Palacký University, Olomouc, for the IR spectra (Infrascan, Hilger and Watts), and Mrs J. Bochořáková of our Institute for the taking of UV spectra (Spectrophotometer Unicam SP 500).

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Translated by Ž. Procházka.

STUDIES IN THE PYRIDINE SERIES. XXXIX.*

RING CLEAVAGE IN LITHIUM ALUMINUM HYDRIDE REDUCTIONS OF SOME DIALKYLPYRIDINE METHIODIDES

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Received July 6th, 1970

It has been shown in one of the earlier papers[1] of this Series that the aluminum hydride (prepared *in situ* from lithium aluminum hydride and aluminum chloride) reductions of 2,5-dimethylpyridine methiodide and 2-methyl-5-ethylpyridine methiodide are accompanied by cleavage of the pyridine ring under the formation of 2-methylaminomethyl-2,4-hexadiene and 5-methylaminomethyl-2,4-heptadiene, respectively. It was of interest if a similar ring cleavage takes place also in reductions of some dialkylpyridine methiodides with the complex hydride alone. In the present paper we wish to report the lithium aluminum hydride reductions of the methiodides of 2,4-dimethylpyridine, 2,5-dimethylpyridine, 2-methyl-5-ethylpyridine, 2,6-dimethylpyridine, and 3-methyl-4-ethylpyridine.

Thus, reduction of 2,4-dimethylpyridine methiodide afforded a mixture containing both stereoisomeric 1,2,4-trimethylpiperidines, 1,2,4-trimethyl-3-piperideine, 1,4,6-trimethyl-3-piperi-

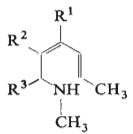
* Part XXXVIII: This Journal *36*, 2057 (1971).

deine, and an additional base which was identified on the basis of elemental analysis and NMR spectra as 1-methylamino-3-methyl-2,4-hexadiene (*Ia*). This dienylamine *Ia* was hydrogenated and the resulting saturated base identified as 1-methylamino-3-methylhexane (*IIa*) on comparison with an authentic specimen obtained by the lithium aluminum hydride reduction of 3-methylcaproic methylamide (*IIe*).

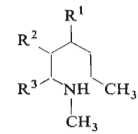
An analogous lithium aluminum hydride reduction of 2,5-dimethylpyridine methiodide and 2-methyl-5-ethylpyridine methiodide gave similar products as the aluminum hydride reduction, namely, both 1,2,5-trimethylpiperidines and 1,2-dimethyl-5-ethylpiperidines, resp., 1,3,6-trimethyl-3-piperideine (*IIIa*) and 1,6-dimethyl-3-ethyl-3-piperideine (*IIIb*), resp., and the dienylamines 2-methylaminomethyl-2,4-hexadiene (*Ib*) and 5-methylaminomethyl-2,4-heptadiene (*Ic*), resp. The dienylamine *Ib* was converted by hydrogenation to the saturated amine which was identified on comparison with an authentic specimen as 2-methylaminomethylhexane (*IIb*). Compound *IIb* was prepared by the lithium aluminum hydride reduction of 2-methylcaproic methylamide (*IId*).

The lithium aluminum hydride reduction of 2,6-dimethylpyridine methiodide afforded both 1,2,6-trimethylpiperidines and 1,2,6-trimethyl-3-piperideines along with an additional base, namely, 6-methylamino-2,4-heptadiene (*Id*). Catalytic hydrogenation of the latter diene *Id* gave a saturated amine which was identified as 2-methylaminoheptane (*IIc*) on comparison with an authentic specimen obtained by reaction of 2-heptanone with methylamine and sodium borohydride with the use of the method reported by Weichet and coworkers[2].

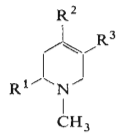
On the other hand, the lithium aluminum hydride reduction products of 3-methyl-4-ethylpyridine methiodide, namely, both 1,3-dimethyl-4-ethylpiperidines and 1,3-dimethyl-4-ethyl-3-piperideine (*IIIc*), were identical with those of an analogous sodium borohydride reduction[3], *i.e.*, no ring cleavage occurred.



Ia, $R^1 = CH_3$, $R^2, R^3 = H$
Ib, $R^1, R^3 = H$, $R^2 = CH_3$
Ic, $R^1, R^3 = H$, $R^2 = C_2H_5$
Id, $R^1, R^2 = H$, $R^3 = CH_3$



IIa, $R^1 = CH_3$, $R^2, R^3 = H$
IIb, $R^1, R^3 = H$, $R^2 = CH_3$
IIc, $R^1, R^2 = H$, $R^3 = CH_3$
IId, $R^1 = H$, $R^2 = CH_3$, $R^3 = O=$
IIe, $R^1 = CH_3$, $R^2 = H$, $R^3 = O=$



IIIa, $R^1, R^2 = CH_3$, $R^3 = H$
IIIb, $R^1 = CH_3$, $R^2 = H$, $R^3 = C_2H_5$
IIIc, $R^1 = H$, $R^2 = C_2H_5$, $R^3 = CH_3$

Conclusively, the ring cleavage occurs in reductions of quaternary salts of 2,4-dialkylpyridines, 2,5-dialkylpyridines, and 2,6-dialkylpyridines.

EXPERIMENTAL

Gas chromatography was performed on a Chrom 2 apparatus (Laboratorní přístroje, Prague), flame-ionization detector, Tridox on Chromosorb (80—100 mesh). Preparative chromatography was performed analogously on an uncommercial apparatus. NMR[4] spectra were taken on JNM-3-60-60 Mc and Tesla BS 487 apparatus, hexamethyldisiloxane as internal standard, carbon tetrachloride solutions.

Reduction of 2,4-Dimethylpyridine Methiodide

2,4-Dimethylpyridine methiodide[5] (49·8 g) was added under stirring to a suspension of lithium aluminum hydride (7·6 g) in ether (400 ml), the whole refluxed for 6 hours, and then decomposed with dilute hydrochloric acid. The aqueous layer was made alkaline and steam-distilled. The distillate was processed as usual to afford 12·2 g of a mixture (b.p. 48—62°C/27 Torr) consisting (as shown by gas chromatography) of both 1,2,4-trimethylpiperidines, 1,4,6-trimethyl-3-piperideine, 1,2,4-trimethyl-3-piperideine, and an additional component which was isolated

TABLE I

Survey of Dienylamines *I* and 3-Piperideines *III*

Compound	B.p., °C (lit.)	Formula (mol. wt.)	Calculated/Found		
			% C	% H	% N
Ia	119·5	$C_8H_{15}N$	76·74	12·07	11·18
	—	(125·2)	76·86	12·19	11·37
Ib	165	$C_8H_{15}N$	76·74	12·07	11·18
	(164)[1]	(125·2)	76·78	11·99	11·13
Ic	78/26 Torr	$C_9H_{17}N$	77·64	12·31	10·06
	(181)[1]	(139·2)	77·52	12·37	9·86
Id	116	$C_8H_{15}N$	76·74	12·07	11·18
	—	(125·2)	76·79	12·08	11·20
IIIa	152—154	$C_8H_{15}N$	76·74	12·07	11·18
	—	(125·2)	76·55	12·11	11·23
IIIb	178—179	$C_9H_{17}N$	77·64	12·31	10·06
	(178—179)[3]	(139·2)	77·85	12·35	9·98
IIIc	178—179·5	$C_9H_{17}N$	77·64	12·31	10·06
	(178—179)[3]	(139·2)	77·99	12·46	10·30

by preparative gas chromatography (b.p. 119·5°C) and identified as 1-methylamino-3-methyl-2,4-hexadiene (*Ia*) with the use of elemental analysis (Table I) and NMR spectra (Table II).

The methiodides of 2,5-dimethylpyridine, 2-methyl-5-ethylpyridine, 2,6-dimethylpyridine, and 3-methyl-4-ethylpyridine were reduced similarly. For analyses and NMR spectra of products see Table I, II, and III.

3-Methylcaproic Methylamide (*IIe*)

A solution of 3-methylcaproyl chloride[6] (11 g) in benzene (50 ml) was added to a solution of methylamine (4·6 g) in benzene (90 ml), the reaction mixture allowed to stand at room temperature overnight, and the methylamine hydrochloride filtered off. Distillation of the filtrate afforded 6·3 g (59·5%) of the methylamide *IIe*, b.p. 129·5–133°C/8 Torr or 135–138°C/11 Torr. For $C_8H_{17}NO$ (143·2) calculated: 67·09% C, 11·96% H, 9·78% N; found: 66·99% C, 12·10% H, 9·99% N.

TABLE II

NMR Spectra of Dienylamines *I* (τ values)

Compound	N<u>H</u>	C<u>H</u>$_3$CH=	C<u>H</u>$_3$C=	C<u>H</u>$_3$NH	NHC<u>H</u>$_2$CH=	—CH=CH—
Ia	8 (s)	8·15 (d)	8·2 (s)	7·64 (s)	5·58 (d)	4·51 (m)
Ib	8·9 (s)	8·29 (d)	8·25 (s)	7·7 (s)	6·82 (s)	4·3 (m)
Ic[a]	8·46 (s)	8·22 (d)	—	7·65 (s)	6·7 (s)	3·98 (m)
Id[b]	9·15 (s)	9·23 (d)	—	7·76 (s)	—	4·37 (m)

[a] $CH_3CH_2C\langle$ 8·99 (t), $CH_3CH_2C\langle$ 7·86; [b] CH_3—CH—N 8·94 (d), =C—CH(—CH_3)—N 6·53 (m).

TABLE III

NMR Spectra of 1-Alkyl-3-piperideines *III* (τ values)

Compound	C<u>H</u>$_3$C=	C<u>H</u>$_3$CH$_2$C=	C<u>H</u>$_3$CH<	>C<u>H</u>CH$_2$C=	C<u>H</u>$_3$N	—C<u>H</u>=C<	—C<u>H</u>$_2$N<
IIIa	8·4 (s)	—	9·01 (d)	8·08 (m)	7·83 (s)	4·75 (m)	7·2 (m)
IIIb	—	9·04 (t)	8·93 (d)	8·11 (m)	7·79 (s)	4·8 (s)	—
IIIc[a]	8·48 (s)	9·12 (t)	—	—	7·75 (s)	—	7·0 (m)

[a] $CH_3\underline{CH_2}C=$ 8·03 (q), N—$\underline{CH_2}$C= 7·32 (s).

1-Methylamino-3-methylhexane (*IIa*)

The methylamide *IIe* (5·1 g) in ether (160 ml) was added to a suspension of lithium aluminum hydride (5·1 g) in ether (230 ml) under stirring, the whole refluxed for 7 hours, decomposed with dilute hydrochloric acid, the aqueous layer made alkaline, and steam-distilled. The distillate was processed as usual to afford 2·8 g of the amine *IIa*, b.p. 46·5°C/8 Torr and 135·5°C/760 Torr. For $C_8H_{19}N$ (129·2) calculated: 74·34% C, 14·82% H, 10·84% N; found: 74·28% C, 14·92% H, 10·85% N. As shown by gas chromatography, amine *IIa* is identical with the saturated component of the mixture obtained by hydrogenation of bases resulting in the lithium aluminum hydride reduction of 2,4-dimethylpyridine methiodide.

1-Methylamino-2-methylhexane (*IIb*)

The methylamide of 2-methylcaproic acid (*IId*) was prepared analogously to the methylamide *IIe* from 2-methylcaproyl chloride[7]. B. p. 131°C/11 Torr; yield, 50·6%. The product was identical with that obtained on heating 2-methylcaproic acid with methylamine[8]. The lithium aluminum hydride reduction of the methylamide *IId* was performed analogously to that of compound *IIe*. B.p. of the amine *IIb*, 60°C/10 Torr. For $C_8H_{19}N$ (129·2) calculated: 74·34% C, 14·82% H, 10·84% N; found: 74·16% C, 15·03% H, 10·71% N. As shown by gas chromatography, the amine *IIb* is identical with the hydrogenation product of the dienylamine *Ib*, obtained in turn by the lithium aluminum hydride reduction of 2,5-dimethylpyridine methiodide.

2-Methylaminoheptane (*IIc*)

Sodium borohydride (0·75 g) was added under cooling and stirring into a mixture of 2-heptanone[9] (2·85 g), 27% aqueous methylamine (10 ml), and methanol (25 ml). Dilute (1 : 1) hydrochloric acid (30 ml) was then added, the mixture evaporated under diminished pressure, and the residue processed as usual to afford the amine *IIc*, b.p. 48—52°C/10—11 Torr; reported[10], b.p. 155°C/760 Torr. For $C_8H_{19}N$ (129·2) calculated: 74·34% C, 14·82% H, 10·84% N; found: 74·14% C, 14·85% H, 10·92% N.

The authors wish to thank Mr J. Hauer, Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, Prague, for interpretation of NMR spectra, and Mrs J. Korbeliusová of this Institute for preparative gas chromatography. Elemental analyses were performed by the staff of Central Laboratories, Institute of Chemical Technology, Prague.

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Translated by J. Pliml.