ON HYDROBORATION OF 2-ALLYL-1,2,3,4-TETRAHYDROISOQUINOLINE*

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Dedicated to Academician J. Mostecký on the occasion of his 60th birthday.

Heating of 2-allyl-1,2,3,4-tetrahydroisoquinoline (*I*) with triethylamine-borane afforded 7,8-benzo-5-aza-1-boraspiro[4,5]decane (*II*) which was hydrolyzed with hydrochloric acid to 3 (1,2,3,4-tetrahydro-2-isoquinolyl)propylboronic acid hydrochloride (*III*). Ethanolysis of *II* led to the diethyl ester *IV*. Compounds *II* and *III* were oxidized to give 3-(1,2,3,4-tetrahydro-2-isoquinolyl)-1-propanol (*V*).

In the preceding[1] paper of this series we described hydroboration of N-allyl derivatives of pyrrolidine, piperidine, hexamethyleneimine and morpholine with triethylamine-borane. This reaction led to a new type of heterocyclic compounds – spirocyclic amine-boranes.

This communication concerns the hydroboration of 2-allyl-1,2,3,4-tetrahydroisoquinoline (*I*) with triethylamine-borane. Similarly to the described cases[1], a spirocyclic amine-borane, 7,8-benzo-5-aza-1-boraspiro[4,5]-decane (*II*), was formed. It was relatively stable towards air and did not change its properties even after standing in a stoppered bottle at −20°C for several months. The structure *II* is supported by the following facts: *a*) In the ^{1}H NMR spectrum the proton signals of methylene groups bonded to the nitrogen atom are shifted downfields as compared with chemical shifts of the corresponding protons in the alcohol *V* and the alkyltetrahydroisoquinolines *VI* and *VII*. *b*) Protons in position 6, corresponding to those in position 1 of the tetrahydroisoquinoline nucleus in compounds *V*–*VII* form in the ^{1}H NMR spectrum a characteristic AB system with a difference of 0·38 ppm whereas the corresponding protons in *V*, *VI* and *VII* appear as a singlet. This non-equivalence of protons can be explained by their different orientation toward the boron atom. *c*) The boron chemical shift in ^{11}B NMR spectrum of compound *II* (−28·1 ppm relative to trimethyl borate) is close to values published for trimethylamine-borane[2], pyridine-

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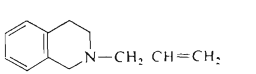
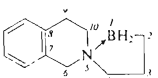
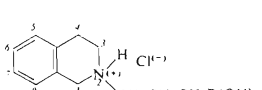
-borane[2], dimethylamine-borane[2] and triethylamine-butylborane[3], indicating an sp^3 hybridization. The filling of the free orbital by a B-H bridge formation (dimerization of the molecule) is not probable since ^{11}B NMR spectrum of 1,2-dimethyldiborane displays a signal at +2·4 ppm[4]; moreover, the molecular weight of *II* fairly agrees with the value calculated for the monomeric structure. *d*) Mass spectrum of compound *II* exhibits no molecular ion signal but it displays a strong $(M-1)^+$ signal, arising by loss of the hydrogen at the boron atom ($-\overset{|}{N^+}-BH-$), which is typical for compounds with dative amine-borane bonds[5,6].



I



II



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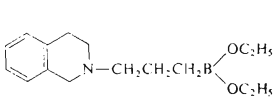
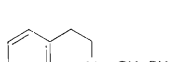


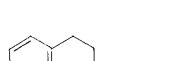
IV

V



VI

VII



VIII

Hydrolysis of the amine-borane *II* with hydrochloric acid afforded 3-(1,2,3,4-tetrahydro-2-isoquinolyl)propylboronic acid hydrochloride (*III*). On oxidation with hydrogen peroxide in alkaline medium, this compound, like the amine-borane *II*, was converted into 3-(1,2,3,4-tetrahydro-2-isoquinolyl)-1-propanol (*V*).

Decomposition of the amine-borane *II* with ethanol gave the diethyl ester *IV*. Unlike the amine-borane *II*, this compound has not the spirocyclic structure because chemical shifts of protons in methylenes bonded to the nitrogen atom are similar to

those of the corresponding protons in compounds *V*, *VI* and *VII* and (similarly to these compounds) the protons in position 1 exhibit only one singlet. The signal in the ^{11}B NMR spectrum of compound *IV* (+6·2 ppm relative to trimethyl borate) corresponds to signals of diethyl phenylboronate[2], dimethyl methylboronate[7], dimethyl ethylboronate[7] and di-tert-butyl ethylboronate[7].

In addition to the alcohol *V*, we isolated, after hydrolysis and oxidation, also 1,2,3,4-tetrahydroquinoline (*VIII*) as a side product of hydroboration of *I*.

EXPERIMENTAL

The temperature data are uncorrected. The IR spectra were taken on a Perkin–Elmer 325 spectrophotometer, ^{1}H NMR spectra were measured on Varian XL-100-15 (100·1 MHz) or Tesla BS-567 (100·1 MHz) instruments at 37°C using tetramethylsilane for solutions in organic solvents or sodium 4,4-dimethyl-4-silapentane-1-sulfonate for solutions in deuterium oxide. The ^{11}B NMR spectra were taken at 37°C on a Varian XL-100-15 (32·1 MHz) spectrometer using trimethyl borate as standard. For the ^{11}B NMR and ^{1}H NMR spectra chemical shifts downfield relative to the

TABLE I

^{1}H NMR spectra of N-substituted 1,2,3,4-tetrahydroisoquinolines

Compound	Chemical shifts, ppm						Coupling constants *J*, Hz	
	H-4	H-9	H-10	H-6 H-6′	H-3	H-2	3, 4	2, 3
II[a]	m 2·62		3·30	3·74[b] 4·12[b]	m 1·84	m 0·56– –1·08	7·5	7·5
	H-9	H-4	H-3	H-1	H-10	H-11	9, 10	10, 11
IV[a,c]	t 2·46	m 2·60	2·99	s 3·59	m 1·68	t 0·76	7·0	8·0
V[d]	m 2·57		3·01	s 3·59	m 1·77	t 3·70	5·5	5·5
VI[a,e]	q 2·54	m 2·60– –2·79	m 2·79– –3·02	s 3·58	t 1·17	—	7·0	—
VII[a]	t 2·45	m 2·57– –2·78	m 2·78– –3·05	s 3·58	m 1·61	t 0·93	7·5	7·5

[a] H_{arom} m 6·85–7·25 ppm; [b] $J_{6,6'}$ = 16 Hz; [c] 2 CH_3 t 1·05 ppm, J = 7·5 Hz; 2 OCH_2 q 3·78 ppm, J = 7·5 Hz; [d] H_{arom} m 6·71–7·15 ppm; OH s 4·59 ppm; [e] Prepared according to ref.[15].

used standard were denoted as positive. Mass spectra were measured on a Gas Chromatograph--Mass Spectrometer LKB 9000 (AB Stockholm). The ions are given in *m/z* units (relative intensity, %). Thin-layer chromatography was carried out on Alufol plates and spots were detected with iodine vapour. Gas–liquid chromatography was performed on a Chrom II chromatograph, using 170 cm columns of 6 mm diameter, carrier gas nitrogen. The column fillings, together with other data, are given for the pertinent compounds. Osmometric molecular weight determination was performed in chloroform on a Dampfdruckosmometer Knauer instrument at 37°C.

2-Allyl-1,2,3,4-tetrahydroisoquinoline (*I*)

A mixture of 2-allylisoquinolinium bromide[8] (30·0 g; 0·12 mol), 85% formic acid (52·2 g; 0·96 mol) and triethylamine (24·3 g; 0·24 mol) was refluxed for 8 h. After alkalisation with 40% NaOH the organic layer was separated, the aqueous one was extracted with ether and the extract was combined with the organic layer. The solution was dried over potassium carbonate and taken down. Distillation afforded 16·8 g (81%) of compound *I*, b.p. 122°C/1·6 kPa (12 Torr). Reported[9] b.p. 117–120°C/12 Torr. ^{1}H NMR spectrum ($CDCl_3$, ppm): 2·58–2·95 (m, 4 H) H on $C_{(3)}$, $C_{(4)}$; 3·09 (d, 2 H, J = 6 Hz) N—CH_2CH=; 3·51 (s, 2 H) H on $C_{(1)}$; 4·97–5·25 (m, 2 H) CH_2=; 5·61–6·05 (m, 1 H) —CH=CH_2; 6·91–7·14 (m, 4 H) aromatic protons.

7,8-Benzo-5-aza-1-boraspiro[4,5]decane (*II*)

A mixture of compound *I* (43·3 g; 0·25 mol) and triethylamine-borane[10] (28·8 g; 0·25 mol) was refluxed under nitrogen. At 130°C (bath temperature) an exothermic reaction occurred and after its end the heating was continued until the temperature reached 150°C. After cooling, triethylamine was distilled off (20·8 g; 82%; identified by gas–liquid chromatography on 15% silicone elastomer E 301 or 15% 1,4-butanediol succinate on Chromosorb N-AW; 80°C, 30 kPa). During the distillation the bath temperature reached 160°C. Distillation *in vacuo* afforded fractions: *a*) b.p. 96–123°C/5·3 Pa (0·04 Torr), 6·3 g; *b*) b.p. 121–135°C/4·7 Pa (0·035 Torr), 34·6 g; distillation residue 5·8 g. Separate redistillation of both fractions afforded 24·8 g (53%) of the product *II* b.p. 144–146°C/8 Pa (0·06 Torr), m.p. 60–68°C (sealed capillary, N_2); R_f 0·7 (thin-layer chromatography in cyclohexane–benzene 1 : 1). For $C_{12}H_{18}BN$ (187·1) calculated: 77·03% C, 9·70% H, 5·78% B, 7·49% N; found: 76·80% C, 9·88% H, 6·23% B, 7·28% N. Mol. wt. (osmometrically) 192. Mass spectrum: 186 (62), 185 (23), 184 (34), 147 (20), 146 (100), 144 (23), 133 (22), 132 (44), 130 (27), 117 (30), 115 (22), 105 (25), 104 (77), 103 (29), 96 (29), 91 (20), 82 (99), 81 (30), 78 (23), 77 (25), 54 (23), 42 (29), 40 (25), 39 (24). IR spectrum ($CHCl_3$, cm^{-1}): 830 (w), 860 (w), 877 (w), 918 (w), 929 (w), 942 (w), 976 (w), 992 (w), 1 006 (w), 1 035 (w), 1 060 (i), 1 070 (m), 1 093 (m), 1 119 (i), 1 128 (s) δ (BH_2), 1 190 (m) δ (BH_2), 1 280 (m), 1 305 (m), 1 318 (m), 1 349 (s), 1 375 (s), 1 394 (s), 1 414 (s), 1 438 (s), 1 445 (s), 1 459 (s), 1 463 (i), 1 485 (w), 1 500 (s), 1 588 (w), 2 200 (i) ν (BH_2), 2 230 (w) ν (BH_2), 2 300 (s) ν (BH_2), 2 340 (i) ν (BH_2), 2 360 (i) ν (BH_2), 2 400 (i) ν (BH_2), 2 850 (m) ν (CH_2), 2 780 (i) ν (CH_2), 2 940 (s) ν (CH_2), 3 015 (s) ν (CH). ^{11}B NMR spectrum ($CDCl_3$, ppm): −28·1 (broad singlet which narrows on proton decoupling).

3-(1,2,3,4-Tetrahydro-2-isoquinolyl)propylboronic Acid Hydrochloride (*III*)

To a stirred solution of *II* (13·1 g; 0·07 mol) in acetone (70 ml), 15% hydrochloric acid (42 ml) was added dropwise. Hydrogen evolved and the mixture became warm. After end of the addition the mixture was stirred under reflux for 15 min. Evaporation *in vacuo* afforded 18·8 g of the crude product of which 9·4 g on crystallization from 2-propanol gave 6·9 g of the hydrochloride *III*, m.p. 152–154°C. For $C_{12}H_{19}BClNO_2$ (255·6) calculated: 56·40% C, 7·49% H, 4·23% B, 13·87% Cl, 5·48% N; found: 56·39% C, 7·63% H, 4·06% B, 13·93% Cl, 5·10% N. ^{1}H NMR

spectrum (D_2O, ppm): 0·84 (t, 2 H, J = 7·5 Hz) H on $C_{(11)}$; 1·90 (m, 2 H, $J_{9,10} = J_{10,11}$ = = 7·5 Hz) H on $C_{(10)}$; 3·03–3·36 (m, 4 H) and 3·57 (t, 2 H, J = 7 Hz) H on $C_{(3)}$, $C_{(4)}$, $C_{(9)}$; 4·41 (s, 2 H) NH; 7·08–7·36 (m, 4 H) aromatic protons. IR spectrum (KBr pellet, cm^{-1}): 735 (s), 745 (s), 770 (i), 780 (s), 810 (w), 910 (m), 980 (m), 990 (m), 1 025 (m), 1 050 (m), 1 070 (m), 1 087 (m), 1 092 (i), 1 120 (w), 1 160 (w), 1 190 (m), 1 200 (m), 1 233 (w), 1 266 (m), 1 276 (m), 1 297 (i), 1 302 (s), 1 310 (m), 1 335 (m), 1 362 (s), 1 380 (s), 1 395 (s), 1 405 (i), 1 422 (m), 1 434 (s), 1 460 (m), 1 473 (m), 1 498 (m), 2 590 (s), 2 610 (m), 2 660 (i), 2 690 (s), 2 720 (s), 2 800 (w), 2 890 (m), 2 960 (s), 2 985 (i), 3 016 (w), 3 310 (s).

Diethyl 3-(1,2,3,4-Tetrahydro-2-isoquinolyl)propylboronate (*IV*)

A mixture of *II* (1·9 g; 0·01 mol) and ethanol (15 ml) was refluxed for 3 h. Evaporation of ethanol left 2·3 g (82%) of a product boiling at 128–130°C/5·3 Pa (0·04 Torr). For $C_{16}H_{26}BNO_2$ (275·2) calculated: 69·83% C, 9·52% H, 3·93% B, 5·09% N; found: 69·54% C, 9·89% H, 3·98% B, 5·09% N.

3-(1,2,3,4-Tetrahydro-2-isoquinolyl)-1-propanol (*V*)

a) A suspension of crude *III* (4·7 g) in water (25 ml) was made homogeneous with tetrahydrofuran (18 ml), mixed with 3M-NaOH (12·5 ml) and treated with 30% H_2O_2 (dropwise addition with stirring). The mixture warmed spontaneously. After addition of 1·8 ml H_2O_2 a test for free H_2O_2 was positive (acidification of a sample + KI + starch). The cold mixture was saturated with solid K_2CO_3, separated in a funnel, the aqueous layer was extracted with tetrahydrofuran and the extract was combined with the first separated part. After drying, the product was repeatedly distilled, affording 2·5 g (75%) of *V*, b.p. 114–114·5°C/2·7 Pa (0·02 Torr); homogeneous according to gas–liquid chromatography (15% silicone elastomer on Chromosorb N-AW, 225°C, 40 MPa). The compound was identical with the product prepared by lithium aluminium hydride reduction of ethyl 3-(1,2,3,4-tetrahydro-2-isoquinolyl)propanoate[11]. Reported[12] b.p. 197°C/13 Torr.

b) A solution of *II* (1·9 g; 0·01 mol) in tetrahydrofuran (30 ml) was mixed with 3M-NaOH (3·5 ml) and 30% H_2O_2 was added dropwise with stirring until unconsumed H_2O_2 was detected (4·5 ml total). After processing as described under *a*), 1·3 g (67%) of *V* was obtained, identical with an authentic sample[11]. Hydrochloride, m.p. 152–155°C (ethanol); reported[12] m.p. 151 to 152°C. ^{1}H NMR spectrum (D_2O, ppm): 1·92–2·26 (m, 2 H) H on $C_{(10)}$; 3·06–3·86 (m, 8 H) H on $C_{(3)}$, $C_{(4)}$, $C_{(9)}$, $C_{(11)}$; 7·44 (s, 2 H) H on $C_{(1)}$; 7·10–7·28 (m, 4 H) aromatic protons.

Oxidation of Side-Products after Isolation of *II*

The mixture of products from the hydroboration of amine *I* (26 g; 0·15 mol) was fractionated into the following fractions: *a*) b.p. 70–152°C/1·6 kPa (12 Torr), 7·3 g; *b*) b.p. 152–178°C/1·6 kPa (12 Torr), 16·0 g; solid residue, 4·8 g. Redistillation of the fraction *b*) afforded the amine-borane *II*. The fraction *a*) was hydrolyzed and oxidized in the usual manner and the product was distilled, yielding the following fractions: *a*) 97–111°C/2·1 kPa (16 Torr), 1·7 g; *b*) b.p. 111–171°C/2·1 kPa (16 Torr), 1·8 g. The fraction *a*) was shown by gas–liquid chromatography (10% Apiezon L/Chromosorb W or 15% silicone elastomer 301 on Chromosorb N-AW, 200°C, 30 kPa) and by ^{1}H NMR spectrum to be 1,2,3,4-tetrahydroisoquinoline (*VIII*). According to ^{1}H NMR spectra, the fraction *b*) was a mixture of 70% (mol) of alcohol *V* and 30% (mol) of compound *VIII*. ^{1}H NMR spectrum of *VIII* ($CDCl_3$; ppm): 1·56 (s, 1 H) NH; 2·70 (t, 2 H, J = 6 Hz) H at $C_{(4)}$; 3·05 (t, 2 H, J = 6 Hz) H at $C_{(3)}$; 3·92 (s, 2 H) H at $C_{(1)}$; 6·78–7·24 (m, 4 H) aromatic protons. 2-*p*-Toluenesulfonyl--1,2,3,4-tetrahydroisoquinoline, m.p. 142–144°C, melted without depression on admixture with the authentic sample[13].

To a stirred solution of the distillation residue (4·8 g) in acetone (25·5 ml) 15% hydrochloric acid (15·5 ml) was added dropwise. The mixture warmed spontaneously and was then refluxed for 15 min with stirring. After evaporation and dissolution in water (10 ml), tetrahydrofuran (25·5 ml) and 40% NaOH (7·5 ml) were added, followed by dropwise addition of 30% H_2O_2 (5·5 ml) to the stirred mixture (strongly exothermic reaction). The mixture was refluxed with stirring for 3 h. The usual work-up procedure afforded 3·8 g of a product, b.p. 165–176°C/2·3 kPa (17 Torr) which was identified (^{1}H NMR spectrum) as *V*.

2-Propylisoquinolinium Bromide

Prepared by boiling isoquinoline with propyl bromide in methanol; m.p. 146–148°C (ethanol). For $C_{12}H_{14}BrN$ (252·2) calculated: 57·16% C, 5·60% H, 5·55% N; found: 56·95% C, 6·18% H, 5·79% N.

2-Propyl-1,2,3,4-tetrahydroisoquinoline (*VII*)

A solution of 2-propylisoquinolinium bromide (10·9 g; 0·043 mol) in 85% formic acid (16 ml) was mixed with triethylamine (8·7 g; 0·086 mol) and refluxed for 12 h. The mixture was worked up as described for *I*, affording 5·8 g (77%) of *VII*; b.p. 115–118°C/2·1 kPa (16 Torr). Reported[14] b.p. 70–72°C/0·4 Torr.

The elemental analyses were carried out in the Analytical Laboratory of our Department (Dr L. Helešic, Head). NMR spectra were measured under supervision of Dr P. Trška. Mass spectra were taken by Dr P. Zachař, IR spectra by Dr E. Janečková and Dr A. Kohoutová, the osmometric determination of molecular weight was performed by Dr J. Podehradská.

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