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Reaction of 1-Alkylbenzimidazolium 3-Ylides with Ethyl 2,2-Dihydropolyfluoroalkanoates[1]

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Abstract: In the presence of base, ethyl 2,2-dihydropolyfluoroalkanoates(**2**) reacted with N-phenacyl(**1a-1b**), N-acetonyl(**1c**), N-ethoxycarbonylmethyl(**1d**) and N-(diethylaminocarbonyl-methyl) benzimidazole bromides(**1e**) in DMF to give the corresponding pyrrolo[1,2-a]quinoxaline derivatives (**3**) respectively. When (**2**) was reacted with N-cyanomethyl benzimidazole bromides (**1f-1g**) , fluoroalkyl substituted 1-aryl pyrrole derivatives (**4**) were formed as the major products. © 1998 Elsevier Science Ltd. All rights reserved.

The reactions of 1-alkyl benzimidazolium 3-ylides with various electron deficient alkynes (such as DMAD, ethyl propiolate etc.) have been widely investigated. With the variation in structure of the ylides , the results obtained are different.[2] When electron deficient alkenes(such as acrylonitrile, methyl acrylate etc.)were employed as dipolarophiles to react with 1-alkyl benzimidazolium 3-ylides in the presence of an oxidant, the expected [3+2] adducts pyrrolo[1,2-a]benzimidazole derivatives were formed as the sole products.[3]

In a previous paper, we have employed ethyl 2-hydropolyfluoroalkenoates, generated in situ from ethyl 2,2-dihydropolyfluoroalkanoates,[4] as dipolarophiles to react with various pyridinium N-ylides.[5] As part of our continuing interest in the utilization of ethyl 2,2-dihydropolyfluoroalkanoates as fluorine-containing building blocks, we have investigated the reactions of ethyl 2,2-dihydropolyfluoroalkanoates with 1-alkylbenzimidazolium 3-ylides. We now wish to report the results of these reactions.

In the presence of base, N-phenacyl benzimidazole bromides(**1a-1b**) reacted with ethyl 2,2-dihydropolyfluoroalkanoates(**2**), the only product isolated was confirmed by spectral data and X-ray crystallography to be the ring expansion product pyrrolo[1,2-a]quinoxaline derivatives, not the expected 4-H- pyrrolo[1,2-a]benzimidazole derivatives.[1] (Scheme 1)

In memory of the late professor Yu Wang (1910-1997)

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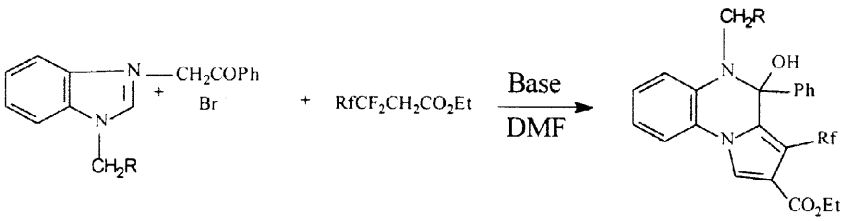


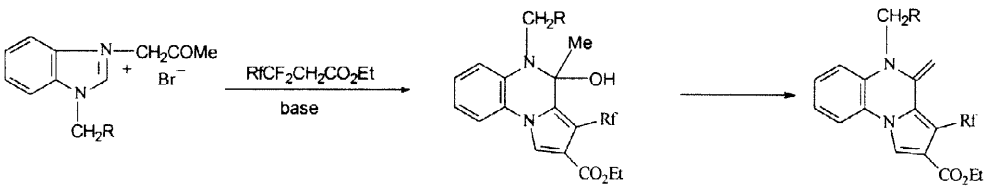
1a, 1b 2h-2j 3ah-3bj

1a: R=H; 1b: R=Ph

2h: Rf=Cl(CF2)3; 2i: Rf=Cl(CF2)5; 2j: Rf=F(CF2)7

Scheme 1

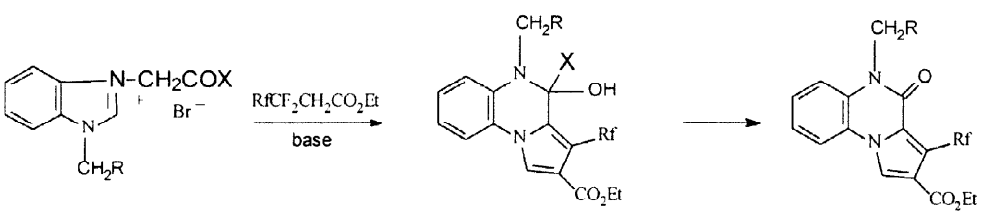
In a similar way, N-acetonyl benzimidazole bromide (**1c**) reacted with ethyl 2,2-dihydropolyfluoro-alkanoates(**2**) to give the corresponding 3-fluoroalkyl-4-methylene pyrrolo[1,2-a]quinoxaline derivatives through the elimination of water from the ring expansion intermediates.(Scheme 2)



1c 2h-2j 3ch-3cj

Scheme 2

When N-ethoxycarbonylmethyl benzimidazole bromide(**1d**) and N-(diethylaminocarbonylmethyl) benzimi-dazole bromides (**1e**) were allowed to react with ethyl 2,2-dihydropolyfluoroalkanoates under similar condition, the same product 3-fluoroalkyl-4-oxo pyrrolo[1,2-a]quinoxaline derivatives were formed resulting from the elimination of ethanol and diethyl amine from the intermediates respectively. (Scheme 3)



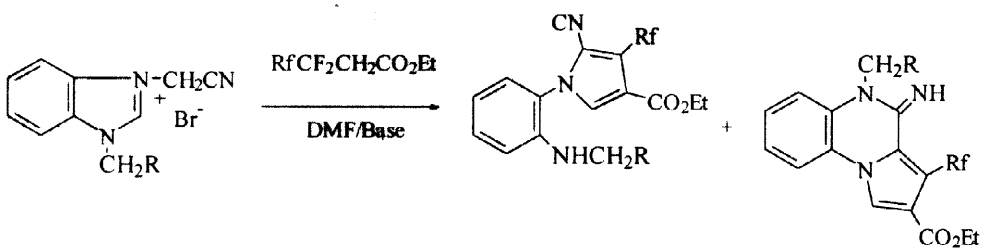
1d (X=OEt) 2h-2j 3dh-3dj

1e (X=NEt2) 2h 3dh

Scheme 3

In order to extend the scope of the ring expansion reactions, we have investigated the reactions of 1-alkylbenzimidazolium 3-cyanomethyl bromides(**1f-1g**)[6] with ethyl 2,2-dihydropoly-fluoroalkanoates. By analogy with the behavior of the 1-alkylbenzimidazolium 3-phenacyl bromide, we expected the formation of

3-fluoroalkyl -4-imino or 4-oxo pyrrolo[1,5-a]quinoxaline derivatives. However, two products were formed from the reactions. The major products were shown by IR, ^{1}H NMR, ^{19}F NMR, MS, elemental analyses or HRMS to be the ring opening products 3-fluoroalkyl 1-(2-alkylaminophenyl)-pyrrole derivatives; and only, the minor products were the expected 3-fluoroalkyl-4-imine pyrrolo[1,5-a]quinoxalines (Scheme 4).



1f-1g 2h-2m 4 3

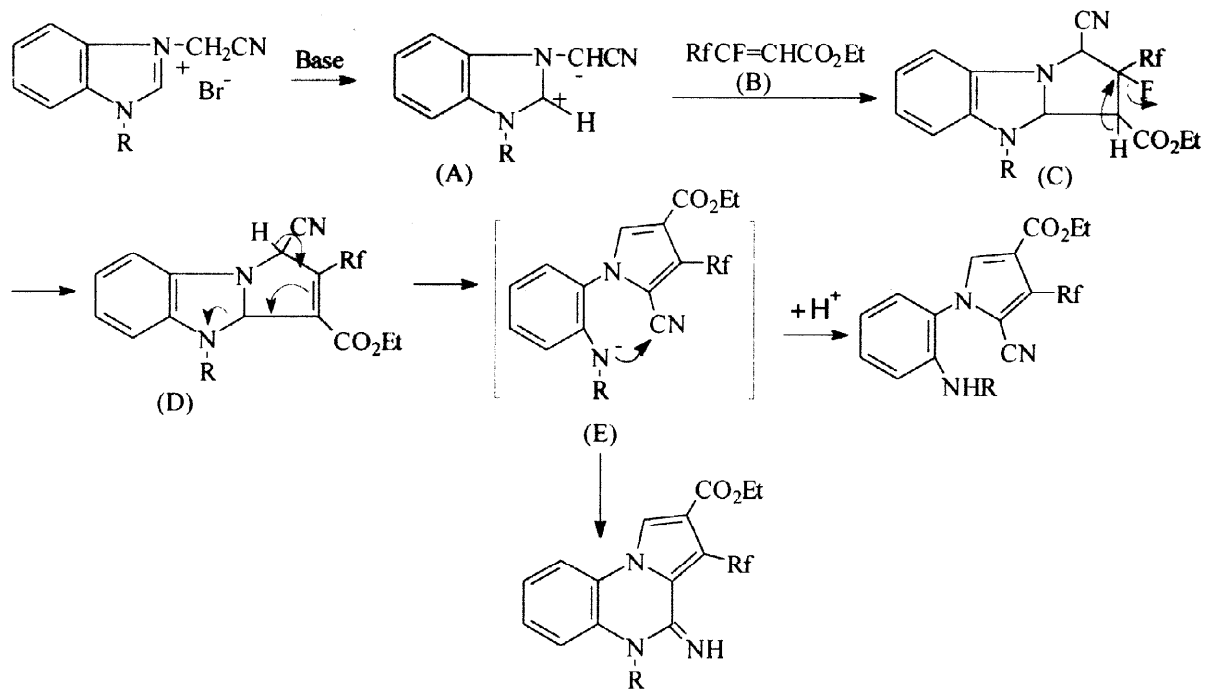
1f: R=H; 1g: R=Ph

2h: Rf=Cl(CF$_2$)$_3$; 2i: Rf=Cl(CF$_2$)$_5$; 2j: Rf=F(CF$_2$)$_7$; 2k: Rf=HCF$_2$; 2l: Rf=ClCF$_2$; 2m: Rf=CF$_3$

Scheme 4

The structure of compound (**4gl**) was further confirmed by X-ray crystallography (Figure 1)

The formation of the two compounds may be depicted as follows (Scheme 5):



Scheme 5

It seems that the lower reactivity of the cyano group has reduced significantly the formation of the ring closure products from the intermediates (E). As a result, the 1-aryl pyrrole derivatives were formed as the

major products.

Ogura et al have reported the formation of 2-substituted benzimidazole and pyrido[1,2-a]benzimidazole derivatives from the reactions of 1-methyl-3-phenacylbenzimidazolium ylide and 1-alkyl-3-methoxycarbonyl-methylbenzimidazolium ylide with dimethyl acetylenedicarboxylate(DMAD) respectively.[2b] They established the structures of these two compounds only by IR, MS and NMR spectroscopy. On view of our present results, it is tempting to suggest that the two products they obtained might actually be N-(2-aminophenyl)-pyrrole and pyrrolo[1,2-a]quinoxaline respectively, since those spectral data could fit both sets of structures.

The detailed results are listed in table 1.

Table 1 The isolated yield of compounds **3** and **4** .

1	R	2	Rf	3(%)	4(%)
1a	H	2h	$Cl(CF_2)_3$	3ah/60	
1a	H	2i	$Cl(CF_2)_5$	3ai/86	
1a	H	2j	$F(CF_2)_7$	3aj/72	
1b	Ph	2h	$Cl(CF_2)_3$	3bh/61	
1b	Ph	2i	$Cl(CF_2)_5$	3bi/85	
1b	Ph	2j	$F(CF_2)_7$	3bj/83	
1c	Ph	2h	$Cl(CF_2)_3$	3ch/75	
1c	Ph	2i	$Cl(CF_2)_5$	3ci/78	
1c	Ph	2j	$F(CF_2)_7$	3cj/76	
1d	Ph	2h	$Cl(CF_2)_3$	3dh/75	
1d	Ph	2i	$Cl(CF_2)_5$	3di/71	
1d	Ph	2j	$F(CF_2)_7$	3dj/73	
1e	Ph	2i	$Cl(CF_2)_3$	3dj/56	
1f	H	2h	$Cl(CF_2)_3$	trace	4fh/65
1f	H	2i	$Cl(CF_2)_5$	3fi/7	4fi/73
1f	H	2j	$F(CF_2)_7$	3fj/12	4fj/48
1f	H	2k	HCF_2	trace	4fk/57
1f	H	2l	$ClCF_2$	trace	4fl/57
1f	H	2m	CF_3	trace	4fm/53
1g	Ph	2h	$Cl(CF_2)_3$	trace	4gh/85
1g	Ph	2j	$F(CF_2)_7$	trace	4gj/91
1g	Ph	2k	HCF_2	trace	4gk/56
1g	Ph	2l	$ClCF_2$	trace	4gl/74
1g	Ph	2m	CF_3	trace	4gm/53

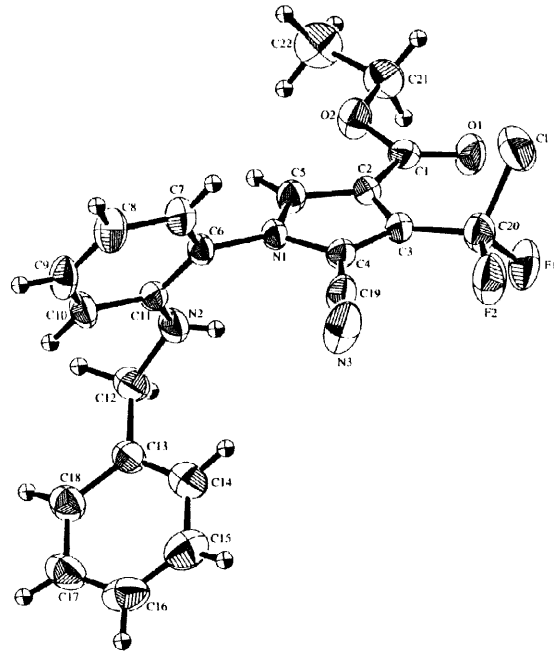


Figure 1: The X-ray structure of compound **4gl**.

In conclusion, the reactions of 1-alkylbenzimidazolium 3-ylides with ethyl 2,2-dihydropolyfluoroalkanoates not only provided a novel and simple access to fluoroalkyl substituted pyrrolo[1,2-a]quinoxaline and 1-aryl pyrrole derivatives, but also enriched the knowledge of the chemical properties of 1-alkyl benzimidazolium 3-ylides.

Experimental section.

General :

All reagents were of chemical pure or analytical reagent. IR spectra were recorded on an Bio-Rad FTS-20E or FTS 185 Spectrometer, using pellets. ^{1}HNMR spectra were measured on Bruker AM 300 (300MHz) Spectrometer, using TMS as internal standard. ^{19}FNMR spectra were recorded on a Varian EM-360L spectrometer (56.4 MHz), using TFA as external standard. In ^{19}FNMR spectra, chemical shifts (in ppm) were positive for upfield shifts and the values are reported as $\delta CFCl_3$ ($\delta CFCl_3=\delta TFA+76.8$). Mass spectra were taken on a Finnegan GC-MS 4021 spectrometer. Column chromatography was performed using silica gel H, particle size 10-40 μ .

*Prepation of compounds **3** and **4***

Typical procedure: A solution of 1.2 molar equiv. of 1-methyl-3-phenacyl benzimidazole bromide(**1a**), 1 molar equiv. of **2h** in 5 ml DMF in the presence of 1.5molar equiv. of potassium carbonate (K_2CO_3) and 2 equiv. of triethyl amine (NEt_3) was heated at 60°C for 4 hours. After the reaction was completed, the mixture was poured into 1N HCl solution to make the final solution with PH=5. The resulting solution was extracted

with dichloromethane(3x20 ml). The organic phase was combined and washed with saturated brine, dried over anhydrous sodium sulfate. After removal of solvent, the residue obtained was purified by column chromatography using petroleum ether and ethyl acetate (6:1) as eluant to give the product **3ah.**

3ah: IR(KBr): 3430(-OH), 1709(C=O) , 1125-1238(C-F) cm^{-1}; δH($CDCl_3$): 8.29(s,1H,C1-H), 7.75-6.43(m, 9H, Ar-H), 4.24(q,2H,-OCH_2-), 2.60(s,3H, -N-CH_3), 1.28(t,3H, -CH_3) ppm; δF($CDCl_3$): 65.8(m,2F), 97.8(m,2F), 115.2(m, 2F) ppm; m/z: 532(M^+, 11.9), 455(45.5), 387(54.18), 105(100.0), 77(43.12); $C_{24}H_{19}N_2F_6O_3Cl$: Calcd: C: 54.10 H: 3.59 N: 5.26 F:21.39; Found: C: 54.16 H: 3.57 N: 5.18 F: 20.84

3ai: IR(KBr): 3435(-OH), 1663(C=O), 1138-1252(C-F)cm^{-1}; δH($CDCl_3$): 7.63-6.46(m,10H, Ar-H), 4.33(q,2H, -OCH_2-), 2.77(s,3H, -N-CH_3), 1.34(t,3H, -CH_3) ppm; δH(d-DMSO): 8.55(s,1H, C1-H), 8.01-6.72(m, 9H, Ar-H), 4.21(q,2H, -OCH_2-), 2.59(s,3H, -N-CH_3), 1.26(t,3H, -CH_3) ppm; δF($CDCl_3$): 67.2(m,2F), 98.8(m,2F), 114.8-118.8(m, 6F) ppm; m/z: 632(M^+, 4.39), 555(M^+-Ph, 13.3), 527(M^+-COPh, 5.3), 487 (34.0), 105(100.0), 77(36.4); $C_{26}H_{19}N_2O_3F_{10}Cl$: Calcd: C: 49.34 H:3.03 N: 4.43; Found: C: 49.13 H: 2.62 N: 4.06

3aj: IR(KBr): 3397(-OH), 1666(C=O), 1131-1214(C-F) cm^{-1}; δH($CDCl_3$): 7.63-6.46(m,10H, Ar-H), 4.33(q,2H, -OCH_2-), 2.73(s,3H, -N-CH_3), 1.34(t,3H, -CH_3) ppm; δF($CDCl_3$): 79.8(m, 3F), 98.8(m, 2F), 117.8-125.8(m, 10F) ppm; m/z: 671(M+-CO2, 2.3), 640(M+-CO2Et, 9.0), 571(74.1), 105(100.0), 77(29.9); $C_{28}H_{19}N_2O_3F_{15}$: Calcd: C: 46.94 H: 2.67 N: 3.91; Found: C: 46.77 H: 2.23 N: 3.60

3bh: IR(KBr): 3400(-OH), 1682(C=O), 1118-1263(C-F)cm^{-1}; δH($CDCl_3$):7.68-6.44(m, 15H, Ar-H), 4.35-4.28(m, 4H, N-CH_2-,-OCH_2-), 1.32(t,3H,-CH_3)ppm; δF($CDCl_3$): 66.8(s,2F), 98.3(m,2F), 117.8(m,2F) ppm; m/z:563(M+-CO_2, 2.8), 535(M+-CO_2Et, 73.2), 503(17.0), 105(41.4), 91(CH_2Ph, 100.0), 77(19.8); $C_{30}H_{23}N_2O_3F_6Cl$: Calcd: C: 59.56 H:3.49 N: 4.63 F:18.84; Found: C: 59.93 H: 4.21 N: 4.28 F:19.04

3bi: IR(KBr): 3425(-OH), 1728(C=O), 1144-1233(C-F) cm^{-1}; δH($CDCl_3$): 7.67-6.45(m, 15H, Ar-H) , 4.36-4.10(m, 4H, N-CH_2-, -OCH_2-), 1.33(t, 3H ,CH_3) ppm; δF($CDCl_3$):53.8(m,2F), 86.1(m,2F), 104.8-108.8(m,6F) ppm; m/z: 631(M+-Ph, 2.0), 603(33.2), 535(14.0), 105(100.0), 91(96.3), 77(27.5); $C_{32}H_{23}N_2O_3F_{10}Cl$: Calcd:C: 54.21 H: 3.27 N: 3.96 F: 26.80; Found: C: 54.47 H: 3.27 N: 4.05 F: 27.25

3bj: IR(KBr): 3420(-OH), 1730(C=O), 1110-1250(C-F) cm^{-1}; δH($CDCl_3$):7.67-6.46(m, 15H, Ar-H), 4.36-4.27(m, 4H, N-CH_2-, -OCH_2-), 1.34(t, 3H,-CH_3) ppm; δF($CDCl_3$): 80.3(s,3F), 98.8(m,2F), 117.8-118.7(m,10F) ppm; m/z 792(M+, 1.7), 747(M+-CO_2, 2.1), 687 (27.6), 105(91.2) , 91(CH_2Ph, 100.0), 77(22.8); $C_{34}H_{23}N_2O_3F_{15}$: Calcd: C: 51.53 H: 2.93 N: 3.53; Found: C: 51.76 H: 2.86 N: 3.39

3ch: IR(KBr): 1697(C=O) , 1111-1280(C-F) cm^{-1}; δH($CDCl_3$): 8.01(s,1H, -C1-H), 7.52-6.65(m,9H, Ar-H),

5.12(d,$^2J_{HH}$=2.3Hz,1H, alkene-H), 5.01(s,2H, -N-CH_2), 4.56(d,$^2J_{HH}$=2.3Hz, 1H, alkene-H), 4..33(q,2H, -OCH_2), 1.35(t,3H, -CH_3) ppm; δF($CDCl_3$): 65.8(m,2F), 85.8(m,2F), 115.3(m,2F)ppm; m/z: 528(M+, 38.6), 343(42.9), 91(100.0); $C_{25}H_{19}N_2O_2F_6Cl$: Calcd: C: 56.78 H: 3.62 N: 5.30 F: 21.55; Found: C: 56.69 H: 3.34 N: 5.14 F: 20.98

3ci: IR(KBr): 1686(C=O), 1143-1276(C-F)cm^{-1}; δH($CDCl_3$): 8.03(s, 1H, C1-H), 7.51-6.67(m,9H, Ar-H), 5.11(d,$^2J_{HH}$=2.3Hz,1H,alkene-H), 5.00(s,2H, -N-CH_2), 4.56(d,$^2J_{HH}$=2.3Hz, 1H, alkene-H), 4.33(q,2H, -O-CH_2), 1.36(t,3H, -CH_3) ppm; δF($CDCl_3$): 66.8(m, 2F), 96.3(m, 2F), 116.8-120.8(m, 6F) ppm; m/z: 628(M+.42.7), 343(45.4), 91(100.0); $C_{27}H_{19}N_2O_2F_{10}Cl$: Calcd: C: 51.57 H: 3.05 N: 4.45 F: 30.21: Found: C: 51.57 H: 2.76 N: 4.29 F: 30.61

3cj: IR(KBr): 1694(C=O), 1129-1273(C-F)cm^{-1}; δH($CDCl_3$):8.03(s,1H, C1-H), 7.52-6.67(m,9H, Ar-H), 5.10(d,$^2J_{HH}$=2.3Hz, 1H, alkene-H), 5.55(s,2H, -N-CH2), 4.57(d,$^2J_{HH}$=2.3Hz, 1H, alkene-H), 4.35(q,2H, -O-CH2), 1.36(t,3H, -CH3) ppm; δF($CDCl_3$): 80.3(s,3F), 96.8(m,2F), 116.8(m,10F) ppm; m/z: 712(M+, 13.7), 343(25.8), 91(100.0); $C_{29}H_{19}N_2O_2F_{15}$: Calcd: C: 48.89 H: 2.69 N: 3.93 F: 40.00; Found: C: 49.32 H: 2.66 N: 3.38 F: 39.27

3dh: IR(KBr): 1748(C=O), 1686(C=O), 1109-1236(C-F)cm^{-1}; δH($CDCl_3$):8.26(s,1H, C1-H), 7.79-7.23(m,9H, Ar-H), 5.53(s,2H, -N-CH_2), 4. 40(q,2H, -OCH_2), 1.39(t, 3H, -CH_3) ppm; δF($CDCl_3$): 65.8(m,2F), 95.3(m,2F),115.8(m,2F) ppm; m/z: 530(M+, 9.4), 375(21.9), 91(100.0); $C_{24}H_{17}N_2O_3F_6Cl$: Calcd: C: 54.30 H: 3.23 N: 5.28 ; Found: C: 53.93 H: 3.02 N: 4.98

3di: IR(KBr): 1721(C=O), 1681(C=O), 1104-1268(C-F) cm^{-1}; δH($CDCl_3$): 8.26(s,1H, C1-H), 7.76-7.22(m,9H, Ar-H), 5.52(s,2H, -N-CH2), 4.34(q,2H, -OCH_2), 1.39(t,3H, -CH_3)ppm; δF($CDCl_3$): 68.3(m, 2F) ,113.8(m,2F), 119.3-121.8(m,6F) ppm; m/z: 630(M+,9.1), 375(26.4), 91(100.0); $C_{26}H_{17}N_2O_3F_{10}Cl$: Calcd: C: 49.50 H: 2.72 N: 4.44 F: 30.11; Found: C: 49.50 H: 2.74 N: 4.40 F: 30.40

3dj: IR(KBr): 1692(C=O), 1682(C=O), 1149-1267(C-F)cm^{-1}; δH($CDCl_3$): 8.28(s,1H, C1-H), 7.79-7.23(m,9H, Ar-H), 5.54(s,2H, -N-CH2), 4.40(q,2H, -CH2), 1.42(t, 3H, -CH3) ppm; δF($CDCl_3$): 79.8(s, 3F), 95.8(m,2F), 116.8-125.8(m,10F) ppm; m/z: 714(M+, 8.8), 375(26.6), 91(100.0); $C_{28}H_{17}N_2O_3F_{15}$: Calcd: C: 47.07 H: 2.40 N: 3.92 F: 39.89; Found: C: 47.05 H: 2.21 N: 3.79 F: 39.42

4fh: IR(KBr): 3431(-NH), 2242(-CN), 1735(C=O), 1120-1207(C-F)cm^{-1}; δH($CDCl_3$): 7.64(s, 1H, C1-H), 7.45-6.78(m,4H, Ar-H), 4.32(q,2H, -OCH2-), 3.43(s, 1H, -NH), 2.85(s, 3H, -N-CH_3), 1.31(t, 3H, -CH_3) ppm; δF($CDCl_3$): 66.8(t, 2F), 101.8(m, 2F), 41.0(s, 2F) ppm; m/z: 454(M^++1, 47.29), 453(M^+, 100.0), 408(22.93), 270(30.10); $C_{18}H_{14}N_3O_2F_6Cl$ Requires 453.0678 HRMS Found 453.0635

4fi: IR(KBr): 3422(-NH) , 2236(-CN), 1728(-C=O), 1104-1207(C-F)cm^{-1}; δH($CDCl_3$): 7.26(s, 1H, C1-H), 7.07-6.41(m, 4H, Ar-H), 3.93(q, 2H, -OCH_2-), 3.15(s, 1H, -NH), 2.50(s, 3H, N-CH_3), 0.95(t, 3H, -CH_3) ppm; δF($CDCl_3$): 66.8(t, 2F), 101.8(s, 2F), 119.3(m,6F) ppm; m/z: 554(M^++1, 39.74), 553(M^+, 100.0), 508(23.01), 328(12.35), 270(50.62); $C_{20}H_{14}N_3O_2F_{10}Cl$: Calcd: C, 43.38 H, 2.55 N, 7.59 F, 34.31 ; Found: C, 43.77 H, 2.45 N, 7.45 F, 34.38

3fi: IR(KBr): 3487(=NH), 1677(C=O), 1613, 1142-1296(C-F)cm^{-1}; δH($CDCl_3$): 8.18(s, 1H, C1-H), 7.67-7.15(m, 4H, Ar-H), 4.36(q, 2H, -OCH_2-), 3.71(s, 3H, -N-CH_3), 1.37(t, 3H, -CH_3) ppm; δF ($CDCl_3$): 67.0(s, 2F), 95.0(m, 2F), 117.0-120.5(m, 6F) ppm; m/z: 554(M^++1, 32.3), 553(M^+, 100.0), 508(19.2), 270(36.5); $C_{20}H_{14}N_3O_2F_{10}Cl$ Requires 553.0614 HRMS Found 553.0660

4fj: IR(KBr): 3431(-NH), 2242(-CN), 1735(C=O), 1120-1207(C-F)cm^{-1}; δH($CDCl_3$): 7.65(s, 1H, C1-H), 7.46-6.79(m,4H, Ar-H), 4.32(q, 2H, -OCH_2-), 3.41(s, 1H, -NH), 2.86(s, 3H, -N-CH_3), 1.35(t, 3H, -CH_3) ppm; δF($CDCl_3$): 80.8(s, 3F), 102.8(s,2F), 119.8-1263(m,10F) ppm; m/z:638(M^++1, 97.41), 637(M^+, 100.0), 328(11.44), 298(16.20), 270(80.10), 171(28.46); $C_{22}H_{14}N_3O_2F_{15}$ Requires 637.0846 HRMS Found 637.0849

3fj: IR(KBr): 3142(=NH), 1676(C=O), 1614, 1149-1283 cm^{-1} δH ($CDCl_3$): 8.17(s, 1H, C1-H), 7.65-7.13(m,4H, Ar-H), 4.34(q, 2H, -OCH_2-), 3.69(s, 3H, -N-CH_3), 1.33(t, 3H, -CH_3) ppm; δF ($CDCl_3$): 78.0(s, 3F), 93.5(m, 2F), 115.0-124.0(m, 10F) ppm; m/z: 638(M^++1, 100.0), 592(19.5), 522(13.9), 270(44.4), 250(18.9); $C_{22}H_{14}N_3O_2F_{15}$: Calcd: C, 41.46 H, 2.21 N, 6.59 F, 44.71; Found: C, 41.70 H, 2.10 N, 6.35 F, 44.62

4fk: IR(KBr): 3422(-NH), 2237(-CN), 1711(C=O), 1115-1237(C-F)cm^{-1}; δH($CDCl_3$):7.50(s, 1H, C1-H), 7.41-6.79(m, 5H, Ar-H +CF_2H), 4.34(q, 2H, -OCH_2-), 3.45(s, 1H, -NH), 2.86(s, 3H, -N-CH_3), 1.36(t, 3H, -CH_3) ppm; δF($CDCl_3$): 111.3(d, J_{FF}=60Hz, 2F) ppm ; m/z: 320(M^++1, 20.29), 319(M^+, 100.0), 270(50.20), 247(33.0), 226(29.43); $C_{16}H_{15}N_3O_2F_2$ Requires 319.1132 HRMS Found 319.1092

4fl: IR(KBr): 3430, 3406 (NH), 3150, 2928, 2237(-CN), 1729(C=O), 1118-1287(C-F) cm^{-1} δH($CDCl_3$): 7.56(s, 1H, C1-H), 7.44-6.77(m,4H, Ar-H), 4.35(q,2H, -OCH_2-), 3.49(s, 1H, -NH), 2.87(s,3H, -N-CH_3), 1.30(t, 3H, -CH_3)ppm; δF($CDCl_3$): 43.8(s, 2F) ppm; m/z: 354(M^++1, 30.63), 353(M^+, 100.0), 317(18.63), 298(24.29), 270(68.28), 245(37.21); $C_{16}H_{14}N_3O_2F_2Cl$ Requires 353.0742 HRMS Found 353.0761

4fm: IR(KBr): 3401(-NH), 3149, 2991, 2237(-CN), 1732(C=O), 1104-1268(C-F) cm^{-1} δH($CDCl_3$):7.59(s,

1H, C1-H), 7.42-6.80(m,4H, Ar-H), 4.33(q, 2H, -OCH2-), 3.50(s, 1H, -NH), 2.90(s, 3H, -N-CH_3), 1.34(t, 3H,-CH_3)ppm; δF($CDCl_3$):55.8(s,3F)ppm; m/z:338(M^++1, 21.85), 337(M^+, 100.0), 292(23.23), 268(37.98), 163(88.90) ; $C_{16}H_{14}N_3O_2F_3$ Requires 337.1038 HRMS Found 337.1010

4gh: IR(KBr): 3420(-NH), 3156, 2235(-CN), 1732(C=O), 1120-1299(C-F) cm^{-1} δH($CDCl_3$):7.66(s, 1H, C1-H), 7.33-6.82(m,9H, Ar-H), 4.38(s, 2H, -N-CH_2-), 4.32(q, 2H, -OCH_2-), 3.75(s, 1H, -NH), 1.31(t, 3H, -CH_3) ppm; δF($CDCl_3$): 64.8(t, 2F), 99.8(t, 2F), 116.3(s, 2F) ppm; m/z:530(M^++1, 69.84), 529(M^+, 100.0), 480(19.23), 91(49.78); $C_{24}H_{18}N_3O_2F_6Cl$ Requires 529.0991 HRMS Found 529.1000

4gj: IR(KBr): 3430(-NH), 3144, 2989, 2239(-CN), 1695(C=O), 1103-1298(C-F) cm^{-1}; δH($CDCl_3$) 7.67(s, 1H, C1-H), 7.39-6.82(m,9H, Ar-H), 4.38(s, 2H, N-CH_2-), 4.32(q,2H, -OCH_2-), 3.72(s, 1H, -NH), 1.36(t, 3H, -CH_3) ppm; δF($CDCl_3$): 80.8(s, 3F), 102.3(s, 2F), 118.8-125.8(m,10F) ppm; m/z: 715(M^++2, 15.12), 714(M^++1, 48.48), 713(M^+, 31.34), 91(100.0); $C_{28}H_{18}N_3O_2F_{15}$: Calcd: C, 47.14 H, 2.54 N, 5.89 ; Found: C, 47.18 H, 2.46 N, 5.62

4gk: IR(KBr): 3396(-NH), 3140, 2236(-CN), 1706(C=O), 1134-1270(C-F)cm^{-1}; δH($CDCl_3$):7.55(s, 1H, C1-H), 7.31-6.79(m, 10H, Ar-H +CF_2H), 4.39(s, 2H, -N-CH_2), 4.30(q, 2H, -OCH_2-), 4.18(s, 1H, -NH), 1.36(t, 3H, -CH_3) ppm; δF($CDCl_3$): 111.3(d, J_{FF}=60Hz, 2F) ppm; m/z:396(M^++1, 29.06), 395(M^+, 94.08), 374(25.43), 326(29.89), 91(100.0); $C_{22}H_{19}N_3O_2F_2$ Requires 395.1445 HRMS Found 395.1446

4gl: IR(KBr): 3409(-NH), 3142, 2233(-CN), 1724(C=O), 1105-1286(C-F)cm^{-1}; δH($CDCl_3$): 7.62(s, 1H, C1-H), 7.33-6.80(m, 9H, Ar-H), 4.41(s, 2H, -N-CH_2-), 4.35(q, 2H, -OCH_2-), 4.04(s, 1H, -NH), 1.37(t, 3H, -CH_3) ppm; δF($CDCl_3$): 43.8(s, 2F)ppm; m/z:430(M^++1.56.14), 429(M^+, 100.0), 394(46.06), 344(30.53), 91(45.83) $C_{22}H_{18}N_3O_2F_2Cl$: Calcd: C, 61.47 H, 4.22 N, 9.78 F, 8.84; Found: C, 61.58 H, 4.21 N, 9.42 F, 8.84

4gm: IR(KBr): 3397(-NH), 3143, 2240(-CN), 1719(C=O), 1143-1267(C-F)cm^{-1}; δH($CDCl_3$):7.61(s, 1H, C1-H), 7.27-6.77(m, 9H, Ar-H), 4.41(s, 2H, -N-CH_2-), 4.30(q, 2H, -OCH_2-), 4.16(s, 1H, -NH), 1.33(t, 3H, -CH_3) ppm; δF($CDCl_3$):56.3(s, 3F) ppm; m/z: 414(M^++1, 26.80), 413(M^+, 87.65), 344(45.94), 91(100.0); $C_{22}H_{18}N_3O_2F_3$ Requires 413.1357 HRMS Found 413.1393

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