Allylboranes: reductive mono- and *trans*-diallylation of aromatic nitrogen-containing heterocyclic compounds*

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Reductive α-mono- and stereoselective trans-α,α′-diallylation of aromatic nitrogen-containing heterocycles by allylic boron derivatives have been discovered. A method for the *trans*-to-*cis* isomerization of *trans*-2,5-diallylpyrrolidines and *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridines by heating with allylboranes has been developed. The above reactions unite the chemistry of nitrogen-containing heterocycles and the chemistry of organoboron compounds on a new level.

Key words: allylboration, triallylborane, trimethallylborane, tricrotylborane, triphenylborane, complexes with pyridines; pyrrole, indole, pyridines, 4,4′-dipyridyl, quinolines, isoquinolines, phenanthridine, reductive monoallylation, reductive diallylation; *cis*- and *trans*-diallypyrrolidine, 1,2,5,6-tetrahydropyridines, stereochemistry, hydrogenation, 1,2-dihydroquinolines, 1,2,3,4-tetrahydroisoquinolines.

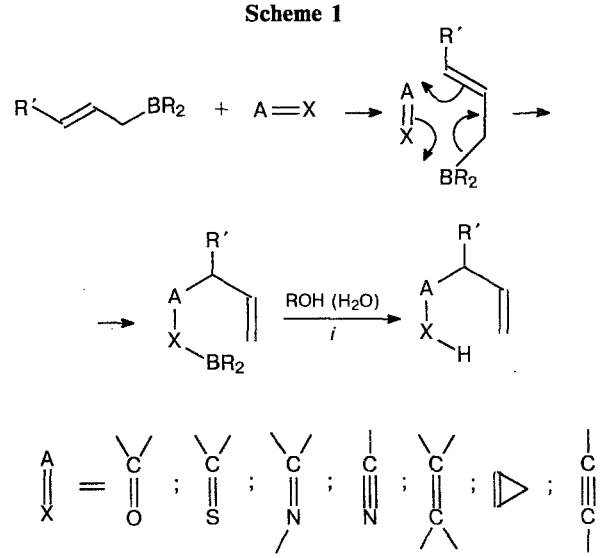
β,γ-Unsaturated (allylic) boron derivatives add to aldehydes, ketones, thioketones, imines, nitriles, acetylenes, and certain olefins.[1–6] Such an addition reaction, *i.e.*, allylboration, proceeds the more readily the more a multiple bond is polarized or strained (Scheme 1).[5–7] This is the fundamental difference between allylboranes and other classes of organoboron derivatives, which, generally, do not add to A=X reagents.[1–4]

The allylboration of carbonyl compounds was discovered in 1964.[8] Later, it was found that all allylboration reactions proceed regio- and stereospecifically, probably *via* a six-membered chair-like transition state (a $2\pi+2\pi+2\sigma$ process).[1–6] Deboronation of the resulting boron-containing adducts gives, respectively, homoallylic alcohols, thiols, amines, 1,4-dienes, 1,4-enynes, *etc.* It should be emphasized that the reactions of allylboranes with carbonyl compounds, nitriles, imines, and thioketones occur under mild conditions (−100 to 20 °C) and are not complicated by side processes.

Allylboration reactions have been used for over twenty years as a key step in the syntheses of various classes of organic compounds, including many natural compounds and their analogs. Several examples of using this general reaction in syntheses are presented in Scheme 2.

In a continuation of the studies on allylic boron derivatives,[5,6] we found a series of new reactions named *reductive mono- and trans-α,α′-diallylation of aromatic nitrogen-containing heterocycles.*[21–30] Some of them are presented below.

Scheme 1



i. Deboronation.

Pyridines: reductive *trans*-2,6-diallylation[21–25]

Triallylborane is a strong Lewis acid and readily forms complexes with pyridine (**1a**),[21,22,31] C_5D_5N (**1b**), and 3-bromopyridine (**1c**),[21] which can be distilled *in vacuo* (Table 1). Adduct **1a** remains unchanged on prolonged heating at 160 °C (20 h).[21,22,24] Its IR, Raman,[32]

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Scheme 2

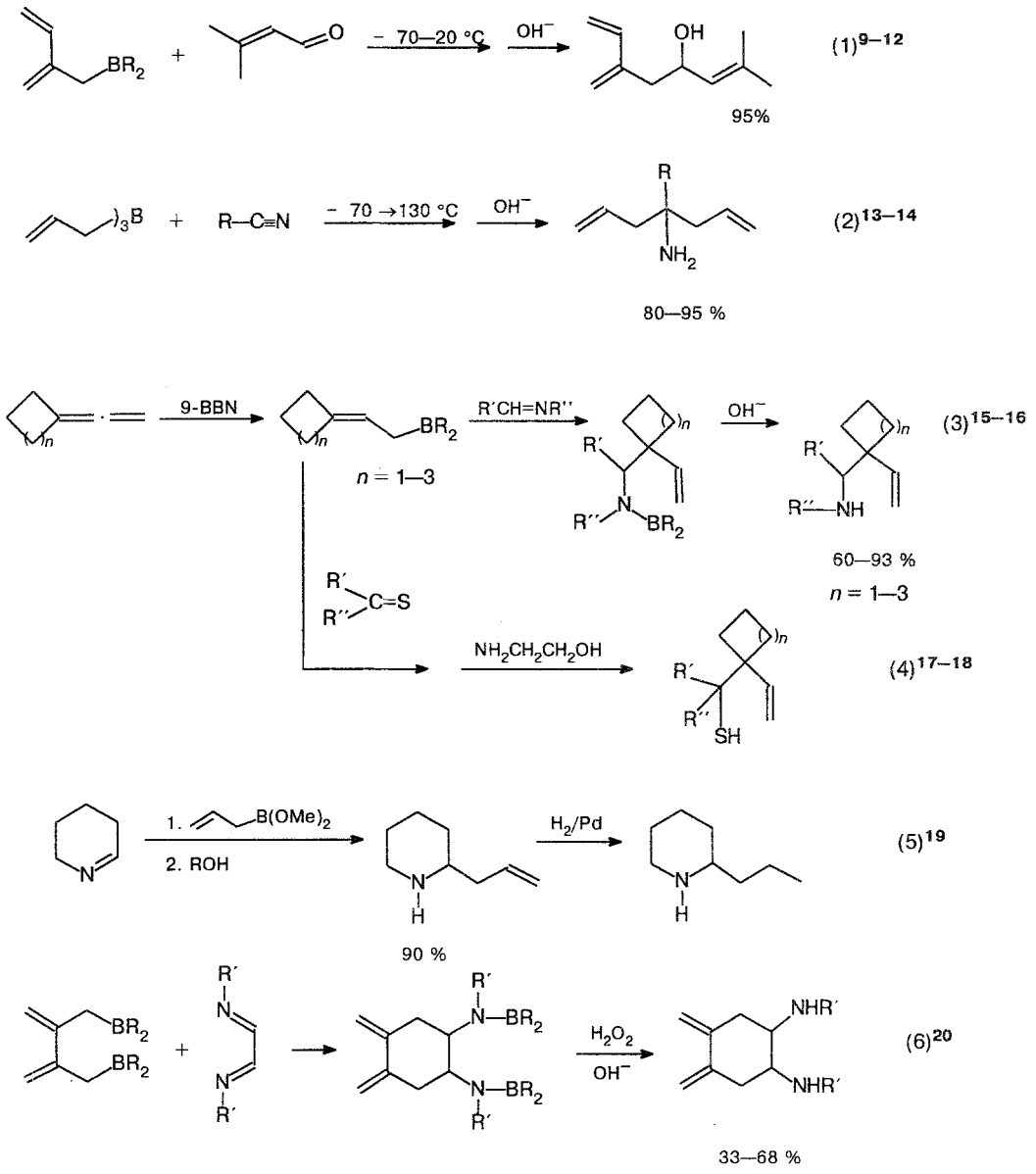
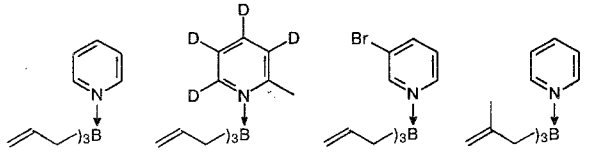


Table 1. Complexes of triallyl- and trimethallylborane **1a—d**



1a **1b** **1c** **1d**

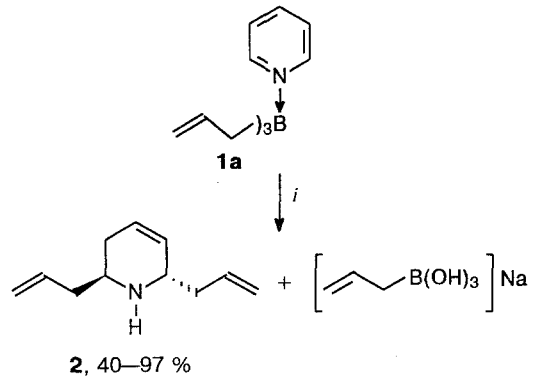
Complex	B.p./°C (*p*/Torr)	n_D^{20}	$\delta^{11}B$
1a*	102 (1)	1.4535	0
1b	103—104 (1)	1.5409	−0.6
1c	106 (1)	1.5643	−0.3
1d	75—77 (2)	1.5391	−0.6

* d_4^{20} 0.932; μ = 4.97 d[34]; m.p. 14—15 °C[21].

and NMR spectra[33,34] have been studied previously. The dipole moment of **1a** equals 4.97 D.[34] Trimethallylborane reacts with Py to give complex **1d**.

We found that the treatment of complex **1a** with alcohols, water, or Et_2NH (40—100 °C, 2—8 h) results in its complete rearrangement into *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine **2** (*trans*-2,6-diallyl-Δ^3-piperideine), whose yield (20—97 %) depends on the nature of the protolytic reagent used and on reaction conditions (Table 2). The maximum yield of **2** (97 %) was obtained when complex **1a** was heated at 95—100 °C with 3—4 equiv. of a secondary alcohol (Pr^iOH) in the presence of 1 equiv. of pyridine.[21—24]

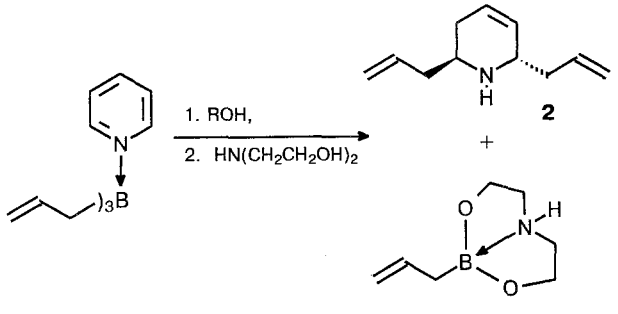
After the process was completed, the reaction mixture was treated with 10 % NaOH (1.2—1.5 equiv. of alkali per 1 equiv. of triallylborane used). Since all



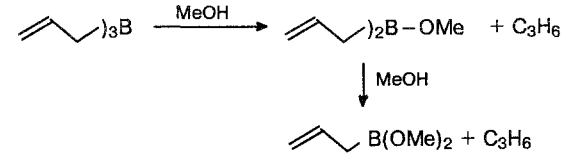
i. 1. ROH (or H_2O, Et_2NH), 20—100 °C,
2. NaOH (MEA or TEA).

MEA = $H_2NCH_2CH_2OH$,
TEA = $N(CH_2CH_2OH)_3$

boron compounds (allylboronic and diallylborinic acids) form borates of $[AllB(OH)_3]Na$ type, they are transferred into the aqueous layer, and product **2** is extracted with ether and distilled *in vacuo*. Isolation of amine **2** from the reaction mixture can also be carried out using another method, namely, by coupling of boron compounds with mono-, di-, or triethanolamine followed by extraction of amine **2** with petroleum ether or by distillation *in vacuo*. Oxidation with hydrogen peroxide in an alkali medium or workup of the mixture with ethereal or aqueous HCl are also efficient methods, but they are less convenient experimentally.



The reductive *trans*-diallylation of pyridine and its derivatives (see below) can be carried out in any solvent, which does not react with triallylborane (ether, THF, benzene, hexane, chloroform, CCl_4, excess pyridine, *etc.*) or without any solvent, which is the most convenient approach. Not less than two equiv. of an alcohol, water, or amine should be used in the reaction. The optimal amount of an alcohol is probably 4 equiv., since the latter is partially consumed in a side process, the protolytic decomposition of the B—C bonds in triallylborane.[1,2]



In the presence of the majority of alcohols and diols studied, the reductive diallylation is completed within 2—4 h, and the yield of **2** is 40—70 %. The best result (92 %) was obtained by heating complex **1a** with 4 equiv. of 2-propanol at 90—100 °C. However, the reaction with this alcohol proceeds 1.5—2 times more slowly than with ethanol and methanol.[21—24,35]

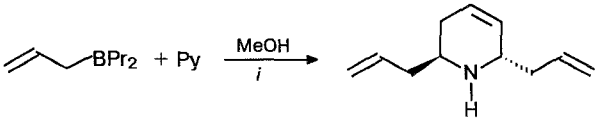
When excess pyridine is used in the reaction, the protolytic decomposition of triallylborane is suppressed, since the equilibrium $All_3B \cdot Py \rightleftharpoons All_3B + Py$ is shifted to the left and the yield of **2** increases. Refluxing (98 °C, 2 h) a mixture of triallylborane, pyridine, and Pr^iOH in the ratio of 1 : 2 : 4 resulted in amine **2** in 97 % yield (Table 2, entry 23), and when the ratio of the components was 1 : 1 : 4, the yield of the amine was 70 % (entries 18—20).

In order to realize the chiral variant of reductive *trans*-2,6-diallylation of pyridine, we carried out a series of reactions in the presence of chiral alcohols, (−)-menthol and 1,4:3,6-dianhydro-*D*-mannitol (Table 2). However, the optical purity of the diallylated product **2** obtained by this method was very low (*ee* < 20 %).

The reaction of pyridine complex **1a** with (−)-menthol (3 equiv.) was carried out at a high pressure (10^4 atm., 24—68 h) and at room temperature. In this case, the yield of amine **2** was 60—65 %. It is interesting to note that the content of the *cis*-isomer in the product increased to 4 % (0.9 % at atmospheric pressure).

trans-2,6-Diallyl-1,2,5,6-tetrahydropyridine **2** obtained in various experiments contained 1—2 % of the *cis*-isomer. In some experiments, in which Bu^tOH (4 equiv., 95—100 °C) was used, the content of the *cis*-isomer reached 9—10 %, and it was 6 % in the experiments with water. This admixture can easily be separated chromatographically by passing hexane solution through a column with a small amount of SiO_2 (when its content in the mixture is 1—2 %) or by distillation using a column (20 theoretical plates).

Compound **2** was also obtained in a 40 % yield by heating pyridine with allyl(dipropyl)borane (1 : 1) in the presence of 4 equiv. of methanol in ether (45 °C, 4 h).

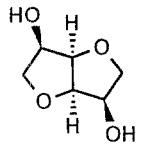


i. 45 °C, 4 h

Table 2. Effect of reaction conditions on the yield of *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine **2**[21,22,24,35]

Entry	ROH (R_2NH)	All_3B : Py : ROH	Solvent	*T*/°C	*t*/h	Yield (%)	Admixture of *cis*-isomer **2c** (%)
1	MeOH	1 : 1 : 1	Ether	40	2	24	—
2	MeOH	1 : 1 : 2	Ether	40	2	35	1.2
3	MeOH	1 : 1 : 4	Ether	40—45	2—6	34—52	1—2
4	MeOH	1 : 1 : 4	Ether	40	20	56	—
5	MeOH	1 : 1 : 4	THF	20	96	57	0.8
6	MeOH	1 : 2 : 4	Ether	45	4	57—63	1—2
7	MeOH	1 : 2 : 4	Benzene	80	4	43	1.1
8	MeOH	1 : 4 : 4	Ether	45	6	75	1.6
9	MeOH	1 : 7 : 4	—	95	1.5	94	1
10	MeOH[a]	1 : 1 : 2	—	20	350	52	1.4
11	MeOH[a]	1 : 3 : 5	Ether	40	4	42	—
12	MeOH[b]	1 : 1 : 4	Ether	45	2	40	0.9
13	EtOH	1 : 1 : 1	Ether	40	2	24	1.3
14	EtOH	1 : 1 : 4	Ether	45	3	50	1.8
15	EtOH	1 : 1 : 4	—	85	4	53	2.1
16	EtOH	1 : 2 : 4	Ether	45	4	60	1.4
17	Pr^iOH	1 : 1 : 4	—	43	2	49	1.4
18	Pr^iOH	1 : 1 : 4	—	98	2	63	—
19	Pr^iOH	1 : 1 : 4	—	98	8	68	1.5
20	Pr^iOH	1 : 1 : 4	—	98	15	70	—
21	Pr^iOH	1 : 1.5 : 4	Ether	50	17	87	1.3
22	Pr^iOH	1 : 2 : 4	—	43	2	53	—
23	Pr^iOH	1 : 2 : 4	—	98	2	97	1.5
24	Pr^iOH	1 : 3 : 4	—	43	2	75	—
25	Bu^tOH	1 : 1 : 4	—	99	6	85	9.8
26	Bu^tOH	1 : 1 : 4	—	99	8	92	10
27	$(CH_2OH)_2$	1 : 1 : 2	—	90	6	36	—
28	Et_2NH	1 : 1 : 4	—	70	2	21	—
29	Et_2NH	1 : 1 : 4	—	70	15	23	—
30	Et_2NH	1 : 1 : 4	—	70	25	45	—
31	H_2O	1 : 2 : 3	THF	40	8	43	—
32	H_2O	1 : 1 : 3	—	50	3	76	5.9
33	10% NaOH[b]	1 : 1 : 3	—	45	2	5	—
34	1,4:3,6-Dianhydro-mannitol[d]	1 : 1 : 4	Hexane	55	5	70	1.5
35	(—)-Menthol[e]	1 : 1.2 : 3	Ether	45	10	66	0.9
36	(—)-Menthol[f]	1 : 1 : 3	—	20	68	61—63	4

[a] Allyl(dipropyl)borane was used instead of triallylborane (the yield of **2** is given with respect to $AllBPr_2$).
[b] A mixture of triallylborane, $AllB(OMe)_2$, pyridine, and alcohol in a ratio of 1 : 1 : 1 : 4 was used in the reaction.
[c] MeOH (3.5 mol) was used in the reaction.
[d] 1,4:3,6-Dianhydromannitol.



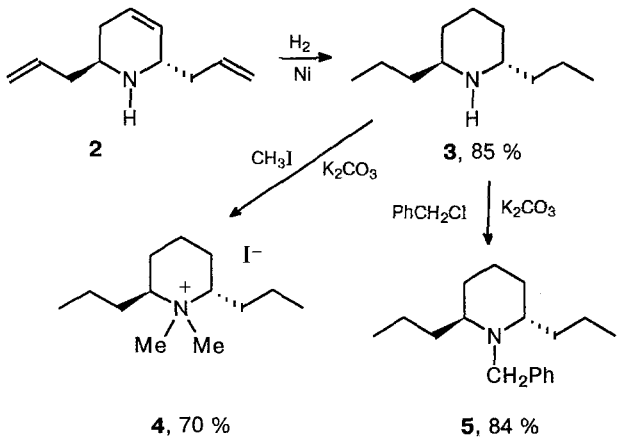
The amine **2** obtained had $[\alpha]_D^{23}$ +4.38° (*c* 10.28; CH_2Cl_2).
[e] The amine **2** obtained had $[\alpha]_D^{23}$ −7.30° (*c* 10.00; CH_2Cl_2).
[f] The reaction was carried out at a pressure of 10^4 atm; the amine **2** obtained had $[\alpha]_D^{23}$ −6.85° (*c* 3.07; CH_2Cl_2).

The *trans*-stereochemistry of diallylic compound **2** was established using NMR spectra of its derivatives.

Hydrogenation of triene amine **2** in acetic acid over Raney nickel (100 atm. H_2, 90—100 °C, 6 h) afforded *trans*-2,6-dipropylpiperidine **3** (85 %).

The *trans*-configuration of the propyl groups in 2,6-dipropyl derivative **3** (and, therefore, allyl groups in amine **2**) was established on the basis of analysis of the ^1H and ^{13}C NMR spectra of *N,N*-dimethyl salt **4** and *N*-benzyl derivative **5**. Compounds **4** and **5** were synthe-

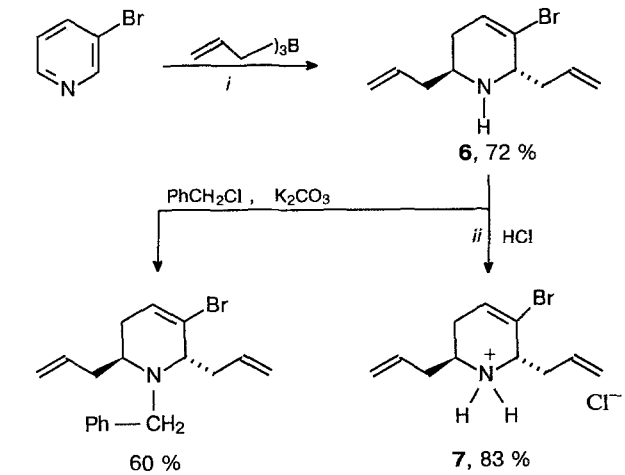
sized by the reaction of **3** with methyl iodide[32] and benzyl chloride, respectively, in the presence of K_2CO_3.



Both methyl groups in salt **4** are equivalent, which is confirmed by the presence of a distinct singlet in the ^1H NMR spectrum (δ 3.38) and one signal in the ^{13}C NMR spectrum (δ 49.02). The methylene protons ($PhCH_2$) of *N*-benzyl derivative **5** appear in the ^1H NMR spectrum as an AB-system with a quartet center at δ 3.65 (δ_A 3.60 and δ_B 3.70, J = 14.04 Hz), which proves their chemical non-equivalence (diastereotopy). These data unambiguously suggest a *trans*-configuration of the propyl groups with respect to the piperidine ring in compounds **3**—**5** and prove the *trans*-stereochemistry of 2,6-diallyl compound **2**.

^1H NMR spectra of similar type were observed previously for the *N,N*-dimethyl salt of *trans*-2,6-dimethylpiperidine[38] and the *N*-benzyl derivative of the latter.[39]

The reductive *trans*-diallylation of 3-bromopyridine with triallylborane in the presence of 4 equiv. of methanol (70 °C, 5 h) afforded compound **6**, in which the bromine atom is linked to the vinyl carbon.[21—24]



i. 4 MeOH, 75 °C, 5 h, *ii*. ether

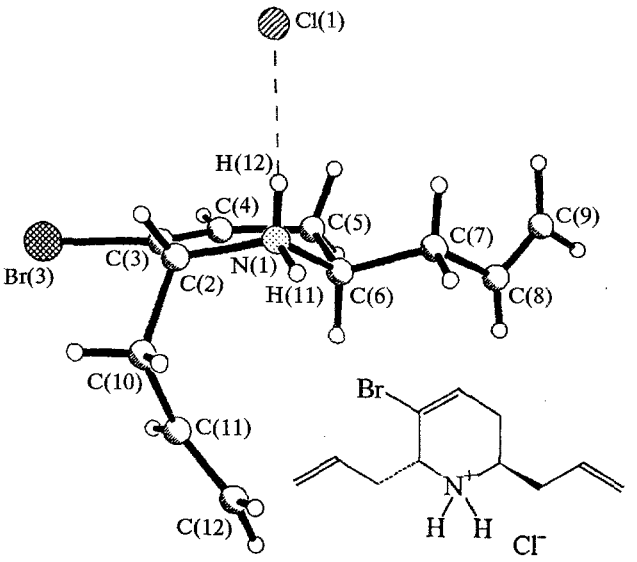
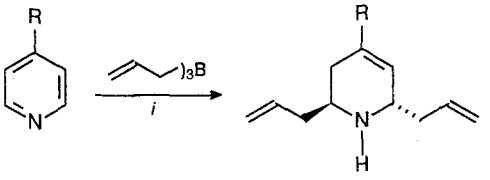


Fig. 1. Structure of hydrochloride **7** (according to X-ray diffraction data).

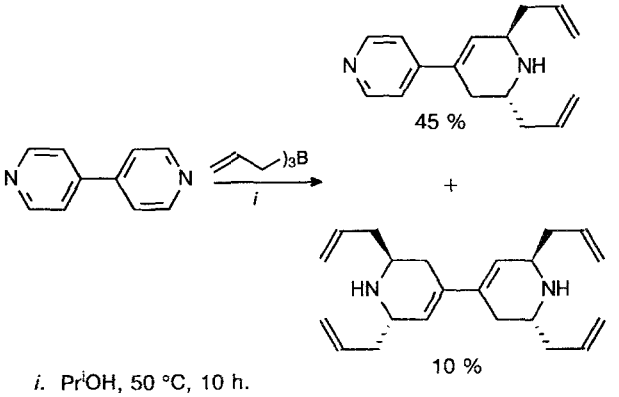
The structure of hydrochloride **7** was confirmed by X-ray diffraction analysis.[24] The bond distances and bond angles in the molecule of this compound are usual; some of the values are given in Fig. 1. As can be seen from the Figure, the allyl groups are in the *trans*-position relative to the cycle.

The similar one-pot methodology was used for transformation of 4-methyl- and 4-benzylpyridine into the corresponding diallylated products.[21,22,35]



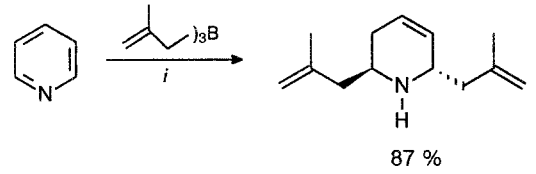
i. 3 MeOH, 95 °C, 5 h. R = Me, 64 % (5 % *cis*-)
R = $PhCH_2$, 66 % (4 % *cis*-)

The reaction of triallylborane with 4,4′-dipyridyl (1 : 1) in the presence of 2-propanol afforded a mixture of di- and tetraallyl compounds.[21,22,35]



i. Pr^iOH, 50 °C, 10 h.

Trimethallylborane also reacts readily with pyridine in the presence of 2-propanol to give a dimethallyl compound in a 87 % yield.



87 %

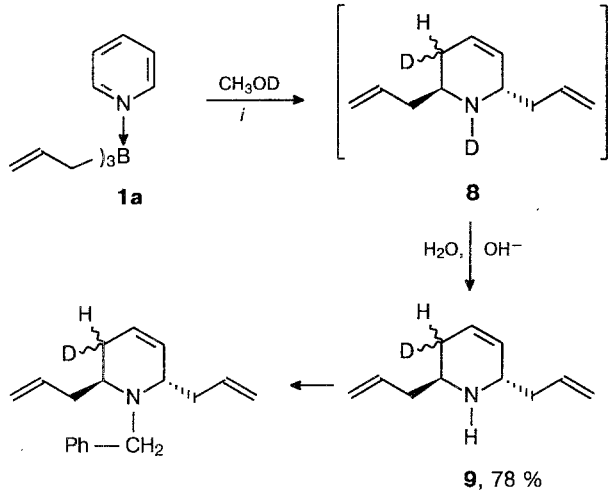
i. 4 PrⁱOH, 95 °C, 4 h.

All these data allow us to conclude that *the reductive trans-2,6-diallylation of pyridines with allylboranes is a general stereospecific reaction*, which affords useful and interesting products with several double bonds and nitrogen-containing groups. Two new carbon-carbon bonds are formed during the process.

Mechanism of reductive *trans*-2,6-diallylation of pyridines

In order to elucidate the mechanism of the reductive *trans*-2,6-diallylation of pyridines, we carried out a series of reactions with the use of deuterated compounds and the reaction of tricrotylborane with pyridine.

Consecutive treatment of complex **1a** with deuteromethanol (46 °C, 4 h) and 10 % NaOH afforded *trans*-2,6-diallyl-5-deutero-1,2,5,6-tetrahydropyridine **9** in 78 % yield.[21,22,24,35]



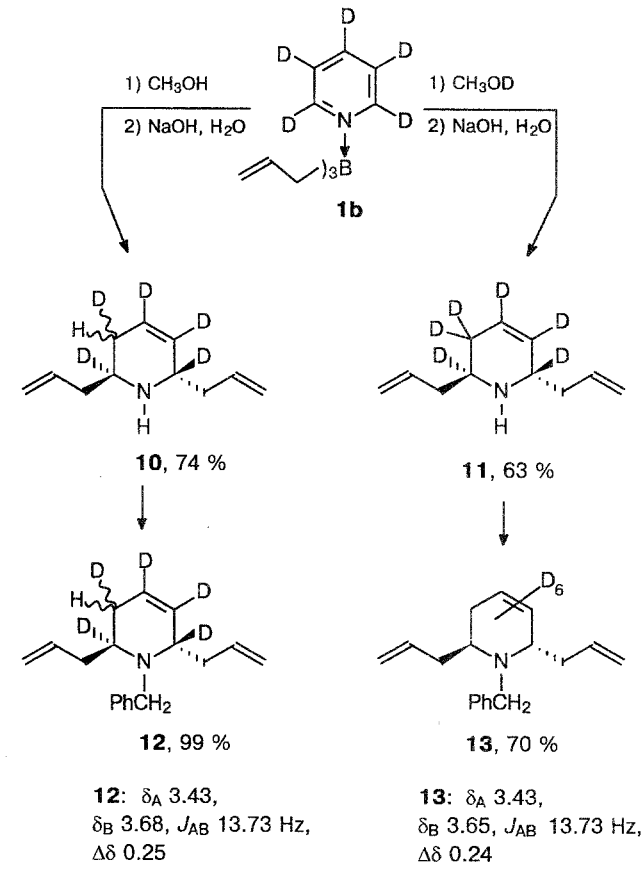
i. 46 °C, 4 h.

There is no doubt that 1,5-dideutero compound **8** is a primary product. It transforms into monodeutero-compound **9** on treatment with an alkaline solution (replacement of N—D by N—H).

Therefore, the proton (deuterium) from the alcohol is localized at position 5 of the tetrahydropyridine ring.

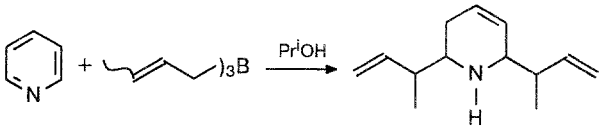
We obtained an additional confirmation of this fact by studying the reductive diallylation of pentadeuteropyridine (complex **1b**) with triallylborane under the action of methanol and deuteromethanol (4 equiv.) (Scheme 3).

Scheme 3



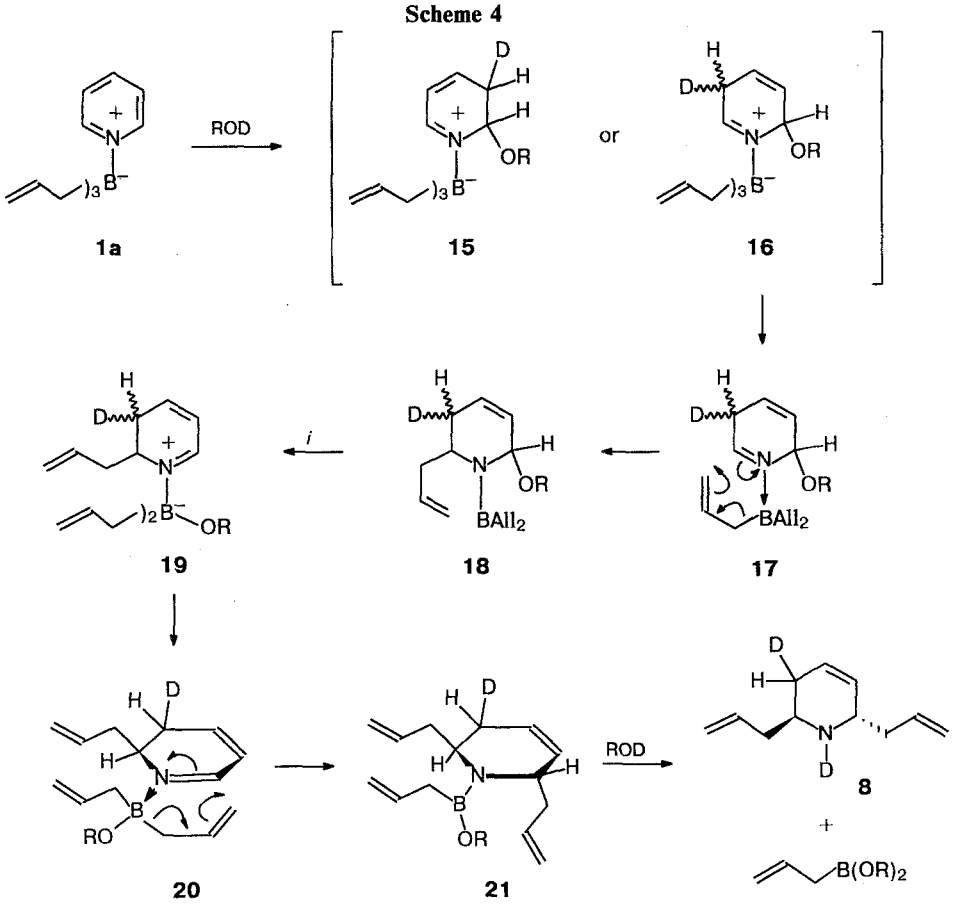
As a result, pentadeutero compound **10** (74 %) containing one hydrogen atom at position 5 and *trans*-2,6-diallyl-2,3,4,5,5,6-hexadeutero-1,2,5,6-tetrahydropyridine **11** (63 %) were synthesized. Starting from **10** and **11**, the corresponding *N*-benzyl derivatives **12** (99 %) and **13** (70 %) were obtained.[21,22,24,35]

Using the reaction of tricrotylborane with pyridine as an example, we established that *both steps of reductive diallylation proceed with full rearrangement of the allylic moiety*. Heating the mixture of tricrotylborane with pyridine (1 : 1) in the presence of 4 equiv. of 2-propanol (97 °C, 10 h) resulted in the formation of 2,6-bis-(1-methylallyl)-1,2,5,6-tetrahydropyridine (**14**) in 62 % yield.[21,22,35]



14, 62 %
diastereomers 80 : 19 : 1

Scheme 4



i. β-Elimination.

The product **14** obtained is a mixture of diastereomers in a 80 : 19 : 1 ratio (GLC). According to NMR spectroscopic data, it does not contain methyl groups at the double bond (crotyl groups). Only the signals of an intra-ring and two terminal double bonds are observed in the ^1H and ^{13}C NMR spectra, along with a multiplet (^1H NMR) of CH_3 groups in the 0.95—1.05 ppm region (^{13}C NMR: 16.50, 16.86, and 17.54 ppm); the ^{13}C NMR spectrum contains no signals at 18—28 ppm (CH_3—C=).

Since complex **1a** does not undergo any transformations with prolonged (20 h) heating at 160 °C, it is quite obvious that alcohols, water, or R_2NH (Table 2) play a decisive role in reductive *trans*-diallylation of pyridines with allylboranes. However, the first step of this complex reaction is still unclear.

Similarly to pyridine adducts with trialkylboranes $Py \cdot BR_3$ (R = H, Me, Et),[40] the nitrogen atom in the complexes of triallyl-, trimethallyl-, tricrotyl-, and allyl(dialkyl)boranes with pyridine and its derivatives is positively charged. Owing to this charge, the nucleophilic attack at the α-position of the cycle should proceed readily.

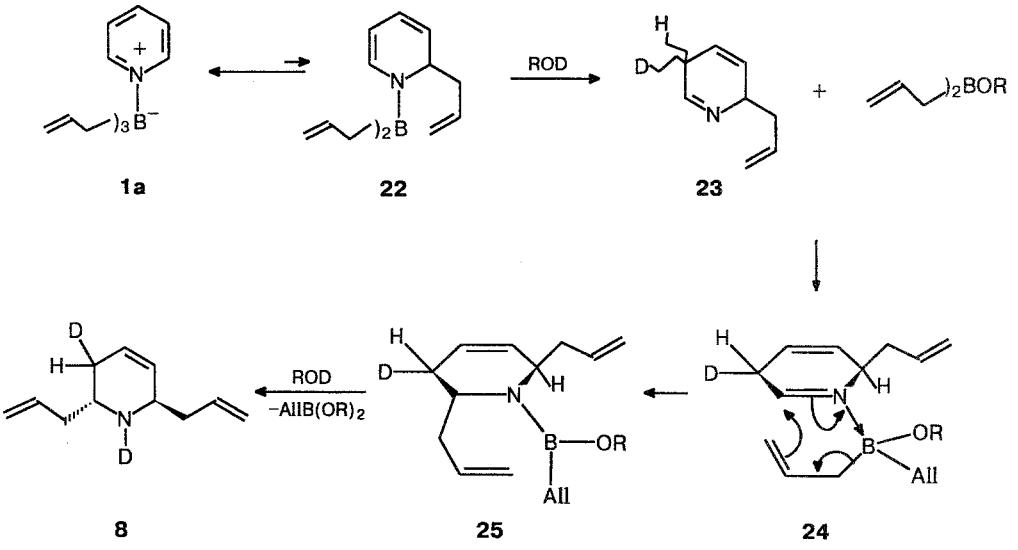
It is well known that pyridinium and quinolinium salts, in which nitrogen is positively charged, readily add alkoxide ions to give 2-alkoxy-1,2-dihydropyridines and 2-alkoxy-1,2-dihydroquinolines.[41—44] For example, the α-addition of the hydroxide ion is the key step of the well known oxidation of pyridinium salts into 2-pyridones on treatment with an alkali solution of potassium ferricyanide.[41—43,45]

Scheme 4 represents a possible mechanism of reductive *trans*-diallylation.

One may assume that a molecule of an alcohol initially attacks the pyridinium cycle of complex **1** with the formation of a product of nucleophilic addition, **15** or **16**. Both these intermediates contain a localized C=N bond, which immediately undergoes allylboration through a six-membered transition state **17**. As a result, allylborane **18** with a covalent B—N bond and an electronegative OR group at position 2 with respect to the boron atom is formed. This compound is unstable and undergoes β-elimination to afford new imine complex **19**.

The next step, allylboration of the C=N bond, *proceeds stereoselectively*. The second allylboron fragment is added in a *trans*-fashion with respect to the allyl group in the ring (through transition state **20**). The B—N bond in aminoborane **21** formed is immediately cleaved with the alcohol used in excess (2—4 equiv.). As a result, the final products of the reaction, *trans*-2,6-diallyl-1,2,5,6-

Scheme 5



tetrahydropyridine **8** and allylboronic ester, are formed. The latter is separated from compound **8** by treatment with an alkaline solution, since it forms a borate complex $[AllB(OH)_3]Na$, which is transferred into the aqueous layer.

Scheme 4 represents a possible mechanism of the reaction with the participation of intermediate **16**, the product of 1,4-addition of an alcohol to the heterocycle (at positions 2 and 5 of the ring of complex **1a**). The scheme will not change essentially if adduct **15**, the product of 1,2-addition of an alcohol to compound **1**, is formed in the first step.

Another possible mechanism involves the participation of alcohol but not in the first step of the process (Scheme 5).

One may assume that reversible intramolecular allylboronation of the C=N double bond in pyridine occurs, the **1a** ⇌ **22** equilibrium being strongly shifted to the left, and at every instant only a very small amount of compound **22** is present in the mixture. The dramatic role of the alcohol consists in the cleavage of the covalent B—N bond in aminoborane **22**. The cleavage occurs *via* allylic type rearrangement resulting in the formation of azomethine **23** and diallylborinic acid.

Further, fast stereospecific allylboration of the double bond of azomethine **23** proceeds, the second allyl group being added in a *trans*-fashion relative to the first one through the transition state **24**. Aminoborane **25** is deboronated with the alcohol to afford allylboronic ester and the final product **8**.

trans→*cis*-Isomerization of 2,6-diallyl-1,2,5,6-tetrahydropyridine[21,22,24,25,27,35]

Having in hands *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine **2** in practically any amount (since pyridine and triallylborane are readily available compounds), we naturally wished to obtain its *cis*-isomer (**2c**), as well as *cis*-2,6-dipropylpiperidine (**30**). Fortunately, this problem was solved very easily.

Our brief studies resulted in finding an original method for an almost quantitative isomerization of *trans*-compound **2** into *cis*-isomer **2c**. The method involves heating of **2** with an equivalent amount of triallylborane at 125—130 °C (Table 3) or allyl(dipropyl)borane at 140—150 °C for 5—10 h (Schemes 6 and 7).[21,22,24,25,27,35]

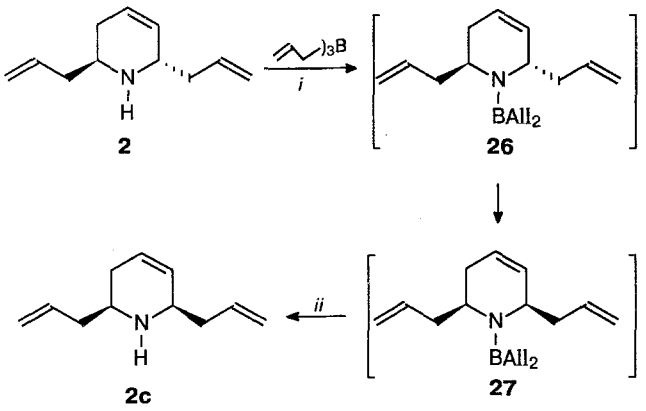
At the first step of the reaction of compound **2** with triallylborane, one B—C bond in triallylborane is cleaved,[1,2] one mol of propene is liberated, and aminoborane **26** is formed. Further heating of the latter resulted in its transformation into isomeric compound **27**, which was not isolated, but was immediately subjected to deboronation by the action of methanol (0—20 °C, cleavage of the B—N bond)[1,2] and 10 % NaOH (1.2 equiv.). *cis*-2,6-Diallyl-1,2,5,6-tetrahydropyridine (**2c**) obtained by this procedure contains 1.5—2 % of *trans*-isomer **2** as an admixture. The latter is easily separated by chromatography on SiO_2. The yield of pure **2c** exceeded 80 % (Table 3).

Furthermore, we found that not only tetraallyl compound **26** but also its *B,B*-dipropyl analog (**28**) under-

Table 3. Isomerization of *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine **2** into *cis*-isomer **2c** by heating with triallylborane[35]

T/°C	Heating time /h	Yield of **2c** (%)	Admixture of **2** (in **2c**) (%)
100—120	2	80	22
120—130	2.5	81	9
120—130	4	84	4
125—130	5	85	2.5
125—130	15	89	1.5

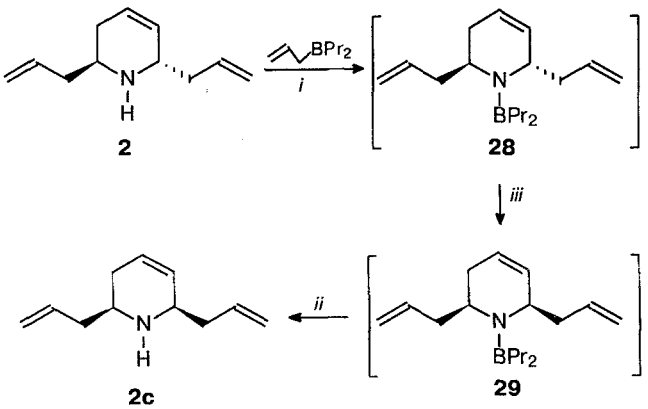
Scheme 6



i. 80—125 °C, 5—10 h, – C_3H_6 ;

ii. 1) MeOH, 0—20 °C, 2) NaOH .

Scheme 7



i. 100 °C, – C_3H_6 .

ii. $N(CH_2CH_2OH)_3$, *iii.* 145 °C, 5 h.

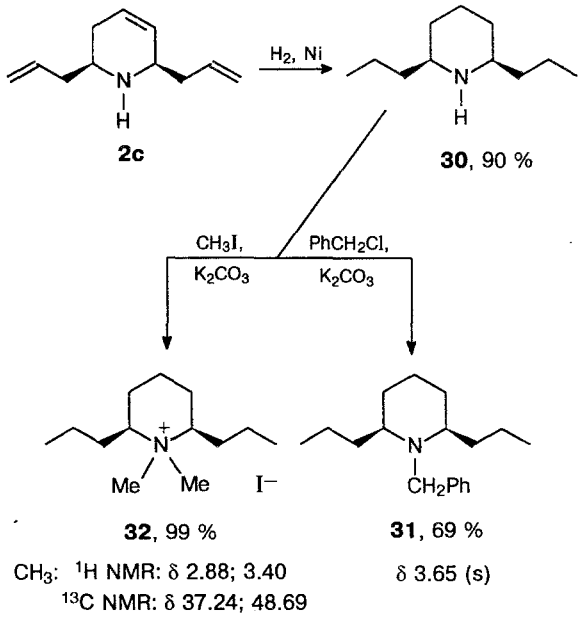
goes *trans*-to-*cis*-isomerization. However, this reaction proceeds at higher temperatures (140—150 °C, 5 h). Deboronation of *cis*-aminoborane **29** obtained was carried out using triethanolamine. *cis*-Compound **2c** prepared by this procedure contained less than 5 % of the *trans*-isomer (**2**).

The stereochemistry of *cis*-isomer **2c** was established by an NMR study of some derivatives of the products of its complete hydrogenation.

The catalytic hydrogenation of compound **2c** over Raney nickel in acetic acid (100 °C, 100 atm. of H_2) gave *cis*-2,6-dipropylpiperidine **30** (90 %), which was further transformed to hydrochloride **30** · HCl (89 %), *N*-benzyl derivative **31** (69 %), and *N,N*-dimethyl salt **32** (99 %) (Scheme 8).

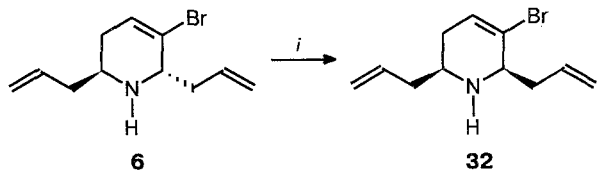
As in *cis*-1,1,2,6-tetramethylpiperidinium iodide,[38] the methyl groups in salt **32** are nonequivalent and gave

Scheme 8



two signals at δ 37.24 and 48.69 in the ^{13}C NMR spectrum. The chemically equivalent (enantiotopic) benzyl protons (CH_2Ph) of compound **31** appear in the ^1H NMR spectrum as a clear singlet at δ 3.65. A similar picture was observed in the case of 1-benzyl-*cis*-2,6-dimethylpiperidine.[39]

As in the case of compound **2**, heating 3-bromo-*trans*-2,6-diallyl-1,2,5,6-tetrahydropyridine **6** with triallylborane (130 °C) followed by deboronation of the aminoborane obtained (of the type **27**) resulted in its transformation into *cis*-isomer **32** (yield 75 %).



i. 1))3B, 130 °C, 2) MeOH, 3) H_2O, OH^-

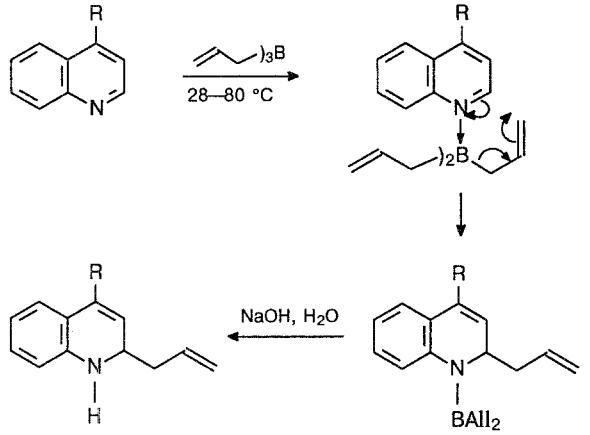
In this case, isomerization was not completed even after heating for 6 h, and amine **32** obtained contained approximately 6 % of *trans*-isomer **6**. The latter was separated by chromatography on SiO_2.

Hence, the present study confirmed that the use of a prochiral benzyl probe and *N,N*-dimethylquaternization makes the determination of the *cis-trans*-stereochemistry of 2,6-disubstituted piperidines surprisingly simple.

Moreover, we have found that ^1H NMR spectroscopy can be successfully used for determining the spatial structure of many 2,6-disubstituted 1,2,5,6-tetrahydropyridines, especially in cases when both isomers are available.[24,35]

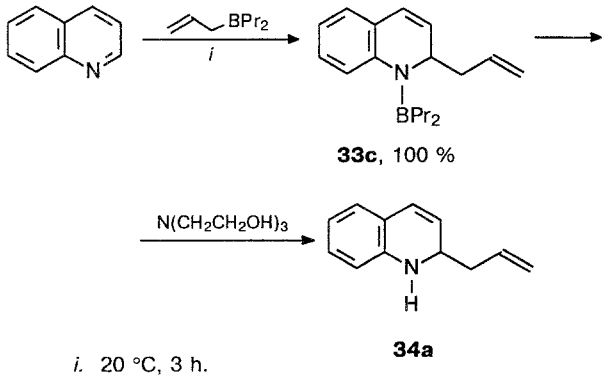
Reductive monoallylation of quinolines and phenanthridine[21,22,26,35]

Quinoline, 4-methyl- and 3-bromoquinoline, and phenanthridine react with triallylborane at room temperature to give aminoboranes **33** (**33a**, δ ^{11}B 46.3), whose deboronation results in the corresponding α-allylated heterocycles **34a—c** and **35**.[21,22,26,35]



Two allylboron fragments of the molecule of triallylborane participate in the reaction, and when the ratio quinoline : All_3B is 2 : 1 (20→80 °C, 1 h), product **34a** is formed in 78 % yield (after hydrolysis of the diaminoborane formed).

Amine **34a** was also synthesized using allyl(dipropyl)borane as the allylborating agent.[35]

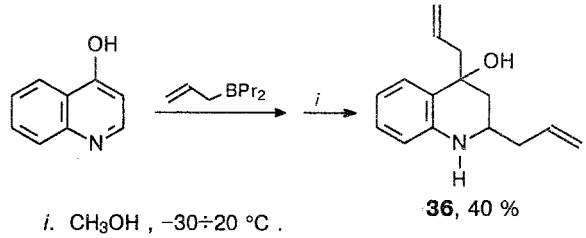


The aminoborane **33c** formed initially was isolated in pure form (b.p. 112 °C (1 Torr), n_D^{20} 1.5376, δ ^{11}B 55.9). Triethanolamine was used for its deboronation. Oxidation of **33** with hydrogen peroxide in an alkali medium also affords amine **34a**, but its yield is only 46 %, since the latter readily undergoes oxidation.

It is noteworthy that compounds **34a** and **35** were obtained previously by the action of allylmagnesium halides on quinoline[46] and phenanthridine,[47] respectively. According to the data obtained by these authors, amine **34a** is converted into 2-propylquinoline by hydrogen migration even during workup of the reaction mixture, and compound **35** is unstable in the air.

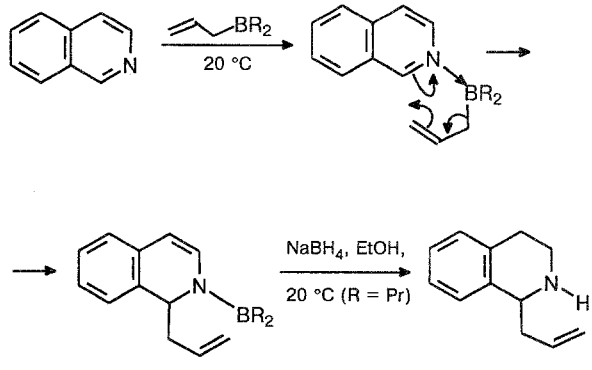
We found that monoallylated compounds **34a** and **35** are stable in an inert atmosphere (nitrogen or argon) up to 100 °C. Compound **34a** isomerizes into 2-propylquinoline at 170 °C in two hours.

The reaction of allyl(dipropyl)borane with 4-hydroxyquinoline (2 : 1, 20 °C) followed by workup with methanol at −30 °C afforded 2,4-diallyl-4-hydroxy-1,2,3,4-tetrahydroquinoline **36** (40 %). The mutual arrangement of allyl groups in compound **36** has not been determined yet.[21,22,35]



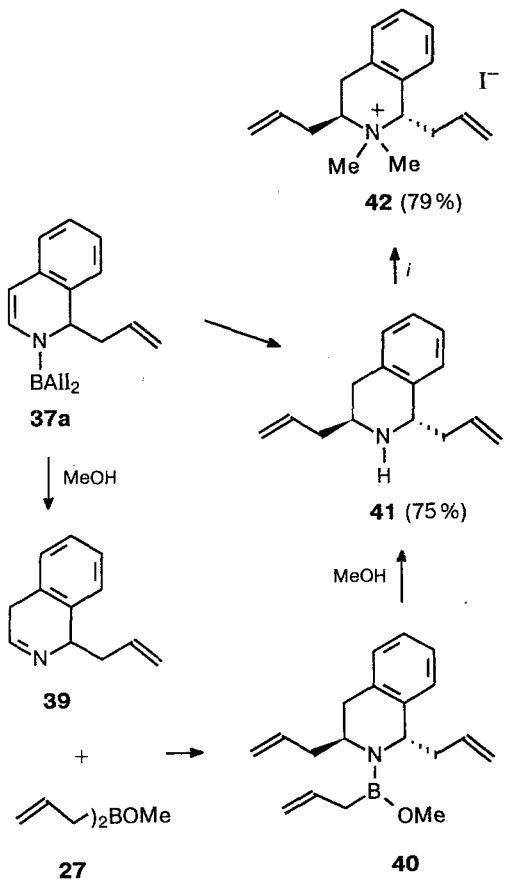
Isoquinoline: reductive mono- and *trans*-1,3-diallylation[21,22,28,35]

Isoquinoline reacts with triallylborane and allyl(dipropyl)borane under mild conditions (0—20 °C) to give the corresponding allylated aminoboranes **37a** (δ ^{11}B 47.7) and **37b** (δ ^{11}B 51.6). These reactions proceed as "thermal addition" of the B—allyl fragment to the C(1)=N double bond, which is localized in isoquinoline to a "larger extent" than in pyridine.[21,28,35]



The products of allylboration of compounds **37** are enaminoboranes of specific type, *i.e.*, compounds with a system of allylic bonds (C=C—N—B). The protolytic cleavage of these compounds proceeds through an allylic type rearrangement and affords imine **39**, whose future fate is determined by the nature of radicals at the boron atom and by the conditions of its subsequent treatment (Scheme 9).

Scheme 9



i. MeI, K_2CO_3, EtOH, 80 °C

The reduction of dipropyl derivative **37b** with $NaBH_4$ in ethanol at room temperature afforded 1-allyl-1,2,3,4-tetrahydroisoquinoline (**38**) in 84 % yield.

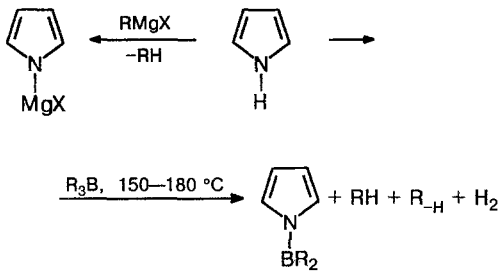
On the other hand, *trans*-1,3-diallyl-1,2,3,4-tetrahydroisoquinoline **41** was synthesized in 75 % yield by treatment of amino(diallylborane) **37a** with methanol (3 equiv., 20 °C, 2 h). The possible mechanism of its formation is presented in the lower part of Scheme 9.

The cleavage of compound **37a** with methanol affords imine **39** and methoxy(diallyl)borane. The latter immediately reacts with imine **39** with the formation of aminoborane **40**, the allylboration proceeding in a *trans*-fashion relative to the allyl group in the cycle. Methylation of **41** gave *N,N*-dimethyl salt **42**.

Pyrrole and indole: reductive mono- and diallylation

It has long been known that organolithium and organomagnesium compounds react with pyrrole (pK_a 17.5) to give the corresponding *N*-derivatives[48] (Scheme 10).

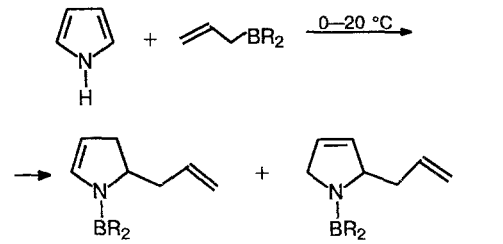
Scheme 10



Köster and Bellut[49,50] found that the reactions of triethyl- and tripropylborane with pyrrole proceed at 150—180 °C to afford the corresponding *N*-dialkylborylpyrroles.

Unlike alkylboranes, allylboranes can add to pyrrole. We found that allyl(dipropyl)borane and triallylborane react with pyrrole at 20 °C with the formation of a mixture of two addition products **43** and **44**, which differ in the position of the double bond in the cycle[21,22,29] (Scheme 11).

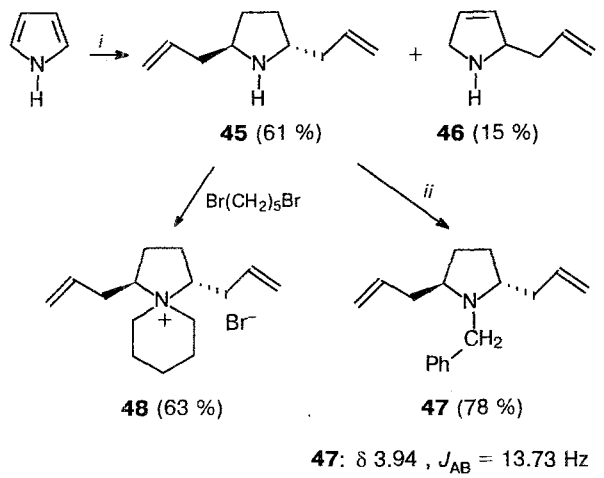
Scheme 11



43a: R = Pr (78%) **44a**: R = Pr (22%)
43b: R = All (70%) **44b**: R = All (30%)

Treatment of the products of the reaction of pyrrole with triallylborane (a mixture of compounds **43b** and **44b**) with methanol (3 equiv., from −30 to 20 °C, 1 h) followed by treatment with 10 % NaOH (1.2 equiv.) afforded a mixture of *trans*-2,5-diallylpyrrolidine **45** and 2-allyl-3-pyrroline **46**, which were isolated by distillation in 61 and 15 % yields, respectively (Scheme 12).

Scheme 12



i. 1. All_3B, 0→20 °C, 1 h,
2. MeOH (3 eqviv., −30 °→20 °C), 3. H_2O, OH^-, 10—20 °C.
ii. $PhCH_2Cl$, K_2CO_3 , EtOH, 80 °C.

The *trans*-orientation of allyl groups in compound **45** was confirmed by NMR spectroscopy using a prochiral benzyl probe. Heating compound **45** with benzyl chloride and K_2CO_3 in ethanol (80 °C) afforded *N*-benzyl derivative **47** (78 %). As in the case of 1-benzyl-*trans*-2,5-dimethylpyrrolidine,[35] the benzyl methylene protons in **47** are diastereotopic and appear in the ^1H NMR spectrum as an AB-quartet at 3.94 ppm (J 13.73 Hz).

The possible mechanism of mono- and diallylation of pyrrole is given in Scheme 13.

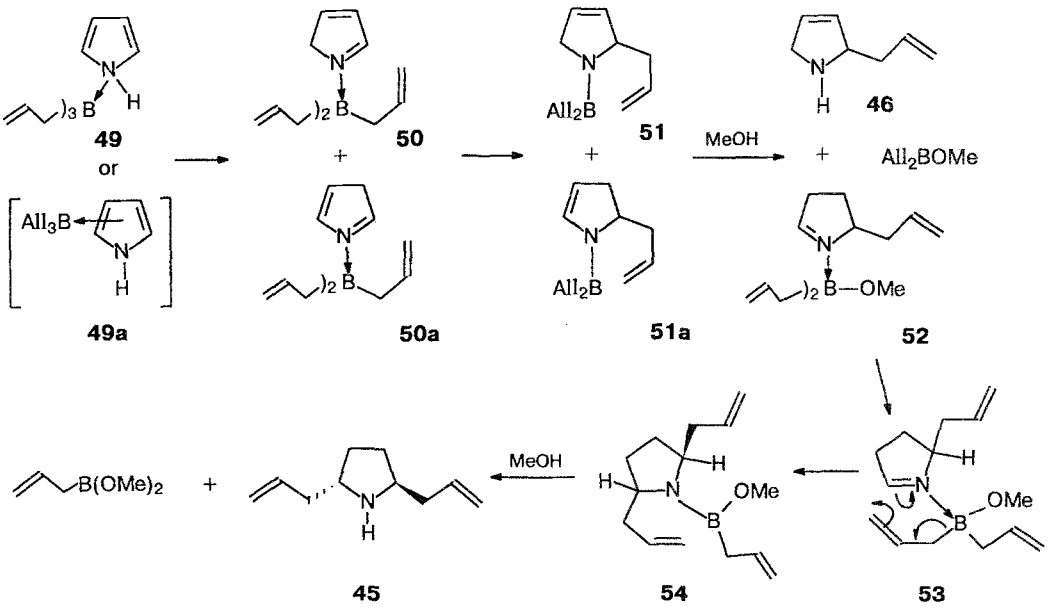
We propose that the first step of the reaction of pyrrole with triallylborane is the formation of N→B complex **49** (or π-complex **49a**). This complex further undergoes isomerization by means of 1,3- or 1,5-migration of hydrogen from the nitrogen atom to C-2 and C-3 to afford two imine adducts **50** and **50a**, in which allylboration of the C=N bonds occurs quickly (through a six-membered cyclic transition state) and gives monoallylated aminoborane **51** and enaminoborane **51a**. Both of them are immediately cleaved with the alcohol to give 2-allyl-3-pyrroline **46** (along with All_2BOMe) and new imine complex **52**. The latter is transformed into aminoborane **54** through six-membered transition state **53**, the addition of the second allylboron fragment proceeding in a *trans-fashion relative to the allyl group already present in the ring.* Subsequent alcoholysis of aminoborane **54** (cleavage of the B—N bond) gives diallylated reaction product **45** and dimethoxy(allyl)borane.

Both steps of the reductive *trans*-diallylation of pyrrole proceed with allyl rearrangement. This fact is unambiguously confirmed by the reaction of tris(3,3-dimethylallyl)borane (triprenylborane) with pyrrole. Subsequent treatment of pyrrole with triprenylborane, methanol (40 °C), and an alkaline solution resulted in two interesting hindered amines **55** and **56** in 65 and 20 % yields[30] (Scheme 14).

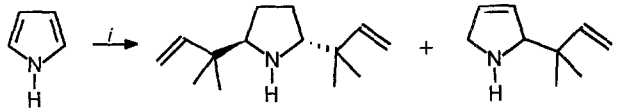
Using two allylborating agents with different structures, one can synthesize non-symmetrical diallylated pyrrolidines. Thus, heterocyclic compound **57** was obtained in 65 % yield as a result of successive treatment of pyrrole with allyl(dipropyl)borane, triprenylborane, methanol, and triethanolamine (Scheme 15).

Similarly to *trans*-2,6-diallyl-1,2,5,6-tetrahydropyridines (see above), *trans*-2,5-diallylpyrrolidine **45** under-

Scheme 13



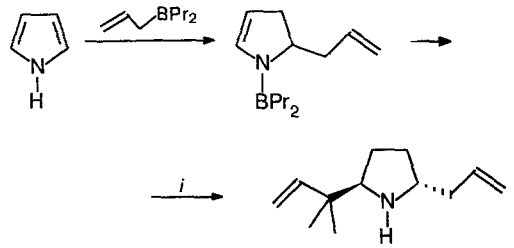
Scheme 14



55 (65 %) **56** (20 %)

i. 1. $(\sim)_3B$
2. MeOH, 40 °C, 3. H_2O, OH^-

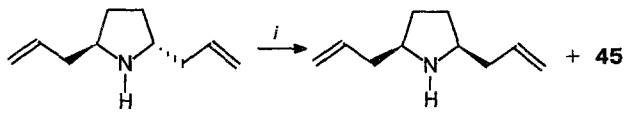
Scheme 15



57 (65 %)

i. 1. $(\sim)_3B$, MeOH, 20 °C
2. $N(CH_2CH_2OH)_3$

goes isomerization on heating with triallylborane to afford *cis*-2,5-diallylpyrrolidine **58**.

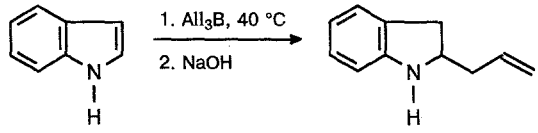


45 **58** (70 %) 30 %

i. 1. All_3B, 160 °C, 10 h, 2. NaOH

However, the isomerization of **45** into **58** is not complete even at 160 °C (10 h). The ratio of compounds **58** and **45** obtained after deboronation (3 : 1) is probably an equlibrium one.

Indole also adds triallylborane (40 °C, 3 h) with the formation (after deboronation with a NaOH solution) of 2-allylindoline **59** in 84 % yield.[29]

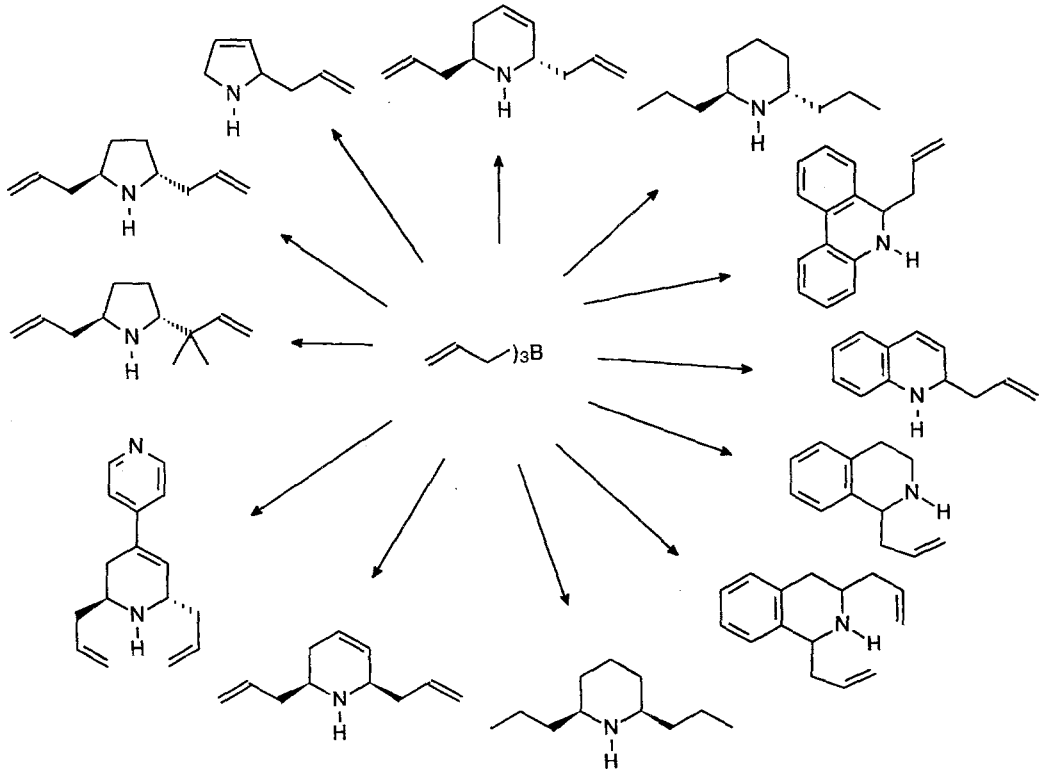


59, 84 %

Conclusions

The reactions presented above unite the chemistry of nitrogen-containing aromatic heterocycles and organobo-

Scheme 16



ron chemistry on a new basis. There is no doubt that these reactions and the new compounds prepared using these reactions will find wide application in organic synthesis.

Scheme 16 shows some compounds synthesized from triallylborane.

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