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A novel precursor for per(poly)fluoroalkyl heterocycles from *N*-aryl per(poly)fluoroalkyl imidoyl iodides

Hong-Bin Yu, Wei-Yuan Huang *

Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

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Abstract

N-aryl 1-per(poly)fluoroalkyl acetylenic imines (**3**), the cross coupling products of *N*-aryl per(poly)fluoroalkyl imidoyl iodides with acetylenes, could be used as novel precursors to synthesize fluorinated heterocycles such as pyrazoles and pyrimidines. © 1998 Elsevier Science S.A.

Keywords: Fluorinated pyrazole; Fluorinated pyrimidine; Imidoyl iodide; Acetylenic imine

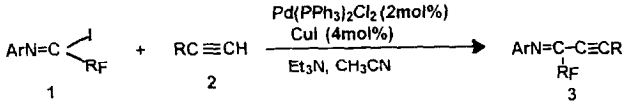
1. Introduction

Many heterocyclic compounds containing fluorine or fluorocarbon groups are either in use or under active investigation in the fields of agrochemistry and medicine [1,2]. The synthetic methods for these compounds include introducing fluorine into the preformed heterocycles, or forming heterocyclic systems by using fluorinated precursors [3]. Usually, the latter was of more interest due to the easy formation of the products and the regioselectivity for the fluorine substituents on the heterocyclic ring. For synthesis of fluorinated pyrazoles or pyrimidines, 1,3-bifunctional fluoro-building blocks were often used [4]; [3+2] or [3+3] cyclization between the 1,3-bifunctional compounds and a bisnucleophilic reagent such as hydrazine or amidine, respectively, gave these products. The 1,3-bifunctional compounds include fluoro-1,3-diketones [5], fluorinated acetylacetylenes [6,7], β-trifluoroacetyllactams, etc. [8]. In addition, there were some reports of other precursors for fluorinated pyrazoles or pyrimidines, such as 1-phenyl 1-trimethylsilyl perfluoroalkanols [9] and enol phosphate derivatives from perfluoroalkyl ketones [10]. In continuation of our investigations on *N*-aryl per(poly)fluoroalkyl imidoyl iodides [11], discovered as new fluorinated precursors for pyrazoles or pyrimidines, we describe herein a synthesis of *N*-aryl 1-per(poly)fluoroalkyl acetylenic imines and their reactions with hydrazine hydrate and amidine.

2. Results and discussion

N-Aryl 1-per(poly)fluoroalkyl acetylenic imines (**3**) were prepared by the Heck reaction between *N*-aryl per(poly)fluoroalkyl imidoyl iodides (**1**) and alkynes (**2**) using $Pd(PPh_3)_2Cl_2/CuI$ as the catalyst in Et_3N/CH_3CN. Similar results were reported by Uneyama and Watanabe [12] using $PhCl_2/PPh_3/CuI$ in toluene/CH_3CN. The reaction proceeded smoothly to give the coupling products in good yields (Scheme 1 and Table 1). When trimethylsilyl acetylene was used, the yield was relatively low for *N*-*p*-methoxyphenyl trifluoromethyl trimethylsilyl acetyl imine (**3dd**) even with a prolonged reaction time. Moreover, attempts at preparing longer chain per(poly)fluoroalkyl derivatives failed.

Then we paid attention to the chemical conversions of the obtained imine derivatives. *N*-Aryl per(poly)fluoroalkyl phenyl acetylenic imines (**3aa–3da**) were treated with excess of hydrazine hydrate in ethanol at 60°C to give the corresponding aryl amine (**9**) and the fluorinated pyrazole derivatives (**6aa–6da**). Under the same conditions, compound **3dd** gave a 3-trifluoromethyl pyrazole (**6dd**) with a cleavage of the trimethylsilyl group (Table 2). Ethanol was the solvent of choice for this reaction due to its low toxicity. Other solvents (e.g., CH_3OH, DMF, CH_3CN) can also be used, but in



Scheme 1.

* Corresponding author. E-mail: wyhuang@pub.sioc.ac.cn.

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Table 1
The Heck reaction of per(poly)fluoroalkyl imidoyl iodides with alkynes

Entry	Ar, RF (**1**)	RC≡CH (**2**)	T (°C)	t (h)	3/Yield (%) [a]
1	p-$CH_3C_6H_4$, C_2F_4Cl (**1a**)	PhC≡CH (**2a**)	Reflux	1	**3aa**/93
2	p-$CH_3OC_6H_4$, C_4F_8Cl (**1b**)	PhC≡CH (**2a**)	Reflux	1	**3ba**/89
3	p-$CH_3OC_6H_4$, C_4F_9 (**1c**)	PhC≡CH (**2a**)	Reflux	1	**3ca**/86
4	p-$CH_3OC_6H_4$, CF_3 (**1d**)	PhC≡CH (**2a**)	Reflux	1	**3da**/91
5	p-$CH_3OC_6H_4$, CF_3 (**1d**)	n-C_4H_9C≡CH (**2b**)	Reflux	2	**3db**/72
6	p-$CH_3OC_6H_4$, CF_3 (**1d**)	CH_3CO_2C≡CH (**2c**)	Reflux	2	**3dc**/70
7	p-$CH_3OC_6H_4$, CF_3 (**1d**)	Me_3SiC≡CH (**2d**)	25	30	**3dd**/25

[a] Isolated yields.

Table 2
The conversion of N-aryl 1-per(poly)fluoroalkyl acetylenic imine (**3**) with hydrazine hydrate or amidine

Entry	**3**	**4** or **5**	Product/yield [a]
1	**3aa**	Hydrazine hydrate (**4**)	**6aa**/94
2	**3ba**	Hydrazine hydrate (**4**)	**6ba**/84
3	**3ca**	Hydrazine hydrate (**4**)	**6ca**/86
4	**3da**	Hydrazine hydrate (**4**)	**6da**/99
5	**3aa**	Phenyl amidine (**5a**)	**7aa**/74
6	**3ba**	Phenyl amidine (**5a**)	**7ba**/85
7	**3ca**	Phenyl amidine (**5a**)	**7ca**/89
8	**3da**	Phenyl amidine (**5a**)	**7da**/80
9	**3aa**	Methyl amidine (**5b**)	**8aa**/70
10	**3ba**	Methyl amidine (**5b**)	**8ba**/84
11	**3ca**	Methyl amidine (**5b**)	**8ca**/82
12	**3da**	Methyl amidine (**5b**)	**8da**/71
13	**3dd**	Hydrazine hydrate (**4**)	**6dd**/59
14	**3dd**	Phenyl amidine (**5a**)	**7dd**/89
15	**3dc**	Hydrazine hydrate (**4**)	**10**/93

[a] Isolated yields.

THF, the reaction did not occur and starting materials were recovered (Scheme 2).

On the other hand, the reaction of benzamidine and methyl amidine with these imine derivatives (**3aa–3da**) in the presence of K_2CO_3 gave the corresponding 4-per(poly)-fluoroalkyl pyrimidines (**7**) and (**8**) and aryl amines (**9**). In the case of compound **3dd**, the product (**7dd**) was the 4-trifluoromethyl pyrimidine without a trimethylsilyl group. This reaction proceeded with good yields in 1,4-dioxane.

However, we were unsuccessful in carrying out these transformations using compounds **3db** and **3dc** as starting materials under a variety of conditions such as increasing the reaction temperature or prolonging the reaction time, or changing the solvent. **3db** was recovered unchanged, whereas **3dc** was hydrolyzed to give **10** (Scheme 3). Compound **10** also failed to cyclize. Therefore, the structure of compound **3** is critical for a successful cyclization to occur.

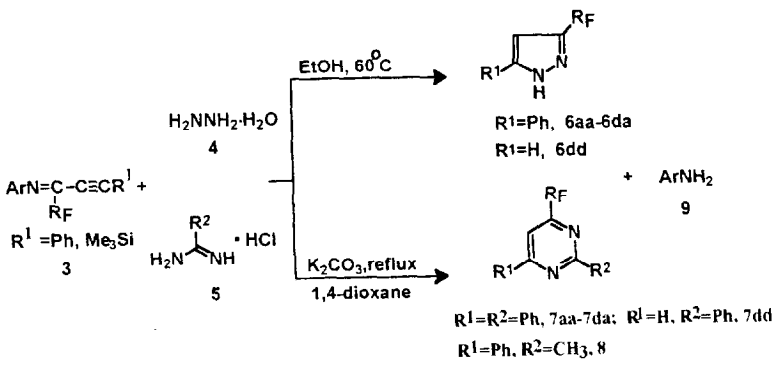
In conclusion, we have used the coupling products from the Heck reaction of N-aryl per(poly)fluoroalkyl imidoyl iodides with acetylenes as a novel precursor to synthesize fluorinated heterocycles such as pyrazoles and pyrimidines.

3. Experimental

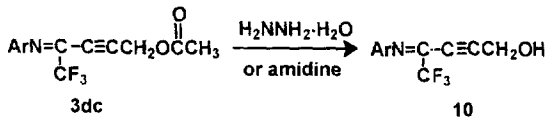
All reactions involving air or moisture-sensitive reagents were run under a nitrogen atmosphere. All melting points are uncorrected. Proton and ^{13}C NMR resonances were obtained at 90 MHz and 75.4 MHz, respectively, and are reported relative to the external tetramethylsilane in ppm. The ^{19}F NMR resonances were obtained at 56.4 MHz using trifluoroacetic acid (TFA) as external standard.

3.1. General procedure for the preparation of N-aryl 1-per(poly)fluoroalkyl acetylenic imines (3)

To a stirred mixture of $Pd(PPh_3)_2Cl_2$ (0.1 mmol), CuI (0.2 mmol), Et_3N (2.5 ml) and CH_3CN (7.5 ml) was added N-aryl per(poly)fluoroalkyl imidoyl iodide (**1**) [11] (5 mmol) and alkyne (**2**) (5 mmol). The reaction mixture was allowed to stir at the required temperature and time. Then the mixture was cooled and filtered. After removal of the solvent



Scheme 2.



Scheme 3.

from the filtrate, the crude product obtained was purified by column chromatography on silica gel (light petroleum b.p. 60–90°C: ethyl acetate = 25: 1 v/v) to give the product (**3**). 1236, 1171, 1136, 1096; MS: 299 (M^+, 4.46), 219 (M^+–CF_3–C + 1, 100.00), Anal. Calcd. for $C_{14}H_{12}F_3NO_3$: C 56.19, H 4.04, N 4.68, F 19.05; C 56.16, H 3.88, N 4.66, F 19.22.

3dd: oil. ^{1}H NMR (90 MHz, $CDCl_3$) 7.72, 7.09 (dd, J = 9 Hz, 4H, ArH), 4.03 (s, 3H, CH_3O), 0.45 (s, 9H, $(CH_3)_3$) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −6.7 (s, 3F, CF_3) ppm; IR (ν, cm^{-1}) 2950, 2820, 1614, 1575, 1505, 1255, 1193, 1163, 1143, 1076; MS: 299 (M^+, 33.74), 230 (M^+–CF_3, 75.21), 226 (M^+–Me_3Si, 61.23); HRMS for $C_{14}H_{16}F_3NO_3Si$: 299.0961.

3.2. General procedure for the preparation of 3-per(poly)fluoroalkyl pyrazoles (6)

Hydrazine monohydrate (6 mmol) (**4**) was added to a solution of **3** (1 mmol) in ethanol (3 ml) and the mixture was heated to 60°C for 2 h with stirring. The cold mixture was then extracted with diethyl ether (20 ml × 3) and the organic layer was washed with brine followed by drying over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by thin layer chromatography on silica gel (light petroleum ether (b.p. 60–90°C)–ethyl acetate 3:1 v/v) to give **6** and **9**.

6aa: m.p. 131–133°C. ^{1}H NMR (90 MHz, $CDCl_3$) 7.65–7.35 (m, 5H, ArH), 6.78 (s, 1H) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −7.2 (s, 2F, CF_2Cl), 31.8 (s, 2F, CF_2) ppm; IR (ν, cm^{-1}) 3128, 1591, 1572, 1475, 1248, 1172, 1152, 1136; MS: 278 (M^+, 50.15), 193 (M^+–CF_2Cl, 100.00); Anal. Calcd for $C_{11}H_7ClF_4N_2$: C 47.42, H 2.53, N 10.05, F 27.27, Found: C 47.48, H 2.37, N 10.13, F 27.24.

6ba: m.p. 104–105°C. ^{1}H NMR (90 MHz, $CDCl_3$) 8.00–7.66 (m, 5H, ArH), 7.20 (s, 1H) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.6 (m, 2F, CF_2Cl), 31.0 (m, 2F, CF_2-ring), 41.0–43.0 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 3100, 3024, 1580, 1502, 1480, 1423, 1284, 1215, 1127; MS: 380(M^+ + 3, 12.64), 378 (M^+ + 1, 37.99), 343 (M^+ + 1–Cl, 10.65), 193(M^+ + 1–Cl$(CF_2)_3$, 100.00); Anal. Calcd for $C_{13}H_7ClF_8N_2$: C 41.24, H 1.86, N 7.40, F 40.14; Found: C 41.09, H 1.73, N 7.33, F 40.08.

6ca: m.p. 94–96°C. ^{1}H NMR (90 MHz, $CDCl_3$) 7.92–7.72 (m, 5H, ArH), 7.59 (s, 1H) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) 3.3 (m, 3F, CF_3), 32.6 (m, 2F, CF_2-pyrazole), 45.6, 49.0 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 3211, 3130, 2984, 2887, 1591, 1502, 1353, 1250, 1193, 1129; MS: 362 (M^+, 67.97), 343 (M^+–F, 10.57), 193 (M^+–$CF_3CF_2CF_2$, 100.00), Anal. Calcd for $C_{13}H_7F_9N_2$: C 43.11, H 1.95, N 7.73, F 47.21; Found: C 43.38,H 1.77, N 7.60, F 47.20.

6da: m.p. 113–115°C. ^{1}H NMR (90 MHz, $CDCl_3$) 7.53–7.31 (m, 5H, ArH), 6.63 (s, 1H) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −5.4 (s, 3F, CF_3) ppm; ^{13}C NMR (75.5 MHz, CDCl3) 145.25 (s, C^5), 143.53 (q, J = 38 Hz, C^3), 121.93 (q. J = 269 Hz, CF_3), 101.45 (s, C^4) ppm; IR (ν, cm^{-1}) 3106, 3024, 1590, 1510, 1439, 1278, 1253, 1210–1120; MS: 213 (M^+ + 1, 12.78), 212 (M^+, 100.00), 193 (M^+–F, 13.23), 143 (M^+–CF_3, 27.03), 77 (Ph, 14.88); Anal. Calcd for $C_{10}H_7F_3N_2$: C 56.61, H 3.33, N 13.20, F 26.86, Found: C 57.03, H 3.41, N 12.88, F 26.40.

6dd: m.p. 47–48°C. ^{1}H NMR (300 MHz, $CDCl_3$) 7.71 (m, 1H), 6.66 (m, 1H) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −7.0 (s, CF_3) ppm; ^{13}C NMR(75.5 MHz, $CDCl_3$) 141.84 (q, J = 38 Hz, C^3), 129.09 (C^5), 102.97 (C^4) ppm; IR (ν, cm^{-1}) 3150, 2970,1500, 1380, 1321, 1170–1140; MS: 136 (M^+, 100.00), 117 (M^+–F, 32.24); HRMS for $C_4H_3F_3N_2$: 136.0251.

3.3. General procedure for the preparation of 4-per(poly)fluoroalkyl pyrimidines from 3 and amidines

Amidine hydrochloride (**5**) (1 mmol) and K_2CO_3 (6 mmol) were added to a stirred solution of **3** (1 mmol) in dioxane (3 ml). The mixture was stirred for 12 h under reflux. Then the cold mixture was washed with saturated aqueous NH_4Cl solution and extracted with diethyl ether (20 ml × 3). The organic extracts were dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (light petroleum (b.p. 60–90°C)–ethyl acetate 100:1 v/v) to give **7** or **8** and arylamine (**9**).

7aa: m.p. 125–127°C. ^{1}H NMR (90 MHz, $CDCl_3$) 8.68–8.38 (m, 4H, ArH), 7.95 (s, 1H, pyrimidine-H), 7.58 (m, 6H, ArH) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −8.6 (s, 2F, CF_2Cl), 37.0 (s, 2F, CF_2) ppm; IR (ν, cm^{-1}) 3093, 3068, 1587, 1572, 1548, 1382, 1367, 1164, 1151, 1087; MS: 368 (M^+ + 2, 35.25), 366 (M^+, 100.00); Anal. Calcd for $C_{18}H_{11}ClF_4N_2$: C 58.95, H 3.02, N 7.64, F 20.72; Found: C 59.06, H 3.06, N 7.53, F 20.25.

7ba: m.p. 90–91°C. ^{1}H NMR(90 MHz, $CDCl_3$) 8.65–8.25 (m, 4H, ArH), 7.94 (s, 1H, pyrimidine-H), 7.55 (m, 6H, ArH) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.8 (s, 2F, CF_2Cl).

3aa: oil. ^{1}H NMR (90 MHz, $CDCl_3$) 7.50–7.28 (m, 9H, Ph), 2.50 (s, 3H, CH_3O) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.30 (s, 2F, CF_2Cl), 35.3 (s, 2F, CF_2) ppm; IR (ν, cm^{-1}) 3131, 2905, 1631, 1504, 1263, 1154; MS: 355 (M^+ + 2, 11.29), 353 (M^+, 30.70), 218 (M^+–CF_2CF_2Cl, 100.00); Anal. Calcd. for $C_{18}H_{12}ClF_4N$: C 61.12, H 3.42, N 3.96, F 21.48; Found: C 62.93, H 3.44, N 3.68, F 21.05.

3ba: oil. ^{1}H NMR (90 MHz, $CDCl_3$) 7.60–6.90 (m, 9H, ArH), 3.89 (s, 3H, CH_3O) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.70 (m, 2F, CF_2Cl), 35.5 (m, 2F, N=CCF_2), 42.0–43.0 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 2940, 2840, 2197, 1613, 1504, 1302, 1256, 1198–1100; MS: 469 (M^+, 13.15), 434 (M^+–Cl, 3.02), 234 (M^+–Cl$(CF_2)_4$, 100.00); HRMS for $C_{20}H_{12}ClF_8NO$: 469.0447.

3ca: oil. ^{1}H NMR (90 MHz, $CDCl_3$) 7.58, 7.18 (dd, 4H, ArH), 7.46 (m, 5H, Ph), 3.87 (s, 3H, CH_3O) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) 3.40 (s, 3F, CF_3), 35.7 (m, 2F, N=CCF_2), 44.7–48.3 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 3009, 2964, 2842, 2202, 1613, 1575, 1505, 1235; MS: 453 (M^+, 20.58), 234 (M^+–$F(CF_2)_4$, 100.00); Anal. Calcd. for $C_{20}H_{12}F_9NO$: C 52.99, H 2.67, N 3.09, F 37.72; Found: C 52.97, H 2.43, N 2.87, F 37.73.

3da: oil. ^{1}H NMR (90 MHZ, $CDCl_3$) 7.60–7.90 (m, 9H, ArH), 3.90 (s, 3H, CH_3O) ppm; ^{19}F NMR(56.4 MHz, $CDCl_3$) −6.6 (s, 3F, CF_3) ppm; IR (ν, cm^{-1}) 2940, 2 820, 2200, 1612, 1574, 1504, 1253, 1161–1140; MS: 303 (M^+, 64.06), 234 (M^+–CF_3, 100.00); Anal. Calcd. for $C_{17}H_{12}F_3N$: C 67.33, H 3.99, N 4.62, F 18.79; Found: C 67.62, H 3.68, N 4.31, F 18.41.

3db: m.p. 100–102°C. ^{1}H NMR (90 MHZ, $CDCl_3$) 8.10–7.25 (m, 4H, ArH), 4.02 (s, 3H,CH_3O), 3.07 (t, J=7.5 Hz, 2H, ≡CCH_2), 2.00–1.30 (m, 4H, $(CH_2)_2$), 1.02 (t, J=7.5 Hz, 3H, CH_3) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −10.3 (s, 3F, CF_3) ppm; IR (ν, cm^{-1}) 3050, 2966, 2933, 2863, 1968, 1622, 1505, 1481, 1287, 1254, 1232, 1184, 1139, 1103; MS: 283 (M^+, 95.96), 264 (M^+–F, 9.07), 241 (M^+–$(CH_2)_3$, 100.00); Anal. Calcd. for $C_{15}H_{16}F_3NO$: C 63.60, H 5.69, N 4.94, F 20.12; Found: C 63.50, H 5.54, N 4.91, F 20.36.

3dc: m.p. 118–120°C. ^{1}H NMR (90 MHZ, $CDCl_3$) 8.23–7.12 (m, 4H, ArH), 5.61 (s, 2H, CH_2), 3.99 (s, 3H, CH_3O), 2.23 (s, 3H, CH_3CO)ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −10.5 (s, 3F, CF_3) ppm; IR (ν, cm^{-1}) 3067, 2992, 1755, 1740, 1625, 1510, 1484, 1293, 1282, 38.0 (s, 2F, CF_2) 42.0–43.0 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 3067, 1590, 1573, 1548, 1382, 1368, 1193, 1151, 1134; MS: 468 (M^+ +2, 30.99), 466 (M^+, 86.84), 431 (M+–Cl, 14.58); Anal. Calcd for $C_{20}H_{11}ClF_8N_2$: C 51.47, H 2.38, N 6.00, F 32.56; Found: C 51.56, H 2.39, N 5.91, F 32.61.

7ca: m.p. 82–83°C. ^{1}H NMR(90 MHz, $CDCl_3$) 8.70–8.30 (m, 4H, ArH), 8.08 (s, 1H, pyrimidine-H), 7.60 (m, 6H, ArH) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) 3.4 (s, CF_3), 38.4 (s, 2F, CF_2), 45.0–48.0 (m, 4F, CF_2CF_2) ppm; IR (ν, cm^{-1}) 3067, 3037, 1589 1572, 1549, 1384, 1253, 1233, 1197, 1131; MS: 450 (M^+, 100.00), 281 (M^+–$CF_2CF_2CF_3$, 5.42); Anal. Calcd for $C_{20}H_{11}F_9N_2$: C 53.35, H 2.46, N 6.22, F 37.97; Found: C 53.27, H 1.77, N 5.95, F 39.82.

7da: m.p. 94–96°C. ^{1}H NMR(90 MHz, $CDCl_3$) 8.88–7.66 (m, 10H, ArH), 7.41 (s, 1H, pyrimidine-H) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −7.7 (s, CF_3) ppm; IR (ν, cm^{-1}) 3068, 1592, 1551, 1392, 1377, 1262, 1190, 1139; MS: 300 (M^+, 100.00), 231 (M^+–CF_3, 5.42); Anal. Calcd for $C_{17}H_{11}F_3N_2$: C 68.00, H 3.69, N 9.33, F 18.98; Found: C 68.63, H 3.84, N 9.29, F 18.98.

7dd: m.p. 101–102°C. ^{1}H NMR (90 MHz, $CDCl_3$) 9.00–8.50, 7.55–7.45 (m, 7H, ArH) ppm, ^{19}F NMR(56.4 MHz, $CDCl_3$) −7.6 (s, CF_3) ppm; IR (ν, cm^{-1}) 3070, 2918, 1576, 1463, 1400, 1342, 1317, 1209, 1182, 1125; MS: 224 (M^+, 100.00), 155 (M^+–CF_3, 71.30); Anal. Calcd for $C_{11}H_7F_3N_2$ C 58.93, H, 3.15, N 12.50, F 25.42; Found: C 59.11, H 3.39, N 12.15, F 25.37.

8aa: oil. ^{1}H NMR(90 MHz, $CDCl_3$) 8.15, 7.60 (m, 5H, ArH), 7.85 (s, 1H, pyrimidine-H), 2.92 (s, 3H, CH_3) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −8.0 (s, 2F, CF_2), 47.5 (s, 2F, CF_2) ppm; IR (ν, cm^{-1}) 3065, 2931, 1565, 1547, 1373, 1256, 1163, 1141; MS: 306 (M^+ +2, 37.71), 304 (M^+, 100.00), 269 (M^+–35, 14.19), 219 (M^+–CF_2Cl, 27.06); HRMS for $C_{13}H_9ClF_4N_2$: 304.0400.

8ba: oil. ^{1}H NMR(90 MHz, $CDCl_3$) 8.16, 7.56 (m, 5H, ArH), 7.86 (s, 1H, pyrimidine-H), 2.91 (s, 3H, CH_3) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.6 (s, 2F, CF_2), 38.5 (s, 2F, CF_2), 42.0, 43.5 (m, 4F, $(CF_2)_2$) ppm; IR (ν, cm^{-1}) 2900, 1585, 1548, 1371, 1200, 1142; MS: 406 (M^+ +2, 30.60), 404 (M^+, 84.89), 369 (M^+–35, 14.19), 219 (M^+–$CF_2CF_2CF_2Cl$, 22.74); HRMS for $C_{15}H_9ClF_8N_2$: 404.0363.

8ca: oil. ^{1}H NMR(90 MHz, $CDCl_3$) 8.15, 7.55 (m, 5H, ArH), 7.84 (s, 1H, pyrimidine-H), 2.81 (s, 3H, CH_3) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) 3.3 (s, CF_3), 39.0 (s, 2F, CF_2), 45.2,48.2 (m, 4F, $(CF_2)_2$) ppm; IR (ν, cm^{-1}) 2900, 1587, 1550, 1370, 1236, 1207, 1136; MS: 388 (M^+, 94.77), 369 (M^+–F, 9.86), 219 (M^+–$CF_2CF_2CF_3$, 18.03); HRMS for $C_{15}H_9F_9N_2$: 388.0625.

8da: oil. ^{1}H NMR (90 MHz, $CDCl_3$) 8.10, 7.76 (m, 5H, ArH), 7.50 (s, 1H, pyrimidine-H), 2.81 (s, 3H, CH_3) ppm, ^{19}F NMR (56.4 MHz, $CDCl_3$) −7.7 (s, CF_3) ppm; IR (ν, cm^{-1}) 3060, 2930, 2860, 1595, 1554, 1512, 1406, 1367, 1367, 1201, 1174–1142; MS: 238 (M^+, 100.00), 219 (M^+–F, 8.69); HRMS for $C_{12}H_9F_3N_2$: 238.0732.

*3.4. Hydrolysis of compound **3dc** with hydrazine hydrate to give compound **10***

The method was the same as procedure (2) and the crude product was recrystallized from ethyl acetate.

10: m.p. 181–183°C. ^{1}H NMR(90 MHz, $(CD_3)_2CO$) 8.01–7.34 (m, 4H, ArH), 5.22 (s, 2 H, CH_2), 4.02 (s, 3H, CH_3O), 3.23 (s, 1H, OH) ppm; ^{19}F NMR (56.4 MHz, $CDCl_3$) −9.5 (s, 3F, CF_3) ppm; IR (ν, cm^{-1}) 3292, 3019, 2941, 2843, 2039, 1625, 1511, 1486, 1296, 1237, 1183, 1143, 1103; MS: 257 (M^+, 100.00), 238 (M^+–F, 10.66), 228(M^+–CH_3O, 51.40), 208 (M^+–49, 50.54); Anal. Calcd. for $C_{12}H_{10}F_3NO_2$: C 56.03, H 3.92, N 5.45, F 22.16; Found: C 56.20, H 3.92, N 5.55, F 21.75.

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