

HETEROCYCLES, Vol. 68, No. 2, 2006, pp. 307 - 321. © The Japan Institute of Heterocyclic Chemistry
Received, 24th November, 2005, Accepted, 12th January, 2006, Published online, 17th January, 2006. COM-05-10633

DESIGNING FLUOROUS DOMAINS. SYNTHESIS OF A SERIES OF PYRIDINIUM SALTS BEARING A PERFLUOROALKYLATED AZOLE MOIETY

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Abstract – The synthesis of a series of *N*-methylpyridinium salts bearing a perfluoroalkylated 1,2,4-oxadiazole or 1,2,4-triazole moiety is reported. X-Ray structures of representative perfluoroalkyl-triazolylpyridine (**15**) and methylpyridinium iodide salt (**5a**) are reported. Their crystal packing clearly shows segregation between the aromatic and parallel double layer fluorinated regions.

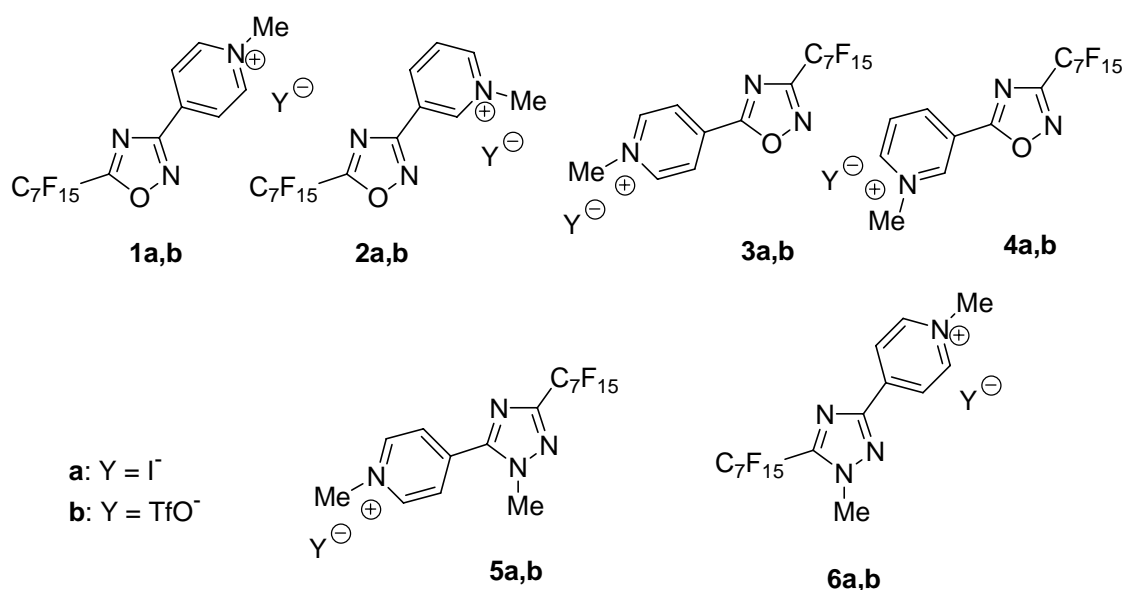
INTRODUCTION

In recent years, there has been a great interest in perfluoroalkylated heterocycles because of their applications in various fields such as agriculture, drug design, materials science and fluorine chemistry.¹ Recent studies reveal that polyfluoro- or perfluoroalkylated azolium or azinium salts find a new and growing interest as *fluorous domains*² and could be used as fluorous surfactants, as phase transfer catalysts, as potential fluorous liquid crystals or ionic liquids. Historically, organic cations of ionic liquids contained *N,N'*-dialkylimidazolium³ or *N*-alkylpyridinium⁴ structures and, more recently *N*-alkyl-*N'*-polyfluoroalkyl-imidazolium,⁴ *N*(4)-polyfluoroalkyl-1,2,4-triazolium,⁵ and C(3)-perfluoroalkyl-1,2,4-triazolium⁶ salts have been also reported. For the synthesis of fluorinated derivatives, it is noteworthy that introduction of a fluorinated chain during quaternization reaction of imidazoles or triazoles can only lead to *N*-polyfluoroalkylated compounds. In fact, quaternization with perfluoroalkyl iodides or bromides is not a feasible route since fluorine atoms decrease the S_N2 reactivity of the perfluoroalkyl halide. On the other hand, the synthesis of C(3)-perfluoroalkyltriazolium salts (the perfluoroalkyl chain being linked at the annular carbon atom) is achieved by construction of the triazole ring from perfluoroalkylated

precursors and subsequent quaternization at the N(4) annular nitrogen atom with an alkyl or a polyfluoroalkyl group.⁶

Related to our ongoing studies on fluorinated heterocyclic compounds,⁷ we became interested in the synthesis and characterization of pyridinium salts containing a five-membered heterocyclic moiety as a spacer between the azinium cation and a perfluoroalkyl chain (Chart 1). Structural features of these molecules represent ideal candidates for different applications; in fact, it is our opinion that a specific tuning of both their physical and chemical properties may be achieved by changing either the central heterocycle, the length and position of a perfluoroalkyl chain, or the linkage to the heterocycle-pyridine. An interesting example of this approach has been reported for non-fluorinated systems such as *N*-alkylpyridinium salts containing the 1,3,4-oxadiazole heterocycle bearing an *S*-alkyl moiety.⁸ Moreover, a combination of oxadiazoles with pyridinium groups for the modification of the electronic properties of the resulting salts has been emphasized in several studies.^{8,9}

Chart 1

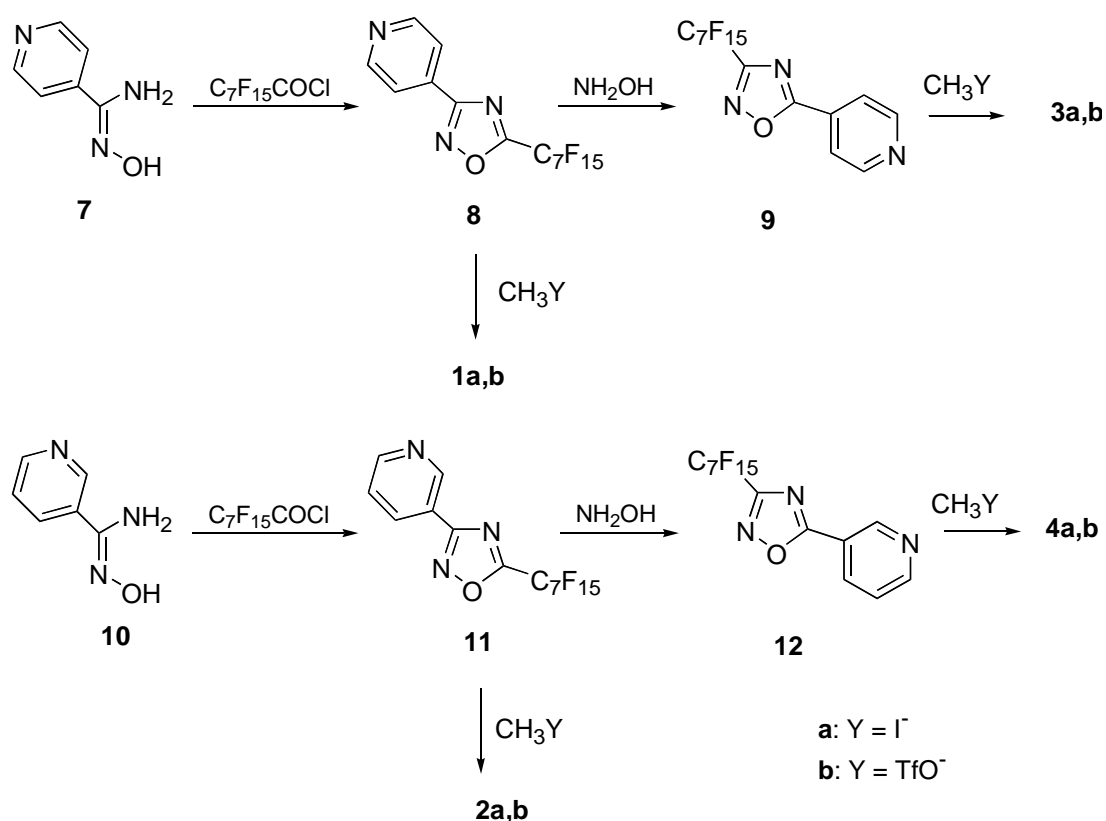


RESULTS AND DISCUSSION

In this work we focused our attention to *N*-methylpyridinium salts bearing a perfluoroalkylated 1,2,4-oxadiazole at C(4) or C(3) [(compounds **1-4**)] or a perfluoroalkylated 1,2,4-triazole moiety at C(4) [(compounds **5**) and (**6**)] (Chart 1). In this series, compounds (**1**) and (**3**) (as well as **2** and **4**, or **5** and **6**) are regioisomers which differ in the reciprocal position of the perfluoroheptyl chain and the pyridyl group with respect to the interspacing azole ring. Therefore we planned the synthesis of oxadiazolylpyridines (**8**, **9**, **11** and **12**) (Scheme 1) and triazolylpyridines (**14**) and (**15**) (Scheme 2), precursors of the corresponding pyridinium salts.

5-Perfluoroalkyloxadiazoles (**8**) and (**11**) have been prepared (in high yields) by exploiting the conventional amidoxime route.^{10,11} Thus, the reaction of the amidoxime (**7**) or (**10**) with pentadecafluorooctanoyl chloride in refluxing toluene in the presence of pyridine directly gave oxadiazole (**8**) or (**11**), respectively, through cyclodehydration of a intermediate *O*-perfluoroalkanoylamidoxime (Scheme 1). Contrary to this, for the preparation of 3-perfluoroalkylated regioisomers (**9**) and (**12**), the amidoxime route gave unsatisfactory results probably because of the low reactivity of the corresponding *O*-perfluoroalkanoylamidoxime towards the cyclodehydration reaction. Therefore, we took advantage of the *ANRORC* methodology¹² which has been successfully implemented in our laboratories.^{7d,7e,7i} Thus, the reaction of 5-perfluoroalkyloxadiazoles (**8**) and (**11**) with hydroxylamine in DMF at room temperature readily gave **9** and **12**, respectively, in good yields (Scheme 1).

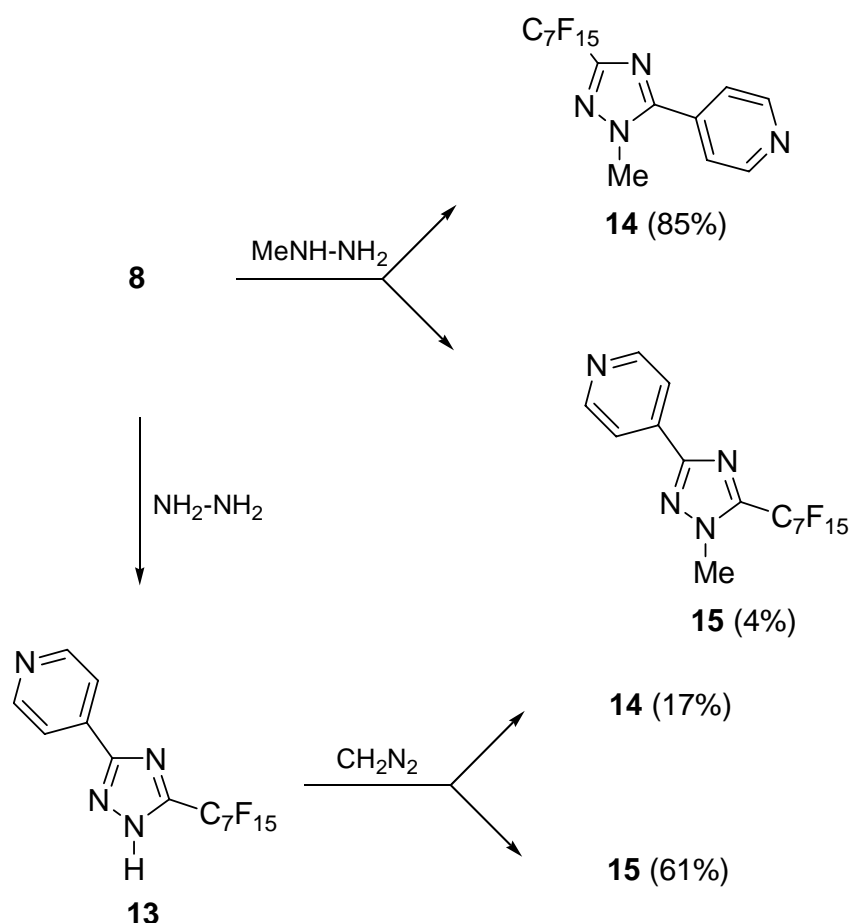
Scheme 1



For the preparation of (C)-perfluoroalkylated 1,2,4-triazoles, the literature reported different methodologies based on the heterocyclization of fluorinated precursors such as perfluoroalkylated amidines, amhydrazones, or perfluoroalkanoylhydrazines.^{6,11} However, for the synthesis of our compounds we again considered *ANRORC*-like rearrangements. Thus, in analogy with the previously observed reactivity,^{7d} hydrazinolysis of the easily prepared 5-perfluoroalkyloxadiazole (**8**) gave the triazole (**13**) (indicated in Scheme 2 as an arbitrary tautomer). On the other hand, the reaction of

compound (**8**) with methylhydrazine mainly gave 1-methyl-3-perfluoroalkyltriazole (**14**) (85%) together with few amounts of the regioisomer 1-methyl-5-perfluoroalkyltriazole (**15**) (4%) (Figure 1). Such a product distribution is the result of a preferential initial attack of the terminal NH₂ nitrogen of the reagent to the electrophilic C(5) of the oxadiazole ring.¹³ This observation is justified by the marked electrophilic character of the C(5), caused by both the fluorinated group and the pyridine moiety at C(3), which will be attacked by the less hindered (even though less nucleophilic) end of the bidentate nucleophile. Nevertheless, to obtain triazole (**15**) as a major product we performed the methylation reaction of compound (**13**) with diazomethane, which yielded a mixture of triazoles (**14**) (17%) and (**15**) (61%). As a matter of facts, both the latter two reactions represent two appealing complementary strategies for the synthesis of regioisomeric methyltriazoles (Scheme 2).

Scheme 2



Quaternization reactions to synthesize the whole series of salts (**1-6**) have been carried out by direct methylation of oxadiazolylpyridines and triazolylpyridines with suitable methylating reagents [methyl iodide (MeI) or methyl trifluoromethanesulfonate (MeOTf)] in MeCN. Both reagents furnished good yields of desired products which were characterized by analytical and spectroscopic data.

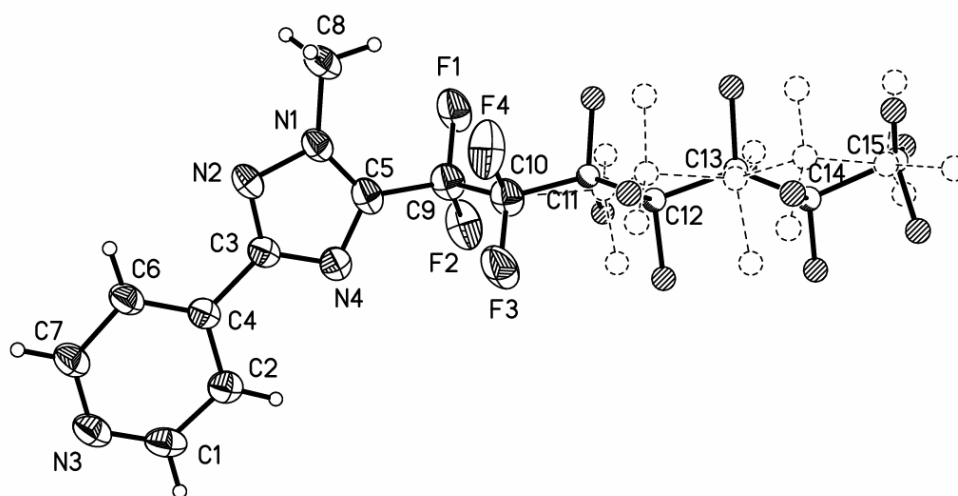


Figure 1. Structure of one of the two independent molecule of **15**, showing crystallographic atomic-numbering scheme (Ortep plot, 20% ellipsoids for non disordered atoms).

As far as it concerns the regiochemistry of the quaternization reaction, the literature reported that pyridine substituted oxadiazoles are quaternized at the pyridine nitrogen rather than at the oxadiazole ring nitrogen.¹⁴ In addition, NMR spectral data show a deshielding of pyridine hydrogens signals of the salts with respect to the starting oxadiazole. In the case of triazoles, instead, X-Ray analyses of compound (**5a**) (Figure 2) confirmed the quaternization at the pyridine nitrogen and, consequently, structure of the precursor (**14**) was also confirmed. Moreover, crystal features of representative perfluoroalkylated neutral molecule (**15**) and ionic structure (**5a**) clearly showed segregation of the fluororous domain from the aromatic region. In summary, the obtained results opened the way to the study of the synthesis of various *azole-spaced* perfluoroalkylated azinium salts as prospective new liquid crystals and fluorinated surfactants.

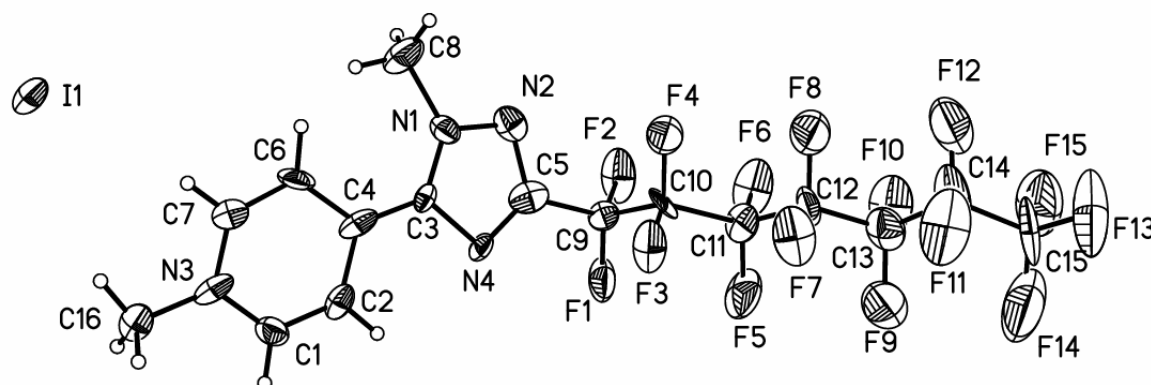


Figure 2. Structure of one of the two independent molecule of **5a**, showing crystallographic atomic numbering scheme (Ortep plot, 20% ellipsoids).

X-Ray crystallographic analyses

Single crystal X-Ray analysis has been performed for **15** and **5a**. Both compounds crystallized with two independent molecules, hereafter named A and B, in the unit cell. The structural refinement required a laborious work due to the poor quality of the crystals and to the flexibility¹⁵ and rotational disorder of the chain moiety,¹⁶ typically found in perfluoroalkylated compounds. However, the triazolylpyridine moiety of both **15** and **5a** refined without any difficulty, confirming the molecular configuration shown in Figure 1 and Figure 2, respectively. Moreover, although disordered, the perfluoroalkyl chains clearly showed an extended zig-zag conformation in both compounds and the peculiarity of crystal packing of each compound was well defined.

In **15**, the disorder of the two independent molecules A and B has been modelled by splitting part of the perfluorinated chains into two positions with site occupation factors refined to about 65% and 35%, respectively. The geometrical details given below refer to the major occupied conformation. In each of A and B molecules, the two heterocycles ring planes are nearly coplanar (mean dihedral angle $7.8(3)^\circ$ and are rotated with respect to the mean plane of the alkyl chain of about 100° . The extended conformation of the chain leads to a C5...C15 distances of about 9.1 and 8.9 Å for A and B, respectively. The connection between the triazolylpyridine moiety and the perfluoroalkyl chain may be described by the angle among the non-bonded atoms N3...C5...C15 which assumes a value of $138.0(5)^\circ$ in both molecules.

In **5a**, the disorder is expressed by the high values of the atomic thermal parameters of some perfluoroalkyl chain atoms and by some significant residual electron density around the iodine atoms. An absorption correction was applied to the intensity data, but this did not improve the least-squares refinement, perhaps due to the poor quality of the crystal and to the crystal intensity decay (about 27%) during data collection.

The two heterocycles ring planes showed different mutual orientation in molecules A and B. In A the pyridine and the triazole plane are rotated to each other of $14.0(2)^\circ$, while in B the corresponding dihedral angle is $52.8(2)^\circ$. The lengths of the alkyl chains (C5...C15 distances) are about 9.1 and 8.9 Å for A and B, respectively. The angles among the non-bonded atoms N3...C5...C15 which describes the dihedral angle between the triazolylpyridine moiety and the perfluoroalkyl chain plane are $141.6(2)$ and $132.2(2)^\circ$ for molecules A and B, respectively.

The crystal packing of both compound (**15**) and (**5a**) showed perfluoroalkyl regions with the chains disposed parallel to each other and well separated aromatic regions (see Figure 3 and Figure 4). This crystal organisation has been usually found in compounds containing a perfluoroalkyl chain.^{15,16,17} In **15** the crystal organisation showed the formation of chains, of alternate A and B molecules, connected by C1-H...F hydrogen bonds: each molecule acts as donor, towards the preceding molecule of the chain, and acceptor, towards the following one, of an hydrogen bond of the C1-H...F3 type [C1B-H...F3A: $2.41(1)\text{Å}$

and $165.0(2)^\circ$; C1A-H \cdots F3B: 2.42(1)Å and $166.2(2)^\circ$]. This hydrogen bonding network, as observed in crystal packing of **5a**, gives rise to zig-zag chains running parallel to *b* axis.

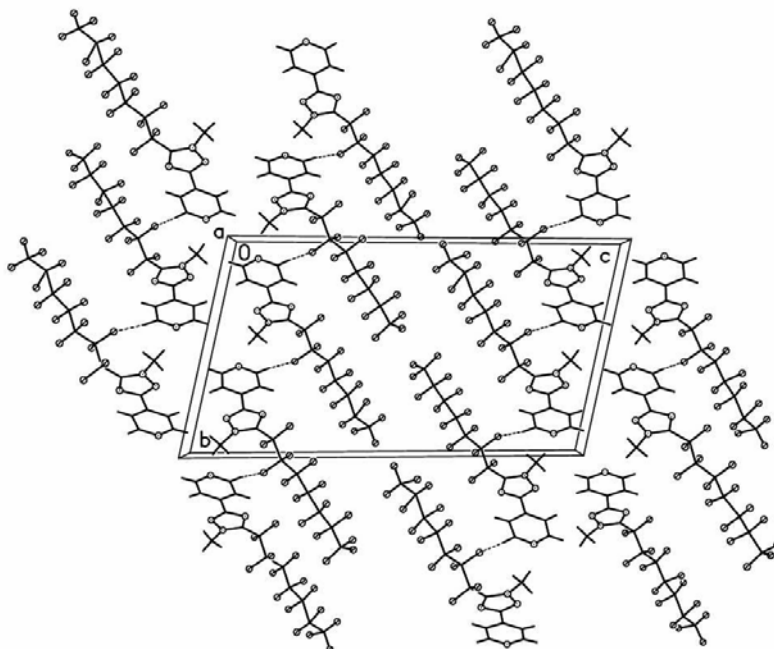


Figure 3. Cross-section of crystal packing of **15**. The figure shows the chains of alternated molecules (**A**) and (**B**), stacked and H-bond connected along *b* direction.

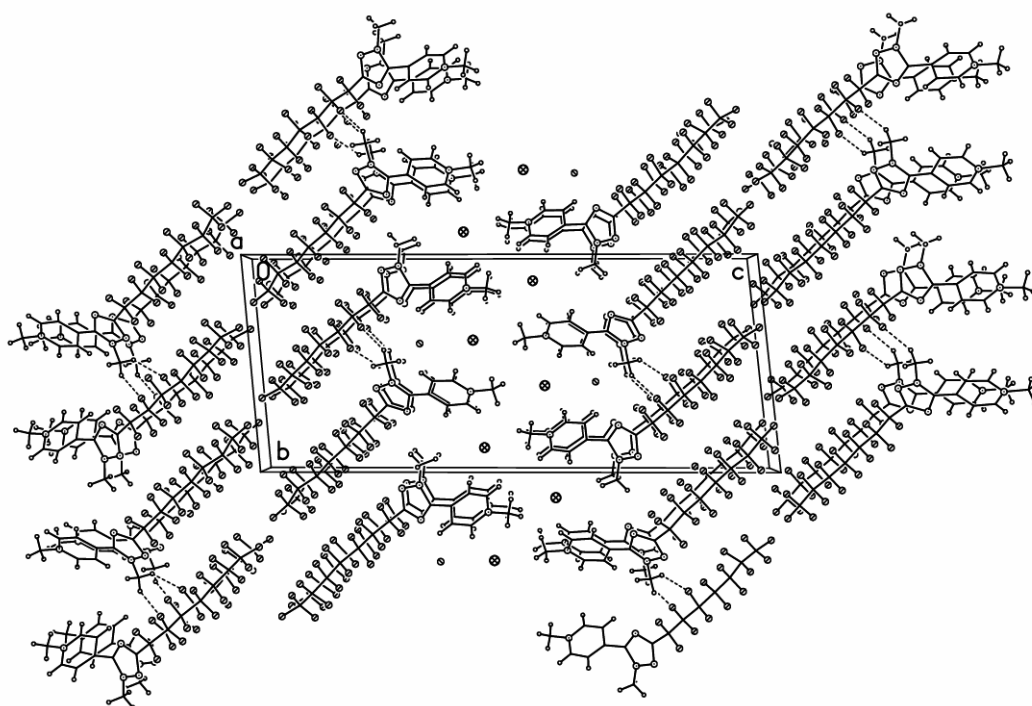


Figure 4. Part of the packing diagram of **5a**. The figure shows the H-bonds between molecules (**A**) and (**B**) of the adjacent columns within the same chain, viewed down *a* axis.

In **5a** the molecules are stacked along the *a* axis, forming chains of two adjacent hydrogen bonded columns, one of molecules A and one of molecules B. The hydrogen bonds are of type C8-H...F : within the single chain they connect the C8 methyl group of each A molecules (which acts as donor of two H-bonds) with F3 atom of the adjacent upper molecule and with F5 atoms of the adjacent lower molecule [C8A-H2...F5B: 2.22(1) Å and 138.9°(2) ; C8A-H3...F3B: 2.53(1) Å and 150.0°(2)]. This hydrogen bonding network gives rise to zig-zag chains extended parallel to *a* axis.

EXPERIMENTAL

General: Melting points were determined on a REICHART-THERMOVAR hot-stage apparatus and are uncorrected. IR spectra (Nujol) were determined with a PERKIN ELMER 257 instrument; ¹H-NMR spectra were recorded on a BRUKER AC 250 E spectrometer. GC/MS spectral determinations were carried out on a VARIAN STAR 3400 CX/SATURN 2000 system and the electron spray ionization (ESI) MS spectra were performed on a Micromass Autospec Ultima instrument. Flash chromatography was performed by using silica gel (Merck, 0.040-0.063 mm), and eluting with light petroleum (fraction boiling in the range 40-60°C), ethyl acetate, or acetonitrile as indicated below.

General procedure for the synthesis of 1,2,4-oxadiazoles (**8**) and (**11**).

A mixture of isonicotylamidoxime (**7**)¹⁸ or nicotylamidoxime (**10**)¹⁸ (1.0 g; 7.3 mmol) and pentadecafluorooctanoyl chloride (3.8 g; 8.8 mmol) in toluene (60 mL) and pyridine (1 mL) was refluxed for 8 h. After removal of the solvent, the residue was treated with water, neutralised with a sat. NaHCO₃ sol. and then extracted with EtOAc. The organic layers were dried over Na₂SO₄ and evaporated. Chromatography of the residue with light petroleum/ethyl acetate at various ratios gave the oxadiazoles (**8**) (3.05 g, 81%) and (**11**) (3.0 g, 80%).

4-(5-Pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridine (8) had mp 96-98°C (EtOH), ¹H NMR (CDCl₃) δ 8.15 (d, *J* = 6.0 Hz, 2H, Ar), 8.91 (d, *J* = 6.0 Hz, 2H, Ar); MS *m/z* (%) 515 (M⁺, 100), 168 (10), 146 (27), 120 (63), 69 (44). Anal. Calcd for C₁₄H₄N₃OF₁₅: C, 32.64; H, 0.78; N, 8.16. Found: C, 32.70; H, 0.90; N, 8.30.:

3-(5-Pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridine (11) had mp 68-70°C (light petroleum), ¹H NMR (CD₃CN) δ 7.56 (dd, *J* = 5.0 and 8.0 Hz, 1H, Ar), 8.39 (dt, *J* = 8.0 and 1.5 Hz, 1H, Ar), 8.80 (dd, *J* = 1.5 and 5.0 Hz, 1H, Ar), 9.25 (s, 1H, Ar); MS *m/z* % 515 (M⁺, 100), 414 (9), 145 (19), 117 (55), 101 (32), 90 (52), 69 (52), 50 (46). Anal. Calcd for C₁₄H₄N₃OF₁₅: C, 32.64; H, 0.78; N, 8.16. Found: C, 32.50; H, 0.70; N, 8.10.

General procedure for the synthesis of 1,2,4-oxadiazoles (**9**) and (**12**).

A sample of oxadiazole (**8**) or (**11**) (0.77 g; 1.5 mmol) was added to a solution of hydroxylamine

hydrochloride (0.31 g, 4.5 mmol) and potassium *tert*-butoxide (0.5 g, 4.5 mmol) in dimethylformamide (3 mL) and then the mixture was left at rt overnight. After dilution with water, the mixture was extracted with EtOAc. The combined extracts were dried over Na₂SO₄ and concentrated. Chromatography of the residue with light petroleum/ethyl acetate at various ratios allowed to recover starting material (**8**) or (**11**) (150 mg, 30%) and compound (**9**) (0.46 g, 60%) or (**12**) (0.43 g, 56%).

4-(3-Pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridine (9) had mp 73-75°C (EtOH). ¹H NMR (CDCl₃) δ 8.05 (d, *J* = 6.0 Hz, 2H, Ar), 8.94 (d, *J* = 6.0 Hz, 2H, Ar); MS *m/z* (%) 515 (M⁺, 100), 196 (68), 174 (20), 106 (28), 69 (32).). Anal. Calcd for C₁₄H₄N₃OF₁₅: C, 32.64; H, 0.78; N, 8.16. Found: C, 32.80; H, 0.90; N, 8.30.

3-(3-Pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridine (12) had mp 53-55°C (light petroleum) ¹H NMR (CD₃CN) δ 7.61 (dd, *J* = 5.0 and 8.0 Hz, 1H, Ar), 8.46 (dt, *J* = 8.0 and 1.5 Hz, 1H, Ar), 8.87 (dd, *J* = 1.5 and 5.0 Hz, 1H, Ar), 9.32 (d, *J* = 2.0 Hz, 1H, Ar); MS *m/z* % 515 (M⁺, 100), 496 (19), 487 (11), 196 (35), 169 (27), 146 (44), 131 (11), 119 (17), 118 (21), 106 (37), 104 (27), 78 (24), 69 (37). Anal. Calcd for C₁₄H₄N₃OF₁₅: C, 32.64; H, 0.78; N, 8.16. Found: C, 32.60; H, 0.80; N, 8.10.

General procedure for the synthesis of triazoles (**13**, **14** and **15**).

To a sample of oxadiazole (**8**) (0.77 g; 1.5 mmol) in dry DMF (2 mL) was added an excess of 99% hydrazine monohydrate (0.37 mL, 7.5 mmol) or methylhydrazine (0.4 mL, 7.5 mmol) and the mixture was left at rt for 1 h. After dilution with water, the mixture was extracted with EtOAc. The combined extracts were dried over Na₂SO₄, the solvent was evaporated and the residue concentrated and chromatographed with light petroleum/ethyl acetate at various ratios.

The reaction of oxadiazole (**8**) with hydrazine gave compound (**13**) (0.50 g, 65%), along with the isolation of oxadiazole (**9**)¹⁹ (0.18 g, 23%).

4-(5-Pentadecafluoroheptyl-1,2,4-triazole-3-yl)pyridine (13) had mp 162-164°C (EtOH). ¹H NMR (DMSO-*d*₆) δ 8.02 (d, *J* = 5.0 Hz, 2H, Ar), 8.87 (d, *J* = 5.0 Hz, 2H, Ar), 15.94 (br s, 1H, NH, exch. with D₂O); MS *m/z* (%) 515 (M+1, 64), 495 (11), 95 (19), 83 (24), 49 (100). Anal. Calcd for C₁₄H₅N₄F₁₅: C, 32.70; H, 0.98; N, 10.90. Found: C, 32.60; H, 1.00; N, 10.80.

The reaction of oxadiazole (**8**) with methylhydrazine gave compounds (**14**) (0.86 g, 85%) and (**15**) (0.03 g, 4%), along with the isolation of oxadiazole (**9**)¹⁹ (0.08 g, 10%).

4-(3-Pentadecafluoroheptyl-1-methyl-1,2,4-triazol-5-yl)pyridine (14) had mp 58-60°C (light petroleum). ¹H NMR (CDCl₃) δ 4.16 (s, 3H, Me), 7.67 (d, *J* = 6.0 Hz, 2H, Ar), 8.85 (d, *J* = 6.0 Hz, 2H, Ar); MS *m/z* (%) 528 (M⁺, 100), 209 (74), 105 (66), 69 (42). Anal. Calcd for C₁₅H₇N₄F₁₅: C, 34.11; H, 1.34; N, 10.61. Found: C, 34.20; H, 1.30; N, 10.70.

4-(5-Pentadecafluoroheptyl-1-methyl-1,2,4-triazol-3-yl)pyridine (15) had mp 76-78°C (light

petroleum). ^1H NMR (CDCl_3) δ 4.15 (s, 3H, Me), 7.97 (d, $J = 6.0$ Hz, 2H, Ar), 8.73 (d, $J = 6.0$ Hz, 2H, Ar); MS m/z (%) 528 (M, 100), 508 (14), 504 (14), 206 (68), 164 (66), 128 (15), 52 (36). Anal. Calcd for $\text{C}_{15}\text{H}_7\text{N}_4\text{F}_{15}$: C, 34.11; H, 1.34; N, 10.61. Found: C, 34.00; H, 1.30; N, 10.50.

Methylation of compound (13) with diazomethane.

To a sample of compound (13) (0.4 g, 0.78 mmol) in ether (20 mL) an ethereal solution of CH_2N_2 was added, and the solution was allowed to stir for 1 h at rt. After removal of the solvent, chromatography of the residue with light petroleum/ethyl acetate at various ratios gave 14 (0.07 g, 17%) and 15 (0.25 g, 61%).

General procedure for the synthesis of pyridinium iodide.

To a solution of the compound (8, 9, 11, 12, 14 or 15) (0.20 g; 0.39 mmol) in anhydrous acetonitrile (20 mL) methyl iodide (0.60 g; 4.22 mmol) was added and the mixture was refluxed for 6 h. After removal of the solvent under reduced pressure the residue was washed with ethyl acetate and filtered off to give the corresponding pyridinium iodide.

***N*-Methyl-4-(5-pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridinium iodide (1a)** (0.16 g; 62%) had mp 98-100°C (MeCN/BuOH); ^1H NMR (CD_3CN) δ 4.41 (s, 3H, Me), 8.60 (d, $J = 6.5$ Hz, 2H, Ar), 9.03 (d, $J = 6.5$ Hz, 2H, Ar); ESI-MS m/z (%) 530 (M^+ , 100). Anal. Calcd for $\text{C}_{15}\text{H}_7\text{N}_3\text{OF}_{15}\text{I}$: C, 27.42; H, 1.07; N, 6.39. Found: C, 27.30; H, 1.00; N, 6.30.

***N*-Methyl-3-(5-pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridinium iodide (2a)** (0.18 g; 71%) had mp 123-125°C (AcCN); ^1H NMR (CD_3CN) δ 4.43 (s, 3H, Me), 8.23 (dd, $J = 6.0$ and 8.0 Hz, 1H, Ar), 8.89 (d, $J = 6.0$ Hz, 1H, Ar), 9.06 (d, $J = 8.0$ Hz, 1H, Ar), 9.37 (s, 1H, Ar); ESI-MS m/z (%) 530 (M^+ , 100). Anal. Calcd for $\text{C}_{15}\text{H}_7\text{N}_3\text{OF}_{15}\text{I}$: C, 27.42; H, 1.07; N, 6.39. Found: C, 27.40; H, 1.10; N, 6.50.

***N*-Methyl-4-(3-pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridinium iodide (3a)** (0.23 g; 90%) had mp 95-97°C (EtOH); ^1H NMR (CD_3CN) δ 4.46 (s, 3H, Me), 8.65 (d, $J = 6.0$ Hz, 2H, Ar), 9.03 (d, $J = 6.0$ Hz, 2H, Ar); ESI-MS m/z (%) 530 (M^+ , 85), 1187 [$(\text{M}^+)_2\text{A}^-$, 100]. Anal. Calcd for $\text{C}_{15}\text{H}_7\text{N}_3\text{OF}_{15}\text{I}$: C, 27.42; H, 1.07; N, 6.39. Found: C, 27.30; H, 1.10; N, 6.40.

***N*-Methyl-3-(3-pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridinium iodide (4a)** (0.16 g; 63%) had mp 150-152°C (AcCN); ^1H NMR (CD_3CN) δ 4.47 (s, 3H, Me), 8.30 (dd, $J = 6.0$ and 8.0 Hz, 1H, Ar), 9.02 (d, $J = 6.0$ Hz, 1H, Ar), 9.11 (d, $J = 8.0$ Hz, 1H, Ar), 9.51 (s, 1H, Ar); ESI-MS m/z (%) 530 (M^+ , 100). Anal. Calcd for $\text{C}_{15}\text{H}_7\text{N}_3\text{OF}_{15}\text{I}$: C, 27.42; H, 1.07; N, 6.39. Found: C, 27.40; H, 1.00; N, 6.30.

***N*-Methyl-4-(3-pentadecafluoroheptyl-1-methyl-1,2,4-triazol-5-yl)pyridinium iodide (5a)** (0.25 g; 96%) had mp 165-167°C (EtOH); ^1H NMR (CD_3CN) δ 4.16 (s, 3H, Me), 4.37 (s, 3H, Me), 8.38 (d, $J = 6.0$ Hz, 2H, Ar), 8.87 (d, $J = 6.0$ Hz, 2H, Ar); ESI-MS m/z (%) 543 (M^+ , 100). Anal. Calcd for $\text{C}_{16}\text{H}_{10}\text{N}_4\text{F}_{15}\text{I}$: C, 28.68; H, 1.50; N, 8.36. Found: C, 28.60; H, 1.40; N, 8.30.

***N*-Methyl-4-(5-pentadecafluoroheptyl-1-methyl-1,2,4-triazol-3-yl)pyridinium iodide (6a)** (0.26 g; 99%) had mp 188-190°C (EtOH); ¹H NMR (CDCl₃) δ 4.23 (s, 3H, Me), 4.77 (s, 3H, Me), 8.62 (d, *J* = 6.5 Hz, 2H, Ar), 9.42 (d, *J* = 6.5 Hz, 2H, Ar); ESI-MS *m/z* (%) 543 (M⁺, 100). Anal. Calcd for C₁₆H₁₀N₄F₁₅I: C, 28.68; H, 1.50; N, 8.36. Found: C, 28.60; H, 1.50; N, 8.40.

General procedure for the synthesis of pyridinium trifluoromethanesulfonate.

To a solution of compound (**8**, **9**, **11**, **12**, **14** or **15**) (0.20 g; 0.39 mmol) in anhydrous acetonitrile (20 mL) methyl trifluoromethanesulfonate (MeSO₃CF₃; TfOMe) (0.73 g, 4.39 mmol) was added and the mixture was allowed to stir at rt overnight. After removal of the solvent under reduced pressure the residue was purified by column chromatography eluting with ethyl acetate and then with MeCN.

***N*-Methyl-4-(5-pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridinium trifluoromethanesulfonate (1b)** (0.22 g, 83%) had mp 130-134°C (EtOH); ¹H NMR (CD₃CN) δ 4.39 (s, 3H, Me), 8.59 (d, *J* = 6.5 Hz, 2H, Ar), 8.86 (d, *J* = 6.5 Hz, 2H, Ar); ESI-MS *m/z* (%) 530 (M⁺, 100). Anal. Calcd for C₁₆H₇N₃O₄F₁₈S: C, 28.29; H, 1.04; N, 6.19. Found: C, 28.20; H, 1.00; N, 6.10.

***N*-Methyl-3-(5-pentadecafluoroheptyl-1,2,4-oxadiazol-3-yl)pyridinium trifluoromethanesulfonate (2b)** (0.12 g, 40%) had mp 119-121°C (EtOH); ¹H NMR (CD₃CN) δ 4.42 (s, 3H, Me), 8.22 (dd, *J* = 6.0 and 8.5 Hz, 1H, Ar), 8.85 (d, *J* = 6.0 Hz, 1H, Ar), 9.06 (d, *J* = 8.5 Hz, 1H, Ar), 9.36 (s, 1H, Ar); ESI-MS *m/z* % 530 (M⁺, 100). Anal. Calcd for C₁₆H₇N₃O₄F₁₈S: C, 28.29; H, 1.04; N, 6.19. Found: C, 28.20; H, 1.10; N, 6.10.

***N*-Methyl-4-(3-pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridinium trifluoromethanesulfonate (3b)** (0.24 g; 91%) had mp 99-102°C (EtOH); ¹H NMR (CD₃CN) δ 4.42 (s, 3H, Me), 8.63 (d, *J* = 6.5 Hz, 2H, Ar), 8.93 (d, *J* = 6.5 Hz, 2H, Ar); ESI-MS *m/z* (%) 530 (M⁺, 60), 1209 [(M⁺)₂A⁻, 100]. Anal. Calcd for C₁₆H₇N₃O₄F₁₈S: C, 28.29; H, 1.04; N, 6.19. Found: C, 28.30; H, 1.10; N, 6.20.

***N*-Methyl-3-(3-pentadecafluoroheptyl-1,2,4-oxadiazol-5-yl)pyridinium trifluoromethanesulfonate (4b)** (0.16 g; 62%) had mp 110-112°C (EtOH); ¹H NMR (CD₃CN) δ 4.44 (s, 3H, Me), 8.27 (dd, *J* = 6.0 and 8.0 Hz, 1H, Ar), 8.91 (d, *J* = 6.0 Hz, 1H, Ar), 9.11 (d, *J* = 8.0 Hz, 1H, Ar), 9.46 (s, 1H, Ar); ESI-MS *m/z* % 530 (M⁺, 100). Anal. Calcd for C₁₆H₇N₃O₄F₁₈S: C, 28.29; H, 1.04; N, 6.19. Found: C, 28.25; H, 1.05; N, 6.20.

***N*-Methyl-4-(3-pentadecafluoroheptyl-1-methyl-1,2,4-triazol-3-yl)pyridinium trifluoromethanesulfonate (5b)** (0.12 g; 46%) had mp 126-129°C (EtOH); ¹H NMR (CD₃CN) δ 4.18 (s, 3H, Me), 4.39 (s, 3H, Me), 8.38 (d, *J* = 6.5 Hz, 2H, Ar), 8.83 (d, *J* = 6.5 Hz, 2H, Ar); ESI-MS *m/z* % 543 (M⁺, 100). Anal. Calcd for C₁₇H₁₀N₄O₃F₁₈S: C, 29.49; H, 1.46; N, 8.09. Found: C, 29.30; H, 1.30; N, 8.00

***N*-Methyl-4-(5-pentadecafluoroheptyl-1-methyl-1,2,4-triazol-3-yl)pyridinium trifluoromethanesulfonate (6b)** (0.13 g, 49%) had mp 113-116°C (EtOH); ¹H NMR (CD₃CN) δ 4.19 (s, 3H, Me), 4.34 (s,

3H, Me), 8.51 (d, $J = 6.5$ Hz, 2H, Ar), 8.72 (d, $J = 6.5$ Hz, 2H, Ar); ESI-MS m/z % 543 (M^+ , 100). Anal. Calcd for $C_{17}H_{10}N_4O_3F_{18}S$ C, 29.49; H, 1.46; N, 8.09. Found: C, 29.40; H, 1.40; N, 8.00.

X-Ray crystallographic analyses

The crystallization of compounds (**5a**) and (**15**) was repeated in different experimental conditions, but it was not possible to obtain good quality crystals. The difficulty of growing single crystals of highly fluorinated compounds suitable for the X-Ray diffraction is proved also by the small number of molecular structures resolved through single crystal X-Ray analysis. This fact together with the disorder typically found in the perfluoroalkylated chains limited the least-squares refinement results. However, in both structures (**5a**) and (**15**) the two heterocyclic moieties were refined without difficulties, while the perfluoroalkyl chains clearly showed an extended zig-zag conformation and the peculiarity of crystal packing of each compound was well defined.

Crystal data for 5a: $C_{16}H_{10}N_4F_{15}I$, Mr = 670.1; triclinic, centrosymmetric, $a = 5.432(1)$, $b = 13.556(2)$, $c = 30.081(9)$ Å, $\alpha = 84.20(1)^\circ$, $\beta = 88.43(2)^\circ$, $\gamma = 86.41(2)^\circ$, $V = 2341.3(7)$ Å³, $Z = 2$, Dc = 1.958 g cm⁻³, $F(000) = 1328$, μ (CuK α) = 12.08 mm⁻¹; colourless crystal (0.5 x 0.4 x 0.01 mm). Diffraction data were collected on a Siemens P4 diffractometer with graphite monochromated Cu-K α radiation ($\lambda = 1.54179$ Å), using $\theta/2\theta$ scan technique. Unit cell parameters were determined using 74 reflections in the range $16.2 \leq 2\theta \leq 48.2^\circ$. Two independent molecules per unit cell. A total of 10865 reflections (8086 unique, $R_{int} = 0.072$) were collected at room temperature in the range $3.5^\circ < 2\theta < 134^\circ$. During data collection, intensity decay up to 27% was observed in the standard reflections and a linear decay correction was applied during data reduction. The structure was solved by direct methods (SIR97, Altomare *et al.*, 1999)²⁰ and refined by full-matrix least-squares on F2 (SHELX97, Sheldrick, 1999).²¹ Due to the presence in the unit cell of the two independent molecules and therefore of a large number of parameters to be refined, the last refinement, with anisotropic temperature factors for non-H atoms, was carried out on each of the two molecules separately. The perfluoroalkyl chain exhibits disorder increasing towards the end of the tail, but any attempt to dislocate the involved carbon and fluorine atoms into well defined positions failed. The final atomic coordinates were obtained applying distance restraints to the perfluoroalkyl chain and the last refinement yielded high values of the anisotropic temperature factor for these atoms. Moreover, a few crystallization water molecules appeared to be dislocated within the crystal lattice, but their position and site occupation factors were completely assigned only for one molecule. The final stage converged to $R = 0.1202$ for 3676 observed reflections after merging and a total of 647 refined parameters.

Crystal data for 15: $C_{15}H_7N_4F_{15}$, Mr = 523.2; triclinic, centrosymmetric, $a = 5.649(1)$, $b = 14.039(3)$, $c = 25.391(5)$ Å, $\alpha = 77.67(2)^\circ$, $\beta = 83.57(2)^\circ$, $\gamma = 89.95(2)^\circ$, $V = 1954.7(7)$ Å³, $Z = 2$, Dc = 1.795 g cm⁻³,

$F(000) = 1040$, μ (CuK α) = 1.95 mm⁻¹; colourless crystal (0.5 x 0.6 x 0.01 mm). Diffraction data were collected on a Siemens P4 diffractometer with graphite monochromated Cu-K α radiation ($\lambda = 1.54179$ Å), using $\theta/2\theta$ scan technique. Unit cell parameters were determined using 83 reflections in the range $14.4 \leq 2\theta \leq 57.1^\circ$. Two independent molecules per unit cell. A total of 8587 reflections (6399 unique, $R_{int} = 0.099$) were collected at room temperature in the range $3.5^\circ < 2\theta < 130^\circ$. No intensity decay was observed during data collection. The structure was solved by direct methods (SIR97, Altomare et al., 1999)²⁰ and refined by full-matrix least-squares on F2 (SHELX97, Sheldrick, 1999).²¹ Due to the presence in the unit cell of the two independent molecules and therefore of a large number of parameters to be refined, the last refinement, with anisotropic temperature factors for non-H atoms, was carried out on each of the two molecules separately. The perfluoroalkyl chain was found to be dislocated in more than one position. Disorder was originally modeled without restraints, allowing each of the chain atoms to be located over two positions with site occupation factors freely refined. This produced some unreasonable bond distances and angles. Distances restraints was thus applied to the perfluoroalkyl chain, but after refinement, the high value of some atomic displacement parameters indicated that disorder could not be completely resolved. The final stage converged to $R = 0.0936$ for 3561 observed reflections, after merging and a total of 890 refined parameters.

ACKNOWLEDGEMENT

Financial support through the Italian MIUR and University of Palermo within the National Research Projects "Fluorinated Compounds: New Materials for Advanced Applications" (PRIN 2001) and "Fluorinated Nanoreactors with Designed Structures and Optimised Functions" (PRIN 2003) is gratefully acknowledged.

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