

STUDIES IN THE PYRIDINE SERIES. XLIII.*

REDUCTION OF QUATERNARY PYRIDINIUM SALTS
WITH SODIUM ALUMINIUM HYDRIDE AND SODIUM
BIS(2-METHOXYETHOXY)ALUMINIUM HYDRIDE

M. FERLES, A. ATTIA and A. ŠILHÁNKOVÁ

*Department of Organic Chemistry,
Institute of Chemical Technology, Prague 6*

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While the reduction of quaternary pyridinium salts with sodium bis(2-methoxyethoxy)aluminium hydride proceeds under the formation of 1-alkylpiperidines and 1-alkyl-3-piperideines, by the action of sodium aluminium hydride along with these products also the fission products of the pyridine ring, the dienylamines *III* are formed.

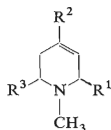
In several papers of this series we have described the reduction of quaternary pyridinium salts with sodium borohydride^{1,2}, lithium aluminium hydride^{3,4}, and aluminium hydride^{5,6}. In all these cases both 1-alkylpiperidines and 1-alkyl-3-piperideines were identified as products. When the reductions were performed with lithium aluminium hydride⁴ and aluminium hydride⁶ respectively, the resulting products were found to contain besides these compounds also the fission products of the pyridine ring *i.e.* the dienylamines. In this connection we were interested to investigate how the quaternary pyridinium salts would behave when treated with sodium aluminium hydride and sodium bis(2-methoxyethoxy)aluminium hydride, resp. Our experience with these complex hydrides gave reasonable hope that this investigation might be successful, as we have already earlier described the reductions of a series of organic nitrogen compounds with sodium aluminium hydride⁷ as well as that of 1-alkoxy-pyridinium salts with the mentioned alkoxy hydride⁸.

The reductions of the quaternary pyridinium salts with sodium bis(2-methoxyethoxy)aluminium hydride afforded similar products as the reductions with sodium borohydride^{1,2}. Thus, from pyridine methiodide we obtained a mixture of 1-methylpiperidine and 1-methyl-3-piperideine (*Ia*), from 2-methylpyridine methiodide a mixture of 1,2-dimethylpiperidine, 1,2-dimethyl-3-piperideine (*Ib*), and 1,6-dimethyl-3-piperideine (*Ic*), from 3-methylpyridine methiodide a mixture of 1,3-dimethylpiperidine, 1,3-dimethyl-3-piperideine (*Iia*), and 1,5-dimethyl-3-piperideine (*Iib*),

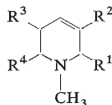
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from 4-methylpyridine methiodide a mixture of 1,4-dimethylpiperidine and 1,4-dimethyl-3-piperideine (*Id*), from 2,4-dimethylpyridine methiodide a mixture of both stereoisomeric 1,2,4-trimethylpiperidines, 1,2,4-trimethyl-3-piperideine (*Ie*), and 1,4,6-trimethyl-3-piperideine (*If*), from 2-methyl-5-ethylpyridine methiodide a mixture of the 1,2-dimethyl-5-ethylpiperidines, 1,2-dimethyl-5-ethyl-3-piperideine (*Iic*), and 1,6-dimethyl-3-ethyl-3-piperideine (*Iid*), and, finally, from 3,5-dimethylpyridine methiodide a mixture of both stereoisomeric 1,3,5-trimethylpiperidines and 1,3,5-trimethyl-3-piperideine (*Iie*). In comparison with the analogous sodium borohydride reduction^{1,2} the obtained yields were lower. Only in one case, namely in the reduction of 2-methyl-5-ethylpyridine methiodide we found in addition to the above mentioned products a negligible amount of a base, which we identified on comparison with the already known product⁶ as 5-methylaminomethyl-2,4-heptadiene (*IIIa*). From the given results it follows that sodium bis(2-methoxyethoxy)aluminium hydride, which in many respects is regarded as equal effective as lithium aluminium hydride, in the reductions of quaternary pyridinium salts, contrary to lithium aluminium hydride⁴ does not cleave the pyridine ring.

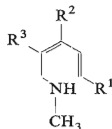
The sodium aluminium hydride reduction of quaternary pyridinium salts led to similar products as the reductions with the above alkoxy hydride. Moreover, with the exception of 4-methylpyridine methiodide, which affords only 1,4-dimethyl-



- Ia*; $R^1 = R^2 = R^3 = H$
Ib; $R^1 = CH_3, R^2 = R^3 = H$
Ic; $R^1 = R^2 = H, R^3 = CH_3$
Id; $R^1 = R^3 = H, R^2 = CH_3$
Ie; $R^1 = R^2 = CH_3, R^3 = H$
If; $R^1 = H, R^2 = R^3 = CH_3$



- Ii*; $R^1 = R^3 = R^4 = H, R^2 = CH_3$
Iib; $R^1 = R^2 = R^4 = H, R^3 = CH_3$
Iic; $R^1 = CH_3, R^2 = R^4 = H, R^3 = C_2H_5$
Iid; $R^1 = R^3 = H, R^2 = C_2H_5, R^4 = CH_3$
Iie; $R^1 = R^4 = H, R^2 = R^3 = CH_3$



- IIIa*; $R^1 = CH_3, R^2 = H, R^3 = C_2H_5$
IIIb; $R^1 = R^2 = R^3 = H$
IIIc; $R^1 = CH_3, R^2 = R^3 = H$
IIId; $R^1 = R^2 = H, R^3 = CH_3$
IIIe; $R^1 = R^2 = CH_3, R^3 = H$

piperidine and 1,4-dimethyl-3-piperidine (*Id*), with all other quaternary salts also a fission of the pyridine ring took place. Thus, on sodium aluminium hydride reduction 5-methylamino-1,3-pentadiene (*IIIb*) was obtained from pyridine methiodide, 1-methylamino-2,4-hexadiene (*IIIc*) from 2-methylpyridine methiodide, 4-methyl-5-methylamino-1,3-pentadiene (*III'd*), from 3-methylpyridine methiodide, 3-methyl-1-methylamino-2,4-hexadiene (*IIIe*) from 2,4-dimethylpyridine methiodide and 5-methylaminomethyl-2,4-heptadiene (*IIIa*) from 2-methyl-5-ethylpyridine methiodide. The dienyamines *IIIa-d* were even the main products of these reductions. The dienyamine *IIIe* was isolated already earlier from the mixtures obtained after the reduction of 2,4-dimethylpyridine methiodide with lithium aluminium hydride⁴ and aluminium hydride⁶, respectively. The structures of the dienyamines *IIIb-d* obtained on reduction of the methiodides of pyridine, 2-methylpyridine, and 3-methylpyridine were determined on the basis of their NMR and IR spectra. The values for the chemical shifts which are in agreement with those for the earlier published substances *IIIa,e* are listed in Table II. In the IR spectra sharp absorption bands appear for the terminal double bond at 912 and 1000 cm^{-1} or at 910 and 990 cm^{-1} , respectively. The IR spectrum of the dienyamine *IIIe* shows an absorption band at 955 cm^{-1} for a trans disubstituted double bond. Hydrogenation of the dienyamine *IIIb*

TABLE I

Sodium Aluminium Hydride (A) and Sodium Bis(2-methoxyethoxy)aluminium Hydride (B) Reduction of the Methiodides of Pyridine Bases

Methiodide of	Agent	Total bases, %	Piperidines, %	Other, %
Pyridine	A	36	1	6 <i>Ia</i> , 89 <i>IIIb</i> ^a
	B	30	15	80 <i>Ia</i> ^a
2-Methylpyridine	A	37	3	13 <i>Ib</i> , 22 <i>Ic</i> , 62 <i>IIIc</i>
	B	55	15	23 <i>Ib</i> , 52 <i>Ic</i> ^a
3-Methylpyridine	A	44	5	35 <i>Ila</i> , 20 <i>Ilb</i> , 35 <i>III'd</i> ^a
	B	51	20	52 <i>Ila</i> , 27 <i>Ilb</i> ^a
4-Methylpyridine	A	28	5	95 <i>Id</i>
	B	39	2	95 <i>Id</i> ^a
2,4-Dimethylpyridine	A	60	6	33 <i>Ie</i> , 37 <i>If</i> , 24 <i>IIIe</i>
	B	52	16	35 <i>Ie</i> , 48 <i>If</i> ^a
2-Methyl-5-ethylpyridine	A	59	5.5 ^b	5.5 <i>Iic</i> , 34 <i>Ild</i> , 55 <i>IIIa</i> ^a
	B	32	4 ^b	16 <i>Iic</i> , 75 <i>Ild</i> , 2 <i>IIIa</i> ^a
3,5-Dimethylpyridine	B	41	5 ^b	95 <i>Iie</i>

^a The rest is made up by unidentified products; ^b mixture of stereoisomers.

from the reduction of pyridine methiodide afforded methylpentylamine identical with the synthetic product⁹.

TABLE II
NMR Spectra of the Dienylamines III (δ Values)

Compound	CH ₃ -C=	CH ₃ -N	=C-CH ₂ -N	CH=	--NH
IIIb	—	2.37 (s)	3.31 (d)	4.80—6.95 (m)	1.82 (s)
IIIc	1.70 (d)	2.38 (s)	3.30 (d)	5.0—6.70 (m)	1.62 (s)
III d	1.77 (s)	2.31 (s)	3.25 (s)	4.8—7.0 (m) ^a	1.25 (s)

^a 4.80—5.30 for =CH₂; (s) singlet, (d) doublet, (m) multiplet.

EXPERIMENTAL

Gas Chromatography was performed on a Chrom 2 apparatus (Laboratorní přístroje, Prague), flame-ionisation detector, Tridox on Chromosorb. Preparative gas chromatography was performed on the same packing on an uncommercial apparatus¹⁰. NMR spectra were taken on a Tesla 487 apparatus in deuteriochloroform (tetramethylsilane as internal standard).

Reduction of 3,5-Dimethylpyridine Methiodide with Sodium Bis(2-methoxyethoxy)aluminium Hydride

A mixture of a 70% benzenic solution of the reduction agent (45 ml) and the quaternary salt (12.46 g; 0.05 mol) was refluxed under stirring for 4 h. Then the reaction mixture was decomposed with dilute hydrochloric acid, the aqueous layer separated, made alkaline and steam distilled. From the distillate the product was isolated in the usual manner; 2.8 g, b.p. 45—46°C/12 Torr. According to gas chromatography it is a mixture which contains 5% of 1,3,5-trimethylpiperidines (*cis*- and *trans*-) and 95% of 1,3,5-trimethyl-3-piperideine. All other reductions were performed by an analogous procedure (Table I).

Reduction of 3-Methylpyridine Methiodide with Sodium Aluminium Hydride

A mixture of 3-methylpyridine methiodide (47 g; 0.2 mol), tetrahydrofuran (800 ml), and sodium aluminium hydride (16 g; 0.296 mol) was refluxed under stirring for 10 h. Then the reaction mixture was decomposed with hydrochloric acid, and after steam distilling the remaining solution was alkalisied and steam distilled. From the distillate the product was isolated in the usual manner; 7.2 g, b.p. 46°C/12 Torr. According to gas chromatography this mixture contains 5% of 1,3-dimethylpiperidine, 35% of 1,3-dimethyl-3-piperideine (IIa), 20% of 1,5-dimethyl-3-piperideine (IIb), and 35% 4-methyl-5-methylamino-1,3-pentadiene (III d). The latter compound was isolated by gas chromatography, b.p. 138°C/756 Torr, n_D^{20} 1.4874. For C₇H₁₃N (111.2) calculated: 75.60% C, 11.78% H, 12.60% N; found: 75.40% C, 12.00% H, 13.06% N. From the analogous performed reductions (Table I) the following further dienylamines were obtained: 5-Methylamino-1,3-pentadiene (IIIb), b.p. 118°C/745 Torr, n_D^{20} 1.4821. For C₆H₁₁N (97.2) calculated: 74.17% C, 11.41% H, 14.42% N; found: 74.42% C, 11.64% H, 14.48% N. This diene was hydrogenated in

methanol solution on Adams catalyst. The product was identified as 1-methylaminopentane by gas chromatographic comparison with an authentic specimen⁹; b.p. 127°C/749 Torr. 1-Methylamino-2,4-hexadiene (*IIIc*), b.p. 116–117°C/761 Torr, n_D^{20} 1.4922. For $C_7H_{13}N$ (111.2) calculated: 75.60% C, 11.78% H, 12.60% N; found: 75.32% C, 12.00% H, 12.42% N.

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