-MS instrument by direct injection and at high resolution using a Thermo LTQ Orbitrap XL instrument. Samples were dissolved in methanol.

*General Method for Preparation of Phthalimides **6**–**9** and **40***

Copper sulfate pentahydrate (0.05 mol equiv.), sodium ascorbate (0.12 mol equiv.), and DMSO (15 mL) were stirred together at room temperature (rt) for 5 min. Phthalimide **1** (1.1 mol equiv.) was added in one portion to the suspension with continuous stirring, followed after 1 min by a solution of the appropriate azide (1.0 mol equiv.) in DMSO (5 mL). The reaction mixture was heated at 80°C for 16 h, then quenched with H_2O (50 mL) and the resulting mixture was extracted with EtOAc (3 × 50 mL). The organic phases were combined and washed with H_2O (50 mL) and brine (2 × 50 mL), then dried over Na_2SO_4 and evaporated to dryness under reduced pressure. Column chromatography on silica gel (EtOAc/Et_2O, 1 : 2), followed by recrystallization from Et_2O/hexane (2 : 1) gave the desired products.

(i) Azide **2** (1.03 g, 3.6 mmol) gave *1-(2-perfluorobutyl) ethyl-4-phthalimidomethyl-1*H-*1,2,3,-triazole* **6** as a white, crystalline powder (1.48 g, 80 %), mp 136–138°C. Found: C 42.72, H 2.21, N 11.56. $C_{20}H_{27}N_6OF_9$ requires: C 43.05, H 2.34, N 11.81 %. ν_{max} (Nujol)/cm^{-1} 3469, 3124, 3080, 1774, 1716, 1616, 1561, 1402, 1356, 1325, 1291, 1219, 1184, 1162, 1133, 1106, 1091, 1072, 1055, 1034, 1014, 994, 942, 916, 901, 878, 848, 832, 775, 749, 716, 695, 671. δ_H (400 MHz, $CDCl_3$) 2.78 (tt, $J_{H–F}$ 18.0, J 7.5, 2H, H2′), 4.63 (t, J 7.5, 2H, H1′), 4.99 (s, 2H, H1″), 7.70 (s, 1H, H5), 7.72 (m, 2H, H5″ and H6″), 7.83 (m, 2H, H4″ and H7″). δ_C (100 MHz) 31.8 (t, $J_{C–F}$ 21.9, C2′), 33.0 (C1″), 42.4 (t, $J_{C–F}$ 5.1, C1′), 123.59 (C5), 123.64 (C4″ and C7″), 132.1 (C3″ and C8″), 134.3 (C5″ and C6″), 143.3 (C4), 167.8 (C2″ and C9″). δ_F (282 MHz, $CDCl_3$) −81.5 (tt, $J_{F–F}$ 9.6, $J_{F–F}$ 2.5, 3F, CF_3CF$_2$), −114.8 (m, 2F), −124.9 (m, 2F), −126.5 (m, 2F). *m/z* (ESI) 496.78 ([M + Na]$^+$, 100 %).

(ii) Azide **3** (1.38 g, 3.60 mmol) gave *1-(2-perfluorohexyl) ethyl-4-phthalimidomethyl-1*H-*1,2,3,-triazole* **7** as a white crystalline powder (1.55 g, 68 %), mp 148–150°C. Found: C 39.85, H 2.02, N 9.65 %. $C_{22}H_{27}N_6OF_{13}$ requires: C 39.74, H 1.93, N 9.76 %. ν_{max} (Nujol)/cm^{-1} 3085, 1460, 1402, 1348, 1250, 1185, 1138, 1100, 1071, 1037, 942, 772, 714, 702. δ_H (300 MHz, $CDCl_3$) 2.78 (tt, $J_{H–F}$ 17.6, J 7.5, 2H, H2′), 4.63 (t, J 7.5, 2H, H1′), 4.98 (s, 2H, H1″), 7.69 (s, 1H, H5), 7.71 (m, 2H, H5″ and H6″), 7.83 (m, 2H, H4″ and H7″). δ_C (75 MHz, $CDCl_3$) 31.9 (t, $J_{C–F}$ 21.6, C2′), 33.0 (C1″), 42.4 (t, $J_{C–F}$ 5.1, C1′), 123.6 (C5), 123.6 (C4″ and C7″), 132.1 (C3″ and C8″), 134.7 (C4″ and C7″), 143.3 (C4), 167.8 (C2″ and C9″). δ_F (282 MHz, $CDCl_3$) −80.9 (tt, $J_{F–F}$ 10.0, $J_{F–F}$ 2.4, 3F, CF_3CF$_2$), −114.2 (m, 2F), −121.9 (m, 2F), −122.9 (m, 2F), −123.5 (m, 2F), −126.2 (m, 2F). *m/z* (ESI) 1171.70 ([2M + Na]$^+$, 19), 598.28 ([M + Na + H]$^+$, 28), 597.37 ([M + Na]$^+$, 100 %).

(iii) Azide **4** (1.53 g, 3.60 mmol) gave *1-(2-perfluorooctyl) ethyl-4-phthalimidomethyl-1*H-*1,2,3,-triazole* **8** as a white crystalline powder (1.34 g, 61 %), mp 142–144°C. Found: C 37.38, H 1.71, N 9.23 %. $C_{19}H_9N_4O_2F_{15}$ requires: C 37.39, H 1.49, N 9.18 %. ν_{max} (Nujol)/cm^{-1} 3130, 3082, 2853, 2337, 1963, 1872, 1819, 1774, 1702, 1612, 1547, 1433, 1404, 1340, 1292, 1257, 1240, 1221, 1178, 1125, 1140, 1100, 1082, 1055, 1046, 1027, 939, 840, 775, 758, 735, 713, 702, 655. δ_H (400 MHz, $CDCl_3$) 5.02 (t, $J_{H–F}$ 14.7, 2H, H1′), 5.02 (s, 2H, H1″), 7.72 (m, 2H, H5″ and H6″), 7.80 (s, 1H, H5), 7.85 (m, 2H, H4″ and H7″). δ_C (100 MHz, $CDCl_3$) 33.0 (C1″), 49.4 (t, $J_{C–F}$ 23.4, C1′), 123.7 (C4″ and C7″), 124.8 (C5), 132.1 (C3″ and C8″), 134.3 (C5″ and C6″), 144.0 (C4), 167.7 (C2″ and C9″). δ_F (282 MHz, $CDCl_3$) −80.8 (tt, $J_{F–F}$ 9.9, $J_{F–F}$ 2.3, 3F, CF_3CF$_2$), −116.8 (m, 2F), −121.6 (m, 4F), −122.7 (m, 4F), −126.1 (m, 2F). *m/z* (ESI) 1243.08 ([2M + Na]$^+$, 8), 633.11 ([M + Na]$^+$, 21 %).

(iv) Azide **5** (2.39 g, 3.60 mmol) gave *1-(2-perfluorooctyl) ethyl-4-phthalimidomethyl-1*H-*1,2,3,-triazole* **9** as a white crystalline powder (0.86 g, 46 %), mp 131–133°C. Found: C 37.60, H 1.53, N 8.15 %. $C_{21}H_{11}N_4O_2F_{17}$ requires: C 37.41, H 1.64, N 8.31 %. ν_{max} (Nujol)/cm^{-1} 3468, 3131, 3086, 1772, 1615, 1558, 1401, 1346, 1251, 1213, 1144, 1111, 1100, 1074, 1054, 1037, 965, 942, 848, 772, 714, 656. δ_H (300 MHz, $CDCl_3$) 2.79 (tt, $J_{H–F}$ 17.7, J 7.5, 2H, H2′), 4.63 (t, J 7.5, 2H, H1′), 5.00 (s, 2H, H1″), 7.68 (s, 1H, H5), 7.72 (m, 2H, H5″ and H6″), 7.85 (m, 2H, H4″ and H7″). δ_C (75 MHz, $CDCl_3$) 32.0 (t, $J_{C–F}$ 21.7, C2′), 33.1 (C1″), 42.5 (t, $J_{C–F}$ 5.1, C1′), 123.56 (C5), 123.61 (C4″ and C7″), 132.1 (C3″ and C8″), 134.3 (C5″ and C6″), 143.3 (C4), 167.8 (C2″ and C9″). δ_F (282 MHz, $CDCl_3$) −80.7 (tt, $J_{F–F}$ 9.9, $J_{F–F}$ 2.1, 3F, CF_3CF$_2$), −114.1 (m, 2F), −121.6 (m, 2F), −121.9 (m, 2F), −122.7 (m, 2F), −123.4 (m, 2F), −126.1 (m, 2F). *m/z* (ESI) 1371.10 ([2M + Na]$^+$, 64), 697.00 ([M + Na]$^+$, 100 %).

(v) Azide **39** (3.07 g, 16.2 mmol) was reacted according to the general procedure, but the product was chromatographed using MeOH/EtOAc (2 : 98) to give *1-(2-(2-(2-methoxyethoxy) ethoxy)ethyl)-4-phthalimidomethyl-1*H-*1,2,3-triazole* **40** as an orange oil (3.75 g, 62 %). Found: C 56.02, H 6.04, N 14.32. $C_{18}H_{22}N_4O_5 \cdot 0.5H_2O$ requires: C 56.38, H 6.05, N 14.62 %. *m/z* (HR-MS ESI) 771.3066 ([2M + Na]$^+$, 56), 397.1476 ([M + Na]$^+$, 100 %). $C_{18}H_{22}N_4O_5$ requires *m/z* 771.3078 ([2M + Na]$^+$),

397.1488 ([M + Na]$^+$). ν_{max} (ATR)/cm^{-1} 3136, 2870, 1769, 1707, 1611, 1550, 1465, 1426, 1392, 1325, 1293, 1221, 1189, 1096, 1047, 934, 846. δ_H (400 MHz, $CDCl_3$) 3.33 (s, 3H, H7′), 3.49 (m, 2H, H6′), 3.57 (m, 6H, H3′–H5′), 3.81 (t, *J* 5.2, 2H, H2′), 4.47 (t, *J* 5.2, 2H, H1′), 4.96 (s, 2H, H1″), 7.68 (m, 2H, H5″ and H6″), 7.76 (s, 1H, H5), 7.81 (m, 2H, H4″ and H7″). δ_C (100 MHz, $CDCl_3$) 33.1 (C1″), 50.3 (C1′), 59.1 (C7′), 69.4 (C2′), 70.54 (C5′), 70.57 (C4′), 70.60 (C3′), 71.9 (C6′), 123.5 (C4″ and C7″), 124.0 (C5), 132.1 (C3″ and C8″), 134.1 (C5″ and C6″), 142.6 (C4), 167.7 (C2″ and C9″).

General Method for Preparation of Amines **10**–**13**

In a modification of the method of Butin et al.,[38] the appropriate phthalimide (1.0 mol equiv.) was dissolved in EtOH (100 mL) with stirring. After 15 min, $NH_2NH_2{\cdot}H_2O$ (5.0 mol equiv.) was introduced into the solution. The reaction mixture was heated in an oil bath at reflux for 16 h, during which time a white precipitate formed. The reaction mixture was cooled to rt and the precipitate removed using vacuum filtration. The filtrate was evaporated under reduced pressure and the resultant solid flash-chromatographed on reverse-phase fluorous silica gel (MeOH) and recrystallized from Et_2O/hexane (1 : 2).

(i) Phthalimide **6** (3.00 g, 6.33 mmol) gave *4-aminomethyl-1-(2-perfluorobutyl)ethyl-1*H-*1,2,3-triazole* **10** as a white microcrystalline powder (1.66 g, 76 %), mp 94–96°C. Found: C 31.49, H 2.62, N 16.03. $C_9H_9N_4F_9$ requires C 31.41, H 2.64, N 16.28 %. ν_{max} (Nujol)/cm^{-1} 3331, 3145, 2854, 2360, 2338, 1950, 1872, 1704, 1596, 1545, 1403, 1358, 1297, 1231, 1216, 1172, 1132, 1098, 1050, 1019, 990, 859, 813, 756, 737, 721, 703. δ_H (400 MHz, CD_3OD) 2.93 (tt, J_{H-F} 14.0, *J* 7.0, 2H, H2″), 3.94 (s, 2H, H1′), 4.78 (t, *J* 7.0, 2H, H1″), 7.96 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 32.1 (t, J_{C-F} 21.4, C2″), 37.3 (C1′), 43.4 (t, J_{C-F} 4.9, C1″), 124.0 (C5), 149.0 (C4). δ_F (282 MHz, CD_3OD) −82.7 (tt, J_{F-F} 9.9, J_{F-F} 3.2, 3F, C*F*$_3$CF$_2$), −115.7 (m, 2F), −125.6 (m, 2F), −127.2 (m, 2F). *m/z* (ESI) 689.16 ([2M + H]$^+$, 18), 367.17 ([M + Na]$^+$, 13), 345.12 ([M + H]$^+$, 100 %).

(ii) Phthalimide **7** (3.00 g, 5.22 mmol) gave *4-aminomethyl-1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazole* **11** as a white microcrystalline powder (1.34 g, 58 %), mp 103–105°C. Found: C 29.90, H 2.07, N 12.34. $C_{11}H_9N_4F_{13}$ requires C 29.74, H 2.04, N 12.61 %. ν_{max} (Nujol)/cm^{-1} 3332, 3144, 2854, 2336, 1937, 1873, 1613, 1545, 1303, 1233, 1209, 1181, 1140, 1098, 1083, 1053, 1027, 991, 941, 908, 809, 701. δ_H (400 MHz, CD_3OD) 2.94 (tt, J_{H-F} 14.1, *J* 7.0, 2H, H2″), 3.91 (s, 2H, H1′), 4.78 (t, *J* 7.0, 2H, H1″), 7.95 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 32.2 (t, J_{C-F} 21.4, C2″), 37.4 (C1′), 43.4 (t, J_{C-F} 4.7, C1″), 123.9 (C5), 149.6 (C4). δ_F (282 MHz, CD_3OD) −82.4 (tt, J_{F-F} 10.2, J_{F-F} 2.1, 3F, C*F*$_3$CF$_2$), −115.4 (m, 2F), −122.9 (m, 2F), −123.9 (m, 2F), −124.5 (m, 2F), −127.3 (m, 2F). *m/z* (ESI) 889.09 ([2M + H]$^+$, 30), 446.13 ([M + 2H]$^+$, 13), 445.07 ([M + H]$^+$, 100 %).

(iii) Phthalimide **8** (3.00 g, 4.92 mmol) gave *4-aminomethyl-1-(2-perfluoroheptyl)ethyl-1*H-*1,2,3-triazole* **12** as a white microcrystalline powder (0.62 g, 27 %), mp 118–120°C. Found: C 27.24, H 1.63, N 11.65. $C_{11}H_7N_4F_{15}$ requires C 27.25, H 1.47, N 11.65 %). ν_{max} (Nujol)/cm^{-1} 3332, 3144, 2854, 2336, 1937, 1873, 1613, 1545, 1303, 1233, 1209, 1181, 1140, 1098, 1083, 1053, 1027, 991, 941, 908, 809, 701. δ_H (400 MHz, CD_3OD) 3.95 (s, 2H, H1′), 5.42 (t, J_{H-F} 15.4, 2H, H1″), 8.04 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 37.4 (C1′), 49.9 (t, J_{C-F} 23.3, C1″), 125.5 (C5), 150.0 (C4). δ_F (282 MHz, CD_3OD) −82.9 (tt, J_{F-F} 10.0, J_{F-F} 2.4, 3F, C*F*$_3$CF$_2$), −117.8 (m, 2F), −122.7 (m, 2F), −123.0 (m, 2F), −123.7 (m, 2F), −124.0 (m, 2F), −127.3 (m, 2F). *m/z* (ESI) 982.9 ([2M + Na]$^+$, 10), 960.9 ([2M + H]$^+$, 31), 502.9 ([M + Na]$^+$, 16), 481.0 ([M + H]$^+$, 100 %).

General Method for Preparation of Amides **14** *and* **15**

Adapting the method of Cohen et al.,[24] the appropriate amine (1.0 mol equiv.) and THF (100 mL) were stirred together at rt before the sequential addition of *N*,*N*-dimethylaniline (0.6 mol equiv.) and either chloroacetyl chloride or chloropropanoyl chloride (2.5 mol equiv.). The reaction mixture was heated at reflux for 16 h. The reaction was quenched with 5 % aq. K_2CO_3 (100 mL) and the resulting mixture extracted with EtOAc (3 × 100 mL). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2 × 100 mL) and brine (100 mL), then dried over Na_2SO_4 and the solvent removed under reduced pressure. The product was flash-chromatographed on reverse-phase fluorous silica gel (MeOH) and recrystallized from EtOAc/hexane (1 : 2).

(i) Amine **10** (3.86 g, 11.2 mmol) gave N-*(((1-(2-perfluorobutyl)ethyl)-1*H-*1,2,3-triazol-4-yl)methyl)-2-chloroacetamide* **14** as a white powder (1.90 g, 40 %), mp 98–100°C. Found: C 31.73, H 2.40, N 13.23. $C_{11}H_{10}N_4OF_9Cl$ requires: C 31.41, H 2.40, N 13.32 %. *m/z* (HR-MS ESI) 865.0639 ([2M + Na]$^+$, 19 %), 863.0670 ([2M + Na]$^+$, 33), 445.0243 ([M + Na]$^+$, 33), 443.0279 ([M + Na]$^+$, 100). $C_{11}H_{10}N_4OF_9Cl$ requires *m/z* 865.0667 ([2M + Na]$^+$), 863.0697 ([2M + Na]$^+$), 445.0268 ([M + Na]$^+$), 443.0297 ([M + Na]$^+$)). ν_{max} (Nujol)/cm^{-1} 3335, 3142, 3077, 2724, 2336, 1934, 1864, 1650, 1541, 1399, 1336, 1294, 1227, 1170, 1133, 1098, 1081, 1054, 1018, 987, 925, 860, 833, 811, 777, 749, 707, 678. δ_H (300 MHz, CD_3OD) 2.92 (tt, J_{H-F} 19.1, *J* 6.9, 2H, H2‴), 4.08 (s, 2H, H2), 4.49 (s, 2H, H1′), 4.76 (t, *J* 6.9, 2H, H1‴), 7.97 (s, 1H, H5″). δ_C (75 MHz, CD_3OD) 32.1 (t, J_{C-F} 21.6, C2‴), 35.9 (t, *J* 9.4, C1′), 43.1 (t, *J* 1.8, C2), 43.4 (t, J_{C-F} 5.2, C1‴), 124.8, 125.4 (C5″), 146.0, 146.1 (C4″), 169.4 (C1). δ_F (282 MHz, CD_3OD) −82.7 (tt, J_{F-F} 9.7, J_{F-F} 3.4, 3F, C*F*$_3$CF$_2$), −115.6 (m, 2F), −125.6 (m, 2F), −127.2 (m, 2F).

(ii) Amine **10** (2.89 g, 8.40 mmol) gave N-*(((1-(2-perfluorobutyl) ethyl)-1*H-*1,2,3-triazol-4-yl)methyl)-3-chloropropanamide* **15** as a white powder (2.43 g, 67 %), mp 104–106°C. Found: C 33.30, H 2.88, N 12.82. $C_{12}H_{12}N_4OF_9Cl$ requires: C 33.16, H 2.78, N 12.89 %. *m/z* (HR-MS ESI) 457.0440 ([M + Na]$^+$, 100 %. $C_{12}H_{12}N_4OF_9Cl$ requires *m/z* 457.0454 ([M + Na]$^+$). ν_{max} (ATR)/cm^{-1} 3286, 3149, 3082, 1634, 1553, 1453, 1443, 1397, 1357, 1333, 1290, 1255, 1225, 1211, 1169, 1129, 1096, 1048, 1017, 987, 960, 923, 857, 816. δ_H (400 MHz, CD_3OD) 2.67 (t, *J* 6.4, 2H, H2), 2.90 (tt, J_{H-F} 19.1, J_{H-H} 7.1, 2H, H2‴), 3.80 (t, *J* 6.4, 2H, H3), 4.46 (s, 2H, H1′), 4.76 (t, *J* 7.1, 2H, H1‴), 7.95 (s, 1H, H5″). δ_C (100 MHz, CD_3OD) 32.1 (t, J_{C-F} 21.4, C2‴), 35.5 (C1′), 39.8 (C2), 41.0 (C3), 43.4 (t, J_{C-F} 4.8, C1‴), 124.72, 124.73 (C5″), 146.46, 146.47 (C4″), 172.5 (C1).

N-*((1-(2-Perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl) trifluoroacetamide* **16**

Amine **11** (2.95 g, 6.64 mmol) and $(CF_3CO)_2O$ (9.22 mL, 66.4 mmol) were stirred together at 0°C under nitrogen for 15 min before the mixture was allowed to warm to rt. After 16 h, the excess reagent and volatiles were removed under reduced pressure. The residue was flash-chromatographed on reverse-phase fluorous silica gel (MeOH) and recrystallized from EtOAc/hexane (1 : 19) to give N-*((1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)trifluoroacetamide* **16** as a pale-green powder (1.70 g, 56 %), mp 110–112°C. Found: C 28.94, H 1.44, N 10.47. $C_{13}H_8N_4OF_{16}$ requires: C 28.90, H 1.49,

N 10.37 %. *m/z* (HR-MS ESI) 563.0317 ($[M+Na]^+$, 100 %). $C_{13}H_8N_4OF_{16}$ requires *m/z* 563.0340 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3313, 1692, 1544, 1430, 1395, 1348, 1332, 1290, 1230, 1178, 1136, 1079, 1054, 1035, 981, 917, 828, 789, 775, 730, 696, 656. δ_H (400 MHz, $CDCl_3$) 2.93 (tt, J_{H-F} 18.8, J 7.1, 2H, H2‴), 4.54 (s, 2H, H1′), 4.77 (t, J 7.1, 2H, H1‴), 8.02 (s, 1H, H5″). δ_C (100 MHz, $CDCl_3$) 32.2 (t, J_{C-F} 21.2, C2‴), 35.7 (t, J_{C-F} 10.1, C1′), 43.5 (t, J_{C-F} 5.3, C1‴), 115.6 (q, J_{C-F} 290, C2), 125.8 (C5″), 144.97, 145.03 (C4″), 158.8, 159.3 (C1). δ_F (282 MHz, $CDCl_3$) −77.4 (s, 3F, CF_3CO), −82.5 (tt, J_{F-F} 10.1, J_{F-F} 2.5, 3F, CF_3CF_2), −115.4 (m, 2F), −122.9 (m, 2F), −123.9 (m, 2F), −124.6 (m, 2F), −127.4 (m, 2F).

*Treatment of Amides **14** and **15** with Alcohol **17** Under Basic Conditions*

2-(2-(2-Methoxyethoxy)ethoxy)ethanol **17** (0.49 mL, 3.04 mmol) was dissolved in dry THF (10 mL) and the solution stirred under nitrogen while cooled in ice for 15 min. KHMDS (8.30 mL of a 0.5 M solution in toluene, 4.15 mmol) was added dropwise by syringe over 30 s, and the mixture was allowed to warm to rt. After 1 h, a solution of amide **14** (1.16 g, 2.76 mmol) in dry THF (10 mL) added by syringe over 1 min. The reaction was maintained at the specified temperature for 16 h, then quenched with sat. aq. NH_4Cl (30 mL) and the product extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with saturated brine (2 × 30 mL), dried over $MgSO_4$, and the solvent removed under reduced pressure to yield crude amide **18** as a yellow oil (0.61 g, 43 %). Purification was attempted using flash-chromatography on reverse-phase fluorous silica gel (MeOH), but the compound could not be purified.

Dry 2-(2-(2-methoxyethoxy)ethoxy)ethanol **17** (0.49 mL, 3.04 mmol) and dry THF (10 mL) were stirred together under nitrogen at 0°C for 15 min. KHMDS (6.07 mL of a 0.5 M solution in toluene, 3.35 mmol) was added dropwise by syringe over 30 s, and the mixture was allowed to warm to rt. After 40 min, the reaction mixture was transferred dropwise by syringe, over 30 s, into a second flask containing a solution of amide **15** (1.2 g, 3.04 mmol) in dry THF (10 mL) at 0°C under nitrogen. The reaction mixture was allowed to warm to rt and stirred for 16 h. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and the resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (2 × 50 mL), dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The product was flash chromatographed on reverse-phase fluorous silica gel (MeOH) and the major product was recrystallized from EtOAc/hexane (1 : 10) to give N-*((1-(2-perfluorobutyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)acrylamide* **20** as a yellow powder (0.47 g, 43 %), mp 107–109°C. Found: C 36.44, H 2.69, N 13.87. $C_{12}H_{11}N_4OF_9$ requires: C 33.19, H 2.78, N 14.07 %. *m/z* (HR-MS ESI) 819.1490 ($[2M+Na]^+$, 37), 399.0869 ($[M+H]^+$, 100 %). $C_{12}H_{11}N_4OF_9$ requires *m/z* 819.1476 ($[2M+Na]^+$), 399.0867 ($[M+H]^+$). ν_{max} (ATR)/cm^{-1} 3287, 3149, 3068, 1652, 1624, 1546, 1452, 1408, 1357, 1334, 1303, 1210, 1168, 1128, 1096, 1047, 1015, 986, 955, 856, 803. δ_H (400 MHz, CD_3OD) 2.92 (tt, J_{H-F} 18.7, J_{H-H} 7.0, 2H, H2‴), 4.51 (s, 2H, H1′), 4.76 (t, J 7.0, 2H, H1‴), 5.67 (dd, J 6.9, 5.1, 1H, H2′), 6.24 (s, 1H, $H3^b$), 6.25 (d, J 1.8, 1H, $H3^a$), 7.97 (s, 1H, H5″). δ_C (100 MHz, CD_3OD) 32.1 (t, J_{C-F} 21.2, C2‴), 35.6 (C1′), 43.4 (t, J_{C-F} 4.7, C1‴), 124.8 (C5″), 127.1 (C2), 131.7 (C3), 146.3 (C4″), 168.1 (C1). δ_F (282 MHz, CD_3OD) −82.6 (tt, J_{F-F} 9.5, 3.2, 3F, CF_3CF_2), −115.6 (m, 2F), −125.5 (m, 2F), −127.2 (m, 2F).

*N-Alkylation of Amine **10** with Mesylate **21***

General Procedure: K_2CO_3 (0.48 g, 2.70 mmol) and amine **10** (1.20 g, 2.70 mmol) were stirred together in MeCN (20 mL) at rt for 30 min. Mesylate **21** (0.58 g, 2.70 mmol) in MeCN (5 mL) was added dropwise over 1 min. The reaction mixture was stirred at rt for 2 h, then heated at reflux for an additional 16 h before quenching with brine (25 mL). The product was extracted into EtOAc (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure to give a pale-yellow powder (0.98 g). Analysis using ^{1}H NMR spectroscopy revealed a mixture of secondary amine **22** and tertiary amine **23**, which could not be separated by chromatography.

*General Method for Preparation of Alcohols **30**–**32***

Based on the method reported by Wang and Read,[12] the appropriate iodide (1.0 mol equiv.) and DMSO (50 mL) were stirred together for 2 min before dropwise addition of propargyl alcohol over 30 s (2.5 mol equiv.). Copper sulfate pentahydrate (0.1 mol equiv.) and sodium ascorbate (0.29 mol equiv.) were added to the reaction mixture. After 2 min, NaN_3 (3.0 mol equiv.) was added and the stirred mixture was heated in an oil bath at 65°C for 16 h. The reaction mixture was quenched with H_2O (200 mL) and the resulting mixture was extracted with EtOAc (3 × 100 mL). The organic fractions were combined, washed with H_2O (100 mL), brine (2 × 100 mL), dried over Na_2SO_4, and the organic solvent was evaporated under reduced pressure. The crude material was flash-chromatographed on reverse-phase fluorous silica gel (MeOH) and recrystallized from EtOAc/hexane (1 : 6).

(i) Iodide **27** (3.74 g, 10.0 mmol) gave *4-hydroxymethyl-1-(2-perfluorobutyl)ethyl-1*H-*1,2,3-triazole* **30** as a pale white powder (3.02 g, 87 %), mp 48–50°C. Found: C 31.26, H 2.28, N 12.08. $C_9H_8N_3OF_9$ requires C 31.21, H 2.34, N 12.17 %. *m/z* (HR-MS ESI) 713.0924 ($[2M+Na]^+$, 24 %), 368.0407 ($[M+Na]^+$, 100). $C_9H_8N_3OF_9$ requires *m/z* 713.0945 ($[2M+Na]^+$), 368.0421 ($[M+Na]^+$. ν_{max} (ATR)/cm^{-1} 3326, 3119, 3073, 1449, 1398, 1356, 1295, 1208, 1126, 1096, 1048, 1006, 853, 814. δ_H (400 MHz, CD_3OD) 2.94 (tt, J_{H-F} 18.7, J 7.0, 2H, H2″), 4.68 (s, 2H, H1′), 4.78 (t, J 7.0, 2H, H1″), 8.00 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 32.1 (t, J_{C-F} 21.4, C2″), 43.4 (t, J_{C-F} 4.8, C1″), 56.5 (C1′), 124.6 (C5), 149.4 (C4). δ_F (282 MHz, CD_3OD) −82.7 (tt, J_{F-F} 10.1, J_{F-F} 3.1, 3F, CF_3CF_2), −115.7 (m, 2F), −125.6 (m, 2F), −127.2 (m, 2F).

(ii) Iodide **28** (4.74 g, 10.0 mmol) gave *4-hydroxymethyl-1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazole* **31** as a pale white powder (4.23 g, 95 %), mp 62–64°C. Found: C 29.59, H 1.81, N 9.27. $C_{11}H_8N_3OF_{13}$ requires C 29.68, H 1.81, N 9.44 %. *m/z* (HR-MS ESI) 913.0790 ($[2M+Na]^+$, 58 %), 468.0338 ($[M+Na]^+$, 100). $C_{11}H_8N_3OF_{13}$ requires *m/z* 913.0817 ($[2M+Na]^+$), 468.0357 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3327, 3120, 3073, 2869, 2321, 2190, 2108, 1852, 1551, 1450, 1398, 1365, 1316, 1291, 1196, 1177, 1135, 1079, 1049, 1007, 988, 916, 850, 776. δ_H (400 MHz, CD_3OD) 2.94 (tt, J_{H-F} 18.8, J 7.0, 2H, H2″), 4.68 (s, 2H, H1′), 4.78 (t, J 7.0, 2H, H1″), 8.00 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 32.2 (t, J_{C-F} 21.4, C2″), 43.4 (t, J_{C-F} 4.8, C1″), 56.5 (C1′), 124.6 (C5), 149.4 (C4). δ_F (282 MHz, CD_3OD) −82.4 (tt, J_{F-F} 10.2, J_{F-F} 2.0, 3F, CF_3CF_2), −115.4 (m, 2F), −122.9 (m, 2F), −123.9 (m, 2F), −124.5 (m, 2F), −127.3 (m, 2F).

(iii) Iodide **29** (5.74 g, 10.0 mmol) gave *4-hydroxymethyl-1-(2-perfluorooctyl)ethyl-1*H-*1,2,3-triazole* **32** as a pale white powder (1.00 g, 33 %), mp 147–149°C. Found: C 28.56, H 1.41,

N 8.03. $C_{13}H_8N_3OF_{17}$ requires C 28.64, H 1.48, N 7.71 %. *m/z* (HR-MS ESI) 568.0278 ($[M+Na]^+$, 100 %). $C_{13}H_8N_3OF_{17}$ requires *m/z* 545.0396 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3320, 3124, 3075, 2946, 2874, 2123, 1667, 1565, 1452, 1399, 1370, 1331, 1291, 1196, 1143, 1036, 987, 955, 842, 817, 766. δ_H (400 MHz, CD_3OD) 2.92 (tt, $J_{H\text{-}F}$ 18.7, J 7.3, 2H, H2″), 4.68 (s, 2H, H1′), 4.78 (t, J 6.5, 2H, H1″), 8.01 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 32.2 (t, J_{C-F} 21.4, C2″), 43.4 (t, J_{C-F} 4.9, C1″), 56.5 (C1′), 124.6 (C5), 149.4 (C4). δ_F (282 MHz, CD_3OD) −82.4 (tt, J_{F-F} 10.1, J_{F-F} 1.8, 3F, CF_3CF_2), −115.4 (m, 2F), −122.8 (m, 2F), −123.8 (m, 6F), −124.6 (m, 2F), −127.3 (m, 2F).

*4-Hydroxymethyl-1-perfluoroheptylmethyl-1*H-*1,2,3-triazole* ***33***

Copper sulfate pentahydrate (0.20 g, 0.80 mmol) and sodium ascorbate (0.44 g, 2.22 mmol) were stirred in DMSO (45 mL) for 2 min before propargyl alcohol (1.16 mL, 1.13 g, 20.2 mmol) was added. After 1 min, a solution of azide **4** (4.90 g, 11.5 mmol) in DMSO (5 mL) was added, and the reaction mixture was heated in an oil bath at 80°C for 16 h with stirring. The reaction was quenched with H_2O (200 mL) and the resultant mixture extracted with EtOAc (3 × 100 mL). The organic fractions were combined and washed with H_2O (100 mL), brine (2 × 100 mL), dried over Na_2SO_4, and the organic solvent was evaporated under reduced pressure. Flash chromatography on reverse-phase fluorous silica gel (MeOH) and recrystallization of the major product from EtOAc/hexane (1 : 6) yielded *4-hydroxymethyl-1-perfluoroheptylmethyl-1*H-*1,2,3-triazole* **33** as pale white powder (2.59 g, 47 %), mp 134–136°C. Found: C 27.09, H 1.42, N 8.92. $C_{11}H_6N_3OF_{15}$ requires C 27.46, H 1.26, N 8.73 %. *m/z* (HR-MS ESI) 481.0495 (M^+, 100 %). $C_{11}H_6N_3OF_{15}$ requires *m/z* 481.0271 ($[M]^+$). ν_{max} (ATR)/cm^{-1} 3294, 3164, 3004, 2966, 2778, 2321, 2119, 2056, 2009, 1563, 1417, 1367, 1325, 1200, 1144, 1100, 1064, 1030, 934, 881, 822, 779, 730, 693. δ_H (400 MHz, CD_3OD) 4.72 (s, 2H, H1′), 5.43 (t, J_{H-F} 15.4, 2H, H1″), 8.07 (s, 1H, H5). δ_C (100 MHz, CD_3OD) 49.9 (t, J_{C-F} 23.4, C1″), 56.4 (C1′), 126.1 (C5), 149.9 (C4). δ_F (282 MHz, CD_3OD) −82.4 (tt, J_{F-F} 10.2, J_{F-F} 2.5, 3F, CF_3CF_2), −117.9 (m, 2F), −122.7 (m, 2F), −123.0 (m, 2F), −123.7 (m, 2F), −124.0 (m, 2F), −127.3 (m, 2F).

*1-(2-Perfluorohexyl)ethyl-1*H-*1,2,3-triazole-4-carbaldehyde* ***34***

A mixture of alcohol **31** (8.39 g, 18.9 mmol) and α,α,α-trifluorotoluene (50 mL) was stirred together while MnO_2 (8.19 g, 94.5 mmol) was added. The reaction mixture was heated at reflux for 16 h, cooled briefly, then filtered through Celite, and the solvent evaporated under reduced pressure. Recrystallization from EtOAc/hexane (1 : 19) gave *1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazole-4-carbaldehyde* **34** as a white powder (7.39 g, 89 %), mp 85–87°C. Found: C 29.81, H 1.36, N 9.48. $C_{11}H_6N_3OF_{13}$ requires C 29.67, H 1.52, N 9.67 %). *m/z* (HR-MS ESI) 973.1010 ($[2M+2CH_3OH^+Na]^+$, 100), 498.0448 ($[M+CH_3OH^+Na]^+$, 96 %). $C_{11}H_6N_3OF_{13}$ requires *m/z* 973.1029 ($[2M+2CH_3OH^+Na]^+$), 498.0463 ($[M+CH_3OH^+Na]^+$). ν_{max} (ATR)/cm^{-1} 3106, 3051, 2844, 2775, 2320, 2206, 2092, 1701, 1539, 1435, 1400, 1365, 1316, 1288, 1230, 1182, 1139, 1077, 1051, 1026, 983, 882, 828, 793, 760, 700. δ_H (400 MHz, $CDCl_3$) 2.88 (tt, J_{H-F} 17.8, J 7.2, 2H, H2′), 4.78 (t, J 7.2, 2H, H1′), 8.19 (s, 1H, H5), 10.1 (s, 1H, H1″). δ_C (100 MHz, $CDCl_3$) 31.7 (t, J_{C-F} 21.8, C2′), 43.2 (t, J_{C-F} 5.0, C1′), 126.0 (C5), 148.1 (C4), 184.9 (C1″). δ_F (376 MHz, $CDCl_3$) −80.8 (tt, J_{F-F} 9.7, J_{F-F} 2.3, 3F, CF_3CF_2), −114.1 (m, 2F), −121.8 (m, 2F), −122.9 (m, 2F), −123.4 (m, 2F), −126.2 (m, 2F).

General Method for Preparation of Amines ***36*** *and* ***42***

Following the method of Łowicki et al.,[30] the phthalimide (1.0 mol equiv.) and $NH_2NH_2{\cdot}H_2O$ (2.0 mol equiv) were dissolved in EtOH (300 mL) and the solution was heated at reflux for 4 h, at which point conc. HCl (3.5 mol equiv.) was added in one portion. The reaction mixture was heated at reflux for a further 16 h, then cooled to rt and filtered through Celite. The filtrate was adjusted to pH 14 through the addition of KOH pellets and extracted with $CHCl_3$ (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and the solvent removed under reduced pressure.

(i) Phthalimide **37** (26.7 g, 91.0 mmol) gave *2-(2-(2-methoxyethoxy)ethoxy)ethylamine* **36** as a pale yellow oil (7.28 g, 49 %), which was used without further purification. ν_{max} (ATR)/cm^{-1} 2864, 1782, 1590, 1453, 1387, 1348, 1288, 1247, 1197, 1106, 1030, 982, 926, 844, 806. δ_H (300 MHz, $CDCl_3$) 2.79 (t, J 3.6, 2H, H1), 3.30 (s, 3H, H5′), 3.43 (m, 2H, H2), 3.49 (m, 2H, H4′), 3.57 (m, 6H, H1′–H3′). δ_C (75 MHz, $CDCl_3$) 41.7 (C1), 59.0 (C5′), 70.2, 70.5, 70.6 (C1′-C3′), 71.9 (C4′), 73.3 (C2).

(ii) Phthalimide **41** (9.94 g, 26.5 mmol) gave *4-aminomethyl-1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-1*H-*1,2,3-triazole* **42** as a slightly impure orange oil (4.73 g, 73 %), which was used in later reactions without further purification. A portion of amine **42** (1.03 g, 4.22 mmol) was stirred together with oxalic acid (0.267 g, 2.11 mmol) in EtOH (5 mL) for 2 h at rt. The solvent was removed under vacuum and the remaining solid was recrystallized from EtOH to give *bis((1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-1*H-*1,2,3-triazol-4-yl)methylammonium) oxalate* **43** as a white powder (1.14 g, 48 %), mp 154–156°C. Found: C 45.26, H 7.57, N 19.20. $C_{22}H_{42}N_8O_{10}$ requires: C 45.67, H 7.32, N 19.37 %. *m/z* (HR-MS ESI) 489.3140 ($[2M+H]^+$, 100), 245.1606 ($[M+H]^+$, 100 %). $C_{10}H_{20}N_4O_3$ requires *m/z* 489.3149 ($[2M+H]^+$), 245.1614 ($[M+H]^+$). ν_{max} (ATR)/cm^{-1} 3131, 3088, 2866, 2815, 2632, 1640, 1542, 1462, 1349, 1226, 1199, 1119, 1048, 980, 948, 856, 829, 770. δ_H (400 MHz, D_2O) 3.36 (s, 3H, H7′), 3.59 (m, 2H, H6′), 3.62 (m, 2H, H4′ or H5′), 3.64 (m, 2H, H4′ or H5′), 3.67 (m, 2H, H3′), 4.00 (t, J 5.2, 2H, H2′), 4.35 (s, 2H, H1″), 4.67 (t, J 5.2, 2H, H1′), 8.17 (s, 1H, H5). δ_C (100 MHz, D_2O) 34.0 (C1″), 50.1 (C1′), 58.0 (C7′), 68.6 (C2′), 69.3 (C4′ or C5′), 69.4 (C4′ or C5′), 69.6 (C3′), 70.9 (C6′), 125.7 (C5), 139.7 (C4), 173.0 (C1‴).

General Method for Preparation of Secondary Amines ***39*** *and* ***44***

Aldehyde **34** (1.0 mol equiv.) and the amine **36** or **42** (1.0 mol equiv.) were dissolved in EtOH (150 mL) and the reaction mixture was heated at reflux for 1 h. The reaction mixture was then cooled to 0°C and $NaBH_4$ (1.0 mol equiv.) was added portionwise while stirring. The reaction was allowed to warm to rt and stirred for 16 h, then quenched with brine (150 mL), and the resultant mixture was extracted with EtOAc (3 × 100 mL). The combined organic layers were dried over $MgSO_4$ and the organic solvent was removed under reduced pressure. The crude product was flash-chromatographed on reverse-phase fluorous silica gel (MeOH) and then on silica gel (acetone/MeOH, 9 : 1), and finally recrystallized from EtOAc/hexane (1 : 10).

(i) Aldehyde **34** (5.97 g, 13.5 mmol) and amine **36** (2.20 g, 13.5 mmol) gave N-(*2-(2-(2-methoxyethoxy)ethoxy)*)-N-*((1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)ethanamine*

39 as a pale white powder (3.82 g, 48 %), mp 36–38°C. Found: C 36.34, H 3.80, N 9.22. $C_{18}H_{23}N_4O_3F_{13}$ requires: C 36.62, H 3.93, N 9.49 %. *m/z* (HR-MS ESI) 1181.3171 ($[2M+H]^+$, 84), 613.1431 ($[M+Na]^+$, 100). $C_{18}H_{23}N_4O_3F_{13}$ requires *m/z* 1181.3203 ($[2M+H]^+$), 613.1460 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3276, 3118, 3069, 2998, 2886, 2837, 1557, 1456, 1366, 1326, 1230, 1185, 1143, 1092, 1026, 987, 940, 879, 853, 807, 771. δ_H (400 MHz, $CDCl_3$) 2.27 (s, 1H, N*H*), 2.79 (tt, J_{H-F} 18.1, J_{H-H} 7.3, 2H, H2′′′′), 2.83 (t, *J* 5.1, 2H, H1), 3.35 (s, 3H, H5′), 3.53 (m, 2H, H4′), 3.61 (m, 8H, H2 and H1′-H3′), 3.93 (s, 2H, H1′′), 4.65 (t, *J* 7.3, 2H, H1′′′′), 7.58 (s, 1H, H5′′′). δ_C (100 MHz, $CDCl_3$) 32.0 (t, J_{C-F} 21.8, C2′′′′), 42.3 (t, J_{C-F} 5.0, C1′′′′), 44.7 (C1′′), 48.7 (C1), 59.1 (C5′), 70.38, 70.41, 70.65 (C2 and C1′-C2′), 70.59 (C3′), 72.0 (C4′), 122.4 (C5′′′), 147.3 (C4′′′). δ_F (282 MHz, $CDCl_3$) −80.8 (tt, J_{F-F} 10.1, 1.9, 3F, CF_3CF$_2$), −114.2 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.5 (m, 2F), −126.1 (m, 2F).

(ii) Aldehyde **34** (1.81 g, 4.08 mmol) and triazolylmethyl amine **42** (1.00 g, 4.10 mmol) gave N-*(1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl)-1*H-*1,2,3-triazol-4-yl)methyl)*-N-*(1-(2-perfluorohexyl)ethyl)-1*H-*1,2,3-triazol-4-yl)amine* **44** as a pale white powder (0.90 g, 33 %), mp 53–55°C. Found: C 37.51, H 4.11, N 14.53. $C_{21}H_{26}N_7O_3F_{13}$ requires: C 37.56, H 3.90, N 14.60 %. *m/z* (HR-MS ESI) 1343.3831 ($[2M+H]^+$, 79), 694.1758 ($[M+Na]^+$, 100 %). $C_{21}H_{26}N_7O_3F_{13}$ requires *m/z* 1343.3857 ($[2M+H]^+$), 694.1787 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3306, 3148, 3109, 3069, 2894, 2815, 1558, 1459, 1397, 1365, 1319, 1288, 1181, 1136, 1101, 1033, 988, 950, 918, 851, 813, 766. δ_H (400 MHz, $CDCl_3$) 2.39 (s, 1H, NH), 2.80 (tt, J_{H-F} 18.0, J_{H-H} 7.5, 2H, H2′), 3.35 (s, 3H, H7′′′), 3.52 (m, 2H, H6′′′), 3.59 (m, 2H, H5′′′), 3.61 (m, 4H, H3′′′–H4′′′), 3.85 (t, *J* 5.2, 2H, H2′′′), 3.93 (s, 2H, H1′′ or H2′′), 3.94 (s, 2H, H1′′ or H2′′), 4.52 (t, *J* 5.2, 2H, H1′′′), 4.65 (t, *J* 7.5, 2H, H1′), 7.61 (s, 1H, H5), 7.70 (s, 1H, H5′′′). δ_C (100 MHz, $CDCl_3$) 32.0 (t, J_{C-F} 21.9, C2′), 42.3 (t, J_{C-F} 5.0, C1′), 43.7 (C1′′ or C2′′), 43.8 (C1′′ or C2′′), 50.3 (C1′′′), 59.1 (C7′′′), 69.6 (C2′′′), 70.6 (C5′′′), 70.7 (C3′′′ and C4′′′), 72.0 (C6′′′), 122.7 (C5), 123.3 (C5′′′), 145.8 (C4′′′), 146.7 (C4). δ_F (282 MHz, $CDCl_3$) −80.7 (tt, J_{F-F} 10.1, 1.7, 3F, CF_3CF$_2$), −114.1 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.4 (m, 2F), −126.1 (m, 2F).

*General Method for the Alkylation of Triazolylmethyl Amines **39** and **44***

The appropriate amine (1.0 mol equiv.), Et_3N (1.1 mol equiv.), and the specified alkylating agent (either **45** or **46**, 1.1 mol equiv.) were dissolved in MeCN (20 mL). The reaction mixture was heated at reflux for 16 h, then quenched with saturated aqueous $NaHCO_3$ (20 mL), and the reaction mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (2 × 20 mL), dried over $MgSO_4$, and the organic solvent removed under reduced pressure. The crude product was flash-chromatographed on reverse-phase fluorous silica gel (MeOH), then on silica gel (MeOH/EtOAc, 3 : 97).

(i) Amine **39** (0.50 g, 0.847 mmol) and ethyl 4-bromobutanoate **45** (0.182 g, 0.932 mmol) gave *ethyl* N-*(2-(2-(2-methoxyethoxy)ethoxy)ethyl)*-N-*(((1-(2-perfluorohexyl)ethyl)-1*H-*1,2,3-triazol-4-yl)methyl)aminobutanoate* **47** as a yellow oil (0.39 g, 65 %). Found: C 40.76, H 4.56, N 8.26. $C_{24}H_{33}N_4O_5F_{13}\cdot 0.5H_2O$ requires: C 40.40, H 4.80, N 7.85 %. *m/z* (HR-MS ESI) 705.2320 ($[M+H]^+$, 100 %). $C_{24}H_{33}N_4O_5F_{13}$ requires *m/z* 705.2322 ($[M+H]^+$). ν_{max} (film)/cm^{-1} 3137, 2878, 1732, 1461, 1368, 1351, 1240, 1204, 1145, 1122, 1047, 948, 850, 809, 781, 746, 736, 708, 698. δ_H (300 MHz, $CDCl_3$) 1.22 (t, *J* 7.1, 3H, H2′), 1.79 (tt, *J* 14.4, 7.2, 2H, H2), 2.29 (t, *J* 7.2, 2H, H3), 2.51 (t, *J* 7.2, 2H, H1), 2.66 (t, *J* 5.7, 2H, H1′′), 2.81 (tt, J_{H-F} 18.1, J_{H-H} 7.6, 2H, H2′′′′′), 3.34 (s, 3H, H7′′), 3.51 (m, 2H, H6′′), 3.56 (m, 2H, H2′′), 3.57 (m, 2H, H3′′ or H4′′), 3.61 (m, 2H, H3′′ or H4′′), 3.63 (m, 2H, H5′′) 3.85 (s, 2H, H1′′′), 4.06 (qr, *J* 7.1, 2H, H1′), 4.65 (t, *J* 7.6, 2H, H1′′′′′), 7.67 (s, 1H, H5′′′′). δ_C (75 MHz, $CDCl_3$) 14.3 (C2′), 22.6 (C2), 31.9 (t, J_{C-F} 21.7, C2′′′′′), 32.0 (C3), 42.2 (t, J_{C-F} 5.0, C1′′′′′), 49.2 (C1′′′), 53.0 (C1′′), 53.5 (C1), 59.0 (C7′′), 60.3 (C1′), 69.9 (C2′′), 70.4, 70.5 (C3′′–C4′′), 70.7 (C5′′), 72.0 (C6′′), 123.7 (C5′′′′), 145.7 (C4′′′′), 173.7 (C4). δ_F (282 MHz, $CDCl_3$) −80.8 (tt, J_{F-F} 9.9, 2.2, 3F, CF_3CF$_2$), −114.1 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.5 (m, 2F), −126.1 (m, 2F).

(ii) Amine **39** (0.50 g, 0.847 mmol) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactos-6-yl triflate **46** (0.365 g, 0.932 mmol) gave N-*(2-(2-(2-methoxyethoxy)ethoxy)ethyl)*-N-*((1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)-6-amino-1,2:3,4-di*-O-*isopropylidene-α-D-galactose* **48** as a colourless oil (0.43 g, 61 %). *m/z* (HR-MS ESI) 833.2783 ($[M+H]^+$, 100 %. $C_{30}H_{41}N_4O_8F_{13}$ requires *m/z* 833.2795 ($[M+H]^+$). ν_{max} (film)/cm^{-1} 3137, 2987, 2897, 1644, 1556, 1457, 1383, 1351, 1241, 1002, 918, 902, 852, 809, 771, 746, 736, 708, 698. δ_H (300 MHz, $CDCl_3$) 1.31 (s, 6H, H1′′ and H1′′′), 1.41 (s, 3H, H2′′′), 1.52 (s, 3H, H7′′A), ∼2.72 (m, 2H, H1′′′′′), ∼2.79 (m, 2H, H6), ∼2.80 (m, 2H, H1′′′′′′′), 3.35 (s, 3H, H7′′′′), 3.52 (m, 2H, H6′′′′), 3.65 (m, 8H, H2′′′′-H5′′′′), 3.97 (s, 2H, H1′′′′′), 4.04 (m, 1H, H5), 4.22 (dd, *J* 7.9, 1.7, 1H, H4), 4.28 (dd, *J* 5.1, 2.3, 1H, H2), 4.57 (dd, *J* 7.9, 2.3, 1H, H3), 4.64 (t, *J* 7.6, 2H, H2′′′′′′′), 5.53 (d, *J* 5.1, 1H, H1), 7.73 (s, 1H, H5′′′′′′). δ_C (75 MHz, $CDCl_3$) 24.6 (C1′′′), 25.0 (C1′′), 26.1 (C2′′), 26.2 (C2′), 32.0 (t, J_{C-F} 21.5, C2′′′′′′′), 42.2 (t, J_{C-F} 5.3, C1′′′′′′′), 49.3 (C1′′′′′), 53.5 (C1′′′′), 54.2 (C6), 59.1 (C7′′′′), 65.9 (C5), 70.3 (C5′′′′), 70.56, 70.74 (C2′′′′–C4′′′′), 70.65 (C2), 71.0 (C3), 72.1 (C6′′′′), 72.3 (C4), 96.8 (C1), 108.6 (C1′), 109.2 (C1′′), 124.0 (C5′′′′′′), 145.9 (C4′′′′′′). δ_F (282 MHz, $CDCl_3$) −80.8 (tt, J_{F-F} 9.7, 1.8, 3F, CF_3CF$_2$), −114.1 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.5 (m, 2F), −126.1 (m, 2F).

(iii) Amine **44** (0.50 g, 0.745 mmol) and ethyl 4-bromobutanoate **45** (0.160 g, 0.820 mmol) gave *ethyl* N-*(((1-(2-(2-methoxyethoxy)ethoxy)ethyl)-1*H-*1,2,3-triazol-4-yl)methyl)*-N-*(((1-(2-perfluorohexyl)ethyl)-1*H-*1,2,3-triazol-4-yl)methyl) aminobutanoate* **52** as a pale white powder (0.15 g, 26 %) mp 38–40°C. Found: C 41.26, H 4.70, N 12.35. $C_{27}H_{36}N_7O_5F_{13}$ requires: C 41.28, H 4.62, N 12.48 %. *m/z* (HR-MS ESI) 808.2432 ($[M+Na]^+$, 100). $C_{27}H_{36}N_7O_5F_{13}$ requires *m/z* 808.2468 ($[M+Na]^+$). ν_{max} (ATR)/cm^{-1} 3117, 3073, 2929, 2879, 2821, 1726, 1643, 1553, 1458, 1434, 1376, 1343, 1321, 1280, 1224, 1179, 1144, 1096, 1050, 962, 931, 885, 836, 818, 762, 745. δ_H (400 MHz, $CDCl_3$) 1.22 (t, *J* 7.2, 3H, H2′), 1.91 (m, 2H, H2), 2.32 (t, *J* 7.2, 2H, H3), 2.53 (m, 2H, H1), 2.83 (tt, J_{H-F} 18.0, J_{H-H} 7.6, 2H, H2′′′′′′), 3.35 (s, 3H, H7′′′), 3.52 (m, 2H, H6′′′), 3.60 (m, 2H, H5′′′), 3.62 (m, 4H, H3′′′–H4′′′), 3.76 (s, 2H, H1′′ or H1′′′′), 3.78 (m, 2H, H1′′ or H1′′′′), 3.88 (t, *J* 5.2, 2H, H2′′′), 4.07 (q, *J* 7.2, 2H, H1′), 4.54 (t, *J* 5.1, 2H, H1′′′), 4.68 (t, *J* 7.6, 2H, H1′′′′′′), 7.78 (m, 2H, H5′′ or H5′′′′′). δ_C (100 MHz, $CDCl_3$) 14.3 (C2′), 22.5 (C2), 31.9 (t, J_{C-F} 21.7, C2′′′′′′), 32.0 (C3), 42.4 (t, J_{C-F} 4.0, C1′′′′′′), 47.5, 47.7 (C1′′ and C1′′′′), 50.4 (C1′′′), 52.5 (C1), 59.1 (C7′′′), 60.4 (C1′), 69.6 (C2′′′), 70.65 (C3′′′–C4′′′), 70.70 (C5′′′), 72.0 (C6′′′), 124.5 (C5′′ and C5′′′′′), ∼144.7 (C4′′ and C4′′′′′), 173.7 (C4).

(iv) Amine **44** (0.50 g, 0.745 mmol) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactos-6-yl triflate **46** (0.320 g, 0.820 mmol)

gave N-*(1-(2-(2-(2-methoxyethoxy)ethoxy)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)*-N-*((1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)-6-amino-1,2 : 3,4-di*-O-*isopropylidene-α-D-galactose* **53** as a colourless gum (0.27 g, 40 %). *m/z* (HR-MS ESI) 914.3091 ($[M+H]^+$, 100 %). $C_{33}H_{44}N_7O_8F_{13}$ requires *m/z* 914.3122 ($[M+H]^+$). ν_{max} (film)/cm^{-1} 3137, 2988, 2936, 2362, 1699, 1644, 1583, 1557, 1457, 1383, 1240, 1145, 1070, 1001, 919, 903, 851, 809, 772, 746, 736, 708. δ_H (600 MHz, $CDCl_3$) 1.30 (m, 3H, H2′ or H2‴), 1.32 (m, 3H, H2‴ or H2‴), 1.40 (m, 3H, H1⁗), 1.54 (m, 3H, H1″), 2.77 (m, 2H, H6), 2.81 (tt, J_{H-F} 16.7, J_{H-H} 7.6, 2H, H2⁗⁗⁗⁗⁗⁗⁗⁗), 3.35 (s, 3H, H7⁗⁗⁗⁗⁗⁗), 3.51 (m, 2H, H6⁗⁗⁗⁗⁗⁗), 3.60 (m, 2H, H5⁗⁗⁗⁗⁗⁗), 3.61 (m, 4H, H3⁗⁗⁗⁗⁗⁗–H4⁗⁗⁗⁗⁗⁗), 3.87 (t, *J* 5.2, 2H, H2⁗⁗⁗⁗⁗⁗), 4.21 (dd, *J* ~7.8, 1.0, 1H, H4), 4.30 (dd, *J* 5.0, 2.0, 1H, H2), 4.52 (t, *J* 5.2, 2H, H1⁗⁗⁗⁗⁗⁗), 4.58 (dd, *J* 7.8, 2.0, 1H, H3), 4.65 (t, *J* 7.6, 2H, H1⁗⁗⁗⁗⁗⁗⁗⁗), 5.56 (d, *J* 5.0, 1H, H1), 7.79 (s, 1H, H5⁗⁗⁗⁗⁗⁗⁗⁗), 7.81 (s, 1H, H5⁗⁗⁗⁗⁗⁗⁗⁗). δ_C (150 MHz, $CDCl_3$) 24.5 (C1″ or C1⁗), 25.0 (C1″ or C1⁗), 26.1 (C2‴), 26.2 (C2′), 32.0 (t, J_{C-F} 21.7, C2⁗⁗⁗⁗⁗⁗⁗⁗), 42.3 (t, J_{C-F} 5.7, C1⁗⁗⁗⁗⁗⁗⁗⁗), 50.3 (C1⁗⁗⁗⁗⁗⁗), 53.2 (C6), 59.1 (C7⁗⁗⁗⁗⁗⁗), 69.6 (C2⁗⁗⁗⁗⁗⁗), 70.61 (C2), 70.65 (C3⁗⁗⁗⁗⁗⁗ or C4⁗⁗⁗⁗⁗⁗), 70.66 (C5⁗⁗⁗⁗⁗⁗), 70.74 (C3⁗⁗⁗⁗⁗⁗ or C4⁗⁗⁗⁗⁗⁗), 71.0 (C3), 72.0 (C6⁗⁗⁗⁗⁗⁗), 72.3 (C4), 96.8 (C1), 108.6 (C1′), 109.2 (C1‴), 124.4 (C5⁗⁗⁗⁗⁗⁗⁗⁗), 124.8 (C5⁗⁗⁗⁗⁗⁗), 143.7 (C4⁗⁗⁗⁗⁗⁗), 144.6 (C4⁗⁗⁗⁗⁗⁗⁗⁗). δ_F (376 MHz, $CDCl_3$) −80.7 (tt, J_{F-F} 9.8, 1.8, 3F, C*F*$_3$CF$_2$), −114.1 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.4 (m, 2F), −126.1 (m, 2F).

Acylation of Bis-(triazolylmethyl)amine ***39*** *with 1-Adamantoyl Chloride* ***49***

1-Adamantanecarboxylic acid (0.38 g, 2.11 mmol) and $SOCl_2$ (1.0 mL) were heated at reflux for 3 h. The excess $SOCl_2$ was removed by distillation under reduced pressure to give acid chloride **49**, which was dissolved in MeCN (20 mL) along with the amine **39** (0.50 g, 0.847 mmol), and Et_3N (0.119 mL, 0.931 mmol). The reaction mixture was heated at reflux for 16 h, then quenched with saturated aqueous $NaHCO_3$ (20 mL) and the resulting mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (2 × 20 mL), dried over $MgSO_4$, and the organic solvent removed under reduced pressure. Flash chromatography on reverse-phase fluorous silica gel (MeOH), followed by flash chromatography on silica gel (acetone/hexane, 15 : 85) afforded *(3r,5r,7r)*-N-*(2-(2-(2-methoxyethoxy)ethoxy)ethyl)*-N-*((1-perfluorohexylethyl-1*H-*1,2,3-triazol-4-yl)methyl)adamantane-1-carboxamide* **50** as a yellow oil (0.30 g, 47 %). Found: C 46.66, H 4.85, N 7.39. $C_{29}H_{37}N_4O_4F_{13}$ requires: C 46.28, H 4.96, N 7.44 %. *m/z* (HR-MS ESI) 1527.5097 ($[2M+Na]^+$, 60), 753.2678 ($[M+H]^+$, 100 %). $C_{29}H_{37}N_4O_4F_{13}$ requires *m/z* 1527.5112 ($[2M+Na]^+$), 753.2685 ($[M+H]^+$). ν_{max} (film)/cm^{-1} 3136, 2908, 2360, 2342, 1621, 1551, 1455, 1406, 1366, 1243, 1145, 990, 939, 850, 810, 780, 746, 735, 708, 698. δ_H (400 MHz, $CDCl_3$) 1.69 (m, 6H, H4, H6 and H1″), 1.97 (m, 6H, H2, H8 and H1′), 2.01 (m, 3H, H3, H5 and H7), 2.80 (tt, J_{H-F} 18.0, *J* 7.5, 2H, H2⁗⁗⁗⁗⁗⁗), 3.35 (s, 3H, H7⁗⁗⁗), 3.52 (m, 2H, H6⁗⁗⁗), 3.53 (m, 2H, H5⁗⁗⁗), 3.61 (m, 4H, H3⁗⁗⁗–H4⁗⁗⁗), 3.64 (t, *J* 5.2, 2H, H1⁗⁗⁗, H2⁗⁗⁗ or H1⁗⁗⁗⁗), 3.72 (m, 2H, H1⁗⁗⁗, H2⁗⁗⁗ or H1⁗⁗⁗⁗), 4.63 (t, *J* 7.5, 2H, H1⁗⁗⁗⁗⁗⁗), 4.68 (m, 2H, H1⁗⁗⁗, H2⁗⁗⁗ or H1⁗⁗⁗⁗), 7.61 (s, 1H, H5⁗⁗⁗⁗⁗⁗). δ_C (100 MHz, $CDCl_3$) 28.6 (C3, C5 and C7), 31.8 (t, J_{C-F} 21.7, C2⁗⁗⁗⁗⁗⁗), 36.6 (C4, C6 and C1″), 39.3 (C2, C8 and C1′), 42.4 (t, J_{C-F} 5.6, C1⁗⁗⁗⁗⁗⁗), 44.6 (C1⁗⁗⁗, C2⁗⁗⁗ or C1⁗⁗⁗⁗), 48.2 (C1⁗⁗⁗, C2⁗⁗⁗ or C1⁗⁗⁗⁗), 59.1 (C7⁗⁗⁗), 69.5 (C1⁗⁗⁗, C2⁗⁗⁗ or C1⁗⁗⁗⁗), 70.64 (C5⁗⁗⁗), 70.67, 70.69 (C3⁗⁗⁗–C4⁗⁗⁗), 72.0 (C6⁗⁗⁗), 124.0 (C5⁗⁗⁗⁗⁗⁗), 146.0 (C4⁗⁗⁗⁗⁗⁗), 177.4 (C1⁗⁗⁗). δ_F (376 MHz, $CDCl_3$) −80.7 (tt, J_{F-F} 9.9, 2.3, 3F, C*F*$_3$CF$_2$), −114.2 (m, 2F), −121.8 (m, 2F), −122.8 (m, 2F), −123.4 (m, 2F), −126.1 (m, 2F).

Subsequent chromatographic fractions yielded what was thought to be N-*(2-(2-(2-methoxyethoxy)ethoxy))*-N-*((1-(2-perfluorohexyl)ethyl-1*H-*1,2,3-triazol-4-yl)methyl)ethanamine* hydrochloride **51** as a solid (0.12 g, 23 %). Found: C 34.03, H 3.81, N 8.60. $C_{18}H_{24}N_4O_3ClF_{13}$ requires: C 34.49, H 3.86, N 8.94 %. *m/z* (HR-MS ESI) 591.1632. $C_{18}H_{24}N_4O_3F_{13}$ requires *m/z* 591.1641. δ_H (400 MHz, $CDCl_3$) 8.55 (s, 1H). δ_H (400 MHz, $CDCl_3$) 2.82 (br m, 2H, $CF_2CH_2CH_2N$). 3.16 (br s, 2H, NCH_2CH_2O), 3.36 (s, 3H, OCH_3), 3.53 (s, 2H, CH_2OCH_3), 3.63 (s, 2H), 3.66 (s, 2H), 3.69 (s, 2H), 3.91 (s, 2H, NCH_2CH_2O), 4.44 (s, 2H, 4-CH_2N), 4.71 (s, 2H, $CF_2CH_2CH_2N$), 8.52 (s, 1H, triazole-H4), 9.79 (br s, 2H, $R_2NH_2^+$). δ_C (100 MHz, $CDCl_3$) 31.8 (t, *J* ~20, $CF_2CH_2CH_2N$), 41.9 (4-CH_2N), 42.8 (t, *J* ~5, $CF_2CH_2CH_2N$), 45.8 (NCH_2CH_2O), 59.1 (OCH_3), 65.7 (NCH_2CH_2O), 70.08, 70.16, 70.21, 71.6 (CH_2OCH_3), 127.3 (C4), 138.4 (C5).

Supplementary Material

Details of method development and copies of spectra for all new compounds are available on the Journal's website.

Acknowledgements

This research was generously supported through small grant funding from the University of New South Wales. The authors thank Mr Ahmed Ahmed for the generous provision of triflate **46**.

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