Stereoselective reductive tetraallylation of pyridinecarboxylic acids with triallylborane

Yu. N. Bubnov,[a,b]* *E. E. Demina,*[a] *V. K. Bel'sky,*[c] *G. V. Zatonsky,*[a] *and A. V. Ignatenko*[a]

[a]*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,*
47 Leninsky prosp., 117913 Moscow, Russian Federation.
Fax: +7 (095) 135 5328. E-mail: bor@cacr.ioc.ac.ru
[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences,*
28 ul. Vavilova, 117813 Moscow, Russian Federation.
Fax: +7 (095) 135 5085
[c]*L. Ya. Karpov Scientific Research Institute of Physical Chemistry,*
10 ul. Vorontsovo pole, 103064 Moscow, Russian Federation.
Fax: +7 (095) 975 2450

Reductive tetraallylation of pyridine-3- and pyridine-4-carboxylic acids with triallylborane in the presence of propan-2-ol proceeded stereoselectively to yield *trans*-2,6-diallyl-3- and *trans*-2,6-diallyl-4-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridines, respectively. Under the same conditions, the reaction with pyridine-2-carboxylic acid gave a mixture of *trans*- and *cis*-2,6-diallyl-2-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridines in a ratio of 57 : 43. When 2,6-diphenylpyridine-4-carboxylic acid reacted with triallylborane, only the carboxylic group underwent reductive diallylation. When heated with triallylborane in *o*-xylene (130—133 °C, 7 h), *trans*-2,6-diallyl-4-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,3,6-tetrahydropyridine was converted to the corresponding *cis*-isomer. The stereochemistry of *trans*-2,6-diallyl-3-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine was confirmed by X-ray diffraction analysis.

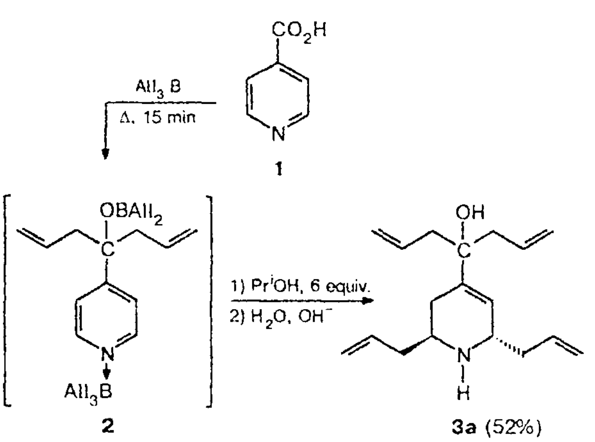
Key words: pyridinecarboxylic acids, reductive allylboration, triallylborane, *trans—cis* isomerization.

Pyridine and its derivatives undergo reductive *trans*-2,6-diallylation under the action of triallylborane and alcohols to give *trans*-2,6-diallyl-Δ^3-piperideines in 70—97% yields.[1—4] This stereospecific reaction proceeds under mild conditions (20—90 °C) and is not complicated by side processes. *trans*-2,6-Diallyl-Δ^3-piperideines obtained by this procedure contain a nitrogen function (NH bond) and three double bonds (two terminal and one endocyclic). Besides, it has long been known that when heated at moderate temperature with triallylborane, organic acids and their esters give the corresponding diallylcarbinols $(CH_2{=}CHCH_2)_2C(OH)R$.[5,6] We believed that reductive di- and tetraallylation of pyridinecarboxylic acids with triallylborane is a promising procedure for the preparation of aminoalcohols of the pyridine and piperideine series containing two or four allyl groups.

Tetraallylation of pyridinecarboxylic acids was carried out in benzene in two stages. The first stage involved reductive diallylation of the carboxylic group and then reductive 2,6-diallylation of the heterocyclic system was performed. The latter process occurs only in the presence of a source of protons, namely, alcohols (usually, propan-2-ol is used), water, or primary or secondary amines.[1—4]

As expected, the reaction of triallylborane with pyridine-4-carboxylic acid (**1**) followed by treatment with isopropyl alcohol proceeded stereoselectively to give aminoalcohol **3a** (52%) with the *trans*-arrangement of the allyl groups relative to the ring (Scheme 1).

Scheme 1



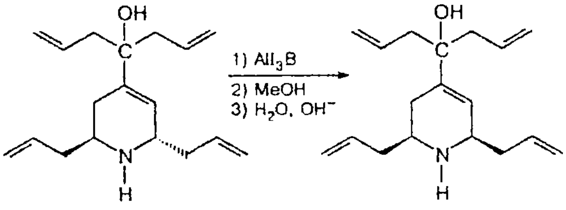
Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 11, pp. 2320—2326, November, 1998.

1066-5285/98/4711-2249$20.00

When triallylborane was added to a suspension of acid **1** (3 : 1) in benzene, propene and boron ester of this acid [RCOOBAll$_2$] were initially formed. The resulting ester underwent reductive diallylation to form diboron compound **2** ("ester—complex"). The ^{11}B NMR spectrum of the reaction mixture (after 4 h at 20 °C) has four signals: at δ 0.1 [B←N], 32.0 [RB(OR)$_2$], 50.2 [R$_2$BOR], and 80.9 [BAll$_3$]. The presence of the signals at δ ^{11}B 0.1 and 50.2 is indicative of the formation of complex **2** containing two boron atoms. One of them belongs to ester R$_2$BOR (δ 50.2). The second signal (δ ~0.0) is assigned to the four-coordinate boron atom. Subsequent treatment of complex **2** (more precisely, of the reaction mixture) with isopropyl alcohol and an alkaline solution afforded aminocarbinol **3a**, *i.e.*, reductive *trans*-2,6-diallylation of the pyridine ring occurred.

Previously, it has been demonstrated that when heated with triallylborane, *trans*-2,6-diallyl-1,2,3,6-tetrahydropyridine, its 3-bromo derivative,[2,3,8] and *trans*-2-allyl-6-alkyl(aryl)-1,2,3,6-tetrahydropyridines[9] were converted to the corresponding *cis* isomers. Homologs of the above-mentioned compounds underwent this isomerization as well. For example, heating of *trans*-2,6-dimetallyl-1,2,3,6-tetrahydropyridine with trimetallylborane (130—135 °C, 2.5 h) afforded its *cis*-2,6-dimetallyl isomer.[10]

We found that *trans*-aminoalcohol **3a** was also converted to *cis* isomer **3b** upon heating with triallylborane (1 : 2) in *o*-xylene (130—133 °C, 7 h) followed by deboration with methanol and alkali. Amine **3b** was identified as picrate (the yield was 82% with respect to **3a**).

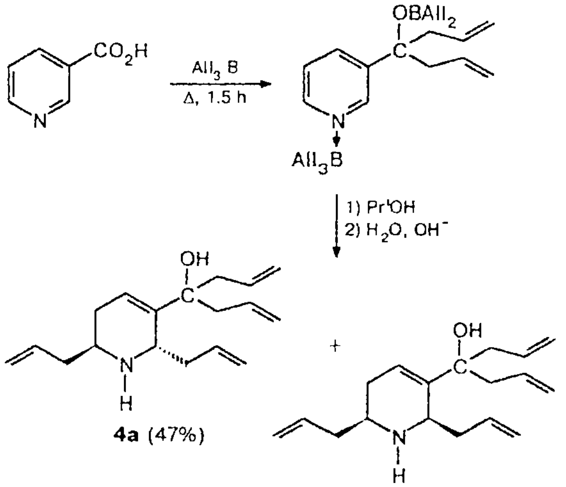


3a **3b**

Therefore, both *trans*- (**3a**) and *cis*-tetraallylated (**3b**) aminoalcohols can be readily prepared starting from pyridine-4-carboxylic acid and triallylborane.

Successive treatment of pyridine-3-carboxylic acid with triallylborane (90 °C, 1.5 h), propan-2-ol, and an alkaline solution afforded a mixture of *trans*- (**4a**) and *cis*-2,6-diallyl-3-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine (**4b**) from which *trans* isomer **4a** was isolated in the pure form by crystallization from pentane (the yield was 47%). The *cis* isomer (**4b**) was isolated (5%) by chromatography of the mother liquor on Al$_2$O$_3$ (Scheme 2). The structure of amine **4a** was determined by X-ray diffraction analysis (see below). The structure of compound **4b** was confirmed by NMR spectroscopy.

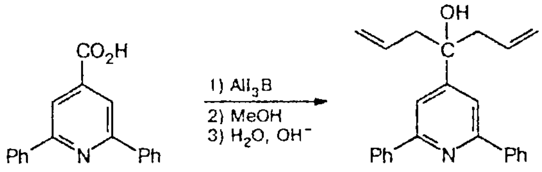
Scheme 2



4a (47%)

4b (5%)

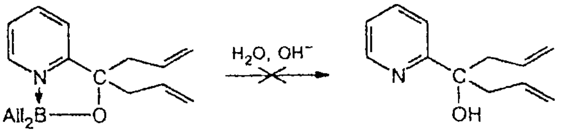
When the pyridine ring contains substituents at positions 2 and 6, selective functionalization of the carboxyl group occurs. Thus, boiling of a mixture of 2,6-diphenylpyridine-4-carboxylic acid and triallylborane in benzene (for 30 min) followed by treatment with methanol and alkali gave diallyl-4-pyridylcarbinol **5** in 75% yield.



5 (75%)

We believed that in the case of the reaction of pyridine-2-carboxylic acid with triallylborane, also only one reaction center, namely, the carboxyl group, would be involved in the reaction to give chelate **6**, whose deboration would afford carbinol **7** (Scheme 3).

Scheme 3

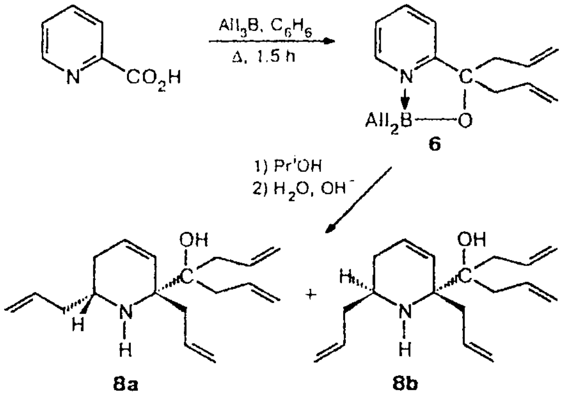


6 **7**

This suggestion is based on the fact that because of steric hindrances, the simplest 2-alkyl derivative of pyridine (α-picoline) reacts with triallylborane (or tripropylborane) to form only an unstable complex.[7] Apparently, this is the reason that α-picoline did not undergo (as we established) reductive 2,6-diallylation under the action of triallylborane and alcohols.

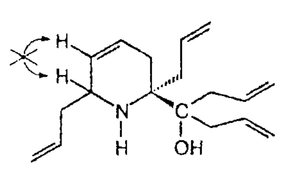
However, successive treatment of pyridine-2-carboxylic acid with triallylborane (boiling in benzene, 1.5 h), isopropyl alcohol, and a 10% NaOH solution afforded a mixture of two tetraallyl compounds, which differ by the mutual arrangement of the substituents with respect to the ring, namely, *trans*-2,6-diallyl- (**8a**) and *cis*-2,6-diallyl-2-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine (**8b**), in a ratio of 57 : 43 (^{1}H NMR data) in a overall yield of 42% (Scheme 4). Both isomers were isolated in the pure form by column chromatography on neutral Al_2O_3. Their structures were confirmed by NMR spectroscopy.

Scheme 4



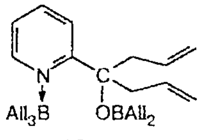
8a : **8b** (57 : 43), 42%

It should be noted that in the mixture of the products of this reaction (**8a** and **8b**), we did not detect their isomers (**9**), which differ in the position of the endocyclic double bond. This is confirmed by the absence of a cross peak between the C(6)H protons and the protons of the double bond in the ^{1}H—^{1}H COSY NMR spectrum.



9

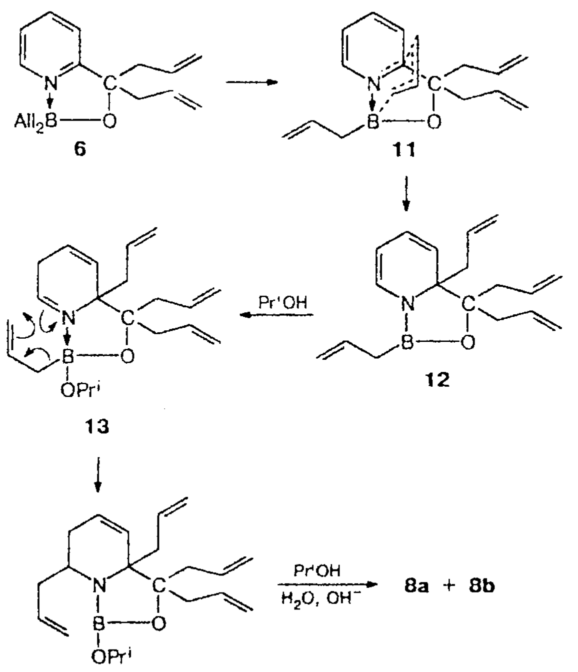
From the aforesaid it follows that allylboration of the pyridine ring (at least, addition of the first allyl group) occurred at position 2. This process occurred in chelate **6** rather than in adduct **10** because the complex-forming ability of carbinol **7** (more precisely, of its boron derivative **6**) with respect to triallylborane should be even smaller than that of α-picoline. Therefore, complex **10** was not formed.



10

A possible mechanism of reductive diallylation of the pyridine ring in compound **6** is shown in Scheme 5.

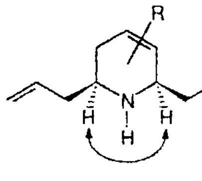
Scheme 5



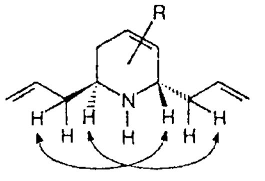
In complex **6**, intramolecular allylboration of the N=C(2) bond of the pyridine ring occurred initially through transition state **11** to give boron bicyclic compound **12**. The cleavage of the B—N covalent bond in **12** was accompanied by allylic rearrangement to give imine complex **13**. Addition of the second allyl fragment (at the C=N bond in **13**) occurred nonstereoselectively because the bulkiness of both groups attached to the C(2) atom of the ring differs insignificantly.

The structures of all the compounds synthesized in this work were confirmed by elemental analysis and spectral methods (^{1}H and ^{13}C NMR and IR).

The *cis* and *trans* arrangements of the allyl groups relative to the piperideine ring were established by the nuclear Overhauser effect experiments (1D NOE and 2D NOESY). In the case of *cis* isomers **3b** and **4b**, pronounced NOE is observed for the C(6)H and C(2)H protons, respectively, under irradiation of the C(2)H and C(6)H protons.

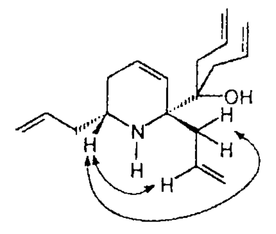


3b, 4b



3a, 4a

For *trans* isomers **3a** and **4a**, NOE is observed only for the protons of the allyl groups under irradiation of C(2)H and C(6)H proton. An analogous situation was also observed in the case of *trans* isomer **8a**. In addition, the structure of *trans* isomer **8a** was confirmed by X-ray diffraction analysis of its picrate (the results will be published elsewhere).



8a

The crystal and molecular structure of compound **4a** was established by X-ray diffraction analysis. The overall view of molecule **4a** is shown in Fig. 1. The bond lengths and bond angles are given in Table 1. The heterocycle adopts a twist conformation. The C(1), C(2), C(3), and C(4) atoms are coplanar to within 0.01 Å. The N and C(5) atoms deviate from this plane by 0.366 and 0.401 Å, respectively. The allyl group at the C(1) atom is in the pseudoaxial position. The corresponding group at the C(5) atom is in the equatorial position. The bond lengths and bond angles in **4a** are close to the standard values.

It is interesting to note that in the crystal compound **4a** exists as achiral dimers formed through OH...N

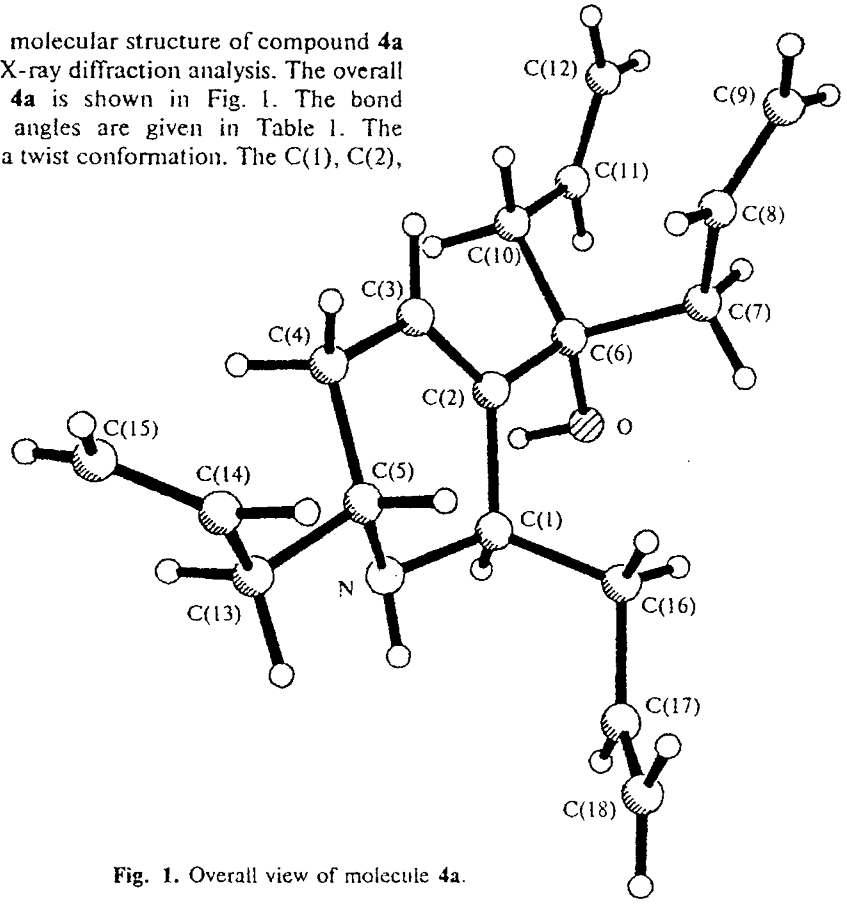


Fig. 1. Overall view of molecule **4a**.

Table 1. Bond lengths (d) and bond angles (ω) in molecule **4a**

Bond	d/Å	Bond	d/Å	Angle	ω/deg	Angle	ω/deg
N—C(5)	1.472(3)	C(6)—C(10)	1.547(4)	C(5)—N—C(1)	114.7(2)	O—C(6)—C(10)	109.1(2)
N—C(1)	1.475(3)	C(6)—C(7)	1.547(4)	N—C(1)—C(2)	110.3(2)	C(2)—C(6)—C(10)	111.4(2)
O—C(6)	1.427(3)	C(7)—C(8)	1.476(5)	N—C(1)—C(16)	112.9(3)	O—C(6)—C(7)	104.2(2)
C(1)—C(2)	1.516(4)	C(8)—C(9)	1.282(5)	C(2)—C(1)—C(16)	113.9(2)	C(2)—C(6)—C(7)	112.3(2)
C(1)—C(16)	1.539(4)	C(10)—C(11)	1.488(4)	C(3)—C(2)—C(1)	119.6(3)	C(10)—C(6)—C(7)	109.1(2)
C(2)—C(3)	1.327(4)	C(11)—C(12)	1.297(5)	C(3)—C(2)—C(6)	122.6(2)	C(8)—C(7)—C(6)	115.8(3)
C(2)—C(6)	1.527(4)	C(13)—C(14)	1.486(5)	C(1)—C(2)—C(6)	117.8(2)	C(9)—C(8)—C(7)	127.2(5)
C(3)—C(4)	1.494(4)	C(14)—C(15)	1.279(5)	C(2)—C(3)—C(4)	125.2(3)	C(11)—C(10)—C(6)	114.8(3)
C(4)—C(5)	1.509(4)	C(16)—C(17)	1.485(5)	C(3)—C(4)—C(5)	112.1(2)	C(12)—C(11)—C(10)	125.3(4)
C(5)—C(13)	1.518(4)	C(17)—C(18)	1.291(6)	N—C(5)—C(4)	106.2(3)	C(14)—C(13)—C(5)	113.9(3)
				N—C(5)—C(13)	109.0(2)	C(15)—C(14)—C(13)	125.9(5)
				C(4)—C(5)—C(13)	113.6(2)	C(17)—C(16)—C(1)	112.1(3)
				O—C(6)—C(2)	110.6(2)	C(18)—C(17)—C(16)	126.1(6)

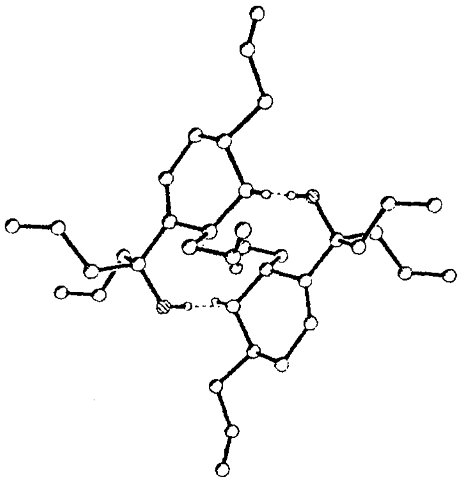


Fig. 2. Crystal structure of compound **4a**.

hydrogen bonds (the length is 2.829 Å) between the hydroxyl groups and the nitrogen atoms of the adjacent enantiomeric molecules (Fig. 2).

Experimental

All operations with organoboron compounds were carried out under an atmosphere of dry argon. The ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on a Bruker AC-200P spectrometer. The chemical shifts are given in the δ scale relative to Me_4Si, $CHCl_3$, and $BF_3 \cdot OEt_2$, respectively. The IR spectra were obtained on a UR-20 spectrometer. The 1D NOE and 2D NOESY experiments were carried out on Bruker AM-300 and Bruker DRX-500 instruments, respectively.

***trans*-2,6-Diallyl-4-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,3,6-tetrahydropyridine (3a).** Triallylborane (11.05 g, 82.44 mmol) was added to a stirred suspension of pyridine-4-carboxylic acid (3.33 g, 27.05 mmol) in benzene (15 mL). The reaction mixture was boiled for 15 min. Isopropyl alcohol (12.61 mL, 164.89 mmol) was added to the resulting homogeneous solution at 20 °C. The reaction mixture was kept at ~20 °C for 19 h and then boiled for 1.5 h. Then ether (10 mL) and a 3.6 *N* NaOH solution (34.7 mL) were added and the reaction mixture was boiled with stirring for 30 min. The organic layer was separated. The aqueous layer was extracted with ether. The combined organic extracts were dried with K_2CO_3. The solvent was evaporated *in vacuo*. Crystallization of the residue from pentane gave compound **3a** in a yield of 3.84 g (52%), m.p. 53—54 °C. Found (%): C, 79.12; H, 9.84. $C_{18}H_{27}NO$. Calculated (%): C, 79.07; H, 9.95. IR (CCl_4), ν/cm^{-1}: 920, 997, 1638, 2980, 3078 ($RCH{=}CH_2$ and $R^1R^2C{=}CHR$); 1437, 2840, 2925 (CH_2 and CH); 1340, 3310, 3565 (NH and OH). ^{1}H NMR, δ: 1.60—2.50 (m, 12 H, CH_2—C=, N—H, O—H); 2.87 (m, 1 H, C(2)—H); 3.44 (m, 1 H, C(6)—H); 4.92—5.25 (m, 8 H, CH_2=C); 5.55—5.90 (m, 5 H, CH=C). ^{13}C NMR, δ: 31.6 (C(3)); 40.0, 40.1, 43.3, 43.4 (CH_2 in the allyl groups); 46.8 and 51.5 (C(2, 6)); 75.0 (C—OH); 117.4, 117.6, 118.1, 118.8 (=CH_2 in the allyl groups); 123.9 (C(5)); 133.2, 133.5, 135.2, 135.6 (=CH— in the allyl groups); 138.5 (C(4)).

Picrate of amine 3a. A solution of picric acid (0.24 g) in ethanol was added to a solution of compound **3a** (0.29 g) in ethanol. The solvent was evaporated. The residue was crystallized from a 1 : 1 ether—hexane mixture. Picrate was obtained in a yield of 0.45 g (85%), m.p. 92—93 °C. Found (%): C, 57.08; H, 6.23. $C_{24}H_{30}N_4O_8$. Calculated (%): C, 57.36; H, 6.02. ^{1}H NMR, δ: 2.13—2.85 (m, 10 H, CH_2—C=); 3.34 (m, 1 H, C(2)—H); 4.12 (m, 1 H, C(6)—H); 5.00—5.50 (m, 8 H, CH_2=C); 5.50—6.00 (m, 5 H, CH=C); 6.40 (br.s, 1 H, NH_A^+); 8.86 (m, 2 H, $C_6H_2(NO_2)_3$); 10.38 (br.s, 1 H, NH_B^+). ^{13}C NMR, δ: 27.5 (C(3)); 36.0, 37.3, 43.2, 43.4 (CH_2 in the allyl groups); 49.0, 51.6 (C(2, 6)); 74.9 (C—OH); 118.7, 119.8, 121.8, 122.1 (=CH_2 in the allyl groups); 126.5 (C(5)); 131.1, 131.4, 132.1, 132.6 (=CH— in the allyl groups); 140.2 (C(4)); 118.1, 127.9, 141.4, 161.7 ($C_6H_2(NO_2)_3OH$).

***cis*-2,6-Diallyl-4-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,3,6-tetrahydropyridine (3b).** Triallylborane (2.00 g, 14.92 mmol) was added to a solution of compound **3a** (2.04 g, 7.46 mmol) in *o*-xylene (3 mL). The mixture was heated at 130—133 °C for 7 h. Then MeOH (0.6 mL) and a 5 *N* NaOH solution (4.48 mL) were added successively upon cooling (below 10 °C). The reaction mixture was extracted with ether. The extract was dried with K_2CO_3. The solvent was evaporated *in vacuo* and compound **3b** was obtained as on oil. ^{1}H NMR, δ: 1.65—2.55 (m, 12 H, CH_2—C=, N—H, O—H); 2.74 (m, 1 H, C(2)—H); 3.47 (m, 1 H, C(6)—H); 4.95—5.30 (m, 8 H, CH_2=C); 5.56—5.64 (m, 1 H, C(5)—H); 5.64—5.95 (m, 4 H, CH=C). ^{13}C NMR, δ: 32.4 (C(3)); 40.9, 41.0, 43.5 (CH_2 in the allyl groups); 52.5, 54.5 (C(2, 6)); 75.0 (C—OH); 117.6, 117.7, 118.2, 118.9 (=CH_2 in the allyl groups); 124.8 (C(5)); 133.3, 133.6, 135.0, 135.1 (=CH— in the allyl groups); 139.4 (C(4)).

Picrate of amine 3b. A solution of picric acid (1.71 g) in ethanol was added to compound **3b**, which was prepared as described above. The hot solution was filtered. The solvent was evaporated *in vacuo*. The residue was crystallized from a 1 : 1 hexane—ether mixture. Picrate was obtained in a yield of 3.09 g (82%), m.p. 102—103 °C. Found (%): C, 57.22; H, 5.89. $C_{24}H_{30}N_4O_8$. Calculated (%): C, 57.36; H, 6.02. ^{1}H NMR, δ: 2.20—2.80 (m, 10 H, CH_2—C=); 3.45 (m, 1 H, C(2)—H); 4.20 (m, 1 H, C(6)—H); 5.00—5.40 (m, 8 H, CH_2=C); 5.50—5.90 (m, 5 H, CH=C); 7.42 (br.s, 1 H, NH_A^+); 8.90 (m, 2 H, $C_6H_2(NO_2)_3$); 9.20 (br.s, 1 H, NH_B^+). ^{13}C NMR, δ: 27.8 (C(3)); 36.9, 37.0, 43.4, 43.6 (CH_2 in the allyl groups); 54.3, 55.0 (C(2, 6)); 75.0 (C—OH); 119.2, 119.9, 121.3, 121.6 (=CH_2 in the allyl groups); 126.7 (C(5)); 130.4, 130.5, 132.2, 132.5 (=CH— in the allyl groups); 141.1 (C(4)); 118.5, 128.72, 141.1, 161.3 ($C_6H_2(NO_2)_3OH$).

***trans*-2,6-Diallyl-3-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine (4a).** Triallylborane (16.72 g, 124.75 mmol) was added to a stirred suspension of pyridine-3-carboxylic acid (4.98 g, 40.45 mmol) in benzene (20 mL). The mixture was boiled for 1.5 h. Isopropyl alcohol (16 mL, 209.15 mmol) was added to the resulting homogeneous solution at 20 °C. The reaction mixture was kept for 14 h and then boiled for 3 h. Isopropyl alcohol (6.2 mL, 80.90 mmol) was added. The reaction mixture was boiled for 1 h. Then a 5.6 *N* NaOH solution (33.42 mL) and mannitol (25 g, 137.22 mmol) were added to the reaction mixture and the mixture was boiled for 45 min. The resulting mixture was extracted with a 1 : 1 benzene—ether mixture. The organic extracts were dried with K_2CO_3. The solvents were evaporated *in vacuo*. Crystallization of the residue from pentane gave compound **4a** in a yield of 4.15 g. The mother liquor was concentrated *in vacuo*. Chromatography of the residue on a column with Al_2O_3 (neutral, L 40/250, a 1 : 3 benzene—ether mixture as the eluent) gave compound **4a** with an admixture of the *cis* isomer. Repeated chromatography of **4a** on a column with Al_2O_3 (a 3 : 1 benzene—ether mixture as the eluent) gave

Table 2. Coordinates of nonhydrogen atoms ($\times 10^4$) and their equivalent isotropic temperature factors U_{eq} ($\times 10^3$/Å^2) in the structure of **4a**

Atom	*x*	*y*	*z*	U_{eq}
N	855(3)	2155(2)	6935(3)	48(1)
O	2720(3)	−364(2)	3940(2)	52(1)
C(1)	2092(3)	1570(3)	6194(3)	46(1)
C(2)	1876(3)	1698(3)	4886(3)	42(1)
C(3)	973(4)	2504(3)	4692(3)	53(1)
C(4)	189(5)	3378(4)	5699(3)	56(1)
C(5)	917(4)	3530(3)	7098(3)	49(1)
C(6)	2664(3)	843(3)	3818(3)	45(1)
C(7)	4665(4)	1583(3)	4009(4)	54(1)
C(8)	5026(4)	2931(4)	4022(4)	74(1)
C(9)	5852(6)	3331(7)	3286(6)	103(2)
C(10)	1542(4)	442(3)	2374(3)	52(1)
C(11)	2093(4)	−524(4)	1270(4)	65(1)
C(12)	2430(6)	−360(6)	242(5)	92(1)
C(13)	−175(6)	4095(4)	8063(4)	64(1)
C(14)	−113(6)	5518(4)	8375(4)	73(1)
C(15)	−1479(9)	5920(6)	8148(6)	107(2)
C(16)	4065(4)	2128(4)	7074(3)	61(1)
C(17)	4210(5)	2010(6)	8356(4)	73(1)
C(18)	4805(8)	3008(8)	9560(6)	121(2)

Table 3. Coordinates of hydrogen atoms ($\times 10^4$) and their equivalent isotropic temperature factors U_{eq} ($\times 10^3$/Å^2) in the structure of **4a**

Atom	*x*	*y*	*z*	U_{eq}
H(1O)	1585(50)	−915(35)	3714(33)	88(12)
H(1N)	1180(34)	2221(26)	7750(29)	47(9)
H(1)	1674(33)	561(28)	5943(24)	50(7)
H(3)	829(33)	2568(24)	3849(28)	54(8)
H(41)	437(34)	4258(31)	5706(26)	62(9)
H(42)	−1176(42)	2939(26)	5387(25)	61(8)
H(5)	2179(35)	4188(23)	7511(22)	38(7)
H(71)	5356(36)	1634(25)	4801(28)	52(8)
H(72)	5030(36)	931(30)	3245(32)	69(9)
H(8)	4669(57)	3647(46)	4655(44)	126(16)
H(91)	6033(61)	4231(55)	3352(44)	139(18)
H(92)	6249(57)	2619(47)	2658(45)	120(18)
H(101)	1546(34)	1248(29)	2238(24)	56(8)
H(102)	292(40)	35(24)	2311(22)	45(7)
H(11)	2132(43)	−1320(37)	1354(33)	88(12)
H(121)	2366(41)	444(36)	180(32)	80(12)
H(122)	2750(54)	−1075(45)	−475(44)	120(14)
H(131)	−1476(47)	3495(30)	7630(28)	69(9)
H(132)	338(42)	4105(32)	8934(38)	89(10)
H(14)	1185(63)	6236(42)	8834(41)	130(15)
H(151)	−1238(47)	6891(45)	8465(37)	102(13)
H(152)	−2608(88)	5226(66)	7616(62)	198(30)
H(161)	4676(40)	1586(30)	6607(29)	64(10)
H(162)	4580(41)	3162(37)	7314(30)	82(10)
H(17)	3777(43)	1111(38)	8211(34)	81(12)
H(181)	5281(56)	3984(52)	9674(44)	138(19)
H(182)	4847(60)	2805(45)	10280(53)	134(18)

an additional amount of pure compound **4a** and *cis* isomer **4b** in yields of 1.04 g and 0.56 g (5.1%), respectively. The total yield of **4a** was 5.19 g (47%).

Table 4. Anisotropic temperature factors ($\times 10^3$/Å^2) in the structure of **4a**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N	47(2)	56(2)	58(2)	35(1)	20(1)	22(1)
O	45(1)	52(1)	71(1)	37(1)	16(1)	20(1)
C(1)	42(2)	51(2)	53(2)	28(2)	15(2)	19(2)
C(2)	33(2)	44(2)	56(2)	29(2)	13(1)	12(1)
C(3)	53(2)	62(2)	58(2)	36(2)	21(2)	25(2)
C(4)	55(2)	58(2)	71(2)	39(2)	21(2)	27(2)
C(5)	43(2)	44(2)	63(2)	28(2)	15(2)	13(2)
C(6)	37(2)	46(2)	63(2)	33(2)	14(2)	15(1)
C(7)	42(2)	64(2)	64(2)	36(2)	17(2)	15(2)
C(8)	56(2)	72(3)	104(3)	49(3)	35(2)	12(2)
C(9)	92(3)	102(4)	125(4)	72(4)	26(3)	11(3)
C(10)	46(2)	56(2)	61(2)	31(2)	15(2)	19(2)
C(11)	72(2)	66(3)	61(2)	31(2)	19(2)	26(2)
C(12)	112(3)	97(4)	80(3)	41(3)	38(2)	47(3)
C(13)	75(3)	65(3)	72(2)	37(2)	35(2)	36(2)
C(14)	86(3)	69(3)	79(2)	34(2)	38(2)	39(3)
C(15)	128(4)	94(4)	130(4)	61(3)	48(3)	66(4)
C(16)	52(2)	79(3)	64(2)	38(2)	15(2)	31(2)
C(17)	67(2)	94(3)	67(3)	39(3)	12(2)	40(2)
C(18)	149(4)	139(5)	73(4)	39(4)	10(3)	71(4)

Compound 4a, m.p. 56—57 °C. Found (%): C, 78.83; H, 9.95. $C_{18}H_{27}NO$. Calculated (%): C, 79.07; H, 9.95. IR (CCl_4), ν/cm^{-1}: 920, 1003, 1639, 2978, 3075 ($RCH=CH_2$ and $R^1R^2C=CHR$); 1436, 2828, 2910 (CH_2 and CH); 3307 (NH); 3564 (OH). ^{1}H NMR, δ: 1.75—2.75 (m, 12 H, CH_2—C=, N—H, O—H); 2.90 (m, 1 H, C(6)—H); 3.45 (d, 1 H, C(2)—H, *J* = 10.4 Hz); 4.95—5.30 (m, 8 H, CH_2=C); 5.54 (t, 1 H, C(4)—H, *J* = 3.8 Hz); 5.77 (m, 4 H, CH=C). ^{13}C NMR, δ: 32.1 (C(5)); 37.6, 41.1, 45.7, 47.1 (CH_2 in the allyl groups); 44.4, 52.4 (C(2, 6)); 75.0 (C—OH); 117.4, 117.6, 118.6, 119.0 (=CH_2 in the allyl groups); 121.1 (C(4)); 133.8, 133.9, 135.2, 136.3 (=CH— in the allyl groups); 143.5 (C(3)).

Single crystals of **4a** suitable for X-ray diffraction analysis were obtained by crystallization from pentane. The crystals are triclinic, $M = 273.41$ [$C_{18}H_{27}NO$], space group $P1$, $Z = 2$, at 20 °C: $a = 7.8640(10)$ Å, $b = 11.256(2)$ Å, $c = 11.218(2)$ Å, $\alpha = 113.38(2)°$, $\beta = 99.26(2)°$, $\gamma = 102.59(2)°$, $V = 854.9(2)$ Å^3, $d_{calc} = 1.062$ g cm^{-3}. The unit cell parameters and intensities of reflections were measured on an automated Nicolet P3 diffractometer (Cu-Kα, β filter, θ/2θ scanning technique, θ ≤ 45°). The structure of **4a** was solved by the direct method. The coordinates of the nonhydrogen atoms were refined anisotropically by the full-matrix least-squares method. The positions of the hydrogen atoms were located from the difference synthesis and refined isotropically by the least-squares method. The final values of the *R* factors were as follows: $R = 0.037$ and $wR_2 = 0.103$ based on 1066 independent reflections with $I > 2\sigma(I)$. All calculations were carried out on an IBM-PC/AT computer with the use of the SHELXL-93 program package. The atomic coordinates and the thermal parameters for the structure of **4a** are given in Tables 2 and 3. The anisotropic temperature factors are listed in Table 4.

Compound 4b, m.p. 34—35 °C (from hexane). ^{1}H NMR, δ: 1.65—2.75 (m, 12 H, CH_2—C=, N—H, O—H); 2.80—3.00 (m, 1 H) and 3.60 (m, 1 H) (C(2)—H and C(6)—H); 4.90—5.30 (m, 8 H, CH_2=C); 5.60—6.00 (m, 5 H, CH=C). ^{13}C NMR, δ: 32.3 (C(5)); 39.2, 40.5, 44.7, 45.5 (CH_2 in the allyl groups); 51.3, 54.6 (C(2, 6)); 75.3 (C—OH); 117.1, 117.6, 118.6, 118.7

(=CH_2 in the allyl groups); 123.9 (C(4)); 133.6, 133.7, 134.9, 135.8 (=CH— in the allyl groups); 141.7(C(3)).

4-(Hydroxydiallylmethyl)-2,6-diphenylpyridine (5). Triallylborane (3.67 g, 27.38 mmol) was added to a stirred suspension of 2,6-diphenylpyridine-4-carboxylic acid (2.48 g, 9.01 mmol) in benzene (10 mL). The reaction mixture was boiled for 35 min (the solution became homogeneous after 20 min). The reaction mixture was treated with MeOH (1.5 mL) and a 4.7 *N* NaOH solution (8.74 mL) and extracted with a 1 : 1 benzene—ether mixture. The extract was dried with Na_2SO_4. The solvent was evaporated *in vacuo*. Crystallization of the residue from hexane gave compound **5** in a yield of 2.3 g (75%), m.p. 71—72 °C. Found (%): C, 84.61; H, 6.88. $C_{24}H_{23}NO$. Calculated (%): C, 84.42; H, 6.79. IR (KBr), ν/cm^{-1}: 1408, 1494, 1552 (with a shoulder), 1578, 1597, 1638, 3037, 3072 (RCH=CH_2, Ph, Py); 3490, 3555 (OH). ^1H NMR, δ: 2.38 (br.s, 1 H, O—H); δ_A = 2.73 and δ_B = 2.56 (AB portion of the ABX spectrum, $^3J_{AB}$ = 13.9 Hz, $^3J_{AX}$ = 5.9 Hz, $^3J_{BX}$ = 8.0 Hz, 4 H, CH_2 in the allyl groups); 5.00—5.25 (m, 4 H, CH_2=C); 5.65 (m, 2 H, CH=C); 7.45 (m, 6 H, *m*- and *p*-H in Ph); 7.72 (s, 2 H, C(3)—H and C(5)—H); 8.20 (d, 4 H, *o*-H in Ph). ^{13}C NMR, δ: 46.3 (CH_2 in the allyl groups); 74.9 (C—OH); 115.6 (=CH_2 in the allyl groups); 119.9 (C(3) and C(5) in Py); 127.0 and 128.5 (*o*-C and *m*-C in Ph); 128.9 (*p*-C in Ph); 132.4 (=CH— in the allyl groups); 139.5 (quaternary C (in Ph)); 156.2 (C(4)); 156.9 (C(2) and C(6)).

***trans*-2,6-Diallyl-2-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine (8a) and *cis*-2,6-diallyl-2-(1-allyl-1-hydroxybut-3-en-1-yl)-1,2,5,6-tetrahydropyridine (8b).** Triallylborane (9.06 g, 67.60 mmol) was added to a stirred suspension of pyridine-2-carboxylic acid (2.65 g, 21.52 mmol) in benzene (5 mL). The mixture was boiled for 1.5 h. Isopropyl alcohol (11.6 mL, 150.67 mmol) was added to the resulting homogeneous solution at 20 °C. The reaction mixture was kept for 19 h and then boiled for 30 min. A 10% NaOH solution (36 mL) was added to the reaction mixture. The mixture was stirred until boron in the organic layer disappeared (control was based on the absence of the green color when the sample was heated over the flame). The organic layer was separated. The aqueous layer was extracted with benzene. The organic extracts were dried with K_2CO_3. Distillation gave a mixture of isomers **8a** and **8b** in a yield of 2.48 g (42%) in a ratio of 57 : 43 (^1H NMR data); b.p. 118—126 °C (1 Torr) or 99 °C (0.3 Torr). Found (%): C, 78.87; H, 9.84. $C_{18}H_{27}NO$. Calculated (%): C, 79.07; H, 9.95. Both isomers were isolated in the individual form by chromatography on a column with Al_2O_3 (neutral, L 40/250, a 60 : 1 hexane—THF mixture as the eluent).

Compound 8a, R_f = 0.17. ^1H NMR, δ: 1.76 (m, 1 H, $C(5)H_A$); 1.92 (m, 1 H, $C(5)H_B$); 2.03 (m, 1 H, H_A in CH_2 at C(6)); 2.24 (m, 1 H, H_B in CH_2 at C(6)); 2.28—2.46 (4 H, CH_2); 2.48—2.57 (2 H, CH_2); 3.05 (1 H, C(6)—H); 5.00—5.18 (8 H, CH_2=); 5.63 (1 H, C(3)—H); 5.73 (1 H, CH= in the allyl group at C(6)); 5.86—6.06 (4 H, C(4)—H in other CH=). ^{13}C NMR, δ: 30.7 (C(5)); 40.3, 40.4 (CH_2 in the allyl group at C—OH); 41.3 (CH_2 in the allyl group at C(6)); 42.1 (CH_2 in the allyl group at C(2)); 48.0 (C(6)); 63.1 (C(2)); 76.9 (C—OH); 116.3, 116.6, 116.7, 117.1 (CH_2=); 126.6 (C(4)); 129.5 (C(3)); 134.7, 135.4, 135.8 (CH=).

Compound 8b, R_f = 0.27. ^1H NMR, δ: 1.63—1.78 (m, 1 H, $C(5)H_A$); 1.95—2.45 (10 H, CH_2—C=, N—H); 3.40 (1 H, C(6)—H); 4.87—5.10 (8 H, CH_2=); 5.42—5.52 (1 H, C(3)—H); 5.56—6.03 (5 H, CH=). ^{13}C NMR, δ: 29.6 (C(5)); 38.4, 40.0, 40.4, 41.0 (CH_2); 48.9 (C(6)); 60.2 (C(2)); 76.7 (C—OH); 116.3, 117.1, 117.2 (CH_2=); 124.4, 127.8 (C(3, 4)); 135.0, 135.2, 135.7 135.9 (CH=).

This work was supported by the Russian Foundation for Basic Research (Project Nos. 96-03-32555 and 95-03-09030) and by the Russian Federation Government (Project No. 96-15-97289).

References

1. Yu. N. Bubnov, E. A. Shagova, S. V. Evchenko, A. V. Ignatenko, and I. D. Gridnev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2644 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 2315 (Engl. Transl.)].
2. Yu. N. Bubnov, E. A. Shagova, S. V. Evchenko, and A. V. Ignatenko, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 693 [*Russ. Chem. Bull.*, 1994, **43**, 645 (Engl. Transl.)].
3. Yu. N. Bubnov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 1203 [*Russ. Chem. Bull.*, 1995, **44**, 1156 (Engl. Transl.)].
4. Yu. N. Bubnov, *Pure Appl. Chem.*, 1994, **66**, 235.
5. B. M. Mikhailov, Yu. N. Bubnov, A. V. Tsyban, and M. Sh. Grigorian, *J. Organomet. Chem.*, 1978, **154**, 131.
6. B. M. Mikhailov, Yu. N. Bubnov, and A. V. Tsyban', *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1978, 1892 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1978, **27**, 1663 (Engl. Transl.)].
7. V. S. Bogdanov, T. K. Baryshnikova, V. G. Kiselev, and B. M. Mikhailov, *Zh. Obshch. Khim.*, 1971, **41**, 1533 [*J. Gen. Chem. USSR*, 1971, **41** (Engl. Transl.)].
8. Yu. N. Bubnov, E. A. Shagova, S. V. Evchenko, and A. V. Ignatenko, *Izv. Akad. Nauk, Ser. Khim.*, 1993, 1672 [*Russ. Chem. Bull.*, 1993, **42**, 1610 (Engl. Transl.)].
9. Yu. N. Bubnov, E. V. Klimkina, A. V. Ignatenko, and I. D. Gridnev, *Tetrahedron Lett.*, 1997, **38**, 4631.
10. Yu. N. Bubnov, E. E. Demina, and A. V. Ignatenko, *Izv. Akad. Nauk, Ser. Khim.*, 1997, 1361 [*Russ. Chem. Bull.*, 1997, **46**, 1306 (Engl. Transl.)].

Received December 29, 1997