Synthesis and molecular structure of *trans*-2-allyl-6-phenyl-1,2,3,6-tetrahydropyridine hydrochloride

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When treated with triallylborane and MeOH, the product of the 1,2-addition of PhLi to pyridine transforms to *trans*-2-allyl-6-phenyl-1,2,3,6-tetrahydropyridine. The structure of its hydrochloride was established by X-ray structural analysis.

Key words: allylboronation, pyridine, 1,2-addition, phenyllithium, triallylborane, *trans*-2-allyl-6-phenyl-1,2,3,6-tetrahydropyridine, X-ray structural analysis.

Pyridine and its derivatives react with triallyl-,1-5 tricrotyl-,^{1,2,6} and trimetallylboranes¹ to form the corresponding trans-2,6-diallylated 1,2,3,6-tetrahydropyridines in 70-97 % yields. This new stereospecific reaction, which is called reductive trans-2,6-diallylation of pyridines, proceeds in the presence of alcohols, water, or amines at 20-100 °C and is not complicated by side processes. However, only symmetrically 2,6-disubstituted Δ^3 -piperideines can be obtained by this reaction. Therefore, we have recently developed⁷ a convenient general procedure for the synthesis of nonsymmetrical trans-2-allyl-6-alkyl(aryl)-1,2,3,6-tetrahydropyridines, which consists of treating pyridine successively with alkyl or aryllithium, triallylborane, and alcohol. The structures of the 2-allyl-6-alkyl- Δ^3 -piperideines obtained by this method were established by NMR spectroscopy (¹H-¹H COSY and 2D NOESY). The stereochemistry of their 6-phenyl analog was determined by X-ray structural analysis.

In this work, we discuss the results of X-ray structural analysis of *trans*-2-allyl-6-phenyl-1,2,3,6-tetrahydropyridine **2** prepared by 1,2-addition of phenyllithium to pyridine followed by *trans*-2-allylation of the enamine that forms with triallylborane in the presence of alcohol.

According to the data of GLC and NMR spectroscopy, amine 1 (94%) and 2-phenylpyridine (6%) are the nitrogen-containing products of this reaction. 2-Phenylpyridine ($pK_a \approx 6$) is readily separated from 1 ($pK_a \approx 10$) when the mixture is acidified with a calculated amount of hydrochloric acid (see Experimental).

The probable mechanism of the formation of heterocycles of type 1 was considered in Ref. 7.

* Deceased in 1995.



The overall view of molecule 2 is shown in Fig. 1. The bond lengths and bond angles are given in Table 1. The piperideine ring of the molecule adopts a distorted



Fig. 1. Overall view of molecule 2.

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d/Å	Bond	d/Å	Angle	ω/deg	Angle	ω/deg
1.503(2) 1.499(3) 1.519(3) 1.527(3) 1.494(3) 1.308(2) 1.513(3) 1.520(2)	$\begin{array}{c} C(7)-C(8)\\ C(8)-C(9)\\ C(10)-C(11)\\ C(10)-C(15)\\ C(11)-C(12)\\ C(12)-C(13)\\ C(13)-C(14)\\ C(14)-C(15) \end{array}$	1.488(3) 1.297(3) 1.394(3) 1.383(3) 1.387(3) 1.370(4) 1.383(3) 1.387(2)	$\begin{array}{c} C(2)-N(1)-C(6)\\ N(1)-C(2)-C(3)\\ N(1)-C(2)-C(7)\\ C(3)-C(2)-C(7)\\ C(2)-C(3)-C(4)\\ C(3)-C(4)-C(5)\\ C(4)-C(5)-C(6)\\ N(1)-C(6)-C(5)\\ N(1)-C(6)-C(6)\\ N(1)-C(6)\\ N(1)-C(6)-C(6)\\ N(1)-C(6)-C(6)\\ N(1)-C(6)-C($	114.5(1) 107.9(2) 108.5(1) 114.2(1) 111.4(1) 123.5(2) 124.6(2) 108.4(1)	$\begin{array}{c} C(2)-C(7)-C(8)\\ C(7)-C(8)-C(9)\\ C(6)-C(10)-C(11)\\ C(6)-C(10)-C(15)\\ C(11)-C(10)-C(15)\\ C(10)-C(11)-C(12)\\ C(11)-C(12)-C(13)\\ C(12)-C(13)-C(14)\\ C(12)-C(13)-C(14)\\ \end{array}$	111.6(2) 125.9(2) 117.1(2) 124.2(2) 118.7(1) 120.7(2) 120.2(2) 119.6(2)
			N(1) = C(6) = C(10) C(5) = C(6) = C(10)	113.8(2)	C(13)-C(14)-C(15) C(10)-C(15)-C(14)	120.5(2)
	d/Å 1.503(2) 1.499(3) 1.519(3) 1.527(3) 1.494(3) 1.308(2) 1.513(3) 1.520(2)	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Table 1. Bond lengths and bond angles for molecule 2

half-chair conformation: the C(3), C(4), C(5), and C(6) atoms are in a single plane (their average deviation is ± 0.004 Å); the C(2) and N(1) atoms deviate from this plane by -0.433 and 0.317 Å, respectively. The allyl group is in an equatorial position, and the phenyl group is in a pseudoaxial position.

The bond lengths in molecule 2 are close to those observed previously in *trans*-2,6-diallyl-3-bromo- Δ^3 -piperideine hydrochloride.⁵

In the crystal, molecules are linked in centrosymmetric dimeric associates $(C_{14}H_{18}NCl)_2$ through hydrogen bonds N(1)-H(1a)...Cl(1) (N...Cl 3.142(3), H...Cl 2.27(3) Å, the N-H-Cl angle is 164°) and N(1)-H(1b)...Cl(1a) (-x+1, -y+1, -z) (N...Cl 3.125(3), H...Cl 2.21(3) Å, the N-H-Cl angle is 175°).

Experimental

All operations with organoboron compounds were carried out under an atmosphere of dry argon. The ¹H and ¹³C NMR spectra were recorded on a Bruker AC-200P spectrometer. The chemical shifts (the δ scale) are given relative to TMS. The IR spectra were obtained on an UR-20 spectrophotometer. The mass spectra were recorded on a Varian-MAT spectrometer.

trans-2-Allyl-6-phenyl-1,2,3,6-tetrahydropyridine (1). Pyridine (14.6 mL, 181.5 mmol) was added to a 0.66 N phenyllithium ether solution (275 mL, 181.5 mmol) at 0 °C, and the mixture was stirred at 0 °C for 1 h (a precipitate formed). The reaction mixture was cooled to -30 °C. Then triallylborane (26.7 g, 200 mmol) was added, and the mixture was stirred at 10 °C for 0.5 h. Absolute methanol (24 mL, 594 mmol) was added dropwise to the reaction mixture at -30 °C. The mixture was stirred, and the temperature was raised to 20 °C. Then the mixture was treated with a 20% NaOH solution (60 mL), refluxed for 1 h, and extracted with ether. According to the data of GLC, the ether solution contained compound 1 (94%) and 2-phenylpyridine (6%). A 3 N HCl solution (47 mL) was added to the ether solution. The aqueous layer was separated and washed with ether. A 20% NaOH solution (60 mL) was added to the aqueous layer. Then the solution was extracted with ether (3×30 mL) and dried with K₂CO₃. Compound 1 was obtained by distillation in a yield of 19.2 g (53 %), b. p. 101-103 °C (1 Torr), n_D²⁰ 1.5510. Found (%): C, 84.39; H, 8.65; N, 6.75. $C_{14}H_{17}N$. Calculated (%): C, 84.37; H, 8.60; N, 7.03. Mass spectrum (EI, 70 eV), m/z: 199 [M]⁺, 158 [M-C₃H₅]⁺, 91 [C₇H₇]⁺. IR (pure compound, v/cm⁻¹): 3320 (br), 3060, 3030, 2910, 1640, 1490, 1450, 1110,

1000, 920, 900, 760, 740, 705. ¹H NMR (CDCl₃, δ): 1.87–2.35 (m, 5 H, CH₂–C= and NH), 2.85–3.08 (m, 1 H, H-2), 4.6 (s, 1 H, H-6), 4.95–5.20 (m, 2 H, CH₂=), 5.55–6.15 (m, 3 H, =CH–), 7.20–7.55 (m, 5 H, Ph). ¹³C NMR (CDCl₃, δ): 31.31 (C-3), 40.27 (C-7), 45.90 (C-2), 56.27 (C-6), 117.16 (C-9), 126.23 (C-4), 126.90 (C_p), 127.48 (C-5), 127.54 and 128.20 (C_p and C_m), 134.96 (C-8), 143.46 (C_i).

Table 2. Atomic coordinates (×10⁴ for nonhydrogen atoms; ×10³ for H atoms) and equivalent temperature factors $(U_{iso}^{eq} \times 10^3/\dot{A}^2 \text{ for nonhydrogen atoms}, \times 10^2/\dot{A}^2 \text{ for H atoms})$

Atom	x	у	z	U	
Cl(1)	2799(1)	3427(1)	837(1)	42(1)	
N(1)	2875(2)	6831(1)	349(1)	32(1)	
C(2)	2128(2)	8031(2)	-919(2)	34(1)	
C(3)	2947(3)	9482(2)	-1337(2)	42(1)	
C(4)	2819(2)	9812(2)	32(2)	43(1)	
C(5)	2534(2)	8798(2)	1397(2)	43(1)	
C(6)	2299(2)	7160(2)	1784(2)	35(1)	
C(7)	2581(3)	7436(2)	-2210(2)	46(1)	
C(8)	1754(3)	8516(3)	-3465(2)	59(1)	
C(9)	2669(4)	9253(2)	-4817(2)	63(1)	
C(10)	351(2)	6799(1)	2721(2)	32(1)	
C(11)	-244(2)	6996(2)	4111(2)	41(1)	
C(12)	-2030(3)	6753(2)	5006(2)	49(1)	
C(13)	-3235(3)	6313(2)	4530(2)	51(1)	
C(14)	-2651(2)	6092(2)	3162(2)	46(1)	
C(15)	-861(2)	6321(2)	2266(2)	38(1)	
H(la)	260(2)	591(2)	54(2)	5(1)	
H(1b)	414(3)	674(2)	6(2)	5(1)	
H(2)	82(2)	819(2)	-52(2)	3(1)	
H(3a)	230(3)	1033(2)	-205(2)	6(1)	
H(3b)	423(3)	941(2)	-188(2)	5(1)	
H(4)	298(3)	1081(2)	-14(2)	5(1)	
H(5)	244(2)	903(2)	221(2)	5(1)	
H(6)	314(2)	647(2)	242(2)	4(1)	
H(7a)	207(3)	645(2)	-179(2)	7(1)	
H(7b)	396(3)	730(2)	-260(2)	5(1)	
H(8)	48(4)	867(3)	-325(3)	8(1)	
H(9a)	404(4)	917(3)	-504(3)	8(1)	
H(9b)	211(3)	998(3)	-549(3)	9(1)	
H(11)	61(2)	725(2)	442(2)	5(1)	
H(12)	-233(3)	688(2)	593(2)	6(1)	
H(13)	-453(3)	614(2)	518(2)	6(1)	
H(14)	-345(3)	580(2)	280(2)	7(1)	
H(15)	-49(2)	619(2)	133(2)	5(1)	

trans-2-Allyl-6-phenyl-1,2,3,6-tetrahydropyridine hydrochloride (2) was prepared by the reaction of an ether solution of HCl with 1, yield 97%, m. p. 145–147 °C. IR (KBr pellets, v/cm⁻¹): 3440 (br), 2960, 2680, 1640, 1590, 1580, 1475, 1450, 1425, 1060, 1020, 1000, 925, 740, 720, 700. ¹H NMR (CDCl₃, δ): 2.32–2.70 (m, 3 H, H-7 and H-3a), 2.75–2.95 (m, 1 H, H-3b), 3.20–3.48 (m, 1 H, H-2), 74.85 (s, 1 H, H-6), 5.05–5.25 (m, 2 H, H-9), 5.55–5.90 (m, 2 H, H-8 and H-4), 6.05–6.25 (m, 1 H, H-5), 7.30–7.70 (m, 5 H, Ph), 9.55 (br.s, 1 H, NH), 10.55 (br.s, 1 H, NH). ¹³C NMR (CDCl₃, δ): 26.79 (C-3), 35.86 (C-7), 48.32 (C-2), 54.57 (C-6), 119.38 (C-9), 122.55 (C_p), 126.67 (C-4), 128.81 (Ph), 129.61 (C-5), 130.25 (Ph), 131.87 (C-8), 133.72 (C_i). Single crystals of hydrochloride 2 (m. p. 145–147 °C) were obtained by crystallization from a 9:1 ether—methanol mixture.

X-ray structural analysis 2. Single crystals of 2 are triclinic, M = 235.8 [C₁₄H₁₈N]Cl, space group $P\overline{I}$, Z = 2; at 296 K a = 7.646(6), b = 9.671(4), c = 9.990(5) Å, $\alpha =$ 66.48(4)°, $\beta = 71.44(5)°$, $\gamma = 76.64(5)°$, V = 637.5(7) Å³, $d_{calc} = 1.228 \text{ g cm}^{-3}$. The unit cell parameters and intensities of 2318 independent reflections with $l \ge 2\sigma(l)$ were measured on an Enraf Nonius Cad 4 diffractometer (Mo- K_{α} radiation, graphite monochromator, $\theta/2\theta$ scanning technique, $2\theta \le 54^\circ$). The structure was solved by the direct method and refined by the full-matrix least-squares method with anisotropic thermal parameters for nonhydrogen atoms. All H atoms were revealed from the difference Fourier synthesis and refined isotropically. The final values of the R factors were as follows: R = 0.0331, $R_{\rm w} = 0.041$. All calculations were carried out on an IBM-PC/AT computer using the SHELXTL PLUS program.⁸ Atomic coordinates and thermal parameters for the structure of 2 are given in Table 2.

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