

REDUCTION OF TERTIARY ALCOHOLS OF THE PYRIDINE SERIES AND CORRESPONDING ALKENYLPYRIDINES WITH ZINC AND FORMIC ACID*

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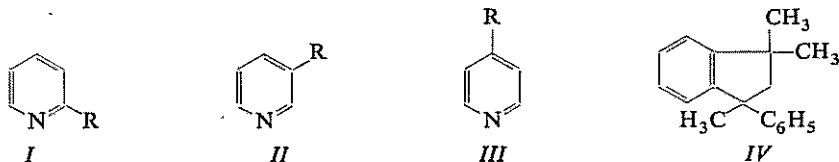
Dedicated to Professor F. Šantavý on the occasion of his 60th birthday.

Reduction of dimethyl(pyridyl)methanols and 1-(2-pyridyl)cyclopentanol and 1-(4-pyridyl)cyclopentanol with zinc and formic acid gives corresponding isopropylpyridine or cyclopentylpyridine, respectively. The same products are formed by this reduction method from isopropenylpyridine or cyclopentenylpyridine, respectively.

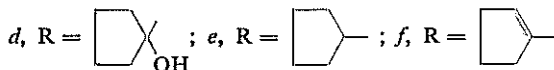
In one of our previous papers we described¹ the reduction of some acylpyridines to corresponding alkylpyridines with zinc and formic acid. In contrast to this, reduction with zinc in acetic acid or hydrochloric acid gives a mixture of alkylpyridine and the corresponding secondary alcohol, or the secondary alcohol alone.

In this paper the reduction of dimethyl(pyridyl)methanols *Ia*, *IIa*, *IIIa*, 1-(2-pyridyl)-cyclopentanol (*Id*) and 1-(4-pyridyl)cyclopentanol (*IIIId*) with zinc and formic acid is described. It was found that this reduction is a suitable synthetic method for the preparation of corresponding isopropylpyridines *Ib*, *IIf*, *IIIb* or cyclopentylpyridines *Ie* and *IIIe*. As the reduction of the mentioned tertiary alcohols is carried out at a relatively elevated temperature, we supposed that corresponding alkenylpyridines *Ic*, *IIf*, *IIIc* could be formed temporarily, which are reduced in a subsequent step to alkylpyridines *Ib*, *IIf*, *IIIb*. For this reason we carried out successfully reductions of alkenylpyridines *Ic*, *IIf*, *IIIc* to alkylpyridines *Ib*, *IIf*, *IIIb* under the same conditions under which the reduction of the tertiary alcohols *Ia*, *IIa*, *IIIa* alone took place (Table I). An attempt in favour of the assumption that isopropenylpyridines are intermediates is the reduction of dimethyl-(3-pyridyl)methanol (*IIa*) with zinc and formic acid, carried out for a shorter time interval², in which a mixture of 3-isopropylpyridine (*IIf*) and 3-isopropenylpyridine (*IIf*) was formed. We also followed the role of formic acid in the mentioned reductions. Substitution of formic acid

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For I—III a, R = $(\text{CH}_3)_2\text{C}$; b, R = $(\text{CH}_3)_2\text{CH}$; c, R = $\text{CH}_2=\text{C}$



by acetic acid in the reduction of dimethyl-(3-pyridyl)methanol (*IIa*) in the presence of zinc led only to a low yield of 3-isopropylpyridine (*IIb*) in addition to a double amount of 3-isopropenylpyridine (*IIc*). From the experiment aiming at the reduction of dimethyl-3-pyridylmethanol (*IIa*) with formic acid alone and also in the presence of potassium formate according to Lukeš³ we obtained only a small amount of 3-isopropenylpyridine (*IIc*). An attempt at the reduction of dimethyl-(3-pyridyl)methanol (*IIa*) with amalgamated zinc and hydrochloric acid was quite unsuccessful. In the reduction of dimethyl-(2-pyridyl)methanol (*Ia*) with formic acid in the presence

TABLE I
Reduction of Dimethyl(pyridyl)methanols and Isopropenylpyridines with Zinc and Formic Acid

Starting substance (ref.)	Yield, %	B.p., °C/Torr (ref.)
<i>Ia</i> ⁹	<i>Ib</i> 65·3	50—54/8—9 (158—159) ¹⁴
<i>IIa</i> ¹⁰	<i>IIb</i> 61	62/10 (179·3/744) ¹⁵
<i>IIIa</i> ¹¹	<i>IIIb</i> 72	65/15 (177—178) ¹⁴
<i>Id</i> ¹²	<i>Ie</i> 64	95/10 (222—223/745) ¹²
<i>IIIa</i> ^a	<i>IIIe</i> 77	112/25 ^b (245—246/738) ⁶
<i>Ic</i> ^{a,13}	<i>Ib</i> 83 ^c	<i>d</i>
<i>IIc</i> ¹³	<i>IIb</i> 38	<i>d</i>
<i>IIIc</i> ^{a,11}	<i>IIIb</i> 75	<i>d</i>
<i>If</i> ^a	<i>Ie</i> 68	<i>d</i>

^a This paper ^b for the analysis see Experimental. ^c 17% of 2-isopropylpiperidine, b.p. 154 to 156°C/748 Torr, lit.¹⁶ gives 162°C (corr.). For $\text{C}_8\text{H}_{17}\text{N}$ (127·2) calculated: 75·52% C, 13·47% H, 11·01% N; found: 76·64% C, 13·49% H, 11·06% N; NMR spectrum (p.p.m.): $\text{CH}_3\text{—C}$ 0·89 (d; 6·5 Hz) and 0·90 (d; 6·5 Hz); NH 1·62 (s); NCH_2H_c 2·09, 2·35 (m); N—CH < 2·62 (m); N—CH_a · H_c 3·0—3·22 (m); other 0·95—1·90; ^d see above.

TABLE II

Reduction of Dimethyl(pyridyl)methanols under Various Conditions

Starting alcohol	Method ^a	Proportion, %		
<i>Ila</i>	<i>A, B</i>	<i>Ila</i> 93	<i>Ilc</i> 7	
<i>Ila</i>	<i>C</i>	<i>Ila</i> 71	<i>Ilb</i> 9.5	<i>Ilc</i> 19.5
<i>Ila</i>	<i>D</i>	<i>Ila</i> 100		
<i>Ia</i>	<i>B</i>	<i>Ia</i> 32	<i>Ib</i> 9.5	<i>Ic</i> 58.5

^a *A* formic acid at 160°C, *B* formic acid and potassium formate at 180°C for 10 hours, *C* zinc and acetic acid at 160°C, *D* amalgamated zinc and hydrochloric acid at 160°C.

of potassium formate the formation of 2-isopropenylpyridine (*Ic*) takes place predominantly, while reduction to 2-isopropylpyridine (*Ib*) took place only to a negligible extent. For comparison the mentioned reductions of some dimethyl(pyridyl)-methanols are listed in Table II.

We were further interested in the question of whether the reduction of tertiary alcohols with zinc and formic acid can have a more general use than in the pyridine series only. For this reason we tried the reduction of dimethyl(phenyl)methanol with zinc and formic acid. Contrary to our expectation isopropylbenzene was not formed; instead, a product was isolated to which we assigned on the basis of analyses and NMR spectra the structure of 1,3,3-trimethyl-1-phenyl-1,2-dihydroindene (*IV*). This compound was also formed from the mentioned tertiary alcohol by mere heating with formic acid. The indene derivative *IV* has been described as a product of reaction of stannic chloride with 2-phenyl-1-propene⁴ or aluminum chloride or stannic chloride with 2,4-diphenyl-4-methyl-2-pentene⁵; both of them are the products of conversion of dimethyl(phenyl)methanol.

The starting tertiary alcohols of the pyridine series were prepared by known methods (Table I). 1-(4-Pyridyl)cyclopentanol (*IIIId*) was obtained on reaction of ethyl isonicotinate with tetramethylenebismagnesium bromide in tetrahydrofuran.

EXPERIMENTAL

The melting points and boiling points are not corrected. The NMR spectra were measured on a Varian XL-100-15 instrument, ¹H at 100.1 MHz in deuteriochloroform; working temperature 37°C.

1-(4-Pyridyl)cyclopentanol (*IIIId*)

Magnesium (14.6 g; 0.6 mol) activated by heating with a few crystals of iodine was suspended in 30 ml of tetrahydrofuran and 1,4-dibromobutane (43 g; 0.2 mol) dissolved in 580 ml of tetra-

hydrofuran was added dropwise to it. The mixture was refluxed under stirring for 10 hours. Ethyl isonicotinate (60.4 g) in 100 ml of tetrahydrofuran was then added dropwise and the mixture refluxed for 12 hours. After decomposition with 140 ml of 10% hydrochloric acid it was steam distilled. The residue in the flask was alkalinized and extracted with chloroform. The usual work-up gave 6 g of product (9.7%), b.p. 130°C/2.5 Torr, m.p. 84.5°C. For $C_{10}H_{13}NO$ (163.2) calculated: 73.59% C, 8.05% H, 8.58% N; found: 73.53% C, 8.37% H, 8.65% N.

Reduction of 1-(4-Pyridyl)cyclopentanol with Zinc and Formic Acid

A solution of 10 g (0.061 mol) of *IIId* in 100 ml of 98% formic acid was heated at 160°C for 2 hours. Zinc dust (78 g) was then added and the mixture refluxed for 3 hours. More formic acid (40 ml of 98%) was added and the heating at 160°C was prolonged for another 10 hours. Zinc was then extracted with boiling water, the solution was alkalinized and steam distilled. The distillate was extracted with ether, the extract dried over magnesium sulfate, ether distilled off and the residue distilled, b.p. 112°C/25 Torr. Yield: 6.9 g (77%). Literature⁶ gives for *IIIe* b.p. 245–246°C/738 Torr. For $C_{10}H_{13}N$ (147.2) calculated: 81.59% C, 8.90% H, 9.51% N; found: 81.50% C, 9.14% H, 9.58% N. Other alcohols and alkenylpyridines were reduced in a similar manner (Table I).

4-(1-Cyclopentenyl)pyridine (*IIIf*)

A mixture of 4.2 g of *IIId*, 7.6 ml of acetic acid, and 7.6 ml of concentrated sulfuric acid was heated on a water bath for 7 hours, then alkalinized and the product steam distilled. Applying the conventional working up procedure 2.85 g (76%) of product were obtained, m.p. 41.5–43°C (after vacuum sublimation). For $C_{10}H_{11}N$ (145.2) calculated: 82.71% C, 7.64% H, 9.65% N; found: 82.88% C, 7.50% H, 9.35% N. NMR spectrum (p.p.m.): CH_2 2.06 (q; 7 Hz), $\text{CH}_2-\text{C}=\text{CH}-\text{CH}_2$ 2.40–2.80 (m), $=\text{CH}$ 6.35–6.45 (m), 3-H 7.18–7.30 (m), 2-H 8.40–8.60 (m).

2-(1-Cyclopentenyl)pyridine (*If*) was prepared in an analogous manner. Yield 77%, b.p. 96°C/10 Torr. Literature⁷ gives b.p. 238–239°C/750 Torr. For $C_{10}H_{11}N$ (145.2) calculated: 82.71% C, 7.64% H, 9.65% N; found: 82.54% C, 7.66% H, 9.89% N. Isopropenylpyridines *Ic*, *Ile*, *IIIc* were prepared analogously.

1,3,3-Trimethyl-1-phenyl-1,2-dihydroindene (*IV*)

A. A mixture of 4.2 g (0.03 mol) of dimethyl(phenyl)methanol⁸ and 50 ml of 98% formic acid was heated at 160°C for 1.5 hours. Additional 50 ml of formic acid were added and the mixture heated at 160°C for 11 hours. The mixture was alkalinized and steam distilled. Crystals separated in the condenser. They were extracted with ether together with the distillate. After conventional working up 1.35 g (37%) of product, m.p. 51–52°C, were obtained, in agreement with lit.⁵. For $C_{18}H_{20}$ (236.35) calculated: 91.47% C, 8.53% H; found: 91.59% C, 8.61% H. NMR spectrum (p.p.m.): CH_3 1.0 (s), 1.30 (s), 1.63 (s); CH_2 2.12 (d; 12 Hz) 2.38 (d; 12 Hz); Ar—H 7.0–7.3 (m).

B. The same amounts of starting materials gave in the presence of 40 g of zinc dust under similar conditions 1.65 g (45.5%) of product of the same quality.

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