Synthesis of Some New Asymmetrical and Symmetrical 2,4,6-Triarylpyridines Using (2-Thiophenoylmethylene)pyridinium Ylide

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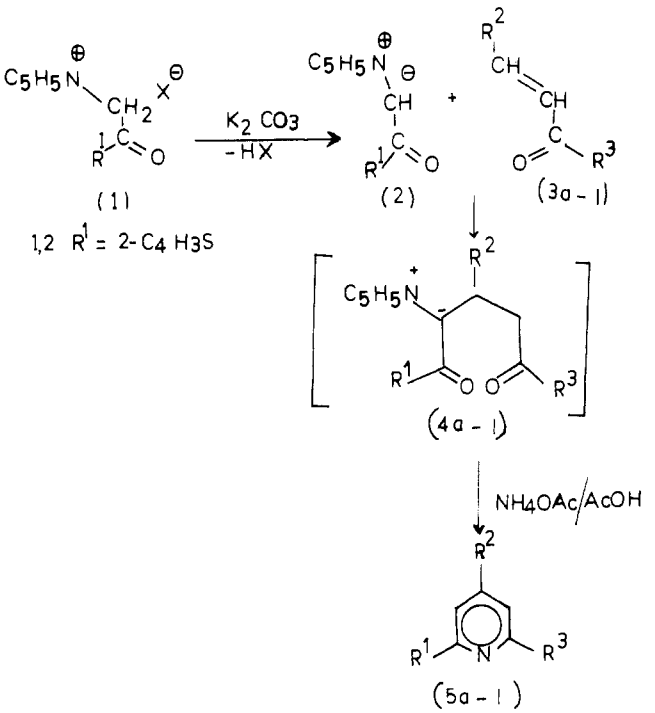
A series of some new 2-thienyl-4,6-di(substituted phenyl)pyridines and 2,6-dithienyl-4-(substituted phenyl)pyridines have been synthesized by the interaction of (2-thiophenoylmethylene)pyridinium ylide with substituted benzylideneacetophenones and substituted benzylidene-2-acetothiophenes, respectively, using ammonium acetate in acetic acid as a cyclization agent. The structures of these pyridines were supported by IR and NMR spectral data.

The earlier methods (*1–4*) for the synthesis of 2,4,6-triarylpyridines were not versatile because of harsh reaction conditions and poor yields of products. Moreover, these could only be used for the synthesis of symmetrical pyridines having identical substitutents at the 2- and 6-positions. However, the synthesis of symmetrical and asymmetrical pyridines having identical substituents at the 2- and 6-positions involving mild reaction conditions and good yields of products could also be applied. Prompted by Krohnke's work and following our earlier researches (*5–10*) on the synthetic and mechanistic aspects of ylides of group-5 elements, we have extended the method for synthesis of symmetrical and asymmetrical 2,4,6-triarylpyridines having thiophene rings at the 2- and 6-positions and a substituted phenyl ring at the 4-position by reacting (2-thiophenoylmethylene)pyridinium ylide with substituted α,β-unsaturated ketones. Such pyridines are expected to possess biological activity.

The (2-thiophenoylmethyl)pyridinium bromide (**1**) on treatment with potassium carbonate in aqueous solution gave (2-thiophenoylmethylene)pyridinium ylide (**2**). The ylide (**2**) reacted with various α,β-unsaturated ketones (**3a–l**) in glacial acetic acid and ammonium acetate under reflux to give 2,4,6-triarylpyridines (**5a–l**) in 50–90% yields. The reaction seems to proceed via the intermediacy of (1,5-dioxo-2-pentyl)pyridinium derivatives (**4a–l**), formed by the nucleophilic attack of **2** on the β-carbon of compounds **3a–l**, ylides which then undergo azo cyclization in the presence of ammonium acetate in acetic acid to give the desired pyridines (**5a–l**) (Scheme I).

All the compounds (**5a–l**) synthesized in the present study were new and gave satisfactory elemental analysis. The structures of the pyridines (**5a–l**) were evidenced by their spectral data. The IR spectra (KBr) of **5a–l** showed characteristic absorption bands in the region 3000–3040 cm^{-1}, which was assigned to the C–H stretching mode of the pyridine ring. The two bands at 1600 cm^{-1} appeared to be a general characteristic of substitutions in the pyridine nucleus. The NMR ($CDCl_3$) spectra of **5a–l** in general exhibited two pyridyl protons in the range δ 6.60–7.30 and aromatic protons at δ 6.78–8.31.

Scheme I



Experimental Section

Melting points were determined on a Gallenkamp apparatus and were uncorrected. IR spectra (KBr) were recorded on a Perkin-Elmer infracord spectrophotometer. NMR ($CDCl_3$) were run by using a Varian A-60 spectrophotometer using Me_4Si as an internal standard. The purity of **5a–l** was checked by TLC.

Pyridinium salt **1** was prepared by the reaction of bromomethyl 2-thienyl ketone with pyridine or by heating 2-acetothiophene with iodine and pyridine using the procedure of King (*11*) and Krohnke (*12*, *13*). The ylide (**2**) was generated by treating a cold aqueous solution of salt (**1**) with aqueous potassium carbonate or treating pyridinium salt (**1**) with sodium hydride in DMF. All the reactions were carried out by using freshly prepared pyridinium ylide (**2**).

Preparation of 2,4,6-Trisubstituted Pyridines (5a–l). General Procedure. A mixture of ylide (**2**, 3 mmol), ammonium acetate (3 g), and glacial acetic acid (50 mL) was stirred at 80 °C. The α,β-unsaturated ketone (**3a–l**, 3 mmol) in glacial acetic acid (25 mL) was added dropwise over 1 h, the temperature was raised to 120 °C, and heating was continued for an additional 6–8 h. The reaction mixture was left overnight at room temperature and ice cold water (50 mL) was added. The re-

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Table I. Physical and Spectral Data of 5a-l[a]

compd	R^2	yield, %	mp, °C	recryst solvent	IR (KBr), cm^{-1} ν_{Ar-H}	$\nu_{C=C}$	$\nu_{C=N}$	$\nu_{C=S}$	ϕ_{C-H}	NMR data ($CDCl_3$), δ
				R^1 = 2-C_4H_3S; R^3 = C_6H_5						
5a	4-$CH_3OC_6H_4$	65	93-95	$CHCl_3$/*n*-hexane	3040	1595	1510	1175	990	3.78 (s, 3 H, OCH_3),
b	4-ClC_6H_4	55	111-12	$CHCl_3$/*n*-hexane	3060	1600	1540	1050	1000	6.78-7.98 (m,
c	3-$NO_2C_6H_4$	60	160-62	C_5H_5N/MeOH	3040	1592	1510	1080	1010	14 H, ArH)
d	3,4-$Cl_2C_6H_3$	65	104-06	$CHCl_3$/*n*-hexane	3060	1595	1515	1178	995	
e	4-FC_6H_4	50	125-27	C_5H_5N/MeOH	3045	1590	1500	1165	1020	
				R^1 = 2-C_4H_3S; R^3 = 4-ClC_6H_4						
f	4-$NO_2C_6H_4$	50	176-78	$CHCl_3$/*n*-hexane	3070	1600	1495	1100	1000	
g	4-FC_6H_4	65	153-55	$CHCl_3$/*n*-hexane	3060	1610	1510	1160	995	7.51-8.31 (m, 13
h	C_6H_5	55	110-12	C_5H_5N/MeOH	3065	1600	1540	1090	1010	H, ArH)
i	3 $NO_2C_6H_4$	70	217-19	C_5H_5N/MeOH	3040	1590	1540	1090	995	
				R^1 = R^3 = 2-C_4H_3S						
j	3-$CH_3OC_6H_4$	60	90-92	C_5H_5N/MeOH	3060	1600	1550	1170	990	3.75 (s, 3 H, OCH_3),
k	3-ClC_6H_4	70	138-40	$CHCl_3$/*n*-hexane	3080	1598	1535	1090	970	6.84-7.82 (m,
l	3-$NO_2C_6H_4$	60	123-25	$CHCl_3$/*n*-hexane	3070	1620	1500	1020	980	12 H, ArH)

[a] All the compounds gave satisfactory elemental analysis for C, H, N. ν = stretching vibrations. ϕ = bending vibrations (out-of-plane vibrations). s = singlet; m = multiplet.

sulting solid mass was filtered, washed twice with water and methanol, dried, and then crystallized from appropriate solvents shown in Table I to give the desired pyridines (**5a–l**).

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Registry No. **5a**, 85957-59-1; **5b**, 82613-22-7; **5c**, 82613-23-8; **5d**, 82613-25-0; **5e**, 85957-60-4; **5f**, 85957-61-5; **5g**, 85957-62-6; **5h**, 73910-99-3; **5i**, 85957-63-7; **5j**, 85957-64-8; **5k**, 85957-65-9; **5l**, 74441-39-7.

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Synthesis of New 2-Pyridylhydrazones and 2-Quinolylhydrazones Containing 2-Thiophene or 2-Furan Groups

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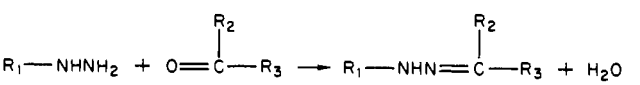
The synthesis of 18 new 2-pyridylhydrazone and 2-quinolylhydrazone compounds containing either 2-thiophene or 2-furan functionalities is described.

Continued interest still exists in the study of a variety of different hydrazones, particularly 2-pyridiyl- and 2-quinolylhydrazones, in addition to many other derivatives, for possible use as complexation reagents for transition metals (*1–7*). Because of this interest, 18 new 2-pyridylhydrazones and 2-quinolylhydrazones containing either various 2-thiophene or 2-furan moieties have been synthesized. The method used to prepare these new hydrazones was the standard procedure where equimolar quantities of the appropriate hydrazine and aldehyde or ketone were refluxed in ethanol, the solid hydrazone formed precipitating out of solution, filtered, and recrystallized from the appropriate solvent.



R_1 = 2-pyridyl or 2-quinolyl
R_2 = H or CH_3
R_3 = 2-thiophene or 2-furan functionality

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