

STUDIES IN THE PYRIDINE SERIES. XLI.*

REDUCTION OF METHIODIDES OF SOME METHYLPYRIDINE BASES WITH RANEY NICKEL IN ALKALINE MEDIUM

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When Raney nickel is allowed to react with methiodides of methylpyridines in sodium hydroxide solution at room temperature the reduction of the pyridine nucleus takes place. From the methiodides of 2,6-dimethylpyridine, 3,5-dimethylpyridine, and 2,4,6-trimethylpyridine, mixtures of the corresponding 1-methylpiperidines and 1-methyl-2-piperidineins are formed. In the mixture after reduction of methiodides of 2-methylpyridine, 3-methylpyridine, and 2,4-dimethylpyridine 1-methyl-3-piperidineins were also identified. After reduction of methiodides of 4-methylpyridine 1,4-dimethyl-3-piperidine was identified as the sole unsaturated base.

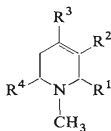
Up to the present time from reduction of corresponding pyridine derivatives only such 2-piperidineins were isolated in which the position β was substituted with a carbonyl¹⁻³ or a nitrile group⁴. These reductions were carried out by catalytic hydrogenation in alkaline medium on palladium in the presence of triethylamine³, or on Raney nickel^{1,2,5}, or eventually rhodium on charcoal.² 1-Trimethylsilyl-2-piperidine was formed parallelly with 3-piperidine and dihydropyridine derivatives by reaction of pyridine with trimethylsilane in the presence of various catalysts based on Pd, Rh, Raney nickel, and other metals⁶.

Sugasawa and Matsuo⁷ described reductive cleavage of benzyltrimethylammonium chloride under the effect of Raney nickel in a sodium hydroxide solution. During this reduction trimethylamine and toluene are formed in a high yield. We were interested in the investigation of the course of this reaction in the series of 1-alkylpyridinium iodides.

During the reductions of methiodides of 2-methylpyridine, 3-methylpyridine, and 4-methylpyridine mixtures of bases were formed which decomposed rapidly even in ethereal solutions during vacuum distillation and also during preparative gas chromatography. From the mixture after reduction of methiodide of 2-methylpyridine and 3-methylpyridine 1,2-dimethylpiperidine or 1,3-dimethylpiperidine resp. were isolated by preparative gas chromatography, and using comparison with standards unsaturated bases could also be identified. On reduction of methiodide of 2-methylpyridine all three possible piperidine bases are formed, *i.e.* 1,2-dimethyl-3-piperi-

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deine⁸ (*Ia*), 1,6-dimethyl-3-piperideine⁸ (*Ib*), and 1,2-dimethyl-2-piperideine¹² (*Ila*), the percentual representation of which is given in Table I. From the methiodide of 3-methylpyridine 1,3-dimethyl-2-piperideine⁹ (*Illa*) is formed in addition to a small amount of 1,3-dimethyl-3-piperideine⁹ (*Ic*). The only case in which 2-piperideine was not identified was the reduction of 4-methylpyridine methiodide. From this reaction mixture 1,4-dimethylpiperidine and 1,4-dimethyl-3-piperideine¹⁰ (*Id*) were isolated. Reduction of 2,4-dimethylpyridine methiodide leads to a mixture of *cis*- and *trans*-1,2,4-trimethylpiperidines¹¹, 1,2,4-trimethyl-3-piperideine⁸ (*Ie*), and 1,2,4-trimethyl-2-piperideine⁸ (*Ilb*).



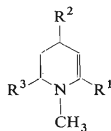
Ia; R¹ = CH₃, R² = R³ = R⁴ = H

Ib; R¹ = R² = R³ = H, R⁴ = CH₃

Ic; R¹ = R³ = R⁴ = H, R² = CH₃

Id; R¹ = R² = R⁴ = H, R³ = CH₃

Ie; R¹ = R³ = CH₃, R² = R⁴ = H

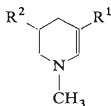


Ila; R¹ = CH₃, R² = R³ = H

Ilb; R¹ = R² = CH₃, R³ = H

Ilc; R¹ = R³ = CH₃, R² = H

Ild; R¹ = R² = R³ = CH₃



Illa; R¹ = CH₃, R² = H

Illb; R¹ = R² = CH₃

During the reduction of methiodides of symmetrically substituted polyalkylpyridines (2,6-dimethylpyridine, 3,5-dimethylpyridine, and 2,4,6-trimethylpyridine) with Raney nickel only 2-piperideines were formed in addition to saturated bases, which could be isolated by preparative gas chromatography. Thus, from 2,6-dimethylpyridine methiodide 1,2,6-trimethyl-2-piperideine (*Ilc*) is formed which is identical with the base prepared on dehydrogenation of 1,2,6-trimethylpiperidine with mercuric acetate¹². 1,3,5-Trimethyl-2-piperideine (*Illb*), the percentual content of which in the mixture is rather high, may be obtained in a pure state by repeated crystallisation of its perchlorate. From the methiodide of 2,4,6-trimethylpyridine all three possible isomeric 1,2,4,6-tetramethylpiperidines and 1,2,4,6-tetramethyl-2-piperideine (*Ild*) were formed. Their structure was determined on the basis of NMR and IR spectra of the bases and their perchlorates. The values of chemical shifts and of characteristic absorptions are given in Table II. Spectral values prove that these 1-methyl-2-piperi-

TABLE I
Composition of the Reaction Mixtures after Reductions of Methiodides of Methylpyridines

Pyridine methiodide	Yield %	Mixture, rel. % of bases	
		saturated	unsaturated
2-Methyl	32	40	10 (<i>Ia</i>), 20 (<i>Ib</i>), 30 (<i>Iia</i>)
3-Methyl	33	51	11 (<i>Ic</i>), 38 (<i>IIIa</i>)
4-Methyl	43	76	17 (<i>Id</i>) ^a
2,4-Dimethyl	41	39 ^b	29 (<i>Ie</i>), 22 (<i>Iib</i>) ^c
2,6-Dimethyl	40	53 ^b	47 (<i>Ic</i>)
3,5-Dimethyl	45	34 ^b	66 (<i>IIIb</i>)
2,4,6-Trimethyl	49	61 ^d	39 (<i>IId</i>)

^a7% of bases were unidentified; ^b*cis* and *trans*; ^c10% of bases were unidentified; ^dthree isomers.

TABLE II
Characteristic Values of NMR (δ_{TMS}) and IR (cm^{-1}) Spectra of 2-Piperideines

Substance ^a	$\text{CH}_3\text{—C}$	$\text{CH}_3\text{—C=}$ $\text{CH}_3\text{—N}$	$\text{—CH}_2\text{—}$	—CH— (CH=)	$\nu(\text{C=C})$ $\nu(\text{C=N})$
<i>Iib</i>	0.83 d	1.68 2.55	2.23 m 2.85 t	1.95 m (4.22)	^b
<i>Iib</i> . HClO_4	0.92 d	2.28 3.48	2.83 m 2.80 m	1.66 m	1 695
<i>Iic</i>	1.08 d	1.78 2.64	2.50—3.33 m	3.42 m (4.24)	1 650 ^c
<i>Iic</i> . HClO_4	1.25 d	2.22 3.36	2.73 m 1.67 m	3.83 m	1 679 ^c
<i>IIIb</i>	0.97 d	1.70 2.49	2.82 m 2.33—1.94 m	2.33—1.94 m (5.57)	1 680
<i>IIIb</i> . HClO_4	1.13 d 1.87 d	— 3.47	2.92 m 1.83—1.42 m	1.94 m (8.53)	1 710
<i>IId</i>	0.88 d 1.17 d	1.73 2.55	1.38 m	2.22 m 2.83 m (4.34)	1 655
<i>IId</i> . HClO_4	0.95 d 1.30 d	2.22 3.29	2.89 m 1.83 m	3.78 m 1.09 m	1 678

^ad Doublet, t triplet, m multiplet; ^bnot measured; ^cliterature¹² gives 1652 cm^{-1} for the base and 1697 cm^{-1} for the perchlorate.

TABLE III

1-Methyl-2-piperideines and Their Perchlorates

Substance	B.p., °C (M.p., °C)	Formula (M. w.)	Calculated/Found			
			% C	% H	% Cl	% N
<i>I Ib</i>	138	C ₈ H ₁₅ N (125.2)	76.75	12.07	—	—
			76.81	12.16	—	—
<i>I Ic</i>	156 ^a	C ₈ H ₁₅ N (125.2)	76.75	12.07	—	11.18
			76.42	12.02	—	11.35
<i>III b</i>	149	C ₈ H ₁₅ N (125.2)	76.75	12.07	—	11.18
			76.72	12.07	—	11.08
<i>III b</i> · HClO ₄	140—141	C ₈ H ₁₆ ClNO ₄ (225.7)	42.58	7.15	15.71	6.21
			42.58	7.23	15.70	5.95
<i>I Id</i>	162	C ₉ H ₁₇ N (139.6)	77.63	12.31	—	10.18
			77.49	12.24	—	9.91
<i>III d</i> · HClO ₄	(172)	C ₉ H ₁₈ ClNO ₄ (240.0)	45.37	7.57	14.79	5.84
			45.57	7.77	14.78	6.05

^aLiterature¹² gives b.p. 146°C and m.p. of perchlorate 201—202°C, found 202°C.

deines are also in the form of bases with an endocyclic double bond, which is probably caused by the greater stability of this bond in the six-membered ring^{13,14}.

The reduction of the 3,5-dimethylpyridine methiodide was carried out under various reaction conditions. We found that an excess of Raney nickel slightly increases the yield of bases. However, the percentage of saturated base in the mixture is higher. The reaction carried out in a more concentrated sodium hydroxide solution leads to the formation of a larger amount of resinous residue. A reduction carried out in hydrogen atmosphere did not bring about an improvement in the yields and the composition of the reaction mixture was practically the same as in the reaction carried out under nitrogen.

EXPERIMENTAL

Gas chromatography was carried out on a Chrom II apparatus (column length 170 cm, diameter 0.6 cm, carrier gas nitrogen). The filling consisted of 20% Tridox on Cellite, working temperature was 110°C. Separation by preparative gas chromatography was carried out on an apparatus of non-commercial origin¹⁵, the filling was 7% of Tridox on porovina. The NMR spectra were

measured on a Tesla BS 477 (60 Mc) apparatus in deuteriochloroform and hexadeuteriodimethyl sulfoxide using tetramethylsilane as an internal standard. The IR spectra were measured on a UR-10 Zeiss Jena spectrophotometer, liquids were measured as such, solid substances were measured in Nujol. All 2-piperideines isolated were very instable and it was necessary to keep them under nitrogen. They had to be stored in a refrigerator. In the case of substances isolated by preparative gas chromatography the spectra were measured and the elemental analyses carried out immediately without delay. For reductions Raney nickel of 0.16 mm particle size was used.

Reduction of 3,5-Dimethylpyridine Methiodide with Raney Nickel

To a solution of 14.9 g (0.06 mol) of 3,5-dimethylpyridine methiodide in 100 ml of water 40 g of 50% NaOH was added at 25°C under stirring, followed by 3 g of Raney nickel. During the addition of sodium hydroxide the starting methiodide separated out partly. The mixture was stirred at room temperature for 6 hours, then extracted twice with ether and the extract was dried over magnesium sulfate. The filtered solution was concentrated and then the crude product distilled, b.p. 58—60°C/20 Torr. Yield 3.4 g (45.5%). This mixture of bases was separated by preparative gas chromatography. The percentual composition of the mixture, analysis, and spectral data of 1,3,5-trimethyl-2-piperideine (*IIIb*) are given in Tables I—III.

1,3,5-Trimethylpiperideinium perchlorate: An ethereal solution of base *IIIb* to which 5% (by volume) of ethanol were added was acidified (Congo red) by a mixture of 65% of perchloric acid and ethanol (1 : 1). The separated perchlorate was crystallised twice from ethanol, m.p. 140—141°C. Analysis see Table III. The reductions of other methiodides were carried out in analogy to the given example.

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