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SYNTHESIS OF FLUORO DERIVATIVES OF 2,4,6-TRIARYLPYRIDINES

R.S. TEWARI* and ANITA BAJPAI

Chemistry Department, H.B.Technological Institute, Kanpur 208002 (India)

SUMMARY

A variety of fluoro-substituted 2,4,6-triarylpyridines have been prepared via the reaction of 4-picolinium 4-chlorophenacyl methylide, with a series of fluorinated α,β-unsaturated ketones in the presence of ammonium acetate in acetic acid.

INTRODUCTION

The chemistry of cycloimmonium ylides has engaged the attention of chemists because of their importance as useful intermediates in the synthesis of novel heterocyclic compounds. In spite of the wide applicability of cycloimmonium ylides[1–4] in synthetic studies, no information is available concerning the syntheses of fluoro-substituted 2,4,6-triarylpyridines. In continuation of our previous researches [5–6] directed towards studies on pyridinium ylides, we report herein the synthesis of some new fluoro-substituted 2,4,6-triarylpyridines by the cyclization reaction of 4-picolinium-4-chloro-phenacyl methylide with fluorine containing α,β-unsaturated ketones.

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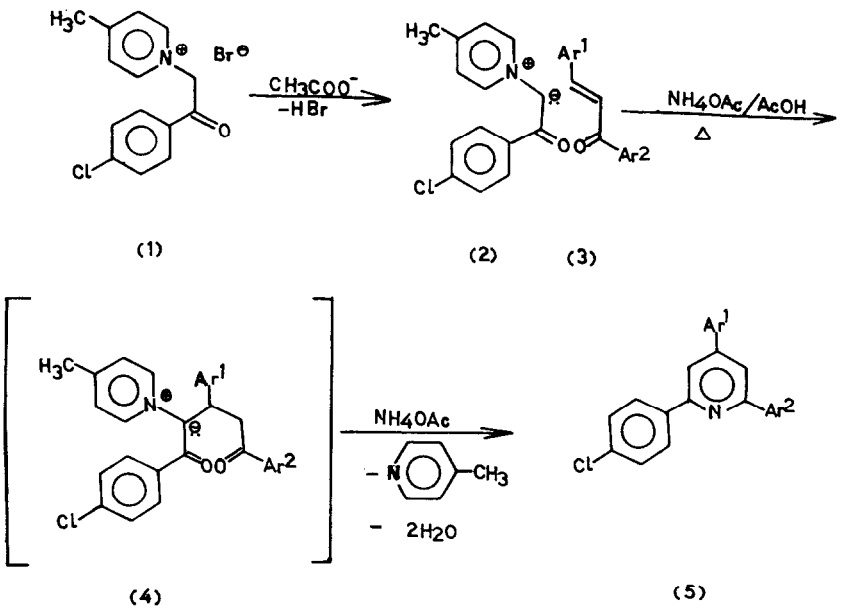
RESULTS AND DISCUSSION

Our syntheses of fluorinated 2,4,6-triarylpyridines (5) consists of the reaction of 4-picolinium-4-chloro-phenacyl methylide (2) with an equimolar amount of a chalcone (3) in the presence of ammonium acetate in glacial acetic acid at reflux temperature. The reaction presumably proceeds via the intermediacy of a 1,5-diketone (4) [7,8], which undergoes cyclo-condensation with ammonium acetate to give (5) (Scheme 1). However it was interesting to note that the fluorinated 2,4,6-triarylpyridines are obtained in better yields when the reaction is allowed with pyridinium salts rather than using corresponding ylides.

The nature of the solvent used has a pronounced influence on the reaction rate. In dimethyl formamide and chloroform, the reaction proceeds much slower than in acetic acid, and in dimethyl sulfoxide no reaction is observed.



Scheme 1

TABLE 1. Melting points and analytical data of fluorinated 2,4,6-triarylpyridines

Comp No.	Ar[1]	Ar[2]	Yield (%)	M.P. (°C)	Recrystallising solvent	Molecular Formula	Elemental Analysis % Calcd.(Found) C	H	N
5a	4-F.C_6H_4	2-naphthyl	75	190-194	Py/MeOH	$C_{27}H_{17}NFCl$	79.12 (79.15)	4.15 (4.16)	3.42 (3.40)
5b	4-F.C_6H_4	4-Br.C_6H_4	78	210-212	Py	$C_{23}H_{14}NFClBr$	65.00 (65.03	3.29 (3.30)	3.29 (3.28)
5c	4-F.C_6H_4	4-Cl.C_6H_4	80	218-220	Py	$C_{23}H_{14}FCl_2N$	70.05 (70.08)	3.55 (3.52)	3.55 (3.58)
5d	3,4$(OCH_3)_2C_6H_4$	4-F.C_6H_4	60	114-116	Py/MeOH/H_2O	$C_{25}H_{19}ClFO_2N$	71.51 (71.54)	4.52 (4.51)	3.34 (3.32)
5e	4-OCH_3.C_6H_4	4-F.C_6H_4	62	138-140	Py/MeOH	$C_{24}H_{17}ONFCl$	73.94 (73.91)	4.36 (4.37)	3.59 (3.61)
5f	4-F.C_6H_4	C_6H_5	70	215-218	Py/MeOH	$C_{23}H_{15}NFCl$	76.77 (76.78)	4.17 (4.15)	3.89 (3.87)
5g	4-NO_2.C_6H_4	4-F.C_6H_4	50	185-188	Py/MeOH/H_2O	$C_{23}H_{14}ClFN_2O_2$	68.23 (68.21)	3.46 (3.47)	6.92 (6.94)
5h	4-Cl.C_6H_4	4-F.C_6H_4	52	185-188	Py	$C_{23}H_{14}Cl_2FN$	70.05 (70.08)	3.55 (3.57)	3.55 (3.52)
5i	4-F.C_6H_4	4-F.C_6H_4	65	188-192	Py/MeOH	$C_{23}H_{14}NF_2Cl$	73.11 (73.10)	3.71 (3.73)	3.71 (3.70)
5j	4-$N(CH_3)_2C_6H_4$	4-F.C_6H_4	40	160-162	Py/H_2O	$C_{25}H_{20}N_2ClF$	74.53 (74.55)	4.97 (4.95)	6.96 (6.98)
5k	3-NO_2.C_6H_4	4-F.C_6H_4	45	205-208	Py/MeOH	$C_{23}H_{14}ClFN_2O_2$	68.23 (68.25)	3.46 (3.42)	6.92 (6.97)
5l	4-F.C_6H_4	4-CH_3.C_6H_4	65	196-198	Py	$C_{24}H_{17}NFCl$	77.21 (77.23)	4.55 (4.56)	3.75 (3.76)
5m	4-F.C_6H_4	4-OCH_3.C_6H_4	70	169-171	$CHCl_3$/MeOH	$C_{24}H_{17}NOClF$	73.94 (73.91)	4.36 (4.38)	3.59 (3.56)

TABLE 2. NMR and IR Data for fluorinated 2,4,6-triarylpyridines

Comp. No.	^{1}H-NMR Data Solution in ($CDCl_3$) Chemical shifts (δppm)	No. of protons	Assignment	IR Data (KBr) cm^{-1} C-H stretching vibrations	C=C Vibrations	C=N Vibration
5a	7.00-8.69	17 H	Aromatic	-	-	-
5b	7.00-8.31	14 H	Aromatic	-	-	-
5c	-	-	-	3008	1600	1540
						1500
5d	3.83 S, 3.90 S	3 H, 3H	Methoxy, Methoxy	3040	1590	1535
	6.83 - 8.52	13 H	Aromatic			1500
5e	3.82 S	3 H	Methoxy	3060	1590	1540
	6.86 - 8.42	14 H	Aromatic			1500
5f	6.85 - 8.40	15 H	Aromatic	3040	1600	1540
						1510
5g	-	-	-	3006	1600	1550
						1510
5h	-	-	-	3010	1605	1540
						1510
5i	6.89 - 8.45	14 H	Aromatic	-	-	-
5j	3.00 S	6 H	Dimethyl	3040	1600	1520
	6.50 - 8.35	14 H	Aromatic			1510
5k	-	-	-	3006	1600	1550
						1510
5l	2.43 S	3 H	Methyl	-	-	-
	7.00 - 8.40	14 H	Aromatic			
5m	3.90 S	3 H	Methoxy	-	-	-
	6.85 - 8.65	14 H	Aromatic			

The structures of the products (5) were established by microanalysis, physical and spectral data (Table 1 and 2). An alternative structure with Ar^1 and Ar^2 interchanged can be excluded because only the β-CH group of compounds (3) will react with the negative site of the ylide (2).

EXPERIMENTAL

Melting points were determined on a Gallenkamp apparatus and are uncorrected. The IR spectra (in potassium bromide) were recorded on a Perkin-Elmer Grating infracord spectrophotometer Model-577. The nuclear magnetic resonance spectra ($CDCl_3$) were run using Varian A-60 and A-90 spectrometers using tetramethylsilane as an internal standard and chemical shifts are expressed in δ ppm values. Analytical samples were purified by column chromatography over silica gel and purity was checked by thin layer chromatography.

4-Chlorophenacyl bromide with 4-picoline at reflux temperature afforded N-4-chlorophenacyl-4-picolinium bromide (mp 239-241°C), which on subsequent treatment with aq.potassium carbonate gave 4-picolinium 4-chlorophenacyl methylide in 90% yield (mp 86-89°C decomp.).

p-Fluoro-substituted α,β-unsaturated ketones were prepared by the reaction of appropriate aromatic aldehydes with methyl aryl ketones in ethanol at ice temperature.

Preparation of fluorinated 2,4,6-triarylpyridines (5)

To a stirred solution of 6 mmol of a 4-picolinium salt in 20 ml of glacial acetic acid containing ammonium acetate (6.0 gm) was added gradually a solution of a fluoro-substituted α,β-unsaturated ketone (6 mmol, 3a-m) in 20 ml of glacial acetic acid under nitrogen. The whole mass was then heated at 120°C under reflux conditions for 6-8 hours. The mixture was left overnight at room temperature and ice cold water (20 ml) was added to precipitate a solid which was separated, washed with methanol, dried and crystallized from appropriate solvent to give a fluorinated triaryl pyridine (5a-m) in 48-80% yield (Table 1).

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