

REDUCTION OF 1-ALKYLPYRIDINIUM HALIDES WITH SODIUM ALUMINUM HYDRIDE*

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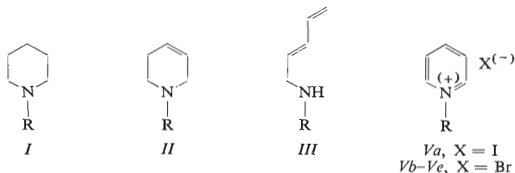
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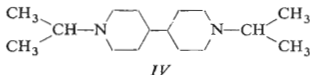
On reduction of 1-alkylpyridinium halides with sodium aluminum hydride 1-alkylpiperidines, 1-alkyl-3-piperidineins, and *trans*-5-alkylamino-1,3-pentadienes are formed.

In a preceding communication¹ we demonstrated that on reduction of methiodides of pyridine and some its homologues with sodium aluminum hydride the products of the cleavage of the pyridine ring – 5-alkylamino-1,3-pentadienes (*III*) – are formed in addition to the usual reduction products – 1-alkylpiperidines (*I*) and 1-alkyl-3-piperidineins (*II*).

In this paper we follow the effect of the alkyl group on the course of the reduction of 1-alkylpyridinium halogenides with sodium aluminum hydride. For this purpose we investigated the reductions of 1-ethylpyridinium iodide, 1-propylpyridinium bromide, and 1-pentylpyridinium bromide. In all instances we isolated in addition to



In formulae *I–III, V*: *a*, R = C₂H₅; *b*, R = n-C₃H₇; *c*, R = i-C₃H₇; *d*, R = n-C₄H₉; *e*, R = n-C₅H₁₁.



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a small amount of the corresponding 1-alkylpiperidine also 1-alkyl-3-piperideine and, similarly as in the cases described¹, also products of pyridine ring cleavage. These were identified on the basis of analyses, IR and PMR spectra as *trans*-5-alkyl-amino-1,3-pentadienes (*III*). It was observed that with increasing alkyl group on nitrogen the fraction of 5-alkylamino-1,3-pentadienes (*III*) decreased, while the amount of 1-alkyl-3-piperideines (*II*) increased. The proportion of 1-alkylpiperidines (*I*) in the reaction mixture was roughly constant. The achieved results show that in the set of the quaternary salts which were reduced only 1-methylpyridinium iodide¹ is suitable for the preparation of dienylamine *III*. For comparison we prepared 1-alkyl-3-piperideines by reduction of the corresponding quaternary pyridinium salt with so-

TABLE I
Reduction of 1-Alkylpyridinium Halogenides with Sodium Aluminum Hydride

Quaternary salt	Relative proportion of components, %		
	<i>I</i>	<i>II</i>	<i>III</i>
<i>Va</i>	1 ^a	39	60
<i>Vb</i>	1 ^b	56	43
<i>Vc</i>	3 ^b	51	46
<i>Vd</i>	1 ^c	55	44
<i>Ve</i>	1 ^b	62	37

^a Preparation see⁷; ^b preparation described in this paper; ^c prepared by Leuckart-Wallach reaction of piperidine with butyraldehyde⁶ (yield 62%).

TABLE II
PMR Spectra of *trans*-5-Alkylamino-1,3-pentadienes

Com- pound	CH_3CH_2 (t; $J = 7$ Hz)	$\text{CH}_3(\text{CH}_2)_n\text{CH}_2$ (m)	NH (s)	$\text{CH}_3(\text{CH}_2)_n\text{CH}_2\text{N}$ (t; $J = 7$ Hz)	$=\text{CHCH}_2\text{N}$ (d; $J = 7$ Hz)	$\text{CH}_2=\text{CHCH}=\text{CH}$ (m)
<i>IIIa</i>	1.12	—	2.09	—	3.43	5.02—6.84
<i>IIIb</i>	0.92	1.2—1.7	1.65	2.59	3.39	4.93—6.90
<i>IIIc</i>	—	—	1.22	—	3.41	5.04—6.86 ^a
<i>III d</i>	0.93	1.1—1.7	2.22	2.63	3.43	5.0—6.86
<i>III e</i>	0.90	1.1—1.7	1.3	2.61	3.43	5.03—6.85

^a $-\text{CH}(\text{CH}_3)_2$ 1.08 (d; $J = 6$ Hz), $(\text{CH}_3)_2\text{CH}-\text{N}$ 2.70—2.99 (m).

dium borohydride. Thus we obtained 1-propyl-3-piperideine (*IIb*), 1-isopropyl-3-piperideine (*IIc*), 1-butyl-3-piperideine (*II d*), and 1-pentyl-3-piperideine (*IIe*). 1-Propylpiperidine (*Ib*) was prepared from piperidine and ethyl propionate on reduction with sodium bis(2-methoxyethoxy)dihydroaluminat. A similar method of synthesis of 1-alkylpiperidines described with lithium aluminum hydride² has not so far appeared with this hydride reagent in the literature. In connection with the preparation of 1-isopropylpiperidine we carried out electrolytic reduction of 1-isopropylpyridinium bromide. From this reaction we isolated in addition to 1-isopropylpiperidine (*Ic*) and 1-isopropyl-3-piperideine (*IIc*) also another crystalline substance

TABLE III
PMR Spectra of 1-Alkyl-3-piperideines

Com- pound	CH_3CH_2 (t; $J = 7$ Hz)	$\text{CH}_3(\text{CH}_2)_n\text{CH}_2$ (m)	$\begin{array}{c} =\text{CHCH}_2\text{CH}_2 \\ \text{N}-\text{CH}_2-\text{R} \\ \text{(m)} \end{array}$	$=\text{CH}-\text{CH}_2\text{N}$ (q; $J = 7$ Hz)	$-\text{CH}=\text{CH}-$ (m)
<i>IIb</i>	0.91	—	1.94—2.74	2.96	5.50—5.90 ^a
<i>IIc</i>	—	—	—	3.03	5.52—5.90 ^b
<i>II d</i>	0.93	1.1—1.7	2.04—2.70	2.95	5.53—5.90
<i>IIe</i>	0.91	1.1—1.68	1.98—2.75	2.93	5.50—5.87

^a $\text{CH}_3\text{CH}_2\text{CH}_2$ 1.55 (sex; $J = 7$ Hz); ^b $(\text{CH}_3)_2\text{CH}$ 1.07 (d; $J = 6$ Hz), $=\text{CH}-\text{CH}_2\text{CH}_2$ 2.16 to 2.25 (m), $\text{N}-\text{CH}_2\text{CH}_2$ 2.3—2.92 (m).

TABLE IV
1-Alkyl-3-piperideines

Com- pound	B.p., °C/Torr	Formula (mol.w.)	Calculated/Found		
			% C	% H	% N
<i>IIb</i>	41.5/10	$\text{C}_8\text{H}_{15}\text{N}$ (125.2)	76.73	12.08	11.19
			77.10	12.25	10.99
<i>IIc</i>	156/747	$\text{C}_8\text{H}_{15}\text{N}$ (125.2)	76.73	12.08	11.19
			76.66	12.12	11.23
<i>II d</i>	62/10	$\text{C}_9\text{H}_{17}\text{N}$ (139.2)	77.63	12.31	10.06
			77.41	12.60	10.23 ^a

^a *IIe* see Experimental.

TABLE V
trans-5-Alkylamino-1,3-pentadienes

Substance	B.p., °C/Torr	Formula (mol.w.)	Calculated/Found		
			% C	% H	% N
<i>IIIa</i>	46.5/12	C ₇ H ₁₃ N (111.2)	75.62	11.78	12.60 ^a
			75.61	11.69	12.58
<i>IIIb</i>	52.5/8	C ₈ H ₁₅ N (125.2)	76.73	12.08	11.19
			76.68	12.06	11.40
<i>IIIc</i>	40.5/7	C ₈ H ₁₅ N (125.2)	76.73	12.08	11.19
			76.62	12.20	11.34
<i>III'd</i>	70/10	C ₉ H ₁₇ N (139.2)	77.63	12.31	10.06
			77.63	12.52	10.28 ^b

^a IR Spectrum: *trans*-R—CH=CH—R 970 cm⁻¹; UV spectrum: λ 215 nm, ε 21 800; ^b *IIIe* see Experimental.

to which we assign the structure of 1,1'-diisopropyl-4,4'-bipiperidyl (*IV*) on the basis of its analysis and spectral evidence.

EXPERIMENTAL

Gas chromatography was carried out on a Chrom 2 apparatus with FID, column length 170 cm, diameter 6 mm, stationary phase 20% Tridox on Celite, carrier gas nitrogen. Preparative gas chromatography was carried out on a non-commercial apparatus³, column length 165 cm, diameter 15 mm, carrier gas nitrogen. The PMR spectra were measured on Varian XL-100-15 (100 Mc) in deuteriochloroform with tetramethylsilane as internal standard the IR spectra on a UR-10 Zeiss Jena spectrophotometer, in chloroform. The UV spectra were recorded with an Optica Milano CS 4 NI apparatus, in methanol. The mass spectra were taken with a Gas Chromatograph-Mass Spectrometer LKB 9000. The melting points and the boiling points are uncorrected.

Reduction of 1-Pentylpyridinium Bromide

a) Reduction with sodium aluminum hydride: To a mixture of 6.1 g (0.11 mol) of sodium aluminum hydride in 220 ml of tetrahydrofuran 1-pentylpyridinium bromide (17.25 g; 0.075 mol; obtained as a syrupy product by refluxing of a methanolic pyridine solution with a calculated amount of pentyl bromide for 20 hours) was added under stirring and the mixture refluxed for 10 hours. After decomposition with 200 ml of dilute hydrochloric acid (1 : 3) tetrahydrofuran was distilled off and the reaction mixture alkalisied and steam distilled. After conventional working up a product was obtained of b.p. 37–82°C/10 Torr, 2 g. Using gas chromatography the following products were identified: 1-pentylpiperidine (*Ie*, 1%), 1-pentyl-3-piperideine (*IIf*, 61%) and 5-pentylamino-1,3-pentadiene (*IIIe*, 38%). The two last mentioned components were isolated by preparative gas chromatography. 1-Pentyl-3-piperideine (*IIf*), b.p. 70°C/10 Torr was identical with the product of reduction of 1-pentylpyridinium bromide (*Ve*) with sodium borohydride

(see below). For the reduction of other 1-alkylpyridinium halogenides see Table I. 5-Pentylamino-1,3-pentadiene (*IIIe*), b.p. 74°C/10 Torr (PMR spectrum see Table II). IR (cm^{-1}): 960 (s) for *trans* R—CH=CH—R, 910 (s) for —CH=CH₂. For C₁₀H₁₉N (153.3) calculated: 78.37% C, 12.49% H, 9.14% N; found: 78.54% C, 12.44% H, 9.07% N.

b) *Reduction with sodium borohydride*: A solution of 11.5 g (0.05 mol) of 1-pentylpyridinium bromide (*Ve*) in 50 ml of water was mixed with 50 ml of 1M-NaOH and after addition of a freshly prepared solution of 2.5 g (0.066 mol) of NaBH₄ in 25 ml of water the mixture was steam distilled. The conventional working up of the distillate afforded 3.25 g of a base, b.p. 28–81°C/10 Torr. Gas chromatography of the mixture indicated: 1-pentylpiperidine (*Ie*, 4%) and 1-pentyl-3-piperidine (*Iie*, 9%) which was isolated (GLC), b.p. 70°C/10 Torr, PMR spectrum in Table III. For C₁₀H₁₉N (153.3) calculated: 78.37% C, 12.49% H, 9.14% N; found: 78.34% C, 12.73% H, 9.13% N. The data on other 1-alkyl-3-piperidines are given in Table IV and the data on 5-alkylamino-1,3-pentadienes in Table V.

1-Pentylpiperidine (*Ie*)

To a suspension of 8.1 g (0.15 mol) of sodium aluminum hydride in 250 ml of tetrahydrofuran a solution of 8.4 g (0.1 mol) of piperidine in 25 ml of tetrahydrofuran was added dropwise under stirring and the mixture refluxed under stirring for 30 minutes. A solution of 13 g (0.1 mol) of ethyl valerate in 25 ml of tetrahydrofuran was then added dropwise over 45 minutes and the mixture refluxed for 15 hours. The reaction mixture was decomposed with 130 ml of hydrochloric acid (1 : 1), alkalisied and worked up in the conventional manner, b.p. 74°3/7 Torr, yield 8.3 g (53.5%). Literature⁴ gives for 1-pentylpiperidine b.p. 196°C/769 Torr. For C₁₀H₂₁N (155.3) calculated: 77.35% C, 13.63% H, 9.02% N; found: 77.43% C, 13.47% H, 9.09% N.

1-Propylpiperidine (*Ib*)

To 59 g (0.2 mol) of a 80% benzene solution of sodium bis(2-methoxyethoxy)-dihydroaluminat a mixture of 4.25 g (0.05 mol) of piperidine and 5.1 g (0.05 mol) of ethyl propionate in 50 ml benzene was added and the mixture refluxed under stirring for 15 hours. The usual work-up gave 3.3 g of product, b.p. 20–40°C/10 Torr. Gas chromatography indicated the presence of piperidine (20%), which was eliminated using Hinsberg's procedure. Thus 1 g (16%) of product was obtained, b.p. 40°C/10 Torr. Literature⁵ gives for 1-propylpiperidine b.p. 149–150°C. For C₈H₁₇N (127.2) calculated: 75.52% C, 13.47% H, 11.01% N; found: 75.68% C, 13.65% H, 11.16% N.

Electrolytic Reduction of 1-Isopropylpyridinium Bromide (*Vc*)

A solution of 15.1 g (0.075 mol) of the quaternary salt in 200 ml of 20% sulfuric acid was reduced electrolytically on lead electrodes (5 A/hour) for 5 hours. The filtered catholyte was alkalisied and steam distilled. Applying the conventional procedure a product was obtained, b.p. 25 to 42°C/8 Torr, 3.5 g. On steam distillation a substance was obtained, m.p. 77–82°C which took moisture from the air and turned yellow; *m/e* 252. For C₁₆H₃₂N₂ (252.4) calculated: 76.12% C, 12.78% H, 11.10% N; found: 76.11% C, 12.65% H, 10.96% N. PMR spectrum (δ -values): —CH(CH₃)₂ 1.06 (d, *J* = 6 Hz), CH_{2ax} and CH_{3ax} 0.9–1.5 (m), —CH_{2ax} and CH_{2eq} 1.5 to 2.3 (m), CH(CH₃)_{2eq} 2.3–3.1 (m). High m.p. and the PMR spectrum indicated 1,1'-diisopropyl-4,4'-bipiperidyl (*IV*). By gas chromatography of the liquid product two components were identified on comparison with standards: 1-isopropylpiperidine (*Ic*, 82.5%) and 1-isopropyl-3-piperidine (*Iic*, 17.5%).

1-Isopropylpiperidine (*Ic*)

Hydrogenation on platinum oxide of a mixture of hydrochlorides of the bases from the preceding experiment (water as solvent) gave a product of b.p. 43–44°C/12 Torr; literature⁵ gives b.p. 149–150°C/757 Torr. For $C_8H_{17}N$ (127.2) calculated: 75.52% C, 13.47% H, 11.01% N; found: 75.74% C, 13.57% H, 11.07% N.

Elemental analyses were carried out in the analytical laboratory of our department, the PMR spectra were measured by Dr P. Trška, the mass spectra under the guidance of Dr V. Kubelka, and the IR spectra under the guidance of Dr P. Adámek.

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