

Reaction of lithiated pyridine with Me_2RSiCl and its identification with NMR spectroscopic methods ($\text{R}=\text{Me}$, ${}^t\text{BuCH}_2\text{CHSiMe}_3$)

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리튬화된 Pyridine과 ME_2RSiCl 의 반응생성물의 NMR 분광학적 연구 ($\text{R}=\text{Me}$, ${}^t\text{BuCH}_2\text{CHSiMe}_3$)

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Abstract: A reactive intermediate 1,2-dihydropyridine derivative 2 has been prepared and isolated from the reaction of pyridine with ${}^t\text{BuLi}$ and trimethylchlorosilane in nonpolar condition at low temperature 2 has characterized by ${}^1\text{H-NMR}$ fine structure analysis with SPINX3. The mechanistic information of formation of 2 was obtained from synthesized 2, 5-disubstituted pyridine derivatives 3 and 4.

요약: Pyridine과 ${}^t\text{BuLi}$ 의 반응생성물과 Me_3SiCl 의 반응에 의해 반응성이 매우 큰 반응 중간체 1,2-dihydropyridine 유도체 (2)를 낮은 온도의 비극성 용매 속에서 합성하여 분리하였으며 SPINX3을 이용한 ${}^1\text{H-NMR}$ 미세 구조 분석에 의해 반응생성물 (2)의 구조를 확인하였다. ${}^1\text{H-NMR}$ spectrum에서 화학적 이동상수와 NH, 그리고 4개의 aromatic CH proton의 coupling에 관한 정보를 분석하였으며, 이 화합물의 형성반응에 의한 반응형성물 3과 4의 합성에 의해 확인하였다.

Key words: ${}^1\text{H-NMR}$ Spectrum, Transition Metal oxides.

I. Introduction

The direct metallation pyridine has been extensively investigated and reviewed.¹⁻⁸ Recently, 1, 2-addition of pyridine by electrophilic reagent on 5-position and 5-substituted-2-alkyl pyridines has been obtained⁹⁻¹², and another the 2,5-dihydropyridine obtained from the reaction of pyridine-alkyllithium complex with alkylhalide is known as unstable reactive intermediate.^{14,15} The 1,2-dihydropyridini-

um salt as highly reactive intermediate in polar medium was prepared by Giam *et al*, but treatment of the salt with RX ($\text{R}=\text{alkyl- and arylhalides}$) yields both N- and C-substituted product.¹⁶ We investigated the reaction of pyridine with ${}^t\text{BuLi}$ in nonpolar condition and isolated a reactive intermediate, 1,2-dihydro-2,5-disubstituted pyridine 2. Treatment of the intermediate 2 with Me_3SiCl afforded a good yield 2,5-disubstituted pyridine 3. We report here a simple synthesis of compound 2

and its derivatives. With these results we also tried to explain the reaction path to the formation of 1,2-dihydropyridine and 2,5-disubstituted pyridine.

1, 2-Dihydro-2, 5-disubstituted pyridine

The reaction of pyridine with $t\text{BuLi}$ in pentane leads probably to pyridine- $t\text{BuLi}$ complex (1a and b) as yellow crystalline product which involve C-alkylation in 2-position at low temperature. This complex reacts further with trimethylchlorosilane and produces 1,2-dihydro-2-tert-butyl-5-trimethylsilyl pyridine 2. The formation of 2 may be explained by assuming the 1,3-exchange of Li/H in this complex (1b). If, in a subsequent step, electrophiles are added, 2,5-disubstituted products are obtained from spontaneous dehydrogenation of 1b in polar medium.^{4, 14} But under the nonpolar condition stable 1, 2-dihydro-5-substituted pyridine 2 is obtained. This unexpected stability of 2 in nonpolar medium is explained by the conjugation of the mesomeric effect¹⁴ of the ring (1,2-, 2,5-, 2,3-dihydropyridine) and with imine bond. But the isomerization of 1a to 1b could be highly increased in pentane medium (Li/H exchange) and the stability of 2 can be explained in connection with po-

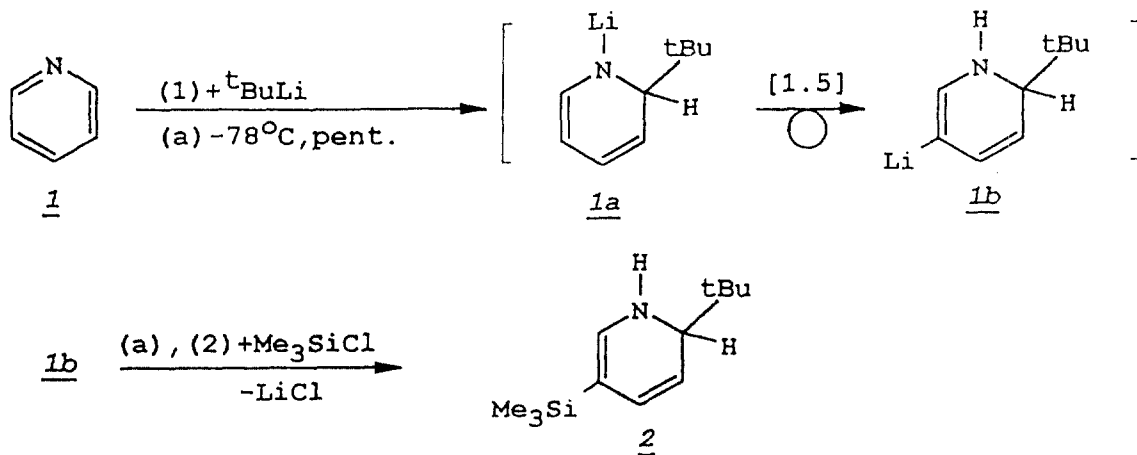
larity of reaction medium as discussed by Marsais *et al.*^{2,14} Therefore, in polar medium such as THF or Et₂O it could be formed deprotonated product.

The lithiation of pyridine in this experiment is carried out with equivalent amounts of pyridine and $t\text{BuLi}$. The resulting product of the reaction with trimethylchlorosilane is the 1,2-dihydro-5-substituted pyridine 2, which is isolated as white crystalline solid and it is not decomposed even heating at 100°C for several days in non polar medium despite of instability against air and moisture condition.

The structure of the 1,2-dihydro-5-substituted pyridine 2 is confirmed by ¹H-NMR, ¹³C-NMR spectra. The hyperfine signals between 3.5~3.6ppm in ¹H-NMR spectrum are essentially nonaromatic and suggest complex coupling pattern between NH proton (3.97ppm) and 4 CH protons. The chemical shift and coupling constants of the 5 protons are exactly analysed (Table 1 and Figure 1) by a computer simulation based on the density matrix method.¹³

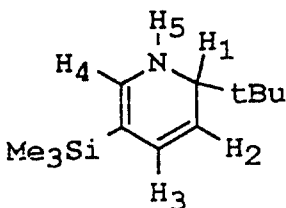
2, 5-Disubstituted pyridine (3 and 4)

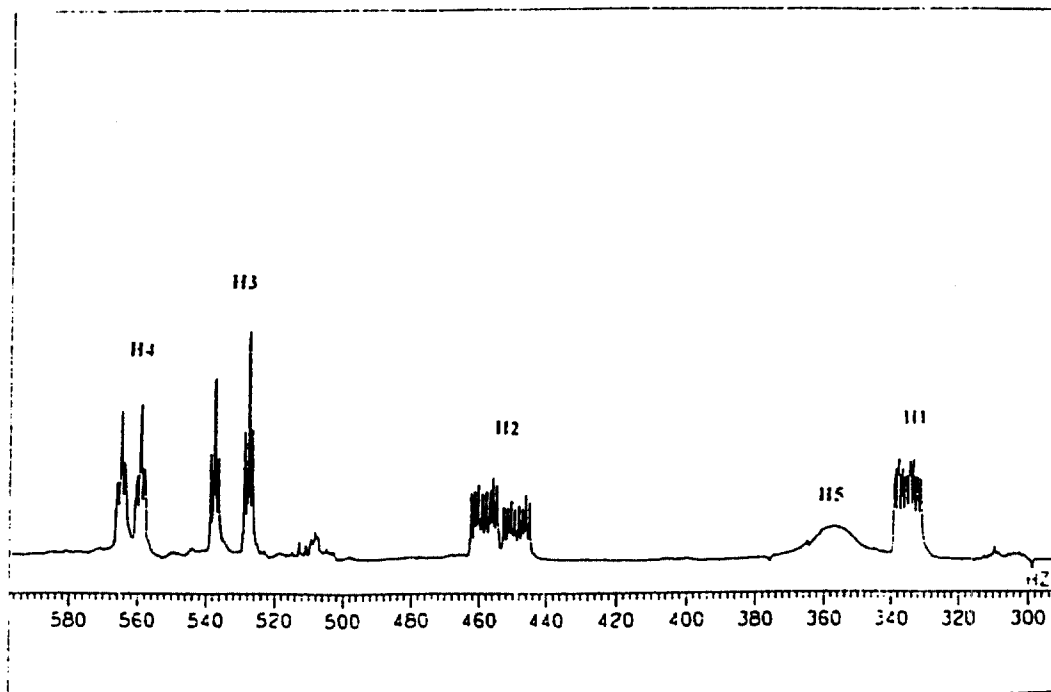
Treatment of 2 with *n*-BuLi at room temperature yields probably *n*-lithiopyridinium salt, which furt-



Scheme 1.

Table 1. ${}^1\text{H}$ -NMR fine structure analysis of comp.(2)

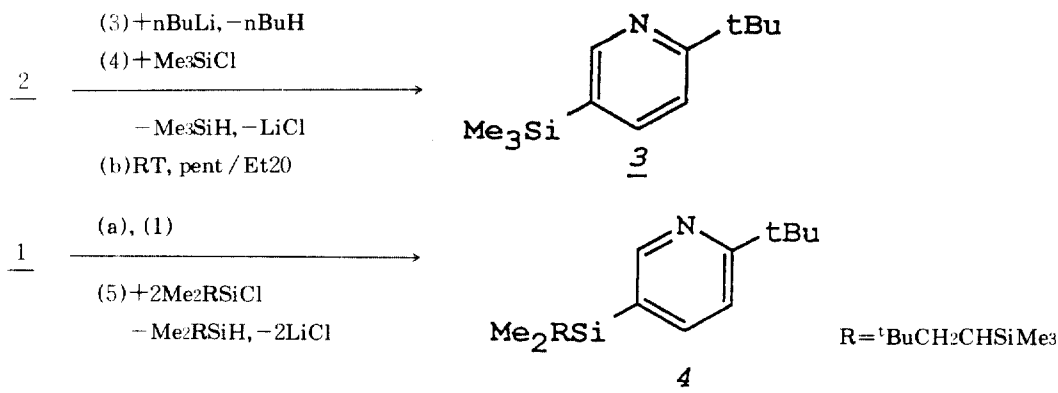
	Chemical Shifts(ppm)								
	H1	H2	H3	H4	H5				
	3.75	5.05	5.92	6.30	3.97				
Coupling constants(Hz)									
J12	J13	J14	J15	J23	J24	J25	J34	J35	J45
4.40	1.10	0.25	2.20	9.80	1.10	2.00	1.10	0.10	5.60


 Fig. 1. ${}^1\text{H}$ -NMR spectrum of comp.(2) between 3.3~ 6.4ppm

her reacts with trimethylchlorosilane to give compound 3 along with LiCl and trimethylsilane. With crystalline compound 3 ($\text{R}=\text{Me}$) is much more stable against air compared to the compound 2. The structure of 3 is confirmed by ${}^1\text{H}$ -NMR spectrum, which shows aromatic protons.

In contrast to the reaction of (1b) with trimethylchlorosilane, analogous reaction with RMe_2SiCl ($\text{R}={}^t\text{BuCH}_2\text{CHSiMe}_3$) proceeds by the subsequent deprotonation from the 1,2-dihydro-5-silylated pyri-

dine to give the deprotonated compound 4 with 44% yield. In this case it appears that the lithiated pyridinium salt reacts with RMe_2SiCl ($\text{R}=\text{Me}$, ${}^t\text{BuCH}_2\text{CHSiMe}_3$) at 5 position through the same mechanism as the formation of compound 3 in Scheme 2. Compound 4 is isolated as colorless liquid (bp $110^\circ\text{C}/10^{-1}\text{torr}$). The structure of 4 is conformed by its ${}^1\text{H}$ -NMR spectroscopic data, which shows the same coupling pattern as in 2,5-lutidine.



Scheme 2.

II. Experiments

All manipulations involving synthesis and transformation of alkyllithium are carried out rigorously dried condition under N₂ atmosphere. All solvents are freshly distilled (Et₂O was dried by boiling with Ph₂C=O/Na; pentane was dried by boiling with Na metal). NMR spectra (¹H and ¹³C) are measured on Jeol EX90(90MHz) spectrometer at and CDCl₃ is used as an internal standard and solvent. The ¹H-NMR simulation for the fine structure of compound 2 is performed using SPHENX3 program¹⁵ on IBM compatible personal computer. Mass spectra (VG70-SEQ) and elemental analysis are performed by Korea Basic Science Center in Seoul.

1, 2-Dihydro-2-tert-butyl-5-trimethylsilyl pyridine (2)

A mixture of 4.80g (43.80mmol) of Me₃SiCl and 3.46g (43.80mmol) of pyridine in 100ml pentane at -78°C is treated slowly with 43.80mmol of ^tBuLi and allowed to warm up to room temperature, where upon LiCl precipitates and then disappear red-yellow solution. For the completion of reaction, the mixture is stirred for 12 hrs at room temperature and then filtered. After removal of pentane by reduced distillation, the residue is subjected to short path distillation at 70°C/10⁻¹ torr. The product 2 is recrystallized from pentane [yield 4.50g (21.53mmol, 55.5%), m.p. 50°C decomp.] and is very air

sensitive compound.

¹H-NMR (90MHz, CDCl₃): δ = -0.01(s, 9H, Me₃Si), 0.85(s, 9H, ^tBu), 3.75(qq, 1H, H), 3.97(m, 1H, NH), 4.98, 5.05, 5.09, 5.15(qq, qq, 1H, H), 5.88, 5.99(tt, 1H, H), 6.24, 6.31(tt, 1H, H), see Fig. 1. ¹³C-NMR (22.5MHz, CDCl₃): δ = -0.00(Me₃Si), 24.70(CH), 38.20(^tBu), 61.10(CH), 112.20(CH), 127.20(CH), 139.80(CH), 98.00(C-Si)

2-tert-Butyl-5-trimethylsilyl pyridine (3)

A solution of 0.80g (3.80mmol) of 1 in 50ml mixed solvent of pentane and diethylether(1:1) is treated with slowly 3.80mmol of n-BuLi at room temperature. 0.5g (4.60mmol) Me₃SiCl is added to the stirred solution, keeping the stirring for 12hrs. White precipitates of lithium chloride are formed, which are filtered off. After removal of mixed solvent, the residue is dissolved in 10ml pentane and recrystallized at -78°C [yield: 0.40g (1.93mmol, 50.7%, white crystal, m.p. 86°C]

¹H-NMR (90MHz, CDCl₃): δ = 0.28(s, 9H, Me₃Si), 1.37(s, 9H, ^tBu), 7.24, 7.35(dd, 1H, H), 7.67, 7.76(dd, 1H, H), 8.65(q, 1H, H). ¹³C-NMR (22.5MHz, CDCl₃): δ = -0.11(Me₃Si), 30.10(C), 37.10(^tBu), 117.90(CH), 141.40(CH), 152.90(CH), 131.09(C), 141.00(C). Mass (70eV): m/z(%) = 207 (M⁺, 30), 192((M-Me)⁺, 100), 165(M-CH₃CHCH₂)⁺, 160, 134(M-Me₃Si)⁺, 4). Anal. Calcd. for C₁₂H₂₁NSi: C, 69.50; H, 10.21; N, 6.75. Found: C,

69.25; H, 11.38; N, 6.72.

2-tert-Butyl-5-[1, 1, 4, 4-tetramethyl-2-trimethylsilyl-1-silapentyl] pyridine (4)

A mixture of 0.67g(3.11mmol) of $\text{Me}_2\text{SiClCH}_2\text{CH}(\text{H})\text{C}(\text{Me}_3)_2$ and 0.24g(3.11mmol) of pyridine in 25ml pentane at -78°C is treated with 2.09mmol of ${}^t\text{BuLi}$ and slowly warmed until room temperature, where upon LiCl precipitate and disappeared yellow solution. After the filtration, pentane is removed by reduced distillation, and the residue is subjected to short path distillation at $130^\circ\text{C}/10^{-1}$ torr [yield: 0.48g(1.38mmol, 45%), colorless liquid].

${}^1\text{H-NMR}$ (90MHz, CDCl_3): $\delta = -0.10$ (t, 1H, CH), -0.05 (s, 9H, Me_3Si), 0.31, 0.35 (d, 6H, Me_3Si), 0.70(s, 9H, ${}^t\text{Bu}$), 1.45, 1.50(d, 2H, CH_2), 1.35(s, 9H, ${}^t\text{Bu}$), 7.20, 7.24(dd, 1H, CH), 7.63, 7.75(dd, 1H, CH), 8.61(q, 1H, H). ${}^{13}\text{C-NMR}$ (22.5MHz, CDCl_3): $\delta = -1.00$ (Me_2Si), 1.00(Me_3Si), 7.00(CH), 29.50, 31.80(${}^t\text{Bu}$ -chain), 38.20(CH_2), 30.00, 37.70(${}^t\text{Bu}$ -ring), 118.00, 142.00, 154.00(CH), 132.00, 170.00(Cquart), Mass (70eV): $m/z(\%) = 349$ (M^+ , 57), 334(($\text{M}-\text{Me}$) $^+$, 48), 292(($\text{M}-{}^t\text{Bu}$) $^+$, 58), 177($\text{M}-\text{Me}_3\text{SiCHCH}_2{}^t\text{Bu}$, Me^+), 61), 73(Me_3Si^+ , 86), 57(${}^t\text{Bu}^+$, 96), 43($\text{M}-\text{CH}_3\text{CHCH}_2^+$, 100), Anal. Calcd. for $\text{C}_{20}\text{H}_{39}\text{NSi}_2$: C, 68.01; H, 11.12; N, 4.18. Found: C, 68.58; H, 11.84; N, 4.35.

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