

Reaction Mechanism of 2-(Trimethylsilylmethyl)pyridine with Benzonitrile^{1)†}

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Synopsis. The mechanism of the reaction of lithiated 2-(trimethylsilylmethyl)pyridine with benzonitrile is discussed. The reaction proceeds through (*E*)- and (*Z*)-1-phenyl-2-(2-pyridyl)-1-(trimethylsilylamino)ethene, which are quantitatively converted to 2-phenacylpyridine by acidic hydrolysis.

Reaction of a nitrile with a Grignard or organolithium reagent has been extensively investigated by many workers.^{2,3)} It is a good synthetic method of ketimines which give ketones by hydrolysis. It is difficult to find a reaction of an α -silyl carbanion with a nitrile, although its reaction with a carbonyl compound has been discussed as the Peterson reaction.⁴⁾ In the course of our investigation of α -silyl carbanion with carbonyl compound or their analogs, we previously reported that *p*-substituted benzonitriles gave the corresponding 2-phenacylpyridine derivatives in high yield when the nitriles were treated with lithiated 2-(trimethylsilylmethyl)pyridine.¹⁾

In this paper, we wish to report a mechanism of the reaction of lithiated 2-(trimethylsilylmethyl)pyridine (**1**) with benzonitrile (**2**). The reaction was found to proceed through (*E*)- and (*Z*)-1-phenyl-2-(2-pyridyl)-1-(trimethylsilylamino)ethene, (**4**) and (**5**), which were isolated in good yield, and converted to 2-phenacylpyridine (**3**) quantitatively by acidic hydrolysis.

Results and Discussion

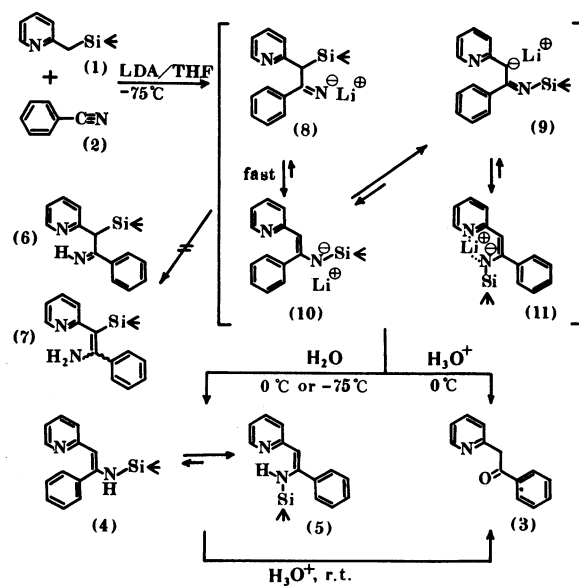
In order to study the behavior of the trimethylsilyl group throughout the reaction, the following three quenching experiments were performed (Table 1). Firstly, the reaction mixture of **1** with **2** was quenched with water at 0 °C (instead of aq ammonium chloride which was used in preparation of **3**¹⁾) after stirring for 1 h at –75 °C and for 2 h at room temperature (method A). The organic extract did not contain any **3**, but did contain (*E*)-1-phenyl-2-(2-pyridyl)-1-(trimethylsilylamino)ethene (**4**) and its *Z*-isomer (**5**) (**4** : **5** = 10 : 90, by GLC) with a small amount of the unreacted **1** (Scheme 1). A mixture of **4** and **5** was isolated in good yield (74%) by distillation under reduced pressure (**4** : **5** = 20 : 80, by GLC; 43 : 57, by ¹H-NMR⁵⁾). Both **4** and **5** were quantitatively converted to **3** by hydrochloric acid, but they did not change to **3** by sodium hydroxide. On the other hand, quenching with aq. THF at –75 °C after 5 min (method B) gave a different ratio (**4** : **5** = 70 : 30, by GLC under the same conditions as method A). This fact suggests that the formation of **4** is kinetically controlled, while that of **5** is thermodynamically controlled.

The structures of **4** and **5** were determined by their spectroscopic properties. The MS of the distillate obtained by method A, showed a molecular ion (*M*⁺) peak at *m/z* 268 (molecular weight of **4** and **5**: C₁₆H₂₀N₂Si = 268.43), and the ¹H-NMR spectrum of the same

TABLE 1. QUENCHING EXPERIMENT IN THE REACTION OF **1** WITH **2**^{a)}

Method	Reaction		Quenching		Ratio of 4 : 5 ^{b)}
	$\theta/^\circ\text{C}$	<i>t</i> /min	Quencher	$\theta/^\circ\text{C}$	
A	–75	60	H ₂ O	0	10 : 90 ^{c)}
	r.t.	120			(25 : 75) ^{d)}
B ^{e)}	–75	5	H ₂ O/THF	–75	70 : 30
C ^{e)}	–75	30	AcOH/THF ^{e)}	–75	100 : $\approx$ 0

a) Molar ratio **1** : **2** : LDA = 1 : 1 : 1; spectra were measured after drying, followed by evaporation of the solvent. b) Determined by GLC (10% Silicone GE SE-30, 80 → 200 °C, 8 °C/min, Rt/min = 21 and 22.5, respectively). c) Analyzed without purification; includes the unreacted **1**. d) Estimated by GLC and ¹H-NMR data of the distillate; **4** : **5** = 20 : 80 by GLC, 43 : 57 by ¹H-NMR. e) Excess acetic acid was removed *in vacuo*, followed by washing with sodium hydroxide.



Scheme 1.

sample consists of two kinds of trimethylsilyl groups (δ = 0.04 for **5** and 0.12 for **4**), two kinds of alkenyl protons (δ = 5.23 for **5** and 5.46 for **4** as singlet respectively), and two kinds of N–H protons (δ = 9.62 for **5** and 7.85 for **4**), together with the ABCX system for the pyridine protons complicated with multiplet phenyl protons. The IR spectrum suggested the presence of the enamine system (ν_{NH} 3470 cm^{–1} and $\nu_{\text{C}=\text{trans}}$ 1620 cm^{–1} for **5** and $\nu_{\text{C}=\text{cis}}$ 1630 cm^{–1} for **4**) together with the trimethylsilyl group (δ_{CH_3} 1253 cm^{–1} and 840 cm^{–1}). No absorption of C=N bond was observed. The absorption band at 930 cm^{–1} was assigned to $\nu_{\text{asSi-N}}$.⁶⁾ Enamines **4** and **5** easily lost the trimethylsilyl group under acidic medium (Scheme 1), although a trimethylsilyl group attached to a *secondary* carbon is less reactive.^{4c)} This does not indicate the presence of the Si–C bond, but the presence of the Si–N bond.⁷⁾ It is

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consistent with the result from the IR spectrum; therefore, an imino compound (**6**) and its enamine tautomer (**7**) derived from (**8**) are not stable intermediates. Moreover, *N*-trimethylsilyl imine derived from **9** by C-protonation was not observed.⁸⁾

Finally, the reaction mixture of **2** was quenched with glacial acetic acid in THF at -75°C after stirring at -75°C for 30 min (method C). Only **4** was included in the reaction mixture (Table 1 and Experimental).

In conclusion, the lithiated **1** reacts with **2** to give the imino compound **8**, which was immediately converted to the (*E*)-enamide **10** by 1,3-migration of the trimethylsilyl group from C to N (Scheme 1).⁷⁾ Through the corresponding imine tautomer **9**, **10** is isomerized to the (*Z*)-enamide **11**, which is thermodynamically more stable. These anions are resonance-stabilized by the electron-attracting 2-pyridyl group and trimethylsilyl group adjacent to the negatively charged nitrogen atom. The anion which would be an intermediate in the reaction of **1** with aldimines⁹⁾ would not become stabilized in this way.

Experimental

The melting points and boiling points were uncorrected. The IR spectra were recorded on a Hitachi Model 260-10 spectrophotometer, and the ^1H -NMR spectra with a JEOL SNM-FX 100 spectrometer for solutions in CDCl_3 . The chemical shift are reported in δ (internal TMS). The mass spectra were recorded with a Hitachi RMU-7M double-focusing mass spectrometer at 70 eV. The analytical GLC determination was carried out with a Shimadzu GC-4CPF apparatus equipped with a 10% Silicone GE SE-30 column (4 mm $\times$ 2 m) and operated in programmed-temperature mode ($80 \rightarrow 200^{\circ}\text{C}$, $8^{\circ}\text{C}/\text{min}$).

Materials. 2-(Trimethylsilylmethyl)pyridine **1** was prepared by a method reported previously.¹⁾

Preparation of 2-Phenacylpyridine 3. A method has been reported in Ref. 1.

Quenching the Reaction of 1 with 2. The reaction was performed in the same way as the preparation of **3**, and the reaction mixture was quenched by the following three methods, before being analyzed by means of IR, GLC, and ^1H -NMR (without purification, except for method A). The results are summarized in Table 1.

Method A: A solution of butyllithium (8.6 g, 0.02 mol) in hexane was added to a solution of diisopropylamine (2.0 g, 0.02 mol) in THF (54 ml) at -75°C with stirring under nitrogen. To the solution, 0.02 mol of **1** was added slowly and stirred for an additional 10 min. The mixture was treated with a THF solution of **2** (0.02 mol), and stirred for 1 h at -75°C and for 2 h at room temperature. The reaction mixture was quenched with 50 ml of water at 0°C . The crude product thus obtained was distilled under reduced pressure. Yield, 74% (the mixture of (*E*)-1-phenyl-2-(2-pyridyl)-1-(trimethylsilylamino)ethene **4** and the *Z*-isomer **5**, **4** : **5** = 10 : 80 by GLC and 43 : 57 by ^1H -NMR), bp $125.2-130^{\circ}\text{C}/1.0\text{ mmHg}$ ($1\text{ mmHg} \approx 133.322\text{ Pa}$). An attempt to separate **5** from **4** by column chromatography on Al_2O_3 (neutral) resulted in failure because of hydrolysis of **4** and **5** during the operation. IR (neat) 3470 (ν_{NH}), 1630 ($\nu_{\text{C}=\text{C}}$ of **4**), 1620 ($\nu_{\text{C}=\text{C}}$ of **5**), 1253 (δ_{SiCH_3}), and 930 ($\nu_{\text{Si-N}}$) cm^{-1} ; MS (70 eV) m/z (rel intensity) 270 ($\text{M}+2$, 1.0), 269 ($\text{M}+1$, 4.1), 268 (M^+ , 14.9), 267 ($\text{M}-1$, 8.2), 256 (1.0), 255 (6.2), 254 (24.0), 253 ($\text{M}-\text{CH}_3$, 100), 197 (2.3), 196 (15.9), 195 ($\text{M}-\text{Si}(\text{CH}_3)_3$, 35.1), 150 (9.7), 132 (8.4), and 73 (28.1); ^1H -NMR δ 0.04 (5.14H, s, $\text{Si}(\text{CH}_3)_3$ of **5**), 0.12 (3.86H, s, $\text{Si}(\text{CH}_3)_3$ of **4**), 5.23 (0.57H, s, $\text{CH}=\text{C}$ of **5**), 5.46 (0.43H, s, $\text{CH}=\text{C}$ of **4**), 6.6–8.35 (9H, ABCX system for 2-Py-H and m for Ph-H), 7.85 (0.43H,

b, NH of **4**) and 9.62 (0.57H, b, NH of **5**). Found: C, 72.32; H, 7.50; N, 10.45%; m/z 268.1385. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{Si}$: C, 71.59; H, 7.51; N, 10.44%; M^+ , m/z 268.1393.

Method B: The reaction was performed on a smaller scale than in method A (**1**, 3 mmol). After stirring for 5 min at -75°C , the reaction mixture was quenched with aq THF ($\text{H}_2\text{O} : \text{THF} = 1 : 2$ v/v, 10 ml) at -75°C . The crude product contained the unreacted **1** and **2**. IR (neat) 1632 ($\nu_{\text{C}=\text{C}}$ of **4**), 1620 ($\nu_{\text{C}=\text{C}}$ of **5**), 1255 (δ_{SiCH_3}), and 930 ($\nu_{\text{Si-N}}$) cm^{-1} ; ^1H -NMR δ 0.14 (s, $\text{Si}(\text{CH}_3)_3$ of **4**), 5.21 (s, $\text{CH}=\text{C}$ of **5**), and 5.43 (s, $\text{CH}=\text{C}$ of **4**), 6.6–8.4 (ABCX system for 2-Py-H and m for Ph-H), 7.8 (b, NH of **4**), and 9.6 (b, NH of **5**).

Method C: The reaction was performed on the same scale as in method B. After stirring for 30 min at -75°C , the reaction mixture was quenched with 2 ml of glacial acetic acid in THF (7 ml) and stirred for 1 h at -75°C . The resultant white precipitate (CH_3COOLi) was removed by filtration under nitrogen atmosphere. The filtrate was concentrated, and excess acetic acid and volatile products were removed under reduced pressure below 40°C . All these operations were performed under nitrogen atmosphere to prevent the product from undergoing acidic hydrolysis. The residue was washed with 2 M NaOH to remove any trace of acetic acid (it was found that the product **4** did not change during the washing). IR (neat) 1635 ($\nu_{\text{C}=\text{C}}$ of **4**), 1240 (δ_{SiCH_3}), and 930 ($\nu_{\text{Si-N}}$) cm^{-1} ; ^1H -NMR δ 0.11 (s, $\text{Si}(\text{CH}_3)_3$ of **4**) and 5.48 (s, $\text{CH}=\text{C}$ of **4**), 6.6–8.4 (ABCX system for 2-Py-H and singlet-like Ph-H), and 7.9 (b, NH of **4**).

Acidic Hydrolysis of 4 and 5. The mixture of **4** and **5** (167 mg) was dissolved in ether (30 ml), and shaken with 2 M HCl (13 ml) for 10 min at room temperature. After washing with ether, the aq. phase was made alkaline (pH 13) with Na_2CO_3 , and completely extracted with ether. Both the enamines **4** and **5** were quantitatively converted to **3**.

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