Studies in fluorinated 1,3-diketones and related compounds. Part XVII. Synthesis and spectroscopic studies of some new 5-alkyl-3-fluoroaryl-1-pentafluoroaryl-pyrazoles and 2-amino-6-alkyl(perfluoroalkyl)-4-aryl pyrimidines*

Vineeta Sareen** and Sunita Jain
Department of Chemistry, University of Rajasthan, Jaipur-302004 (India)

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Abstract

Six new 3-(4′-fluorophenyl)-1,5-trisubstituted pyrazoles have been synthesized from the appropriate fluorinated 1,3-diketones and pentafluorophenylhydrazine in the presence of absolute ethanol and hydrochloric acid, viz., 1-pentafluorophenyl-3-(4′-fluorophenyl)-5-methylpyrazole, 1-pentafluorophenyl-3-(4′-fluorophenyl)-5-trifluoromethylpyrazole, 5-ethyl-1-pentafluorophenyl-3-(4′-fluorophenyl) pyrazole, 5-(pentafluoroethyl)-1-pentafluorophenyl-3-(4′-fluorophenyl) pyrazole, 1-pentafluorophenyl-3-(4′-fluorophenyl) 5-n-propylpyrazole and 5-(heptafluoropropyl)-1-pentafluorophenyl-3-(4′-fluorophenyl) pyrazole. In addition, six new 2-amino-4-(4′-fluorophenyl)-6-alkyl(perfluoroalkyl)-trisubstituted pyrimidines have been prepared from the same diketones and guanidine carbonate in the presence of hydrochloric acid using absolute ethanol as a solvent, viz., 2-amino-4(4′-fluorophenyl)-6-methylpyrimidine, 2-amino-4(4′-fluorophenyl)-6-trifluoromethylpyrimidine, 2-amino-6-ethyl-4-(4′-fluorophenyl)pyrimidine, 2-amino-6-pentafluoroethyl-4-(4′-fluorophenyl)pyrimidine, 2-amino-4-(4′-fluorophenyl)-6-n-propylpyrimidine and 2-amino-6-(heptafluoropropyl)-4-(4′-fluorophenyl)pyrimidine. All new fluorinated pyrazoles as well as pyrimidines have been characterized by elemental analyses as well as spectral studies.

Introduction

The use of 1,3-diketones and related compounds is well recognized. Pyrazole derivatives are well known for various biological activities, e.g. hypotensive [1], hypoglycemic [2], cytostatic [3] and psychotropic [4], and as coronary vasodilators [5].

In continuation of our comprehensive programme of developing new fluorinated 1,3-diketones and related compounds [6–10], we now report, via reactions with pentafluorophenylhydrazine, the synthesis and characterization of some new fluorinated pyrazoles. Using guanidine carbonate, pyrimidines can be prepared.

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**To whom all correspondence should be addressed.

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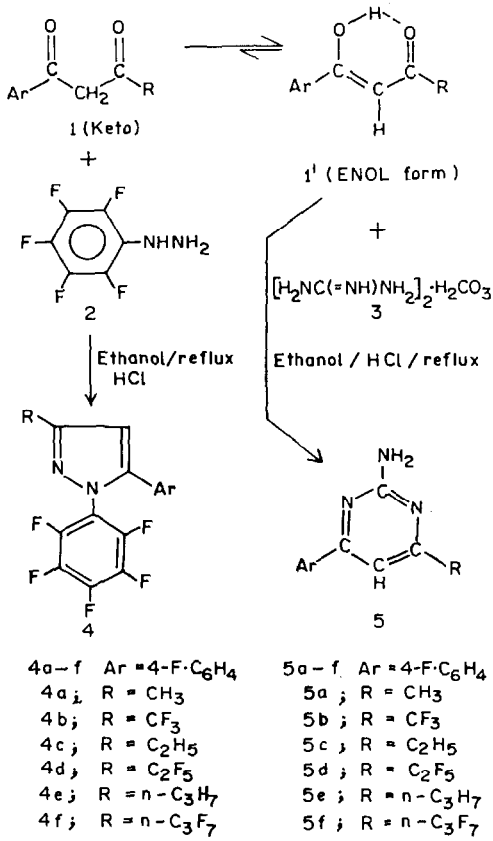

Results and discussion

The IR spectra of the substituted fluorinated pyrazoles **4** showed very strong absorption bands in the region 1180–1010 cm^{-1} due to $\rangle C-F$ stretching vibrations. Similar absorption bands were also observed in the fluorinated pyrimidines **5**. Stretching vibrations of the type $\rangle C-N$ were found in the region 1240–1220 cm^{-1} while $\rangle C=N$ stretching vibrations were observed in the region 1680–1470 cm^{-1}.

In the ^1H NMR spectra, the methine ($=\overset{|}{C}H$) resonance signal was observed for compounds **4** and **5** in the region δ 6.5–7.4 ppm, methyl ($-CH_3$) while methylene ($-CH_2$) signals were noticed in the region δ 1.0–1.5 ppm respectively. Ar–H protons were observed in the region δ 6.5–8.5 ppm. In addition to these, 6-alkyl(perfluoroalkyl)-2-amino-5-arylpyrimidines (**5**) showed amino, $-NH_2$, proton signals at δ 4.00 ppm as confirmed by deuterium-exchange studies.

The structures were further confirmed by mass spectral analysis, e.g. **4d** $[M]^{+\cdot}$ at *m/z* 446 and **5d** $[M]^{+\cdot}$ at *m/z* 307.

TABLE 1

Analytical and characteristic data of 5-alkyl-3-fluoroaryl-1-pentafluoroarylpyrazoles

Compound No.	Molecular formula	M.p. (°C)	Yields (%)	C (%)		H (%)		N (%)		F (%)	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
4a	$C_{16}H_8F_6N_2$	140	70	56.14	56.10	2.34	2.32	8.18	8.17	33.33	33.32
4b	$C_{16}H_5F_9N_2$	135	75	48.48	48.46	1.26	1.25	7.07	7.05	43.19	43.18
4c	$C_{17}H_{10}F_6N_2$	145	78	57.30	57.29	2.81	2.79	7.86	7.86	32.02	32.00
4d	$C_{17}H_5F_{11}N_2$	151	80	45.74	45.74	1.12	1.10	6.28	6.27	46.86	46.84
4e	$C_{18}H_{12}F_6N_2$	156	70	58.38	58.36	3.24	3.23	7.57	7.52	30.81	30.80
4f	$C_{18}H_5F_{13}N_2$	172	72	43.55	43.54	1.01	1.00	5.64	5.62	49.80	49.75

TABLE 2

Analytical and characteristic data of 2-amino-6-alkyl/perfluoroalkyl-4-arylpyrimidines

Compound No.	Molecular formula	M.p. (°C)	Yield (%)	C (%)		H (%)		N (%)		F (%)	
				Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
5a	$C_{11}H_{10}FN_3$	153	75	65.02	65.00	4.92	4.92	20.69	20.68	9.35	9.30
5b	$C_{11}H_7F_4N_3$	158	78	51.36	51.36	2.72	2.71	16.34	16.35	29.57	29.50
5c	$C_{12}H_{12}FN_3$	148	80	66.36	66.35	5.52	5.51	19.35	19.35	8.75	8.74
5d	$C_{12}H_7F_6N_3$	168	82	46.90	46.89	2.28	2.27	13.68	13.65	37.13	37.10
5e	$C_{13}H_{14}FN_3$	172	76	67.53	67.52	6.06	6.05	18.18	18.17	8.22	8.20
5f	$C_{13}H_7F_8N_3$	182	73	43.69	43.68	1.96	1.95	11.76	11.74	42.58	42.56

TABLE 3

Spectroscopic data for fluorinated pyrazoles and pyrimidines

Compound No.	IR (cm^{-1})			^1H NMR δ (ppm)			Mass spectrum $[M]^{+\cdot}$
	>C=N	>C–N	>C–F	R	=CH	Ar	
4a	1675	1240	1180	1.2 (s)	6.6 (s)	6.5–8.5 (m)	
4b	1600	1230	1170	–	6.8 (s)	6.5–8.5 (m)	
4c	1580	1235	1110	1.1 (t); 1.5 (q)	6.7 (s)	6.5–8.5 (m)	
4d	1545	1220	1010	–	6.82 (s)	6.5–8.5 (m)	446
4e	1490	1225	1160	1.0 (t); 1.2 (m); 1.5 (t)	6.9 (s)	6.5–8.5 (m)	
4f	1470	1228	1140	–	6.85 (s)	6.5–8.5 (m)	
5a	1600	1235	1175	1.3 (s)	7.3 (s)	6.5–8.5 (m)	
5b	1610	1220	1160	–	7.45 (s)	6.5–8.5 (m)	
5c	1590	1238	1130	1.0 (t); 1.4 (q)	7.2 (s)	6.5–8.5 (m)	
5d	1510	1230	1070	–	7.1 (s)	6.5–8.5 (m)	307
5e	1575	1240	1060	1.05 (t); 1.20 (m); 1.45 (m)	7.0 (s)	6.5–8.5 (m)	
5f	1560	1236	1010	–	7.25 (s)	6.5–8.5 (m)	

Experimental

IR spectra were recorded on a Perkin-Elmer 337 spectrometer using Nujol mulls while ^1H NMR spectra were measured by means of a Perkin-Elmer RB-12 spectrometer in $CDCl_3$ solution with TMS as the internal standard. The purity of all the compounds was checked by TLC on silica gel plates.

Synthesis of pentafluorophenylhydrazine

A mixture of hexafluorobenzene (0.11 mol, 20.0 g) and hydrazine hydrate (0.31 mol, 12.5 g) was refluxed in absolute ethanol for 12 h on a steam bath. Excess ethanol was then distilled off and the residue poured into water. The solid was filtered and recrystallized from petroleum ether, m.p. 77 °C (lit value [11], m.p. 78 °C), yield 11.6 g (58%).

Synthesis of fluorinated 1,3-diketones

These were prepared by Claisen condensation of the fluorinated acetophenones with the appropriate esters in the presence of sodamide [7].

Synthesis of 1,3,5-trisubstituted pyrazoles

These were prepared by refluxing a mixture of fluorinated 1,3-diketones for 10–14 h with pentafluorophenylhydrazine in absolute ethanol containing

a drop of hydrochloric acid. Excess ethanol was then distilled off and the residue poured into ice cold water. All these compounds were recrystallized from ethanol until they gave single spots on TLC analysis. All are recorded along with their analytical data in Table 1 and Table 3.

Synthesis of 2,4,6-trisubstituted pyrimidines

These were prepared by refluxing a mixture of fluorinated 1,3-diketones with guanidine carbonate for 10–14 h in absolute ethanol containing a few drops of hydrochloric acid. Excess ethanol was then distilled off and the residue poured into ice cold water. All these compounds were recrystallized from ethanol until they gave single spots on TLC analysis. All are recorded along with their analytical data in Table 2 and Table 3.

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