REACTION OF α-SILYL CARBANION WITH OXIME ETHERS[1]

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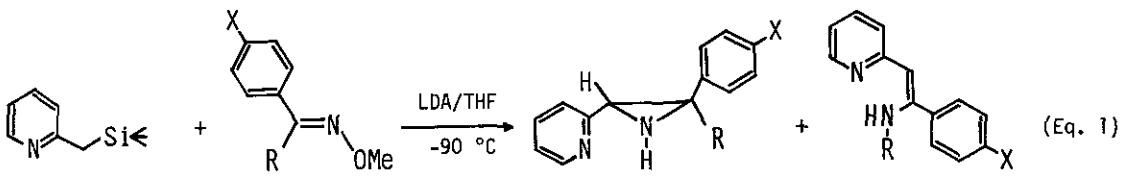
Abstract —— In the presence of LDA, 2-(trimethylsilylmethyl)pyridine reacts with *p*-substituted benzaldoxime methyl ethers to give stereoselectively *trans*-2-aryl-3-(2-pyridyl)aziridines and (*z*)-1-amino-1-aryl-2-(2-pyridyl)-ethenes. From the temperature-dependent ^{1}H-nmr spectra of *trans*-2-phenyl-3-(2-pyridyl)aziridine, ΔF^* was estimated to be about 14 kcal/mol at the coalescence temperature (T_c = 0 °C).

Aziridine derivatives are inflammable, explosive, and very poisonous. These problems slowed down any research on their chemistry. But recently these derivatives have attracted considerable attention, because of their easy conversion into high polymers, their use as aminoalkylating agents, and their powerful physiological action.[2] Generally, aziridine derivatives are prepared from (i) β-amino alcohols, (ii) ketoximes and excess Grignard reagents, (iii) 1,2,3-triazolines, (iv) benzyl ketoximes and lithium aluminum hydride, or (v) alkenes and nitrenes (or imines and carbenes).[2,3] The forth reaction is stereoselective, but the yield is not so high. Although the fifth reaction gives aziridines in high yields, its stereospecificity depends upon the spin-state of a nitrene or carben.

In the course of our investigation of α-silyl carbanion with carbonyl compounds or their analogs, we have reported that lithiated 2-(trimethylsilylmethyl)pyridine reacted with imines to give (*E*)-2-alkenylpyridines stereospecifically,[4] and with benzonitrile to give (*E*)-1-phenyl-2-(2-pyridyl)-1-(trimethylsilylamino)ethene under the kinetically controlled conditions and the *z*-isomer under the thermodynamically controlled conditions.[5,6]

As an extension of our investigation mentioned above, we now wish to report a reaction of 2-(trimethylsilylmethyl)pyridine (1) with *p*-substituted benzaldoxime methyl ethers, (2a) ~ (2d), to give the corresponding *trans*-2-aryl-3-(2-pyridyl)aziridines (3) and (*z*)-1-amino-1-aryl-2-(2-pyridyl)-ethenes (4). In a typical run, twenty-five mmol of 1 was lithiated with LDA in THF at -90 °C, and the resultant solution was treated with a THF solution of 2 (25 mmol) at -90 °C to afford 3 and 4 (Eq. 1).



(Eq. 1)

1 2 3 4

Their yields were determined by means of ^{1}H-nmr spectra, and the result is shown in Table. Benzaldoxime methyl ether (2a) gave *trans*-2-phenyl-3-(2-pyridyl)aziridine (3a)[7] in 38% (isolated) yield and (z)-1-amino-1-phenyl-2-(2-pyridyl)ethene (4a) in 11% yield. The *p*-chloro derivative 2b gave the corresponding aziridine and enamine derivatives, 3b and 4b,[8] in 12 and 30% (isolated) yields. The *p*-methyl and *p*-methoxyl derivatives, 2c and 2d, also gave the corresponding products, 3c, 4c, 3d, and 4d, in 15, 30, 17, and 28% yields. Thus, the replacement of the X group in 2 by chloro, methyl, or methoxyl group decreases the yield of 3 to *ca.* 15% and increases that of 4 to *ca.* 30%. On the other hand, if the R group in 2 was replaced by a methyl or phenyl group, the yield of 3 diminished greatly and 4 was undetectable (see Table). The reason for this lower reactivity of 2e and 2f may be explained by steric hindrance around the methoxyimino carbon. In all cases, the unreacted 1 was quantitatively recovered, but 2 was partially decomposed.[9]

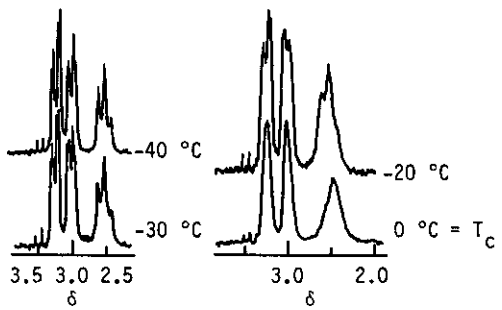
The structure of 3 was spectrometrically determined.[7,10] The ir spectrum of 3a, measured in KBr disk, suggested the presence of the hydrogen-bonded NH group at 3230 cm^{-1}, but the *cis* isomer was reported[11] to exhibit an absorption band of the free NH group at 3300 cm^{-1}. This suggests that the inversion of the nitrogen atom in 3a is fixed in *syn* form (5) in crystal because of the intramolecular hydrogen bond. At room temperature, the ^{1}H-nmr spectrum of the aziridine 3a shows singlets at

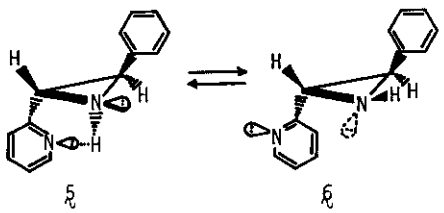
Table. Yields of the products 3 and 4 and their ratio

Entry	X	R	Yield, %[a,b,c]		Ratio
			3	4	3 : 4
a	H	H	(38)	11	78 : 22
b	Cl	H	12	(30)	29 : 71
c	CH_3	H	15	30	33 : 67
d	OCH_3	H	17	28	38 : 62
e	H	CH_3	trace	-[d]	——
f	H	C_6H_5	trace	-[d]	——

a) Based on 1 charged initially. b) Determined by means of ^{1}H-nmr spectra using benzyl alcohol as an internal standard, and yield of the pure product isolated in parentheses. c) Most of the unreacted 1 was recovered. d) Undetectable.

δ 3.2 and 2.99, assignable to the aziridine-ring protons, and a broad signal at δ 2.46 assignable to the imino proton. This broad signal disappeared when deuterium oxide was added. The *cis* isomer was reported to show a singlet at δ 3.7 for the aziridine-ring protons and a singlet at δ 1.92 for an imino proton.[11] The signals for the aziridine-ring protons of 3a at first broaden with decreasing temperature and ultimately split into AB quartets, as shown in Figure. The coupling constant J_{AB} obtained from conventional analyses of these AB-like patterns at low temperature is 2.2 Hz, which is nearly equal to those of other *trans*-aziridine derivatives.[12] This temperature dependence of the ^{1}H-nmr spectrum of 3a is explained by the inversion of the imino nitrogen as shown in Eq. 2. Intramolecular hydrogen bonding between the NH group and the pyridine-ring nitrogen in the invertomer 5 will stabilize this *syn* form. These temperature-dependent spectra of 3a show us that $\Delta\nu = \nu_A - \nu_B$ = 295.10 - 285.36 = 8.74 Hz for the ring proton attached to C-3, and that the coalescence temperature, T_c = 0 °C, from which half of the life time of either site, τ = 0.0258 sec, and ΔF^* is about 14 kcal/mol at T_c. This value is large compared with that for 2,2,3,3-tetramethylaziridine, perhaps, because of the intramolecular hydrogen bonding.[13]

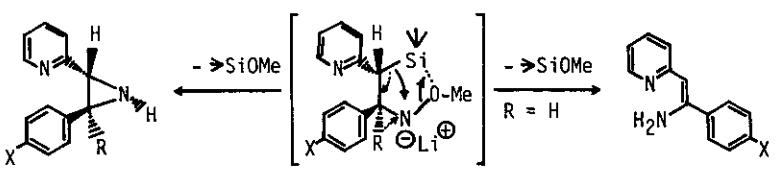




5 6 (Eq. 2)

Figure. Temperature-dependent ^{1}H-nmr of 3a

The structure of 4 was also determined spectrometrically.[8,10] The aziridine 3 was not converted into the enamine 4 by the action of excess LDA. This simultaneous formation of 3 and 4 suggests that the intermediate adduct (7) should eliminate methyl trimethylsilyl ether to form the aziridine 3 as shown in solid-line arrows, and the enamine 4 as shown in dotted-line arrows (Scheme). Like some other methods to prepare aziridines, this method has the advantage of complete stereoselectivity. For example, the Kitahonoki-Kotera's method gives the *cis* isomer of 3a in the reaction of 2-(2-pyridyl)acetophenone oxime,[11] while the present method gives the *trans* isomer, 3a, in the reaction of benzaldoxime methyl ether. In addition, the reaction of 1 with nitrones, reported



3 7 4

Scheme

by Tsuge and his coworkers,[12] gave mixtures of *cis*- and *trans*-aziridine derivatives. The present method, however, has regrettably a disadvantage that it gives a considerable amount of the enamine. Further investigation is now in progress.

Experimental procedure has been reported previously.[4] To the reaction mixture was added water at 0 °C after stirring for 1 h at -90 °C and 2 h at room temperature, and the ethereal extract was evaporated. The condenced reaction mixture was (a) dissolved in carbon tetrachloride for ^{1}H-nmr analysis after addition of an internal standard (benzyl alcohol), and (b) separated by column chromatography on Florisil, or by preparative hplc (Shodex Polymer HP-125).

REFERNCES AND NOTES

1. A preliminary report of this work was presented at the 9th International Congress of Heterocyclic Chemistry, Tokyo, August, 1983, Abstr. p. 138.
2. R. Livingstone, 'Rodd's Chemistry of Carbon Compounds', 2nd ed, ed by S. Coffey, Elsevier Scientific Pub., Amsterdam(1973), Vol. IV-A, p. 15.
3. R. S. Atkinson, B. D. Judkins, and N. Khan, *J. Chem. Soc. Perkin Trans. I*, 1982, 2491.
4. T. Konakahara and Y. Takagi, *Tetrahedron Lett.*, 1980, **21**, 2073.
5. T. Konakahara and K. Sato, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 1241.
6. T. Konakahara and Y. Takagi, *Heterocycles*, 1980, **14**, 393.
7. Physical and spectral properties of **3a**: mp 61.4 ∿ 62.2 °C (from ether); uv(EtOH) $\lambda_{max}(\varepsilon)$ 210 (13500), 232(15900), and 267 nm (7500); ir(KBr) 3230(ν_{NH}), 1210, 835 cm^{-1} (ν_s, ν_{as} of aziridine ring); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 2.46(1H, b, NH), 2.99(1H, s, H on C-3), 3.2(1H, s, H on C-2), 7.3(5H, s-like, Ph-H), 7.0 ∿ 8.6(4H, ABCX system for 2-Py-H); ms(70 eV) m/z(rel intensity) 197 (4), 196(M^+, 31), 195(29), 181(14), 180(100), 168(15), 119(42), 92(27). Found: C, 79.57; H, 6.08; N, 14.28%. Calcd for $C_{13}H_{12}N_2$: C, 79.56; H, 6.16; N, 14.28%.
8. Physical and spectral properties of **4b**: mp 125.0 ∿ 125.5 °C (from ethanol); uv(EtOH) $\lambda_{max}(\varepsilon)$ 236(13000), 267(8500), and 355 nm (23500); ir(KBr) 3500, 3430(ν_{NH}), 1618($\nu_{C=C}$), and 810 cm^{-1} ($\delta_{=CH}$); ^{1}H-nmr(60 MHz, $CDCl_3$) δ 5.4(1H, s, =CH), 5.7(2H, b, NH_2), 6.7 ∿ 8.38(8H, ABCX system for 2-Py-H and m for phenylene-H); ms(70 eV) m/z(rel intensity) 233(4), 232(41), 231(54), 230 (M^+, 100). Found: C, 67.60; H, 4.71; N, 12.07; Cl, 15.31%. Calcd for $C_{13}H_{11}N_2Cl$: C, 67.69; H, 4.81; N, 12.14; Cl, 15.37%.
9. For example; the recoveries of **1** and **2c** (or **1** and **2d**) were 55 and 30% (or 60 and 35%). Consequently, the yields of **3c**, **4c**, **3d**, and **4d** are 33, 67, 43, and 70% based on the consumed **1**.
10. The other aziridine (**3b**) and enamines (**4a**, **4c**, and **4d**) were exhibited spectral properties in accordance with assigned structures.
11. K. Kotera, S. Miyazaki, H. Takahashi, T. Okada, and K. Kitahonoki, *Tetrahedron*, 1968, **24**, 3681.
12. O. Tsuge, K. Sano, S. Urano, and K. Matsuda, *J. Org. Chem.*, 1982, **47**, 5157.
13. T. J. Bardos, C. Szantay, C. K. Navada, *J. Am. Chem. Soc.*, 1965, **87**, 5796.

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