Synthesis of Fluorinated Indolizines and 4*H*-Pyrrolo[1,2-*a*]benzimidazoles via 1,3-Dipolar Cycloaddition of Fluoroalkenes to *N*-Ylides

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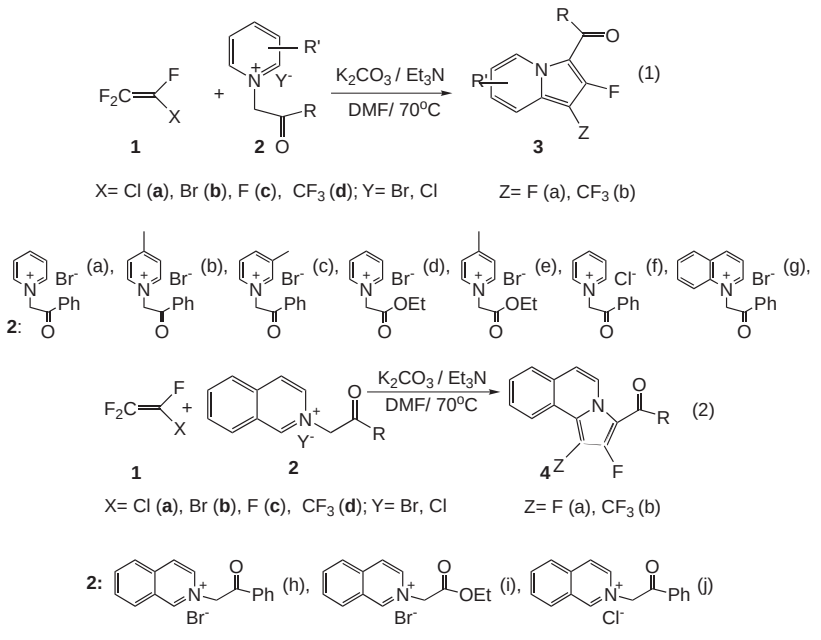
Abstract: In the presence of K_2CO_3 and Et_3N, pyridinium, quinolinium, isoquinolinium and benzimidazolinium *N*-ylides, generated in situ from their halides, react with gaseous flouroalkenes [CF_2=CFX (**1**), X = Cl (**a**), Br (**b**), CF_3 (**d**)] in DMF under atmospheric pressure in normal glassware at 70 °C to give the corresponding fluorinated indolizines or *H*-pyrrolo[1,2-*a*]benzimidazoles via 1,3-dipolar [3+2] cycloaddition. Similar results are obtained with tetrafluoroethene in an autoclave.

Key words: 1,3-dipolar addition, [3+2] cycloaddition, fluoroalkene, fluorinated indolizine, fluorinated *H*-pyrrolo[1,2-*a*]benzimidoazole

Heterocyclic compounds such as indolizines and 4*H*-pyrrolo[1,2-*a*]benzimidazoles are important bioactive compounds which have wide applications in biology, pharmacology and agrochemistry.[1,2] Since the introduction of fluorine atom(s) often confers unique properties on a molecule in terms of increased lipophilicity, which could change in vivo absorption and transport rates,[3] much effort has been paid to the development of methodologies for synthesizing fluorinated heterocycles. In 1980s, Banks et al. first reported the synthesis of a few fluorinated indolizines via [3+2] cycloaddtion reactions between pyridinium methylide and fluorinated dipolarophiles, such as trifluoroacetonitrile, hexafluorobut-2-yne, 3,3,3-trifluoropropyne and hexafluoropropene.[4] However, these reactions were so complicated and the yields were so low that they did not optimize the reaction conditions.[4]

We recently found[5] that chlorofluorocarbons (CFCs) and hydrofluorocarbon (HFCs) such as HCFC-133a (CF_3CH_2Cl, bp 6 °C) and HFC-134a (CF_3CH_2F, bp –27 °C) possess high solubility in some aprotic organic solvents, such as *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and *N*-methyl-2-pyrrolidone (NMP). This enabled to carry out their nucleophilic substitution reactions in these solvents at 80–100 °C under atmospheric pressure in normal glassware rather than in an autoclave or sealed pyrex tube.[5] We envisioned that this solvent effect could also be applied to the fluoroalkenes



Scheme 1

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[CF_2=CFX (**1**), X = Cl (**a**), bp –26.8 °C; Br (**b**), bp –4.5 °C; F (**c**), bp –76 °C; CF_3 (**d**), bp –29 °C], from which fluorinated indolizines and 4*H*-Pyrrolo[1,2-*a*]benzimidazoles may be synthesized through [3+2] cycloaddition reaction in normal glassware. And it was, indeed, found to be the case and we herein report the results.

Table 1 Yields of the Reaction of **1** with **2** in DMF[a]

Entry	1	2	Product	Yield (%)
1	**1a**	**2a**	**3aaa**	58
2[b]	**1a**	**2a**	**3aaa**	66
3	**1a**	**2b**	**3aba**	64
4[c]	**1a**	**2c**	**3aca**	60
5	**1a**	**2d**	**3ada**	37
6	**1a**	**2f**	**3aaa**	52
7	**1a**	**2g**	**3aga**	11
8	**1a**	**2h**	**4aha**	85
9	**1a**	**2i**	**4aia**	79
10	**1a**	**2j**	**4aha**	74
11	**1b**	**2a**	**3aaa**	57
12	**1b**	**2b**	**3aba**	77
13	**1b**	**2d**	**3ada**	75
14	**1b**	**2g**	**3aga**	20
15	**1b**	**2h**	**4aha**	86
16	**1b**	**2i**	**4aia**	91
17	**1b**	**2j**	**4aha**	74
18[b]	**1c**	**2b**	**3aba**	32
19[b,c]	**1c**	**2c**	**3aca**	37
20[b]	**1c**	**2h**	**4aha**	74
21[b]	**1c**	**2i**	**4aia**	71
22	**1d**	**2a**	**3dab**	62
23	**1d**	**2b**	**3dbb**	71
24	**1d**	**2d**	**3ddb**	57
25	**1d**	**2e**	**3deb**	53
26	**1d**	**2g**	trace	–
27	**1d**	**2h**	**4dhb**	81
28	**1d**	**2i**	**4dib**	67

[a] **1**–**2**–K_2CO_3–Et_3N = 5:1:1:1; 70 °C, 24 h.
[b] The reaction was carried out in an autoclave at 70 °C for 24 h.
[c] A mixture of 6- and 8-methylindolizine derivatives was obtained in nearly a 1:1 ratio.

To DMF was added fluoroalkenes **1a**, **1b** or **1d** cooled with dry ice/acetone, followed by pyridinium, quinolinium or isoquinolinium halides (**2**), K_2CO_3 and Et_3N. After stirring at 70 °C for 24 hours, the fluorinated indolizines **3** (equation 1) or their analogues **4** (equation 2) were obtained in moderate to good yields (Scheme 1, Table 1).

The structures of **3** were readily assigned on the basis of ^{1}H NMR, ^{19}F NMR, MS and elemental analyses. However, it is difficult to determine the exact structures of products **4dhb** and **4dib**, which might be **4dhb′** and **4dib′** (Figure 1) from the reactions of isoquinolinium halides **2h**–**j**, based only on ^{1}H NMR and ^{19}F NMR spectroscopy. Therefore the structure of the cycloadduct **4dhb** was established by a single-crystal X-ray analysis (Figure 2).

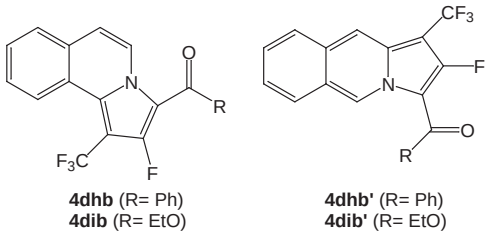


Figure 1 Possible structures of Products **4dhb**, **4dhb′** and **4dib**, **4dib′**

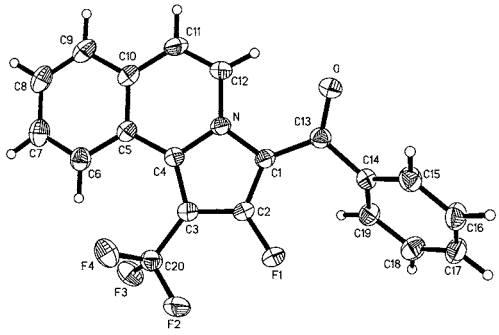


Figure 2 The X-ray structure of **4dhb**

If **2c** was used, a mixture of 6-methyl- and 8-methylindolizine derivatives **3aca**, **3aca′** (Figure 3) was obtained in nearly 1:1 ratio (Entries 4,19, Table 1).

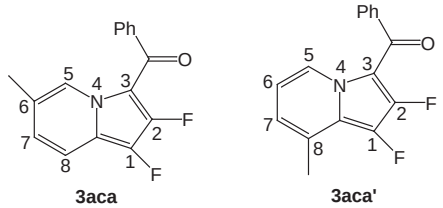


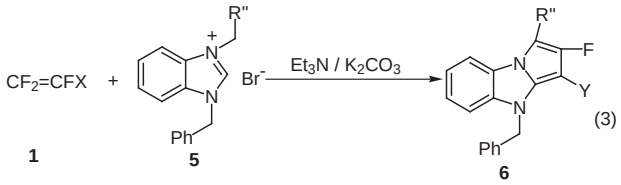
Figure 3 Structures of 6-methyl- and 8-methylindolizine derivatives **3aca** and **3aca′**

The yields of the reactions of **1** with isoquinolinium halides **2h**,**i** are always much higher than those with quinolinium halides **2g** (Entries 8,9,10,15,16,17,27,28 vs. 7,14,26 in Table 1).

In order to show the advantage of the solvent effect, the same reaction of **1a** with **2a**, was also carried out in an autoclave and the yield of **3aaa** was found to be only slightly higher than that in normal glassware (Entry 1 vs. 2 in Table 1). Unfortunately, the reaction of tetrafluoroethene (**1c**) with **2** has to be carried out in an autoclave probably due to its extremely low boiling point (–76 °C) (Entries 18–21, Table 1).

In the presence of base, benzimidazolinium bromide **5**, which was reported to form an *N*-ylide,[6] also reacted with **1** to produce fluorinated 4*H*-pyrrolo[1,2-*a*]benzimidazoles via 1,3-dipolar cycloaddition reaction under similar reaction conditions. The results are listed in Table 2.

Table 2 The Yields of the Reaction of **1** with **5** in DMF[a]



X = Cl (a), Br (b), F (c), CF_3 (d);
R" = COPh (a), COOEt (b), CN (c)

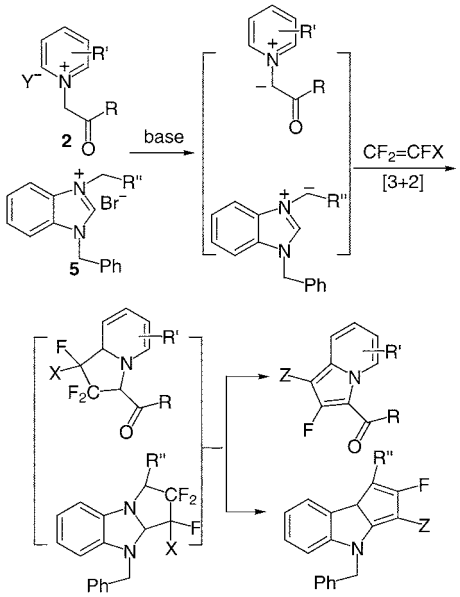
Y=F (a), CF_3 (b)

Entry	1	5	Product	Yield (%)
1[b]	**1a**	**5a**	**6aaa**	61
2[b]	**1a**	**5b**	**6aba**	58
3[b]	**1a**	**5c**	**6aca**	54
4[c]	**1b**	**5a**	**6aaa**	72
5[c]	**1b**	**5b**	**6aba**	79
6[c]	**1b**	**5c**	**6aca**	62
7[d]	**1c**	**5a**	**6aaa**	66
8[d]	**1c**	**5b**	**6aba**	79
9[e]	**1d**	**5a**	**6dab**	58
10[e]	**1d**	**5b**	**6dbb**	47
11[e]	**1d**	**5c**	**6dcb**	73
12[d,e]	**1d**	**5a**	**6dab**	67

[a] 70 °C, 18 h.
[b] **1**–**5**–K_2CO_3–Et_3N = 4:1:6:1.5.
[c] **1**–**5**–K_2CO_3–Et_3N = 6:1:8:1.5; the solvent was DMSO.
[d] The reaction was carried out in an autoclave.
[e] **1**–**4**–K_2CO_3–Et_3N = 2.5:1:1.5:1.1.

Similarly, the yield of **6dab** from the reaction between **1d** and **5** was also only slightly higher in autoclave than that in normal glassware (Entry 9 vs. 12 in Table 2) and tetrafluoroethene (**1c**) reacted with **5** only in an autoclave under pressure (Entries 7,8 in Table 2).

As reported by Banks et al.,[4] the reaction mechanism might be described as shown in Scheme 1. Namely, the 1,3-dipolar [3+2] cycloaddition of pyridinium, quinolinium isoquinolinium and benzimidazolinium *N*-ylide, generated in situ from the corresponding salts in the presence of the base, with the fluoroalkene **1**, followed by HX (X = F, Cl, Br) elimination, yields the fluorinated indolizine and 4*H*-pyrrolo[1,2-*a*]benzimidazole, respectively (Scheme 2).



Scheme 2

Clearly, from Scheme 1, it is essential to choose a suitable base for these reactions. The base should not only be able to deprotonate the pyridinium, quinolinium, isoquinolinium and benzimidazolinium halides to form the corresponding *N*-ylides, but also to effectively eliminate HX (X = F, Cl, Br) to produce the indolizines or 4*H*-pyrrolo[1,2-*a*]benzimidazoles after the 1,3-dipolar cycloaddition. A mixture of organic and inorganic base, i.e. K_2CO_3 and Et_3N, was found to give the best results. If only the inorganic base, either KOH or K_2CO_3, was used, the yields of the reaction between **1a** and **2a** were much lower, only 21 and 14%, respectively. When Et_3N or DBU was employed solely, none of the products were formed. This is, probably, the reason why Banks et al. failed to isolate the target compounds in good yields from the complicated mixture in the reaction of **1d** with **2a** or **2d**,[4] because sodium hydride was used as the only base, which could not effectively eliminate HF, thus causing the complexity of the reaction.

In summary we have presented a convenient method for synthesizing some fluorinated indolizines and 4*H*-pyrrolo[1,2-*a*]benzimidazoles from gaseous fluoroalkenes in DMF under atmospheric pressure in normal glassware.

Boiling points are uncorrected. ^{1}H NMR spectra were taken on a Varian Mercury-300 (300 MHz) NMR spectrometer. ^{19}F NMR spectra were obtained on a Varian Mercury-300 (282 MHz) spectrometer. Chemical shifts were reported in parts per million relative to TMS as an internal standard ($\delta_{TMS} = 0$) for ^{1}H NMR spectra and $CFCl_3$ as an external standard [δ ($CFCl_3$) = 0] for ^{19}F NMR (upfield shift being designated as negative) spectra. Acetone-d_6 was used as the solvent for NMR measurements. IR spectra were recorded on a Perkin-Elmer Jeol 983 spectrometer. MS and HRMS spectra were recorded on a Hewlett-Packard HP-5989A spectrometer.

Caution: Fluoroalkenes **1a**, **1b**, **1d** are toxic on inhalation and their reactions must be performed in an efficient fume cupboard.

Fluorinated Indolizines and 4*H*-Pyrrolo[1,2-*a*]benzimidazoles 3; (1,2-Difluoroindolizin-3-yl)phenylmethanone (3aaa); Typical Procedure

Precooled CF_2=CFCl (**1a**; 0.814 g, 6.99 mmol), with dry ice/acetone in a trap, was added quickly to DMF (15 mL). To this solution were added K_2CO_3 (0.193 g, 1.40 mmol), Et_3N (0.155 g, 1.54 mmol), and **2a**[7] (0.389 g, 1.40 mmol). After stirring at 70 °C for 24 h, brine (50 mL) was added to the reaction mixture and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined extracts were washed with brine (3 × 10 mL) and dried (Na_2SO_4). After removal of EtOAc, the residue was subjected to column chromatography on silica gel to give **3aaa** (0.207 g, 58%) as a yellow solid; mp 70–72 °C.

IR (KBr): 3100, 1609, 1394, 1233, 980, 834, 747, 701, 604 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 6.96–7.65 (m, 8 H), 9.58 (dd, J_{HH} = 8.4, 1.2 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –155.78 (d, J_{FF} = 12.7 Hz, 1 F), –188.14 (d, J_{FF} = 12.7 Hz, 1 F).

MS (EI): *m*/*z* (%) = 257 (M^+, 85), 228 (31), 180 (25), 152 (43), 105 (59), 77 (100), 51 (42).

HRMS (EI): *m*/*z* Calcd for $C_{15}H_9F_2NO$: 257.065220. Found: 257.06595.

(1,2-Difluoro-7-methylindolizin-3-yl)phenylmethanone (3aba)

Mp 87–89 °C.

IR (KBr): 2999, 1615, 1477, 1394, 1235, 797, 708, 670, 555 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 2.47 (s, 3 H), 6.99–7.02 (m, 1 H), 7.50–7.61 (m, 4 H), 7.73–7.76 (m, 2 H), 9.63 (d, J_{HH} = 7.2 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): = –155.52 (d, J_{FF} = 11.3 Hz, 1 F), –189.13 (d, J_{FF} = 11.3 Hz, 1 F).

MS (EI): *m*/*z* (%) = 271 (M^+, 100), 242 (46), 194 (23), 166 (37), 105 (40), 77 (78), 51 (26).

Anal. Calcd for $C_{16}H_9F_2NO$: C, 70.84; H, 4.09; N, 5.16. Found: C, 70.29; H, 4.22; N, 5.04.

(1, 2-Difluoro-6-methylindolizin-3-yl)phenylmethanone (3aca) and (1,2-Difluoro-8-methylindolizin-3-yl)phenylmethanone (3aca′)

IR (KBr): 3036, 2926, 1612, 1473, 1419, 1396, 1261, 1053, 798, 714, 690 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 2.26 (s, 3 H × 0.5), 2.45 (s, 3 H × 0.5), 6.82–7.63 (m, 7 H), 9.41–9.44 (m, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –156.55 (d, J_{FF} = 12.7 Hz, 1 F × 0.5), –156.64 (d, J_{FF} = 10.3 Hz, 1 F × 0.5), –185.28 (d, J_{FF} = 10.3 Hz, 1 F), –188.48 (d, J_{FF} = 12.7 Hz, 1 F).

MS (EI): *m*/*z* (%) = 271 (M^+, 100), 243 (36), 166 (30), 105 (44), 77 (79), 51 (22).

Ethyl 1,2-Difluoroindolizine-3-carboxylate (3ada)

Mp 39–41 °C.

IR (KBr): 3105, 2927, 1691, 1592, 1477, 1418, 1241, 1118, 1042, 962, 748 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.22 (t, J_{HH} = 6.9 Hz, 3 H), 4.21 (q, J_{HH} = 6.9 Hz, 2 H), 6.79 (m, 1 H), 7.04 (m, 1 H), 7.40 (dd, J_{HH} = 8.7, 1.2 Hz, 1 H), 9.12 (dd, J_{HH} = 6.9, 1.2 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –159.58 (d, J_{FF} = 12.1 Hz, 1 F), –188.74 (d, J_{FF} = 12.1 Hz, 1 F).

MS (EI): *m*/*z* (%) = 225 (M^+, 100), 197 (57), 180 (32), 153 (70), 125 (20), 57 (16).

Anal. Calcd for $C_{11}H_9F_2NO_2$: C, 58.67; H, 4.03; N, 6.22; F, 16.87. Found: C, 58.90; H, 4.02; N, 6.24; F, 16.79.

2,3-Difluoropyrrolo[1, 2-*a*]quinolin-1-yl)phenylmethanone (3aga)

Mp 171–173 °C.

IR (KBr): 2925, 1726, 1378, 755, 691 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 7.39–7.78 (m, 9 H), 8.04–8.08 (m, 1 H), 9.31 (d, J_{HH} = 8.1 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –158.79 (d, J_{FF} = 13.50 Hz, 1 F), –180.47 (d, J_{FF} = 13.50 Hz, 1 F).

MS (EI): *m*/*z* (%) = 307 (M^+, 47), 279 (18), 230 (11), 202 (20), 105 (51), 77 (70), 43 (100).

Anal. Calcd for $C_{19}H_{11}F_2NO$: C, 74.25, H, 3.61, N, 4.56, F, 12.36. Found: C, 73.99, H, 3.96, N, 4.38, F, 12.12.

(2-Fluoro-1-trifluoromethylindolizin-3-yl)phenylmethanone (3dab)[4c]

Mp 99–101 °C.

IR (KBr): 3132, 1616, 1555, 1410, 1226, 1108, 958, 759, 691 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 7.33–7.36 (m, 1 H), 7.53–7.66 (m, 4 H), 7.79–7.84 (m, 3 H), 9.75 (d, J_{HH} = 6.9 Hz, 1 H).

^{19}F NMR (282MHz, acetone-d_6): δ = –55.71 (d, J_{FF} = 10.72 Hz, 3 F), –138.10 (d, J_{FF} = 10.72 Hz, 1 F).

MS (EI): *m*/*z* (%) = 307 (M^+, 64), 289 (17), 280 (34), 230 (22), 105 (26), 77 (25).

(2-Fluoro-7-methyl-1-trifluoromethylindolizin-3-yl)phenylmethanone (3dbb)

Mp 116–118 °C.

IR (KBr): 2922, 1652, 1408, 1110, 790, 692, 662 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 2.52 (s, 3 H), 7.14–7.16 (m, 1 H), 7.51–7.63 (m, 4 H), 7.76–7.80 (m, 2 H), 9.63 (d, J_{HH} = 7.5 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –55.62 (d, J_{FF} = 10.53 Hz, 3 F), –137.79 (d, J_{FF} = 10.53 Hz, 1 F).

MS (EI): *m*/*z* (%) = 321 (M^+, 100), 302 (15), 261 (40), 244 (25), 216 (16), 105 (17), 77 (21).

HRMS (EI): *m*/*z* Calcd for $C_{17}H_{11}F_4NO$: 321.07768. Found: 321.07545.

Ethyl 2-Fluoro-1-trfluoromethylindolizine-3-carboxylate (3ddb)[4c]

Mp 100–102 °C.

IR (KBr): 3123, 3000, 1699, 1435, 1214, 951, 758, 713, 675 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.30 (t, J_{HH} = 7.1 Hz, 3 H), 4.02 (q, J_{HH} = 7.1 Hz, 2 H), 7.24–7.26 (m, 1 H), 7.52–7.54 (m, 1 H), 7.76 (d, J_{HH} = 9.6 Hz, 1 H), 9.53 (d, J_{HH} = 8.1 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –55.60 (d, J_{FF} = 9.87 Hz, 3 F), –141.34 (d, J_{FF} = 9.87 Hz, 1 F).

MS (EI): *m*/*z* (%) = 275 (M^+, 99), 256 (12), 247 (55), 230 (66), 203 (100), 184 (33), 152 (25).

Ethyl 2-Fluoro-7-methyl-1-trifluoromethylindolizine-3-carboxylate (3deb)
Mp 71–73 °C.

IR (KBr): 3141, 2999, 1695, 1472, 1265, 1220, 1108, 799, 691 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.37 (t, J_{HH} = 7.2 Hz, 3 H), 2.47 (s, 3 H), 4.39 (d, J_{HH} = 7.2 Hz, 2 H), 7.08 (d, J_{HH} = 7.2 Hz, 1 H), 7.51 (s, 1 H), 9.36 (d, J_{HH} = 7.2 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –55.48 (d, J_{FF} = 10.25 Hz, 3 F), –141.25 (d, J_{FF} = 10.25 Hz, 1 F).

MS (EI): *m*/*z* (%) = 289 (M^+, 100), 293 (37), 244 (41), 217 (55), 167 (14).

HRMS (EI): *m*/*z* Calcd for $C_{13}H_{11}F_4NO_2$: 289.07259. Found: 289.07325.

(1,2-Difluoropyrrolo[2,1-*a*]isoquinlin-3-yl)phenylmethanone (4aha)
Mp 166–168 °C.

IR (KBr): 3011, 1735, 1624, 1536, 1417, 1383, 930, 794, 675 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): = 7.33 (d, J_{HH} = 7.8 Hz, 1 H), 7.54–7.93 (m, 8 H), 8.34 (dd, J_{HH} = 0.9, 6.9 Hz, 1 H), 9.26 (d, J_{HH} = 7.8 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): = –160.53 (d, J_{FF} = 12.56 Hz, 1 F), –180.39 (d, J_{FF} = 12.56 Hz, 1 F).

MS (EI): *m*/*z* (%) = 307 (M^+, 100), 279 (36), 230 (18), 202 (22), 105 (15), 77 (21).

Anal. Calcd for $C_{19}H_{11}F_2NO$: C, 74.25; H, 3.61; N, 4.56; F, 12.36. Found: C, 74.09; H, 3.86; N, 4.54; F, 11.96.

Ethyl 1,2-Difluoropyrrolo[2,1-*a*]isoquinlin-3-carboxylate (4aia)
Mp 121–123 °C.

IR (KBr): 3132, 2980, 1691, 1595, 1424, 1253, 1066, 797, 771, 679 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.40 (t, J_{HH} = 7.0 Hz, 3 H), 4.42 (q, J_{HH} = 7.0 Hz, 2 H), 7.26 (d, J_{HH} = 7.8 Hz, 1 H), 7.64–7.70 (m, 2 H), 7.85 (d, J_{HH} = 7.8 Hz, 1 H), 8.27 (d, J_{HH} = 7.8 Hz, 1 H), 9.12 (d, *J* = 7.8 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –160.61 (d, J_{FF} = 11.68 Hz, 1 F), –180.47 (d, J_{FF} = 11.68 Hz, 1 F).

MS (EI): *m*/*z* (%) = 275 (M^+, 86), 247 (66), 230 (27), 202 (79), 182 (21), 176 (29), 152 (81).

Anal. Calcd for $C_{15}H_{11}F_2NO$: C, 65.45, H, 4.03, N, 5.09, F, 13.80. Found: C, 65.47, H, 4.19, N, 4.89, F, 13.51.

(2-Fluoro-1-trifluoromethylpyrrolo[2,1-*a*]isoquinlin-3-yl)phenylmethanone (4dhb)
Mp 174–176 °C.

IR (KBr): 3148, 1685, 1617, 1458, 1421, 1207, 1106, 919, 805, 735 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 7.17–7.35 (m, 3 H), 7.56–8.05 (m, 6 H), 8.43–8.46 (m, 1 H), 9.36 (d, J_{HH} = 7.5 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –54.72 (d, J_{FF} = 23.12 Hz, 3 F), –141.25 (d, J_{FF} = 23.12 Hz, 1 F).

MS (EI): *m*/*z* (%) = 357 (M^+, 100), 329 (9), 280 (30), 252 (18), 105 (29), 77 (37).

Anal. Calcd for $C_{20}H_{11}F_4NO$: C, 67.23; H, 3.10; N, 3.92; F, 21.27. Found: C, 66.92; H, 3.28; N, 3.74; F, 21.07.

Ethyl 2-Fluoro-1-trifluoromethylpyrrolo[2,1-*a*]isoquinlin-3-carboxylate (4dib)
Mp 156–158 °C.

IR (KBr): 3136, 2964, 1700, 1261, 1109, 798, 709 cm^{-1}.

^{1}H NMR (300 MHz, acetone-d_6): δ = 1.41 (t, J_{HH} = 6.9 Hz, 3 H), 4.44 (q, J_{HH} = 6.9 Hz, 2 H), 7.52 (d, J_{HH} = 7.8 Hz, 1 H), 7.75–7.79 (m, 2 H), 7.95–7.99 (m, 1 H), 8.37–8.39 (m, 1 H), 9.37 (d, J_{HH} = 7.8 Hz, 1 H).

^{19}F NMR (282 MHz, acetone-d_6): δ = –54.73 (d, J_{FF} = 23.59 Hz, 3 F), –141.37 (d, J_{FF} = 23.59 Hz, 1 F).

MS (EI): *m*/*z* (%) = 325 (M^+, 54), 306 (5), 298 (47), 281 (43), 253 (82).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{11}F_4NO_2$: 325.07259. Found: 325.07363.

(4-Benzyl-2,3-difluoro-4*H*-pyrrolo[1,2-*a*]benzimidazol-1-yl)phenylmethanone (6aaa)
Mp 142–144 °C.

IR (KBr): 2910, 1595, 1542, 1407, 873, 695 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.38 (s, 2 H), 7.22–7.54 (m, 11 H), 7.79–7.83 (m, 2 H), 8.82 (d, J_{HH} = 6.5 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –145.52 (d, J_{FF} = 12.4 Hz, 1 F), –197.32 (d, J_{FF} = 12.4 Hz, 1 F).

MS (EI): *m*/*z* (%) = 386 (M^+, 28), 295 (8), 105 (42), 91 (100), 77 (27).

Anal. Calcd for $C_{24}H_{16}F_2N_2O$: C, 74.60; H, 4.17; N, 7.25; F, 9.83. Found: C, 74.34; H, 4.50; N, 6.89; F, 9.67.

Ethyl 4-Benzyl-2,3-difluoro-4*H*-pyrrolo[1,2-*a*]benzimidazole-1-carboxylate (6aba)
Mp 138–140 °C.

IR (KBr): 2998, 1695, 1499, 1419, 1302, 1059, 742 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.41 (t, J_{HH} = 7.2 Hz, 3 H), 4.39 (q, J_{HH} = 7.2 Hz, 2 H), 5.30 (s, 2 H), 7.18–7.31 (m, 8 H), 8.75 (d, J_{HH} = 8.7 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –150.45 (d, J_{FF} = 11.0 Hz, 1 F), –199.15 (d, J_{FF} = 11.0 Hz, 1 F).

MS (EI): *m*/*z* (%) = 354 (M^+, 25), 235 (7), 91 (100), 65 (11), 76 (5).

HRMS: *m*/*z* calcd for $C_{15}H_9F_2NO$: 354.11798. Found: 354.11602.

4-Benzyl-2, 3-difluoro-4*H*-pyrrolo[1,2-*a*]benzimidazole-1-carbonitrile (6aca)
Mp 175–177 °C.

IR (KBr): 3063, 2206, 1654, 1548, 1417, 1090, 744, 703 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.32 (s, 2 H), 7.25–7.36 (m, 8 H), 7.86 (d, J_{HH} = 7.8 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –152.75 (d, J_{FF} = 10.9 Hz, 1 F), –192.26 (d, J_{FF} = 10.9 Hz, 1 F).

MS (EI): *m*/*z* (%) = 307 (M^+, 17), 216 (11), 91 (100), 65 (32), 51 (11).

HRMS: *m*/*z* Calcd for $C_{15}H_9F_2NO$: 307.092104. Found: 307.09063.

(4-Benzyl-2-fluoro-3-trifluoromethyl-4*H*-pyrrolo[1,2-*a*]benzimidazol-1-yl)phenylmethanone (6dab)
Mp 151–153 °C.

IR (KBr): 3068, 1693, 1223, 736 cm^{-1}

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.50 (s, 2 H), 7.16–7.34 (m, 8 H), 7.48–7.58 (m, 3 H), 7.84–7.88 (m, 2 H), 8.72 (d, J_{HH} = 9.3 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –50.71 (d, J_{FF} = 14.9 Hz, 3 F), –129.80 (q, J_{FF} = 14.9 Hz, 1 F).

MS (EI): *m*/*z* (%) = 307 (M^+, 10), 384 (6), 223 (15), 105 (52), 91 (100), 56 (70).

HRMS: *m*/*z* calcd for $C_{25}H_{16}F_4N_2O$: 436.11988. Found: 436.11736.

Ethyl 4-Benzyl-2-fluoro-3-trifluoromethyl-4*H*-pyrrolo[1,2-*a*]benzimidazole-1-carboxylate (6dbb)
Mp 147–149 °C.

IR (KBr): 2978, 1697, 1500, 1240, 745, 703 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.41 (t, J_{HH} = 7.2 Hz, 3 H), 4.41 (q, J_{HH} = 7.2 Hz, 2 H), 5.36 (s, 2 H), 7.19–7.37 (m, 8 H), 8.88 (d, J_{HH} = 8.1 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –50.63 (d, J_{FF} = 13.3.Hz, 3 F), –129.73 (q, J_{FF} = 13.3 Hz, 1 F).

MS (EI): *m*/*z* (%) = 404 (M^+, 9), 354 (15),180 (8), 91 (100), 65 (10).

HRMS: *m*/*z* calcd for $C_{21}H_{16}F_4N_2O_2$: 404.11479. Found: 404.11153.

4-Benzyl-2-fluoro-3-trifluoromethyl-4*H*-pyrrolo[1,2-*a*]benzimidazole-1-carbonitrile (6dcb)
Mp 183–185 °C.

IR (KBr): 2929, 2208, 1640, 1511, 1306, 1127, 746, 707 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.35 (s, 2 H), 7.29–7.43 (m, 8 H), 8.04 (d, J_{HH} = 7.8 Hz, 1 H).

^{19}F NMR ($CDCl_3$, 282 MHz): δ = –50.81 (d, J_{FF} = 16.9 Hz, 3 F), –129.87 (q, J_{FF} = 16.9 Hz, 1 F).

MS (EI): *m*/*z* (%) = 357 (M^+, 16), 339 (2), 91 (100), 65 (10).

HRMS: calcd for $C_{19}H_{11}F_4N_3$: 357.08891. Found: 357.08815.

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