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Dearomatization Reactions of Aryl-Substituted Silaaziridines

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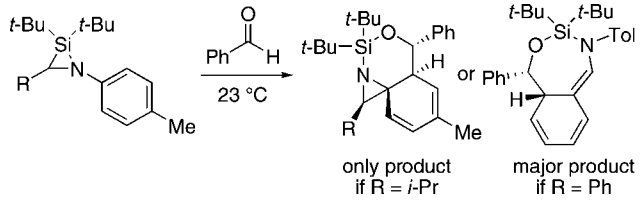
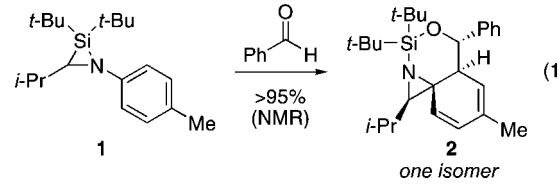


Silaaziridines with an aryl group on either the carbon or the nitrogen atom undergo dearomatization reactions upon treatment with benzaldehyde. The reactions form new bonds *ortho* to the nitrogen substituents with high diastereoselectivity. These dearomatization processes likely are driven by relief of the considerable ring strain of the silaaziridine.

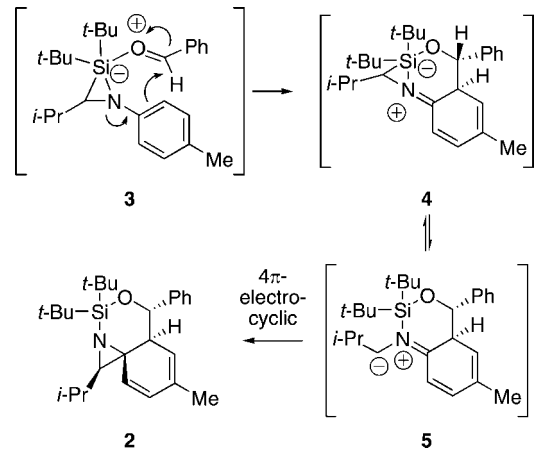
Three-membered ring compounds, including cyclopropanes[1] and aziridines,[2] are valuable synthetic intermediates because their ring-opening reactions provide synthetically useful products. These ring-opening reactions are accelerated by relief of strain in the transition state and by favorable interactions of reagents with the distorted bonding orbitals of the three-membered ring.[3] The relief of ring strain can also be large enough to overcome aromaticity.[4] For example, aryl-substituted silacyclopropanes and silaaziridines undergo rearrangement reactions that break the aromaticity of the aryl group.[5−7] In this Note, we report two carbon−carbon bond-forming reactions of silaaziridines that form ring-expanded, dearomatized products with unusual carbon frameworks.

As part of our studies of the reactions of silaaziridines such as **1** (eq 1),[8] we examined their carbon−carbon bond-forming reactions with aldehydes. Aldehydes can insert into the carbon−silicon bonds of silacyclopropanes thermally,[9,10] but di-*tert*-butylsilacyclopropanes react with electrophiles more cleanly using Lewis bases or metal salts as catalysts.[10−12] On the other hand, the *N*-aryl silaaziridine **1** reacted with benzaldehyde at room temperature without a catalyst to form a highly sensitive product as a single diastereomer.[13] The adduct showed multiple downfield doublets (δ 5.0−5.9) in its ^{1}H NMR spectrum, which suggested that the *N*-aryl group was no longer aromatic. The structure of the product **2**, including the relative configurations of the four contiguous stereocenters, was established by X-ray crystallography.[14]



A stepwise mechanism can be proposed to account for the dearomatization reaction observed for *N*-aryl silaaziridine **1** (Scheme 1). Coordination of the carbonyl oxygen atom to the

SCHEME 1. Proposed Mechanism for the Formation of Aziridine 2



Lewis acidic silicon atom of the three-membered ring[15] would form the Lewis acid-base adduct **3**. Attack of the electron-rich aromatic ring through a chair-like six-membered transition state would position the two hydrogen atoms of intermediate **4** trans to each other. This strained zwitterion could be converted to

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(3) Hoz has argued that orbital effects and ground state destabilization contribute to rate accelerations observed in reactions of strained rings: (a) Sella, A.; Basch, H.; Hoz, S. *J. Am. Chem. Soc.* **1996**, *118*, 416–420. (b) Sella, A.; Basch, H.; Hoz, S. *Tetrahedron Lett.* **1996**, *37*, 5573–5576.
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(11) Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **1999**, *121*, 949–957.
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(13) The sensitivity of this compound has thwarted our attempts to derivatize it by either reducing it or engaging the diene in cycloadditions. Under all conditions, either recovered starting materials or numerous decomposition products were observed.
(14) The details of the crystallographic studies are provided as Supporting Information.
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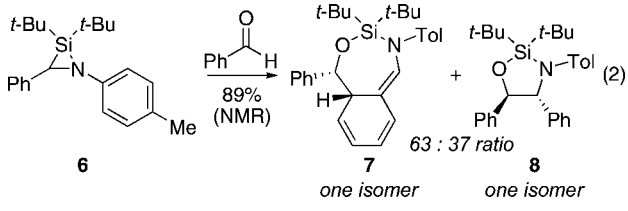
the corresponding azomethine ylide **5** by cleavage of a carbon−silicon bond. The azomethine ylide **5**, in which the isopropyl group is positioned to minimize allylic strain,[16] could be converted to the aziridine **2** by a conrotatory 4-π electrocyclic ring closure.[17,18] The cis-fused isomer **2** formed from this conrotatory motion is favored because the diene moiety can remain coplanar in the product.

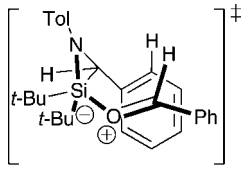
The thermodynamic driving force for dearomatization is likely to be the release of the strain of the three-membered ring silane. Silacyclopropanes possess considerably more ring strain than cyclopropanes do (estimates range from 41[19] to 52[20] kcal/mol), and the ring strain of a silaaziridine may be even higher because the silicon−nitrogen bond would be shorter.[21] The relief of the ring strain of the silaaziridine also appears to be sufficient to compensate for the ring strain (27 kcal/mol)[22] that results from formation of the aziridine ring of dearomatized product **2**.

A silaaziridine with an aromatic substituent on the carbon atom displayed a different mode of dearomatization than silaaziridine **1**. Treatment of silaaziridine **6** with benzaldehyde provided dearomatized enamine **7** and silyl-protected amino alcohol **8** in a 63:37 ratio (eq 2). The structures of both products were determined by spectroscopic methods and confirmed by X-ray crystallography.[14] The major product, **7**, resulted from dearomatization of the aryl group on the carbon atom of silaaziridine **6** instead of the aryl group on the nitrogen atom. The minor product, **8**, was formed by insertion into the carbon−silicon bond of the silaaziridine, a transformation that has also been observed for silacyclopropanes.[9−12] As observed for other carbon−carbon bond-forming reactions of silaaziridines, the carbon−silicon bond was more reactive than the nitrogen−silicon bond.[8]



The dearomatized product **7** may result from a sigmatropic rearrangment reaction (Scheme 2). Formation of a Lewis acid-

SCHEME 2. Proposed Transition State for the Formation of Enamine 7



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base adduct, as suggested in Scheme 1, would result in a three-membered ring attached to two unsaturated functional groups. Subsequent [3,3]-sigmatropic rearrangement through six-membered boat-like transition state[23] **9** would provide the dearomatized enamine **7** with the observed stereochemistry.[4]

In conclusion, we have demonstrated that aryl silaaziridines undergo reactions with aldehydes that result in loss of aromaticity. These transformations occur rapidly at room temperature (<20 min) and proceed with high diastereoselectivity in the absence of catalysts.

Experimental Section

Representative Procedure for the Synthesis and Isolation of Silaaziridines 1 and 6. Silaaziridine 1. To a round-bottom flask were added imine (2.13 g, 13.2 mmol), di-*tert*-butylcyclohexensilirane (2.96 g, 13.2 mmol), and toluene (57 mL, 0.23 M).[8] To the reaction mixture was added AgOTf (0.34 g, 10 mol %) to give a dark brown solution. The reaction mixture was stirred at 23 °C and was monitored by ^{1}H NMR spectroscopy. After 24 h, the reaction mixture was concentrated in vacuo. Purification by bulb-to-bulb distillation (90−100 °C/0.05 mmHg) gave silaaziridine **1** as a clear liquid (1.92 g, 48%): ^{1}H NMR (C_6D_6, 500 MHz, distinctive peaks) δ 2.37 (d, J = 10.0 Hz, 1H), 2.21 (s, 3H), 1.17 (s, 9H), 0.90 (s, 9H); ^{29}Si NMR (C_6D_6, 99.3 MHz) δ −46.0; HRMS (APCI) m/z calcd for $C_{19}H_{34}NSi$ $(M + H)^+$ 304.2461, found 304.2469.

Dearomatization of Silaaziridine 1 (NMR Experiment). To an NMR tube with silaaziridine **1** (0.12 mmol) was added benzaldehyde (35 μL, 0.35 mmol). The reaction mixture was left at 23 °C and monitored by ^{1}H NMR spectroscopy. After 20 min, aziridine **2** was formed in >95% yield, as determined by ^{1}H NMR spectroscopy: ^{1}H NMR (C_6D_6, 400 MHz, distinctive peaks) δ 5.86 (dd, J = 9.8, 1.7 Hz, 1H), 5.41 (d, J = 9.8 Hz, 1H), 5.00 (d, J = 9.7 Hz, 1H), 4.70 (br d, J = 5.8 Hz, 1H), 1.25 (s, 9H), 1.20 (s, 9H).

Aziridine 2. To a round-bottom flask were added silaaziridine **1** (0.17 g, 0.57 mmol), benzaldehyde (58 μL, 0.57 mmol), and toluene (2.5 mL, 0.23 M). The reaction mixture was stirred at 23 °C for 1 h. Concentration of the reaction mixture in vacuo yielded the product as a viscous oil. X-ray quality crystals were grown from hexane: mp 144−145 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.32−7.23 (m, 5H), 5.94 (dd, J = 9.8, 1.8 Hz, 1H), 5.39 (d, J = 9.7 Hz, 1H), 4.79 (d, J = 9.6 Hz, 1H), 4.58 (br d, J = 5.8 Hz, 1H), 1.93 (d, J = 9.0 Hz, 1H), 1.75 (dd, J = 9.5, 5.9 Hz, 1H), 1.68 (s, 3H), 1.29 (sept d, J = 6.7, 2.3 Hz, 1H), 1.13 (s, 9H), 1.09 (s, 9H), 1.06 (d, J = 6.7 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.8, 132.2, 131.1, 130.7, 128.0, 127.4, 127.2, 119.9, 74.9, 59.1, 48.6, 44.1, 30.8, 28.7, 27.8, 22.9, 22.0, 21.5, 19.6; IR (thin film) 3032, 2959, 2858, 1472, 1060 cm^{-1}; HRMS (ES) m/z calcd for $C_{27}H_{44}NO_2Si$ $(M + CH_3OH + H)^+$ 442.3141, found 442.3135. Anal. Calcd for $C_{26}H_{39}NOSi$: C, 76.23; H, 9.60; N, 3.42. Found: C, 76.40; H, 9.69; N, 3.44.

Dearomatization of Silaaziridine 6 (NMR Experiment). To an NMR tube with silaaziridine[8] **6** (0.12 mmol) was added benzaldehyde (35 μL, 0.35 mmol). The reaction mixture was left at 23 °C and monitored by ^{1}H NMR spectroscopy. After 10 min, enamine **7** and silyl-protected amino alcohol **8** were formed in 89% yield as a 63:37 ratio, as determined by ^{1}H NMR spectroscopy. **Enamine 7:** ^{1}H NMR (C_7D_8, 400 MHz, distinctive peaks) δ 6.12 (s, 1H), 6.05 (d, J = 9.5 Hz, 1H), 5.62 (br dd, J = 9.6, 5.6 Hz, 1H), 5.48 (br dd, J = 9.6, 5.8 Hz, 1H), 5.20 (dd, J = 9.5, 5.6 Hz, 1H), 4.97 (d, J = 6.2 Hz, 1H), 4.45 (br s, 1H), 2.08 (s, 3H), 1.29 (s, 9H), 1.14 (s, 9H). **Silyl-Protected Amino Alcohol 8:** ^{1}H NMR (C_7D_8, 400 MHz, distinctive peaks) δ 5.04 (d, J = 9.1 Hz, 1H), 4.70 (d, J = 9.1 Hz, 1H), 1.97 (s, 3H), 1.42 (s, 9H), 1.13 (s, 9H).

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Enamine 7 and Silyl-Protected Amino Alcohol 8. To a round-bottom flask were added silaaziridine **6** (0.684 g, 2.03 mmol), benzaldehyde (0.21 mL, 2.03 mmol), and toluene (9 mL, 0.23 M). The reaction mixture was stirred at 23 °C for 1 h. Concentration of the reaction mixture in vacuo yielded the crude as a viscous oil. Separation of the products was possible by trituration. X-ray quality crystals for **7** were grown from hexane at −22 °C to give a white opaque solid (0.59 g, 66%): mp = 136 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33−7.31 (m, 2H), 7.23−7.19 (m, 5H), 7.08 (d, J = 8.2 Hz, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.18 (s, 1H), 6.12 (d, J = 9.5 Hz, 1H), 5.70 (br dd, J = 9.7, 5.5 Hz, 1H), 5.63 (br dd, J = 9.6, 4.7 Hz, 1H), 5.26 (dd, J = 9.4, 5.5 Hz, 1H), 5.00 (d, J = 6.2 Hz, 1H), 4.38 (br s, 1H), 2.32 (s, 3H), 1.22 (s, 9H), 1.12 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.3, 142.1, 137.9, 132.7, 129.5, 128.4, 127.8, 127.3, 126.8, 125.0, 124.7, 124.6, 124.1, 119.6, 75.8, 44.4, 29.8, 29.4, 24.0, 23.9, 20.9; IR (thin film) 3031, 2859, 1594, 1509, 1216, 1144 cm^{-1}; HRMS (APCI) m/z calcd for $C_{29}H_{38}NOSi$ $(M + H)^+$ 444.2723, found 444.2719. Anal. Calcd for $C_{29}H_{37}NOSi$: C, 78.50; H, 8.41; N, 3.16. Found: C, 78.42; H, 8.36; N, 3.13.

Silyl-Protected Amino Alcohol 8. X-ray quality crystals were grown from hexane at −22 °C to give the product as a white solid (0.15 g, 17%): mp = 147−149 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.29−7.28 (m, 3H), 7.16−7.12 (m, 5H), 7.04−7.01 (m, 2H), 6.85 (d, J = 8.2 Hz, 2H), 6.63 (d, J = 8.5 Hz, 2H), 4.89 (d, J = 9.1 Hz, 1H), 4.63 (d, J = 9.1 Hz, 1H), 2.15 (s, 3H), 1.41 (s, 9H), 1.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.8, 140.7, 139.6, 129.5, 128.41, 128.38, 128.2, 128.1, 128.0, 127.4, 118.8, 85.2, 71.6, 29.5, 28.3, 23.7, 23.3, 20.6; IR (thin film) 3030, 2859, 1614, 1514, 1292, 1043, cm^{-1}; HRMS (ES) m/z calcd for $C_{29}H_{38}NOSi$ $(M + H)^+$ 444.2723, found 444.2712.

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Supporting Information Available: Complete experimental procedures and product characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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