HYDROBORATION OF UNSATURATED AMINES. VIII.*

HYDROBORATION OF 1,4-DIMETHYL-3-PIPERIDEINE, 1,4-DIETHYL-3-PIPERIDEINE, AND 1-METHYL-4-ETHYL-3-PIPERIDEINE

M.FERLES, J.HAUER, J.KOLÁŘ, Z.POLÍVKA and P.ŠTERN

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

Received July 26th, 1971

On hydroboration of 1,4-dimethyl-3-piperideine, 1,4-diethyl-3-piperideine, and 1-methyl-4-ethyl-3-piperideine at room temperature and subsequent oxidation with hydrogen peroxide in alkaline medium a mixture of amino alcohols *II* and *III* is formed, accompanied by a small amount of *IV*. When hydroboration is carried out at higher temperature a small amount of *V* is also formed.

In our preceding papers we have described the course of hydroboration of 1-methyl-3-piperideine[1] and 1,3-dimethyl-3-piperideine[1,2]. In this paper we describe the hydroboration of 1,4-dialkyl-3-piperideines: 1,4-dimethyl-3-piperideine (*Ia*), 1,4-diethyl-3-piperideine (*Ic*), and 1-methyl-4-ethyl-3-piperideine (*Ib*). When hydroboration was carried out with diborane created directly in the reaction mixture from sodium borohydride and boron trifluoride in diglyme, oxidation of the reaction mixture of bases *Ia* and *Ic* with hydrogen peroxide in alkaline medium led to two amino alcohols for each base, while base *Ib* gave three amino alcohols. The main products of these hydroborations were 1,4-dimethyl-3-piperidinol, 1,4-diethyl-3-piperidinol, and 1-methyl-1,4-ethyl-3-piperidinol, respectively, as shown on the basis of their NMR spectra. Although we did not determine the configuration of these amino alcohols we believe that in analogy to the hydroboration of 1,3-dimethyl-3-piperideine[2] the products are *trans*-isomers (*IIa,b,c*).

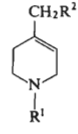
We obtained both stereoisomeric 1,4-dimethyl-3-piperidinols (possessing identical mass spectra) from 4-methyl-3-pyridinol by its conversion to methobromide and hydrogenation on Raney-nickel. The by-products of the hydroboration of *Ia* were shown to be 1,4-dimethyl-4-piperidinol (*IVa*), 1,4-diethyl-4-piperidinol (*IVc*), 1-methyl-4-ethyl-4-piperidinol (*IVb*), and 1-methyl-4-α-hydroxyethylpiperidine (*Vb*) on the basis of their analyses and comparison with synthetic samples. Amino alcohols *IVa*, *IVb* and *IVc* were prepared from the corresponding 1-alkyl-4-piperidone with methyl-

* Part VII: This Journal *36*, 4099 (1971).

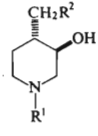
lithium or ethyllithium. Amino alcohol *Vb* was identified by comparison with a product prepared from 1-methyl-4-acetylpyridinium iodide on reduction with sodium borohydride and subsequent hydrogenation.

Hydroboration of bases *Ia,b,c* with triethylamine-borane at elevated temperature in all instances gave mixtures of both stereoisomeric 1,4-dialkyl-3-piperidinols (*II, III*), further 1,4-dialkyl-4-piperidinols (*IV*), and a negligible amount of 1-alkyl-4-α-hydroxyethylpiperidines (*V*). As the minor isomers from each pair of stereoisomeric amino alcohols *II* and *III* have identical mass spectra and similar NMR spectra as the main product of hydroboration carried out in the cold, we consider that they are *cis*-isomers *IIIa,b,c*. This is in agreement with the hydroboration of 1-methyl-1-cyclohexene where, in the cold, *trans*-2-methylcyclohexanol is formed upon *cis*-addition, while at elevated temperature a minor fraction of the *cis*-product[3] is also formed. The *cis*-products are not formed primarily by *trans*-addition, but by isomerisation of the primary hydroboration product which possesses *trans*-configuration[4]. We consider that the configurational relationships of the further two pairs of amino alcohols formed by hydroboration of *Ib* and *Ic* at elevated temperature and subsequent oxidation will be analogous, *i.e.* that the main components in the stereoisomeric mixture will be *trans*-isomers *IIb,c*, and the minor components the *cis*-isomers *IIIb* and *IIIc*.

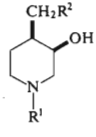
Derivative *Vc* was obtained from 4-acetylpyridine. This was reduced with lithium aluminum hydride to 4-α-hydroxyethylpyridine, the latter was transformed to ethobromide, and this quaternary salt then reduced with sodium borohydride to 1-ethyl-4-α-hydroxyethyl-3-piperideine (*VI*) and eventually hydrogenated.



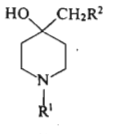
I



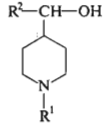
II



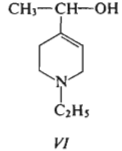
III



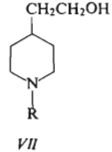
IV



V



VI



VII

I–V, a, $R^1 = CH_3$, $R^2 = H$; *b*, $R^1 = R^2 = CH_3$; *c*, $R^1 = C_2H_5$, $R^2 = CH_3$

It is worth mentioning that on hydroboration at elevated temperature of bases *Ib* and *Ic* the expected amino alcohols *VII* with the hydroxy group in the position β are not formed. The formation of these amino alcohols would require a temporary formation of bicyclic amine-boranes with two seven-membered rings. On the other hand, when base *Ia* is submitted to hydroboration at elevated temperature the formation of additional products has been observed the structure of which we have been unable to solve satisfactorily so far. We suppose that a ring cleavage is involved in this case.

EXPERIMENTAL

The melting points and the boiling points were not corrected. Crystalline substances were dried for analysis *in vacuo* at 0·5 Torr for 8 hours. The IR spectra were measured on a Zeiss UR 10 spectrograph, the PMR spectra on Tesla BS 487 (80 Mc/s) and Varian (100 Mc/s) spectrometers in deuteriochloroform, with hexamethyldisiloxan as internal standard. The mass spectra were measured on a Gas Chromatograph — Mass Spectrometer LKB 9000 Produkter AB Stockholm. The samples were dosed *via* the gas chromatographic column (length 2·5 m, 20% Carbowax 20M on Chromosorb W, carrier gas helium). The gas chromatographic analyses were carried out on a Chrom II apparatus (2 m column, diameter 0·6 cm, 15% Tridox on Celite or 20% Carbowax M on Chromosorb W, carrier gas nitrogen or argon, ionisation detection). Preparative gas chromatography was carried out on an apparatus of non-commercial origin[5]. Thin-layer chromatography was carried out on neutral alumina, activity III according to Brockmann, detection with iodine vapours. Diglyme for hydroboration was purified and dried by distillation with lithium aluminum hydride[6,7]. Hydroborations were carried out under dry nitrogen.

1,4-Diethylpyridinium Iodide

A mixture of 30 g of 4-ethylpyridine[8] in 100 ml of ethanol and 57 g of ethyl iodide in 50 ml of ethanol was refluxed for 6·5 hours. On evaporation of the solvent and excess ethyl iodide a hygroscopic product was obtained in 99% yield (73·1 g), m.p. 49—56°C.

1,4-Diethyl-3-piperideine (*Ic*)

a) *By reduction with lithium aluminum hydride*: 1,4-Diethylpyridinium iodide (26·3 g) was added under stirring to a suspension of 7·9 g of lithium aluminum hydride in 150 ml of ether, and the reaction mixture was refluxed for 6 hours. Dilute hydrochloric acid (8%, 130 ml) was then added to the mixture, followed by 100 ml of water, and the ethereal layer was separated. The aqueous layer was alkalised with a 40% NaOH and the base was steam distilled. The base was then salted out from the distillate with sodium hydroxide and dried over potassium hydroxide. By distillation through a Němec column 9·45 g (68%) of a product were obtained, b.p. 82°C/22 Torr, containing 78% of compound *Ia*. The distillate was diluted with water (1 : 3) and neutralised with hydrobromic acid. The hydrobromide solution was evaporated to dryness and the residue dissolved in chloroform. To this solution a 10% solution of bromine in chloroform was added and the mixture allowed to stand overnight. It was then evaporated under reduced pressure and the residue crystallised from ethyl acetate–acetone 3 : 1. M.p. of the product 154·5—155°C, yield 15·03 g. For $C_9H_{18}Br_3N$ (380·0) calculated: 28·45% C, 4·78% H, 3·69% N; found: 28·64% C, 4·74% H, 3·94% N. To a solution of 14·43 g of 3,4-dibromo-1,4-diethylpiperidinium bromide in a minimum amount of water zinc (7·8 g) was added and the mixture stirred for 2 hours. The excess zinc was separated by filtration and the filtrate alkalised with a 40% NaOH and steam distilled. The base was salted out and dried over potassium hydroxide, b.p. 67·5—68°C/14 Torr.

Yield 2·98 g (57%) of base *Ic*. For $C_9H_{17}N$ (139·2) calculated: 77·63% C, 12·30% H, 10·06% N; found: 77·89% C, 12·33% H, 10·22% N. PMR spectrum: CH_3CH_2 1·0 (t; *J* 5 Hz), CH_3CH_2N 1·1 (t; *J* 7Hz), CH_2—N (1·77–2·26 (m), CH_2C=C (2·39–2·63 (m), C=CH—CH_2—N 2·93 (m), CH= 5·35 (m) (in δ values).

b) *By reduction with sodium borohydride*: A solution of 95 g of 1,4-diethylpyridinium iodide in 238 ml of water was mixed with a solution of 14·7 g of sodium hydroxide in 238 ml of water. To this mixture sodium borohydride (14·7 g) in 121 ml of water was added and the mixture steam distilled. The base was salted out and dried over potassium hydroxide; b.p. 68–69°C/12 Torr. Yield 34·83 g (68%) of compound *Ic*, identical with that prepared under *a*).

Hydroboration of 1,4-Dimethyl-3-piperideine (*Ia*)

A) To a mixture of 11·1 g (0·1 mol) of compound[9] *Ia* and 6·3 g (0·16 mol) of 96·5% sodium borohydride in 150 ml of diglyme a solution of 31·7 g (0·21 mol) of a 94% boron trifluoride etherate in 50 ml of diglyme was added dropwise at 25°C over 30 minutes. The mixture was stirred for another 60 minutes at the same temperature, then decomposed with 11 ml of water, 52 ml 36% hydrochloric acid, and eventually alkalised under stirring with 85 ml of 40% NaOH. Hydrogen peroxide (70 ml of a 30% solution) was then added over 60 minutes and the reaction mixture stirred for 3 hours. The mixture was extracted twice with 50 ml of ether and twice with 50 ml of chloroform and the combined extracts were acidified with an ethereal hydrogen chloride solution. The solution was evaporated to dryness and the residual hydrochlorides were dissolved in 50 ml of water and the solution extracted with chloroform. The combined extracts were dried over potassium carbonate, the solvent was evaporated through a column, and the residue was vacuum-distilled, b.p. 85–90°C/12 Torr. The mixture of amino alcohols was analysed by gas chromatography.

B) The reaction was carried out in a manner analogous to the preceding case. After hydroboration was ended the mixture was stirred for another 60 minutes, then heated at 160°C and stirred for 15 minutes. After cooling the mixture was worked up as under *A*). The yield and the composition of the mixture are given in Table I.

Hydroboration of 1-Methyl-4-ethyl-3-piperideine (*Ib*) with Triethylamine Borane at Elevated Temperature

20 g of 1-methyl-4-ethyl-3-piperideine[10] were mixed with a solution of 18·4 g of triethylamine borane in 183 ml of toluene and refluxed for 6 hours (bath temperature 140–145°C, nitrogen atmosphere). The solvent and triethylamine were distilled off under nitrogen through a Němec column (bath 155°C). The residue (17·3 g) was dissolved in 143 ml of acetone and 39·5 ml of 6M-HCl and the solution refluxed for 20 minutes. The solvents were evaporated and the syrupy residue was mixed with 35 ml of tetrahydrofuran and alkalised with 50 ml of a 40% NaOH. Hydrogen peroxide (50 ml of a 30% solution) was then added dropwise over 30 minutes and the tetrahydrofuran layer was separated and the aqueous layer extracted with chloroform. The solvents were evaporated at normal pressure using a Němec column. Vacuum distillation gave 8·09 g of a mixture, b.p. 110·5–111°C/15 Torr, the composition of which is given in Table I. From the reaction mixture the following fractions were isolated: *a*) b.p. 105°C/15 Torr, which could not be obtained by fractional distillation in a purity better than 70% of the main component; *b*) b.p. 110·5–111°C/15 Torr, chromatographically pure. For $C_8H_{17}NO$ (143·2) calculated: 67·09% C, 11·96% H, 9·78% N; found: 67·23% C, 12·20% H, 9·63% N. The mass spectra of both fractions are identical, from which we conclude that the products are stereoisomeric.

Hydroboration of 1,4-Diethyl-3-piperideine (*Ic*) in the Cold

To a solution of 3·15 g of sodium borohydride in 75 ml of diglyme 7 g of compound *Ic* and 15·8 g of boron trifluoride etherate in 25 ml diglyme were added over 20 minutes at 25–26°C. The mixture was stirred for 2 hours, decomposed with 5·5 ml of water and 26 ml of 36% hydrochloric acid, alkalised with 42·5 ml of a 40% NaOH, and additioned dropwise with 35 ml of 30% hydrogen peroxide. The mixture was stirred for another 3 hours, allowed to stand overnight, and extracted with chloroform. The extract was acidified with 27 g of hydrogen chloride in ether, the solvents were evaporated, the residue dissolved in 25 ml of water, and the solution extracted with

TABLE I

Review of Hydroborations of 1,4-Dialkyl-3-piperideines (*I*)

Starting base	Procedure[a]	Yield, %	*II*, %	*III*, %	*IV*, %	*V*, %
Ia	A	22·4	98	—	2	—
Ia	B	24·7	26	18	18	3
Ia	C	75	23	14	14	—
Ib	A	34·4	86	7	7	—
Ib	D	35	74	23·5	1·5	1
Ic	A	41	94·5	—	5·5	—
Ic	D	55	66	30	3	1

[a] A, $NaBH_4$ and BF_3, diglyme, 25°C; B, $NaBH_4$ and BF_3, diglyme, 160°C; C, $(C_2H_5)_3N\text{-}BH_3$, xylene, 140°C; D, $(C_2H_5)_3N\text{-}BH_3$, toluene, 140°C.

TABLE II

NMR Spectra of Amino Alcohols *II*–*V* (δ values)

Compound	CH_3—C	CH_3—N	OH	CH—OH	CH_2—N	CH_2
IIa	0·98 ud[a] $J = 2·5$	2·14 s	4·97 s	3·03 m	2·44–2·98 m	1·63 m
IIb	0·97 t[b]	2·23 s	4·2 s	3·38 m	2·6 –3·05 m	1·65–2·0 m
IIc[c]	0·95 t[b]	—	3·41 s	3·41 m	2·47–3·1 m	1·66–2·0 m
IIIa	0·93 d[d]	2·12 s	2·9 s	3·55 m	2·53–2·86 m	1·37–2·09 m
IVa	1·1 s	2·12 s	3·5 s	—	2·29 t[b]	1·47 t[b]
IVb	0·9 t[b]	2·08 s	3·07 s	—	2·0 –2·9 m	1·1 –2·0 m
IVc[e]	0·92 t[f]	—	1·7 s	—	2·0 –2·9 m	1·3 –1·83 m
Vb	1·15 d[d]	2·23 s	2·12 s	3·53 s	2·2 –3·1 m	1·7 –2·0 m

[a] Methine proton on $C_{(4)}$ is shifted to the CH_3—C region, J 25 Hz; [b] J 6 Hz; [c] N—CH_2CH_3 2·42 t, J 7 Hz; [d] J 7 Hz; [e] N—CH_2—CH_3 1·07, J 6 Hz; [f] J 6·5 Hz.

chloroform. The aqueous layer was alkalised with 40% sodium hydroxide solution and extracted with chloroform. The extracts were dried over potassium carbonate, chloroform was evaporated, and the residue distilled using a Němec column; b.p. 110—114°C/15 Torr. Yield 2·95 g (41%). Composition of the product is given in Table I.

1,4-Dimethyl-3-hydroxypyridinium Bromide

A mixture of 17·1 g (0·157 mol) of 4-methyl-3-pyridinol[11], 74·5 g (0·785 mol) of methyl bromide and 70 ml of methanol was heated in a glass autoclave (400 ml) at 55°C for 20 hours. The mixture was evaporated to dryness and the residue crystallised from methanol; Yield 28·1 g (87·8%) of a compound, m.p. 145·5—146°C. For $C_7H_{10}BrNO$ (204·1) calculated: 41·20% C, 4·94% H, 39·16% Br, 6·86% N; found: 41·12% C, 5·13% H, 39·18% Br, 6·73% N.

1,4-Dimethyl-3-piperidinol (*IIa, IIIa*)

A mixture of 22·8 g (0·112 mol) of 1,4-dimethyl-3-hydroxypyridinium bromide, 5 g of Raney nickel, and 200 ml of methanol was hydrogenated in a 0·5 l autoclave at 120°C, at a starting pressure of 150 atm, for 3 hours. After cooling the catalyst was filtered off and the filtrate evaporated to dryness. The residue was dissolved in a small amount of water, the solution alkalised with 15% NaOH, and extracted with chloroform. The combined extracts were dried over potassium carbonate and chloroform was evaporated using a column. Distillation of the residue gave 1·65 g (11·4%) of a liquid boiling at 60—95°C/15 Torr, which according to gas chromatography represents a mixture of *cis* and *trans*-1,4-dimethyl-3-piperidinols in a 64 : 36 ratio (Tridox, 150°C, 0·4 kp/cm^2). Preparative gas chromatography (Tridox, 150°C) gave:

Isomer IIIa: B.p. 155—156°C/745 Torr. For $C_7H_{15}NO$ (129·2) calculated: 65·07% C, 11·70% H, 10·84% N; found: 65·25% C, 11·80% H, 11·02% N. NMR spectrum (100 Mc/s) see Table II. Mass spectrum, *m/e* (relative intensity): 129 (26·0), 128 (13·8), 114 (2·6), 112 (9·6), 110 (3·4), 100 (6·0), 98 (5·2), 96 (5·8), 86 (9·2), 71 (22·6), 70 (12·0), 58 (99·5), 57 (16·6), 44 (82·8), 43 (100), 42 (68·5), 39 (13·4).

Isomer IIa: B.p. 90—91°C/12 Torr. For $C_7H_{15}NO$ (129·2): calculated: 65·07% C, 11·70% H, 10·84% N; found: 65·10% C, 11·72% H, 10·79% N. Mass spectrum, prominent ions *m/e* (relative intensity): 129 (24·4), 128 (14·0), 114 (2·6), 112 (8·4), 110 (3·4), 100 (1·4), 98 (5·0), 96 (6·0), 86 (6·0), 71 (23·2), 70 (11·4), 58 (99·5), 57 (16·3), 44 (61·2), 43 (100), 42 (67·2), 39 (13·2).

1,4-Dimethyl-4-piperidinol (*IVa*)

As the product prepared according to literature[12] contained the starting 1-methyl-4-piperidone, a five-fold molar excess of methyllithium was used for the reaction. On crystallisation from light petroleum a compound of m.p. 66—67°C was obtained; literature[17] gives m.p. 66·4—68°C. NMR spectrum (deuteriochloroform, 100 Mc/s) see Table II. Mass spectrum (prominent ions) *m/e* (relative intensity): 129 (24·2), 128 (20·2), 114 (4·4), 112 (7·8), 110 (9·5), 86 (43·2), 71 (22·8), 70 (50·2), 58 (11·4), 44 (48·6), 43 (100), 42 (76·4), 41 (18·8), 39 (8·8).

1-Methyl-4-ethyl-4-piperidinol (*IVb*)

To a suspension of 2·1 g of lithium in 30 ml of ether a solution of 17·75 g of ethyl bromide in 70 ml of diethyl ether was added and the mixture refluxed under stirring for 2 hours. The liquid was transferred using nitrogen (pressure) into another flask and a solution of 2·1 g of 1-methyl-

4-piperidone[13] in 25 ml of benzene was added to it over 55 minutes, under external cooling. The reaction mixture was refluxed for 11·5 hours under stirring and then decomposed with 40 ml of water and 25 ml of 40% NaOH. The solvent layer was separated and the aqueous layer extracted with chloroform. The combined extracts were dried over potassium carbonate. After evaporation of the solvent compound *IVb* was obtained, b.p. 97–98°C/12 Torr, 1·1 g (41%). For $C_8H_{17}NO$ (143·3) calculated: 67·09% C, 11·96% H, 9·78% N; found: 66·96% C, 11·89% H, 9·73% N. Mass spectrum, *m/e* (relative intensity): M 157 (25), M − 1 (18), M − CH_3 (100), M − HO—CH—CH_3 (15); 28 (28), 29 (17), 42 (26), 43 (20), 44 (15), 55 (25), 58 (49), 124 (10), 143 (15).

1,4-Diethyl-4-piperidinol (*IVc*)

To a suspension of 5·62 g of lithium in 80 ml of ether 48·5 g of ethyl bromide in 160 ml of ether was added and the mixture refluxed for one hour. After the elimination of the unreacted lithium the ethyllithium solution in ether was additioned with a solution of 3·2 g of 1-ethyl-4-piperidone[14,15] in 33·5 ml of ether over 20 minutes at −30°C. The mixture was kept for one hour at −30°C and then for 3 hours at room temperature. Eventually it was refluxed for 10 hours. The reaction mixture was decomposed with 107 ml of water and 67 ml of 40% NaOH, then extracted with chloroform and dried over potassium carbonate. Yield 1·87 g *IVc*, b.p. 102°C/16 Torr. For $C_8H_{17}NO$ (143·3) calculated: 67·09% C, 11·96% H, 9·78% N; found: 66·96% C, 11·89% H, 9·73% N. Mass spectrum, *m/e* (relative intensity): M − 157 (27), M − CH_3 (100%), M − OH (9), M − C_2H_5 (19); 28 (38), 29 (29), 32 (63), 42 (58), 56 (36), 57 (45), 58 (39), 84 (37), 110 (19), 112 (15), 124 (43), 143 (13).

1-Methyl-4-hydroxymethylpiperidine (*Va*)

A solution of 0·65 g (5·1 mmol) of 1-methyl-4-hydroxymethyl-3-piperideine[16] in 30 ml of methanol was mixed with 30 mg of Adams catalyst and hydrogenated at 21°C and 745 Torr for 5 hours. The hydrogen consumption was 114 ml (90·5%). The catalyst was filtered off and methanol evaporated using a column. Distillation of the residue gave 0·60 g (91·2%) of a liquid, b.p. 104 to 105°C/20 Torr; literature[17] gives 110–111°C/16 Torr. For $C_7H_{15}NO$ (129·2) calculated: 65·07% C, 11·70% H, 10·84% N; found: 65·01% C, 11·79% H, 10·95% N. Mass spectrum, *m/e* (relative intensity): 129 (34·6), 128 (49·2), 112 (9·6), 110 (6·8), 98 (22·2), 71 (12·4), 70 (27·2), 58 (16·0), 57 (16·4), 55 (35·4), 45 (15·0), 44 (100), 43 (60·8), 42 (73·9), 41 (21·8), 39 (16·4).

1-Methyl-4-α-hydroxyethylpiperidine (*Vb*)

To a solution of 5 g of 1-methyl-4-acetylpyridinium iodide[18] in 25 ml of water 1·45 g of sodium borohydride was added under stirring over 30 minutes. After 7 hours stirring the separated crystals were filtered off under suction and the filtrate was extracted with chloroform and dried over potassium carbonate. After evaporation of the chloroform the residue was vacuum-distilled to yield 2 g of a liquid, b.p. 104°C/10 Torr. To a solution of 1·6 g of this product in 20 ml of ethanol 50 mg of Adams catalyst were added and the mixture hydrogenated at ordinary pressure and room temperature. After 5 hours 250 ml of hydrogen were absorbed (98% per one double bond). The catalyst was filtered off, ethanol was evaporated under reduced pressure, and the residue distilled to give 1·4 g (65%) of *Vb*, b.p. 104°C/10 Torr. Literature[18] gives b.p. 104 to 111°C/3 Torr, or[19] 111–112°C/15 Torr. For $C_8H_{17}NO$ (143·2) calculated: 67·08% C, 11·96% H, 9·79% N; found: 67·15% C, 12·09% H, 9·70% N. For NMR see Table II.

4-α-Hydroxyethylpyridine

Into a suspension of 4·03 g of lithium aluminum hydride in 100 ml of ether a solution of 25·7 g of 4-acetylpyridine[20] in 100 ml of ether was added and the reaction mixture refluxed for one hour. It was decomposed, under cooling, with 4 ml of water, 4 ml of a 15% sodium hydroxide solution, and finally with 12 ml of water. The salt formed was filtered off using a sintered glass filter and the ethereal solution was dried over potassium carbonate. Ether was distilled off and the residue distilled *in vacuo*. Yield 10·83 g (42%), b.p. 139—142·5°C/10 Torr. Literature[21] gives b.p. 138 to 140°C/30 Torr.

1-Ethyl-4-α-hydroxyethyl-3-piperideine (*VI*)

To a solution of 10·83 g of 4-α-hydroxyethylpyridine in 35 ml of ethanol a solution of 8·1 ml of ethyl bromide in 15 ml of ethanol was added and the mixture refluxed for 32 hours. Ethanol was evaporated and the non-crystalline residue (bromide) weighed (20·1 g; 97%). 1-Ethyl-4-α-hydroxyethylpyridinium bromide was dissolved in 60 ml of water and 3·7 g of sodium hydroxide in 60 ml of water. A solution of 3·7 g of sodium borohydride in 30 ml of water was added to the above solution and the reaction mixture stirred for 30 minutes, then extracted with chloroform and the extract dried over potassium carbonate. After evaporation of the solvent the residue was distilled, b.p. 129—132°C/10 Torr. Yield 9·17 g (62%). For $C_9H_{17}NO$ (155·2) calculated: 69·63% C, 11·04% H, 9·02% N; found: 69·42% C, 11·10% H, 9·26% N. NMR spectrum: $C\underline{H}_3—CH_2—N$ 1·1 (t; $J = 7$ Hz), $C\underline{H}_3—CH—OH$ 1·22 (d; $J = 7$ Hz), CH_2 2·16—2·63 (m) $CH_2—C{=}C$ 2·93 (m), OH 3·98 (s), $HO—CH—CH_3$ 4·15 (q; $J = 7$ Hz), CH = 5·58 (m) (in δ values). Mass spectrum, *m/e* (relative intensity): M 155 (12), M — 1 (10%), M — CH_3 (16), M — HO—CH—CH_3 (100); 29 (18), 42 (27), 43 (34), 58 (16), 111 (18), 122 (9), 142 (9).

1-Ethyl-4-α-hydroxyethylpiperidine (*Vc*)

A mixture of 4·66 g of compound *VI* and 140 mg of Adams catalyst in 100 ml of ethanol was hydrogenated for 15 hours. Ethanol was evaporated off and the residue distilled in a vacuum, b.p. 121—122·5°C/10 Torr. *Picrate*, m.p. 160°C (ethyl acetate). For $C_{15}H_{22}N_4O_8$ (386·4) calculated: 46·63% C, 5·74% H, 14·50% N; found: 46·92% C, 5·84% H, 14·68% N. The picrate was decomposed with a lithium hydroxide solution in hot water and the base was extracted with chloroform. The extract was dried over potassium carbonate and distilled, b.p. 117°C/10 Torr. Yield 1·1 g of compound *Vc*. For $C_9H_{19}NO$ (157·3) calculated: 68·74% C, 12·18% H, 8·91% N; found: 69·03% C, 12·32% H, 9·15% N. Mass spectrum, *m/e* (relative intensity): M 157 (24), M — 1 (17), M — CH_3 (100), M — HO—CH—CH_3 (15); 28 (28), 29 (17), 42 (26), 43 (20), 55 (25), 58 (49), 124 (10), 143 (15).

Elemental analyses were carried out in the Analytical Laboratory of our Department. Mass spectra were measured by Dr V. Kubelka, NMR spectra by Dr P. Trška (both from the Institute of Chemical Technology, Prague), Dr M. Masojídková, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague, and Dr D. Doskočilová, Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, Prague.

REFERENCES

1. Polívka Z., Ferles M.: This Journal *35*, 2392 (1970).
2. Ferles M., Hauer J., Polívka Z.: This Journal *36*, 4099 (1971).
3. Brown H. C., Zweifel C.: J. Am. Chem. Soc. *83*, 2544 (1961).
4. Tichý M., Hapala J., Sicher J.: Unpublished results.
5. Lukeš V., Herout V.: This Journal *25*, 2770 (1960).
6. Brown H. C., Mead E. J., Subba Rao B. C.: J. Am. Chem. Soc. *77*, 6209 (1955).
7. Brown H. C., Tierney P. A.: J. Am. Chem. Soc. *80*, 1552 (1958).
8. Frank R. L., Smith P. V.: Org. Syn. *27*, 38 (1947).
9. Ferles M.: This Journal *23*, 479 (1958).
10. Ferles M., Kovařík M., Vondráčková Z.: This Journal *31*, 1348 (1966).
11. Traynelis V. J., Martello R. F.: J. Am. Chem. Soc. *82*, 2744 (1960).
12. McElvain S. M., Berger R. S.: J. Am. Chem. Soc. *77*, 2848 (1955).
13. McElvain S. M., Rorig K.: J. Am. Chem. Soc. *70*, 1820 (1948).
14. Duson R. C., Parham W. E., Reed L. J.: J. Am. Chem. Soc. *68*, 1239 (1946).
15. Barbulescu N., Greff C.: Rev. Chim. (Bucharest) *17*, 202 (1966); Chem. Abstr. *65*, 8870 (1966).
16. Ferles M.: This Journal *24*, 2221 (1959).
17. Lukeš R., Ferles M., Štrouf O.: This Journal *24*, 212 (1959).
18. Nielsen A. T., Moore D. W., Mazur J. H., Berry K. H.: J. Org. Chem. *29*, 2898 (1964).
19. Lukeš R., Štrouf O., Ferles M.: This Journal *22*, 326 (1957).
20. Kolloff H. G., Hunter J. H.: J. Am. Chem. Soc. *63*, 490 (1941).
21. Clemo G. R., Hoggarth E.: J. Chem. Soc. *1941*, 41.

Translated by Ž. Procházka.