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THE PREPARATION OF SOME 1-VINYLPYRIDINIUM SALTS

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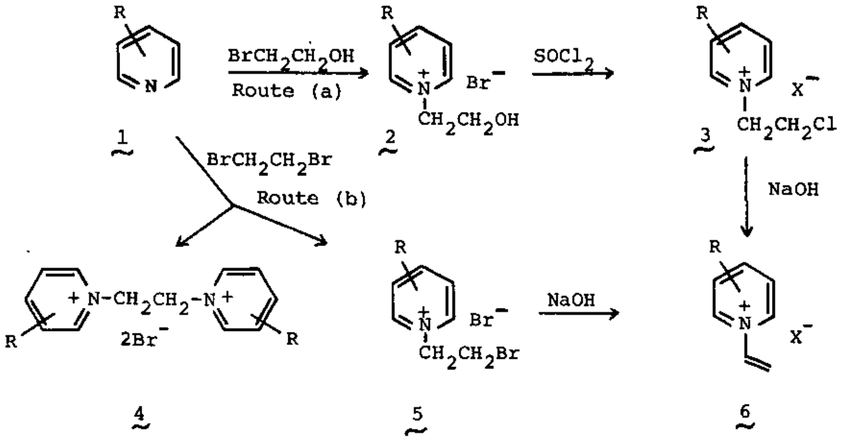
Abstract - A variety of substituted pyridines are converted into the corresponding 1-vinylpyridinium bromides or perchlorates. The conjugation in these salts is discussed with reference to the ir spectral characteristics.

1-Vinylpyridinium cations are of potential interest as polymer components, but in contrast to the much studied 2- and 4-vinylpyridines, have been little investigated. A recent publication[1] from this laboratory described the first practical synthesis of an unsubstituted 1-vinylpyridinium salt - the sparse earlier work[2] had utilized silver oxide as a reagent. Other work by our group has concerned the preparation of 2,4,6-trisubstituted 1-vinylpyridinium salts[3] and interesting ring transformations of such cations[4] and of the 1,2-dihydropyridines[5] derived from them. The present paper generalizes the preparation of simple 1-vinylpyridinium salts and describes some of their physical properties.



Scheme I

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Table I Preparation of N-(hydroxyethyl)- and N-(haloethyl)-pyridinium bromides

Comp. No.	Ring Substituent	M p °C Recrys.solv.	Yield %	Molecular formula	Analysis Calcd. (%) C	H	Found (%) C	H
2a	4-N(CH$_3$)$_2$	147-149 acetonitrile	74	$C_9H_{15}BrN_2O$	43.72	6.12	43.55	6.18
2b	3-CH$_3$	95-99 acetone-EtOH	47	$C_8H_{12}BrNO\cdot\frac{1}{2}H_2O$	42.30	5.77	42.52	5.77
2c	4-Ph	120-122 acetone EtOH	79	$C_{13}H_{14}BrNO$	55.73	5.04	55.79	5.09
2d	4-(4-methyl-1-piperidinyl)	thick oil	74	$C_{13}H_{21}BrN_2O$	+			
3a	4-N(CH$_3$)$_2$	200-201.5 acetone	77	$C_9H_{14}N_2ClBr$	40.69	5.31	40.47	5.43
3b*	4-Ph	115-117 ethanol	78	$C_{13}H_{13}Cl_2NO_4$	49.08	4.12	48.86	4.39
3c	4-(4-methyl-1-piperidinyl)	162-164 acetone-EtOH	47	$C_{13}H_{20}BrClN_2$	48.83	6.30	48.76	6.34
5a	4-N(CH$_3$)$_2$	202-203 ethanol	59	$C_9H_{14}Br_2N_2$	34.86	4.55	35.09	4.59
5b**	H	95-102 acetone-EtOH	58	$C_7H_9Br_2N_2$	31.49	3.40	31.36	3.40
5c	3-CH$_3$	thick oil	68	$C_8H_{11}Br_2N$	+			
5d	4-CH$_3$	145-147 acetone-EtOH	76	$C_8H_{11}Br_2N\cdot\frac{1}{2}H_2O$	33.13	4.17	33.09	4.20
5e	4-(4-methyl-1-piperidinyl)	208-210 acetone-EtOH	51	$C_{13}H_{20}Br_2N_2$	42.88	5.54	42.97	5.60

*Perchlorate. **Ref.2 gives mp 126-128°C; E. Schmidt Arch. Pharm., 251, 183 (1913), mp 100-103°C. +Characterized spectrally ++Analysis of Nitrogen, calcd. (found): 2a, 11.33(11.29); 2c, 5.00(4.95); 3a, 10.55(10.89); 3b, 4.40(4.39); 3c, 8.76(8.73); 5a, 9.04(9.00); 5b, 5.25(5.25); 5e, 7.69(7.67).

Formation of 1-(2-haloethyl)pyridinium salts - We have used two routes for the preparation of these N-haloethyl derivatives from the appropriate pyridine (Scheme I): (a) simple reaction with 1,2-dibromoethane or (b) quaternization by 2-bromoethanol, followed by transformation of the hydroxy into a chloro group with $SOCl_2$.

1,2-Dibromoethane reacted with pyridine[2] in boiling ethanol given 1-(2-bromoethyl)pyridinium bromide and 1,1'-ethylenebispyridinium dibromide as a by-product. The same procedure applied to the other pyridines gave the corresponding 1-(2-bromoethyl) derivatives (Table I) (average yield 60%) with the 1,1'-ethylenebispyridinium salts (Table II) as byproducts.

The second, two-step pathway, utilizes the reaction between pyridines and 2-bromoethanol in boiling acetonitrile which was previously used for this compound[6] and for 1-(2-hydroxyethyl)isoquinolinium bromide.[7] 1-(2-Hydroxyethyl)pyridinium was also obtained from pyridine and ethylene oxide.[8,9] The 1-(2-hydroxyethyl) derivatives (Table I) were obtained in yields of 50-70%. Treating them with $SOCl_2$ directly[8] provides 1-(2-chloroethyl)pyridinium salts in about 70% yield (Table I). However, the reaction with 2-bromoethanol also gives polymers which were sometimes inseparable from the required product; for this reason attempted preparation of 1-vinyl-4-methylpyridinium from 4-picoline by this route failed.

Table II Properties of 1,1'-ethylenebispyridinium bromides [a]

Comp. No.	Ring Substit.	Mp °C	Lit. Mp	Yield %	Molecular Formula	Analysis Calcd. (%)		Found (%)	
						C	H	C	H
4a	H	280	>265[c]	28	$C_{12}H_{14}Br_2N_2$[b]	41.64	4.08	41.68	4.10
4b	4-$N(CH_3)_2$	>300		9	$C_{16}H_{24}Br_2N_4 \cdot H_2O$	42.68	5.82	42.56	5.85
4c	4-CH_3	>300	>265[c]	8	$C_{14}H_{18}Br_2N_2 \cdot H_2O$	42.87	5.14	42.84	5.16
4d	3-CH_3	266-268	256.4-258.7[c]	5	$C_{14}H_{18}Br_2N_2$[b]	44.94	4.85	44.66	4.89
4e	4-Ph	301-302		17	$C_{24}H_{22}Br_2N_2 \cdot 2H_2O$	53.95	4.90	53.96	4.93

[a] All compounds were recrystallized from ethanol, 4d from ethanol-water. [b] Analysis of nitrogen, calcd.(found): 4a, 8.09(8.07); 4d, 7.49(7.38). [c] J.L. Hartwell and M.A. Pogorelskin, J.Am.Chem.Soc., 1950, 2040.

The ^1H n.m.r. data of the 1-(2-hydroxyethyl)- and 1-(2-haloethyl)-pyridinium salts are given in Table III and those for the 1,1'-ethylenebispyridinium salts in Table IV. These spectra show expected features and confirm the structures assigned.

Table III ^{1}H n.m.r. spectra of hydroxyethyl- and haloethyl-pyridinium salts

Comp.	$^+NCH_2$- (2H)			$-CH_2X$ (2H)			R substituent			Pyridine ring						
No.	δ [p.p.m.]	m	J	δ [p.p.m.]	m	J	δ [p.p.m.]	H	m	δ [p.p.m.]	H	m	δ [p.p.m.]	H	m	J
2a[a]	4.0-4.5	m		4.0-4.5	m		2.70	6	s	7.90	2	d	8.90	2	d	8
2b[a]	4.90	t[c]		4.20	t[c]		2.53	3	s	7.7-8.8	4	m				
2c[a]	4.90	t[c]		4.43	t[c]		7.73	5	m	8.30	2	d	8.90	2	d	7
2d[b]	2.8-4.8	m[d]		2.8-4.8	m[d]		0.8-2.1	7	m	7.06	2	d	8.50	2	d	7
							2.8-4.8	5	m[d]							
3a[b]	4.90	t[c]		4.13	t[c]		3.33	6	s	7.03	2	d	8.80	2	d	8
3b[a]	4.8-5.2	m[d]		3.9-4.3	m[d]		7.5-8.1	5	m	8.30	2	d[c]	8.60-9.00	2	m[c]	
3c[b]	4.90	t	6	4.20	m[d]		0.8-2.1	7	m	7.17	2	d	8.77	2	d	8
							2.6-3.5	5	m							
5a[b]	5.00	t	5	4.00	t	5	2.32	6	s	7.00	2	d	8.80	2	d	8
5b[b]	5.27	t	6	4.00	t	6	-			8.0-9.3	5	m				
5c[a]	5.33	t[c]		4.13	t[c]		2.67	3	s	7.8-9.4	4	m				
5d[b]	5.60	t[c]		4.20	t[c]		2.80	3	s	8.07	2	d	9.70	2	d	6
5e[b]	4.95	t	6	3.8-4.5	m[d]		0.7-2.1	7	m	7.20	2	d	8.80	2	d	8
							2.9-4.5	5	m[d]							

[a] $CDCl_3+CF_3COOH$ solution [b] $CDCl_3$ [c] Distorted signal [d] Obscured by signals in the same region

Table IV ^{1}H n.m.r. spectra of 1,1'-ethylenebispyridinium bromides[a]

Comp.	R	$^+NCH_2-CH_2N^+$	R			Pyridine ring						
No.		4H s	δ	H	m	δ [p.p.m.]	H	m	δ [p.p.m.]	H	m	J
4a	H	5.65	-			8.1-9.5	10	m				
4b	4-$N(CH_3)_2$	4.65	3.15	12	s	6.80	4	d	8.00	4	d	8
4c	4-CH_3	5.43	2.70	6	s	7.93	4	d	9.27	4	d	7
4d	3-CH_3[b]	5.60	2.66	6	s	8.20	2	m	9.27	4	m	
4e	4-Ph	5.40	7.4-8.0	10	m	8.20	4	d	9.33	4	d	6

[a] $CDCl_3+CF_3COOH$ solution. [b] 8.52 (2H, d).

Formation of 1-vinylpyridinium salts - As expected from the earlier work[1,3,4] elimination reactions of the β-haloethyl- to 1-vinylpyridiniums (6) proceed smoothly in ethanol-methanol at -5°C with aqueous 10M NaOH. Particularly for 1-vinylpyridinium itself and for the 1-vinylpicoliniums, to prevent polymerization it is necessary to avoid temperatures above -5°C and to work at low concentration. Isolation of the products as halosalts is difficult because some are hygroscopic: the perchlorates are easier to crystallize. The physical properties of the N-vinylpyridinium salts prepared are given in Table V.

Table V Preparation of 1-vinylpyridinium salts

Comp. No.	R	M p °C Recrys.solv.	Yield %	Mol.formula	Analysis Calcd. C	Analysis Calcd. H	Analysis Found C	Analysis Found H
6a[a]	4-N(CH$_3$)2	159-160 ethanol	80	$C_9H_{13}ClN_2O_4$	43.47	5.27	43.53	5.32
6b[b]	4-(4-methyl-1-piperidinyl)	180-182 acetone-EtOH	77	$C_{13}H_{19}BrN_2.\frac{1}{2}H_2O$	53.42	6.55	53.57	6.87
6c[a]	4-Ph	152-154 ethanol	81	$C_{13}H_{12}ClNO_4$	55.43	4.29	55.27	4.31
6d[b]	4-CH$_3$	168-170 acetone-EtOH	74	$C_8H_{10}NBr.H_2O$	44.05	5.55	43.93	5.58
6e[c]	3-CH$_3$	82-84 acetone-ether	77	$C_8H_{10}IN$	38.89	4.08	38.80	4.10
6f[b]	H	148-150	70	$C_7H_8BrN.H_2O$	41.20	4.94	41.12	4.96

[a] Perchlorate [b] Bromide [c] Iodide *Analysis of Nitrogen, calcd.(found): 6a, 11.27(11.23); **6c**, 4.97(4.92); **6e**, 5.67(5.65).

Spectra of 1-vinylpyridinium cation - In 1-vinylpyridinium itself and in the 3- and 4-methyl derivatives the uv absorption maximum (Table VII) is almost unchanged in relation to the corresponding des-vinylpyridiniums, although the extinction coefficient is significantly increased. However, the more conjugated 4-dimethylamino and 4-phenyl derivatives show pronounced bathochromic shifts on introduction of the N-vinyl group as well as increased extinction coefficients.
In the infrared spectra all the compounds show a strong ν C=C at 1664-1649 cm^{-1} (cf. styrene 1650 cm^{-1} and diethylvinylamine 1648 cm^{-1}), together with other characteristic bands as expected (Table VII).
The vinyl protons show an ABC pattern in the ^{1}H n.m.r. spectrum with CH at

7.0-8.1 p.p.m. CH_2(cis) at 5.3-6.1 p.p.m. and CH_2(trans) at 5.8-6.6 p.p.m. As the 4-substituent increases in electron-donor character all of the signals tend to higher field while the *J* values show no significant changes from typical values. All ^1H nmr data are given in Table VI.

Table VI ^{1}H N.m.r. spectra of 1-vinylpyridinium salts

Comp. No.	Ring Substituent	δ [p.p.m.] =CH	=CH_2 cis	=CH_2 trans	*J* [Hz] gem	cis	trans	Pyridine ring δ_α	*J*	δ_β	δ_γ
6a[a]	4-NMe_2	7.03	5.38	5.67	4	9	15	8.13	8	6.97	-
6b[b]	[c]	7.40	5.30	5.90	3	9	15	8.87	8	7.35	-
6c[a]	4-Ph	7.70	5.77	6.15	4	8	15	8.93	7	8.33	-
6d[b]	4-CH_3	8 13	5.80	6.60	3	8	15	9.80	7	8.15	-
6e[a]	3-CH_3	7.77	6.07	6.40	4	8	16	9.07	-	8.30	8.55
6f[a]	H	7.77	5.87	6.30	4	8	14	9.27	-	8.27	8.70

[a] $CDCl_3+CF_3COOH$ solution [b] $CDCl_3$ [c] 4-(4-methyl-1-piperidinyl)

Table VII UV. and I.R. spectra of 1-vinylpyridinium salts

Comp. No.	Pyridinium cation U.V. λ[nm]	ε	1-Vinylpyridinium cation U.V. λ[nm]	ε	I.R. ν[cm^{-1}] C=C	=CH_2	C=C,C=N arom.	CH arom.
6a	285	-	310	25000	1664	1404	1640,1577,1475	1210,1215
6b	-	-	315	26300	1653	1410	1635,1550,1517	1200,1180
6c	386	17400	312	20800	1649	1410	1624,1488	1195
6d	252	4470	256	7710	1656	1419	1634,1560,1520	1190
6e	262	5010	265	7780	1654	1410	1620,1585,1490	1100
6f	256	5010	257	8860	1650	1410	1628,1495,1475	1195

Addition reactions - N-Vinylpyridiniums undergo Michael addition reactions with nucleophiles in the presence of base giving the corresponding adducts.[1] As illustrations of such reactions, we have obtained adducts from thiophenol and 4-dimethylamino-1-vinylpyridinium and from 2-nitropropane and 4-phenyl-1-vinylpyridinium.

Other attempts of preparation of N-vinyl derivatives- We have also investigated quinoline and isoquinoline. N-(2-Hydroxyethyl)-quinolinium[7] and -isoquinolinium bromides[10] have been described previously and we have obtained the corresponding N-(2-chloroethyl) derivatives. However, reaction with base gave only deep red polymers.

EXPERIMENTAL

Melting points were determined using a Hoover capillary melting point apparatus and are uncorrected. ^{1}H n.m.r. spectra were recorded with a Varian Model EM 360L using TMS as internal standand, uv spectra were recorded in water solution ($c=2x10^{-5}$) with Perkin Elmer 330 apparatus. Ir spectra were taken in CCl_4 using Perkin Elmer 283B apparatus.

General procedure for preparation of 1-(2-hydroxyethyl)pyridinium bromides 2a-d - Equimolar amounts of the appropriate pyridine and 2-bromoethanol were refluxed in acetonitrile (10 ml for 1g pyridine) for 20 h. The mixture was cooled. If the product did not separate, the solvent was evaporated and the remaining oil dissolved in ethanol-acetone. After cooling, the crystals were filtered off and recrystallized (Table I).

General procedure for preparation of 1-(2-chloroethyl)pyridinium salts 3a-c - 1-(2-Hydroxyethyl)pyridinium bromide (0.036mol) was treated in portions with $SOCl_2$ (10 ml). After half an hour the excess $SOCl_2$ was removed *in vacuo* (30°C/20 mm Hg) and the remaining oil treated with hot acetone. The resulting crystals were filtered off and recrystallized (Table I). For compound 3b, the oil was dissolved in acetone and an equimolar amount of $NaClO_4$ added. After filtration of inorganic salt, acetone was removed and the remaining solid recrystallized from ethanol.

General procedure for preparation of 1-(2-bromoethyl)pyridinium bromides 5a-e - The pyridine (8mmol), 1,2-dibromoethane (24 mmol) and ethanol (5 ml) were refluxed for 6 h. The reaction mixture was left overnight at 0°C. The dimeric by-product was filtered off (Table II). The ethanol was removed and the residue dissolved in acetone-ethanol solution. After cooling, the resulting 1-(2-bromoethyl)pyridinium bromide was filtered off and recrystallized (Table I).

General procedure for preparation of 1-vinylpyridinium salts 6a-f - Aqueous NaOH (10M, 1.1 mmol) was added dropwise at -5°C to the 1-(2-haloethyl)pyridinium salt (8mmol) in ethanol-methanol (3:1, 20 ml). After 16 h the solution was neutralized with HCl, inorganic salts were filtered off and the solution concentrated *in vacuo* (30°C/20 mm Hg). Addition of acetone-ethanol gave the product which was filtered off and recrystallized (Table V).

1-(2-Phinylthioethyl)-4-dimethylaminopyridinium perchlorate - 1-Vinyl-4-dimethylaminopyridinium perchlorate (1.3g), thiophenol (1.5 ml), methanol (20 ml) and sodium methoxide (2 ml containing 0.08g Na) were refluxed for 12 h. Removal of the solvent followed by addition of acetone (5 ml) gave a white solid (consisting of starting material 0.65g and inorganic salt) which was filtered off. A few drops of $HClO_4$ were added to the mother liquid, which on cooling gave white crystals which were collected (0.5g) (53%), mp 149-150°C. $\delta(CDCl_3+CF_3COOH)$: 3.20 (6H, s, $-N(CH_3)_2$), 3.36 (2H, t, *J* 6 Hz, $-CH_2S-$), 4.30 (2H, t, *J* 6 Hz, $N-CH_2-$), 7.30 (5H, s, phenyl), 6.73 (2H, d, pyridine *J* 8 Hz), 7.78 (2H, d, pyridine *J* 8 Hz). Anal. Calcd. for $C_{15}H_{19}ClN_2O_4S$: C, 50.20; H, 5.37; N, 7.74. Found: C, 50.00; H, 5.37; N, 7.74.

1-(3-Nitro-3-methylbutyl)-4-phenylpyridinium perchlorate - 1-Vinyl-4-phenylpyridinium perchlorate (0.3g), 2-nitropropane (0.2 ml), methanol (3 ml) and sodium methoxide (1 ml containing 0.017g Na) were refluxed for 20 h. The mixture was neutralized with HCl and the precipitate filtered off, purified by refluxing in methanol with charcoal and recrystallized from ethanol to give a yellow amorphous solid (0.17g) (43%), mp 186-188°C. $\delta(CDCl_3+CF_3COOH)$: 1.70 (6H, s, $2x-CH_3$), 2.70 (2H, m, $-CH_2C$), 4.73 (2H, m, $N-CH_2-$), 7.5-8.0 (5H, m, phenyl), 8.30 (2H, d, *J* 7 Hz), 8.87 (2H, d, *J* 7 Hz). Anal. Calcd. for $C_{16}H_{19}ClN_2O_6$: C, 51.82; H, 5.16; N, 7.56. Found: C, 51.87; H, 5.20; N, 7.50.

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