

## Pyrido[1,2-*a*]pyrimidinium Salts. Part I. Synthesis from 2-Aminopyridines and Interconversion with 2-(2-Acylvinylamino)pyridines

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The scope and steric restrictions of a route for the preparation of pyrido[1,2-*a*]pyrimidinium salts from 2-aminopyridines and 1,3-dicarbonyl compounds, or their acetals, have been investigated. 2-(2-Acylvinylamino)pyridines and not, as formerly suggested, acylethylidenaminopyridines, are shown to be the intermediates in this type of reaction, and the previous claim for the synthesis of a 1,8-naphthyridine under similar conditions is disproved. Good yields of twenty-six pyrido[1,2-*a*]pyrimidinium perchlorates and bromides have thus been obtained from the 2-aminopyridines in one step by reactions carried out at room temperature. Spectroscopic evidence is presented for all the products, including those where the formation of positional isomers is theoretically possible.

SEVERAL pyrido[1,2-*a*]pyrimidin-4-ones are reported to have antihypertensive and hypoglycemic properties,<sup>1</sup> and antiparasitic activity has been observed in a number of quinolizinium salts.<sup>2</sup> In view of this, and of our general interest in the preparation, substitution, and ring-opening reactions of *N*-bridgehead compounds,<sup>3</sup> we embarked on the synthesis of a series of pyrido[1,2-*a*]pyrimidinium salts (13)—(38).

Many pyrido[1,2-*a*]pyrimidin-2- and -4-ones have been prepared by the reaction of 2-aminopyridines with a variety of acetylenic esters and  $\beta$ -keto-esters,<sup>4</sup> but only five papers concerning pyrido[1,2-*a*]pyrimidinium salts not bearing an oxo- or an imino-substituent have appeared.<sup>5-9</sup> We have now extended the method of Nesmeianov and Rybinskaia,<sup>6</sup> which involved the treatment of 2-aminopyridine with keto-aldehyde acetals in the presence of acids, to the treatment of 2-aminopyridine (1) and eight variously substituted alkyl 2-aminopyridines (2)—(9) with pentane-2,4-dione (10), 1,1,3,3-tetramethoxypropane (12), and 4,4-dimethoxybutan-2-one (11) in the presence of perchloric acid to give the pyrido[1,2-*a*]pyrimidinium perchlorates (13)—(35) recorded in Table 3. The pyrido[1,2-*a*]pyrimidinium

perchlorates were clearly distinguished from the isomeric perchloric acid salts of 1,8-naphthyridines by the absence of NH absorptions in their i.r. spectra (see Experimental section) and the presence of <sup>1</sup>H n.m.r. signals due to the 9-protons in all the salts derived from 2-aminopyridines not bearing a 3-substituent (see Table 2).

The use of hydrobromic acid generally gave lower yields and the bromides were less stable than the corresponding perchlorates. No rigorous attempts were made to establish optimum reaction conditions, since the yields were usually very good after reaction at room temperature for 15—18 h and since the varying solubilities of the products appeared to be a complicating factor. The parent pyrido[1,2-*a*]pyrimidinium perchlorate (13) and the 2,4-dimethyl derivative (15) have been obtained<sup>7</sup> by conversion of bromides, obtained in similar reactions conducted in boiling methanol and hydrobromic acid. Seven of the salts recorded in Table 3 have recently been prepared in good yields by treatment of the appropriate isolated 2-aminopyridine perchlorate with the dicarbonyl compound at 120—140°.<sup>8</sup>

2-Amino-3,5-dimethylpyridine appeared to be the most

<sup>1</sup> C. M. Gupta, A. P. Bhaduri, N. M. Khanna, and S. K. Mukherjee, *Indian J. Chem.*, 1971, **9**, 201.

<sup>2</sup> R. J. Alaimo, C. J. Hatton, and M. K. Eckman, *J. Medicin. Chem.*, 1970, **13**, 554; R. J. Alaimo, B.P. 1,170,230/1969 (*Chem. Abs.*, 1970, **72**, 55,286q).

<sup>3</sup> J. A. Hickman and D. G. Wibberley, *J.C.S. Perkin I*, 1972, 2958.

<sup>4</sup> W. L. Mosby, 'Heterocyclic Systems with Bridgehead Nitrogen Atoms,' Interscience, New York, 1961, part 2, p. 1141, and references cited therein.

<sup>5</sup> A. N. Nesmeianov, M. I. Rybinskaia, and N. K. Belsky, *Proc. Acad. Sci. (U.S.S.R.)*, 1957, **113**, 213.

<sup>6</sup> A. N. Nesmeianov and M. I. Rybinskaia, *Proc. Acad. Sci. (U.S.S.R.)*, 1958, **118**, 43.

<sup>7</sup> A. Pollak, B. Stanovnik, and M. Tišler, *J. Org. Chem.*, 1971, **36**, 2457.

<sup>8</sup> A. M. Khmaruk, Yu. M. Volovenko, and V. A. Chuiguk, *Ukrain. Khim. Zhur.*, 1972, **38**, 262 (*Chem. Abs.*, 1972, **76**, 153,698c).

<sup>9</sup> S. Huenig and K. H. Oette, *Annalen*, 1961, **640**, 98.



Further evidence for the structure of 2,6-dimethylpyrido[1,2-*a*]pyrimidinium perchlorate (26) was afforded by treatment with aqueous sodium hydroxide, to yield 2-(2-formyl-1-methylvinylamino)-6-methylpyridine (44)

ment of 2,4,8-trimethylpyrido[1,2-*a*]pyrimidinium perchlorate (21) with sodium hydroxide, and both products formed the pyrido[1,2-*a*]pyrimidinium perchlorate (21) with perchloric acid. Treatment of the initial product

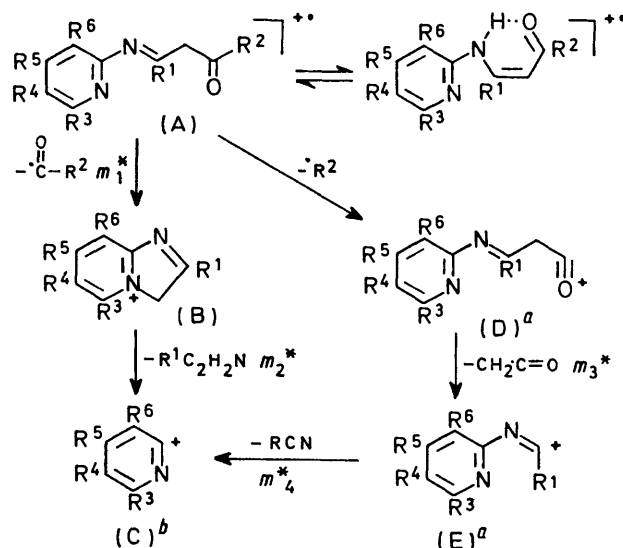
TABLE I  
Mass spectra of 2-(2-acylvinylamino)pyridines

	(A)		(B)		(C)		(D)		(E)		$m_1^*$	$m_2^*$	$m_3^*$	$m_4^*$
	$m/e$	%	$m/e$	%	$m/e$	%	$m/e$	%	$m/e$	%				
(39)	162	13.6	119	100	78	67.5	147	12.7	105	16.4	87.5	51.1	75.0	57.9
(40)	176	12.5	133	100	92	46.7	161	9.9	119	5.6	100.5	63.7	88.0	71.1
(41)	176	11.1	133	100	78	36.8	161	4.5	119	15.7	100.6	45.7	88.0	51.1
(42)	190	7.1	147	100	92	34.6	175	5.2	133	14.4	113.7	57.6	101.1	63.6
(43)	204	5.1	161	100	106	2.08	189	3.9	147	17.7	127.0	69.9	114.3	76.5
(44)	176	7.9	147	100	92	22.9	175	3.1	133	3.3	123.0	57.6		63.7

and not 2-(2-acetylvinylamino)-6-methylpyridine (40), which was the product of direct condensation of 2-amino-6-methylpyridine (5) with 4,4-dimethoxybutan-2-one (11). That the products (40) and (44) were not identical was seen from comparison of their i.r. spectra. More detailed study by  $^1\text{H}$  n.m.r. showed the presence of an aldehydic proton in (44) but not in (40). The mass spectrum of (44) showed a base peak at  $M - 29$ , indicating the loss of a formyl group and that of (40) showed a base peak at  $M - 43$  indicating loss of an acetyl group (see Table I and Scheme). Treatment of (44) with perchloric acid in ether-methanol gave an immediate precipitate of the pyrido[1,2-*a*]pyrimidinium perchlorate (26) in excellent yield, but similar treatment of the derivative (40) yielded only 2-(2-acetylvinylamino)pyridine perchlorate.

Singh, Taneja, and Narang<sup>12</sup> have claimed that 2,4,5-trimethyl-1,8-naphthyridine (46) is obtained by the action of pentane-2,4-dione (10) on 2-amino-4-methylpyridine (3) in the presence of phosphoric acid at 100°, and subsequent treatment with base. The formation of a naphthyridine under these conditions appeared unlikely on steric grounds, and we repeated the reaction. Under the stated conditions the sole product which we

(42) with picric acid gave a yellow picrate, m.p. 164–165 °C, which proved to be 2,4,8-trimethylpyrido[1,2-*a*]-



SCHEME

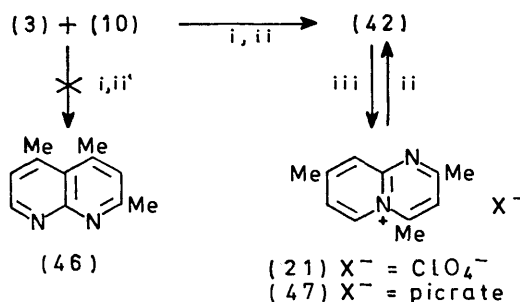
<sup>a</sup> For alternative bicyclic structures see T. Kato, H. Yamataka, N. Katagiri, and S. Masuda, *Chem. and Pharm. Bull. (Japan)*, 1972, **20**, 142. <sup>b</sup> Possibility of azatropylium structure when methyl substituent present.

pyrimidinium picrate (47) and not the isomeric 1,8-naphthyridine picrate.

#### EXPERIMENTAL

I.r. spectra were measured for Nujol mulls, on a Unicam SP 200 spectrometer.  $^1\text{H}$  N.m.r. spectra were recorded on Varian A-60A (internal Me<sub>4</sub>Si standard) and HA100 (external Me<sub>4</sub>Si lock standard) spectrometers. Mass spectra were recorded on an A.E.I. MS9 instrument, operating at 70 eV. M.p.s were determined on an Electrothermal apparatus and microanalyses were carried out by Dr. Strauss, Microanalytical Labs., Oxford.

*Pyrido[1,2-*a*]pyrimidinium Salts. General Method.*—The 2-aminopyridine (1 g) and an equimolar quantity of the appropriate β-dicarbonyl compound, or its acetal, were dissolved in methanol (5 cm<sup>3</sup>), 60% perchloric acid (2 cm<sup>3</sup>) was added, and the mixture was stirred at room temperature for 15–18 h. In most cases a precipitate separated. Sufficient diethyl ether was added to complete



Reagents: i, heat, H<sub>3</sub>PO<sub>4</sub>; ii, NaOH; iii, HX.

isolated was a pale yellow oil, identified as 2-(2-acetylvinylamino)-4-methylpyridine (42), presumably formed by basic ring opening of an intermediate pyrido[1,2-*a*]pyrimidinium phosphate, which we were unable to isolate. The same compound was obtained by treat-

<sup>12</sup> S. Singh, R. S. Taneja, and K. S. Narang, *Indian J. Chem.*, 1968, **6**, 11.

TABLE 2  
<sup>1</sup>H N.m.r.<sup>a</sup> spectra of pyrido[1,2-*a*]pyrimidinium perchlorate

	Ring protons														Other protons <sup>b</sup> ( $\tau$ values)	
	$\tau$ Values							$J$ /Hz								
	2-H	4-H	6-H	8-H	9-H	3-H	7-H	2,3	3,4	2,4	6,7	7,8	6,8	8,9		7,9
(13) <sup>c</sup>	0.37—0.59		0.83	(1.21—1.44)	(1.64—1.96)	n.r. <sup>d</sup>	n.r.	n.r.	ca. 7	n.r.	n.r.	n.r.	n.r.	n.r.		
(14) <sup>e</sup>	0.55	Me	0.75	(1.18—1.38)	1.87	1.69	5.0		7.4	n.r.	n.r.	n.r.	n.r.	n.r.	6.78	
(15) <sup>e</sup>	Me	Me	0.87	(1.25—1.55)	2.02	1.83			7.0	n.r.	n.r.	n.r.	n.r.	n.r.	7.02, 6.87	
(16) <sup>f,g</sup>	0.61	0.79	1.21	1.64	Me	2.05	2.09	4.2	6.9	1.7	6.5	7.7	ca. 0		7.11	
(17)	0.60	Me	0.99	1.49	Me	2.03	1.92	4.5			7.3	8.0	n.r. <sup>h</sup>		6.99, 6.82	
(18) <sup>f</sup>	Me	Me	1.48	1.97	Me	2.51	2.40				7.0	7.0	ca. 1		7.42, 7.42, 7.28	
(19) <sup>f,g</sup>	0.61	0.74	1.11	Me	1.67	2.05	2.05	4.0	7.0	1.5	6.8			ca. 0	7.22	
(20)	0.58	Me	0.88	Me	1.49	1.96	1.85	4.0			7.0			ca. 0	7.11, 6.81	
(21)	Me	Me	0.93	Me	1.55	2.08	1.91				7.5			ca. 0	7.15, 7.00, 6.87	
(22) <sup>f,g</sup>	0.61	0.73	1.14	1.54	1.54	1.96	Me	4.5	7.0	1.5			ca. 1	0.0	7.32	
(23)	0.62	Me	0.99	1.41	1.41	1.91	Me	4.5					ca. 0	0.0	7.18, 6.80	
(24)	Me	Me	1.07	1.44	1.44	2.05	Me						ca. 1	0.0	7.22, 6.97, 6.83	
(24) <sup>i</sup>	(0.33—0.50)		Me	(1.25—1.45)	(1.61—1.86)	n.r.	n.r.	n.r.				n.r.	n.r.	n.r.	n.r.	6.82
(26) <sup>f,g</sup>	Me	0.68	Me	1.48	1.53	1.95	2.03				7.4			8.8	1.6	6.91, 6.87
(27) <sup>i</sup>	(0.33—0.50)		Et	(1.12—1.49)	(1.66—1.91)	n.r.	n.r.	n.r.				n.r.	n.r.	n.r.	n.r.	Et 8.37(t), 6.50(q)
(28) <sup>f,g</sup>	Me	1.19	Et	1.88	2.00	2.42	2.45				7.5			8.8	1.3	7.43, Et 8.88(t), 7.03(q)
(29) <sup>i</sup>	(0.37—0.48)		Pr	(1.15—1.50)	(1.66—1.92)	n.r.	n.r.	n.r.				n.r.	n.r.	n.r.	n.r.	Pr 8.80(t), 7.99(m)
(30) <sup>f,g</sup>	Me	0.74	Pr	1.49	1.60	1.91	2.05			7.3				8.8	1.3	7.02, Pr 8.86(t), 8.07(m), 6.64(t)
(31) <sup>f,g</sup>	0.63	0.83	1.36	1.74	Me	2.04	Me	4.1	7.0	1.5			ca. 0		7.40, 7.17	
(32)	0.58	Me	1.13	1.56	Me	1.95	Me	4.0					ca. 1		7.23, 7.02, 6.82	
(33)	Me	Me	1.26	1.65	Me	2.12	Me						ca. 0		7.30, 7.07, 7.03, 6.90	
(34) <sup>g</sup>	0.46	0.56	Me	1.49	Et	1.84	1.97	4.4	7.6	1.8				8.3	6.91, Et 8.55(t), 6.56(q)	
(35)	Me	0.78	Me	1.65	Et	2.02	2.14				7.5			7.5	6.99, 6.99, Et 8.55(t), 6.59(q)	

<sup>a</sup> Recorded at 60 MHz; solvent CF<sub>3</sub>·CO<sub>2</sub>H unless otherwise stated. <sup>b</sup> Singlet methyl groups, unless otherwise stated. <sup>c</sup> Includes ABMX and ABX spectra, where X regions overlap. <sup>d</sup> n.r. = Not resolvable. <sup>e</sup> Includes ABMX spectrum. <sup>f</sup> Recorded at 100 MHz; solvent CF<sub>3</sub>·CO<sub>2</sub>H. <sup>g</sup> Includes ABX spectrum, calculated according to C. N. Banwell, in 'Nuclear Magnetic Resonance for Organic Chemists,' ed. D. W. Mathieson, Academic Press, London, 1967, p. 85. <sup>h</sup> 6-H and 8-H are broad doublets. <sup>i</sup> Includes 2 ABX systems, where X regions overlap.

TABLE 3  
 Pyrido[1,2-*a*]pyrimidinium perchlorates and bromides

	M.p. (°C)	Yield <sup>a</sup> (%)	Formula	Found (%)			Calc. (%)		
				C	H	N	C	H	N
(13) <sup>b,c</sup>	216 *	90.0	C <sub>8</sub> H <sub>7</sub> ClN <sub>2</sub> O <sub>4</sub>	42.0	3.2	12.0	41.65	3.0	12.5
(14) <sup>d</sup>	232—233 *	66.7, 92.8 <sup>e</sup>	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>4</sub>	44.2	3.8	11.3	44.3	3.7	11.5
(15) <sup>b,c</sup>	228—230 *	85.3, 88.5 <sup>e</sup>	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.3	4.3	10.6	46.4	4.3	10.8
(16) <sup>e</sup>	156—158	95.0	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>4</sub>	44.4	3.9	11.4	44.3	3.7	11.5
(18) <sup>e</sup>	167—169	91.5	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.7	4.9	10.35	48.4	4.8	10.3
(19) <sup>e</sup>	191—193 *	91.1	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>4</sub>	44.0	3.7	11.4	44.3	3.7	11.5
(21) <sup>e</sup>	190—191	83.2, 90.6 <sup>e</sup>	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.3	4.7	10.4	48.4	4.8	10.3
(25) <sup>e</sup>	224—225 *	79.5	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>4</sub>	44.4	3.8	11.5	44.3	3.7	11.5
							Required (%)		
(17)	185—186 *	46.0	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.3	4.2	10.7	46.4	4.3	10.8
(20)	188—190	43.3	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.2	4.2	10.75	46.4	4.3	10.8
(22)	183—185	48.6	C <sub>9</sub> H <sub>9</sub> ClN <sub>2</sub> O <sub>4</sub>	44.0	3.7	11.2	44.3	3.7	11.5
(23)	196—199 *	79.4	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.6	4.3	10.8	46.4	4.3	10.8
(24)	226—227 *	68.2	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.7	4.9	10.3	48.4	4.8	10.3
(26)	224—226 *	66.8, 95.3 <sup>e</sup>	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.1	4.4	10.85	46.4	4.3	10.8
(27)	187—190	42.5	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.3	4.45	10.6	46.4	4.3	10.8
(28)	194—195 *	33.6	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.1	5.0	10.0	48.4	4.8	10.3
(29)	143—144	79.9	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.3	4.9	10.1	48.4	4.8	10.3
(30)	103—105	23.7	C <sub>12</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>4</sub>	50.2	5.4	9.6	50.3	5.2	9.8
(31)	164—165	89.6	C <sub>10</sub> H <sub>11</sub> ClN <sub>2</sub> O <sub>4</sub>	46.3	4.3	10.6	46.4	4.3	10.8
(32)	162—163	82.8	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.2	4.8	10.1	48.4	4.8	10.3
(33)	141—142	86.0, 99.7 <sup>e</sup>	C <sub>12</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>4</sub>	50.5	5.5	9.6	50.3	5.2	9.8
(34)	192—195	88.6	C <sub>11</sub> H <sub>13</sub> ClN <sub>2</sub> O <sub>4</sub>	48.75	5.0	10.2	48.4	4.8	10.3
(35)	121—123	30.9	C <sub>12</sub> H <sub>15</sub> ClN <sub>2</sub> O <sub>4</sub>	50.2	5.4	9.5	50.3	5.2	9.8
(36)	268 *	83.3	C <sub>8</sub> H <sub>7</sub> BrN <sub>2</sub>	45.7	3.6	13.3	45.5	3.3	13.3
(37)	265—266 *	66.7	C <sub>10</sub> H <sub>11</sub> BrN <sub>2</sub>	50.3	4.7	11.7	50.2	4.6	11.7
(38)	ca. 292 <sup>f</sup>	83.3	C <sub>9</sub> H <sub>9</sub> BrN <sub>2</sub>	47.7	4.05	12.2	48.0	4.0	12.4

<sup>a</sup> Yield obtained by direct condensation. <sup>b</sup> Previously prepared.<sup>7</sup> <sup>c</sup> Previously prepared<sup>8</sup> but characterised on the basis of Cl analysis only. <sup>d</sup> Previously prepared.<sup>5,6</sup> <sup>e</sup> Yield obtained by treatment of the intermediate 2-(2-acylvinylamino)pyridine with perchloric acid. Melts only when placed in preheated m.p. apparatus.

precipitation of the *perchlorate* which was collected, recrystallised from methanol containing a few drops of perchloric acid, and dried at 50° *in vacuo* [perchlorates (13)—(15) and (17)—(35), Table 3]. By this general procedure 2-amino-3-methylpyridine and 1,1,3,3-tetramethoxypropane yielded an unidentified intermediate which was converted into the *perchlorate* (16) by heating under reflux in dimethyl sulphoxide for 10 min. The same salt was also obtained by the general procedure but with stirring for 5 h at 50°.

A similar procedure with 60% hydrobromic acid in place of the perchloric acid yielded the *bromides* (36)—(38), which were recrystallised from methanol containing a few drops of hydrobromic acid. The bromides were less stable than the perchlorates and tended to darken on recrystallisation or when kept at room temperature for several weeks.

I.r. spectra of all salts showed a strong absorption in the range 1650—1630  $\text{cm}^{-1}$  ( $\text{C}=\text{N}^+$ ); none showed NH bands. Perchlorates showed a very strong absorption at *ca.* 1100  $\text{cm}^{-1}$  ( $\text{ClO}_4^-$ ).

2-(2-Acetylvinyllamino)pyridine (39) was prepared by the method of Nesmeianov and Rybinskaia,<sup>5</sup> except that the mixture was refluxed in xylene overnight and not heated in a sealed tube at 140°. The *enaminone* (39) was isolated in 64.5% yield; m.p. 114—115° (lit.,<sup>5</sup> 61.3°; m.p. 121°) (Found: C, 66.3; H, 6.25; N, 17.3%;  $M^+$ , 162.079342. Calc. for  $\text{C}_9\text{H}_{10}\text{N}_2\text{O}$ : C, 66.7; H, 6.2; N, 17.3%;  $M$ , 162.079308),  $\nu_{\text{max}}$ . 3250 (NH), 1645 (C=O), 1600, 1565, and 1515  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CDCl}_3$ ; 60 MHz) —1.69br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 1.75br (1H, d, 6-H), 2.07 (1H, dd,  $J$  12.0 and 8.6 Hz, —NH—CH=CH—), 2.46 (1H, ddd, 4-H), 3.00—3.40 (2H, m, 3- and 5-H), 4.62 (1H, d,  $J$  8.6 Hz, —NH—CH=CH—), and 7.86 (3H, s, COMe) (3-H, 5-H, 4-H, and 6-H  $\equiv$  ABMX system; from first-order analysis  $J_{3,4}$  and  $J_{4,5}$  7.6 and 8.4,  $J_{4,6}$  1.8, and  $J_{5,6}$  6.0 Hz).

2-(2-Acetylvinyllamino)-6-methylpyridine (40).—Similar treatment of 6-amino-2-methylpyridine and 4,4-dimethoxybutan-2-one for 42 h yielded, after chromatography on neutral alumina with  $\text{CCl}_4\text{—CHCl}_3$  (60 : 40) as eluant, the *enaminone* (40) (55.2%), pale yellow needles, m.p. 85—87° (Found: C, 68.0; H, 6.75; N, 16.05%;  $M^+$ , 176.09451.  $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$  requires C, 68.2; H, 6.8; N, 15.9%;  $M$ , 176.094958),  $\nu_{\text{max}}$ . 3230 (NH), 1650 (C=O), 1600, 1570, and 1500  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CCl}_4$ ; 60 MHz) —1.61br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 2.09 (1H, dd,  $J$  12.2 and 8.6 Hz, —NH—CH=CH—), 2.63 [1H, t (deg. dd),  $J$  8.2 and 8.2 Hz, 4-H], 3.36 and 3.51 (2H, 2  $\times$  d,  $J$  8.2 and 8.2 Hz, 3- and 5-H), 4.74 (1H, d,  $J$  8.6 Hz, —NH—CH=CH—), 7.62 (3H, s, 6-Me), and 7.93 (3H, s, COMe) (first-order analysis for 3-H, 5-H, and 4-H, ABX system).

Ring Opening of the Pyrido[1,2-a]pyrimidinium Perchlorates.—The perchlorate was suspended in water, and an excess of 40% sodium hydroxide solution was added, in some cases a brightly coloured solution was obtained and in others a brown oil separated. The mixture was stirred for 5 min and extracted with  $\text{CCl}_4$ . The *enaminone* was purified by direct chromatography on a neutral, or basic, alumina column with elution by  $\text{CCl}_4$  or  $\text{CCl}_4\text{—CHCl}_3$ , as appropriate. The following products were thus obtained: 2-(2-acetyl-1-methylvinyllamino)-3,5-dimethylpyridine (43), needles, m.p. 89—91° [from light petroleum (b.p. 40—60°)] (Found: C, 70.4; H, 7.7; N, 13.6.  $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}$  requires C, 70.6; H, 7.8; N, 13.7%),  $\nu_{\text{max}}$ . 1630 (C=O), 1605, 1570, and 1500  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CCl}_4$ ; 60 MHz) —2.72br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 2.36br (1H, s, 6-H), 3.05br (1H, s, 4-H), 5.03

(1H, q,  $J$  0.5 Hz, —NH—CMe=CH—), 7.62 (3H, d,  $J$  0.5 Hz, —NH—CMe=CH—), 7.77 and 7.87 (6H, 2  $\times$  s, 3- and 5-Me), and 8.04 (3H, s, COMe); 2-(2-formyl-1-methylvinyllamino)-6-methylpyridine (44), pale yellow microprisms, m.p. 82.5—84° [from light petroleum (b.p. 30—40°) by evaporation; not chromatographed] (Found: C, 68.1; H, 6.8; N, 15.85%;  $M^+$ , 176.094862.  $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$  requires C, 68.2; H, 6.8; N, 15.9%;  $M$ , 176.094958),  $\nu_{\text{max}}$ . 3290 (NH), 1625 (C=O), 1605, 1585, and 1540  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CCl}_4$ ; 60 MHz) —2.76br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 0.91 (1H, d,  $J$  2.6 Hz, CHO), 2.52 [1H, t (deg. dd),  $J$  8.3 and 8.3 Hz, 4-H], 3.22br and 3.35br (2H, 2  $\times$  d,  $J$  8.3 and 8.3 Hz, 3- and 5-H), 4.85 (1H, dq,  $J$  2.6 and 0.5 Hz, —NH—CMe=CH—), 7.54 (3H, d,  $J$  0.5 Hz, —NH—CMe=CH—), and 7.57 (3H, s, 6-Me) (first-order analysis for 3-H, 5-H, and 4-H, ABX system); 2-(2-acetyl-1-methylvinyllamino)pyridine (41), pale yellow oil (lit.,<sup>13</sup> m.p. 36°, assigned imine-type structure) (Found: C, 67.8; H, 6.8; N, 15.9%;  $M^+$ , 176.094686.  $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$  requires C, 68.2; H, 6.8; N, 15.9%;  $M$ , 176.094958),  $\nu_{\text{max}}$ . 3200 (NH), 1625 (C=O), 1595, 1570, and 1505  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CCl}_4$ ; 60 MHz) —2.91br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 1.82 (1H, m, 6-H), 2.51 (1H, ddd, 4-H), 3.10—3.32 (2H, m, 3- and 5-H), 4.88 (1H, q,  $J$  0.6 Hz, —NH—CMe=CH—), 7.58 (3H, d,  $J$  0.6 Hz, —NH—CMe=CH—), and 8.0 (3H, s, COMe) (first-order analysis for 3-H, 5-H, 4-H, and 6-H, ABMX system); 2-(2-acetyl-1-methylvinyllamino)-4-methylpyridine (42), pale yellow oil (Found: C, 69.5; H, 7.4; N, 14.8%;  $M^+$ , 190.109389.  $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}$  requires C, 69.5; H, 7.4; N, 14.7%;  $M$ , 190.110607),  $\nu_{\text{max}}$ . 1625 (C=O), 1605, 1560, and 1505  $\text{cm}^{-1}$ ,  $\tau$  ( $\text{CCl}_4$ ; 60 MHz) —2.69br (1H, s, exchanges  $\text{D}_2\text{O}$ , NH), 1.97 (1H, dd,  $J$  5.1 and 0.8 Hz, 6-H), 3.36br (2H, d, 3- and 5-H), 4.90 (1H, q,  $J$  0.6 Hz, —NH—CMe=CH—), 7.58 (3H, d,  $J$  0.6 Hz, —NH—CMe=CH—), 7.75 (3H, s, 4-Me), and 8.0 (3H, s, COMe) (first-order analysis for 3-H, 5-H, and 6-H, ABX system).

Treatment of 2-amino-4-methylpyridine (5 g) with pentane-2,4-dione (5  $\text{cm}^3$ ) and phosphoric acid, followed by sodium hydroxide, under the conditions described by Singh, Taneja, and Narang,<sup>12</sup> gave, after chromatography on basic alumina, a pale yellow oil (7.1 g, 80.5%), i.r. and  $^1\text{H}$  n.m.r. spectra identical with those of the *enaminone* (42). Cyclisation of the oil as described below yielded 2,4,8-trimethylpyrido[1,2-a]pyrimidinium perchlorate. Treatment with picric acid yielded the 2,4,8-trimethylpyrido[1,2-a]pyrimidinium picrate (47), yellow needles (from ethanol, m.p. 164—165°) (Found: C, 50.9; H, 3.8; N, 17.65.  $\text{C}_{17}\text{H}_{15}\text{N}_5\text{O}_7$  requires C, 50.9; H, 3.7; N, 17.5%),  $\tau$  [ $(\text{CD}_3)_2\text{SO}$ ; 60 MHz] 0.63 (1H, d,  $J$  7.5 Hz, 6-H), 1.27 (2H, s, picryl protons), 1.56 (1H, d,  $J$  2.0 Hz, 9-H), 1.77 (1H, dd,  $J$  7.5 and 2.0 Hz, 7-H), 1.79 (1H, s, 3-H), and 6.80, 7.02, and 7.07 (9H, 3  $\times$  s, 2-, 4-, and 8-Me).

Cyclisation of 2-(2-Acylvinyllamino)pyridines.—The 2-(2-acylvinyllamino)pyridine [(39), (41)—(44)] (0.1 g) was dissolved in ether (100  $\text{cm}^3$ ) and methanol (2  $\text{cm}^3$ ) and stirred during the addition of 60% perchloric acid (0.2  $\text{cm}^3$ ). The solution immediately went milky and then cleared as the perchlorate [(14), (15), (21), (33), (26)] coagulated. When washed with ether and dried, the salts (Table 3) had m.p.s and i.r. spectra identical with those of the samples prepared directly from the 2-aminopyridines.

Similar treatment of 2-(2-acetylvinyllamino)-6-methylpyridine (40) yielded only the *perchloric acid salt* of (40)

<sup>13</sup> A. S. Kudryavtsev and I. A. Savich, *J. Gen. Chem. (U.S.S.R.)* 1963, **33**, 1321.

(95.5%), m.p. 139—141° (decomp.) (Found: C, 43.4; H, 4.9; Cl, 12.6; N, 9.9.  $C_{10}H_{13}ClN_2O_5$  requires C, 43.4; H, 4.7; Cl, 12.8; N, 10.1%),  $\nu_{\max}$ . 3300, 3180 (NH), 1640 (C=O), 1595, 1545, and 1520  $cm^{-1}$ .

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