

STUDIES IN THE PYRIDINE SERIES. XLII.*

REDUCTION OF ACETYLPIRIDINES AND PROPIONYLPIRIDINES WITH ZINC AND HYDROCHLORIC, ACETIC, AND FORMIC ACID, RESP.

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Reduction of acetylpyridines and propionylpyridines with zinc and formic acid affords the corresponding ethylpyridine and propylpyridine, resp. in preparative yield. Reduction with zinc and acetic acid gives in the α - and γ -series a mixture of the alkylpyridine and the corresponding secondary alcohol. This alcohol is the main product on reduction with amalgamated zinc and hydrochloric acid. Reduction of the ketones in the β -series takes place with small yields: from 3-acetylpyridine is produced by the action of zinc and acetic acid besides 1-(3-pyridyl)-1-ethanol also 2,3-di-(3-pyridyl)-2,3-butanediol, and the analogous reduction of 3-propionylpyridine afforded 1-(3-pyridyl)-1-propanol and 3-propylpyridine.

Some time ago we have described the electrolytic reduction of acetylpyridines¹. We were now interested to find out how the acetylpyridines and propionylpyridines will behave on reduction with zinc in hydrochloric, acetic, and formic acid, resp. In the literature we find only a few cases of the reduction of compounds with a keto group attached in position 2 of the pyridine ring with amalgamated zinc and hydrochloric acid²⁻⁵. In some cases this reduction proceeds to the secondary alcoholic group, in other cases up to the methylene group.

The reduction of 2-acetylpyridine (*Ia*) and 2-propionylpyridine (*Ib*) with amalgamated zinc and hydrochloric acid and with zinc dust and acetic or formic acid gave rise to similar products as γ -derivatives *Ic*, *Id*. On reduction with amalgamated zinc in boiling hydrochloric acid as main products the secondary alcohols *II* along with a small quantity of the corresponding ethylpyridine and propylpyridine were obtained. The reduction with zinc dust and acetic acid afforded already a larger amount of ethylpyridine and propylpyridine, resp. in addition to the secondary alcohols. Under similar conditions, the reduction with zinc dust and formic acid furnished almost exclusively ethylpyridine and propylpyridine, resp. The mentioned reduction course of 2-acetylpyridine to 1-(2-pyridyl)-1-ethanol with amalgamated zinc and hydrochloric acid shows that Holland and Nayler⁵ were right who,

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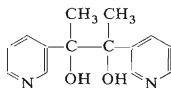
contrary to the assertion of Furst⁴, obtained also the alcohol *Ila*, and not 2-ethylpyridine. The reduction with zinc and formic acid seems to be a preparative route for the alkylpyridines from the corresponding ketones. This reduction proceeds probably *via* the stage of the secondary alcohol *II*. This is proved by the reduction of 1-(2-pyridyl)-1-ethanol (*Ila*) with zinc dust and formic acid affording exclusively 2-ethylpyridine. The reduction with zinc dust and formic acid was also found to be suitable for 3-acetylpyridine (*Ie*) and 3-propionylpyridine (*If*) which are converted into the corresponding alkylpyridine. The reduction of 3-acetylpyridine with zinc and acetic acid affords besides 1-(3-pyridyl)-1-ethanol (*IIf*) also 2,3-di-(3-pyridyl)-2,3-butanediol (*III*).



- Ia*; $R^1 = \text{CH}_3\text{CO}$, $R^2, R^3 = \text{H}$
Ib; $R^1 = \text{C}_2\text{H}_5\text{CO}$, $R^2, R^3 = \text{H}$
Ic; $R^1, R^2 = \text{H}$, $R^3 = \text{CH}_3\text{CO}$
Id; $R^1, R^2 = \text{H}$, $R^3 = \text{C}_2\text{H}_5\text{CO}$
Ie; $R^1, R^3 = \text{H}$, $R^2 = \text{CH}_3\text{CO}$
If; $R^1, R^3 = \text{H}$, $R^2 = \text{C}_2\text{H}_5\text{CO}$



- Ila*; $R^1 = \text{CH}_3\text{CHOH}$, $R^2, R^3 = \text{H}$
Ilb; $R^1 = \text{C}_2\text{H}_5\text{CHOH}$, $R^2, R^3 = \text{H}$
Ilc; $R^1, R^2 = \text{H}$, $R^3 = \text{CH}_3\text{CHOH}$
IId; $R^1, R^2 = \text{H}$, $R^3 = \text{C}_2\text{H}_5\text{CHOH}$
IIf; $R^1, R^3 = \text{H}$, $R^2 = \text{C}_2\text{H}_5\text{CHOH}$



III

The formation of this glycol (of undetermined configuration) is in analogy to the electrolytic reduction of 3-acetylpyridine⁶.

EXPERIMENTAL

Gas chromatography was performed on a Chrom II apparatus (column length 2 m, 0.6 cm diameter; 15% of Tridox on Celite, nitrogen as carrier gas).

A. Reduction with amalgamated zinc and hydrochloric acid: A mixture of 2-acetylpyridine^{7,8} (10 g) was refluxed under stirring for 8 hours with concd. hydrochloric acid (25 ml), water (19 ml), and amalgamated zinc prepared from zinc dust (25 g), mercuric chloride (3.9 g), conc. HCl (1.75 ml), and water (38 ml). The liquid was poured off from the zinc and made alkaline. The bases were extracted with chloroform and the dried chloroform extract (MgSO_4) was distilled; b.p. 102/13 Torr, 8.3 g. According to gas chromatography and by comparison with authentic specimens it was identified as a mixture of 1-(2-pyridyl)-1-ethanol and traces of 2-ethylpyridine. Literature⁹ gives b.p. of 1-(2-pyridyl)-1-ethanol 95–97°C/13 Torr. *B. Reduction with zinc and acetic acid:* A mixture of 2-acetylpyridine⁷ (10 g), zinc dust (25 g), glacial acetic acid (25 ml), and water (19 ml) was refluxed for 9 hours. Working up as under *A*) gave: *a*) a fraction with b.p. 95°C to

155 Torr (3.2 g) identified as 2-ethylpyridine, and *b*) a fraction with b.p. 100°C/12 Torr (5.5 g) identified as 1-(2-pyridyl)-1-ethanol. *C. Reduction with zinc and formic acid*: A mixture of 2-acetylpyridine⁷ (6.05 g), zinc dust (40 g), and 80% formic acid (100 ml) was refluxed for 8 h. Working up as under *A*) gave 5 g of a fraction with b.p. 158°C/752 Torr, identical with 2-ethylpyridine (literature¹⁰ gives b.p. 148–149°C). For the results of the other reductions see Table I.

1-(2-Pyridyl)-1-ethanol

A solution of 2-acetylpyridine⁷ (9.08 g) in diethyl ether (100 ml) was added dropwise to a suspension of lithium aluminium hydride (1.9 g) in diethyl ether (100 ml), and the mixture was refluxed under stirring for 1 h. After work-up according to Micović and Mihailović²⁰ the title compound (4.5 g; 49%) was obtained by distillation, b.p. 92°C/9 Torr. Literature⁹ gives b.p. 95–97°C/12 Torr.

TABLE I

Survey of Reduction of Acetylpyridines and Propionylpyridines

Ketone	Method ^a	B.p. of the product °C/Torr	Yield %	Alcohol <i>II</i> %	Alkylpyridine %
<i>Ia</i>	A	102/13 ^a	83	100	traces
<i>Ia</i>	B	95–100/12 ^a	87	85	15
<i>Ia</i>	C	158/752 ^a	86	—	100
<i>Ib</i>	A	105/10 ^a	86	100	—
<i>Ib</i>	B	103–106/13 ^a	61	85	15
<i>Ib</i>	C	56/9 ^a	70	—	100
<i>Ic</i>	A	56–57 ^b	85	100	—
<i>Ic</i>	B	55–56 ^b	48	8	92
<i>Ic</i>	C	158 ^c	64	—	100
<i>Id</i>	A	189/770 ^d ; 118/2.3 ^e	55	87	13
<i>Id</i>	B	60/3 ^d ; 115/2 ^e	45	67	33
<i>Id</i>	C	52/2.8 ^d	48	—	100
<i>Ie</i>	A	126/17 ^f	14	100	—
<i>Ie</i>	B	130/9 ^f ; 243 ^g	34	77	—
<i>Ie</i>	C	75–78/739 ^h	64	—	100
<i>If</i>	A	106/2.3 ⁱ	26	100	—
<i>If</i>	B	138/13 ⁱ	24	83	17
<i>If</i>	C	185/755 ^j	30	—	100

^a For the boiling points of the standard substances and their preparation see the references given in the experimental part of this paper. ^b B.p. of 1-(4-pyridyl)-1-ethanol¹¹ 54°C; ^c B.p. of 4-ethylpyridine¹² 163–165°C. ^d B.p. of 4-propylpyridine¹³ 189°C/776 Torr. ^e B.p. of 1-(4-pyridyl)-1-propanol¹⁴ 128–129°C/3.6 Torr. ^f B.p. of 1-(3-pyridyl)-1-ethanol¹⁵ 123–125°C/5 Torr. ^g M.p. of 2,3-di-(3-pyridyl)-2,3-butanediol¹⁶ 244–245°C. For C₁₄H₁₆N₂O₂ (244.3) calculated: 68.83% C, 6.60% H, 11.47% N; found: 68.84% C, 6.64% H, 11.21% N. ^h B.p. of 3-ethylpyridine¹⁷ 165–165.3°C. ⁱ B.p. of 1-(3-pyridyl)-1-propanol¹⁸ 133–134°C/6 Torr. ^j B.p. of 3-propylpyridine¹⁹ 182–184°C/753 Torr.

1-(2-Pyridyl)-1-propanol

To a suspension of lithium aluminium hydride (0.95 g) in diethyl ether (100 ml) a solution of 2-propionylpyridine²¹ (6.75 g) in diethyl ether (50 ml) was dropwise added and the reaction mixture boiled for 1 h. Working up as above afforded the title compound (3.8 g; 56%), b.p. 115°C/10 Torr. Literature²² gives b.p. 213–218°C.

2-Propylpyridine

A mixture of 2-propionylpyridine²¹ (13.5 g), 80% hydrazine hydrate (15 ml), ethylene glycol (50 ml), and KOH (10.6 g) was refluxed for 2 h. Then the fraction boiling at 105–120°C was distilled from the reaction mixture. The product was taken up in ether, dried with KOH, and distilled, b.p. 57–58°C/12 Torr, 6.5 g (54%). Literature²³ gives b.p. 165–166°C.

Reduction of 1-(2-Pyridyl)-1-ethanol with Zinc and Formic Acid

A mixture of 1-(2-pyridyl)-1-ethanol (6 g), zinc dust (40 g), and 85% formic acid (100 ml) was refluxed for 9 h. The work-up as in the analogous reduction of 2-acetylpyridine yielded the product (4.14 g) boiling at 147–149°C/749 Torr which was identical with 2-ethylpyridine (lit.¹⁰ gives b.p. 148–149°C).

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