

**REDUCTION OF 1,2-DIALKYLPIRIDINIUM IODIDE
WITH SODIUM ALUMINUM HYDRIDE***

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The reduction of 1,2-dialkylpyridinium iodides with sodium aluminium hydride gives a mixture of 1,2-dialkyl-3-piperidineines, 1,6-dialkyl-3-piperidineines and 1-alkylamino-*trans-trans*-2,4-alkadienes. For the sake of comparison the reductions of methiodides of 2-ethylpyridine, 2-propylpyridine and 2-isopropylpyridine were also carried out electrolytically. The reduction of the methiodide of 2-methylpyridine with sodium borohydride was repeated.

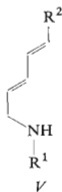
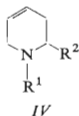
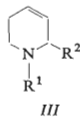
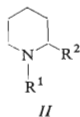
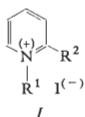
In preceding papers we studied the reductions of 1-alkylpyridinium iodides^{1,2}, 1,2-, 1,3-, 1,4-dimethylpyridinium iodides¹, 1,2,4-trimethylpyridinium iodide¹, and 1,2-dimethyl-5-ethylpyridinium iodide¹ with sodium aluminium hydride. In this paper we study the effect of the substituent in the position two on the ratio of the bases formed during the reductions of methiodides of 2-alkylpyridines. In all instances a mixture of 1,2-dialkylpiperidine (*II*), 1,2-dialkyl-3-piperidine (*III*) and 1,6-dialkyl-3-piperidine (*IV*) is formed. However, the main products of reduction are dienylamines *V* of *trans-trans* configuration. The formation of these dienylamines was already observed during the reductions of quaternary pyridinium salts with aluminium hydride³, lithium aluminium hydride⁴ and sodium aluminium hydride¹. While the alkyl group on the nitrogen atom affects the content of dienylamine in the reaction mixture quite appreciably² (with increasing length, or branching of the alkyl the amount of dienylamine decreases), the increase in the alkyl length in the position two of the series methyl, ethyl, propyl, isopropyl did not practically affect the amount of dienylamine in the mixture. The substitution of the methyl group for the ethyl group on the nitrogen atom when compared with one of the reduction of the methiodide and ethiodide of 2-methylpyridine leads to a decrease in dienylamine content, in agreement with the results of the reductions of 1-alkylpyridinium iodides². The dienylamine content is also affected by the ratio of the quaternary salt and the reducing agent. The highest yields of dienylamine were achieved when the molar ratio of the quaternary salt to sodium aluminium hydride was 1 : 2. We could observe

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this effect earlier during the reductions with aluminum hydride⁵, lithium aluminum hydride⁵ and sodium aluminum hydride⁶.

As said before, in addition to diethylamine *V* 1,6-dialkyl-3-piperideines (*IV*) and 1,2-dialkyl-3-piperideines (*III*) are also formed as unsaturated bases. In the mentioned series of reductions the content of 1,6-dialkyl-3-piperideine (*IV*) in the reaction mixture decreases with increasing substituent in the position two. The determination of a more accurate content of the isomeric 1,2-dialkyl-3-piperideine *III* is made more difficult in the case of the reduction of methiodides of 2-ethyl-, 2-propyl-, and 2-isopropylpyridine, due to a larger or smaller superimposition of the chromatographic peaks of 1,2-dialkylpiperidine *II* and 1,2-dialkyl-3-piperideine *III*. 1-Methyl-2-ethyl-3-piperideine (*IIIc*), 1-methyl-2-propyl-3-piperideine (*III d*) and 1-methyl-2-isopropyl-3-piperideine (*III e*) were isolated by repeated preparative gas chromatography from analogous reductions of methiodides with sodium borohydride^{7,8}.

After reduction of ethiodide of 2-methylpyridine (*Ib*) we were unable to isolate pure 1-ethyl-2-methyl-3-piperideine (*III b*) by preparative gas chromatography. Its structure was assigned on the basis of the following data. Its mass spectrum contains the signals M 125, $M-15$ (100%). Hydrogenation of its mixture with 1-ethyl-6-methyl-3-piperideine (*IV b*) gave pure 1-ethyl-2-methylpiperidine (*II b*). In GLC analysis the peak of this substance appears between the peak belonging to 1-ethyl-6-methyl-



- In formulae *I-Va*; $R^1 = R^2 = \text{CH}_3$
b; $R^1 = \text{C}_2\text{H}_5$, $R^2 = \text{CH}_3$
c; $R^1 = \text{CH}_3$, $R^2 = \text{C}_2\text{H}_5$
d; $R^1 = \text{CH}_3$, $R^2 = \text{CH}_3\text{CH}_2\text{CH}_2$
e; $R^1 = \text{CH}_3$, $R^2 = \begin{array}{l} \text{CH}_3 \\ \diagdown \\ \text{CH} \end{array}$

-3-piperideine (*IVb*) and 1-ethyl-2-methylpiperidine (*IIB*), which corresponds to the position of the chromatographic peaks of other 1,2-dialkyl-3-piperideines.

We also repeated the reduction of the methiodide of 2-methylpyridine (*Ia*) with sodium borohydride⁹. During this reduction 1,6-dimethyl-3-piperideine (*IVa*) is mainly formed, in addition to small amounts of 1,2-dimethylpiperidine (*IIa*) and 1,2-dimethyl-3-piperideine (*IIIa*). Electrolytic reductions of the methiodides of 2-ethylpyridine (*Ic*), 2-propylpyridine (*Id*) and 2-isopropylpyridine (*Ie*) also always give a mixture of three compounds – the saturated bases *II* and both isomeric 3-piperideines *III* and *IV*.

EXPERIMENTAL

Gas chromatography was carried out on a Chrom II apparatus (stationary phase 5% or 15% of Tridox on Chromaton NAW-HMDS, in some instances also Carbowax 20M, 1,2,3-tris(2-cyanoethoxy)propane, Reoplex), using nitrogen as carrier gas and FID. Preparative gas chromatography was carried out in an apparatus of non-commercial origin¹⁰ (stationary phase 7% of Tridox on porovina). The NMR spectra were measured on a Varian 100 instrument in deuteriochloroform, using tetramethylsilane as internal standard (δ values). The IR spectra were measured with a UR 10 Zeiss Jena spectrophotometer, in chloroform, and the mass spectra on a Gas Chromatograph – Mass Spectrometer LKB 9000.

Reduction of 1-Methyl-2-ethylpyridinium Iodide with Sodium Aluminum Hydride

Quaternary salt (18,7g, 0.075 mol) was added to a mixture of 6.1 g (0.113 mol) of sodium aluminum hydride and 300 ml of tetrahydrofuran and the mixture was refluxed for 10 hours. After decomposition with 75 ml of dilute hydrochloric acid (1 : 1) tetrahydrofuran was distilled off. The reaction mixture was alkalinized and the base steam-distilled. According to titration with hydrochloric acid the yield was 30%. From the solution of hydrochlorides, which were concentrated, bases were set free, dried over potassium hydroxide and distilled. Yield 1.3 g of a mixture of bases, b.p. 23–63°C/10 Torr.

TABLE I
List of Reductions Performed

Quaternary salt	B. p. °C/Torr	Yield %	<i>II</i> ^a	<i>III</i> ^a	<i>IV</i> ^a	<i>V</i> ^a
<i>Ia</i>	23–46/8	31.5	1 (11)	6 (12)	44 (13)	49 (1)
<i>Ib</i>	22.5–56/8	31.5	5 (14)	12	59 (15) ^b	24 ^b
<i>Ic</i>	23–63/10	30	13 (7, 16) ^{b,c}		33 (7)	50 ^b
<i>Id</i>	25–53/7	34	25 (7, 17, 18) ^{b,c}		30 (7)	45 ^b
<i>Ie</i>	40–62/8	25	26 (7, 19) ^c		19 (7)	49 ^b

^a The number of reference is in brackets; ^b see Table II. ^c Mixture of *II* and *III*.

Gas chromatography indicated three peaks. The first one, an asymmetric wave (13%), comprises a mixture of 1-methyl-2-ethylpiperidine (*Iic*) and 1-methyl-2-ethyl-3-piperideine⁷ (*IIic*), as it follows from a comparison with standards. The further component of the mixture is 1-methyl-6-ethyl-3-piperideine⁷ (*IVc*), and the substance with the longest elution time is 1-methylamino-2,4-heptadiene (*Vc*). Both last mentioned substances were isolated by preparative gas chromatography and their structure determined on the basis of NMR and IR spectroscopy (Table II, III).

Electrolytic Reduction of 1-Methyl-2-ethylpyridinium Iodide (*Ic*)

A solution of 18.7 g (0.075 mol) of *Ic* in 200 ml of 20% sulfuric acid was reduced in an electrolyser with lead electrodes (4 hours, 24 Ah). The catholyte was alkalinized with 40% sodium hydride and steam-distilled. After neutralization (22 ml 2.66M-HCl, yield 78%) the solution of hydrochlorides

TABLE II
List of Isolated Bases

Base Method ^a	B.p., °C/Torr lit. data	Formula (mol. w.)	Calculated/Found		
			% C	% H	% N
<i>Iib</i>	39/15	C ₈ H ₁₇ N	75.52	13.47	11.01
A + C	(147–148/760) ¹⁴	(127.2)	75.68	13.49	11.29
<i>Iic</i>	34/9	C ₈ H ₁₇ N	75.52	13.47	11.01
A + C	(150–151) ¹⁶ (148–149) ⁵	(127.2)	75.61	13.70	10.86
<i>Iid</i>	56.5/8	C ₉ H ₁₉ N	76.53	13.56	9.92
A + C	(175.5/760) ¹⁷ (65–66/10) ⁷ , (175.5) ¹⁸	(141.3)	76.75	13.50	9.75
<i>IVb</i>	39/7	C ₈ H ₁₅ N	76.74	12.08	11.19
B	(150–151) ¹⁵	(125.2)	77.02	12.22	11.35
<i>IVd</i>	57/8	C ₉ H ₁₇ N	77.63	12.30	10.06
B	(171–172) ⁷	(139.2)	77.70	12.55	10.35
<i>IVe</i>	54.5/10	C ₉ H ₁₇ N	77.63	12.30	10.06
B	(73–74/22) ⁷	(139.2)	77.70	12.31	10.35
<i>Vb</i>	64/8	C ₈ H ₁₅ N	76.74	12.08	11.19
B		(125.2)	76.73	12.32	11.25
<i>Vc</i>	60/8	C ₈ H ₁₅ N	76.74	12.08	11.19
B		(125.2)	76.73	12.26	11.23
<i>Vd</i>	66/10	C ₉ H ₁₇ N	77.63	12.30	10.06
B		(139.2)	77.42	12.45	10.09
<i>Ve</i>	66/10	C ₉ H ₁₇ N	77.63	12.30	10.06
B		(139.2)	77.65	12.31	10.25

^a A + C electrolytic reduction followed by hydrogenation; B reduction with sodium aluminum hydride

TABLE III

NMR and IR Spectra of Alkylaminoalkadienes (δ -values, cm^{-1})

Compound	$\text{=CH(CH}_2)_n\text{CH}_3$ t, $J = 7 \text{ Hz}$	NH s	NHCH_3 s	$\text{=CHCH}_2\text{N}$ d, $J = 7 \text{ Hz}$	CH= m	$\gamma(\text{CH})$ R-CH=CH-Q (trans)
Va^a	—	1.08	2.44	3.34	5.2–6.5	985, 960, 924
Vb^b	—	1.25	—	3.39	5.2–6.5	985, 950, 924
Vc^c	1.03 (n = 1)	1.20	2.45	3.35	5.2–6.5	985, 950
Vd^d	0.92 (n = 2)	1.39	2.46	3.36	5.2–6.5	985, 945
Ve^e	—	1.44	2.46	3.36	5.2–6.5	985, 945

a =CH-CH_3 1.78 (d, $J = 7 \text{ Hz}$); b NCH_2CH_3 1.13 (t, $J = 7 \text{ Hz}$), =CH-CH_3 1.79 (d, $J = 7 \text{ Hz}$), NCH_2CH_3 2.69 (q, $J = 7 \text{ Hz}$); c $\text{=CH-CH}_2\text{CH}_3$ 2.14 (m, $J = 7 \text{ Hz}$); d $\text{-CHCH}_2\text{CH}_3$ 1.44 (sext., $J = 7 \text{ Hz}$), $\text{CH}_2\text{CH}_2\text{CH}_3$ 2.10 (q, $J = 7 \text{ Hz}$); e $\text{-CH(CH}_3)_2$ 1.03 (d, $J = 6 \text{ Hz}$), $\text{CH(CH}_3)_2$ 2.1–2.6 (m).

was concentrated, the bases set free and dried. Distillation gave 5.4 g of bases, b.p. 24–43°C/7 Torr.

Analysis by gas chromatography indicated two peaks identical with the first two peaks of substances from the reduction of the same quaternary salt with sodium aluminum hydride. The first peak belongs to the mixture of 1-methyl-2-ethyl-3-piperidine (*IIIc*) and 1-methyl-2-ethylpiperidine (*IIC*). In the mentioned mixture base *IIC* prevails, as it follows from the NMR and the mass spectra and from the comparison with the standards⁷. The second substance, purified by preparative gas chromatography, was identified as 1-methyl-6-ethyl-3-piperidine⁷ (*IVc*).

An aqueous solution of hydrochlorides, prepared from 3 g of a mixture of bases, was hydrogenated on 0.17 g of Adams catalyst at atmospheric pressure and room temperature until the consumption of hydrogen ceased (260 ml). The catalyst was filtered off, the solution of hydrochlorides concentrated, the base separated, dried, and distilled. B.p. 34°C/7 Torr, yield 1.9 g of 1-methyl-2-ethylpiperidine (*IIC*) (Table II).

Other reductions were carried out in an analogous manner. The results of the reductions, boiling points, analyses, and spectral data are given in Tables I–III.

NMR Spectra (δ -values)

1-Ethyl-6-methyl-3-piperidine (*IVb*): >CHCH_3 1.05 (d, $J = 7 \text{ Hz}$), $\text{>NCH}_2\text{CH}_3$ 1.06 (t, $J = 7 \text{ Hz}$), $\text{=CHCH}_2\text{CHNCH}_2\text{-}$ 1.42–2.92 (m), $\text{=CHCH}_2\text{N}$ 2.94–3.28 (m), -CH=CH- 5.50–5.84 (m). 1-Methyl-6-propyl-3-piperidine (*IVd*): $\text{>CHCH}_2\text{CH}_3$ 0.93 (t, $J = 7 \text{ Hz}$), CHCH_2CH_3 1.07–1.68 (m), $\text{=CHCH}_2\text{CH<}$ 1.74–2.18 (m), NCH_3 2.34 (s), CHCH_2CH_3 (m) 2.18–2.64, $\text{=CHCH}_2\text{N}$ 2.74–3.34 (m), -CH=CH- 5.49–5.85 (m). 1-Methyl-6-isopropyl-3-piperidine (*IVe*): $\text{-CH(CH}_3)_2$ 0.94 (d, $J = 6 \text{ Hz}$), $\text{=CHCH}_2\text{CH<}$, $\text{-CH(CH}_3)_2$, CHCH_2CH_3 1.6–2.5 (m), >NCH_3 2.30 (s), $\text{=CHCH}_2\text{N}$ 2.78–3.40 (m), -CH=CH- 5.44–5.90 (m).

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