# HYDROBORATION OF 1-(5-HEXENYL)PIPERIDINE AND *trans*-1-(3-HEXENYL)PIPERIDINE*

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1-(5-Hexenyl)piperidine (*Ia*) and *trans*-1-(3-hexenyl)piperidine (*Ib*) were hydroborated with tetrahydrofuran–borane, diborane *in situ*, 9-borabicyclo[3.3.1]nonane and triethylamine–borane. The hydroboration products were converted to 1-piperidinylhexanols *IIa*—*IIe* by hydrolysis with hydrochloric acid and subsequent oxidation with hydrogen peroxide in an alkaline medium. In addition to the alcohols *IIa*—*IIe*, the reaction also gave 1-hexylpiperidine (*Ic*). In the reactions with diborane *in situ* and triethylamine–borane, thermal isomerisation of the hydroboration products was also studied. Hydroboration of *Ia* with triethylamine–borane afforded a mixture of spirocyclic amine–boranes *IIIa*—*IIIc* from which 6-(1-piperidinyl)-3-hexylboronic acid hydrochloride (*IV*) was obtained by hydrolysis with hydrochloric acid. Compounds *IIIa*—*IIIc* were slowly decomposed with ethanol to give esters of boronic acids *Id*—*If*. The synthesis of compounds *Ia* and *Ib* is described.

In our previous papers we described the results of hydroboration of ω-alkenyldimethylamines[1–5], N-allyl derivatives of pyrrolidine, piperidine, hexahydroazepine and morpholine[6], 1-(3-butenyl)piperidine[7] and 1-(4-pentenyl)-piperidine[7]. Since hydroboration products of ω-alkenyldimethylamines containing alkenyl longer than pentenyl undergo isomerization upon heating[3], we expected an analogous behaviour also for hydroboration products from 1-(5-hexenyl)piperidine (*Ia*). We studied therefore not only hydroboration of compound *Ia* but also of *trans*-1-(3-hexenyl)-piperidine (*Ib*). In case of isomerization equilibrium, the composition should be the same in both cases.

The hydroborations were carried out with four reagents: tetrahydrofuran–borane, diborane generated *in situ* from sodium borohydride and boron trifluoride etherate in diethylene glycol dimethyl ether, 9-borabicyclo[3.3.1]nonane (9-BBN), and triethylamine–borane. The hydroboration products were oxidized to mixtures of the corresponding alcohols which were analysed by gas–liquid chromatography. The oxidation was invariably accompanied by hydrolysis to 1-hexylpiperidine (*Ic*), present in the final mixtures in amounts up to 10%. The results are summarized in Table I.

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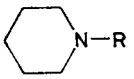
TABLE I

Percentage of compounds in the mixtures after hydrolysis and oxidation of hydroboration products from *Ia* and *Ib*

| Reagent | Temperature °C | Substrate | *Ia* | *Ib* | *Ic* | *IIa*[a,b] | *IIb*[b] | *IIc*[b] | *IId*[b] | *IIe*[b] |
|---|---|---|---|---|---|---|---|---|---|---|
| Tetrahydro-furan–borane | 22 | *Ia* | 26·5 | — | 9·3 | 56·9 (88·6) | 7·3 (11·4) | 0 | 0 | 0 |
| | 22 | *Ib* | — | 3·2 | 4·1 | 0 | 0 | 27·5 (29·7) | 59·8 (64·5) | 5·4 (5·8) |
| 9-BBN[c] | 65 | *Ia* | 4·9 | — | 2·1 | 92·7 (99·7) | 0·3 (0·3) | 0 | 0 | 0 |
| | 65 | *Ib* | — | 22·1 | 5·9 | 0 | 0 | 20·6 (28·6) | 49·3 (68·5) | 2·1 (2·9) |
| Diborane *in situ* | 22 | *Ia* | 39·2 | — | 9·6 | 46·0 (89·8) | 5·2 (10·2) | 0 | 0 | 0 |
| | 160[d] | *Ia* | 0 | — | 4·2 | 75·5 (78·8) | 9·6 (10·0) | 10·7 (11·2) | 0 0 | 0 0 |
| | 22 | *Ib* | — | 54·5 | 8·2 | 0 | 0 | 12·6 (33·8) | 22·1 (59·2) | 2·6 (7·0) |
| | 160[d] | *Ib* | — | 0 | 8·3 | 0 | 0 | 18·7 (20·4) | 66·6 (72·6) | 6·7 (7·0) |
| Triethylamine–-borane | 150 | *Ia* | 12·5 | — | 9·5 | 61·3 (78·6) | 16·7 (21·4) | 0 | 0 | 0 |
| | 200[e] | *Ia* | 0 | — | 6·6 | 53·8 (57·6) | 13·7 (14·7) | 12·8 (13·7) | 13·1 (14·0) | 0 |
| | 150 | *Ib* | — | 57·7 | 3·4 | 0 | 0 | 13·9 (35·7) | 22·2 (57·1) | 2·8 (7·2) |
| | 200[e] | *Ib* | — | 0 | 4·2 | 0 | 1·3 (1·4) | 36·5 (38·1) | 57·3 (59·8) | 0·7 (0·7) |

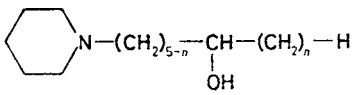
[a] Prepared according to ref.[8]; [b] in parentheses percentage of the total amount of *IIa*–*IIe*; [c] 9-borabicyclo[3.3.1]nonane; [d] reaction time 3 h; [e] reaction time 2 h.

Hydroborations of compounds *Ia* and *Ib* with tetrahydrofuran–borane were carried out at room temperature at which the products did not isomerize. The presence of *Ia* or *Ib* in the products indicates that in a concurrent reaction a part of the reagent

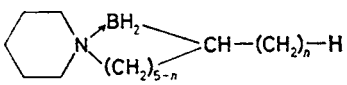


*Ia*, R = $(CH_2)_4CH=CH_2$ (7–10, 11, 12)
*Ib*, R = $CH_2CH_2C(H)=C(H)CH_2CH_3$
*Ic*, R = $(CH_2)_5CH_3$
*Id*, R = $(CH_2)_4CH(B(OC_2H_5)_2)-CH_3$
*Ie*, R = $(CH_2)_3CH(B(OC_2H_5)_2)-CH_2CH_3$
*If*, R = $(CH_2)_2CH(B(OC_2H_5)_2)-CH_2CH_2CH_3$

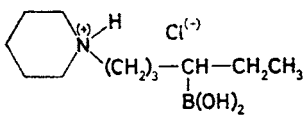
*Ig*, R = $CO(CH_2)_3CH=CH_2$
*Ih*, R = $COCH_2C(H)=C(H)CH_2CH_3$
*Ii*, R = $CO(CH_2)_3COCH_3$
*Ij*, R = $CO(CH_2)_2COCH_2CH_3$
*Ik*, R = $CO-CHOH-(CH_2)_3CH_3$



*IIa*, *n* = 0
*IIb*, *n* = 1
*IIc*, *n* = 2
*IId*, *n* = 3
*IIe*, *n* = 4



*IIIa*, *n* = 1
*IIIb*, *n* = 2
*IIIc*, *n* = 3



*IV*

is bonded to the nitrogen lone electron pair, loosing thus (at room temperature) its ability of addition to the double bond. Compound *Ia* gave 6-(1-piperidinyl)-1--hexanol (*IIa*) and 6-(1-piperidinyl)-2-hexanol (*IIb*) in the ratio 89 : 11, the reaction being less selective than hydroboration of 1-hexene[9] (94 : 6). Evidently, compound *Ia* is hydroborated only to the first stage and further hydroboration is precluded by formation of an intramolecular or intermolecular B—N bond, whereas 1-hexene is converted into trihexylborane the total selectivity of the reaction being determined by the selectivity of all three steps. It is known that the anti-Markovnikov addition

of monoalkylboranes, and even more dialkylboranes, to alkenes is more selective than of the unsubstituted diborane. Thus, *e.g.*, hydroboration of 1-hexene with bis(1,2-dimethylpropyl)borane, followed by oxidation, gave 1-hexanol and 2-hexanol in the ratio 99 : 1 (ref.[10]).

Hydroboration of *trans*-1-(3-hexenyl)piperidine (*Ib*) afforded a mixture of 6-(1-piperidinyl)-3-hexanol (*IIc*), 1-(1-piperidinyl)-3-hexanol (*IId*), and 1-(1-piperidinyl)-2-hexanol (*IIe*). We regard the presence of the alcohol *IIe* as a proof that *trans*-3-hexenoic acid, obtained according to Boxer and Linstead[11] and Jutz[12] and used as starting compound for preparation of *Ib*, was contaminated with 2-hexenoic acid. However, our attempts to detect the isomeric 1-(2-hexenyl)piperidine in *Ib* by NMR spectroscopy or gas–liquid chromatography failed. As seen from the percentage of alcohols *IIc*–*IIe*, in hydroboration of *Ib* the boryl group attacks more the position 3 than position 4 because the double bond is polarized by the inductive effect of the nitrogen atom.

Because of large errors in determination of concentration of the reagent and its dosage we could not assess separately the reactivity of the double bonds in *Ia* and *Ib*. Therefore, we hydroborated an equimolecular mixture of *Ia* and *Ib* and evaluated the ratio of *IIa* + *IIb* to *IIc* + *IId* + *IIe* (compounds *Ia* and *Ib* were not separated by gas–liquid chromatography). The found value (55 : 45) shows a slightly higher reactivity of the terminal double bond in *Ia*, as expected.

Hydroboration of 1-(5-hexenyl)piperidine (*Ia*) with 9-borabicyclo[3.3.1]nonane afforded – with the expected high selectivity – the primary alcohol *IIa*; compound *Ib* was converted mainly into alcohol *IId*, similarly as in hydroboration with tetrahydrofuran–borane. The greater amount of *Ib* in the reaction mixture corresponds to a lower reactivity of the disubstituted double bond as compared with the monosubstituted double bond in *Ia*.

Hydroboration of compounds *Ia* and *Ib* with diborane generated *in situ* at 22°C afforded alcohols *IIa*–*IIe* in amounts similar to those obtained by hydroboration with tetrahydrofuran–diborane. These hydroboration mixtures also contained the starting compounds *Ia* or *Ib*. In both cases, heating the products to 160°C resulted in hydroboration of all the hexenyl groups and isomerization of the hydroboration products. After heating for 3 h to this temperature, we found in the mixture from *Ia* also the alcohol *IIc*. The percentage of the primary alcohol *IIa* decreased whereas that of the secondary alcohol *IIb* remained practically constant. Under the same conditions, in the mixture obtained from compound *Ib* the amount of alcohol *IId* increased at the expense of *IIc*; the percentage of *IIe* did not change. We may assume that under the given conditions the hydroboration product which affords *IId* is preferred, and that with *Ia* an equilibrium composition (if exists) could be achieved only after much longer reaction time.

Hydroboration of *Ia* and *Ib* with triethylamine–borane proceeded vigorously; immediately after the reaction we isolated the same products as with tetrahydrofuran–

–borane or with diborane *in situ* at 22°C. However, because of higher reaction temperature and partial isomerization, the formation of primary alcohol *IIa* from *Ia* was less selective (79% rel. compared with about 90% rel. in the latter two methods). The large difference in the content of the substrate is ascribed to the different reactivity of the double bonds in *Ia* and *Ib*.

On heating to 200°C for 2 h, the hydroboration mixture liberated triethylamine. After this treatment, compound *Ia* afforded a mixture containing alcohols *IIc* and *IId*, in addition to *IIa* and *IIb*. The percentage decrease of not only the primary alcohol *IIa* but also of the alcohol *IIb* indicates that shift of the boryl group from the chain end into the neighbouring position is slower than other shifts inside the chain. This agrees with many reports that on heating the boryl group in non-nitrogen boranes shifts preferentially to the carbon chain end[13]. The population of alcohol *IId* was approximately the same as of *IIc*, showing that the boryl group prefers the γ-position relative to the nitrogen atom. Heating the hydroboration mixture from compound *Ib* to 200°C resulted in a substantial drop in the percentage of *IIe* and appearance of a minor amount (1·4% rel.) of alcohol *IIb*. As expected from the experiments with *Ia*, the most populated compound remained the alcohol *IId*.

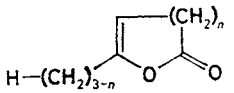
Distillation *in vacuo* of the hydroboration product from *Ia* gave a mixture of 8-methyl-6-aza-7-boraspiro[5.6]dodecane (*IIIa*), 2-ethyl-6-aza-1-boraspiro[5.5]undecane (*IIIb*), and 2-propyl-5-aza-1-boraspiro[4.5]decane (*IIIc*). After conversion to the corresponding alcohols *IIb*, *IIc*, and *IId*, their ratio was determined to be 8·5 : : 77 : 14·5.

We interpret the obtained results as follows: The boryl group of 1-(borylhexyl)-piperidines is stabilized by an intermolecular or intramolecular dative bond N→B. The latter type means ring formation which prefers isomer with the thermodynamically most stable ring. During the distillation the intermolecular N→B bonds must dissociate and in a monomer the boryl group can be stabilized only by an intramolecular bond. Therefore, during the distillation of the hydroboration product, although shorter than 2 h at 200°C, the isomerization in the gas phase proceeded much faster than in the liquid phase. The distillate did not contain any eight-membered cyclic amine–borane because such species is too unstable. In the gas phase, the thermodynamically most stable isomer is the amine–borane *IIIb* with the six-membered ring formed by the N→B bond.

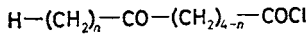
We hydrolyzed the mixture of amine–boranes *IIIa*–*IIIc* with hydrochloric acid and isolated 6-(1-piperidinyl)-3-hexylboronic acid hydrochloride (*IV*) which on oxidation with hydrogen peroxide in alkaline medium afforded alcohol *IIc* without any isomeric alcohols. The reaction of the amine–boranes *IIIa*–*IIIc* with ethanol was slow: After boiling with excess ethanol for 18 h the mixture contained 32% of *IIIa*–*IIIc* and 68% of the corresponding esters of boronic acids *Id*–*If*.

The starting 1-(5-hexenyl)piperidine (*Ia*) was prepared by lithium aluminium hydride reduction of 1-(5-hexenoyl)piperidine (*Ig*) which in turn was obtained by

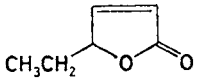
reaction of piperidine with 5-hexenoyl chloride. The compound *Ib* was prepared by analogous reduction of *trans*-1-(3-hexenoyl)piperidine (*Ih*), prepared by treatment of piperidine with the reaction product from *trans*-3-hexenoic acid and thionyl chloride. Reaction of 5-oxohexanoic acid with thionyl chloride afforded a mixture of 5-methyl-4-pentenolide (*Va*) and 5-oxohexanoyl chloride (*VIa*) which was converted into 1-(5-oxohexanoyl)piperidine (*Ii*). The derivative *Ii* was reduced with li-



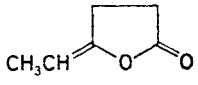
*Va*, $n = 2$
*Vb*, $n = 1$



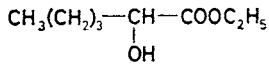
*VIa*, $n = 1$
*VIb*, $n = 2$



*VII*



*VIII*



*IX*

thium aluminium hydride to give the alcohol *IIb*. In an analogous way, 4-oxohexanoic acid and thionyl chloride furnished a mixture of 4-ethyl-3-butenolide (*Vb*), 4-ethyl-2--butenolide (*VII*), 4-ethylidenebutanolide (*VIII*), and 4-oxohexanoyl chloride (*VIb*) from which we prepared 6-(1-piperidinyl)-3-hexanol (*IIc*) *via* 1-(4-oxohexanoyl)-piperidine (*Ij*). 1-(1-Piperidinyl)-3-hexanol (*IId*) was obtained by reduction of 1-(1-piperidinyl)-3-hexanone with lithium aluminium hydride, 1-(1-piperidinyl)-2--hexanol (*IIe*) was synthesized from 2-hydroxyhexanoylpiperidine (*Ik*) formed from ethyl 2-hydroxyhexanoate (*IX*) and piperidine. Reaction of piperidine with 1-bromo-hexane in 2-butanone in the presence of potassium carbonate gave 1-hexylpiperidine (*Ic*).

## EXPERIMENTAL

The temperature data are uncorrected. Gas–liquid chromatography was performed on a Chrom 5 chromatograph (Laboratorní přístroje, Prague) on 2 500 × 3 mm columns, FID, carrier gas nitrogen. The columns were packed with 15% Carbowax 20M on Chromaton N-AW-DMCS (0·125—0·16 mm) or with 3% OV-225 on the same support. Quantitative analyses were carried out on the former phase (temperature programme 130°C—220°C, 5°C/min) and the chromatograms were evaluated by cutting the peak areas. The relative responses of the compounds were not determined and are assumed to be the same. $^1$H NMR spectra were measured on a Varian XL-100-15, Tesla BS-567 (100·1 MHz) or a Bruker AM-400 (400·134 MHz; stated with the spectral data) instrument; internal standard tetramethylsilane (for deuteriochloroform solutions) or sodium 4,4-dimethyl-4-silapentane-1-sulfonate (for deuterium oxide solutions). The chemical

shifts are given in $\delta$(ppm), coupling constants in Hz. $^{11}$B NMR spectra were obtained with a Varian XL-100-15 (32·1 MHz) or a Varian XL-200 (64·2 MHz) spectrometer with trimethyl borate as external standard. Chemical shifts downfield relative to the standard are taken as positive, in the $^{11}$B NMR spectra a correction of 18·1 ppm was added to boron trifluoride diethyl etherate signal used as standard. IR spectra were recorded on a Perkin–Elmer 325 spectrometer, the values are in inverse centimeters.

1-(5-Hexenoyl)piperidine (*Ig*)

A solution of 5-hexenoyl chloride[14] (23·8 g; 179 mmol) in diethyl ether (25 ml) was added dropwise during 40 min to a stirred and cooled solution of piperidine (30·6 g; 359 mmol) in diethyl ether (40 ml). The formed suspension was diluted with diethyl ether (50 ml), stirred for 1 h, filtered and the solid was washed with diethyl ether (80 ml). The filtrate was taken down and the residue distilled affording *Ig* (30·1 g; 92·5%), b.p. 136–138°C/1·3 kPa. For $C_{11}H_{19}NO$ (181·3) calculated: 72·88% C, 10·56% H, 7·73% N; found: 72·86% C, 10·66% H, 7·96% N. $^1$H NMR ($C^2HCl_3$): 1·36–1·92 m, 8 H (2 H-3, 2 H-4, 2 H-5, 2 H-9); 2·12 m, 2 H (2 H-10, $J$(9, 10) = = $J$(10, 11) = 7); 2·32 t, 2 H (2 H-8, $J$ = 8); 3·20–3·80 m, 4 H (2 H-2, 2 H-6); 4·96 m, 1 H (H-12-*cis*, $^2J$ = 2; $J$(11, 12-*cis*) = 10); 5·00 m, 1 H (H-12-*trans*, $^2J$ = 2; $J$(11, 12-*trans*) = 17); 5·80 m, 1 H (H-11, $J$(10, 11) = 7; $J$(11, 12-*cis*) = 10; $J$(11, 12-*trans*) = 17). IR ($CCl_4$): 916 m 1 007 m (γ(CH)); 1 650 s (ν(CO)); 2 980 sh (ν(=$CH_2$)); 3 085 w; 3 015 w (ν(=CH)).

1-(5-Hexenyl)piperidine (*Ia*)

A solution of *Ig* (25·0 g; 138 mmol) in diethyl ether (55 ml) was added during 15 min to a stirred suspension of 70% lithium aluminium hydride (7·5 g; 140 mmol) in diethyl ether (690 ml). The mixture was stirred and refluxed for 3 h and decomposed with 4% sodium hydroxide solution (21 ml). After filtration and washing the solid with diethyl ether the filtrate was dried over potassium carbonate, the solvent was evaporated and the product distilled; yield 21·7 g (94%) of *Ia*, b.p. 91°C/1·9 kPa (reported[15] b.p. 115–117°C/5·3 kPa). $^1$H NMR ($C^2HCl_3$): 1·21–1·83 m, 10 H (2 H-3, 2 H-4, 2 H-5, 2 H-8, 2 H-9); 2·14 m, 2 H (2 H-10, $J$(9, 10) = $J$(10, 11) = 6·5); 2·25–2·57 m, 6 H (2 H-2, 2 H-6, 2 H-7); 5·00, 1 H (H-12-*cis*, $^2J$ 2; $J$(11, 12-*cis*) = 10); 5·04 m, 1 H (H-12-*trans*, $^2J$ = 2; $J$(11, 12-*trans*) = 17); 5·87 m, 1 H (H-11, $J$(10, 11) = 6·5; $J$(10, 12-*cis*) = = 10; $J$(11, 12-*trans*) = 17). IR ($CCl_4$): 914 s; 995 s (γ(CH)); 1 828 w (first overtone); 2 980 s (ν(=$CH_2$)); 3 085 m (ν(=CH)); 3 010 m.

*trans*-1-(3-Hexenoyl)piperidine (*Ih*)

Thionyl chloride (23·0 g; 195 mmol) was added dropwise with stirring to *trans*-3-hexenoic acid[11,12] (20·0 g; 175 mmol) during 20 min at room temperature. The mixture was stirred for 1·5 h at 30°C, set aside at room temperature overnight, diluted with diethyl ether (60 ml) and added dropwise with stirring and ice-cooling in the course of 45 min to piperidine (30·15 g; 389 mmol) in diethyl ether (120 ml). After stirring at room temperature for 2 h, water (100 ml) was added to dissolve the solids. The organic layer was separated, washed with water (2 × 50 ml), dried over potassium carbonate and the solvent was evaporated. Distillation of the residue afforded *Ih* (19·8 g; 62%), b.p. 90–91°C/40 Pa. For $C_{11}H_{19}NO$ (181·3) calculated: 72·88% C, 10·56% H, 7·73% N; found: 72·44% C, 10·60% H, 7·87% N. $^1$H NMR ($C^2HCl_3$): 1·00 t, 3 H (3 H-12, $J$ = 6·6); 1·40–1·72 m, 6 H (2 H-3, 2 H-4, 2 H-5); 2·00–2·11 m, 2 H (2 H-11); 3·09 d, 2 H (2 H-8, $J$ = 6·6); 3·26–3·69 m, 4 H (2 H-2, 2 H-6); 5·48–5·63 m, 2 H (H-9, H-10). IR ($CCl_4$): 970 m (γ(CH) in CH=CH *trans*).

*trans*-1-(3-Hexenyl)piperidine (*Ib*)

The title compound (12·6 g; 69%), b.p. 106–107°C/1·2 kPa, was prepared by reduction of *Ih* (19·8 g; 118 mmol) with lithium aluminium hydride (4·7 g; 123 mmol) analogously as described for *Ia*. For $C_{11}H_{21}N$ (167·3) calculated: 78·97% C, 12·65% H, 8·38% N; found: 78·67% C, 12·79% H, 8·47% N. $^1$H NMR ($C^2HCl_3$): 0·96 t, 3 H (3 H-12, $J$ = 7·5); 1·43–1·62 m, 6 H (2 H-3, 2 H-4, 2 H-5); 1·98–2·03 m, 2 H (2 H-11, $J$(10, 11) = 6·7; $J$(11, 12) = 7·5); 2·19 m, 2 H (2 H-8, $J$(7, 8) = $J$(8, 9) = 7·2); 2·31–2·40 m, 6 H (2 H-2, 2 H-6, 2 H-7); 5·35–5·40 m, 1 H (H-9, $J$(9, 10) = 15·2; $J$(8, 9) = 5·2); 5·46–5·52 m, 1 H (H-10, $J$(9, 10) = 15·2; $J$(10, 11) = 6·4).

Reaction of 5-Oxohexanoic Acid with Thionyl Chloride

Thionyl chloride (15·4 g; 130 mmol) was added dropwise during 20 min to 5-oxohexanoic acid[16] (15·3 g; 117 mmol). After heating to 50°C for 1 h and evaporation of excess thionyl chloride *in vacuo*, the product was distilled (b.p. 83–84°C/1·9 kPa), affording a mixture of *Va* and *VIa* in the ratio 84 : 16 (7·65 g; 56%). For a mixture of 84% $C_6H_8O_2$ (112·1) and 16% $C_6H_9ClO_2$ (148·6) calculated: 61·75% C, 7·02% H, 3·82% Cl; found: 61·64% C, 6·95% H, 3·67% Cl. $^1$H NMR ($C^2HCl_3$): 1·89 s ($CH_3$ in *Va*); 2·02 s ($CH_3$ in *VIa*); 2·15–2·46 m (=C—$CH_2$ in *Va* and CO—C—$CH_2$ in *VIa*); 2·46–2·80 m ($CH_2CO$ in *Va* and $COCH_2C$—$CH_2CO$ in *VIa*); 5·02 t (=CH, $J$ = 4). IR ($CCl_4$): 1 700 m (ν(C=C)); 1 770 s (ν(CO)).

1-(5-Oxohexanoyl)piperidine (*Ii*)

A solution of the mixture of *Va* and *VIa*, obtained in the preceding experiment (7·0 g; 60 mmol), in diethyl ether (7 ml) was added dropwise during 35 min under stirring and cooling with ice to a solution of piperidine (8·0 g; 94 mmol) in diethyl ether (20 ml). After stirring for 1 h at room temperature, the mixture was filtered, the solvent evaporated and the residue distilled to give *Ii* (7·35 g; 62%), b.p. 132°C/20 Pa. For $C_{11}H_{19}NO_2$ (197·3) calculated: 66·97% C, 9·71% H, 7·10% N; found: 66·94% C, 9·99% H, 7·10% N. $^1$H NMR ($C^2HCl_3$): 1·35–1·72 m, 6 H (2 H-3, 2 H-4, 2 H-5); 1·72–2·06 m, 2 H (2 H-9); 2·15 s, 3 H (3 H-12); 2·21–2·64 m, 4 H (2 H-2, 2 H-6); 3·19–3·70 m, 4 H (2 H-8, 2 H-9).

6-(1-Piperidinyl)-2-hexanol (*IIb*)

The compound, b.p. 135–136°C/1·7 kPa (4·7 g; 86%), was prepared by reduction of *Ii* (5·8 g; 29 mmol) with lithium aluminium hydride (2·0 g; 53 mmol) analogously to *Ia*. For $C_{11}H_{23}NO$ (185·3) calculated: 71·30% C, 12·51% H, 7·56% N; found: 71·23% C, 12·72% H, 7·36% N. $^1$H NMR ($C^2HCl_3$): 1·16 d, 3 H ($CH_3$, $J$ = 6); 1·27–1·73 m, 12 H (2 H-3, 2 H-4, 2 H-5, 2 H-8, 2 H-9, 2 H-10); 2·16–2·46 m, 6 H (2 H-2, 2 H-6, 2 H-7); 2·57 s, 1 H (OH); 3·76 m, 1 H (H-11, $J$(10, 11) = $J$(11, 12) = 6).

Reaction of 4-Oxohexanoic Acid with Thionyl Chloride

A mixture of 4-oxohexanoic acid[17] (9·75 g; 75 mmol) and thionyl chloride (9·8 g; 82 mmol) was treated as described for preparation of the mixture of *Va* and *VIa* to give a mixture (6·5 g; 74%), b.p. 93–95°C/2·3 kPa, containing *Vb* (44%), *VII* (12%), *VIII* (27%), and *VIb* (17%). For a mixture of 83% $C_6H_8O_2$ (*Vb*, *VII*, and *VIII*; 112·1) and 17% $C_6H_9ClO_2$ (*VIb*; 148·6) calculated: 61·59% C, 7·01% H, 4·06% Cl; found: 61·49% C, 6·96% H, 3·98% Cl. $^1$H NMR ($C^2HCl_3$): 0·90–1·28 m ($CH_3$ in *Vb*, *VIb*, and *VII*); 1·58–1·73 m ($CH_3$ in *VIII*); 1·90–3·03 m ($CH_2$—CO in *Vb* and *VII*, $CH_2CH_2$ in *VIII* and $CH_2COCH_2CH_2$ in *VIb*); 3·10–3·24 m ($CH_2COO$ in *Vb*);

4·62 q (—CH= in *VIII*, $J = 7$); 4·93—5·40 m (=CH— in *Vb* and CH—O in *VII*); 6·12 m (=CH—COO in *VII*, $J(2, 3) = 6$, $J(3, 4) = 2$); 7·50 d (=CHCO in *VII*, $J = 6$). IR ($CCl_4$): 1 710 (ν(C=O) in $CH_3COCH_2$ in *VIb*); 1 760 (ν(C=O) in *VII* and *VIII*); 1 810 (ν(C=O) in *Vb* and COCl in *VIb*).

1-(4-Oxohexanoyl)piperidine (*Ij*)

The title compound, b.p. 130°C/30 Pa (6·55 g; 76%), was obtained from piperidine (5·9 g; 68 mmol) and the mixture from the preceding experiment (5·1 g; 44 mmol) as described for the preparation of *Ii*. For $C_{11}H_{19}NO_2$ (197·3) calculated: 66·97% C, 9·71% H, 7·10% N; found: 67·14% C, 10·01% H, 6·88% N. $^1$H NMR ($C^2HCl_3$): 1·08 t, 3 H (3 H-12, $J = 7·5$); 1·38—1·72 m, 6 H (2 H-3, 2 H-4, 2 H-5); 2·30—2·85 m, 6 H (2 H-8, 2 H-9, 2 H-11); 3·36—3·57 m, 4 H (2 H-2, 2 H-6). IR ($CCl_4$): 1 650 (ν(C=O) in N—CO); 1 720 (ν(CO) in C—CO—C).

6-(1-Piperidinyl)-3-hexanol (*IIc*)

Prepared from *Ij* (5·6 g; 28 mmol) by reduction with lithium aluminium hydride (1·9 g; 51 mmol) as described for the preparation of *Ia*; yield 4·4 g (84%), b.p. 126—128·5°C/1·7 kPa. For $C_{11}H_{23}NO$ (185·3) calculated: 71·30% C, 12·51% H, 7·56% N; found: 71·48% C, 12·73% H, 7·69% N. $^1$H NMR ($C^2HCl_3$): 0·92 t, 3 H (3 H-12, $J = 7$); 1·14—1·92 m, 13 H (2 H-3, 2 H-4, 2 H-5, 2 H-8, 2 H-9, 2 H-11, OH); 2·10—2·70 m, 6 H (2 H-2, 2 H-6, 2 H-7); 3·24—3·54 m, 1 H (H-10). IR ($CCl_4$): 3 400 m (ν(OH)).

1-(1-Piperidinyl)-3-hexanol (*IId*)

This compound, b.p. 111°C/1·7 kPa, was prepared by reduction of 1-(1-piperidinyl)-3-hexanone[18] (4·0 g; 22 mmol) with 70% lithium aluminium hydride (1·2 g; 22 mmol), analogously as described for *Ia*; yield 3·6 g (89%). For $C_{11}H_{23}NO$ (185·3) calculated: 71·30% C, 12·51% H, 7·56% N; found: 71·36% C, 12·59% H, 7·59% N. $^1$H NMR ($C^2HCl_3$): 0·92 t, 3 H (3 H-12, $J = 6$); 1·18 to 1·87 m, 13 H (2 H-3, 2 H-4, 2 H-5, 2 H-8, 2 H-10, 2 H-11, OH); 2·11—2·45 m, 2 H (2 H-7); 2·45—2·80 m, 4 H (2 H-2, 2 H-6); 3·60—3·92 m, 1 H (H-9). IR ($CCl_4$): 1 330 m; 1 355 s; 1 380 m; 1 448 s; 1 460 s; 1 475 s (δ(CH, $CH_2$, $CH_3$)), 2 740 m; 2 770 s; 2 820 s; 2 860 s; 2 880 s; 2 940 s (ν(CH, $CH_2$, $CH_3$)), 3 260 s (ν(OH)).

Ethyl 2-Hydroxyhexanoate (*IX*)

A mixture of (±)-2-hydroxyhexanoic acid[19] (21·7 g; 164 mmol), ethanol (20 ml), benzene (18 ml), and sulfuric acid (8 drops) was slowly distilled (7 h; bath temperature 105—110°C) until clear distillate was obtained. The distillation residue was neutralized with calcium carbonate, filtered and the filtrate distilled to give 15·1 g (58%) of *IX*, b.p. 85°C/1·3 kPa (reported[20] b.p. 67—68°C/400 Pa).

1-(2-Hydroxyhexanoyl)piperidine (*Ik*)

A mixture of ester *IX* (15·1 g; 94 mmol) and piperidine (48·1 g; 565 mmol) was refluxed under stirring for 17 h. The excess piperidine and the formed ethanol were evaporated *in vacuo* and the residue on distillation afforded *Ik* (10·9 g; 58%), b.p. 140—141°C/20 Pa. For $C_{11}H_{21}NO_2$ (199·3) calculated: 66·29% C, 10·62% H; found: 66·14% C, 10·81% H. $^1$H NMR ($C^2HCl_3$): 0·90 t, 3 H ($CH_3$, $J = 6·3$); 1·25—1·53 m, 6 H (2 H-9, 2 H-10, 2 H-11); 1·53—1·80 m, 6 H (2 H-3, 2 H-4, 2 H-5); 3·34 t, 2 H and 3·60 t, 2 H (2 H-2, 2 H-6, $J = 5·3$); 4·32—4·37 m, 1 H (H-8); 4·45 s, 1 H (OH); IR ($CCl_4$): 1 640 s (ν(C=O)); 3 440 m (ν(OH)).

1-(1-Piperidinyl)-2-hexanol (*IIe*)

The title compound, b.p. 113–116°C/1·3 kPa, was prepared by reduction of *Ik* (5·0 g; 25 mmol) with lithium aluminium hydride (1·7 g; 45 mmol) as described for *Ia*; yield 3·0 g (64%). For $C_{11}H_{23}NO$ (185·3) calculated: 71·30% C, 12·51% H, 7·56% N; found: 71·52% C, 12·69% H, 7·34% N. $^1$H NMR ($C^2HCl_3$, 400·134 MHz): 0·91 t, 3 H ($CH_3$, $J$ = 5·3); 1·23–1·70 m, 12 H (2 H-3, 2 H-4, 2 H-5, 2 H-9, 2 H-10, 2 H-11); 2·12–2·37 m, 4 H and 2·55–2·65 m, 2 H (2 H-2, 2 H-6, 2 H-7); 3·59–3·68 m, 1 H (H-8); 3·78 s, 1 H (OH). IR ($CCl_4$): 3 450 m (ν(OH)).

1-Hexylpiperidine (*Ic*)

A solution of 1-bromohexane (33·0 g; 200 mmol) in 2-butanone (20 ml) was added to a stirred mixture of potassium carbonate (30·0 g; 220 mmol), piperidine (16·8 g; 200 mmol), and 2-butanone (50 ml). After stirring and refluxing for 7 h, the solid was filtered off and the filtrate taken down. Distillation at 98–99°C/1·9 kPa gave 23·6 g (83%) of *Ic* (reported[21] b.p. 110°C/2·9 kPa).

Hydroboration of *Ia* and *Ib*

*A*) A solution of the substrate (0·5 g; 3 mmol) in tetrahydrofuran (3 ml) was added dropwise under nitrogen at 22°C to a stirred solution of tetrahydrofuran–borane (3·3 mmol, ref.[22]) in the course of 5 min. After stirring for 1 h (the same conditions), the mixture was decomposed with 15% hydrochloric acid (1 ml), made alkaline with 40% NaOH (1 ml) and oxidized with 30% $H_2O_2$ (0·6 ml, reflux for 1 h). The mixture was saturated with potassium carbonate, the organic layer was separated and the aqueous one was extracted with tetrahydrofuran (2 × 3 ml). The extract was combined with the original organic phase, dried over potassium carbonate and analyzed by gas–liquid chromatography (Table I). In the hydroboration of equimolar mixture of *Ia* and *Ib*, only the ratio (*IIa* + *IIb*) : (*IIc* + *IId* + *IIe*) was determined (55 : 45).

*B*) A solution of the unsaturated amine *Ia* or *Ib* (2·0 g; 12 mmol) in tetrahydrofuran (6 ml) was added dropwise under nitrogen to a stirred suspension of 9-borabicyclo[3.3.1]nonane[23] (1·5 g; 12 mmol) in tetrahydrofuran (15 ml) during 5 min. After boiling for 3 h, the mixture was acidified with 15% hydrochloric acid (3·5 ml), made alkaline with 40% NaOH (5 ml) and oxidized with 30% $H_2O_2$ (4·3 ml, reflux for 1 h). The mixture was saturated with potassium carbonate, the organic layer was separated, the aqueous one was extracted with tetrahydrofuran (2 × 7 ml) and the extract was combined with the original organic phase. After drying over potassium carbonate the solution was analyzed by gas–liquid chromatography (Table I).

*C*) A solution of boron trifluoride diethyl etherate (1·8 ml; 14 mmol) in diglyme (3·5 ml) was added dropwise at 22°C under nitrogen to a stirred mixture of sodium borohydride (0·4 g; 10 mmol), *Ia* or *IIb* (1·7 g; 10 mmol), and diglyme (15 ml) during 10 min. After stirring for 1 h (the same conditions) a sample (2 ml) was withdrawn through a rubber septum by means of a syringe. The mixture was heated to 160°C (bath) during 15 min and stirred under nitrogen for 3 h. A sample of the mixture was decomposed with 15% HCl (0·8 ml), made alkaline with 40% NaOH (1·0 ml) and boiled with 30% $H_2O_2$ (0·7 ml) under stirring for 1 h. The organic layer was separated, the aqueous layer was extracted with tetrahydrofuran (2 × 3 ml), and the extract was combined with the original organic layer and analyzed by gas–liquid chromatography (Table I).

*D*) In a flask equipped with reflux condenser, a mixture of the unsaturated amine (2·0 g; 12 mmol) and triethylamine–borane[24] was heated under nitrogen until the reaction started (at about 120°C). After the reaction ceased, the mixture was heated to 150°C (bath) for 2 min, cooled to room temperature and a sample for analysis was withdrawn. The mixture was heated

to 200°C (bath) for 2 h and the liberated triethylamine was distilled. Samples of the reaction mixture (0·5 ml) were decomposed with 15% HCl (1 ml), diluted with tetrahydrofuran (2 ml), made alkaline with 40% NaOH (2·5 ml) and oxidized with 30% $H_2O_2$ (1 ml, reflux for 1 h). The mixture was cooled, saturated with potassium carbonate, the organic layer was separated and the aqueous one was extracted with tetrahydrofuran (2 × 5 ml). The extract was combined with the original organic layer, dried over potassium carbonate and analyzed by gas–liquid chromatography (Table I).

According to the procedure described in the preceding paragraph, compound *Ia* (20·0 g; 120 mmol) was treated with triethylamine–borane[7] (13·8 g; 120 mmol). Triethylamine was removed by distillation and the residue was three times distilled *in vacuo* (nitrogen introduced through a capillary), affording a mixture of *IIIa* (8·5%), *IIIb* (77%), and *IIIc* (14·5%), b.p. 152 to 154°C/1·9 kPa (15·3 g; 70%). The population of the amine–boranes in the mixture was determined by gas–liquid chromatography after conversion into alcohols *IIb*–*IId* by hydrolysis with hydrochloric acid and oxidation with hydrogen peroxide. For $C_{11}H_{24}BN$ (181·1) calculated: 72·94% C, 13·36% H, 5·97% B, 7·73% N; found: 73·13% C, 13·58% H, 6·12% B, 7·58% N. $^1$H NMR ($C^2HCl_3$): 0·17–0·61 m, 1 H (B—CH); 0·72—1·40 m, 7 H (B—C—$CH_2$ and $CH_3$); 1·40–2·05 m, 8 H (C—$CH_2$—C in the rings); 2·40–3·18 m, 6 H (N—$CH_2$). $^{11}$B NMR ($C^2HCl_3$): −9·7 t ($J(^{11}B, H) = 85$). IR ($CCl_4$): 1 180 s (δ($BH_2$)), 1 140 m; 1 451 s; 1 459 s; 1 469 s; 1 472 m (δ(CH, $CH_2CH_3$)), 2 240 m; 2 250 sh; 2 290 s; 2 340 m, 2 360 sh (ν($BH_2$)), 2 810 m; 2 840 s; 2 870 w; 2 890 s; 2 930 s; 2 950 s; 3 000 sh (ν(CH, $CH_2$, $CH_3$)).

6-(1-Piperidinyl)-3-hexylboronic Acid Hydrochloride (*IV*)

Hydrochloric acid (15%; 20 ml) was added dropwise under stirring to a solution of the mixture of *IIIa*–*IIIc* obtained above (6·0 g; 33 mmol) in acetone (33 ml). Hydrogen was evolved and the mixture warmed spontaneously. After stirring and reflux for 15 min, the acetone and excess acid were evaporated *in vacuo*. Crystallization of the residue from 2-butanone-2-propanol afforded 4·9 g (59%) of *IV*, m.p. 82–85°C. For $C_{11}H_{25}BClNO_2$ (249·6) calculated: 52·93% C, 10·10% H, 4·33% B, 14·21% Cl, 5·61% N; found: 53·08% C, 9·97% H, 4·06% B, 14·38% Cl, 5·47% N. $^1$H NMR ($^2H_2O$): 0·66–1·08 m, 4 H (3 H-12, H-10); 1·14–2·02 m, 12 H (2 H-3, 2 H-4, 2 H-5, 2 H-8, 2 H-9, 2 H-11); 2·74—3·52 m, 6 H (2 H-2, 2 H-6, 2 H-7).

*Oxidation*: To a solution of *IV* (1·85 g; 7·4 mmol) in water (5·9 ml) and tetrahydrofuran (7·4 ml) was added 3M-NaOH (5·2 ml) and 30% $H_2O_2$ (1·0 ml). After stirring at room temperature for 1 h, the mixture was saturated with potassium carbonate, the organic layer was separated and the aqueous one was extracted with diethyl ether (4 × 4 ml). The extract was combined with the original organic layer, dried over potassium carbonate and evaporated; yield 1·1 g (80%) of *IIc*, b.p. 134–136°C/2·9 kPa. The product was identified with an authentic specimen (gas–liquid chromatography, $^1$H NMR and IR spectra). For $C_{11}H_{23}NO$ (185·3) calculated: 71·30% C, 12·51% H, 7·56% N; found: 71·45% C, 12·37% H, 7·59% N.

Ethanolysis of Mixture of *IIIa*–*IIIc*

A solution of a mixture of amine–boranes *IIIa*–*IIIc* (0·40 g; 2·2 mmol) in ethanol (3·3 ml) was refluxed for 18 h. Evaporation and distillation *in vacuo* afforded material (0·3 g, 58%), boiling at 130–140°C/2·1 kPa, consisting of the starting compounds (32%) and diethyl esters of the corresponding boronic acids *Id*–*If* (68%). For a mixture of 32% $C_{11}H_{24}BN$ (181·1) and 68% $C_{15}H_{32}BNO$ (269·2) calculated: 68·84% C, 12·42% H, 4·64% B, 6·01% N; found: 68·60% C, 12·51% H, 4·69% B, 5·92% N. $^1$H NMR ($C^2HCl_3$): in addition to signals of the starting amine–boranes 1·18 t ($CH_3$, $J = 7$); 2·13–2·48 m, (N—$CH_2$); 3·89 q ($OCH_2$, $J = 7$). $^{11}$B NMR ($C^2HCl_3$; 64·2 MHz): −3·57 t ($BH_2$, $J = 94$); 31·0 s ($B(OC_2H_5)_2$).

*The elemental analyses were performed under supervision of Dr L. Helešic, the* NMR *spectra were measured under supervision of Dr P. Trška, and the* IR *spectra were taken by Dr E. Janečková and Dr A. Kohoutová, Central Laboratories, Prague Institute of Chemical Technology, Prague. The spectra, measured on Varian* XL-200 *instrument, were taken by Dr D. Šaman, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague.*

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