

Table I. Urea Reaction Products of RNCO and 2-Amino-2-methyl-1,3-propanediol

R	reaction solvent	% yield	mp, °C	proton chemical shift data (δ) ^a		
				RNHC=O	O=CNH $\leftarrow$	CH ₃ C(CH ₂ OH)
n-dodecyl	2-PrOH(aq)	86	63	6.20 t	5.65 s	5.10 t
n-octadecyl	CHCl ₃	81	85	6.18 t	5.65 s	5.13 t
cyclohexyl	2-PrOH(aq)	63	155	6.10-6.20 d	5.65 s	5.13 t
phenyl	CHCl ₃	63	133-135	8.70 s	6.00 s	4.90 t
naphthyl	CHCl ₃	95	176	8.75 s	6.55 s	4.93 t

^a Key: s = singlet; d = doublet; t = triplet.

Chloroform as Solvent. A 13-g sample (0.12 mol) of 2-amino-2-methyl-1,3-propanediol was slurried into 100 mL of chloroform and heated to gentle reflux. Isocyanate (0.10 mol) was added dropwise and then finished as above.

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Studies on Cycloimmonium Ylides: Synthesis of Some New 2,4,6-Trisubstituted Pyridines. 2

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A wide range of 2,6-di(2-thienyl)-4-arylpyridines, 2-(4-biphenyl)-4-aryl-6-(2-thienyl)pyridines, and 2-(4-biphenyl)-4-aryl-6-(2-naphthyl)pyridines have been synthesized by the interaction of 1-(2-thiophenylmethyl)pyridinium iodide, 1-(4-phenylphenacyl)pyridinium bromide, and 1-(2-naphthylmethyl)pyridinium bromide with a variety of α,β -unsaturated ketones. Ammonium acetate in glacial acetic acid was used as cyclization agent. The structures of the resulting products were confirmed by IR and NMR spectral analyses.

Introduction

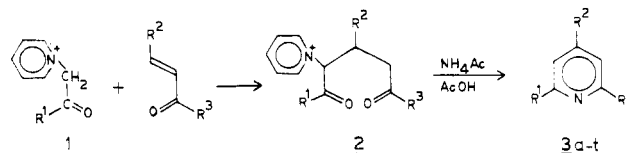
Continuing our previous studies on the reactivity of cycloimmonium ylides,¹ we wish to report herein the reactivity of (2-thiophenylmethylene)pyridinium ylide, (4-phenylphenacyl)pyridinium ylide, and (2-naphthylmethylene)pyridinium ylide with a variety of α,β -unsaturated ketones, leading to the formation of some new substituted 2,4,6-triarylpyridines.

Results and Discussion

(2-Thiophenylmethyl)pyridinium iodide (**1a**) was prepared by the Ortoleva-King reaction² which involved the reaction of pyridine with 2-acetylthiophene and iodine at reflux. Treatment of the salt (**1a**) with α,β -unsaturated ketones, i.e., substituted benzylidene-2-acetothiophene, in the presence of ammonium acetate and glacial acetic acid at reflux temperature afforded 2,6-di(2-thienyl)-4-(substituted phenyl)pyridine (**3a-f**). However,

the salt **1a** when treated with substituted benzylidene-4-acetobiphenyl under similar reaction conditions gave 2-(4-biphenyl)-4-(substituted phenyl)-6-(2-thienyl)pyridines (**3g-j**) (Scheme I).

Scheme I



The reaction of (2-naphthylmethyl)pyridinium bromide (**1b**), prepared by the quaternization of pyridine with ω -bromo-2-acetonaphthone with substituted benzylidene-4-acetobiphenyl in the presence of ammonium acetate and glacial acetic acid gave 2-(4-biphenyl)-4-(substituted phenyl)-6-(2-naphthyl)pyridines (**3k-t**) (Scheme I).

The synthesis of pyridines **3k-t** has also been achieved by an alternative route which involved the reaction of (4-phenylphenacyl)pyridinium bromide **1c** with substituted benzylidene-2-acetonaphthone. Ammonium acetate in glacial acetic acid was used for bringing about aza ring closure of the intermediate (**2**), formed by the nucleophilic attack of the ylide carbanion on the β -carbon atom of α,β -unsaturated ketones.

Various 2,4,6-trisubstituted pyridines synthesized above are listed in Table I. All the pyridines **3a-t** gave satisfactory elemental analyses. The spectral data for the resulting pyridines were also consistent with the proposed structures. The IR^{3,4} spectra showed a characteristic absorption band in the region 3090-3000 cm^{-1} which may be assigned to the C-H stretching mode of the pyridine ring. Two bands in the region 1600 cm^{-1}

Table I. Physical Properties of 2,4,6-Triphenylpyridines (3a-t)

compd	R ¹	R ²	R ³	% yield	mp, °C	recryst solvent
3a	2-C ₄ H ₉ S	C ₆ H ₅	2-C ₄ H ₉ S	50	118-120	C ₅ H ₅ N-MeOH
3b		4-ClC ₆ H ₄		50	146-148	CHCl ₃ -MeOH
3c		3-NO ₂ C ₆ H ₄		40	158-161	C ₅ H ₅ N-MeOH
3d		4-CH ₃ C ₆ H ₄		45	114-115	
3e		3,4-O ₂ CH ₂ C ₆ H ₃		60	100-102	
3f		2-C ₄ H ₉ O		35	315	
3g		C ₆ H ₅	4-C ₆ H ₅ C ₆ H ₄	30	315-316	
3h		4-ClC ₆ H ₄		51	140-142	CHCl ₃ -MeOH
3i		3-CH ₃ C ₆ H ₄		50	208-209	
3j		4-CH ₃ C ₆ H ₄		53	160-162	
3k	2-C ₁₀ H ₇	2-OCH ₃ C ₆ H ₄		48	130-132	
3l		3-OCH ₃ C ₆ H ₄		53	165-166	
3m		4-OCH ₃ C ₆ H ₄		55	132-134	C ₅ H ₅ N-MeOH
3n		3,4-(OCH ₃) ₂		30	165-167	
3o		6-Br-C ₆ H ₂				
3p		2-ClC ₆ H ₄		46	186	CHCl ₃ -MeOH
3q		3-ClC ₆ H ₄		50	176-178	
3r		3,4-O ₂ CH ₂ C ₆ H ₃		65	178	C ₅ H ₅ N-MeOH
3s		4-NO ₂ C ₆ H ₄		70	208-210	CHCl ₃ -MeOH
3t		4-N(CH ₃) ₂ C ₆ H ₄		48	209-211	
		2-C ₄ H ₉ O		50	150-152	

Table II. Spectral Data of 2,4,6-Trisubstituted Pyridines (3a-t)

compd	¹ H NMR data ^a (CDCl ₃) δ	IR data (KBr), cm ⁻¹			
		Ar-H	C=C	C=N	PyH ^b
3a	7.10 (s, 2 H, pyridyl); 7.36-8.13 (m, 11 H, ArH)	3050	1585	1535	995
3b	7.05 (s, 2 H, pyridyl); 7.20-8.18 (m, 10 H, ArH)	3050	1600	1570	1010
3c	7.02 (s, 2 H, pyridyl); 7.15-8.15 (m, 10 H, ArH)	3090	1605	1530	1005
3d	2.38 (s, 3 H, -CH ₃); 7.00-7.75 (m, 12 H, ArH)	3070	1600	1545	1010
3e	6.08 (s, 2 H, -O ₂ CH ₂); 6.95-7.81 (m, 11 H, ArH)	3040	1595	1500	1030
3f	6.90 (s, 2 H, pyridyl); 7.12-8.25 (m, 9 H, ArH)	3060	1635	1510	1055
3g	7.30 (s, 2 H, pyridyl); 7.53-8.33 (m, 17 H, ArH)	3050	1620	1520	1045
3h	7.16 (s, 2 H, pyridyl); 7.50-8.48 (m, 16 H, ArH)	3000	1595	1530	1010
3i	2.35 (s, 3 H, CH ₃); 7.23-8.26 (m, 18 H, ArH)	3000	1610	1530	1020
3j	2.40 (s, 3 H, -CH ₃); 7.08-8.36 (m, 18 H, ArH)	3000	1595	1530	1010
3k	3.81 (s, 3 H, -OCH ₃); 6.82-8.50 (m, 22 H, ArH)	3000	1595	1540	950
3l	3.85 (s, 3 H, -OCH ₃); 6.98-8.81 (m, 22 H, ArH)	3050	1590	1535	960
3m	3.88 (s, 3 H, -OCH ₃); 7.05-8.80 (m, 22 H, ArH)	3000	1590	1505	1020
3n	3.84 (d, 6 H, (OCH ₃) ₂); 6.92-8.64 (m, 20 H, ArH)	3000	1600	1560	1010
3o	7.03 (s, 2 H, pyridyl); 7.26-8.33 (m, 20 H, ArH)	3000	1595	1480	985
3p	7.18 (s, 2 H, pyridyl); 7.20-8.63 (m, 20 H, ArH)	3050	1615	1495	1020
3q	5.95 (s, 2 H, O ₂ CH ₂); 6.80-8.60 (m, 21 H, ArH)	3000	1550	1480	1030
3r	7.13 (s, 2 H, pyridyl); 7.25-8.40 (m, 20 H, ArH)	3050	1595	1515	1010
3s	3.02 (s, 6 H, N(CH ₃) ₂); 6.75-8.86 (m, 22 H, ArH)	3000	1590	1510	970
3t	7.08 (s, 2 H, pyridyl); 6.75-8.23 (m, 19 H, ArH)	3000	1600	1495	1018

^a Key: s = singlet; m = multiplet. ^b Out of plane deformations of the hydrogen atom of the pyridine ring.

and near 1500 cm⁻¹ have been assigned to the interaction between C=C and C=N vibrations of the pyridine ring. The former band, appearing as a double adsorption maxima near 1600 cm⁻¹, seems to be the general characteristic of trisubstitution at the pyridine nucleus. The NMR spectra in general exhibited aromatic protons in the range δ 6.95-8.81 (Table II).

Experimental Procedure

Melting points were determined on a Gallenkamp apparatus and are uncorrected. A Perkin-Elmer infracord spectrometer was used to record the IR spectra in KBr. The NMR spectra (CDCl₃) were run on a Varian A-60 spectrometer using tetramethylsilane as an internal standard. Purity of the products was checked by thin-layer chromatography. All the reactions were carried out under an atmosphere of nitrogen.

(2-Thiophenylmethyl)pyridinium iodide (1a) was prepared by the Ortoleva-King reaction.⁵ (2-Naphthylmethyl)pyridinium bromide (1b)⁶ and (4-phenylphenacyl)pyridinium bromide (1c) were prepared by the quaternization of ω-bromo-2-acetonaphthone⁷ and 4-phenylphenacyl bromide,⁸ respectively. Various α,β-unsaturated ketones were prepared by the interaction of 2-acetothiophene, 2-acetonaphthone, and 4-aceto-

biphenyl with the suitably substituted benzaldehydes.⁹

Preparation of 2,6-Di-(2-thienyl)-4-arylpyridines (3a-f).

An equimolar amount of (2-thiophenylmethyl)pyridinium iodide (1a) (3 mmol) and arylidene-2-acetothiophene (3 mmol) was heated under reflux for 4-8 h in the presence of ammonium acetate (3.0 g) and glacial acetic acid (6.0 mL). After the reaction mixture was maintained at room temperature overnight, ice cold water (20.0 mL) was added to it. The precipitated solid thus obtained was filtered, washed with methanol, dried, and recrystallized from appropriate solvent to afford 2,6-di-(2-thienyl)-4-arylpyridines (3a-f) in quantitative yields (Table I).

Preparation of 2-(4-Biphenyl)-4-aryl-6-(2-thienyl)pyridines (3g-j). A mixture of (4-phenylphenacyl)pyridinium bromide (1c) (3 mmol) and arylidene-2-acetothiophene in glacial acetic acid (10.0 mL) and ammonium acetate (3.0 g) was heated under reflux for 6 h in an atmosphere of nitrogen. The reaction mixture, after being allowed to stand overnight at room temperature, was poured into ice cold water (25.0 mL). The product, thus obtained, was filtered, washed successively with cold water and methanol, and recrystallized from appropriate solvent to afford title compounds in fair to good yields (Table I).

Preparation of 2-(4-Biphenyl)-4-aryl-6-(2-naphthyl)pyridines (3k-l). Route A. To a solution of (2-naphthyl-

methylpyridinium bromide (**1b**) (3 mmol) and arylidene-2-acetobiphenyl (3 mmol) in glacial acetic acid (6.0 mL) was added ammonium acetate (3.0 g), and the mixture was allowed to reflux for 6-8 h. Ice cold water (10.0 mL) was then added to the solution for complete precipitation. The precipitated solid was filtered, washed with methanol, dried, and recrystallized from suitable solvents to yield pyridines (**3k-t**) (Table I).

Route B. An equimolar amount of (4-phenylphenacyl)-pyridinium bromide (**1c**) (3 mmol) and substituted arylidene-2-acetonaphthone was refluxed in the presence of ammonium acetate (3.0 g) in glacial acetic acid (10.0 mL) for 3 h. Similar workup of the reaction mixture led to the formation of a solid mass, recrystallization of which from appropriate solvents gave the title pyridines in fair to good yields (Table I).

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Preparation and Properties of Some Halohydroxamic Acids

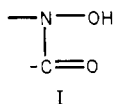
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The preparation and properties of some new *N*-(*p*-chlorophenyl)hydroxamic acids have been described. They are characterized by their melting point, elemental analysis, and IR and UV spectra.

Introduction

The hydroxamic acids, with functional group (I), are excellent



complexing reagents and are generally used in organic and inorganic analysis.

In the present investigation the halo-substituted hydroxamic

Table I^a

hydroxamic acids, <i>N</i> - <i>p</i> -chlorophenyl	formula	mp, °C	yield %	IR spectra, cm ⁻¹			UV spectra λ _{max} , nm
				ν _{O—H}	ν _{C=O}	ν _{N—O}	
<i>p</i> -ethoxybenzohydroxamic acid	C ₁₁ H ₁₄ O ₃ NCI	162	65	3150	1620	810	278
<i>o</i> -bromobenzohydroxamic acid	C ₁₃ H ₉ O ₂ NCIBr	130	62	3130	1620	825	288 332
<i>p</i> -bromobenzohydroxamic acid	C ₁₃ H ₉ O ₂ NCIBr	161	66	3180	1640	830	240 275
<i>p</i> -iodobenzohydroxamic acid	C ₁₃ H ₉ O ₂ NCII	190	60	3150	1635	820	238 338
<i>n</i> -stearohydroxamic acid	C ₂₄ H ₄₀ O ₂ NCI	90	68	3175	1620	830	285
<i>n</i> -chloroacetohydroxamic acid	C ₈ H ₇ O ₂ NCI ₂	117	72	3160	1635	825	284
<i>2</i> -naphthohydroxamic acid	C ₁₇ H ₁₂ O ₂ NCI	202	67	3350	1632	810	286
<i>cinnamohydroxamic acid</i>	C ₁₅ H ₁₂ O ₂ NCI	181	69	3150	1640	828	292

^a Elemental analysis (C, H, N), in agreement with theoretical values, were obtained and submitted for review.