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

$RNHCONHC(CH_2OH)_2$ (CH₃ on the central C)

R	reaction solvent	% yield	mp, °C	proton chemical shift data (δ)[a] RNHC=O	O=CNHC	CH₃C(CH₂OH)
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.

Acknowledgment

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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-thiophenoylmethyl)pyridinium iodide, 1-(4-phenylphenacyl)pyridinium bromide, and 1-(2-naphthoylmethyl)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.

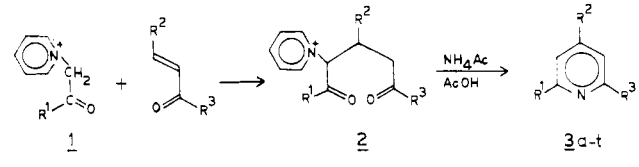
Introduction

Continuing our previous studies on the reactivity of cycloimmonium ylides,[1] we wish to report herein the reactivity of (2-thionylmethylene)pyridinium ylide, (4-phenylphenacyl)pyridinium ylide, and (2-naphthoylmethylene)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-Thiophenoylmethyl)pyridinium iodide (**1a**) was prepared by the Ortoleva–King reaction[2] 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., subsituted 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



1 2 3a-t

The reaction of (2-naphthoylmethyl)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}

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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_4H_3S	C_6H_5	2-C_4H_3S	50	118-120	C_5H_5N-MeOH
3b		4-ClC_6H_4		50	146-148	$CHCl_3$-MeOH
3c		3-$NO_2C_6H_4$		40	158-161	C_5H_5N-MeOH
3d		4-$CH_3C_6H_4$		45	114-115	
3e		3,4-$O_2CH_2C_6H_3$		60	100-102	
3f		2-C_4H_3O		35	315	
3g		C_6H_5	4-$C_6H_5C_6H_4$	30	315-316	
3h		4-ClC_6H_4		51	140-142	$CHCl_3$-MeOH
3i		3-$CH_3C_6H_4$		50	208-209	
3j		4-$CH_3C_6H_4$		53	160-162	
3k	2-$C_{10}H_7$	2-$OCH_3C_6H_4$		48	130-132	
3l		3-$OCH_3C_6H_4$		53	165-166	
3m		4-$OCH_3C_6H_4$		55	132-134	C_5H_5N-MeOH
3n		3,4-$(OCH_3)_2$ 6-Br-C_6H_2		30	165-167	
3o		2-ClC_6H_4		46	186	$CHCl_3$-MeOH
3p		3-ClC_6H_4		50	176-178	
3q		3,4-$O_2CH_2C_6H_3$		65	178	C_5H_5N-MeOH
3r		4-$NO_2C_6H_4$		70	208-210	$CHCl_3$-MeOH
3s		4-$N(CH_3)_2C_6H_4$		48	209-211	
3t		2-C_4H_3O		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, $-O_2CH_2$); 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_2CH_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 ($CDCl_3$) 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-Thiophenoylmethyl)pyridinium iodide (**1a**) was prepared by the Ortoleva-King reaction.[5] (2-Naphthoylmethyl)pyridinium bromide (**1b**)[6] and (4-phenylphenacyl)pyridinium bromide (**1c**) were prepared by the quaternization of ω-bromo-2-acetonaphthone[7] and 4-phenylphenacyl bromide,[8] respectively. Various α,β-unsaturated ketones were prepared by the interaction of 2-acetothiophene, 2-acetonaphthone, and 4-acetobiphenyl with the suitably substituted benzaldehydes.[9]

Preparation of 2,6-Di(2-thienyl)-4-arylpyridines (3a-f). An equimolar amount of (2-thiophenoylmethyl)pyridinium iodine (**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-arylpyridenes (**3a-f**) in quantitative yields (Table I).

Preparation of 2-(4-Biphenyl)-4-aryl-6-(2-thienyl)pyridines (3g-l). A mixture of (4-phenylphenacyl)pyridinum 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-t). Route A. To a solution of (2-naphthoyl-

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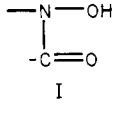
The preparation and properties of some new *N*-(*p*-chlorophenyl)hydroxamic acids have been described. They are characterized by their melting point, elemental analysis, and IR and UV spectra.

Introduction

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



I

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

In the present investigation the halo-substituted hydroxamic acids have been synthesized to develop new analytical methods for the detection, determination, and separation of trace elements in tracer and ultratracer levels.

Experimental Section

All the chemicals used were of A.R. or G.R. quality, unless otherwise stated.

The IR spectra of the synthesized hydroxamic acids were recorded on the Perkin-Elmer Model 221 spectrophotometer in the range 2000–15 000 nm as KBr pellets. The UV spectra were recorded on a Beckman DU-2 spectrophotometer in ethanol.

Ethanol was purified by the method of Vogel (*3*).

Acid Chlorides. The acid chlorides were prepared by the action of thionyl chloride on the respective carboxylic acids. The yields and their boiling points are in agreement with the literature (*4*).

Table I[a]

hydroxamic acids, *N*-*p*-chlorophenyl	formula	mp, °C	% yield	IR spectra, cm^{-1} ν_{O-H}	$\nu_{C=O}$	ν_{N-O}	UV spectra λ_{max}, nm
-*p*-ethoxybenzohydroxamic acid	$C_{15}H_{14}O_3NCl$	162	65	3150	1620	810	278
-*o*-bromobenzohydroxamic acid	$C_{13}H_9O_2NClBr$	130	62	3130	1620	825	288, 332
-*p*-bromobenzohydroxamic acid	$C_{13}H_9O_2NClBr$	161	66	3180	1640	830	240, 275
-*p*-iodobenzohydroxamic acid	$C_{13}H_9O_2NClI$	190	60	3150	1635	820	238, 338
-stearohydroxamic acid	$C_{24}H_{40}O_2NCl$	90	68	3175	1620	830	285
-chloroacetohydroxamic acid	$C_8H_7O_2NCl_2$	117	72	3160	1635	825	284
-2-naphthohydroxamic acid	$C_{17}H_{12}O_2NCl$	202	67	3350	1632	810	286
-cinnamohydroxamic acid	$C_{15}H_{12}O_2NCl$	181	69	3150	1640	828	292

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

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