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Synthesis of fluorinated pyrazolone compounds

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ABSTRACT

Various fluorine containing (4*Z*)-2-(4-fluorophenyl)-4-[(1-phenyl-1*H*-pyrazol-4-yl)methylidene]-5-(trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 3a-e, (4*E*)-2-(4-fluorophenyl)-4-[(4-oxo-3,4-dihydro-2*H*-chromen-3-yl)methylidene]-5-(trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 5a-e and (4*E*)-4-[(2-chloroquinolin-3-yl)methylidene]-2-(4-fluorophenyl)-5-(trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 7a-e have been synthesized. The compounds have been characterized by IR, ^{1}H, NMR, MS study and further confirmed by elemental analysis.

Keywords: Fluorinated compound, 4-formyl pyrazole, 4-oxo 3-formyl chromene, 3-formyl Quinoline, Pyrazolone, anti-inflammatory, ant diabetic.

INTRODUCTION

In recent years design of environmentally benign reactions is an important goal in organic synthesis. Day by day hazardous chemicals and by-products of various reactions increase the pollution in the environment.

Fluorinated organic compounds are associated with antimicrobial[1], antitumour[2], antibacterial[3], anti-lung cancer[4] and act as selective inhibitors of biosynthesis of aminergic neurotransmmitters[5].

Pyrazole as well as pyrazole containing compounds have been reported to show a broad spectrum of biological activities such as antimicrobial[6], antitumor[7], anti-HCV[8] and antiinflammatory[9] agents. Due to bioactivity associated with pyrazole and pyrazole containing compounds, researchers and chemist are very much interested in pyrazole chemistry[10, 11]. Pyrazolone are associated with broad spectrum of biological activities[12, 13]. Pyrazolone exhibit analgesic[14], antiinflammatoty[15] and anaesthetic activity[16] and act as potential antidiabetic agents in rats[17].

RESULTS AND DISCUSSION

In the present work various 3-substituted-1-phenyl-1*H*-pyrazole-4-carbaldehyde 1 are treated with 2-substituted 5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 in acetic acid to give (4)-2-(4-fluorophenyl)-4-{[1-aryl-3-aryl-1*H*-pyrazol-4-yl]methylidene}-5- (trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 3.

Equivalent mole of 4-oxo 3-formyl 4*H* chromene 4 and 2-substituted 5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 are refluxed in acetic acid to give (4*E*)-4-[(aryl)-4-oxo-4*H*-chromen-3-yl)methylidene]-2-(4-fluorophenyl)-5-(trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 5 Similarly 2-chloro 3-formyl quinoline 6 and 2-substituted 5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 are refluxed in acetic acid to give (4*E*)-4-[aryl-2-chloroquinolin-3-yl)methylidene]-2-(4-fluorophenyl)-5- (trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 7

EXPERIMENTAL

(4)-2-(4-fluorophenyl)-4-{[1-aryl-3-aryl-1*H*-pyrazol-4-yl]methylidene}-5- (trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 3

3- Chloro phenyl -1-Fluro phenyl-1*H*-pyrazole-4-carbaldehyde 1 (0.001 mole) and 2-(4-flurophenyl)-5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 (0.001 mole) was refluxed in 10 mL acetic acid in a 50 mL RBF for 30-45 min. Reaction was monitored by TLC. After the TLC indicated complete consumption of the starting material heating was stopped and the reaction mixture was cooled to 25-27^{0}C and quenched in water and solid obtained was separated by filtration and was washed thoroughly with water to obtain free flowing solid. The product obtained was again dissolved in acetic acid and quenched in water to obtain pure 3a. This typical experimental procedure was followed to prepare other analogs of this series. The compounds synthesized by above procedure are listed in Table I.

3d

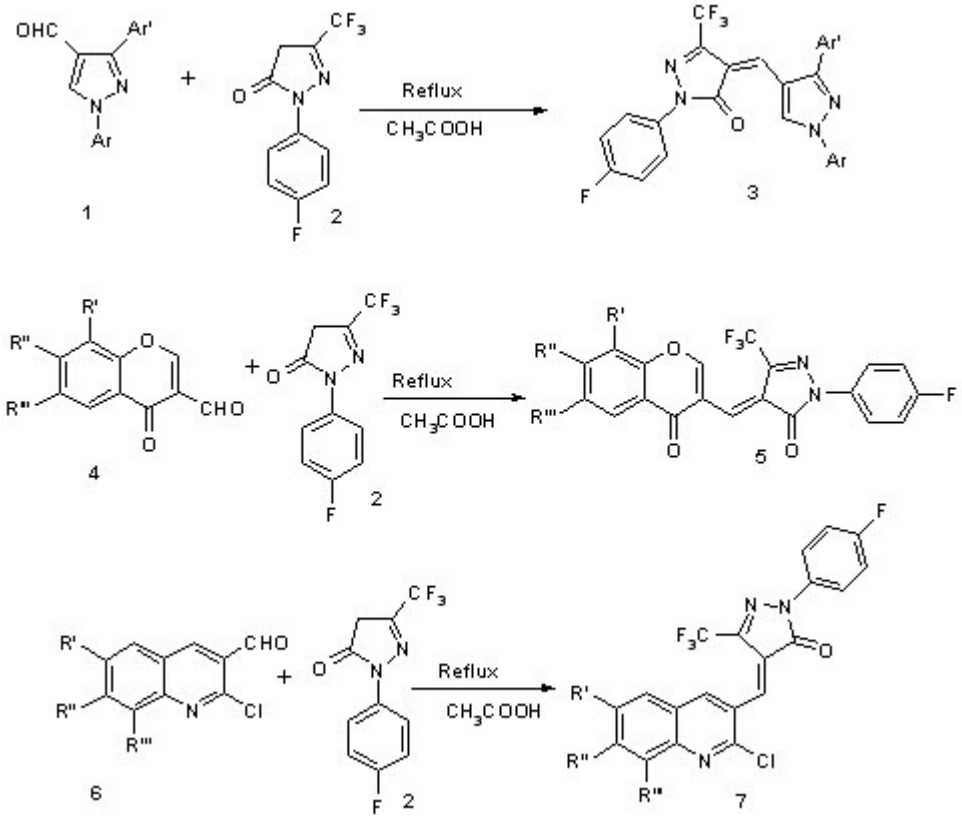
IR (KBr): 3140, 1690, 1596, cm^{-1}; ^{1}H NMR (DMSO-d$_6$): □ 7.39-8.0 (m, 14H aromatic and 1H olefinic proton) 10.23 (s, 1H); MS: *m/z* 477 (M+1)

3b

^{1}H NMR ($CDCl_3$): □ 7.13-7.91 (m, 13H aromatic and 1H olefinic proton) 10.26 (s, 1H); The structures were confirmed by IR, NMR and MS data All the structures were reconfirmed by elemental analysis

(4*E*)-4-[(aryl)-4-oxo-4*H*-chromen-3-yl)methylidene]-2-(4-fluorophenyl)-5-(trifluoromethyl)-2,4-dihydro-3*H*-pyrazol-3-one 5

4-oxo 3-formyl 4*H* chromene **4** (0.001 mole) and 2-(4-flurophenyl)-5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 (0.001 mole) are refluxed in acetic acid in 10 mL acetic acid in a 50 mL RBF for 25-50 min. Reaction was monitored by TLC. After the TLC indicated complete consumption of the starting material, heating was stopped and the reaction mixture was cooled to 25-27^{0}C and quenched in water to obtain a sticky solid from which the aqueous layer was decanted and then the sticky solid was washed thoroughly with water to obtain free flowing solid. The product obtained was again



Scheme 1:

dissolved in acetic acid and quenched in water to obtain pure 5a. This typical experimental procedure was followed to prepare other analogs of this series. The compounds synthesized by above procedure are listed in Table 2.

5d

^{1}H NMR ($CDCl_3$): δ 2.53 (s, 3H), 7.14-8.37 (m, 6H aromatic and 1H olefinic proton) 10.73 (s, 1H), **5a:** ^{1}H NMR ($CDCl_3$): δ 7.13-8.44 (m, 8H aromatic and 1H olefinic proton) 10.79 (s, 1H). All the structures were reconfirmed by elemental analysis

(4*E*)-4-[aryl-2-chloro quinolin-3-yl) methylidene]-2-(4-fluorophenyl)-5- (trifluoromethyl)-,4-dihydro-3*H*-pyrazol-3-one 7

2-chloro 3-formyl quinoline **6** (0.001 mole) and 2-(4-flurophenyl)-5-(trifluoromethyl)-2,4 dihydro 3*H* - pyrazol-3-one 2 (0.001 mole) are refluxed in acetic acid in 10 mL acetic acid in a 50 mL RBF for 25-350 min. Reaction was monitored by TLC. After the TLC indicated complete consumption of the starting material, heating was stopped and the reaction mixture was cooled to 25-27^{0}C and quenched in water to obtain a solid which was filtered and the upper residue was washed thoroughly with water to obtain free flowing solid. The product obtained was again dissolved in acetic acid and quenched in water to obtain pure 7a. This typical experimental procedure was followed to prepare other analogs of this series. The compounds synthesized by above procedure are listed in Table III.

Table 1: Characterization data of 3a-e

Compd. No.	Ar group	Ar'	M.P. (°C)	Time (min)	Yield (%)	elemental analysis found/calcd		
						C	H	N
3a	Fl phenyl	Cl phenyl	218	30	80	59.05 59.00	2.67 2.62	10.59 10.62
3b	phenyl	Cl phenyl	209	45	82	61.13 61.19	2.96 3.09	10.97 10.85
3c	phenyl	2,4-dichloro-5-fluro phenyl	237	40	81	55.44 55.49	2.33 2.38	9.95 9.94
3d	phenyl	phenyl	220	30	84	65.55 65.54	3.39 3.43	11.76 11.75
3e	phenyl	Me phenyl	214	35	82	66.12 66.16	3.70 3.73	11.42 11.45

Table 2: Characterization data of 5a-e

Compd. No.	R^I	R^{II}	R^{III} (^{0}C)	M.P. (min)	Time (%)	Yield	Elemental analysis found/ calcd		
							C	H	N
5a	H	H	H	223	25	85	59.71 59.73	2.51 2.54	6.96 7.00
5b	H	H	Me	244	30	86	60.58 60.54	2.91 2.93	6.73 6.69
5c	H	H	F	212	45	80	57.16 57.20	2.16 2.14	6.67 6.70
5d	H	Me	Cl	263	40	80	55.96 55.98	2.46 2.49	6.21 6.18
5e	Cl	H	Cl	257	50	77	50.98 60.00	1.71 1.73	5.95 5.91

Table 3: Characterization data of 7a-e

Compd. No.	R^{I}	R^{II}	R^{III}	M.P. (^{0}C)	Time (min)	Yield (%)	Elemental analysis found/ calcd		
							C	H	N
7a	H	H	H	278	25	80	57.23	2.40	10.01
							57.26	2.44	9.97
7b	H	Ome	H	214	30	68	56.08	2.69	9.34
							56.09	2.73	9.34
7c	H	H	Me	211	35	72	58.15	2.79	9.69
							58.14	2.81	9.67
7d	H	Me	H	227	35	77	58.15	2.79	9.69
							58.20	2.75	9.72
7e	Me	H	Me	208	30	75	58.15	2.79	9.69
							58.11	2.71	9.65

7b

IR (KBr): 3150, 1695, 1661, 1605, cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 3.81 (s, 1H), 7.40-8.27 (m, 8H aromatic and 1H olefinic proton), **7c:** IR (KBr): 2990, 1694, 1648, 1605, cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.35 (s, 1H), 7.28-8.27 (m, 8H aromatic and 1H olefinic proton). All the structures were reconfirmed by elemental analysis

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