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Synthesis of some new 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluoro- phenyl)-5-arylpyrazolines and their iodine(III) mediated oxidation to corresponding pyrazoles

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The reaction of fluorinated chalcones **2** and 6-fluorobenzothiazol-2-ylhydrazine **1** in presence of catalytic amount of glacial acetic acid in refluxing ethanol yields 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-arylpyrazolines **3**, which undergo facile oxidation to the corresponding pyrazoles **4** in good yield using iodobenzene diacetate (IBD). The structures of the synthesized compounds have been established on the basis of their elemental analysis, MS and ^{1}H and ^{13}C NMR spectroscopy.

Keywords: Fluorinated chalcones, pyrazolines, iodobenzene diacetate, pyrazoles, NMR spectroscopy

Pyrazoline derivatives constitute an interesting class of organic compounds, which are associated with diverse chemical and pharmacological properties[1-4]. These compounds are known for their antitumor, analgesic, anti-inflammatory, insecticidal, antiarthritic, cerebroprotective effect and antidepressant properties[5-8]. Several substituted pyrazolines are found to be effective bleaching agents, luminescents and fluorescents[9]. They are also useful as biodegradable agrochemicals[10].

Moreover, several pyrazole derivatives have emerged as a group of compounds possessing a broad spectrum of useful medicinal properties such as analgesic, antipyretic, anti-inflammatory, germicidal and antifungal activity[11,12].

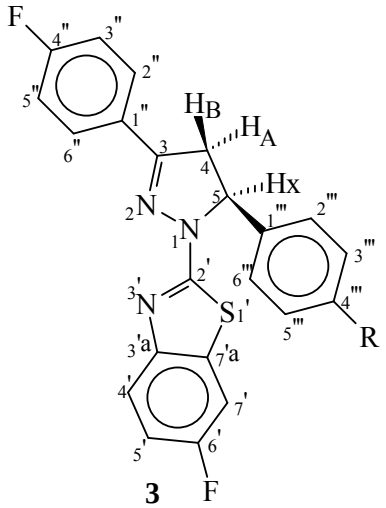
The biological properties of fluorine or multifluorine containing compounds have been recently investigated. Owing to their unique properties, such as high thermal stability and lipophilicity, fluoro-organic compounds have been frequently used as biorelated materials, medicines and agrochemicals[13,14].

Encouraged by these results and in continuation with the work related to the synthesis, spectral studies and biological properties of heteroarylpyrazoles[15], herein is reported the synthesis of some novel fluorine incorporated 1-heteroarylpyrazolines **3** and pyrazoles **4**.

Results and Discussion

Synthesis of 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-arylpyrazolines **3a-f** and their oxidation to corresponding pyrazoles **4a-f** is summarized in **Scheme I**.

The starting compounds 1-(4-fluorophenyl)-3-arylprop-2-enones (chalcones) **2a-f** were prepared by the Claisen-Schmidt condensation of *p*-fluoroacetophenone with various substituted aromatic aldehydes in presence of methanol/KOH[16]. The reaction of 6-fluorobenzothiazol-2-ylhydrazine **1** with chalcones **2a-f** in refluxing ethanol under the influence of glacial acetic acid gave 1-(6-fluorobenzothiazol-2-yl)-



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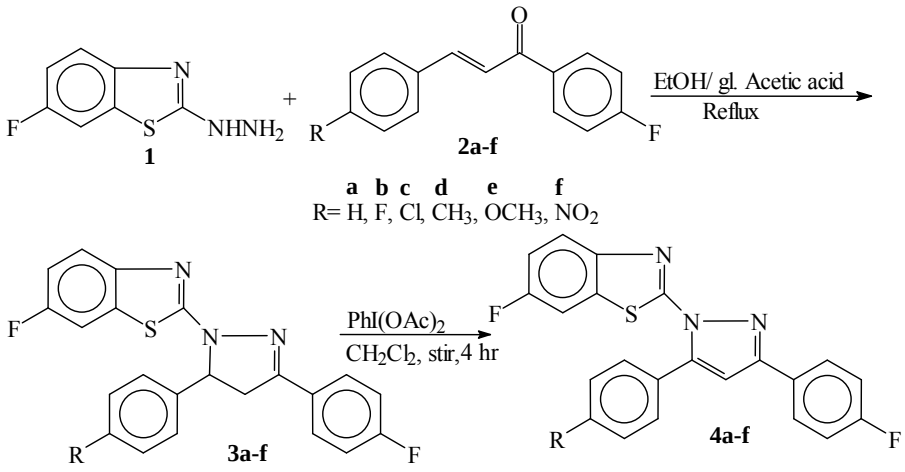

Scheme I

3-(4-fluorophenyl)-5-arylpyrazolines **3a-f** in good yield.

The compounds **3a-f** were characterized by the combined application of elemental analysis, mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy. The ^{1}H NMR spectra of pyrazolines **3a-f** displayed the three characteristic signals due to diastereotopic protons (H_A, H_B and H_X). The H_A proton which is *cis* to H_X resonates upfield in the range δ 3.25-3.35 as a doublet of doublet (dd, J_{HAHB} = ~ 17.7 Hz, J_{HAHX} = ~ 5.4 Hz) while H_B, the other proton which is *trans* to H_X resonates downfield in the range δ 3.89-3.99 as a dd (J_{HAHB} = ~ 17.7 Hz, J_{HBHX} = ~ 12 Hz). The H_X proton which is vicinal to two methylene protons (H_A and H_B) resonates as dd in the range δ 5.81-5.87 (J_{HBHX} = ~ 12 Hz, J_{HAHX} = ~ 5.4 Hz).

The structures of **3a-f** were further supported by their ^{13}C NMR in which C-3, C-4 and C-5 resonated in the range of 146-149, 41-44 and 61-64 ppm, respectively. These values are in close agreement with the reported values[17] for pyrazoline carbons 3, 4 and 5.

It may be mentioned here that many conventional oxidizing agents namely potassium ferricyanide, silver nitrate, mercuric nitrate, colloidal platinum, manganese oxide, mercuric acetate and lead oxide have been used for the dehydrogenation of pyrazolines. A careful examination of the literature reveals that most of the methods suffer from one drawback or the other. To illustrate, catalytic dehydrogenation using colloidal platinum results in the formation of a mixture containing the corresponding pyrazoles and pyrazolidines[18]. Similarly, the oxidation of pyrazolines involving manganese dioxide results in the formation of biphenyl in addition to the desired pyrazoles[19]. Moreover, toxicity associated with the mercury and lead reagents makes their use rather undesirable.

In view of the difficulties encountered in these methods and encouraged by previous observations[20] resulting in the successful conversion of pyrazolines to pyrazoles using IBD, this reagent has been adopted to convert the pyrazoline **3** to pyrazoles **4**.

The pyrazolines **3a-f** were treated with one equivalent of iodobenzene diacetate (IBD) in dichloromethane at RT for 4 hr. The reaction smoothly afforded the desired products **4a-f** in good yield.

The compounds **4a-f** were also characterized on the basis of NMR and mass spectrometry, and elemental analysis. The ^{1}H NMR spectra of pyrazoles **4a-f** showed a characteristic singlet due to C_4-H at δ ~6.6. In ^{13}C NMR spectra of the compound **4a-f**, the three carbon atoms C-3, C-4 and C-5 of pyrazole nucleus resonated at δ 152-153, 108 and 145-146, respectively[21].

The complete assignments of the carbon signals of the compounds **3** and **4** are given in **Tables I** and **II**.

Experimental Section

Melting points were determined in open capillaries in electrical apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were run on a Brucker instrument at 300 MHz and 75 MHz, respectively using TMS as an internal standard. ^{19}F NMR spectra were run on DRX 300 and DPX 400 at 282 and 376 MHz, respectively, using $CDCl_3$ as solvent. The internal standard for ^{19}F spectra was $CFCl_3$, setting the $CFCl_3$ signal at δ 0.00. High resolution mass spectra (HRMS) were measured in EI mode on a Kratos MS-50 spectrometer.

Table I — ^{13}C NMR data of compounds **3a-e**

Carbons	3a	3b*	3c	3d	3e
C-3	146.21	147.48	145.93	147.98	148.21
C-4	41.80	43.88	44.00	43.96	43.86
C-5	61.75	63.53	63.49	63.73	63.51
C-2'	160.70	162.72	162.67	162.79	162.79
C-3'a	149.95	152.47	153.56	152.37	152.23
C-4'	118.27(d, $^3J_{C\text{-}F}$ = 9 Hz)	120.40(d, $^3J_{C\text{-}F}$ = 9 Hz)	120.04(d, $^3J_{C\text{-}F}$ = 9 Hz)	120.30(d, $^3J_{C\text{-}F}$ = 9 Hz)	120.34(d, $^3J_{C\text{-}F}$ = 9 Hz)
C-5'	111.34(d, $^2J_{C\text{-}F}$ = 24 Hz)	113.39(d, $^2J_{C\text{-}F}$ = 24 Hz)	114.05(d, $^2J_{C\text{-}F}$ = 23.75 Hz)	113.49(d, $^2J_{C\text{-}F}$ = 24 Hz)	113.45(d, $^2J_{C\text{-}F}$ = 24 Hz)
C-6'	156.41(d, $^1J_{C\text{-}F}$ = 240 Hz)	158.52(d, $^1J_{C\text{-}F}$ = 240 Hz)	158.86(d, $^1J_{C\text{-}F}$ = 240.75 Hz)	158.54(d, $^1J_{C\text{-}F}$ = 240 Hz)	158.54(d, $^1J_{C\text{-}F}$ = 240 Hz)
C-7'	105.40(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.58(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.78(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.52(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.50(d, $^2J_{C\text{-}F}$ = 26.25 Hz)
C-7'a	130.04(d, $^3J_{C\text{-}F}$ = 10.5 Hz)	131.98(d, $^3J_{C\text{-}F}$ = 10.5 Hz)	131.04(d, $^3J_{C\text{-}F}$ = 9.75 Hz)	131.93(d, $^3J_{C\text{-}F}$ = 9.75 Hz)	132.05(d, $^3J_{C\text{-}F}$ = 10.5 Hz)
C-1"	125.18(d, $^4J_{C\text{-}F}$ = 3 Hz)	127.05(d, $^4J_{C\text{-}F}$ = 3 Hz)	126.78(d, $^4J_{C\text{-}F}$ = 3 Hz)	127.01(d, $^4J_{C\text{-}F}$ = 3.75 Hz)	126.14(d, $^4J_{C\text{-}F}$ = 3.75 Hz)
C-2", 6"	126.41(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	128.45(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	128.81(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	128.55(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	128.53(d, $^3J_{C\text{-}F}$ = 8.25 Hz)
C-3", 5"	113.81(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.90(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	116.11(d, $^2J_{C\text{-}F}$ = 22.50 Hz)	115.94(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.89(d, $^2J_{C\text{-}F}$ = 21.75 Hz)
C-4"	161.77(d, $^1J_{C\text{-}F}$ = 249.75 Hz)	163.95(d, $^1J_{C\text{-}F}$ = 249.75 Hz)	164.20(d, $^1J_{C\text{-}F}$ = 250.50 Hz)	163.91(d, $^1J_{C\text{-}F}$ = 249 Hz)	163.90(d, $^1J_{C\text{-}F}$ = 249.75 Hz)
C-1'"	125.86	127.37(d, $^4J_{C\text{-}F}$ = 3 Hz)	134.09	127.32	132.86
C-2'", 6'"	126.87	127.92(d, $^3J_{C\text{-}F}$ = 8.75 Hz)	129.26	129.65	127.36
C-3'", 5'"	123.85	114.52(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	127.59	125.93	114.31
C-4'"	138.71	163.81(d, $^1J_{C\text{-}F}$ = 249 Hz)	138.67	137.77	159.34
CH_3	-	-	-	21.11	55.23

* The assigned carbon values for double prime and triple prime phenyl ring may be interchangeable.

Table II — ^{13}C NMR data of compounds **4a-e**

Carbons	4a	4b*	4c	4d	4e
C-3	153.03	153.13	153.08	153.01	152.99
C-4	108.51	108.22	108.70	108.31	108.10
C-5	146.39	146.45	146.15	146.53	146.34
C-2'	159.72	159.92	159.80	159.82	159.85
C-3'a	147.39	147.88	147.51	147.41	147.42
C-4'	123.96(d, $^3J_{C\text{-}F}$ = 9 Hz)	123.89(d, $^3J_{C\text{-}F}$ = 9 Hz)	123.93(d, $^3J_{C\text{-}F}$ = 9 Hz)	123.98(d, $^3J_{C\text{-}F}$ = 9 Hz)	123.93(d, $^3J_{C\text{-}F}$ = 9.75 Hz)
C-5'	114.58(d, $^2J_{C\text{-}F}$ = 24 Hz)	114.5(d, $^2J_{C\text{-}F}$ = 24 Hz)	114.68(d, $^2J_{C\text{-}F}$ = 24 Hz)	114.54(d, $^2J_{C\text{-}F}$ = 24 Hz)	114.54(d, $^2J_{C\text{-}F}$ = 24 Hz)
C-6'	160.21(d, $^1J_{C\text{-}F}$ = 243.75 Hz)	160.26(d, $^1J_{C\text{-}F}$ = 240 Hz)	160.31(d, $^1J_{C\text{-}F}$ = 243.75 Hz)	160.19(d, $^1J_{C\text{-}F}$ = 243.75 Hz)	160.20(d, $^1J_{C\text{-}F}$ = 243 Hz)
C-7'	107.59(d, $^2J_{C\text{-}F}$ = 26.25 Hz)	107.52(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.66(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.57(d, $^2J_{C\text{-}F}$ = 27 Hz)	107.56(d, $^2J_{C\text{-}F}$ = 27 Hz)
C-7'a	134.67(d, $^3J_{C\text{-}F}$ = 11.25 Hz)	134.24(d, $^3J_{C\text{-}F}$ = 10.5 Hz)	134.74(d, $^3J_{C\text{-}F}$ = 10.5 Hz)	134.70(d, $^3J_{C\text{-}F}$ = 9.75 Hz)	134.64(d, $^3J_{C\text{-}F}$ = 10.5 Hz)
C-1"	127.25(d, $^4J_{C\text{-}F}$ = 3.25 Hz)	127.35(d, $^4J_{C\text{-}F}$ = 3 Hz)	127.48(d, $^4J_{C\text{-}F}$ = 3.25 Hz)	127.40(d, $^4J_{C\text{-}F}$ = 3.75 Hz)	127.45(d, $^4J_{C\text{-}F}$ = 3.25 Hz)
C-2", 6"	128.02(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	128.10(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	127.98(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	127.98(d, $^3J_{C\text{-}F}$ = 8.25 Hz)	127.95(d, $^3J_{C\text{-}F}$ = 8.25 Hz)
C-3", 5"	115.82(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.84(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.85(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.78(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	115.77(d, $^2J_{C\text{-}F}$ = 21.75 Hz)
C-4"	163.33(d, $^1J_{C\text{-}F}$ = 246.75 Hz)	163.41(d, $^1J_{C\text{-}F}$ = 246.75 Hz)	163.41(d, $^1J_{C\text{-}F}$ = 246.75 Hz)	163.31(d, $^1J_{C\text{-}F}$ = 246.75Hz)	163.30(d, $^1J_{C\text{-}F}$ = 246.75 Hz)
C-1'"	129.58	127.32(d, $^4J_{C\text{-}F}$ = 3.75 Hz)	130.10	126.53	121.75
C-2'", 6'"	129.76	128.32(d, $^3J_{C\text{-}F}$ =8.25 Hz)	131.12	129.62	131.18
C-3'", 5'"	128.00	115.96(d, $^2J_{C\text{-}F}$ = 21.75 Hz)	128.23	128.75	113.67
C-4'"	129.24	163.02(d, $^1J_{C\text{-}F}$ = 249.75 Hz)	135.36	139.35	160.43
CH_3	-	-	-	21.48	55.35

* The assigned carbon values for double prime and triple prime phenyl ring may be interchangeable.

6-Fluorobenzothiazol-2-ylhydrazine was prepared according to literature procedure[22].

General procedure for synthesis of 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-arylpyrazolines, **3**

1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-phenylpyrazoline, 3a.

A solution of 1-(4-fluorophenyl)-3-phenylprop-2-enone **2a** (0.45 g, 0.002 mole) and 6-fluorobenzothiazol-2-ylhydrazine **1** (0.37 g, 0.002 mole) in ethanol (25 mL) containing 4-5 drops of glacial acetic acid was heated under reflux for 8 hr. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and then allowed to cool when a solid product crystallized out. The product was collected by filteration & washed with ethanol to give **3a**. This was further purified by recrystallization from ethanol. Yield 80%; m.p. 182-83ºC; ^{1}H NMR ($CDCl_3$): δ 3.27-3.35 (dd, 1H, H_A, J_{HAHB} = 17.7 Hz, J_{HAHX} = 5.4 Hz), 3.89-3.98 (dd, 1H, H_B, J_{HAHB} = 17.4 Hz, J_{HBHX} = 12 Hz), 5.82-5.87 (dd, 1H, H_X, J_{HXHB} = 11.7 Hz, J_{HXHA} = 5.4 Hz), 6.95-7.02 (m, 1H, 5'-H), 7.11-7.17 (m, 2H, 3", 5"-H), 7.28-7.37 (m, 6H, Ph'"-H, 7'-H), 7.44-7.48 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.75-7.79 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 6'-F), -109 (s, 1F, 4"-F); HRMS: *m/z* M^+ $C_{22}H_{15}F_2N_3S$ requires 391.0954. Found: 391.0943. Anal. Calcd. for $C_{22}H_{15}F_2N_3S$: N, 10.74. Found 10.65%.

The compounds **3b-f** were similarly prepared.

3b: Yield 76%; m.p. 146ºC; ^{1}H NMR ($CDCl_3$): δ 3.23-3.39 (dd, 1H, H_A, J_{HAHB} = 17.7 Hz, J_{HAHX} = 5.4

Hz), 3.87-3.96 (dd, 1H, H_B, J_{HAHB} = 17.4 Hz, J_{HBHX} = 12 Hz), 5.74-5.79 (dd, 1H, H_X, J_{HXHB} = 11.7 Hz, J_{HXHA} = 5.4 Hz), 6.94-7.78 (m, 11H, FBz', *p*-FPh" and *p*-FPh"'-H); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 6'-F), -109 (s, 1F, 4"-F)*, -111(s, 1F, 4"'-F)*; MS: *m/z* M^+ 409. Anal. Calcd. for $C_{22}H_{14}F_3N_3S$: N, 10.27. Found 9.94%.

3c: Yield 78%; m.p. 186ºC; ^{1}H NMR ($CDCl_3$): δ 3.25-3.32 (dd, 1H, H_A, J_{HAHB} = 17.5 Hz, J_{HAHX} = 5.4 Hz), 3.90-4.00 (dd, 1H, H_B, J_{HAHB} = 17.5 Hz, J_{HBHX} = 12 Hz), 5.85-5.90 (dd, 1H, H_X, J_{HXHB} = 11.7 Hz, J_{HXHA} = 5.4 Hz), 6.78-7.06 (m, 1H, 5'-H), 7.09-7.18 (m, 2H, 3", 5"-H), 7.33-7.38 (m, 5H, *p*-ClPh"'-H, 7'-H), 7.43-7.51 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.74-7.78 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 6'-F), -109 (s, 1F, 4"-F); HRMS: *m/z* M^+ $C_{22}H_{14}ClF_2N_3S$ requires 425.0565 for lower isotope. Found: 425.0552 M^+ and 427.0515 M^++2 in the ratio showing typical chlorine isotope profile (3:1); Anal. Calcd. for $C_{22}H_{14}ClF_2N_3S$: N, 9.87. Found 9.81%.

3d: Yield 82%; m.p. 163ºC; ^{1}H NMR ($CDCl_3$): δ 2.22 (s, 3H, CH_3), 3.14-3.22 (dd, 1H, H_A, J_{HAHB} = 17.4 Hz, J_{HAHX} = 5.4 Hz), 3.75-3.85 (dd, 1H, H_B, J_{HAHB} = 17.5 Hz, J_{HBHX} = 12 Hz), 5.67-5.72 (dd, 1H, H_X, J_{HXHB} = 11.7 Hz, J_{HXHA} = 5.4 Hz), 6.84-6.91 (m, 1H, 5'-H), 7.00-7.08 (m, 2H, 3", 5"-H), 7.04-7.07 (d, 2H, 3"', 5"'-H, J_o = 8.4 Hz), 7.14-7.17 (d, 2H, 2"', 6"'-H, J_o = 8.4 Hz), 7.22-7.25 (dd, 1H, 7'-H, J_o = 8.4 Hz, J_m = 2.7 Hz), 7.33-7.38 (dd, 1H, 4'-H, J_o = 8.8 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.63-7.68 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 6'-F), -109 (s, 1F, 4"-F); HRMS: *m/z* M^+ $C_{23}H_{17}F_2N_3S$ requires 405.1111. Found: 405.1115; Anal. Calcd. for $C_{23}H_{17}F_2N_3S$: N, 10.37. Found 10.26%.

3e: Yield 74%; m.p. 168ºC; ^{1}H NMR ($CDCl_3$): δ 3.28-3.36 (dd, 1H, H_A, J_{HAHB} = 17.4 Hz, J_{HAHX} = 5.1 Hz), 3.78 (s, 3H, OCH_3), 3.88-3.98 (dd, 1H, H_B, J_{HAHB} = 17.4 Hz, J_{HBHX} = 12 Hz), 5.86-5.91 (dd, 1H, H_X, J_{HXHB} = 11.5 Hz, J_{HXHA} = 5.1 Hz), 6.86-6.89 (d, 2H, 3"', 5"'-H, J_o = 8.7 Hz), 6.97-7.04 (m, 1H, 5'-H), 7.12-7.18 (m, 2H, 3", 5"-H), 7.31-7.38 (m, 3H, 7', 2"', 6"'-H), 7.49-7.54 (dd, 1H, 4'-H, J_o = 8.8 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.76-7.81 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 6'-F), -109 (s, 1F, 4"-F); MS: *m/z* M^+ 421. Anal. Calcd. for $C_{23}H_{17}F_2N_3OS$: N, 9.97. Found 9.82%.

3f: Yield 75%; m.p. >250ºC; ^{1}H NMR ($CDCl_3$+ DMSO-d_6): δ 3.30-3.38 (dd, 1H, H_A, J_{HAHB} = 17.7 Hz, J_{HAHX} = 5.1 Hz), 4.03-4.16 (dd, 1H, H_B, J_{HAHB} = 17.7 Hz, J_{HBHX} = 11.7 Hz), 6.16-6.25 (dd, 1H, H_X, J_{HXHB} = 11.7 Hz, J_{HXHA} = 5.1 Hz), 6.99-7.06 (m, 1H, 5'-H), 7.13-7.19 (m, 2H, 3", 5"-H), 7.36-7.39 (dd, 1H, 7'-H, $J_{(o)\ HF}$ = 8.1 Hz, J_m = 2.7 Hz), 7.49-7.58 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.59-7.62 (d, 2H, 2"', 6"'-H, J_o = 8.7 Hz), 7.77-7.81 (m, 2H, 2", 6"-H), 8.21-8.24 (d, 2H, 3"', 5"'-H, J_o = 8.7 Hz); ^{19}F NMR ($CDCl_3$): δ -120 (s, 1F, 4'-F), -109 (s, 1F, 4"-F); HRMS: *m/z* M^+ $C_{22}H_{14}F_2N_4O_2S$ requires 436.0805. Found: 436.0796. $C_{22}H_{14}F_2N_4O_2S$ requires 436.0805. Anal. Calcd. for $C_{22}H_{14}F_2N_4O_2S$: N, 12.84. Found 12.69%.

General procedure for synthesis of 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-arylpyrazoles, **4**

1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-phenylpyrazole, ***4a***

To a stirred solution of 1-(6-fluorobenzothiazol-2-yl)-3-(4-fluorophenyl)-5-phenylpyrazoline **3a** (0.391 g, 0.001 mole) in dichloromethane (20 mL) was added IBD (0.386 g, 0.0012 mole) at RT. The resulting mixture was stirred for 4 hr. Dichloromethane was distilled off on a steam bath to give a gum which was triturated with pet-ether to remove iodobenzene and then was purified by recrystallization from ethanol to afford the product **4a**. Yield 81%; m.p. 170ºC; ^{1}H NMR ($CDCl_3$): δ 6.79 (s, 1H, 4-H), 7.10-7.21 (m, 3H, 5', 3", 5"-H), 7.47-7.53 (m, 4H, 3"', 4"', 5"', 7'-H), 7.61-7.66 (m, 3H, 2", 6", 4'-H), 7.92-7.96 (dd, 2H, 2", 6"-H, J_o = 8.1 Hz, $J_{(m)\ HF}$ = 5.4 Hz), 7.75-7.79 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s, 1F, 4"-F); HRMS: *m/z* M^+ $C_{22}H_{13}F_2N_3S$ requires 389.0798. Found: 389.0782. Anal. Calcd. for $C_{22}H_{13}F_2N_3S$: N, 10.79. Found 10.58%.

The compounds **4b-f** were similarly prepared.

4b: Yield 84%; m.p. 152ºC; ^{1}H NMR ($CDCl_3$): δ 6.79 (s, 1H, 4-H), 6.98-7.95 (m, 11H, FBz', *p*-FPh" and *p*-FPh"'-H); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s, 1F, 4"-F)*, -114 (s, 1F, 4"'-F)*; MS: *m/z* M^+ 407; Anal. Calcd. for $C_{22}H_{12}F_3N_3S$: N, 10.32. Found 10.22%.

4c: Yield 79%; m.p. 240ºC; ^{1}H NMR ($CDCl_3$): δ 6.77 (s, 1H, 4-H), 7.09-7.20 (m, 3H, 5', 3", 5"-H), 7.42-7.45 (d, 2H, 3"', 5"'-H, J_o = 8.4 Hz), 7.49-7.52 (dd, 1H, 7'-H, $J_{(m)\ HF}$ = 8.1 Hz, J_m = 2.7 Hz), 7.54-7.57 (d, 2H, 2"', 6"'-H, J_o = 8.4 Hz), 7.62-7.66 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.88-7.91 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s,

* May be interchangeable

1F, 4"-F); HRMS: *m/z* M^+ $C_{22}H_{14}ClF_2N_3S$ requires 423.0385 for lower isotope. Found: 423.0394 M^+ and 425.0366 M^++2 in the ratio showing typical chlorine isotope profile (3:1). Anal. Calcd. for $C_{22}H_{12}ClF_2N_3S$: N, 9.92. Found 9.78%.

4d: Yield 83%; m.p. 182-83ºC; ^{1}H NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 6.67 (s, 1H, 4-H), 7.00-7.44 (m, 8H, 5', 7', 3", 5", *p*-CH_3Ph"-H), 7.57-7.61 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.82-7.87 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s, 1F, 4"-F); MS: *m/z* M^+ 403. Anal. Calcd. for $C_{23}H_{15}F_2N_3S$: N, 10.42. Found 10.24%.

4e: Yield 75%; m.p. 187ºC; ^{1}H NMR ($CDCl_3$): δ 3.82 (s, 3H, OCH_3), 6.65 (s, 1H, 4-H), 6.85-6.95 (d, 2H, 3"', 5"'-H, J_o = 8.7 Hz), 7.04-7.10 (m, 3H, 5', 3", 5"-H), 7.39-7.43 (dd, 1H, 7'-H, $J_{(o)\ HF}$ = 8.1 Hz, J_m = 2.7 Hz), 7.45-7.48 (d, 2H, 2"', 6"'-H, J_o = 8.7 Hz), 7.57-7.62 (dd, 1H, 4'-H, J_o = 9 Hz, $J_{(m)\ HF}$ = 4.8 Hz), 7.81-7.86 (m, 2H, 2", 6"-H); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s, 1F, 4"-F); MS: *m/z* M^+ 419. Anal. Calcd. for $C_{23}H_{15}F_2N_3OS$: N, 10.02. Found 9.79%.

4f: Yield 78%; m.p. >250ºC; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 6.78 (s, 1H, 4-H), 7.04-7.10 (m, 3H, 5', 3", 5"-H), 7.52-8.02 (m, 7H, FBz', 2", 6", 2"' and 6"'-H), 8.26-8.29 (d, 2H, 3"', 5"'-H, J_o = 9 Hz); ^{19}F NMR ($CDCl_3$): δ -116 (s, 1F, 6'-F), -112 (s, 1F, 4"-F); MS: *m/z* M^+ 434. Anal. Calcd. for $C_{22}H_{14}F_2N_4O_2S$: N, 12.90. Found 12.78%.

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