Studies on Cycloimmonium Ylids. Synthesis of some New 2,4,6-Triaryl-substituted Pyridines via Pyridinium, Picolinium and Isoquinolinium Ylids

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Reaction of pyridinium phenacylids and their picolinium and isoquinolinium counterparts with substituted benzylideneacetophenones gave a wide variety of 2,4,6-triaryl-substituted pyridines which are expected to have some potential biological activities. Ammonium acetate in glacial acetic acid was used as the cyclization agent. The structures of resulting pyridines are supported by nmr and ir spectral data.

J. Heterocyclic Chem., 17, 953 (1980).

Although considerable work has been done by various workers (1,2) in order to examine the reactivity of pyridinium ylids towards benzylideneacetophenones, the synthetic potentialities of picolinium and isoquinolinium ylids have been comparatively less explored after the only report of Krohnke, et al., (3). Continuing our previous researches, (4-7), presently we wish to report the synthesis of some new 2,4,6-triaryl-substituted pyridines via pyridinium, picolinium and isoquinolinium ylids generated in situ from their respective precursors.

Pyridinium phenacylids, 4-picolinium phenacylids and isoquinolinium phenacylids were generated in situ from their respective cycloimmonium salts (1-3) and were made to react with wide range of substituted benzylideneaceto-phenones (4a-s) in refluxing acetic acid in presence of ammonium acetate to afford a wide variety of 2,4,6-triaryl-substituted pyridines (6a-s) presumably via the intermediacy of pentane-1,5-dionylpyridinium, 4-picolinium and isoquinolinium derivatives (5a-s), respectively (Scheme 1).

$$\begin{aligned} & \text{Id} = \text{X} = \text{C}_5\text{H}_5\text{N} & \text{R}^{\dagger} = \text{4} - \text{OCH}_3 - \text{C}_6\text{H}_4 \\ & \text{Ib} = \text{X} = & & \text{R}^{\dagger} = \text{4} - \text{CH}_3 - \text{C}_6\text{H}_4 \\ & \text{Ic} = \text{X} = & & \text{R}^{\dagger} = \text{4} - \text{CI} - \text{C}_6\text{H}_4 \\ & \text{Id} = \text{X} = & & \text{R}^{\dagger} = \text{4} - \text{CI} - \text{C}_6\text{H}_4 \\ & \text{2d} = \text{X} = \text{4} - \text{CH}_3 - \text{C}_5\text{H}_4\text{N} & \text{R}^{\dagger} = \text{4} - \text{CI} - \text{C}_6\text{H}_4 \\ & \text{2b} = \text{X} = \text{4} - \text{CH}_3 - \text{C}_5\text{H}_4\text{N} & \text{R}^{\dagger} = \text{4} - \text{CH}_3 - \text{C}_6\text{H}_4 \\ & \text{3d} = \text{X} = \text{C}_9\text{H}_7\text{N} & \text{R}^{\dagger} = \text{4} - \text{CH}_3 - \text{C}_6\text{H}_4 \\ & \text{3b} = \text{X} = \text{C}_6\text{H}_4\text{N} & \text{R}^{\dagger} = \text{3} - \text{NO}_3 - \text{C}_6\text{H}_4 \end{aligned}$$

All the pyridines synthesized in this study are listed in Table 1. The products (6a-s), most of which are new, gave satisfactory elemental analysis. The structures of the final products were supported by nmr and ir spectral data (Table 2).

EXPERIMENTAL

Melting points were measured on Gallen kamp apparatus and are uncorrected. The ir spectra were recorded on Perkin-Elmer infracord spectrophotometer in potassium bromide. The nmr spectra (deuteriochloroform) were determined using a Varian A-60 spectrometer with tetramethylsilane as an internal standard. Analytical samples were purified by column chromatography over neutral alumina and purity was checked by thin layer chromatography (tlc).

Pyridinium, 4-picolinium and isoquinolinium salts (1-3) were prepared by the quaternization of tertiary bases viz., pyridine, 4-picoline and isoquinoline with the respective α -bromoketones.

Preparation of 2,4,6-Triaryl-substituted Pyridines (6a-s).

A general procedure was used in all the reactions. A mixture of N-acylcycloimmonium salts (1-3, 3 mmoles) and ammonium acetate (3 g.) in acetic acid (15 ml.) was stirred at 80°. Benzylideneacetophenones (4a-s, 3 mmoles) in 10 ml. of acetic acid was added dropwise during 1 hour after which the temperature was allowed to raise up to 120°. Heating was continued for additional 3 hours. The mixture was left overnight at room temperature and ice cold water was then added to precipitate a solid which was separated, washed with methanol, dried and crystallized from an appropriate solvent to yield 2,4,6-triaryl-substituted pyridines (6a-s).

Acknowledgements.

Thanks are due to the Director, H. B. Technological Institute, Kanpur for providing facilities. One of us (N. K. M.) is thankful to Principal, D. B. S. College for facilities and the U. G. C., New Delhi for financial assistance. A. K. D. is thankful to CSIR, New Delhi for the award of senior research fellowship.

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Table 1
Structure and Physical Properties of 2,4,6-Triarylsubstituted Pyridines

			-	-		•	•			
Compound	ł R¹	R²	R³	Salt	%	M.p. °C	Crystallization	Analysis	Found (Ca	alcd.) %
•				used	Yield	-	solvent (a)	C	H	N
_			0 NO O W	,	60	146 147	A	70.60	E 00	£ 21
6а	4-UCH ₃ -C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	3-NO ₂ -C ₆ H ₄	la	60	146-147	A	70.60 (70.58)	5.00 (4.97)	6.31 (6.33)
6b	4-CH ₃ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	4-CH ₃ -C ₆ H ₄	1 b	55	140-141	A	85.50	6.28	3.84
UD.	4-0113-06114	T-00113-06114	4-0113-06114	10	00	110 111	••	(85.48)	(6.30)	(3.83)
6c	4-CH ₈ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	1b	45	116-117	A	82.72	6.12	3.72
								(82.76)	(6.10)	(3.71)
6d	4-CH ₃ -C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	C ₆ H ₅	1b	55	97-99	A	82.73	6.08	3.73
_						100 100		(82.76)	(6.10)	(3.71)
6e	4-CH ₃ -C ₆ H ₄	4-N(CH ₃) ₂ -C ₆ H ₄	4-Cl-C ₆ H ₄	lb	62	138-139	A	78.76	5.74	7.00 (7.02)
6f	4-CH ₃ -C ₆ H ₄	4-Cl-C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	1b	58	145-146	A	(78.79) 77.80	(5.77) 5.16	3.65
01	4-Un ₃ -U ₆ n ₄	4-GI-G ₆ П ₄	4-0Cn ₃ -C ₆ n ₄	110	50	140-140	А	(77.82)	(5.19)	(3.63)
6g	4-CH ₃ -C ₆ H ₄	4-N(CH ₃) ₂ -C ₆ H ₄	4-OCH ₈ -C ₆ H ₄	1b	52	122-123	A	82.21	6.58	7.11
~8		111(0113/2 06114						(82.23)	(6.60)	(7.10)
6h	4-CH ₃ -C ₆ H ₄	C ₆ H ₅	4-OCH ₃ -C ₆ H ₄	1b	48	101-102	В	85.43	5.96	3.98
								(85.47)	(5.98)	(3.99)
				3b	56	100-101	В	85.42	5.96	3.96
				•	4-	100 105		(85.47)	(5.98)	(3.99)
6i	4-Cl-C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	1c	45	123-125	A	74.68	4.97	3.48
6 j	4-Cl-C ₆ H ₄	4-N(CH ₃) ₂ -C ₆ H ₃	4-Cl-C ₆ H ₄	1c	48	155-156	A	(74.71) 71.58	(4.98) 4.79	(3.49) 6.69
o)	4-CI-C ₆ П ₄	4-N(Cn ₃) ₂ -C ₆ n ₃	4-CI-C ₆ П ₄	16	40	100-100	Л	(71.60)	(4.77)	(6.68)
6k	4-Cl-C ₆ H ₄	3,4-(OCH ₈) ₂ -C ₆ H ₃	4-Cl-C ₆ H ₄	1 c	50	169-170	A	68.78	4.38	3.20
	. 0. 0,	o,1 (o dang/2 dang						(68.80)	(4.36)	(3.21)
				2a	52	168-170	A	68.76	4.37	3.21
								(68.80)	(4.36)	(3.21)
61	4-C ₆ H ₅ -C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	4-CH ₃ -C ₆ H ₄	1d	50	69-70	A	84.04	5.84	3.09
_						145140		(84.02)	(5.90)	(3.06)
6m	4-C ₆ H ₅ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	4-CH ₃ -C ₆ H ₄	ld	54	147-148	A	87.28 (87.32)	5.61 (5.63)	3.26 (3.28)
6n	4-CH ₃ -C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	4-Cl-C₀H₄	1b	50	130-131	A	75.08	5.28	3.37
VII	4-G11 ₃ -G ₆ 11 ₄	5, 1 (0011 ₃ / ₂ -0 ₆ 11 ₃	T-G1-G114		00	100 101	••	(75.09)	(5.29)	(3.36)
				2b	55	132-133	A	75.08	5.30	3.38
								(75.09)	(5.29)	(3.36)
6 0	4-Cl-C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	C_6H_5	2a	58	59-60	В	74.68	4.97	3.48
							12	(74.71)	(4.98)	(3.49)
6р	4-CH ₃ -C ₆ H ₄	3,4-(OCH ₃) ₂ -C ₆ H ₃	C ₆ H ₅	2b	52	112-113	A	81.22	6.75	3.62
				3a	50	116-117	A	(81.25) 81.24	(6.77) 6.78	(3.64) 3.63
				Ja	30	110-117	A	(81.25)	(6.77)	(3.64)
6q	4-CH ₃ -C ₆ H ₄	4-CH ₃ -C ₆ H ₄	4-CH ₃ -C ₆ H ₄	3a	62	176-177	A	89.41	6.61	4.04
94	1 0113 06114	. 0.13 06-14	. cary c64		***			(89.39)	(6.59)	(4.01)
6r	4-CH ₃ -C ₆ H ₄	C_6H_5	4-CH ₃ -C ₆ H ₄	3a	58	145-146	A	89.52	6.22	4.21
								(89.55)	(6.26)	(4.18)
6s	3-NO ₂ -C ₆ H ₄	4-OCH ₃ -C ₆ H ₄	4-Cl-C ₆ H ₄	3b	60	181-183	A	69.13	4.10	6.69
								(69.15)	(4.08)	(6.72)

⁽a) Solvent for crystallization. A = Pyridine-methanol. B = Chloroform-methanol.

Table 2

Nmr and Ir Data for 2,4,6-Triarylsubstituted Pyridines (6a-s)

•••		Nmr data (deuterio			Ir data (potassium bromide), cm-1			
Vibrations Vib	Compound	δ (ppm)	No of	Assignment		C=C	C=N	
6a 4.02 d 9H methoxy — — — — 6b 2.62 s 6H methyl — — — — 6b 2.62 s 6H methyl — — — — 6c — — — 3010 1601 1550, 6c — — — — — — 6d 2.36 s 3H methyl — — — — 6d 2.36 s 3H methyl — — — — 6e 2.62 s 3H methyl — — — — 6e 2.62 s 3H methyl — — — — 6f 2.42 s 3H methyl — — — — 6g 2.76 s 9H methyl — — — — 6g 2.76 s 9H			protons		· ·	Vibration	Vibration	
6.94-8.44 m 13H aromatic a.398 s 3H methoy 6.94-8.60 m 14H aromatic 6.60					vibrations			
6b 2.62 s 6H methory —	6а	4.02 d	9H	methoxy	_	_	_	
3.98 s		6.94-8.44 m	13H	aromatic				
6c - - - 3010 1601 1550, 1500 6d 2.36 s 3H methyl - - - - 6d 2.58 s 3H methyl - - - - 6e 2.62 s 9H methyl - - - - 6f 2.42 s 3H methyl - - - - - 6g 2.76 s 9H methyl - - - - - 6g 2.76 s 9H methyl - <	6b	2.62 s	6H	methyl				
6c — — — 3010 1601 1550. 1500 6d 2.36 s 3.84 d 6H methoxy — — — — 6.84.8.15 m 14H aromatic — — — — 6e 2.62 s 9H methyl — — — 6f 2.42 s 3H methoxy — — — 6g 2.76 s 9H methyl — — — 6g 2.76 s 9H methoxy — — — 6g 2.76 s 9H methyl — — — 3.82 s 3H methoxy — — — 6.90-8.38 m 15H aromatic — — — 6i — — — — 6.90-8.38 m 15H aromatic — — — 6i — — — 3060 1600 1510, 490 — — — 3060 1601 1520, 6i — — — 3040 1600 <th< td=""><td></td><td>3.98 s</td><td>3H</td><td>methoxy</td><td>_</td><td></td><td>_</td></th<>		3.98 s	3H	methoxy	_		_	
1500 1500		6.94-8.60 m	14H	aromatic				
6d 2.36 s 3H methyl methyl	6 c	_		_	3010	1601		
Section Sect	6d	2.36 s	3H	methyl			1000	
6.84-8.15 m				· ·	_	_		
6e 2.62 s 9H methyl aromatic —				•				
66 80-8.32 m 14H aromatic —	6e							
6f 2.42 s 3H methyl — <				•	_	_	_	
3.88 s	6f							
6g 2.76 s 9H methyl 3.82 s 3H methoxy — — — 6.72-8.36 m 14H aromatic — — — — 6h 2.42 s 3H methoxy — — — — 6.99.8.38 m 15H aromatic —				•		<u></u>	_	
6g 2.76 s 9H methyl 3.82 s 3H methoxy — — 6.72-8.36 m 14H aromatic 6h 2.42 s 3H methyl 3.82 s 3H methoxy — — 6.90-8.38 m 15H aromatic 6i — — — 3010 1600 1510, 1490 — — — 1490 6j — — — 3060 1600 1530, 1490 — — — — 1490 6k — — — — 1601 1520, 1490 — — — — 1601 1520, 1490 — — — 3060 1599 1535, 6l — — — 3040 1600 1542, 1510 — — — 3020 1600 1510, 6p 2.34 s 3H methyl — — —				•				
3.82 s 3H methoxy	6g	2.76 s						
6h 6.72-8.36 m	J	3.82 s		•	_	_		
6h 2.42 s 3H methoxy — — — 6.90-8.38 m 15H aromatic — — — — 6i — — — 3010 1600 1510, 1490 6j — — — 3060 1600 1530, 1490 6k — — — — — 1601 1520, 1490 6k — — — — — — 1601 1520, 1495 6l — — — — 3060 1599 1535, 1508 6m — — — — 3040 1600 1542, 1510 6n — — — — 3020 1600 1510, 1490 6o 3.28 d 6H methoxy — — — — 6p 2.34 s 3H methyl — — — — 5.74-6.82 m 14H <td></td> <td></td> <td></td> <td>•</td> <td></td> <td></td> <td></td>				•				
3.82 s	6h							
6i — — — 3010 1600 1510, 1510, 1490 6j — — — 3060 1600 1530, 1490 6k — — — — 1490 6k — — — — 1601 1520, 1530, 1500 6l — — — 3060 1599 1535, 1508 6m — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 1510, 1510, 1510 6o 3.28 d 6H methoxy — — — — 6p 2.34 s 3H methyl — — — — 3.76 d 6H methyl — — — — 6q 2.42 s 9H methyl — — — — 7.168.54 m 14H aromatic — — — — 6c 2.40 s 6H methyl — — — —				•	***	_	_	
6i — — — 3010 1600 1510, 1490 6j — — — 3060 1600 1530, 1490 6k — — — — 1601 1520, 1495 6l — — — 3060 1599 1535, 1508 6m — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 1510, 1510, 1510, 1510 6o 3.28 d 6H methoxy — — — — 5.74-6.82 m 14H aromatic — — — — 6p 2.34 s 3H methoxy — — — — 6c 3.24 s 3H methoxy — — — — 6c 2.42 s 9H methyl — — — — 7.08-8.56 m 15H aromatic — — — — — 6s 3.90 s 3H methoxy				•				
1490	6i	_		_	3010	1600	1510	
6j — — — — 1530, 1490 6k — — — — 1601 1530, 1520, 1520, 1495 6l — — — 3060 1599 1535, 1508 6m — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 15							•	
6k — — — 1601 1520, 1495 6l — — — 3060 1599 1535, 1508 6m — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 1510, 1549 6o 3.28 d 6H methoxy — — — 5.74-6.82 m 14H aromatic — — — 6p 2.34 s 3H methyl — — — 3.76 d 6H methoxy — — — — 6q 2.42 s 9H methyl — — — — 7.16-8.54 m 14H aromatic — — — — 6r 2.40 s 6H methyl — — — — 7.08-8.56 m 15H aromatic — — — — — 6s 3.90 s 3H methoxy — — — — —	6j	_	_	_	3060	1600		
6k — — — — 1601 1520, 1495 6l — — — — 3060 1599 1535, 1508 6m — — — — 3040 1600 1542, 1510 6n — — — — 1510 6o 3.28 d 6H methoxy — — — 5.74-6.82 m 14H aromatic — — — — 6p 2.34 s 3H methyl — — — — 3.76 d 6H methyl — — — — 6q 2.42 s 9H methyl — — — — 7.16-8.54 m 14H aromatic — — — — 6c 3.90 s 3H methoxy	·							
1495 1596 1597 1535, 1508 1508 1508 1508 1508 1508 1508 1508 1508 1508 1509 1510, 1510 1510 1510, 1510 1600 1510, 1490 1509 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1490 1600 1510, 1600 1600, 1600 1510, 1600 1510, 1600 1510, 1600 1600, 1600 1510, 1600 1600,	6k	<u> </u>	_	_	_	1601		
6l — — — — 3060 1599 1535, 1508 6m — — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 1490 6o 3.28 d 6H methoxy — — — 5.74-6.82 m 14H aromatic — — — 6p 2.34 s 3H methyl — — — 3.76 d 6H methoxy — — — — 6q 2.42 s 9H methyl — — — — 6r 2.40 s 6H methyl — — — — 6s 3.90 s 3H methoxy — — — —								
1508	61	_	_	_	3060	1599		
6m — — — — 3040 1600 1542, 1510 6n — — — 3020 1600 1510, 1510, 1510, 1490 6o 3.28 d 6H methoxy — — — — 5.74-6.82 m 14H aromatic —								
6n — — — — 1510 6o 3.28 d 6H methoxy — — — 1490 6o 3.28 d 6H methoxy — — — — 5.74-6.82 m 14H aromatic — — — — 6p 2.34 s 3H methoxy — — — — 6c 6.63-8.11 m 14H aromatic — — — — 6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — — — 6s 3.90 s 3H methoxy	6m	_		_	3040	1600		
6n — — — 3020 1600 1510, 1490 6o 3.28 d 6H methoxy — — — — 5.74-6.82 m 14H aromatic — <th< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>								
60 3.28 d 6H methoxy 5.74-6.82 m 14H aromatic — — 6p 2.34 s 3H methyl 3.76 d 6H methoxy — — 6.63-8.11 m 14H aromatic 6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — — 6s 3.90 s 3H methoxy	6 n	_	_	_	3020	1600		
60 3.28 d 6H methoxy 5.74-6.82 m 14H aromatic — — 6p 2.34 s 3H methyl 3.76 d 6H methoxy — — 6.63-8.11 m 14H aromatic 6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — — 6s 3.90 s 3H methoxy								
6p 2.34 s 3H methyl 3.76 d 6H methoxy — — 6.63-8.11 m 14H aromatic 6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — 6s 3.90 s 3H methoxy	6 0	3.28 d	6Н	methoxy				
3.76 d 6H methoxy — — — — — — — — — — — — — — — — — — —		5.74-6.82 m	14H	aromatic	_	_	_	
6.63-8.11 m 14H aromatic 6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — — — 6s 3.90 s 3H methoxy	6р	2.34 s	3H	methyl				
6q 2.42 s 9H methyl 7.16-8.54 m 14H aromatic — — 6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — — 6s 3.90 s 3H methoxy		3.76 d	6Н	methoxy		_		
7.16-8.54 m 14H aromatic — — — — — — — — — — — — — — — — — — —		6.63-8.11 m	14H	aromatic				
6r 2.40 s 6H methyl 7.08-8.56 m 15H aromatic — — 6s 3.90 s 3H methoxy	6 q	2.42 s	9H	methyl				
7.08-8.56 m 15H aromatic — — — — — — — — — — — — — — — — — — —		7.16-8.54 m	14H	aromatic	_		_	
6s 3.90 s 3H methoxy	6r	2.40 s	6H	methyl				
		7.08-8.56 m	15H	aromatic	_	_	_	
6.98-8.60 m 14H aromatic	6s		3 H	methoxy				
		6.98-8.60 m	14H	aromatic		_		

s = singlet; d = doublet; m = multiplet.