The Reaction of Aryl and Heteroarylhydrazines with Aryl-Trifluoromethyl β-Diketones

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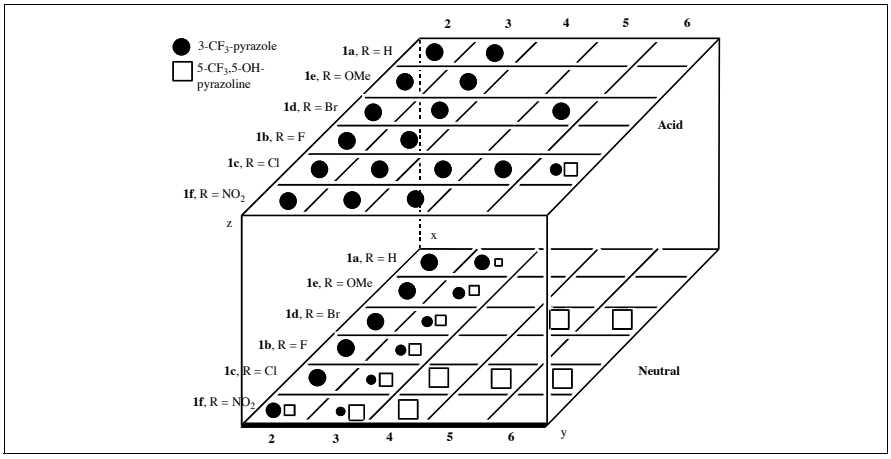

We report the results obtained when five aromatic or heteroaromatic hydrazines react with six β-diketones bearing trifluoromethyl and aryl substituents. Forty-two compounds have been isolated corresponding to two isomeric trifluoromethyl pyrazoles and the intermediate 5-CF_3, 5-OH pyrazolines. The results have provided useful information for establishing the mechanism of the synthesis of pyrazoles.

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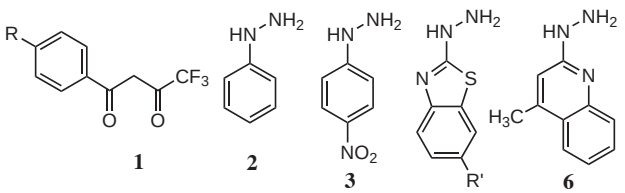
Introduction.

The reaction of *N*-substituted hydrazines with β–dicarbonyl compounds is one of the most useful methods to prepare *N*-substituted pyrazoles. The main problem with this reaction is that it usually yields the isomeric pyrazoles and the reasons for obtaining them are generally not well understood [1-6]. It is the aim of the present paper to report the study of the reaction between a series of 1-aryl-4,4,4-trifluorobutane-1,3-diones **1**, which are differently substituted on the phenyl ring with five hydrazines: phenylhydrazine **2**, *p*-nitrophenylhydrazine **3**, 6-methylbenzothiazol-2-ylhydrazine **4**, 6-fluorobenzothi-azol-2-ylhydrazine **5** and 4-methylquinolin-2-ylhydrazine **6** (Scheme I).

Scheme I



1 **2** **3** **4** **6**

a, R = H; **b**, R = F; **c**, R = Cl;
d, R = Br; **e**, R = OCH_3; **f**, R = NO_2

4, R' = CH_3
5, R' = F

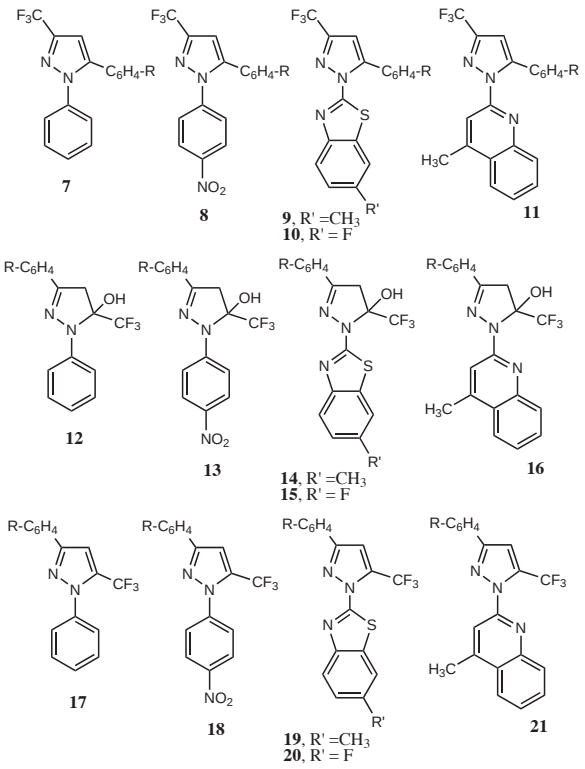
Owing to the presence of the trifluoromethyl group, it is possible to isolate the corresponding 5-hydroxy-5-trifluoromethyl-Δ^2 -pyrazolines [7-10] in some cases.

Therefore, three kinds of compounds are expected from the reaction between **1** and hydrazines **2**-**6**: 3-trifluoromethyl-5-arylpyrazoles **7**-**11**, 3-aryl-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines **12**-**16** and their dehydration products, 3-aryl-5-trifluoromethylpyrazoles **17**-**21** (Scheme II). It is interesting to note that pyrazoles **1**-**11** are related to compounds important as COX-2 inhibitors or as starting materials to prepare them [11,12].

Results and Discussion.

The combination of six β-diketones, five hydrazines may generate three kinds of pyrazole derivatives leading to 90 possible compounds. Using two experimental conditions, neutral and acidic media, and a selection of reagents, 42 compounds were actually isolated (Table 1). Out of these compounds, **7a**, **7b**, **7c**, **7d**, **7e**, **7f**, **8a** and **8b** have been previously reported (see Experimental Part). The second reaction of Table 1 corresponds to the dehydration of the 5-hydroxy-5-

Scheme II



results in two hydrazones and two enehydrazines: **xA**, **yA**, **yB** and **xB**. These compounds neither do necessarily represent the reality (the compounds are probably hydrated) nor is the following step the formation of hydroxypyrazolines but most probably dihydroxy-pyrazolidine is involved as an intermediate [7,9,13,14]. What is more important is that these four possibilities ended in only two 5-hydroxy-Δ^2-pyrazolines which are precursors of two types of pyrazoles. A plausible explanation why the presence of a CF_3 group at the 5-position stabilizes the two 5-hydroxy-Δ^2-pyrazolines (in the present case **12**-**16**) has been proposed previously [3,7,15].

We will now discuss the role of R and R^1 in neutral and acidic conditions on the orientation of the reaction. It is evident that R and R^1 act only on the molecule that bears them, *i.e.*, on the β-diketones and the hydrazines, respectively. This point is of fundamental importance, and thus, changes in the final products associated with R must be assigned to differences in the reactivity of **1** while those associated with R^1 must be due to modifications in the relative reactivity of the NH and the NH_2 of **2**.

In neutral conditions and in what concerns the hydrazine, to explain the results of Table 1, it must be assumed that the reactivity of phenylhydrazine (**2**) is different than that of the other hydrazines. Even if for the

Table 1

Products obtained in the reactions between **1** and **2**-**6**.

Hydrazine	β-diketone	Conditions	Products	2nd Reaction
2	**1a-1e**	Neutral	**7a-7e**	
2	**1f**	Neutral	70% **7f** / 30% **12f**	**12f** → **17f**
2	**1a-1f**	Acid	**7a-7f**	
3	**1a-1f**	Neutral	19-38% (**8a-8f**) / 62-81% (**13a-13f**)	**13a-13f** → **18a-18f**
3	**1a-1f**	Acid	**8a-8f**	
4	**1c**&**1f**	Neutral	**14c** & **14f**	**14c** & **14f** → **19c** & **19f**
4	**1c**&**1f**	Acid	**9c** & **9f**	
5	**1c**-**1d**	Neutral	**15c-15d**	**15c-15d** → **20c-20d**
5	**1c**-**1d**	Acid	**10c-10d**	
6	**1c-1d**	Neutral	**16c-16d**	**16c** → **21c**
6	**1c**	Acid	54% **11c** / 38% **16c** with ~8% **21c**	

trifluoromethyl-Δ^2-pyrazolines into the corresponding 5-trifluoromethyl pyrazoles. In the case of the reaction between **3** and all six β-diketones in neutral conditions, the relative proportions of 3-trifluoromethylpyrazoles and 5-hydroxypyrazolines are reported in Table 2.

The results of Tables 1 and 2 can be interpreted using Scheme III. Both, the β-diketone (electrophilic centers **x** and **y**) and the monosubstituted hydrazine (nucleophilic centers **A** and **B**) have two possibilities for reacting. This

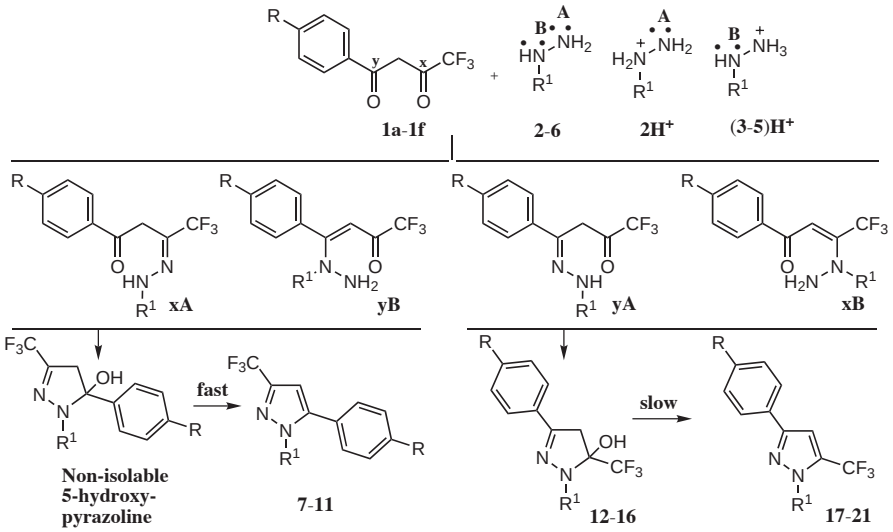
five hydrazines the most basic nitrogen should be the NH_2, the only reasonable hypothesis is that the reactivity changes from the NH for **2** to the NH_2 for **4**-**6** [*p*-nitrophenylhydrazine (**3**) occupying an intermediate position]. The opposite assumption is meaningless, thus, the data of Table 1 correspond to **2** reacting by the **yB** way, **3** by the **yB** + **yA** ways and **4**-**6** by **yA** one. Note that only the reactivity of the hydrazine changes, **A** or **B**, while apparently the β-diketone always reacts by the

Table 2

Ratios determined by ^{1}H NMR spectroscopy from the crude reaction mixtures obtained by treating the *p*-nitrophenylhydrazine (**3**) with β–diketones (**1a-f**).

Compound	% (**8**)	% (**13**)	Ln ratio **8**/**13**	*F*
a, R = H	38	62	–0.490	0.000
b, R = F	27	73	–0.995	0.708
c, R = Cl	24	76	–1.153	0.690
d, R = Br	25	75	–1.099	0.727
e, R = OCH_3	30	70	–0.847	0.413
f, R = NO_2	19	81	–1.450	1.109

Scheme III



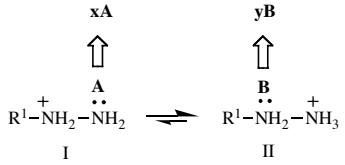
COAr (**y**), although probably the $COCF_3$ is more electrophilic. This apparent inconsistency is probably related to β-diketones reacting in the enol form.

In the case of the reaction of **3** with different β-diketones, the effect of the nitro group at the *para* position of the **y** carbonyl group (compound **1f**) lowers its reactivity and the proportions of **8** and **13** changes accordingly. The lowering effect of the nitro group on the rates is related to the dehydration step [16,17]. This indicates a change in the **y**/**x** ratio. Therefore, the data of Table 2 cannot be explained by a simple change in the **yB**/**yA** ratio and imposes to assume that **x** ways are implicated. However, as it is difficult to decide if it is **xA** or **xB** ways, we have assumed that it is the **xB**.

The **yB** way decreases and the **xB** one increases when the electron-withdrawing ability of R increases. Using as descriptor the Swain and Lupton *F* (field effect [18]) the data of Table 2 are relatively well correlated:

$$\text{Ln ratio} = -(0.49\pm0.05) - (0.86\pm0.08) * F,\ n = 6,\ r^2 = 0.97$$

In acid medium, hydrazines should be protonated and a reverse of reactivity is expected if one assumes that the most nucleophilic nitrogen atom would be protonated [19]. Here again, probably the five hydrazines protonate in both nitrogen atoms (structures I and II) the equilibrium being shifted towards II but less in **2** than in the other hydrazines. Thus, the change in reactivity between **2** and the other hydrazines could correspond to **2** using the **A** lone pair and the other the **B** lone pair.



Since in most cases only 3-trifluoromethyl derivatives **7**-**10** are isolated, the phenylhydrazinium cation could react by the **xA** way and the others cations by the **yB** one. But this implies a change in the reactivity of the β-diketones, which is not reasonable. Hence it is more probable that in all cases the **yB** way is followed (structure II). With the quinolylhydrazine **6** a mixture in nearly equal proportions of **11** and of (**16**+**21**) is obtained. Probably, the last compounds result from a **6H**$^+$ species protonated in the quinoline ring (**yA**).

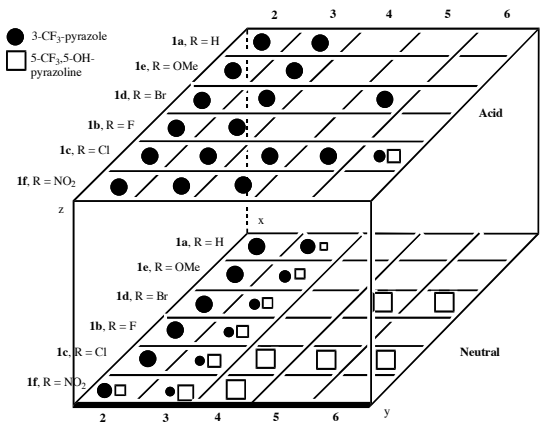


Figure 1

Within the experimental space we have plotted (represented in three dimensions in Fig. 1) the three axis corresponding to:

i) Vertical or z-axis: on going from neutral to acidic conditions, the proportion of 3-trifluoromethyl-pyrazoles always increases (if there are not the 100% of the mixture).

ii) Horizontal or y-axis: the more the electron-withdrawing effect of the substituent on the hydrazine (from **2** to **6**) the percentage of hydroxypyrazoline increases.

iii) Tilted or x-axis: the more electron-withdrawing the substituent on the phenyl ring of the β-diketone (classified according to Swain and Lupton field parameter, from **1a** to **1f**) the larger the proportion of hydroxypyrazoline.

Conclusions.

We have reported in this paper a large collection of pyrazole derivatives bearing a trifluoromethyl group. The combined use of different hydrazines, different β-diketones and two experimental conditions (neutral and acid-catalyzed) has allowed to propose a mechanism that although explaining the results is not grounded on kinetics data. For this reason, it should be considered as tentative accepting that other possibilities remain open.

EXPERIMENTAL

Melting points were determined in open capillaries in an electrical apparatus and are uncorrected. The ir spectra (in potassium bromide) of all the compounds were recorded on a Buck Scientific IR M500 instrument and ^{1}H nmr and ^{13}C nmr spectra were run on a Brucker instrument at 300 MHz and 75 MHz, respectively. ^{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 ppm. ^{13}C and ^{19}F nmr data for the compounds are presented in Tables 3, 4, 5 and 6, respectively. High resolution mass spectra (hrms) were measured in EI mode on a Kratos MS-50 spectrometer.

Fluorinated β-diketones (**1a-f**) and heteroarylhydazines (**4, 5, 6**) are well-known compounds often described in the literature: **1a** (CAS 326-06-7) is a commercial product (Alfa), the others **1b** (CAS 582-65-0), **1c** (CAS 18931-60-7), **1d** (CAS 18931-61-8), **1e** (CAS 15191-68-1), **1f** (CAS 35999-53-2) were synthesized according to literature procedures [12,20,21]. Phenylhydrazine (**2**) and *p*-nitrophenylhydrazine (**3**) are commercially available, **4** (CAS 20174-69-0), **5** (CAS 78364-55-3) and **6** (21703-52-6) were prepared according to literature procedures [22,23].

Reactions Performed in Neutral Medium (EtOH).

Synthesis of 1-Phenyl-5-aryl-3-trifluoromethylpyrazoles (**7a-e**).

1-Phenyl-5-(*p*-chlorophenyl)-3-trifluoromethylpyrazole (**7c**).

An ethanolic solution (20 ml) of 1-(*p*-chlorophenyl)-4,4,4-trifluorobutane-1,3-dione **1c** (1.25 g, 5 mmoles) and phenylhydrazine **2** (0.54 g, 5 mmoles) was refluxed for 3 hours. The excess of solvent was evaporated and on cooling, a solid appeared which was recrystallized from ethanol, mp 80° (Lit [12] yellow syrup), yield 72%; ^{1}H nmr ($CDCl_3$): δ 6.75 (s, 1H, 4-H), 7.15-7.48 (m, 9H, Ph'-H & *p*-ClPh''-H); ms: m/z 322 (M^+) 324 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{16}H_{10}ClF_3N_2$: C, 59.53; H, 3.10; N, 8.68. Found: C, 59.32; H, 3.01; N, 8.69.

Other pyrazoles (**7a, 7b, 7d, 7e, 7f**) were prepared similarly.

1,5-Diphenyl-3-trifluoromethylpyrazole (**7a**).

The compound had mp 79° (Lit [7] 80°, Lit [11] 95°); ^{1}H nmr ($CDCl_3$): δ 6.75 (s, 1H, 4-H), 7.23-7.34 (m, 10 H, Ph'-H & Ph''-H).

Anal. Calcd. for $C_{16}H_{11}F_3N_2$: C, 66.66; H, 3.82; N, 9.72. Found: C, 66.43; H, 4.02; N, 9.55.

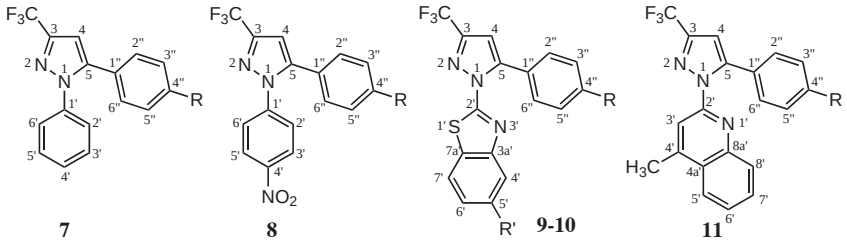


Table 3

^{13}C NMR data for 3-trifluoromethylpyrazoles (ppm).

Compds.	**7 c**	**7 d**	**8 b**	**8 c**	**8 d**	**8 e**	**8 f**	**9 c**	**9f**	**10c**	**10d**	**11 c**
C-3	143.32 (q, $^{2}J_{C-F}$ = 38.25 Hz)	143.34 (q, $^{2}J_{C-F}$ = 38.25 Hz)	144.56 (q, $^{2}J_{C-F}$ = 39 Hz)	144.65 (q, $^{2}J_{C-F}$ = 38.25 Hz)	144.67 (q, $^{2}J_{C-F}$ = 38.25 Hz)	143.94 (q, $^{2}J_{C-F}$ = 38.25 Hz)	144.43 (q, $^{2}J_{C-F}$ = 39 Hz)	144.90 (q, $^{2}J_{C-F}$ = 39 Hz)	145.08 (q, $^{2}J_{C-F}$ = 39.75 Hz)	144.50 (q, $^{2}J_{C-F}$ = 39 Hz)	144.80 (q, $^{2}J_{C-F}$ = 39 Hz)	143.90 (q, $^{2}J_{C-F}$ = 39 Hz)
C-4	105.7	105.67	107.0	107.15	107.13	106.51	108.0	108.20	109.06	106.0	108.5	107.10
C-5	143.48	143.50	144.30	143.63	143.63	145.23	145.20	145.35	143.90	143.48	145.45	145.83
C-1′	139.0	138.97	143.79	144.06	144.09	144.08	143.23	-	-	-	-	-
C-2′	125.52	125.51	124.69	124.74	124.75	124.57	124.98	157.91	157.85	158.54	158.57	149.99
C-3′	129.28	129.29	125.47	125.49	125.49	125.42	125.67	-	-	-	-	116.58
C-3′a	-	-	-	-	-	-	-	148.29	148.37	146.94	146.84	-
C-4′	128.71	128.72	146.94	147.0	147.0	146.75	147.33	123.10	122.98	124.72 (d, $^{3}J_{C-F}$ =9.75Hz	124.62 (d, $^{3}J_{C-F}$ =9.75Hz	144.66
C-4′a	-	-	-	-	-	-	-	-	-	-	-	129.59
C-5′	129.28	129.29	125.47	125.49	125.49	125.42	125.67	128.19	128.33	115.29 (d, $^{2}J_{C-F}$ =24.75Hz	115.27 (d, $^{2}J_{C-F}$ =24.75Hz	127.06
C-6′	125.52	125.51	124.69	124.74	124.75	124.57	124.98	136.20	136.43	160.60 (d, $^{1}J_{C-F}$ = 245.25Hz	160.70 (d, $^{1}J_{C-F}$ = 245.25Hz	123.75
C-7′	-	-	-	-	-	-	-	121.16	121.21	108.10 (d, $^{2}J_{C-F}$ = 27.75 Hz	107.85 (d, $^{2}J_{C-F}$ = 27.75 Hz	128.33
C-7′a	-	-	-	-	-	-	-	134.08	133.90	134.92 (d, $^{3}J_{C-F}$ = 11.0 Hz	134.85 (d, $^{3}J_{C-F}$ = 11.0 Hz	-
C-8′	-	-	-	-	-	-	-	-	-	-	-	130.19
C-8′a	-	-	-	-	-	-	-	-	-	-	-	148.21
C-1″	127.63	128.08	124.75	126.99	127.44	120.75	134.62	127.01	135.00	126.88	127.34	127.50
C-2″, 6″	130.04	130.20	130.90 (d, $^{3}J_{C-F}$ = 9 Hz)	130.13	130.32	130.28	129.76	131.02	130.78	131.09	131.30	130.42
C-3″, 5″	129.04	131.99	116.5 (d, $^{2}J_{C-F}$ = 22.5 Hz)	129.55	132.50	114.60	124.43	128.50	124.30	128.99	131.47	128.85
C-4″	135.24	122.96	163.40 (d, $^{1}J_{C-F}$ =249.75 Hz)	136.16	124.38	160.61	148.33	135.89	148.12	135.82	124.56	134.79
CH_3	-	-	-	-				21.59	21.57	-	-	18.98
CF_3	121.2 (q, $^{1}J_{C-F}$ = 267 Hz)	121.17 (q, $^{1}J_{C-F}$ = 267.75 Hz)	120.90 (q, $^{1}J_{C-F}$ =267.75 Hz)	120.83 (q, $^{1}J_{C-F}$ =267.75 Hz)	120.81 (q, $^{1}J_{C-F}$ =267.75 Hz)	121.0 (q, $^{1}J_{C-F}$ =267.75 Hz)	120.65 (q, $^{1}J_{C-F}$ =267.75 Hz)	120.65 (q, $^{1}J_{C-F}$ =267.75Hz)	120.57 (q, $^{1}J_{C-F}$ =267.75Hz)	120.31 (q, $^{1}J_{C-F}$ = 270.0Hz)	120.39 (q, $^{1}J_{C-F}$ = 270.0Hz)	120.75 (q, $^{1}J_{C-F}$ =267.75 Hz)
OCH_3						55.40						

Table 4

^{13} C NMR data for 5-hydroxy-5-trifluoromethylpyrazolines (ppm).

Compds.	**12 f**	**13 a**	**13 b**	**13 c**	**13 d**	**13 e**	**13f**	**14c**	**14f**	**15c**	**15d**	**16 c**	**16 d**
C-3	145.90	149.56	148.53	148.42	148.41	149.45	148.05	148.47	148.32	147.11	147.41	147.0	148.47
C-4	43.65	44.64	44.72	44.46	44.46	44.85	43.98	44.14	43.89	44.19	44.15	44.05	43.98
C-5	94.12 (q, $^{2}J_{C-F}$ = 31.5 Hz)	93.54 (q, $^{2}J_{C-F}$ = 32.25 Hz)	93.62 (q, $^{2}J_{C-F}$ = 33 Hz)	93.70 (q, $^{2}J_{C-F}$ = 33 Hz)	93.70 (q, $^{2}J_{C-F}$ = 33Hz)	93.39 (q, $^{2}J_{C-F}$ = 33 Hz)	94.17 (q, $^{2}J_{C-F}$ = 33Hz)	92.90 (q, $^{2}J_{C-F}$ = 34.5 Hz)	93.36 (q, $^{2}J_{C-F}$ = 33.75 Hz)	92.85 (q, $^{2}J_{C-F}$ = 34.5 Hz)	92.86 (q, $^{2}J_{C-F}$ = 34.5 Hz)	93.70 (q, $^{2}J_{C-F}$ = 33 Hz)	93.70 (q, $^{2}J_{C-F}$ = 33.75 Hz)

Table 4 (continued)

Compds.	12 f	13 a	13 b	13 c	13 d	13 e	13f	14c	14f	15c	15d	16 c	16 d
C-1′	140.10	140.61	140.72	140.77	140.86	140.37	141.34	-	-	-	-	-	-
C-2′	124.10	115.55	115.55	115.62	115.68	115.30	116.08	162.97	162.47	163.21	163.18	155.13	155.10
C-3′	126.32	124.86	124.88	124.84	124.87	125.72	125.04	-	-	-	-	112.77	112.76
C-3′a	-	-	-	-	-	-	-	151.58	150.21	152.0	152.06	-	-
C-4′	124.63	147.94	147.85	147.76	147.71	148.0	147.08	121.03	121.09	121.26 (d, $^3J_{C\text{-}F}$ =9Hz	121.27 (d, $^3J_{C\text{-}F}$ =9Hz	144.89	144.79
C-4′a	-	-	-	-	-	-	-	-	-	-	-	124.74	124.74
C-5′	126.32	124.86	124.88	124.84	124.87	125.72	125.04	127.54	127.73	114.3 (d, $^2J_{C\text{-}F}$ =24Hz	114.3 (d, $^2J_{C\text{-}F}$ =24Hz	124.20	124.21
C-6′	124.10	115.55	115.55	115.62	115.68	115.30	116.08	136.85	135.85	159.21 (d, $^1J_{C\text{-}F}$ = 241.5Hz	159.0 (d, $^1J_{C\text{-}F}$ = 241.0Hz	123.82	123.82
C-7′	-	-	-	-	-	-	-	120.18	120.43	107.8 (d, $^2J_{C\text{-}F}$ = 27 Hz	107.8 (d, $^2J_{C\text{-}F}$ = 27 Hz	127.13	127.13
C-7′a	-	-	-	-	-	-	-	131.14	131.13	132.0 (d, $^3J_{C\text{-}F}$ = 10.5Hz	132.1 (d, $^3J_{C\text{-}F}$ = 8.25 Hz	-	-
C-8′	-	-	-	-	-	-	-	-	-	-	-	129.94	129.94
C-8′a	-	-	-	-	-	-	-	-	-	-	-	149.07	149.12
C-1″	137.44	130.99	127.36 (d,$^4J_{C\text{-}F}$ = 3 Hz)	129.56	129.99	123.65	137.10	128.92	131.75	128.31	128.74	129.55	125.79
C-2″, 6″	129.07	128.84	128.95 (d, $^3J_{C\text{-}F}$ = 8.25 Hz)	129.50	127.40	127.61	126.57	129.18	127.19	129.23	127.96	129.05	127.58
C-3″, 5″	126.72	125.70	115.95 (d, $^2J_{C\text{-}F}$ = 21.75 Hz)	127.22	132.04	114.27	124.10	127.75	124.17	127.79	131.94	127.38	132.0
C-4″	147.87	130.11	163.78 (d, $^1J_{C\text{-}F}$ =250.0 Hz)	135.91	124.27	161.20	147.32	133.25	148.32	137.05	125.42	135.99	122.25
CH_3	-	-	-	-	-	-	-	21.35	21.39	-	-	19.09	19.09
CF_3	123.0 (q, $^1J_{C\text{-}F}$ = 282.75Hz)	123.66 (q, $^1J_{C\text{-}F}$ = 265.5 Hz)	123.74 (q, $^1J_{C\text{-}F}$ =285.75 Hz)	123.72 (q, $^1J_{C\text{-}F}$ =285. 75 Hz)	123.69 (q, $^1J_{C\text{-}F}$ =267. 75 Hz)	123.82 (q, $^1J_{C\text{-}F}$ =285. 75 Hz)	123.60 (q, $^1J_{C\text{-}F}$ =285. 75 Hz)	123.0 (q, $^1J_{C\text{-}F}$ =285Hz)	123.4 (q, $^1J_{C\text{-}F}$ =285.2Hz)	123.12 (q, $^1J_{C\text{-}F}$ = 285.5Hz)	123.11 (q, $^1J_{C\text{-}F}$ = 285.0Hz)	123.9 (q, $^1J_{C\text{-}F}$ =286.5Hz)	123.88 (q, $^1J_{C\text{-}F}$ =286.5 Hz)
OCH_3						55.43							

Table 5

^{13}C NMR data for 5-trifluoromethylpyrazoles (ppm).

Compds.	17 f	18a	18 b	18 c	18 d	18 e	18 f	19 c	19 f	20 c	20 d	21 c
C-3	149.30	152.93	152.01	151.82	151.84	152.76	150.55	148.87	148.76	147.41	147.42	147.65
C-4	106.8	108.00	107.00	107.83	107.83	107.62	108.42	109.56	110.10	109.82	109.85	108.92
C-5	134.64 (q, $^2J_{C\text{-}F}$ = 39 Hz)	133.95 (q, $^2J_{C\text{-}F}$ = 39Hz)	134.08 (q, $^2J_{C\text{-}F}$ = 39Hz)	134.15 q, $^2J_{C\text{-}F}$ = 39.75Hz)	134.16 (q, $^2J_{C\text{-}F}$ = 39Hz)	133.80 (q, $^2J_{C\text{-}F}$ = 39Hz)	134.71 (q, $^2J_{C\text{-}F}$ = 39Hz)	133.81 (q, $^2J_{C\text{-}F}$ = 42 Hz)	133.80 (q,$^2J_{C\text{-}F}$= 42 Hz)	134.38 (q, $^2J_{C\text{-}F}$ = 42 Hz)	134.34 (q, $^2J_{C\text{-}F}$ = 42.75 Hz)	134.06 (q, $^2J_{C\text{-}F}$ =42 Hz)
C-1′	138.83	143.96	143.87	143.81	143.79	144.04	143.53	-	-	-	-	-
C-2′	125.67	124.74	124.76	124.77	124.76	124.72	124.86	157.38	157.32	157.82	158.82	150.69
C-3′	129.30	125.60	125.59	125.63	125.61	125.46	125.83	-	-	-	-	114.61
C-3′a	-	-	-	-	-	-	-	151.77	150.50	152	152.15	-
C-4′	126.40	147.49	147.54	147.58	147.58	147.35	147.89	123.06	123.25	124.55 (d, $^3J_{C\text{-}F}$ =9.75Hz	124.56 (d, $^3J_{C\text{-}F}$ =9.75Hz	146.03
C-4′a	-	-	-	-	-	-	-	-	-	-	-	127.42

Table 5 (continued)

Compds.	**17 f**	**18a**	**18 b**	**18 c**	**18 d**	**18 e**	**18 f**	**19 c**	**19 f**	**20 c**	**20 d**	**21 c**
C-5′	129.30	125.60	125.59	125.63	125.61	125.46	125.83	128.14	128.34	115.15 (d, $^2J_{C\text{-}F}$ =24 Hz	115.22 (d, $^2J_{C\text{-}F}$ =24.75Hz	126.64
C-6′	125.67	124.74	124.76	124.77	124.76	124.72	124.86	135.80	136.22	160.57 (d, $^1J_{C\text{-}F}$ = 245.25Hz	160.71 (d, $^1J_{C\text{-}F}$ = 245.25Hz	123.73
C-7′	-	-	-	-	-	-	-	121.06	121.16	107.80 (d, $^2J_{C\text{-}F}$ = 27 Hz	107.83 (d, $^2J_{C\text{-}F}$ = 27 Hz	129.64
C-7′a	-	-	-	-	-	-	-	133.71	133.75	134.31 (d, $^3J_{C\text{-}F}$ = 11.0 Hz	134.28 (d, $^3J_{C\text{-}F}$ = 10.50 Hz	-
C-8′	-	-	-	-	-	-	-	-	-	-	-	130.10
C-8′a	-	-	-	-	-	-	-	-	-	-	-	149.40
C-1″	137.91	130.99	127.25 (d, $^4J_{C\text{-}F}$ = 3.75 Hz)	126.51	129.96	123.64	137.10	129.00	136.50	128.79	129.27	127.42
C-2″, 6″	129.79	128.97	127.80 (d, $^3J_{C\text{-}F}$ = 8.25 Hz)	129.21	127.45	127..30	126.59	129.18	126.81	129.24	127.66	129.04
C-3″, 5″	124.25	125.95	116.00 (d, $^2J_{C\text{-}F}$ = 21.75 Hz)	127.19	132.50	114.35	124.35	127.38	124.30	127.39	132.21	127.21
C-4″	147.79	129.25	163.40 (d, $^1J_{C\text{-}F}$ =247.50 Hz)	135.19	123.40	160.49	148.13	135.51	148.27	135.70	123.94	134.78
CH_3	-	-	-	-				21.59	21.63	-	-	19.04
CF_3	119.52 (q, $^1J_{C\text{-}F}$ = 267.75 Hz)	119.72 (q, $^1J_{C\text{-}F}$ = 285 Hz)	119.55 (q, $^1J_{C\text{-}F}$ =267.75 Hz)	119.49 (q, $^1J_{C\text{-}F}$ =267.75 Hz)	119.50 (q, $^1J_{C\text{-}F}$ =267.75 Hz)	119.66 (q, $^1J_{C\text{-}F}$ =267 Hz)	119.34 (q, $^1J_{C\text{-}F}$ =267.75 Hz)	119.22 (q, $^1J_{C\text{-}F}$ =267.75 Hz)	119.21 (q, $^1J_{C\text{-}F}$ = 267.75 Hz)	119.14 (q, $^1J_{C\text{-}F}$ = 267.75Hz)	119.21 (q, $^1J_{C\text{-}F}$ = 267.75Hz)	120.00 (q, $^1J_{C\text{-}F}$ = 267.75Hz)
OCH_3						55.38						

Table 6

^{19} F NMR values (ppm) for compounds **7**-**21**.

Compds	CF_3,	F	Compds	CF_3,	F	Compds	CF_3,	F	Compds	CF_3,	F
7a	-63.1	-	**8f**	-63.2,	-	**13e**	-80.9	-	**18c**	-57.7	-
7b	-63.0,	-112	**9c**	-62.7	-	**13f**	-80.9,	-	**18d**	-57.7	-
7c	-62.9	-	**9f**	-62.7	-	**14c**	-81.4	-	**18e**	-57.6	-
7d	-62.9	-	**10c**	-63.4,	-115	**14f**	-81.2	-	**18f**	-57.2	-
7e	-62.9	-	**10d**	-62.8,	-114	**15c**	-82.0,	-119	**19c**	-59.6	-
7f	-63.1	-	**11c**	-63.0	-	**15d**	-81.7,	-119	**19f**	-59.7	-
8a	-63.0	-	**12f**	-77.94	-	**16c**	-81.6	-	**20c**	-60.0,	-115
8b	-62.9	-	**13a**	-76.0	-	**16d**	-81.6	-	**20d**	-59.8,	-115
8c	-63.1,	-110	**13b**	-81.0,	-111	**17f**	-57.8	-	**21c**	-59.7	-
8d	-63.1	-	**13c**	-80.8	-	**18a**	-57.6	-	-	-	-
8e	-63.1	-	**13d**	-80.8	-	**18b**	-57.7,	-112	-	-	-

1-Phenyl-5-(*p*-fluorophenyl)-3-trifluoromethylpyrazole (**7b**).

The compound had mp 99° (Lit [24] 101°); ^{1}H nmr ($CDCl_3$): δ 6.73 (s, 1H, 4-H), 6.99-7.38 (m, 9H, Ph'-H & *p*-FPh"-H).

Anal. Calcd. For $C_{16}H_{10}F_4N_2$: C, 62.75; H, 3.27; N, 9.15. Found: C, 62.55; H, 3.12; N, 8.99.

1-Phenyl-5-(*p*-bromophenyl)-3-trifluoromethylpyrazole (**7d**).

The compound had mp 94° (Lit [13] 92-94°), yield 74%; ^{1}H nmr ($CDCl_3$): δ 6.76 (s, 1H, 4-H), 7.08 (d, 2H, 2"& 6"-H, *J* = 8.7 Hz.), 7.28-7.41 (m, 5H, Ph'-H), 7.46 (d, 2H, 3"& 5"-H, *J* = 8.4 Hz.); ms: m/z 366 (M^+) and 368 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{16}H_{10}BrF_3N_2$: C, 52.46; H, 2.73; N, 7.65. Found: C, 52.34; H, 2.45; N, 7.65.

1-Phenyl-5-(*p*-methoxyphenyl)-3-trifluoromethylpyrazole (**7e**).

Compound was obtained as a liquid (Lit [24] bp 159°); ^{1}H nmr ($CDCl_3$): δ 3.78 (s, 3H, OCH_3), 6.69 (s, 1H, 4-H), 6.83 (d, 2H, 3"& 5"-H, *J* = 9 Hz), 7.14 (d, 2H, 2"& 6"-H, *J* = 9 Hz), 7.29-7.38 (m, 5H, Ph'-H).

Anal. Calcd. for $C_{17}H_{13}F_3N_2O$: C, 64.15; H, 4.10; N, 8.80. Found: C, 63.97; H, 3.97; N, 8.67.

1-Phenyl-5-(*p*-nitrophenyl)-3-trifluoromethylpyrazole (**7f**) and 1-Phenyl-3-(*p*-nitrophenyl)-5-hydroxy-5-trifluoro-methyl-Δ^2-pyrazoline (**12f**).

A solution of 1-(*p*-nitrophenyl)-4,4,4-trifluoro-butane-1,3-dione **1f** (1.3 g, 5 mmoles) and phenylhydrazine 2 (0.54 g, 5 mmoles) in ethanol (20 ml) was refluxed for 3 hours. The reaction was monitored by tlc. The solvent was evaporated completely. The tlc and ^{1}H nmr of crude reaction mixture showed the formation of two products in a 70:30 (**7f**:**12f**) ratio. Column chromatographic separation using silica gel (100-200 mesh) with petroleum ether (60-80°) as eluent afforded 7f, mp 104° (Lit [24] 56°), yield 50%; ^{1}H nmr ($CDCl_3$): δ 6.89 (s, 1H, 4-H), 7.28-7.45 (m, 7H, Ph', 2"& 6"-H), 8.19 (d, 2H, 3"& 5"-H, *J* = 8.7 Hz).

Anal. Calcd. for $C_{16}H_{10}F_3N_3O_2$: C, 57.66; H, 3.00; N, 12.61. Found: C, 57.33; H, 2.89; N, 12.46.

Further elution of column with petroleum ether afforded the other product (**12f**). The compound had mp 144°, yield 22%; ir: ν OH 3430 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 3.53 (d, 1H, 4-H, *J* = 18 Hz), 3.74 (d, 1H, 4-H, *J* = 18 Hz), 7.28-7.45 (m, 5H, Ph'-H), 7.82 (d, 2H, 2"& 6"-H, *J* = 8.7 Hz), 8.11 (bs, 1H, OH), 8.25 (d, 2H, 3" & 5"-H, *J* = 8.7 Hz); ms: m/z 351 (M^+).

Anal. Calcd. for $C_{16}H_{12}F_3N_3O_3$: C, 54.71; H, 3.42; N, 11.96. Found: C, 54.95; H, 3.40; N, 11.90.

Synthesis of 1-(*p*-Nitrophenyl)-5-aryl-3-trifluoromethyl-pyrazoles (**8a-f**) and 1-(*p*-Nitrophenyl)-3-aryl-5-hydroxy-5-trifluoro-methyl-Δ^2- pyrazolines (**13a-f**).

1-(*p*-Nitrophenyl)-5-phenyl-3-trifluoromethylpyrazole (**8a**) and 1-(*p*-nitrophenyl)-3-phenyl-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**13a**).

An ethanolic solution of 1-phenyl-4,4,4-trifluorobutane-1,3-dione **1a** (1.075 g, 5 mmoles) and *p*-nitrophenyl-hydrazine **3** (0.77 g, 5 mmoles) in ethanol (20 ml) was refluxed for 8 hours. The reaction was monitored by tlc. The solvent was evaporated completely to give the solid reaction product. The tlc and ^{1}H nmr of the crude reaction mixture showed the formation of two products in a ratio given in the Table 2. Column chromatographic separation using silica gel (100-200 mesh) and petroleum ether (60-80°) as eluent afforded **8a**, mp 87° (Lit [9] 91°), yield 27%; ^{1}H nmr ($CDCl_3$): δ 6.78 (s, 1H, 4-H), 7.22-7.51 (m, 5H, Ph"-H), 7.50 (d, 2H, 2' & 6'-H, *J* = 9 Hz), 8.23 (d, 2H, 3' & 5'-H, *J* = 9 Hz).

Anal. Calcd. for $C_{16}H_{10}F_3N_3O_2$: C, 57.66; H, 3.00; N, 12.61. Found: C, 57.45; H, 2.94; N, 12.44.

Further elution of the column with petroleum ether: ethyl acetate (99:1) afforded the other product (**13a**). The compound had mp 198-99°, yield 45%; ir: ν OH 3410 cm^{-1}; ^{1}H nmr ($CDCl_3$ + DMSO-d_6): δ 3.65 (d, 1H, 4-H, *J* = 18.6 Hz), 3.80 (d, 1H, 4-H, *J* = 18.6 Hz), 7.43-7.48 (m, 3H, 3", 4", 5"-H), 7.71-7.75 (m, 4H, 2", 6", 2' & 6'-H), 8.10 (bs, 1H, OH), 8.15 (d, 2H, 3' & 5'-H, *J* = 9 Hz); ms: m/z 351 (M^+).

Anal. Calcd. for $C_{16}H_{12}F_3N_3O_3$: C, 54.71; H, 3.42; N, 11.96. Found: C, 54.65; H, 3.29; N, 11.76.

Using similar procedure, compounds **8b-f** and **13b-f** were also prepared and purified. The ratio of the two products is given in the Table 2.

1-(*p*-Nitrophenyl)-5-(*p*-fluorophenyl)-3-trifluoromethyl-pyrazole (**8b**).

The compound had mp 98° (Lit [11] 111-113°), yield 21%; ^{1}H nmr ($CDCl_3$): δ 6.78 (s, 1H, 4-H), 7.07-7.13 (m, 2H, 3", 5"-H), 7.21-7.27 (m, 2H, 2", 6"-H), 7.50 (d, 2H, 2' & 6'-H, *J* = 9 Hz), 8.24 (d, 2H, 3' & 5'-H, *J* = 9 Hz); ms: m/z 351 (M^+).

Anal. Calcd. for $C_{16}H_9F_4N_3O_2$: C, 54.71; H, 2.56; N, 11.96. Found: C, 54.65; H, 2.40; N, 11.45.

1-(*p*-Nitrophenyl)-3-(*p*-fluorophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**13b**).

The compound had mp 176°, yield 45%; ir: ν OH 3410 cm^{-1}; ^{1}H nmr ($CDCl_3$ + DMSO-d_6): δ 3.63 (d, 1H, 4-H, *J* = 18.3 Hz), 3.77 (d, 1H, 4-H, *J* = 18.6 Hz), 7.09-7.16 (m, 2H**,** 3", 5"-H), 7.69-7.75 (m, 4H, 2", 6", 2' & 6'-H), 8.06 (bs, 1H, OH), 8.15 (d, 2H, 3' & 5'-H, *J* = 9 Hz); ms: m/z 369 (M^+).

Anal. Calcd. for $C_{16}H_{11}F_4N_3O_3$: C, 52.04; H, 2.98; N, 11.38. Found: C, 52.15; H, 2.87; N, 11.39.

1-(*p*-Nitrophenyl)-5-(*p*-chlorophenyl)-3-trifluoromethyl-pyrazole (**8c**).

The compound had mp 124°, yield 19%; ^{1}H nmr ($CDCl_3$): δ 6.80 (s, 1H, 4-H), 7.18 (d, 2H, 2", 6"-H, *J* = 8.1 Hz), 7.39 (d, 2H, 3", 5"-H, *J* = 8.1 Hz), 7.51 (d, 2H, 2' & 6'-H, *J* = 8.7 Hz), 8.25 (d, 2H, 3' & 5'-H, *J* = 8.7 Hz); ms: m/z 367 (M^+) and 369 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{16}H_9ClF_3N_3O_2$: C, 52.24; H, 2.45; N, 11.43. Found: C, 52.03; H, 2.33; N, 11.66.

1-(*p*-Nitrophenyl)-3-(*p*-chlorophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**13c**).

The compound had mp 192-94°, yield 58%; ir: ν OH 3410 cm^{-1}; ^{1}H nmr ($CDCl_3$+DMSO-d_6): δ 3.60 (d, 1H, 4-H, *J* = 18.6Hz), 3.77 (d, 1H, 4-H, *J* = 18.6 Hz), 7.40 (d, 2H, 2", 6"-H, *J* = 8.4 Hz), 7.65 (d, 2H**,** 3", 5"-H, *J* = 8.4 Hz), 7.70 (d, 2H, 2' & 6'-H, *J* = 9.3 Hz), 7.79 (bs, 1H, OH), 8.16 (d, 2H, 3' & 5'-H, *J* = 9.3 Hz); ms: m/z 385 (M^+) and 387 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{16}H_{11}ClF_3N_3O_3$: C, 49.81; H, 2.85; N, 10.89. Found: C, 49.80; H, 2.71; N, 11.05.

1-(*p*-Nitrophenyl)-5-(*p*-bromophenyl)-3-trifluoromethyl-pyrazole (**8d**).

The compound had mp 160°, yield 23%; ^{1}H nmr ($CDCl_3$): δ 6.80 (s, 1H, 4-H), 7.12 (d, 2H, 2", 6"-H, J = 8.7 Hz), 7.54 (m, 4H, 3", 5", 2' & 6'-H), 8.25 (d, 2H, 3' & 5'-H, J = 9.3 Hz); ms: m/z 411 (M^+) and 413 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{16}H_9BrF_3N_3O_2$: C, 46.71; H, 2.18; N, 10.22. Found: C, 46.29; H, 2.12; N, 10.20.

1-(*p*-Nitrophenyl)-3-(*p*-bromophenyl)-5-hydroxy-5-trifluoro-methyl-Δ^2-pyrazoline (**13d**).

The compound had mp 199-200°, yield 56%; ir: ν OH 3414 cm^{-1}; ^{1}H nmr ($CDCl_3$ + DMSO-d_6): δ 3.61 (d, 1H, 4-H, J = 19.5 Hz), 3.76 (d, 1H, 4-H, J = 18.9 Hz), 7.55-7.61 (m, 4H**,** *p*-BrPh"-H), 7.70 (d, 2H, 2' & 6'-H, J = 9.3 Hz), 7.88 (bs, 1H, O-H), 8.16 (d, 2H, 3' & 5'-H, J = 9.3 Hz); ms: m/z 429 (M^+) and 431 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{16}H_{11}BrF_3N_3O_3$: C, 44.75; H, 2.56; N, 9.79. Found: C, 44.31; H, 2.65; N, 9.78.

1-(*p*-Nitrophenyl)-5-(*p*-methoxyphenyl)-3-trifluoro-methyl-pyrazole (**8e**).

The compound had mp 135°, yield 22%; ^{1}H nmr ($CDCl_3$): δ 3.84 (s, 3H, OCH_3), 6.73 (s, 1H, 4-H), 6.90 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.16 (d, 2H, 2", 6"-H, J = 8.7 Hz), 7.52 (d, 2H, 2' & 6'-H, J = 9Hz), 8.22 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 363 (M^+).

Anal. Calcd. for $C_{17}H_{12}F_3N_3O_3$: C, 56.20; H, 3.31; N, 11.57. Found: C, 55.95; H, 3.21; N, 11.60.

1-(*p*-Nitrophenyl)-3-(*p*-methoxyphenyl)-5-hydroxy-5-trifluoro-methyl-Δ^2-pyrazoline (**13e**).

The compound had mp 176°, yield 57%; ir: ν OH 3417 cm^{-1}; ^{1}H nmr ($CDCl_3$ + DMSO-d_6): δ 3.58 (d, 1H, 4-H, J = 19 Hz), 3.77 (d, 1H, 4-H, J = 18.6 Hz), 3.86 (s, 3H, O-CH_3), 6.95 (d, 2H**,** 3", 5"-H, J = 9 Hz), 7.65-7.71 (m, 4H, 2', 6', 2", 6"-H), 7.93 (bs, 1H, O-H), 8.15 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 381 (M^+).

Anal. Calcd. for $C_{17}H_{14}F_3N_3O_4$: C, 53.54; H, 3.67; N, 11.02. Found: C, 53.39; H, 3.47; N, 10.87.

1, 5-Bis (*p*-nitrophenyl)-3-trifluoromethylpyrazole (**8f**).

The compound had mp 188°, yield 13%; ^{1}H nmr ($CDCl_3$): δ 6.93 (s, 1H, 4-H), 7.44-7.53 (m, 4H, 2',6',2" & 6"-H), 8.26-8.30 (m, 4H, 3',5', 3" & 5"-H); ms: m/z 378 (M^+).

Anal. Calcd. for $C_{16}H_9F_3N_4O_4$: C, 50.80; H, 2.38; N, 14.81. Found: C, 50.58; H, 2.33; N, 14.68.

1,3-Bis(*p*-nitrophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**13f**).

The compound had mp 192-94°, yield 65%; ir: ν OH 3421 cm^{-1}; ^{1}H nmr ($CDCl_3$ + DMSO-d_6): δ 3.70 (d, 1H, 4-H, J = 18.9 Hz), 3.83 (d, 1H, 4-H, J = 18.9 Hz), 7.70-8.29 (m, 8H, *p*-NO_2Ph' & p-NO_2Ph"-H), 8.30 (bs, 1H, OH); ms: m/z 396 (M^+).

Anal. Calcd. for $C_{16}H_{11}ClF_3N_3O_5$: C, 48.49; H, 2.78; N, 14.14. Found: C, 48.42; H, 2.80; N, 13.97.

Synthesis of 1-(6'-Substitutedbenzothiazol-2'-yl)-3-aryl-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines (**14c, 14f, 15c, 15d**).

1-(6'-Methylbenzothiazol-2'-yl)-3-(*p*-chlorophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2–pyrazoline (**14c**).

An ethanolic solution of 1-(*p*-chlorophenyl)-4,4,4-trifluoro-butane-1, 3-dione **1c** (1.25 g, 5 mmoles) and 6-methyl-benzothiazol-2-ylhydrazine **4** (0.90 g, 5 mmoles) was refluxed in ethanol (20 ml) for 8 hours. The reaction was monitored by tlc. The solvent was evaporated completely to yield a solid reaction product. The tlc and ^{1}H nmr of the crude reaction mixture showed the formation of an exclusive single product. The product was recrystallized from ethanol to yield the pure product **14c**, mp 142°, yield 78%; ir: ν OH 3290 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 2.57 (s, 3H, CH_3), 3.62 (d, 1H, 4-H, J = 18.6 Hz), 3.77 (d, 1H, 4-H, J = 18.6 Hz), 7.17 (d, 1H, 5'-H, J = 8.1 Hz), 7.40 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.50 (s, 1H, 7'-H), 7.55 (d, 1H, 4'-H, J = 8.4 Hz), 7.64 (d, 2H, 2", 6"-H, J = 8.7 Hz); ms: m/z 411 (M^+) and 413 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{18}H_{13}ClF_3N_3OS$: C, 52.49; H, 3.16; N, 10.21. Found: C, 52.43; H, 3.09; N, 10.10.

Compounds **14f, 15c** and **15d** were prepared and purified by similar procedure.

1-(6'-Methylbenzothiazol-2'-yl)-3-(*p*-nitrophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**14f**).

The compound had mp 175-76°, yield 81%; ir: ν OH 3287 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 2.43 (s, 3H, CH_3), 3.69 (d, 1H, 4-H, J = 18.3 Hz), 3.84 (d, 1H, 4-H, J = 18.3 Hz), 7.21 (d, 1H, 5'-H, J = 8.1 Hz), 7.54 (s, 1H, 7'-H), 7.58 (d, 1H, 4'-H, J = 8.4 Hz), 7.88 (d, 2H, 2", 6"-H, J = 8.7 Hz), 8.3 (d, 2H, 3", 5"-H, J = 9 Hz); ms: m/z 422 (M^+).

Anal. Calcd. for $C_{18}H_{13}F_3N_4O_3S$: C, 51.18; H, 3.08; N, 13.27. Found: C, 51.12; H, 2.98; N, 13.01.

1-(6'-Fluorobenzothiazol-2'-yl)-3-(*p*-chlorophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline (**15c**).

The compound had mp 136-37°, yield 75%; ir: ν OH 3305 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 3.64 (d, 1H, 4-H, J = 18.6 Hz), 3.79 (d, 1H, 4-H, J = 18.6 Hz), 7.06-7.66 (m, 8H, OH, 6-FBz'-H & *p*-ClPh"-H); ms: m/z 415 (M^+) and 417 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{17}H_{10}ClF_4N_3OS$: C, 49.10; H, 2.41; N, 10.11. Found: C, 48.93; H, 2.33; N, 9.89.

1-(6'-Fluorobenzothiazol-2'-yl)-3-(*p*-bromophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines (**15d**).

The compound had mp 152-54°, yield 76%; ir: ν OH 3298 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 3.70 (d, 1H, 4-H, J = 18.3 Hz), 3.79 (d, 1H, 4-H, J = 18.3 Hz), 7.06-7.66 (m, 7H, 6-FBz'-H & p-BrPh"-H); ms: m/z 459 (M^+) and 461 (M^++2) in the ratio showing typical isotope bromine profile (1:1).

Anal. Calcd. for $C_{17}H_{10}BrF_3N_3OS$: C, 44.44; H, 2.18; N, 9.15. Found: C, 44.39; H, 1.99; N, 9.18.

Synthesis of 1-(4'-methylquinolin-2'-yl)-3-aryl-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines (**16c, 16d**).

1-(4'-Methylquinolin-2'-yl)-3-(*p*-chlorophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines (**16c**).

An ethanolic solution of 1-(*p*-chlorophenyl)-4,4,4-trifluoro-butane-1, 3-dione **1c** (1.25 g, 5 mmoles) and 4-methylquinolin-2-ylhydrazine **6** (0.87 g, 5 mmoles) was refluxed in ethanol (20

ml) for 8 hours. The reaction was monitored by tlc. The solvent was evaporated completely to provide a solid reaction mixture. The tlc and ^{1}H nmr of the crude reaction mixture showed the formation of an exclusive single product. The compound was recrystallized from ethanol to give pure solid **16c**, mp 180°, yield 72%; ir: ν OH 3310 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 2.69 (s, 3H, CH_3), 3.59 (d, 1H, 4-H, *J* = 18.4 Hz), 3.74 (d, 1H, 4-H, *J* = 18.3 Hz), 7.37-7.88 (m, 9H, Qu'-H, & *p*-ClPh"-H), 9.31 (bs, 1H, OH); ms: m/z 405 (M^+) and 407 (M^++2) in the ratio of a typical Cl isotope profile (3:1).

Anal. Calcd. for $C_{20}H_{15}ClF_3N_3O$: C, 59.20; H, 3.69; N, 10.35. Found: C, 59.02; H, 3.57; N, 10.26.

Compound **16d** was prepared and purified by similar procedure.

1-(4'-Methylquinolin-2'-yl)-3-(*p*-bromophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazolines (**16d**).

The compound had mp 196-97°, yield 74%; ir: ν OH 3306 cm^{-1}; ^{1}H nmr ($CDCl_3$): δ 2.69 (s, 3H, CH_3), 3.59 (d, 1H, 4-H, *J* = 18.6 Hz), 3.74 (d, 1H, 4-H, *J* = 18.3 Hz), 7.37-7.88 (m, 9H, Qu'-H, & *p*-BrPh"-H), 9.40 (bs, 1H, OH); ms: m/z 449 (M^+) and 451 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{20}H_{15}BrF_3N_3O$: C, 53.45; H, 3.34; N, 9.35. Found: C, 53.08; H, 3.31; N, 9.23.

Reactions performed under acidic condition (EtOH/ H_2SO_4).

Synthesis of 1-Phenyl-5-aryl -3-trifluoromethylpyrazoles (**7a-f**).

1, 5-Diphenyl-3-trifluoromethylpyrazole (**7a**).

An ethanolic solution (20 ml) of 1-phenyl 4,4,4-trifluorobutane-1, 3-dione **1a** (1.075 g, 5 mmoles) and 0.1 ml conc. sulfuric acid was stirred for 15 minutes. An equimolar amount of phenylhydrazine **2** (0.54 g, 5 mmoles) was subsequently added at 50° temperature in small lots with constant stirring. The reaction mixture was allowed to reflux for 3 hours. Reaction was monitored by tlc. The excess of solvent was evaporated and ^{1}H nmr of the crude product so obtained showed the formation of only single product **7a** exclusively. The solid was recrystallized from ethanol to provide the pure compound **7a**, mp 80°, yield 71%, identical to that obtained above.

Compounds **7b-f** were obtained as exclusive products under the similar conditions.

Synthesis of 1-(*p*-Nitrophenyl)-5-aryl-3-trifluoromethyl-pyrazole (**8a-f**).

Compounds **8a-f** were obtained exclusively by performing the similar reactions when refluxed for 5 hours and were recrystallized from ethanol.

Synthesis of 1-(6'-Substitutedbenzothiazol-2'-yl)-5-aryl-3-trifluoromethylpyrazoles (**9c, 9f, 10c, 10d**).

Compounds **9c, 9f, 10c, 10d** were obtained exclusively by performing the similar reactions when refluxed for 15 hours and were recrystallized from ethanol.

1-(6'-Methylbenzothiazol-2'-yl)-5-(*p*-chlorophenyl)-3-trifluoromethylpyrazole (**9c**).

The compound had mp 150°, yield 69%; ^{1}H nmr ($CDCl_3$): δ 2.48 (s, 3H, CH_3), 6.74 (s, 1H, 4-H), 7.25 (d, 1H, 5'-H, *J* = 6.6 Hz), 7.40 (d, 2H, 2", 6"-H, *J* = 8.7 Hz), 7.47 (d, 2H, 3", 5"-H, *J* = 8.7 Hz), 7.62 (s, 1H, 7'-H), 7.64 (d, 1H, 4'-H, *J* = 6.8 Hz); ms: m/z 393 (M^+) and 395 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{18}H_{11}ClF_3N_3S$: C, 54.90; H, 2.79; N, 10.67. Found: C, 54.77; H, 2.68; N, 10.60.

1-(6'-Methylbenzothiazol-2'-yl)-5-(*p*-nitrophenyl)-3-trifluoromethylpyrazole (**9f**).

The compound had mp 188-190°, yield 76%; ^{1}H nmr ($CDCl_3$): δ 2.40 (s, 3H, CH_3), 6.77 (s, 1H, 4-H), 7.15 (d, 1H, 5'-H, *J* = 8.4 Hz), 7.47 (d, 1H, 4'-H, *J* = 8.4 Hz), 7.57 (s, 1H, 7'-H), 7.65 (d, 2H, 2", 6"-H, *J* = 8.7 Hz), 8.22 (d, 2H, 3", 5"-H, *J* = 8.7 Hz); ms: m/z 404 (M^+).

Anal. Calcd. for $C_{18}H_{11}F_3N_4O_2S$: C, 53.46; H, 2.72; N, 13.86. Found: C, 53.33; H, 2.56; N, 13.657.

1-(6'-Fluorobenzothiazol-2'-yl)-5-(*p*-chlorophenyl)-3-trifluoromethylpyrazole (**10c**).

The compound had mp 152°, yield 71%; ^{1}H nmr ($CDCl_3$): δ 6.75 (s, 1H, 4-H), 7.17-7.19 (m, 1H, 5'-H), 7.44-7.69 (m, 6H, 6-FBz'-H & *p*-ClPh"-H); ms: m/z 397 (M^+) and 399 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{17}H_8ClF_4N_3S$: C, 51.33; H, 2.01; N, 10.56. Found: C, 51.30; H, 1.86; N, 10.56.

1-(6'-Fluorobenzothiazol-2'-yl)-5-(*p*-bromophenyl)-3-trifluoromethylpyrazole (**10d**).

The compound had mp 150-52°, yield 73%; ^{1}H nmr ($CDCl_3$): δ 6.75 (s, 1H, 4-H), 7.16 (m, 1H, 5'-H), 7.41 (d, 2H, 2", 6"-H, *J* = 8.7 Hz), 7.52 (m, 1H, 7'-H), 7.61 (d, 2H, 3", 5"-H, *J* = 8.7 Hz), 7.72 (m, 1H, 4'-H); ms: m/z 441 (M^+) and 443 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{17}H_8BrF_3N_3S$: C, 46.26; H, 1.81; N, 9.52. Found: C, 45.84; H, 1.70; N, 9.54.

Synthesis of 1-(4'-Methylquinolin-2'-yl)-5-(*p*-chloro-phenyl)-3-trifluoromethyl pyrazole (**11c**), 1-(4'-Methylquinolin-2'-yl)-3-(*p*-chlorophenyl)-5-hydroxy-5-trifluoro-methyl-Δ^2-pyrazolines (**16c**) and 1-(4'-Methylquinolin-2'-yl)-3-(*p*-chlorophenyl)-5-trifluoromethyl pyrazoles (**21c**).

An ethanolic solution (20 ml) of 1-(*p*-chlorophenyl)-4,4,4-trifluorobutane-1, 3-dione **1c** (1.25 g, 5 mmoles) and 0.1ml conc. sulfuric acid was stirred for 15 minutes. An equimolar amount of 4-methylquinolin-2-ylhydrazine **6** (0.87 g, 5 mmoles) was subsequently added at 50° temperature in small lots with constant stirring. The reaction mixture was allowed to reflux for 14 hours. Reaction was monitored by tlc. The excess of solvent was evaporated and tlc and ^{1}H nmr of the crude reaction mixture showed the formation of three products **11c**, **16c**, **21c** in a ratio 54:38:8, respectively. These compounds were separated by column chromatographic technique. Column chromatographic separation using silica gel (100-200 mesh) and petroleum ether (60-80°) as eluent afforded **11c**, mp 134-135°, yield 44%; ^{1}H nmr ($CDCl_3$): δ 2.79 (s, 3H, CH_3), 6.80 (s, 1H, 4-H), 7.32-7.33 (m, 4H, *p*-ClPh"-H), 7.60-7.69 (m, 3H, Qu'-H), 7.76 (s, 1H, 3'-H), 8.02 (d, 1H, 8'-H, *J* = 8.7 Hz); ms: m/z 387 (M^+) and 389 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{20}H_{13}ClF_3N_3$: C, 61.93; H, 3.35; N, 10.83. Found: C, 61.77; H, 3.19; N, 10.66.

Further elution then afforded **21c**, mp 130°, yield 4% and other product (**16c**) was afforded by further elution of the column with petroleum ether: ethyl acetate (99:1), mp 180°, yield 26%. ^{1}H nmr data and elemental analysis of compounds **16c** and **21c** were given in experimental section.

Dehydration of 5-Hydroxy-5-trifluoromethyl-Δ^2-pyrazolines into 5-trifluoromethyl- pyrazoles.

Synthesis of 1-Phenyl-3-(*p*-nitrophenyl)-5-trifluoro-methyl-pyrazole (**17f**).

An ethanolic solution (20 ml) of 1-phenyl-3-(*p*-nitrophenyl)-5-hydroxy-5-trifluoromethyl-Δ^2-pyrazoline **12f** (0.4 g, 1.2 mmoles) and 0.1 ml conc. sulfuric acid was refluxed for 4 hours. The excess of solvent was evaporated and on cooling a solid appeared which was recrystallized from ethanol, mp 82 ºC, yield 87 %; ^{1}H NMR ($CDCl_3$): δ 7.21 (s, 1H, 4-H), 7.52-7.55 (m, 5H, Ph'-H), 8.03 (d, 2H, 2" & 6"-H, J = 9 Hz), 8.30 (d, 2H, 3" & 5"-H, J = 9 Hz); ms: m/z 333 (M^+).

Anal. Calcd. for $C_{16}H_{10}F_3N_3O_2$: C, 57.66; H, 3.00; N, 12.61. Found: C, 57.44; H, 2.91; N, 12.24.

Synthesis of 1-(*p*-Nitrophenyl)-3-aryl-5-trifluoromethyl-pyrazoles (**18a-18f**).

Compounds **18a-18f** were prepared by employing similar procedure when refluxed for 6 hours.

1-(*p*-Nitrophenyl)-3-phenyl-5-trifluoromethylpyrazole (**18a**).

The compound had mp 102°, yield 74%; ^{1}H nmr ($CDCl_3$): δ 7.20 (s, 1H, 4-H), 7.39-7.49 (m, 3H, 3", 4" & 5"-H), 7.79-7.88 (m, 4H, 2', 6', 2" & 6"-H), 8.39 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 333 (M^+).

Anal. Calcd. for $C_{16}H_{10}F_3N_3O_2$: C, 57.66; H, 3.02; N, 12.61. Found: C, 57.79; H, 3.13; N, 12.68.

1-(*p*-Nitrophenyl)-3-(*p*-fluorophenyl)-5-trifluoromethyl-pyrazole (**18b**).

The compound had mp 101°, yield 72%; ^{1}H nmr ($CDCl_3$): δ 7.15 (m, 3H, 4, 3", 5"-H), 7.79-7.86 (m, 4H, 2', 6', 2" & 6"-H), 8.39 (d, 2H, 3′& 5′-H, J = 9 Hz); ms: m/z 351 (M^+).

Anal. Calcd. for $C_{16}H_9F_4N_3O_2$: C, 54.70; H, 2.56; N, 11.96. Found: C, 54.573; H, 2.47; N, 11.87.

1-(*p*-Nitrophenyl)-3-(*p*-chlorophenyl)-5-trifluoromethyl-pyrazole (**18c**).

The compound had mp 121ºC, yield 76%; ^{1}H nmr ($CDCl_3$): δ 7.18 (s, 1H, 4-H), 7.43 (d, 2H, 3", 5"-H, J = 8.4 Hz), 7.78-7.81 (m, 4H, 2', 6', 2" & 6"-H), 8.40 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 385 (M^+) and 387 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{16}H_9ClF_3N_3O_2$: C, 52.25; H, 2.45; N, 11.43. Found: C, 51.99; H, 2.34; N, 11.40.

1-(*p*-Nitrophenyl)-3-(*p*-bromophenyl)-5-trifluoromethyl-pyrazole (**18d**).

The compound had mp 138°, yield 78%; ^{1}H nmr ($CDCl_3$): δ 7.18 (s, 1H, 4-H), 7.59 (d, 2H, 3", 5"-H, J = 8.4 Hz), 7.73 (d, 2H, 2" & 6"-H, J = 8.7 Hz), 7.79 (d, 2H, 2' & 6'-H, J = 9 Hz.), 8.39 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 411 (M^+) and 413 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{16}H_9BrF_3N_3O_2$: C, 46.71; H, 2.19; N, 10.22. Found: C, 46.56; H, 2.00; N, 10.20.

1-(*p*-Nitrophenyl)-3-(*p*-methoxyphenyl)-5-trifluoro-methyl-pyrazole (**18e**).

The compound had mp 106-07°, yield 70%; ^{1}H nmr ($CDCl_3$): δ 3.86 (s, 3H, OCH_3), 6.98 (d, 2H, 3",5"-H, J = 8.7 Hz), 7.13 (s, 1H, 4-H), 7.77-7.82 (m, 4H, 2', 6', 2" & 6"-H), 8.15 (d, 2H, 3' & 5'-H, J = 9 Hz); ms: m/z 363 (M^+).

Anal. Calcd. for $C_{17}H_{12}F_3N_3O_3$: C, 56.20; H, 3.31; N, 11.57. Found: C, 56.11; H, 3.00; N, 11.55.

1,3-Bis(*p*-nitrophenyl)-5-trifluoromethylpyrazole (**18f**).

The compound had mp 186°, yield 77%; ^{1}H nmr ($CDCl_3$): δ 7.31 (s, 1H, 4-H), 7.82 (d, 2H, 2', 6'-H, J = 9 Hz), 8.05 (d, 2H, 2" & 6"-H, J = 9.3 Hz), 8.33 (d, 2H, 3' & 5'-H, J = 9 Hz), 8.39 (d, 2H, 3" & 5"-H, J = 9.3Hz); ms: m/z 378 (M^+).

Anal. Calcd. for $C_{16}H_9F_3N_4O_4$: C, 50.79; H, 2.38; N, 15.38. Found: C, 52.54; H, 2.27; N, 15.08.

Synthesis of 1-(6'-Substitutedbenzothiazol-2'-yl)-3-aryl-5-trifluoromethylpyrazoles (**19c**, **19f**, **20c** and **20d**).

Compounds **19c**, **19f**, **20c** and **20d** were prepared employing similar reaction conditions when refluxed for 24 hours.

1-(6'-Methylbenzothiazol-2'-yl)-3-(*p*-chlorophenyl)-5-trifluoro-methylpyrazole (**19c**).

The compound had mp 172°, yield 75%; ^{1}H nmr ($CDCl_3$): δ 2.50 (s, 3H, CH_3), 7.18 (s, 1H, 4-H), 7.31 (d, 1H, 5'-H, J = 8.4 Hz), 7.44 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.64 (s, 1H, 7'-H), 7.81-7.86 (m, 3H, 4', 2", 6"-H); ms: m/z 393 (M^+) and 395 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{18}H_{11}ClF_3N_3S$: C, 54.90; H, 2.79; N, 10.67. Found: C, 54.77; H, 2.50; N, 10.37.

1-(6'-Methylbenzothiazol-2'-yl)-3-(*p*-nitrophenyl)-5-trifluoromethyl-pyrazole (**19f**).

The compound had mp 192°, yield 79%; ^{1}H nmr ($CDCl_3$): δ 2.45 (s, 3H, CH_3), 7.19 (s, 1H, 4-H), 7.26 (d, 1H, 5'-H, J = 8.4 Hz), 7.61 (s, 1H, 7'-H), 7.82 (d, 1H, 4'-H, J = 8.1 Hz), 8.27 (d, 2H, 3", 5"-H, J = 8.7 Hz), 8.01 (d, 2H, 2", 6"-H, J = 8.7 Hz), 8.27 (d, 2H, 3", 5"-H, J = 8.7 Hz); ms: m/z 404 (M^+).

Anal. Calcd. for $C_{18}H_{11}F_3N_4SO_2$: C, 53.46; H, 2.72; N, 13.86. Found: C, 53.27; H, 2.55; N, 13.68.

1-(6'-Fluorobenzothiazol-2'-yl)-3-(*p*-chlorophenyl)-5-trifluoro-methylpyrazole (**20c**).

The compound had mp 166-68°, yield 74%; ^{1}H nmr ($CDCl_3$): δ 7.18 (s, 1H, 4-H), 7.21-7.22 (m, 1H, 5′-H), 7.44 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.51 (m, 1H, 7'-H), 7.81 (d, 2H, 2", 6"-H, J = 8.7 Hz), 7.89-7.93 (m, 1H, 4'-H); ms: m/z 397 (M^+) and 399 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{17}H_8ClF_4N_3S$: C, 51.32; H, 2.01; N, 10.58. Found: C, 51.23; H, 1.94; N, 10.58.

1-(6'-Fluorobenzothiazol-2'-yl)-3-(*p*-bromophenyl)-5-trifluoro-methylpyrazole (**20d**).

The compound had mp 160°, yield 75%; ^{1}H nmr ($CDCl_3$): δ 7.21 (s, 1H, 4-H), 7.22-7.24 (m, 1H, 5'-H), 7.53-7.56 (m, 1H, 7'-H) 7.61 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.76 (d, 2H, 2", 6"-H, J = 8.7 Hz), 7.90-7.95 (m, 1H, 4'-H); ms: m/z 441 (M^+) and 441 (M^++2) in the ratio showing typical bromine isotope profile (1:1).

Anal. Calcd. for $C_{17}H_8BrF_4N_3S$: C, 46.26; H, 1.81; N, 9.52. Found: C, 45.77; H, 1.71; N, 9.42.

Synthesis of 1-(4'-Methylquinolin-2'-yl)-3-(*p*-chloro-phenyl)-5-trifluoromethyl pyrazole (**21c**).

An acetic acid solution (15 ml) of compound **16c** (0.41 g, 1.2 mmol) and 0.1ml conc. sulfuric acid was refluxed for 20 hours. The excess of solvent was evaporated and poured the reaction mixture in cold water. Solid so obtained was recrystallized from ethanol, mp 130ºC, yield 69%; ^{1}H nmr ($CDCl_3$): δ 2.81 (s, 3H, CH_3), 7.21 (s, 1H, 4-H), 7.45 (d, 2H, 3", 5"-H, J = 8.7 Hz), 7.58-7.64 (m, 1H, 6'-H), 7.74-7.79 (m, 1H, 7'-H), 7.99 (s, 1H, 3'-H), 8.03 (dd, 1H, 5'-H, J_o = 8.4 Hz, J_m = 0.9 Hz), 8.08 (dd, 1H, 8'-H, J_o = 8.4 Hz, J_m = 0.9 Hz); ms: m/z 387 (M^+) and 389 (M^++2) in the ratio showing typical chlorine isotope profile (3:1).

Anal. Calcd. for $C_{20}H_{13}ClF_3N_3$: C, 61.93; H, 3.35; N, 10.83. Found: C, 61.87; H, 3.29; N, 10.63.

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