Synthesis and molecular structure of 3-bromo-*trans*-2,6-diallyl-Δ^3-piperideine hydrochloride

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The structure of 3-bromo-*trans*-2,6-diallyl-Δ^3-piperideine hydrochloride was determined by X-ray diffraction analysis. The corresponding base was prepared by reductive diallylation of 3-bromopyridine with triallylborane. 3-Bromo-*cis*-2,6-diallyl-Δ^3-piperideine **3** was prepared by heating *trans*-isomer **2** with triallylborane at 130 °C followed by deboronation of the resulting aminoborane with a solution of sodium hydroxide.

Key words: reductive allylation, allylboration, triallylborane, pyridines, X-ray diffraction analysis, 3-bromo-2,6-diallyl-Δ^3-piperideines, *trans*- to *cis*-isomerization,.

Complexes of triallylborane with pyridine and some of its derivatives undergo complete reconstruction when treated with alcohols, water, or secondary amines to give the corresponding *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridines (*trans*-2,6-diallyl-Δ^3-piperideines) in a yield of up to 98 %.[1,2] The latter isomerize nearly quantitatively when heated (125-150 °C) with triallyl- or allyl(dipropyl)borane to give *cis*-2,6-diallyl-Δ^3-piperideines.[2,3]

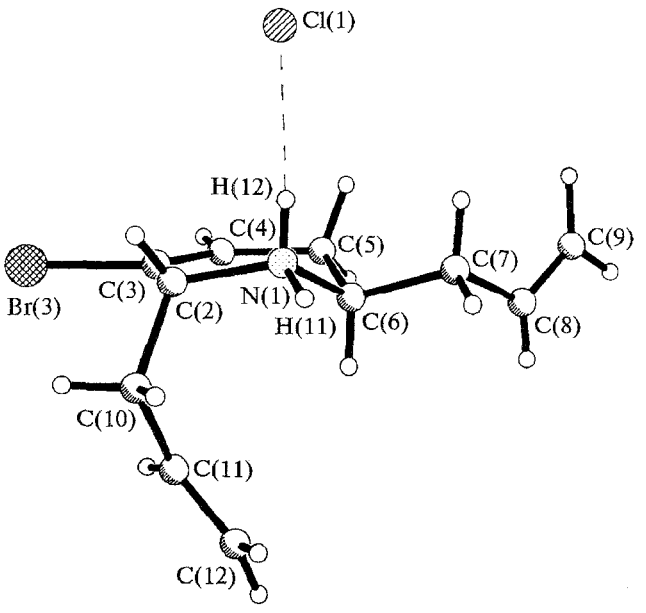

Fig. 1. General view of molecule **2a**

The structures of *trans*- and *cis*-2,6-diallyl-Δ^3-piperideines as well as the products of their hydrogenation and other transformations were confirmed by NMR spectroscopy (introduction of a prochiral benzyl probe and *N*,*N*-dimethyl quaternization).[2]

However, determination of the stereochemistry of the products of reductive 2,6-diallylation of some asymmetrically substituted pyridines based on the NMR spectra involved certain difficulties.

In the present paper we describe the conversion of the 3-bromopyridine complex of triallylborane (**1**) to 3-bromo-*trans*-2,6-diallyl-Δ^3-piperideine (**2**) and present the results of an X-ray structural study of its hydrochloride (**2a**).

The general view of molecule **2a** is shown in Fig. 1; Tables 1 and 2 list the bond lengths and angles. The piperideine ring in molecule **2a** has a distorted half-

Table 1. Bond lengths in molecule **2a**

Bond	*d*, Å
N(1)–C(2)	1.518(6)
N(1)–C(6)	1.513(6)
C(2)–C(3)	1.501(6)
C(2)–C(10)	1.534(7)
C(3)–C(4)	1.323(7)
C(4)–C(5)	1.506(7)
C(5)–C(6)	1.521(6)
C(6)–C(7)	1.526(6)
C(7)–C(8)	1.503(7)
C(8)–C(9)	1.320(8)
C(10)–C(11)	1.503(7)
C(11)–C(12)	1.315(8)
Br(3)–C(3)	1.912(4)

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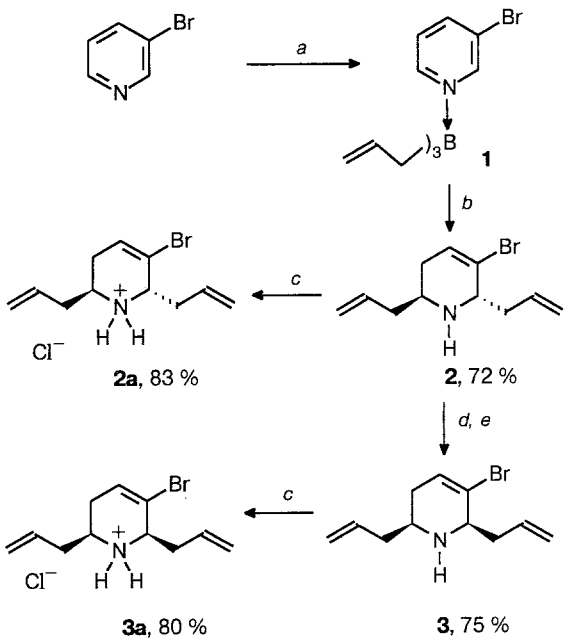
chair conformation: the C(6) and N(1) atoms deviate from the root-mean-square plane (with an accuracy of ±0.04 Å) by 0.442 Å and −0.239 Å; the Br atom actually lies in this plane (0.01 Å). The allyl group at the C(2) atom is oriented pseudoaxially and that at C(6) is equatorial. The bond lengths in molecule **2a** are close to the standard values.[4]

Molecules in the crystal are united by N(1)—H(12)···Cl (N···Cl is 3.060(8), H···Cl is 2.25(5), and the NHCl angle 173°) and N(1)—H(11)···Cl (1.5−x, 0.5+y, 1.5−z; N···Cl is 3.098(8), H···Cl is 2.18(5), the NHCl angle is 164°) hydrogen bonds in infinite chains directed along the 2_1 axis.



Reagents and conditions: *a*. All_3B, 0–20 °C (100 %). *b*. MeOH (4 equiv.), 75 °C, 6 h. *c*. $Et_2O \cdot HCl$ in ether, 20 °C. *d*. All_3B, 125–130 °C, 6 h. *e*. MeOH, 0–20 °C, 10% NaOH solution, 20 °C.

By heating with 1 mol of triallylborane (140 °C, 6 h) compound **2** is converted to *cis*-isomer **3**, which has been transformed to hydrochloride **3a**.[3]

Experimental

All operations with organoboron compounds were carried out under dry argon. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200P spectrometer, chemical shifts are given in the δ scale (ppm) with respect to TMS. IR spectra were run on an UR-20 spectrophotometer and mass spectra were obtained on Varian-MAT and MS-30 spectrometers.

3-Bromo-*trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine (2). 13.8 mL (143.1 mmol) of 3-bromopyridine and then 15.5 mL (382 mmol) of methanol were added with cooling (−70 °C) to 12.79 g (95.4 mmol) of triallylborane. The reaction mixture was refluxed for 6 h, then treated with 20 % NaOH (30 mL), and extracted with ether. The extract was dried with K_2CO_3. Distillation gave 16.75 g (72 %) of compound **2**, b.p. 80–85 °C (1 Torr). After repeat distillation the compound had a b.p. of 85–86 °C (1 Torr), n_D^{20} 1.5251. Found (%): C, 54.41; H, 6.76; Br, 33.36; N, 5.83. $C_{11}H_{16}NBr$. Calculated (%): C, 54.55; H, 6.66; Br, 33.00; N, 5.78. MS (EI, 70 eV), *m/z*: 201 $[M-C_3H_5]^+$. IR (neat, ν/cm^{-1}): 1435, 1452, 1640, 3079 (CH_2=CH and CH=CH); 3318 (NH). ^1H NMR ($CDCl_3$) δ: 1.78–2.4 (6 H, CH_2–C=); 2.6 (m, 1 H, NH); 2.94 (m, 1 H, H-6); 3.41 (d, 1 H, H-2); 5.0–5.18 (4 H, CH_2=C); 5.63–5.9 (2 H, CH=C); 6.0–6.1 (1 H, H-4). ^{13}C NMR ($CDCl_3$) δ: 34.09 (C-5); 36.16, 39.66 (–CH_2– of the allyl group); 44.91, 58.11 (C-2, C-6); 117.09, 117.69 (=CH_2 of the allyl group); 124.34 (C-3); 127.34 (C-4); 134.55, 134.92 (=CH– of the allyl group).

3-Bromo-*trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine hydrochloride (2a) was prepared by treatment of compound **2** with an ethereal solution of HCl, yield 83 %, m.p. 165–166 °C. Found (%): C, 47.47; H, 6.29; Br, 28.47; Cl, 12.51; N, 5.03. $C_{11}H_{17}NBrCl$. Calculated (%): C, 47.41; H, 6.15; Br, 28.68; Cl, 12.72; N, 5.03. IR ($CHCl_3$, ν/cm^{-1}): 1434, 1648 (CH_2=CH and CH=CH); 1580 (NH_2^+). ^1H NMR ($CDCl_3$), δ: 2.35–2.6 (3 H, CH_2–C=); 2.8–3.18 (3 H, CH_2–C=); 3.55 (br.s, 1 H, H-6); 4.1 (c, 1 H, H-2); 5.12–5.53 (4 H, CH_2=C); 5.64–6.1 (2 H, CH=C); 6.25 (m, 1 H, H-4); 9.7 and 10.6 (br.s, 2 H, NH_2^+). ^{13}C NMR ($CDCl_3$), δ: 29.15, 34.84, 35.88 (C-5, CH_2 of the allyl group); 49.27, 55.93 (C-2, C-6); 116.24 (C-3); 120.03, 121.35 (=CH_2 of the allyl group); 128.29 (C-4); 131.18, 131.40 (=CH– of the allyl group). Single crystals of hydrochloride **2a** (m.p. 165–166 °C) were prepared by crystallization from a mixture of ether and methanol. X-ray structural study: single crystals of **2a** are monoclinic, M = 278.63 $[C_{11}H_{17}NBr]Cl$, space group $P2_1/n$, $Z = 4$, at −130 °C: $a = 9.826(2)$, $b = 7.662(1)$, $c = 16.691(3)$ Å, $\beta = 95.12(2)°$, $V = 1251.6(7)$ Å^3, $d_{calc} = 1.479$ g cm^{-3}. Unit cell parameters and intensities of 2099 independent reflections with $I \geq 4\sigma(I)$ were measured on a Siemens P3/PC diffractometer (λMoK_α, graphite monochromator, $\theta/2\theta$-scanning, $2\theta \leq 60°$). The structure was solved by the direct method and refined in the full-matrix anisotropic approximation for nonhydrogen atoms. All of the H atoms were revealed from the differential synthesis and refined isotropically in the final cycles. The residual factors $R = 0.043$, $R_w = 0.047$.

Table 2. Bond angles in molecule **2a**

Angle	ω°, degrees
C(2)–N(1)–C(6)	116.8(3)
N(1)–C(2)–C(3)	109.0(4)
N(1)–C(2)–C(10)	111.8(4)
C(3)–C(2)–C(10)	114.9(4)
Br(3)–C(3)–C(2)	113.5(3)
Br(3)–C(3)–C(4)	120.0(3)
C(2)–C(3)–C(4)	126.5(4)
C(3)–C(4)–C(5)	121.5(4)
C(4)–C(5)–C(6)	113.6(4)
N(1)–C(6)–C(5)	108.6(4)
N(1)–C(6)–C(7)	107.5(3)
C(5)–C(6)–C(7)	112.2(4)
C(6)–C(7)–C(8)	112.7(4)
C(7)–C(8)–C(9)	125.0(5)
C(2)–C(10)–C(11)	114.2(4)
C(10)–C(11)–C(12)	124.3(5)

Table 3. The coordinates of the atoms (×10⁴ or ×10³ for H) and their heat parameters (U_{iso}^{equiv} (Å² ×10³, Å² ×10² for H)

Atom	*x*	*y*	*z*	*U*
Br(3)	8010(1)	810(1)	4244(1)	26(1)
Cl(1)	6171(1)	−1301(2)	7001(1)	21(1)
N(1)	6968(4)	2392(5)	6525(2)	14(1)
C(2)	7886(5)	1974(6)	5866(3)	17(1)
C(3)	7018(5)	1703(6)	5089(2)	16(1)
C(4)	5697(5)	2040(7)	4954(3)	20(1)
C(5)	4884(5)	2748(7)	5604(3)	21(1)
C(6)	5760(5)	3574(6)	6300(3)	16(1)
C(7)	4985(5)	3789(7)	7046(3)	19(1)
C(8)	3769(5)	4977(7)	6905(3)	22(1)
C(9)	2489(6)	4505(8)	6959(3)	31(2)
C(10)	9031(5)	3325(6)	5829(3)	19(1)
C(11)	8568(5)	5039(7)	5462(3)	22(1)
C(12)	8611(6)	6532(8)	5852(4)	32(2)
H(11)	746(9)	300(12)	694(5)	6(3)
H(12)	669(6)	143(8)	665(3)	2(1)
H(2)	827(5)	96(7)	598(3)	1(1)
H(4)	523(5)	170(7)	447(3)	1(1)
H(51)	430(7)	352(9)	539(4)	4(2)
H(52)	427(5)	181(6)	580(3)	0(1)
H(6)	609(6)	470(8)	618(3)	2(1)
H(71)	467(6)	270(9)	721(3)	2(2)
H(72)	560(5)	432(7)	744(3)	1(1)
H(8)	388(6)	601(9)	678(3)	3(2)
H(91)	179(7)	536(10)	689(4)	4(2)
H(92)	227(7)	329(10)	711(4)	4(2)
H(101)	965(6)	280(8)	548(3)	2(1)
H(102)	950(5)	343(6)	639(2)	0(1)
H(111)	824(5)	499(7)	486(3)	1(1)
H(121)	826(6)	768(8)	559(3)	3(2)
H(122)	892(7)	663(9)	632(4)	3(2)

The calculations were carried out on an IBM PC/AT computer by SHELXTL PLUS programs.[5] Coordinates and heat parameters of the atoms of structure **2a** are listed in Table 3.

3-Bromo-*cis*-2,6-diallyl-1,2,5,6-tetrahydropyridine (3). 8.67 g (35.8 mmol) of compound **2** was added at 20 °C to 4.80 g (35.8 mmol) of triallylborane. Weak self-heating of the reaction mixture was observed. The mixture was heated at 125—130 °C for 3 h and then MeOH (1 mL) and 20 % NaOH (11 mL, 54 mmol) were successively added. The mixture was extracted with ether and the ethereal solution was dried with K_2CO_3. Distillation gave 6.46 g (75 %) of *cis*-isomer **3**, b.p. 104 °C (2 Torr). The admixture of *trans*-isomer (6 %) was separated by chromatography on SiO_2 (with pentane as the eluent). Pure compound **3** has b.p. 98 °C (1.5 Torr), n_D^{20} 1.5242. Found (%): C, 54.50; H, 6.82; Br, 33.37; N, 5.70. $C_{11}H_{16}NBr$. Calculated (%): C, 54.55; H, 6.66; Br, 33.00; N, 5.78. MS (EI, 70 eV), *m/z*: 201 $[M-C_3H_5]^+$. IR (CH_2Cl_2) ν/cm^{-1}: 1440, 1450, 1460, 1641, 3005, 3042, 3081 (CH_2=CH and CH=CH); 3324 with the shoulder 3294 (NH). 1H NMR ($CDCl_3$), δ: 1.8—2.25 (m, 5 H, CH_2+NH); 2.35—2.6 (m, 2 H, CH_2); 2.78—2.93 (m, 1 H, H-6); 3.58 (m, 1 H, H-2); 4.97—5.24 (m, 4 H, CH_2=C); 5.63—5.88 (m, 2 H, CH=C); 6.15 (m, 1 H, H-4). 13C NMR ($CDCl_3$), δ: 34.63, 38.13, 40.00 (C-5, $-CH_2-$ of the allyl group); 51.24, 58.08 (C-2, C-6); 117.32, 118.43 (CH_2= of the allyl group); 125.65 (C-3); 129.13 (C-4); 133.47, 134.30 (CH= of the allyl group).

3-Bromo-*cis*-2,6-diallyl-1,2,5,6-tetrahydropyridine hydrochloride (3a). Yield 80 %, m.p. 162—162.5 °C (from a mixture of ether with methanol). Found (%): C, 47.54; H, 6.00; Br, 28.83; Cl, 12.79; N, 4.96. $C_{11}H_{17}NBrCl$. Calculated (%): C, 47.41; H, 6.15; Br, 28.68; Cl, 12.72; N, 5.03. IR (pressed with KBr), ν/cm^{-1}: 1430, 1642, 3038, 3080 (CH_2=CH and CH=CH); 1578 with the shoulder 1594 (NH_2^+). 1H NMR ($CDCl_3$, δ: 2.5—3.2 (m, 6 H, CH_2); 3.3 (br.s, 1 H, H-6); 4.15 (br.s, 1 H, H-2); 5.1—5.46 (m, 4 H, CH_2=C); 5.6—5.83 (m, 1 H, H-4); 6.04—6.37 (m, 2 H, CH=C); 9.35 and 10.3 (br.s, 2 H, NH_2^+); ^{13}C NMR ($CDCl_3$), δ: 29.26, 35.78, 36.20 (C-5, $-CH_2-$ of the allyl group); 53.93, 58.38 (C-2, C-6); 119.84, 121.28 (CH_2= of the allyl group); 124.82 (C-3); 129.25 (C-4); 130.84, 131.46 (=CH− of the allyl group).

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