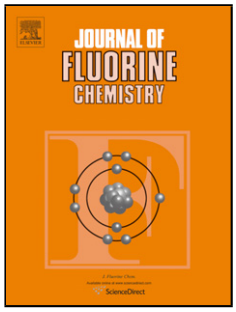

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***Manuscript**

Convenient Synthesis of Pure Fluorous Alkyl Azides at Multigram Scale

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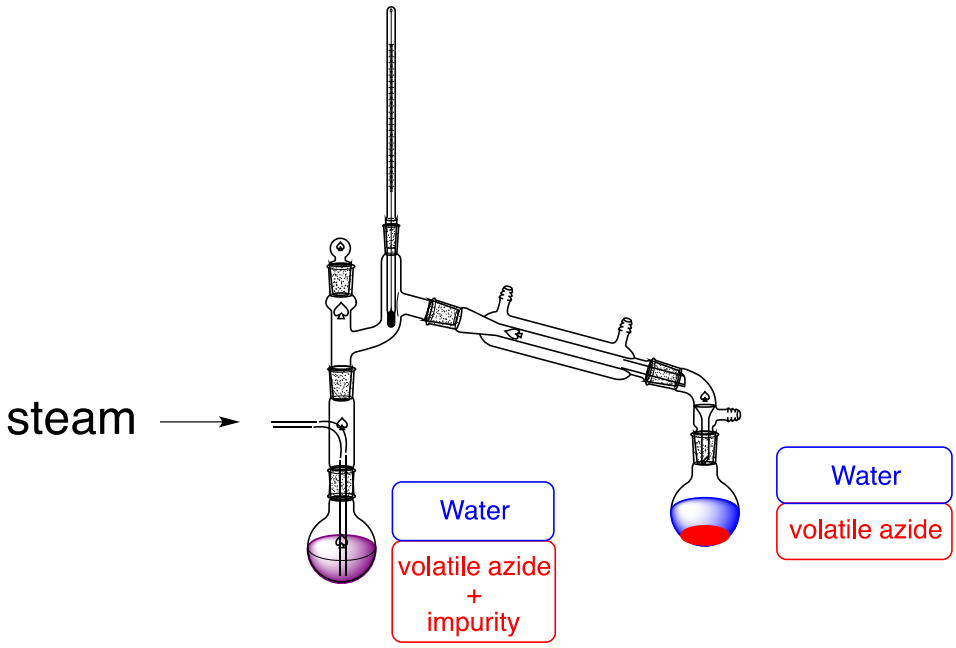
***Graphical Astract – Pictogram**



***Graphical Abstract – Synopsis**

Convenient Synthesis of Pure Fluorous Alkyl Azides at Multigram Scale

Máté Berta,[a] András Dancsó,[b] Anikó Nemes,[a] Zoltán Pathó,[a] Dénes Szabó [a] and József Rábai*[a]

The reaction of (perfluoroalkyl)alkyl halides and sulfonates and a slight excess of NaN_3 in DMSO at 100 °C for 5 h, followed by steam distillation, gave the corresponding azides $C_nF_{2n+1}(CH_2)_xN_3$ in good to excellent yields with high purity (GC≥98%). 4-$CF_3C_6F_4N_3$ and $CH_3(CH_2)_7N_3$ were similarly prepared starting from $CF_3C_6F_5$ or 1-iodooctane.

***Highlights (for review)**

Highlights:

- Efficient synthetic route for fluorous-, polyfluoroaryl- and alkyl azides are disclosed here
- Steam-distillation enabled cost-effective separation of highly volatile fluorous azides
- Synthesis and isolation of stable fluorous azides can easily be upscaled to safe processes

This article is dedicated to Professor Steven H. Strauss on the occasion of his 2016 ACS Award for Creative Work in Fluorine Chemistry.

The reaction of *F*-alkylation reagents including (perfluoroalkyl)alkyl halides and sulfonates [$R_{fn}(CH_2)_mX$ (X = Br, I, OTs, OTf)], and a slight excess of NaN_3 in DMSO at 100 °C for 5 h, followed by steam distillation, allowed the isolation of azides $R_{fn}(CH_2)_mN_3$ in good to excellent yields with high purity (GC assay ≥98%). Due to the stability of these fluorous azides they can be distilled at atmospheric or lower pressures for further purification. 4-Azidoperfluorotoluene (*p*-$CF_3C_6F_4N_3$) and 1-azidooctane were also prepared under similar conditions starting from perfluorotoluene ($CF_3C_6F_5$) or 1-iodooctane, respectively. Steam distillation allowed easy and safe product isolations up to 50 g scale.

1. Introduction

The chemistry of organic azides started with the synthesis of phenyl azide one and one-half century ago [1], flourished in the 1950's [2], and has today emerged as a broad area of chemistry of a unique class of compounds with exploding diversity in their synthesis and applications [3]. Since organic azides are the derivatives of the explosive HN_3, many of them belong to the class of high-energy-density molecules [3a, 4]. Similarly to the parent hydrogen azide and the heavy metal azides, many organic azides may have explosive properties, triggered by friction, impact or excess of heating [5].

However, certain structural patterns (e.g. longer fluorinated chains [6]) of the molecules result in the formation of *shock-insensitive* and *nonexplosive* azides that can be manipulated safely [7]. In addition, the recent technology of a continuous-flow microreactor enables the safe syntheses, in the laboratory and on a larger scale, of potentially hazardous substances like organic azides [8].

Organic azides can be applied to such diverse fields as rocket fuels, explosives, photoaffinity labeling (PAL) agents [9], surface functionalization [10] and nanomaterial synthesis [11]. The synthesis of amines [12] and nitrogen heterocycles including aziridines, azirines, azepines, carbazoles, furoxanes, tetrazoles and triazoles [3, 13] are based on organic azide; as is the generation of nitrenes [3, 14].

Several synthetic routes have been developed for the synthesis of azides, which include nucleophilic substitution, diazotization and diazotransfer reactions.

Contemporary azide syntheses mostly are based on nucleophilic substitutions (S_N) reaction, which are the method of choice for making alkyl-, benzyl-, allyl-, acyl- and heteroaryl-azides [15]. Sodium or potassium azide is used as source of the nucleophile and reactions performed in DMF [16] or DMSO [17] solution.

Azide chemistry has been associated with the hazards of working with high-energy-density substances since its beginning. **Explosions** *and* **detonations** *occurred during the preparation of certain azides. Therefore guides and rules were developed for the safe handling and estimation of the explosive nature of such substances* [18].

In the early days of azide chemistry steam distillation was used to isolate aromatic azides from reaction mixtures [19]. In the case of alkyl azides, the crude product usually was obtained by liquid-liquid extraction. The laboratory scale purification of crude azides is possible by distillation or flash chromatography [20]; however large scale chromatography should normally be avoided.

2. Results and discussion

Fluorous chemistry, introduced more than two decades ago, offers an exceedingly valuable technique for isolation processes [21]. Dispersion interactions between fluorous molecules such as perfluoroalkanes, perfluoroalkyl ethers, and perfluoro(trialkylamines) are weak thus such compounds are volatile. Moreover, intermolecular attraction forces between fluorous and organic

molecules or water are even weaker [22] which results in their low solubility in each other (cf. Hildebrand solubility parameters of fluorocarbons, common organic solvents and water [23]).

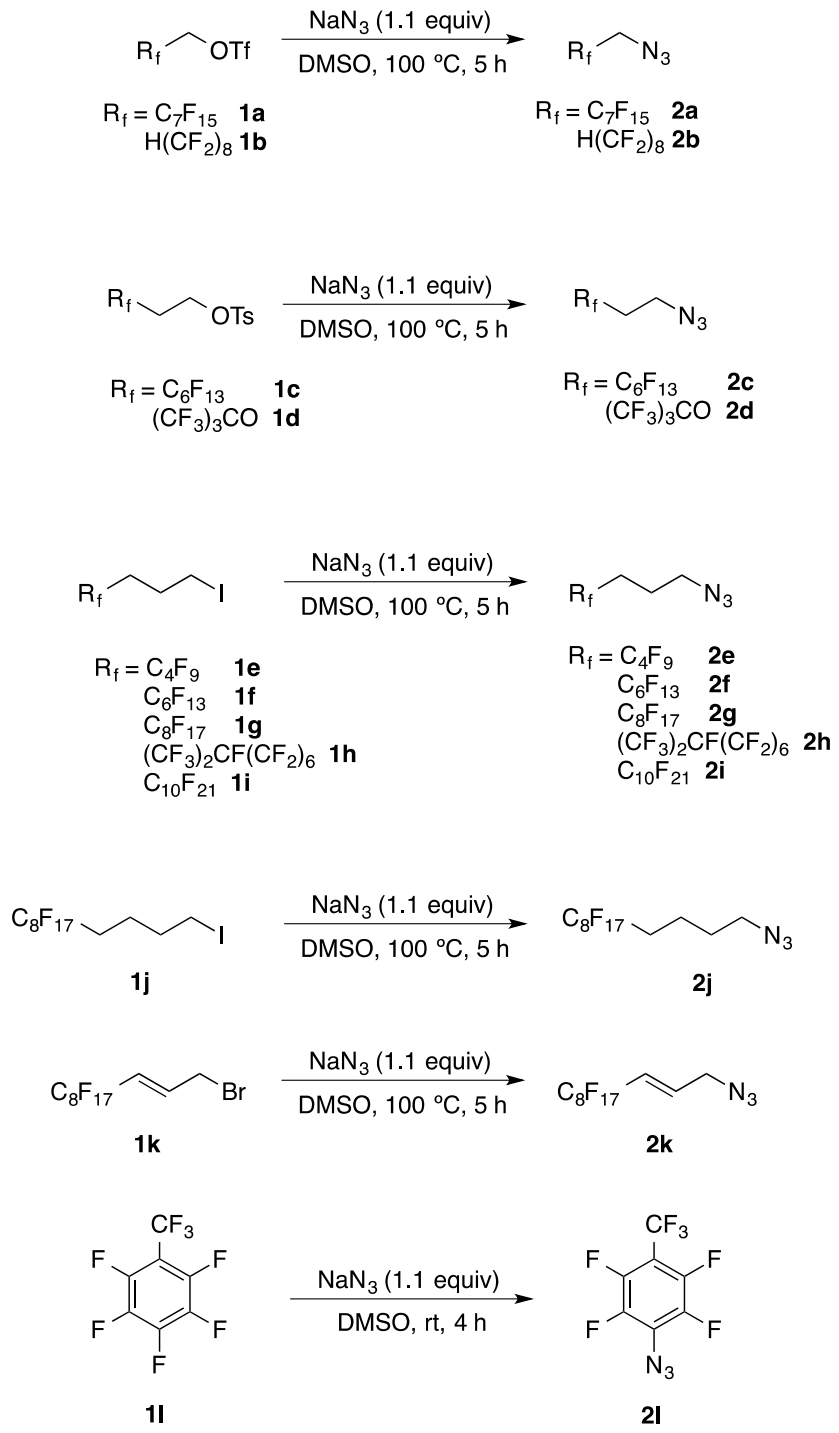
Azidotrifluoromethane (b. p. -28.5°C) [24], which is formally a combination of the shortest fluorous ponytail (R_{f1} = CF_3) and the azido group, is considered to be the parent compound for all fluorous azides (Figure 1.). We thought that the substitution of CF_3-group with longer perfluoroalkyl groups (C_nF_{2n+1} = R_{fn}) and the introduction of different length of insulating groups between the trifluoromethyl and the azido groups could allow the construction of F-organic azides with tunable reactivity and acceptable stability (e.g. nonexplosive, long shelf life).

$F\text{-}CF_2\text{-}N_3$
$R_f\text{-}CF_2\text{-}CH_2\text{-}N_3$
$R_f\text{-}CF_2\text{-}CH_2\text{-}CH_2\text{-}N_3$
$(CF_3)_3C\text{-}O\text{-}CH_2\text{-}CH_2\text{-}N_3$
$R_f\text{-}CF_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}N_3$
$R_f\text{-}CF_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}N_3$
$p\text{-}CF_3\text{-}C_6F_4\text{-}N_3$

Figure 1. Evolution of fluorous azides

We also considered whether steam distillation would be a suitable method for the isolation of fluorous azides, since they are immiscible with water and volatile. *Indeed, we observed that this was the case.* As a limiting factor, however, azides should be stable at the steam distillation temperature (~100 °C).

Fluorous azides (**2a-l**) were synthesized by the reaction of (perfluoroalkyl)alkyl sulfonates (**1a-d)** or (perfluoroalkyl)alkyl halides (**1e-k**) and $CF_3C_6F_5$ (**1l**) and a slight excess of ~0.5 M sodium azide in DMSO at 100 °C for 5 h. The crude fluorous azides (**2a-l**) were isolated from the reaction mixture by steam distillation in good to excellent yields and in high purity (GC assay ≥98%) (Scheme 1, Table 1.). The precursor (perfluoroalkyl)alkyl sulfonates (**1a-d**) and halides (**1e-k**) were synthesized and purified as published (GC assay ≥98%, cf. Experimental Section).



Scheme 1. Synthesis of *F*-azides by nucleophilic substitution reactions

Table 1. Selected Physical Properties and Yields of Fluorous Azides [a]

Azide [a]	**MW [g/mol]**	**N [%]**[b]	**Boiling Point** [c] **[°C/mmHg]**	**Yield** [d] **[%]**	**Scale [mmol]**
2a (p.n.c.) [25]	425.10	9.88	61-62/$_{1}$	85	50
2b (n.c.)	457.11	9.19	86-87/$_{15}$	78	20
2c [13, 26]	389.12	10.80	67-68/$_{15}$	85	120
2d [27]	305.10	13.77	140/$_{760}$	81	60
2e (n.c.)	303.13	13.86	53-55/$_{15}$	85	8
2f (p.n.c.) [28]	403.14	10.42	84-85/$_{15}$	95	100
2g (p.n.c.) [29]	503.16	8.35	104-105/$_{15}$	84	10
2h (n.c.)	553.17	7.60	114-116/$_{15}$	77	6
2i (n.c.)	603.17	6.97	mp 52-53	88	7
2j (p.n.c.) [30]	517.18	8.12	118-120/$_{15}$	79	7
2k (n.c.)	501.14	8.38	103-104/$_{15}$	43	6
2l [16, 31][e]	259.08	16.22	54-55/$_{5}$	81	9 [e]
1-$C_8H_{17}N_3$ [32]	155.24	27.07	73-75/$_{3}$	89	14

[a] n. c. = new compound; p.n.c = prepared or purchased, but not characterized.

[b] Using the rule of the carbon to nitrogen ratio only 1-octyl azide should be considered as an unsafe azide [5b].

[c] Boiling point values for **2a-k** were determined by distillation of pure azides and disclosed first time here.

[d] The steam-distilled azides are of high purity (GC assay: ≥98%, cf.: Experimental Section).

[e] At larger scale the exothermic reaction of **1l** and NaN_3 should be controlled by the addition of the NaN_3 solution.

Dipolar-aprotic solvents DMSO, DMF and CH_3CN are the most suitable for azidation of R-X type compounds and for their work-up water – ether partition is the method of choice for azide isolation. However, when we used this technique for the isolation of **2d** (b. p. = 140 °C) significant product loss was observed during the atmospheric evaporation of the ether solvent due to its volatility, which is an unusual property compared with classical organic compounds having similar boiling points. Consequently we adapted the so-called 'concentrate' work-up procedure, without using solvents for collecting the lower fluorous phase [33].

All but one azide **2k** were obtained in good to excellent yields (Table 1.). Although the precursor *F*-allylic bromide **1k** was consumed quantitatively, only 43% yield of azide **2k** was obtained as a colorless liquid using steam distillation. However, on longer standing at room temperature this oily product became amorphous white solid insoluble in common organic solvents. The other fluorous azides appeared unchanged if they were kept at ambient temperature for several weeks.

For the synthesis of azides with one methylene spacer, we used triflates **1a** and **1b** due to the well documented reluctance of $R_fCH_2OSO_2R$ type sulfonates to react with nucleophiles [34]. Some $R_fCH_2N_3$ type azides with one methylene spacer have been prepared using mesylates $R_fCH_2OSO_2CH_3$ under forcing conditions (NaN_3-DMSO/110 °C, 24 h, 18-crown-6) allowed by their higher stability [6].

Tosylates **1c** and **1d** with a two-carbon spacer showed adequate reactivity with sodium azide to afford **2c** and **2d,** respectively, in excellent yields. Perfluoroalkyl-ethyl azide **2c** has been prepared

for the first time by the reaction of $C_6F_{13}CH_2CH_2I$ with NaN_3 in wet *t*-butyl alcohol, but as a difficult to separate mixture of the product and unreacted $C_6F_{13}CH_2CH_2I$ [26b].

The reaction of fluorous iodides **1e**-**1j** with sodium azide occurs as easily as with 1-iodooctane, since the propylene- and butylene spacers almost completely insulate the electron withdrawing effect of the perfluoroalkyl-chain from the reaction center [21].

The fluorine to azide exchange reaction in DMSO on the activated aromatic system of octafluorotoluene **1l** occurred in *para*-position, as reported for the cases of using CH_3CN [30] or DMF [16] solvents and NaN_3, and azide **2l** was isolated in excellent yield.

All crude azide products isolated by steam distillation showed high GC purity (GC assay ≥98%). Their purity can further be improved by distillation at atmospheric or reduced pressure (Table 1.)

Table 2. Selected spectral data of fluorous azides.

	$\nu_{as}(cm^{-1})$	$\nu_{ps}(cm^{-1})$	$\sigma^{15}N$, ppm	$\sigma^{15}N$, ppm
2a	2116	1306	-340.6	-154.1
2b	2116	1308	-340.7	-154.1
2c	2109	1238	-330.5	-152.9
2e	2103	1225	-329.8	-152.4
2f	2103	1239	-329.7	-152.3
2g	2103	1241	-329.7	-152.3
2h	2104	1255	-329.9	-152.5
2i	2106	1258	-329.9	-152.6
2j	2102	1242	-329.9	-151.8

IR spectra of azides **2a**-**l** show that asymmetric stretching vibrations of azide groups appear near 2100 cm^{-1}, and their frequency depends on the number of methylene groups between the azide group and the fluorous chain (**2a**, **2c**, **2f**) but varied only slightly with the length of the perfluorinated moiety (**2e**-**i**). The frequency of the symmetric stretching vibration of the azide group (between 1306 and 1225 cm^{-1}) depends both on the length of the spacer and the fluorous chain. ^{15}N NMR data show the same tendency. The difference in the chemical shifts is more pronounced in the case of the α nitrogen atom (Table 2.).

3. Conclusion

In conclusion a series of fluorous azides were synthesized by nucleophilic substitution reactions. Steam distillation proved to be a mild and effective method for isolation of pure azides from the reaction mixture up to 50 g scale. They can be distilled under reduced pressure without decomposition to further improve their purity.

4. Experimental Section

4.1. General description of methods and materials

The precursor fluorous alkylation reagents were prepared as reported: **1a** [35], **1c** [36], **1d** [30], **1e-j** [37]. NMR spectra (^{1}H, ^{19}F, ^{1}H-^{15}N HMBC, ^{1}H-^{19}F HMBC) were recorded on a Bruker Avance III 400 MHz instrument using a 5 mm ^{1}H- and BB-channel probe head at room temperature (295 ± 2 K) in $CDCl_3$. Chemical shifts (δ) are given in ppm units relatively to the internal standards: TMS (δ = 0.00 for ^{1}H) and $CFCl_3$ (δ = 0.00 for ^{19}F). The ^{15}N spectra were projected from ^{1}H-^{15}N HMBC experiment: reference was CH_3NO_2 (δ = 0.00 for^{15}N). GC-MS spectra were recorded on a Perkin Elmer Precisely (Clarus 500 Gas Chromatograph, Clarus 560 D Mass Spectrometer, 70eV). IR spectra were recorded on Bruker Alpha Spectrophotometer. Melting points were determined on a Boetius micro melting point apparatus and are uncorrected. Purity of *F*-azides was determined by GC (Hewlett-Packard 5890 Series II; PONA [crosslinked methylsilicon gum] 50 m × 0.2 mm × 0.5 mm column, H_2 carrier gas, FID detection); the liquid ones with neat injection.

Warning: *Organic azides are considered as explosives whenever the azido content is remarkably high. Of course, there is no sharp threshold at which the explosive hazard starts. However, as a rule of thumb violent decomposition reactions are expected for azido compounds having a (C + O)/N ratio of < 3 [4c, 5b]. Appropriate safety measures (e.g small scale reactions, safety shields, manipulators, etc) should be used when working with explosive azides (e.g. copper(I) azide, mono-, di- and polyazido alkanes or arenes of lower molecular weight) and their incidental formation should be avoided; for more details, see [3, 4, 18]. In addition the toxic nature of hydrazoic acid and sodium azide should also be considered [3, 4, 18].*

*2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9-Hexadecafluorononyl-1-trifluoromethanesulfonate (**1b**)*

To a stirred solution of $H(CF_2)_8CH_2OH$ (13.0 g, 30 mmol) and 2.85 g (36 mmol) of pyridine in 60 ml of CH_2Cl_2 at 0-5°C was added 10.2 g (36 mmol) trifluoromethanesulfonic anhydride during 1 h. The mixture was stirred for 36 h at 20°C and ice-water added to dissolve the precipitated salt, while some CH_2Cl_2 to dissolve the phase separating oil. Then the separated organic layer was washed with brine, dried (Na_2SO_4), filtered and the solvent evaporated. The residual oil was purified by short-path distillation to afford **1b** as a colorless liquid. Yield: 15.0 g (93%) bp = 135-140 °C/30 mmHg (Lit. [38] bp = 117-119 °C/20 mmHg). GC-FID assay: 98.0 %.

^{1}H NMR ($CDCl_3$): δ 4.82 (t, 2H, $^{3}J_{HF}$ = 12.3 Hz, C**H**$_2$O); 6.05 (tt, 1H, $^{2}J_{HF}$= 51.8 Hz, $^{3}J_{HF}$ = 5.1Hz, **H**CF_2,). ^{19}F NMR ($CDCl_3$): δ -74.94 (s, 3F), -120.51 (m, 2F), -122.46 (m, 6F), -123.53 (m, 2F), -123.93 (m, 2F), -130.09 (m, 2F), -137.96 (m, 2F). IR (KBr) ν, cm^{-1}: 1432, 1212, 1144, 1027, 820, 764, 703, 661, 612, 540, 504, 477. MS (EI) *m/z* 564 [M$^+$], 495, 345, 231, 213, 181, 163, 151, 131, 113, 100, 99, 83, 69, 51 Da.

*(E)-1-Bromo-4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundec-1-ene (**1k**)* (n. c.)

To a solution of *E*-$C_8F_{17}CH{=}CHCH_2OH$ [39] (30.0 g, 63 mmol) in 100 ml of ether PBr_3 (7.21 g, 2.50 ml, 26.6 mmol) was added drop-by-drop at 0°C with stirring, then refluxed and stirred for 9 h. Cooled to 10 °C and the excess of PBr_3 decomposed by addition of water. The water and ether layer were separated, the water phase was extracted with ether, and then the combined organics were washed with brine and dried (Na_2SO_4). It was filtered and the solvent evaporated then the title F-allyl bromide was isolated by fractional distillation. Yield: 30.2 g (89%) colorless liquid; bp = 150-155 °C/15 mmHg. GC-FID assay: 98.1% (96.1% *E* – 3.9 % *Z* ratio).

^{1}H NMR ($CDCl_3$): δ 3.99 (2H, m, C**H**$_2$Br), 5.90 (dt, 1H, $^3J_{HH(E)}$ = 15.39 Hz, $^3J_{HH}$= 11.95 Hz, CH_2C**H**), 6.55 (dtt, 1H, $^3J_{HH(E)}$ = 15.39 Hz, $^3J_{HF}$ = 7.1 Hz, $^4J_{HF}$ = 2.2 Hz, CF_2C**H**). ^{19}F NMR ($CDCl_3$): δ -81.60 (t, 3F, $^3J_{FF}$ = 10.1 Hz), -112.68 (m, 2F), -121.87 (m, 2F), -122.38 (m, 4F), -123.23 (m, 2F), -123.78 (m, 2F), -126.74 (m, 2F). IR (KBr) ν, cm^{-1}: 1721, 1675, 1440, 1369, 1314, 1206, 1150, 1014, 1068, 970, 876, 792, 722, 705, 656, 559, 531. MS (EI) *m/z* 538 [M^+], 459, 389, 345, 219, 181, 169, 119, 90, 69 Da.

4. 2. General procedure for the synthesis of azides

A stirred solution of NaN_3 (0.715 g, 11 mmol) and perfluoroalkyl-alkyl halide or perfluoroalkyl-alkyl sulfonate (10 mmol) in DMSO (22 ml) was heated to 100 °C for 5 h. Then the reaction mixture was allowed to cool to room temperature and water (60 ml) was added. The resulting mixture was steam distilled applying an external steam generator. The phases of the distillate were separated; the fluorous layer was dried over Na_2SO_4. The obtained *"crude product"* (GC-FID assay ≥98%) can further be purified by distillation or crystallization (GC-FID assay ≥99.5%).

*4.2.1. 8-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6,7,7-pentadecafluorooctane (**2a**)*

A solution of NaN_3 (3.90 g, 60 mmol) and **1a** (28.8 g, 54.1 mmol) in DMSO (120 ml) was reacted. Yield: 21.4 g (93%) crude by steam distillation, which on distillation gave 19.6 g (85%) colorless viscous oil, bp 61-62 °C/12 mmHg, GC-FID assay: 99.0 %. ^{1}H NMR ($CDCl_3$): δ 3.77 (t, 2H, $^3J_{HF}$ = 14.5 Hz). ^{19}F NMR ($CDCl_3$): δ -81.33 (t, 3F, $^3J_{FF}$ = 9.9 Hz), -117.94 (m, 2F), -122.50 (m, 4F), -123.22 (m, 4F), -126.63 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -154.1, -340.6. IR (KBr) ν, cm^{-1}: 2116, 1306, 1205, 1147, 436. MS (EI) *m/z* 425 [M^+], 397 [M-N_2]$^+$, 378, 328, 231, 219, 181, 169, 131, 119, 100, 78, 69, 56 Da.

*4.2.2. 9-Azido-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorononane (**2b**)*

A solution of NaN_3 (1.43 g, 22 mmol) and **1b** (11.3 g, 20.0 mmol) in DMSO (18 ml) was reacted. Yield: 7.13 g (78 %) colorless viscous oil, bp 86-87 °C/15 mmHg, GC-FID assay: 99.0. ^{1}H NMR ($CDCl_3$): δ 3.76 (t, 2H, $^3J_{HF}$ = 14.51 Hz, C**H**$_2N_3$), 6.03 (tt, 1H, $^2J_{HF}$ = 51.80 Hz, $^3J_{HF}$ = 5.13 Hz, **H**CF_2). ^{19}F NMR ($CDCl_3$): δ -117.72 (m, 2F), -122,10 (m, 6F), -123.36 (m, 2F), -123.55 (m, 2F), -129.61 (m, 2F), -137.32 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -154.1, -340.7. IR (KBr) ν, cm^{-1}: 2116, 1308, 1208, 1146, 434. MS (EI) *m/z* 457 [M^+], 430, 410, 360, 181, 131, 119 Da.

*4.2.3. 8-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorooctane (**2c**)*

A solution of NaN_3 (8.33 g, 128 mmol) and **1c** (60.4 g, 117 mmol) in DMSO (260 ml) was reacted. Yield: 42.8 g (94%) crude by steam distillation, which on distillation gave 38.6 g (85%) colorless viscous oil, bp 67-68 °C/15 mmHg, GC-FID assay: 98.80%. ^{1}H NMR ($CDCl_3$): δ 3.61 (t, 2H, $^3J_{HH}$ = 7.2 Hz, C**H**$_2$N$_3$), 2.39 (tt, 2H, $^3J_{HH}$ = 7.2 Hz, $^3J_{FH}$ = 18.5 Hz, C**H**$_2$CH$_2$N$_3$). ^{19}F NMR ($CDCl_3$): δ -88.36 (t, 3F, $^3J_{FF}$ = 9.9 Hz), -114.44 (m, 2F), -122.36 (m, 2F), -123.35 (m, 2F), -124.01 (m, 2F), -126.63 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -152.9, -330.5. IR (KBr) ν, cm^{-1}: 2109, 1238, 1202, 1145, 441. MS (EI) *m/z* 389 [M$^+$], 361 [M-N$_2$]$^+$, 340, 169, 131, 119, 100, 95, 69, 42 Da.

*4.2.4. 5-Azido-1,1,1-trifluoro-2,2-bis(trifluoromethyl)-3-oxapentane (**2d**)*

A solution of NaN_3 (4.161 g, 64 mmol) and **1d** (25.00 g, 58 mmol) in DMSO (75 ml) was reacted. Yield: 14.2 g (81 %) colorless easily moving liquid, bp 140 °C/760 mmHg, GC-FID assay: 98.80%. The spectroscopic data were in agreement with a sample prepared and reported previously in this laboratory [27].

*4.2.5. 7-Azido-1,1,1,2,2,3,3,4,4-nonafluoroheptane (**2e**)*

A solution of NaN_3 (0.572 g, 8.8 mmol) and **1e** (3.10 g, 8.0 mmol) in DMSO (17 ml) was reacted. Yield: 2.05 g (85 %) colorless viscous oil, 53-55 °C/15 mmHg, GC-FID assay: 98.0%. ^{1}H NMR ($CDCl_3$): δ 3.42 (t, 2H, $^3J_{HH}$ = 6.5 Hz, C**H**$_2$N$_3$), 2.18 (m, 2H, C**H**$_2$CH$_2$N$_3$), 1.90 (m, 2H, C**H**$_2$CH$_2$CH$_2$N$_3$). ^{19}F NMR ($CDCl_3$): δ -81.21 (t, 3F, $^3J_{FF}$ = 9.4 Hz), -114.62 (m, 2F), -124.54 (m, 2F), -126.16 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -152.5, -329.7. IR (KBr) ν, cm^{-1}: 2103, 1225, 1133, 442. MS (EI) *m/z* 303 [M$^+$], 275 [M-N$_2$]$^+$, 169, 119, 69, 42 Da.

*4.2.6. 9-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluorononane (**2f**)*

A solution of NaN_3 (7.37g, 0.113 mol) and **1f** (50.4 g, 0.103 mol) in DMSO (205 ml) was reacted. Yield: 39.75 g (95 %) colorless viscous oil, bp 104-105 °C/15 mmHg, GC-FID assay: 98.30%. ^{1}H NMR ($CDCl_3$): δ 3.43 (t, 2H, $^3J_{FH}$ = 6.5 Hz, C**H**$_2$N$_3$), 2.18 (m, 2H, C**H**$_2$CH$_2$N$_3$), 1.91 (m, 2H, C**H**$_2$CH$_2$CH$_2$N$_3$). ^{19}F NMR ($CDCl_3$): δ -81.31 (t, 3F, $^3J_{FF}$ = 9.9 Hz), -114.71 (m, 2F), -122.40 (m, 2F), -122.36 (m, 2F), -122.95 (m, 2F), -126.65 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -152.5, -329.7. IR (KBr) ν, cm^{-1}: 3444, 2955, 2879, 2103, 1456, 1357, 1239, 1204, 1145. MS (EI) *m/z* 403 [M$^+$], 375 [M-N$_2$]$^+$, 169, 119, 69, 42 Da.

*4.2.7. 11-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluoroundecane (**2g**)*

A solution of NaN_3 (0.501 g, 7.7 mmol) and **1g** (4.13 g, 7.0 mmol) in DMSO (15 ml) was reacted. Yield: 2.37 g (84 %) colorless viscous oil, bp 104-105 °C/15 mmHg, GC-FID assay: 98.8%. ^{1}H NMR ($CDCl_3$): δ 3.43 (t, 2H, $^3J_{HH}$ = 9.9 Hz, C**H**$_2$N$_3$), 2.18 (m, 2H, C**H**$_2$CH$_2$N$_3$), 1.90 (m, 2H, C**H**$_2$CH$_2$CH$_2$N$_3$). ^{19}F NMR ($CDCl_3$): δ -81.47 (t, 3F, $^3J_{FF}$ = 10.1 Hz), -114.77 (m, 2F), -122,18 (m, 2F), -122.40 (m, 4F), -123.23 (m, 2F), -123.93 (m, 2F), -126.69 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -152.4, -329.7. IR (KBr) ν, cm^{-1}: 3358, 2955, 2879, 2103, 1642, 1456, 1357, 1320, 1205, 1150,

1116, 1076, 1031, 1000, 876, 825, 780, 737, 722, 705, 656, 622, 585, 560, 529, 431, 411, 408). MS (EI) *m/z* 503 [M^+], 475 [M-N_2]$^+$, 456, 169, 131, 119, 69, 42 Da.

*4.2.8. 11-Azido-1,1,1,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluoro-2-(trifluoromethyl)undecane (**2h**)*

A solution of NaN_3 (0.415 g, 6.4 mmol) and **1h** (3.72 g, 5.8 mmol) in DMSO (12 ml) was reacted. Yield: 2.36 g (73 %) colorless viscous oil, bp 114-116 °C/15 mmHg, GC-FID assay: 98.0 %. ^{1}H NMR ($CDCl_3$): δ 3.42 (t, 2H, $^3J_{HH}$ = 6.5 Hz, CH_2N_3), 2.18 (m, 2H,C**H**$_2$$CH_2N_3$), 1.90 (m, 2H,C**H**$_2$$CH_2CH_2N_3$). ^{19}F NMR ($CDCl_3$): δ -72.13 (m, 6F), -114.49 (m, 2F), -115.17 (m, 2F), -120.92 (m, 2F), -121.67 (m, 2F), -121.84 (m, 2F), -123.63 (m, 2F), -186.30 (m, 1F). ^{15}N NMR ($CDCl_3$): δ -152.4, -330.0. IR (KBr) ν, cm^{-1}: 2104, 1255, 1207, 1115, 985, 440. MS (EI) *m/z* 553 [M^+], 506, 131, 69, 56, 42 Da.

*4.2.9. 13-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10-henicosafluorotridecane (**2i**)*

A solution of NaN_3 (0.465 g, 7.2 mmol) and **1i** (4.49 g, 6.5 mmol) in DMSO (16 ml) was reacted. After steam distillation the solid product was extracted with DCM (30 ml). The organic phase was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Yield: 3.47 g (88 %) white wax-cloth, mp 52-53 °C, GC-FID assay: 99.3 %. ^{1}H NMR ($CDCl_3$): δ 3.43 (t, 2H, $^3J_{HH}$ = 6.1 Hz, CH_2N_3), 2.18 (m, 2H, C**H**$_2$$CH_2N_3$), 1.90 (m, 2H, C**H**$_2$$CH_2$ CH_2N_3). ^{19}F NMR ($CDCl_3$): δ -81.38 (t, 3F, $^3J_{FF}$ = 9.9 Hz), -114.77 (m, 2F), -122.23 (m, 10F), -123.24 (m, 2F), -123.96 (m, 2F), -126.68 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -152.3, -329.9. IR (KBr) ν, cm^{-1}: 2106, 1212, 1152, 588. MS (EI) *m/z* 575 [M-N_2]$^+$, 556, 504, 169, 131, 119, 104, 69, 56, 42 Da.

*4.2.10. 12-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluorododecane (**2j**)*

A solution of NaN_3 (0.508 g, 7.8 mmol) and **1j** (4.25 g, 7.1 mmol) in DMSO (15 ml) was reacted. After steam distillation the product was extracted with DCM (30 ml). The organic phase was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Yield: 2.88 g (79 %), bp 118-120 °C/15 mmHg, GC-FID assay: 97.7 %. ^{1}H NMR ($CDCl_3$): δ 3.34 (t, 2H, $^3J_{FH}$ = 6.1 Hz), 2.11 (m, 2H), 1.70 (m, 4H). ^{19}F NMR ($CDCl_3$): δ -81.36 (t, 3F, $^3J_{FF}$ = 9.8 Hz), -114.93 (m, 2F), -122.22 (m, 2F), -122.42 (m, 4F), -123.22 (m, 2F), -123.99 (m, 2F), -126.64 (m, 2F). ^{15}N NMR ($CDCl_3$): δ -151.9, -329.0. IR (KBr) ν, cm^{-1}: 3351, 2957, 2882, 2102, 1659, 1462, 1442, 1352, 1326, 1242, 1206, 1150, 1117, 1038, 974, 919, 873, 826, 791, 736, 722, 705, 656, 585, 560, 529, 447, 441, 422, 408. MS (EI) *m/z* 487, 467, 440, 389, 181, 169, 148, 131, 121, 90, 69, 56 Da.

*4.2.11. 11-Azido-1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptadecafluoroundec-9-ene (**2k**)*

A solution of NaN_3 (0.436 g, 6.7mmol) and **1k** (3.28 g, 6.1 mmol) in DMSO (13 ml) was reacted. After steam distillation the solid product was extracted with DCM (20 ml). The organic phase was dried over Na_2SO_4, and the solvent was removed under reduced pressure. Yield: 1.32 g (43 %) colorless oil, bp 103-104 °C/15 mmHg, GC-FID assay: 97.6%. ^{1}H NMR ($CDCl_3$): δ 6.42 (m, 1H), 5.95 (1H, ~q, J=13.1 Hz), 4.04 (m, 2H). ^{19}F NMR ($CDCl_3$): δ -81.40 (t, 3F, $^3J_{FF}$ = 9.8 Hz), -112.47 (m, 2F), -121.87 (m, 2F), -122.42 (m, 4F), -123.22 (m, 2F), -123.87 (m, 2F), -126.65 (m,

2F). ^{15}N NMR ($CDCl_3$): δ -152.9, -331.3. IR (KBr) ν, cm^{-1}: 2113, 1682, 1438, 1354, 1209, 1150, 989, 437, 415. MS (EI) *m/z* 501[M^+], 473 [M-N_2]$^+$, 381, 169, 135, 131, 119, 104, 77, 69, 54 Da.

*4.2.12. 1-Azido-4-trifluoromethyl-2,3,5,6-tetrafluorobenzene (**21**)*

Warning: *multiple fluorine substitution with formation of explosive side products should be avoided* (Table 1.). A solution of NaN_3 (0.608 g, 9.4 mmol) and $CF_3C_6F_5$ (2.00 g, 8.5 mmol) in DMSO (17 ml) was stirred at room temperature for 4 h. Yield: 1.78 g (81 %) yellow oil, 54-55 °C/5 mmHg, GC-FID assay: 99.8%. ^{19}F NMR ($CDCl_3$): δ -55.92 (m, 3F), -140.39 (m, 2F), -150.09 (m, 2F). MS (EI) *m/z* 259 [M-N_2]$^+$, 231, 212, 181, 162, 131, 117, 93, 69 Da.

4.2.13. 1-Azido-n-octane

A solution of NaN_3 (1.02 g, 15.6 mmol) and 1-iodooctane (3.42g, 14.2 mmol) in DMSO (30 ml) was reacted. Yield: 1.97 g (89 %) colorless oil, bp 73-75 °C/3 mmHg, GC-FID assay: 99.9%. ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 3H), 1.28 (m, 10H), 1.59 (m, 2H), 3.25 (t, 2H, $^3J_{HH}$ = 6.84 Hz).

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