

Application of the Silicon-Tether Strategy for Controlling the Regioselectivity and Diastereoselectivity of Intramolecular Nitrono Cycloadditions for Aminopolyol Synthesis

Teruhiko Ishikawa,* Takayuki Kudo, Kazunori Shigemori, and Seiki Saito*

Contribution from the Department of Bioscience and Biotechnology, Faculty of Engineering, Okayama University, Tsushima, Okayama, Japan 700-8530

Received January 24, 2000. Revised Manuscript Received May 8, 2000

Abstract: Highly regioselective and diastereoselective intramolecular chiral nitrono cycloaddition reactions with a vinyl group tethered by a silicon atom have been developed as a general method for the synthesis of stereodefined amino polyols. This strategy features a series of one-pot reactions involving (1) DIBAH reduction of the carbonyl groups of chiral α - or β -hydroxy carbonyl compounds, in which the hydroxy group is protected as diphenylvinylsilyl ethers, at $-78\text{ }^\circ\text{C}$ to give an aldehyde, (2) condensation of the aldehyde with *N*-benzylhydroxylamine to furnish nitrono ($-78\text{ }^\circ\text{C} \rightarrow \text{rt}$), and (3) intramolecular [3 + 2] dipolar cycloaddition reaction between the nitrono and the silicon-tethered vinyl group ($\text{rt} \rightarrow 70\text{ }^\circ\text{C}$, 3–15 h) to give isoxazolidine derivatives as direct precursors for amino polyols. Since the cycloaddition reaction is concerted in nature and passes through a fused-bicyclic transition state, the substituents, the nitrono substrate, and the silicon atom bias the stereochemical course of this addition, resulting in highly diastereoselective and synthetically useful transformations.

Introduction

Polyhydroxylated alkaloids and amino sugars are important classes of compounds which are ubiquitous in nature and play an important role in biological functions such as recognition, transport, adhesion, etc. in the form of glycoproteins, oligosaccharides, or glycolipids.¹ Other compounds of biological interest sometimes contain amino polyol functions or amino sugars attached to aglycons as illustrated by HIV protease inhibitors and macrolide and anthracycline antibiotics.² The search for effective mimetics or large-scale production of these glycoconjugates by organic or chemical-enzymatic synthesis requires an efficient and practical synthetic route to stereodefined amino sugars. In the early 1980s, specific amino sugars were targeted, and diastereoselective inter- or intramolecular nitrono-olefin cycloaddition reactions,³ Henry reactions,⁴ or intramolecular amino Michael addition reactions⁵ have been employed as key steps in their total synthesis. However, these methods are not always highly stereoselective for a broad range of substrates.

Asymmetric epoxidation⁶ and dihydroxylation⁷ followed by the appropriate nucleophilic carbon–nitrogen bond formation has become one of the more widely applied strategies for enantiocontrolled synthesis of amino alcohols. More recently,

asymmetric aminohydroxylation⁸ has appeared as a method for introducing the 1,2-amino alcohol functionality directly to carbon–carbon double bonds. Although these reactions are quite effective, the complete carbon chains required for the target amino sugars must be prepared either before or after the reactions. Thus, other versatile concepts that satisfy simultaneous introduction of both the carbon chain and the amino alcohol functionality are desirable. We have succeeded in realizing such objectives by means of the silicon-tether strategy for controlling the regioselectivity and diastereoselectivity of intramolecular nitrono cycloadditions.⁹ New oxygen- and nitrogen-bearing stereogenic centers are introduced in a 1,2-fashion following the nitrono cycloaddition step by application of the Tamao oxidation.¹⁰

The outline of our concept is shown in Scheme 1. This plan features a series of reactions involving (1) DIBAH reduction of the carbonyl function of **2**, itself prepared by silylation of the hydroxy group of chiral hydroxy carbonyl compounds (**1**), to an aldehyde group at $-78\text{ }^\circ\text{C}$, (2) condensation of the aldehyde with *N*-benzylhydroxylamine to give nitrono **3** ($-78\text{ }^\circ\text{C} \rightarrow \text{rt}$), and (3) intramolecular [3 + 2] dipolar cycloaddition reaction between the nitrono (**3**) and the vinyl group on the silicon atom to furnish isoxazolidine derivatives (**4**) ($\text{rt} \rightarrow 70\text{ }^\circ\text{C}$, 3–15 h). Ten chiral compounds (**1a–j**) were used as substrates for this series of reactions. On the basis of

(1) (a) Springer, T. A. *Nature* **1990**, *346*, 425–434. (b) Sharon, N.; Lis, H. *Science* **1989**, *246*, 227–234.

(2) See, for example: Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585–607.

(3) (a) Wovkulich, P. M.; Uskoković, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 3956–3958. (b) DeShong, P.; Leginus, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 1686–1688. See also: DeShong, P.; Dicken, C. M.; Leginus, J. M.; Whittle, R. R. *J. Am. Chem. Soc.* **1984**, *106*, 5598–5602.

(4) Hanessian, S.; Kloss, J. *Tetrahedron Lett.* **1985**, *26*, 1261–1264. See also: Rosini, G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 2, pp 321–340. Shibasaki, M.; Gröger, H. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. III, pp 1075–1090.

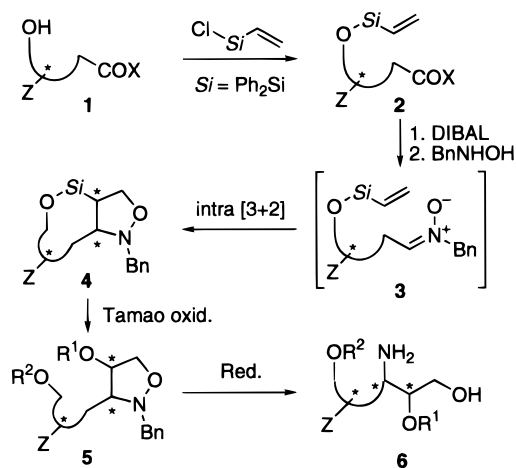
(5) Hirama, M.; Shigemoto, T.; Tamazaki, Y.; Ito, S. *J. Am. Chem. Soc.* **1985**, *107*, 1797–1798.

(6) For reviews, see: (a) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1985; Vol. 5, pp 247–308. (b) Rossiter, R. E. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1985; Vol. 5, pp 193–246.

(7) For reviews, see: (a) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; pp 227–272. (b) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547.

(8) (a) Goossen, L. J.; Liu, H.; Dress, K. R.; Sharpless, K. B. *Angew. Chem. Int. Ed.* **1999**, *38*, 1080–1083 and references therein. Acetamidoglycosylation with glycol donors also has gained entry to this category, see: Bussolo, V. D.; Liu, J.; Huffman, L. G., Jr.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 204–207.

Scheme 1

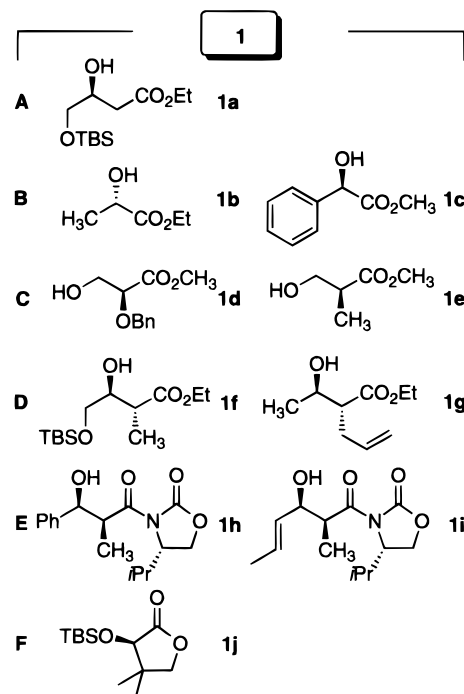


(1) the concerted nature of nitron-olefin [3 + 2] cycloaddition,¹¹ (2) the fused bicyclic architecture of the transition states, (3) the geometrical homogeneity (*Z*) of the nitron C=N bond,^{3b,12} and (4) the steric influence exerted by the phenyl groups on the silicon atom and the substituents on the carbon chain of **3**, it was expected that a highly diastereoselective transformation should result. If so established, the stereodefined isoxazolidines **4** would serve as precursors for variety of chiral amino polyols (**6**) via oxidation of the Si-C bond¹⁰ and reductive cleavage of the N-O bond.¹³

Results and Discussion

Chiral α - or β -Hydroxy Carbonyl Compounds. Six classes (A–F) of chiral α - or β -hydroxy carbonyl compounds were used in this work as shown in Chart 1. The conversion of (*S*)-malic acid to ethyl (3*S*)-3-*O*-*tert*-butyldimethylsilyl-3,4-dihydroxybutanoate (A-type: **1a**) was reported from our laboratory.¹⁴ This β -hydroxy ester (**1a**) and commercially available ethyl (3*R*)-3-hydroxybutanoate were employed as precursors to 2,3-anti-disubstituted esters **1f** and **1g** (D-type), respectively, which were prepared using Fráter's procedure.¹⁵ Commercially

Chart 1. Structural Types (A–F) of Chiral Hydroxy Carbonyl Compounds (**1**): These Were Synthesized Using Standard Methods, As Outlined in the Supporting Information, or Are Commercially Available in the Cases of **1b** and **1e**



available methyl (2*S*)-2,3-*O*-isopropylidene-2,3-dihydroxypropanoate was converted to methyl (2*S*)-2-*O*-benzyl-2,3-dihydroxypropanoate (C-type: **1d**) via a series of routine reactions involving acetone deprotection, selective primary hydroxy protection (TBDMS), secondary hydroxy protection (benzyl), and final deprotection of the TBDMS group. Evans asymmetric aldol protocol¹⁶ was employed for the synthesis of syn-aldols (E-type: **1h,i**). Esterification of (*R*)-mandelic acid and TBDMS-protection of (*R*)-pantolactone led to **1c** (B-type) and **1j** (F-type), respectively. The remaining chiral hydroxy compounds **1b** (B-type) and **1e** (C-type) are commercially available and were used as received.

Cycloaddition Reactions and Absolute Structure Determination. Hydroxy carbonyl compounds **1a–i** were converted to the corresponding α - or β -*O*-diphenylvinylsilyl derivatives (**2a–i**) using a standard method [Ph₂(CH=CH)Si-Cl/imidazole/THF/rt, 1 h]. A typical one-pot procedure for the intramolecular nitron cycloaddition reaction is as follows. To a solution of **2a–i** in toluene was added DIBAH (toluene solution, 1.0 equiv) at -78 °C. The reaction mixture was stirred at -78 °C for 30 min followed by the addition of BnNHOH (1.5–3.0 equiv). Without isolating nitron intermediates (**3**), the resulting mixture was warmed to room temperature and stirred at that temperature in the case of B-type substrates leading to the cycloadducts of a bicyclo[3.3.0] backbone (**4b,c**) or at elevated temperature (70 °C) in the case of A- and C–E-type substrates leading to the cycloadducts of a bicyclo[4.3.0] framework (**4a,d–i**). Purification or diastereomer separation for these cycloadducts was conducted by means of silica gel column chromatography.

(14) Saito, S.; Ishikawa, T.; Kuroda, A.; Koga, K.; Moriwake, T. *Tetrahedron* **1992**, *48*, 4067–4086. See also: Saito, S.; Hasegawa, T.; Inaba, M.; Nishida, R.; Fujii, T.; Nomizu, S.; Moriwake, T. *Chem. Lett.* **1984**, 1389–1392.

(15) Fráter, G. *Helv. Chim. Acta* **1979**, *62*, 2825–2828.

(16) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737–1739.

(9) To the best of our knowledge, this is the first example of generalized silicon-tether strategy for an intramolecular nitron-olefin cycloaddition reaction. For only one fragmentary example of the reaction of this class, see: (a) Rong, J.; Roselt, P.; Plavec, J.; Chattopadhyaya, J. *Tetrahedron* **1994**, *50*, 4921–4936. For intermolecular nitron-vinylsilyl cycloaddition reactions, see: (b) Padwa, A.; MacDonald, J. G. *J. Org. Chem.* **1983**, *48*, 3189–3195. (c) DeShong, P.; Leginus, J. M. *J. Org. Chem.* **1984**, *49*, 3421–3423. (d) DeShong, P.; Leginus, J. M.; Lander, S. W., Jr. *J. Org. Chem.* **1986**, *51*, 574–576. For the silicon-tether strategy for intramolecular [3 + 2] cycloaddition reactions other than nitrones, see: (e) Righi, P.; Marotta, E.; Landuzzi, A.; Rosini, G. *J. Am. Chem. Soc.* **1996**, *118*, 9446–9447. (f) Denmark, S. E.; Hurd, A. R.; Sacha, H. J. *J. Org. Chem.* **1997**, *62*, 1668–1674. (g) Garner, P.; Cox, P. B.; Anderson, J. T.; Protasiewicz, J.; Zaniewski, R. *J. Org. Chem.* **1997**, *62*, 493–498. (h) Young, D. G. J.; G.-Bengoa, E.; Hoveyda, A. H. *J. Org. Chem.* **1999**, *64*, 692–693. (i) Marrugo, H.; Dogbeáou, R.; Breaux, L. *Tetrahedron Lett.* **1999**, *40*, 8979–8983.

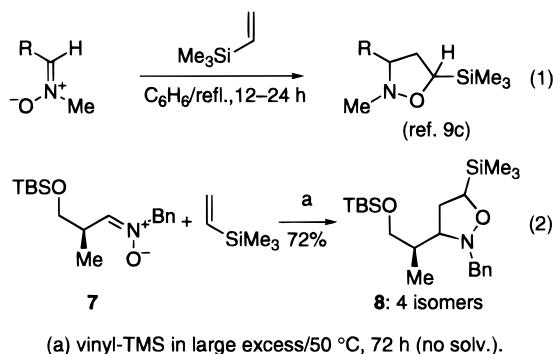
(10) For reviews, see: (a) Tamao, K. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; Vol. 3, Jai Press: 1996; pp 1–62. (b) Fleming, I. *Chemtracts, Org. Chem.* **1996**, *9*, 1–64. (c) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599–7662. See also: (d) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694–1696.

(11) Saito, S.; Ishikawa, T.; Moriwake, T. *J. Org. Chem.* **1994**, *59*, 4375–4377 and references therein.

(12) Saito, S.; Ishikawa, T.; Kishimoto, N.; Kohara, T.; Moriwake, T. *Synlett* **1994**, 282–284.

(13) It is well-known that an N–O bond of isoxazolidine can easily be cleaved, see: Dondoni, A.; Merchán, F. L.; Merino, P.; Tejero, T. *Synth. Commun.* **1994**, *24*, 2551–2555. The combination of Pearlman's catalyst and hydrogen is also known to work well in this transformation. For simultaneous introduction of a Boc group into a nitrogen atom under such conditions, see ref 23.

Scheme 2



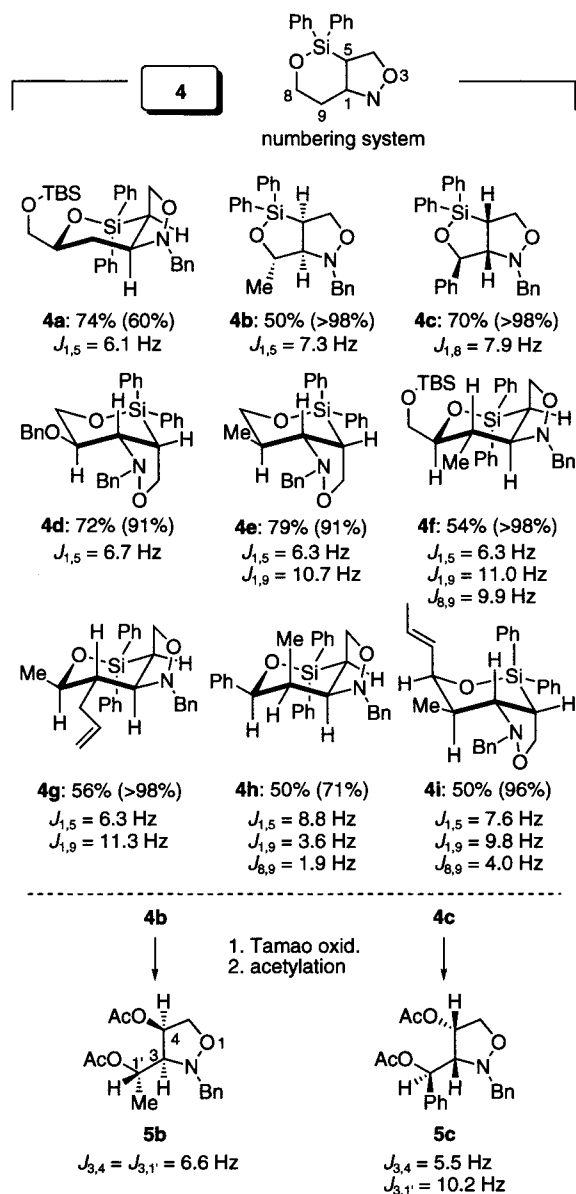
Careful NMR analysis involving $^3J_{\text{H-H}}$ values and NOESY or NOEDIF data for predominant (**4a,d,e,h,i**) or exclusive (**4f,g**) cycloadducts made the unambiguous determination of their absolute structures possible. Two- or one-dimensional NOE data clearly indicated that they are cis-fused. The spin-coupling constants between hydrogens on fused carbons ($J_{1,5}$) were observed in the range of 6.1–8.8 Hz for these cycloadducts, which are reasonably compatible with the conclusion based on the NOE data. The typical cis- $J_{1,5}$ value seems to be 6.1 Hz as observed for **4a** in this bicyclo[4.3.0] system. The largest $J_{1,5}$ value (8.8 Hz) observed for **4h** can be explained by assuming that **4h** adopts a twist chair conformation in order to relieve 1,3-type nonbonded repulsion between the C(9)-axial methyl group and the C(4)–C(5) σ -bond, for which the dihedral angle [$\angle\text{H}(1)\text{--C}(1)\text{--C}(5)\text{--H}(5)$] become nearly zero.

Although **4b,c** were difficult to purify because of the inclusion of a vinylsilane-derived contaminants even after column chromatography, the cis-fused structures for the major products were assured on the basis of careful NMR analysis involving NOE and $^3J_{\text{H-H}}$ measurements. Under such a situation, however, diastereoselectivity was difficult to determine. This analysis was performed at the stage of derivatives **5b,c** obtained through Tamao oxidation¹⁰ and subsequent acetylation (Scheme 2): both ^1H and ^{13}C NMR spectra indicated that they are exclusive products. These results are summarized in Chart 2 [chemical yields (% de)] together with some critical NMR data.

The Origin of Diastereoselectivity. On the basis of the stereostructures of the cycloadducts in Chart 2, we considered the transition state structures illustrated as **A_L**–**E_L** in Chart 3 to be reasonable, together with the corresponding disfavored higher energy transition states **A_{H1}**, **A_{H2}**, and **B_H**–**E_H**.

First of all, the important role of the phenyl groups on the silicon atom should be mentioned: **A_{H1}** is presented to draw attention to the fact that transition states of this class must be the highest energy ones because of severe 1,3-diaxial type interaction between one of the phenyl groups on the silicon atom and the nitron group. Hence **A_{H1}** should be ruled out. Indeed, the absolute structures of minor diastereomers never have their origin in **A_{H1}**-type transition states. Therefore, although not indicated in Chart 3, similar transition states with respect to type **C**–**E** should be also ruled out.

Model considerations indicate that bicyclo[3.3.0] or -[4.3.0] transition states leading to trans-fused cycloadducts would not be feasible because the interatomic distance between the oxygen atom of the nitron and the carbon atom of the dipolarophile is improbably long. Those transition states (**A_{H2}**–**E_H**) leading to alternative cis-fused cycloadducts would suffer from steric constraints involving the axial “Z” substituents, while **A_L**–**E_L** would be free from such disadvantages: transition state **B_L** leading to **4b** or **4c** minimizes the torsional strain between the

Chart 2. Absolute Configuration of the Major Cycloadducts (**4**): Yield, % (de), and Typical $^3J_{\text{H-H}}$ Values

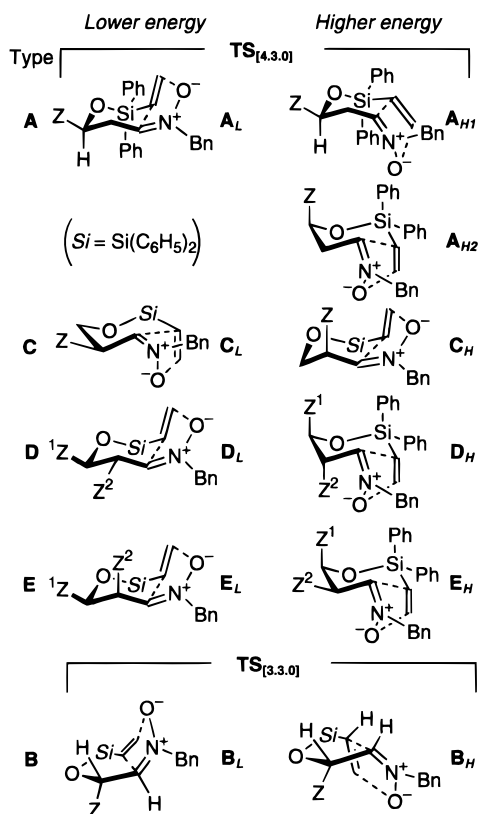
Z substituent and the nitron moiety; **C_L** avoids not only an $\text{A}^{(1,3)}$ -type destabilizing interaction between the nitron moiety and the Z group but also is free from 1,3-diaxial-type destabilizing interactions between the Z group and the vinyl group on the silicon atom (**C_H**).

The moderate diastereomeric excess (60% de) observed in the case of **2a** may be a consequence of the rather longer O–Si bond length¹⁷ by which the 1,3-diaxial interaction between the Z group (TBSOCH₂ in this case) and the axial phenyl group on the silicon atom at the transition state (**A_{H2}**) may become weak in comparison to that for the normal carbocyclic structure. Thus, the proportion of the route to a minor cis-fused isomer via **A_{H2}** becomes significant.

The anti-aldols **1f** and **1g** can afford exclusive cycloadducts **4f** and **4g**, respectively, because both substituents **Z**¹ and **Z**² are equatorially arranged in the lowest energy bicyclic transition state (**D_L**); there seems to be no chance of the 1,2-diaxial transition state **D_H** being utilized. On the other hand, syn-aldols

(17) Typical bond length of Si–O = 1.633 ± 0.005 Å. See: Gordon, A. J.; Ford, R. A. *The Chemist Companion*; Wiley: New York, 1972; pp 107–108.

Chart 3. Transition State Structures



1h and **1i** led only to cis-fused cycloadducts but with different diastereofacial senses (**4h** and **4i**). As a consequence of the *A* value difference between a phenyl and methyl (2.80–1.74 = 1.06 kcal/mol),¹⁸ **1h** preferred *E_L* to *E_H* (*Z*¹ = Ph, *Z*² = Me) with a diastereomeric excess of 71%. Particularly interesting is the case of **1i** where a diastereomeric excess as high as 96% was observed: **1i** preferred *E_H* to *E_L* (*Z*¹ = CH₃CH=CH–, *Z*² = Me). Such a high % de is surprising because the *A* value difference between methyl and 1-propenyl is estimated to be small.¹⁹ At the corresponding transition state (*E_H*) leading to **4i** the propenyl group apparently prefers an axial (*Z*¹ in *E_H*) disposition judging from the stereochemistry of **4i**.²⁰

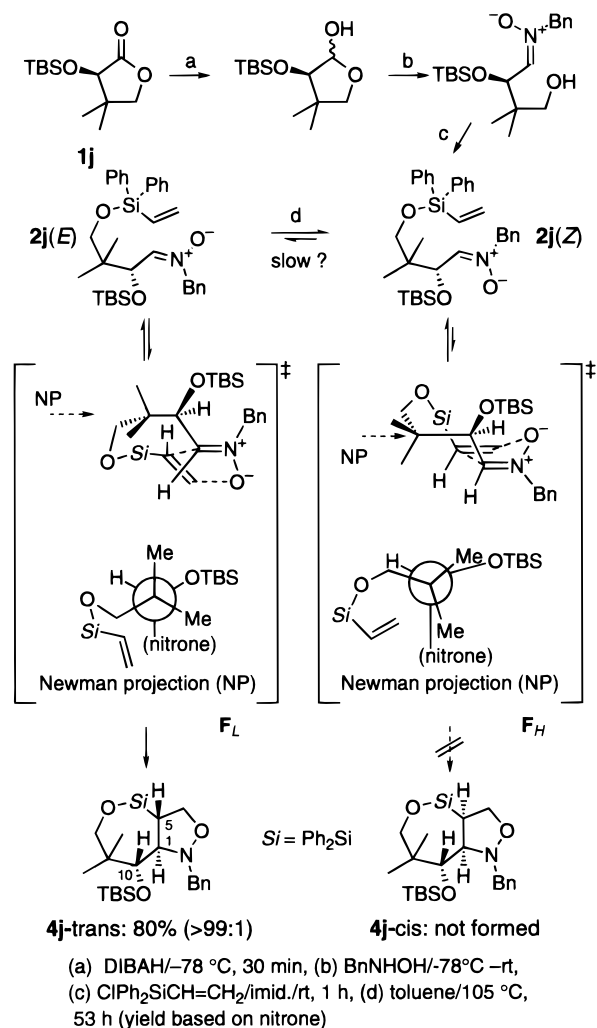
Regiochemical Aspect of Silicon-Tether Strategy. Intermolecular cycloaddition reactions between nitrones and unsubstituted vinylsilanes such as trimethylvinylsilane were reported by DeShong.^{9c} In this case the cycloaddition proceeded with completely reversed regiochemical sense in comparison to that of the intramolecular examples reported here to give 5-(trimethylsilyl)-substituted isoxazolidine (eq 1, Scheme 2). This regioselectivity appears to be general for the intermolecular reactions. Indeed, when unsubstituted trimethylvinylsilane was reacted with chiral nitron (7), 5-(trimethylsilyl)-substituted isoxazolidine (**8**) was obtained (72%) as shown in eq 2. Thus, only the present intramolecular silicon-tether strategy can realize

(18) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 695–698.

(19) *A* value for –CH=CHCH₃ is not available from the exhaustive listing in ref 18. However, we can roughly estimate that the *A* value difference ($\Delta\Delta G^\ddagger$) between Me (*A* value = 1.74 kcal/mol) and –CH=CHCH₃ may be small. The *A* value for the CH₂=CH– group is 1.68 kcal/mol.

(20) At present we have no other plausible idea than an attractive CH/ π interaction to explain why 1-propenyl and phenyl groups arrange cis in a 1,3-diaxial fashion in transition state *E_H*: see Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/ π Interaction: Evidence, Nature, and Consequences*; Wiley-VCH: New York, 1998.

Scheme 3



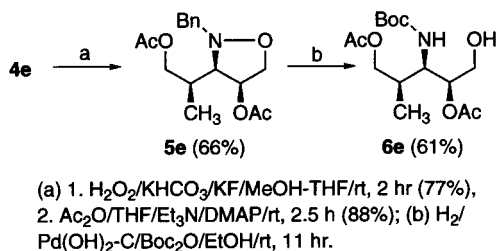
the formation of 4-(trimethylsilyl)-substituted isoxazolidines (**4**), which are the direct precursors of the targeted 1,2-amino alcohol functionality.²¹ Aside from the regiochemical problem, the intermolecular reactions (eq 2) also exhibited an unacceptable level of stereochemical control. Careful NMR analysis of **8** indicated that it consists of four diastereoisomers in a 3:3:1:1 ratio.²² Thus, the intramolecular cycloaddition reaction of chiral nitrones with unsubstituted vinylsilane via the silicon-tether strategy is required to achieve concurrent access to the 1,2-amino alcohol functionality following Tamao oxidation.¹⁰

Application and Prospect for Amino Sugar Synthesis. Chiral γ -lactone **1j** can be used as a substrate for the present protocol. In this case the introduction of the diphenylvinylsilyl ether followed DIBAH reduction and nitron formation. From this nitron (**2j**), trans-fused cycloadduct (**4j-trans**) was exclusively formed in 80% yield. No nuclear Overhauser effect between the two hydrogens on the fused carbons was observed at all. The NMR signal of hydrogen at C(1) appeared at 3.43 ppm as a triplet with a *J*_{1,5} value of 8.9 Hz which strongly suggests that three contiguous protons attached to C(10), C(1), and C(5) are trans to each other. These results clearly indicated that the cycloadduct should be a trans-fused bicyclo[5.3.0]

(21) Cycloadducts with the regiochemistry of **4** may be obtained in the intermolecular cycloaddition if substituted vinylsilanes such as β -trimethylsilylstyrene is used as a dipolarophile: see ref 9d.

(22) This ratio was conveniently determined by the signal intensity of the methyl carbons on the stereocenter (see Supporting Information).

Scheme 4



structure. This result is highly surprising because we expected that nitronc **2j**(*Z*) might lead to an alternative product **4j**-*cis* through transition state \mathbf{F}_H .

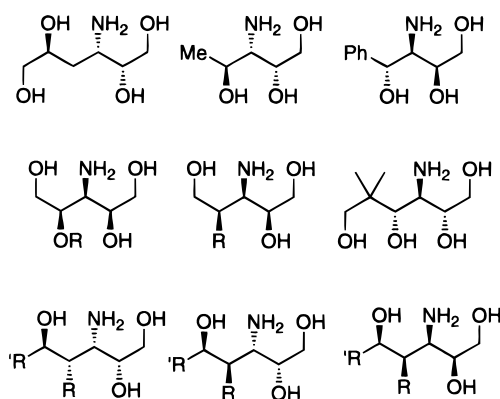
Inspection of models suggests that transition state \mathbf{F}_H might be avoided because it should suffer from severe torsional strain between the substituents on the stereogenic center and the neighboring geminal dimethyl groups (Scheme 3, Newmann projection, right). We also had the additional insight that **2j**(*Z*) could not lead to **4j**-*trans* because the interatomic distance between the oxygen atom of the (*Z*)-nitronc and the carbon atom of the dipolarophile is too long to achieve an effective overlap of molecular orbitals. However, we realized that *trans*-selectivity might be realized if the (*Z*)-nitronc isomerized to the (*E*)-isomer (**2j**(*E*)) under the reaction conditions (105 °C for 53 h).²³ If this is the case, the reaction might proceed through the transition state (\mathbf{F}_L), which features a *gauche* conformation around the C(2)–C(3) bond (Scheme 3; Newmann projection, left) and is free from torsional strain, to furnish **4j**-*trans* exclusively. A final assessment of this analysis, however, must await future systematic studies.

The carbon–silicon bonds in **4a–j** can be cleaved by using the Tamao protocol¹⁰ to introduce the stereodefined hydroxyl group. For example, **4e** led to isoxazoline **5e** in 66% overall yield via the oxidative cleavage of the carbon–silicon bond of **4e** and subsequent acetylation of two hydroxyl groups. The final reductive cleavage²⁴ of the N–O bond using catalytic hydrogenolysis afforded **6e** (Scheme 4). Thus, the cycloadducts

(23) LeBel discussed the possibility of nitronc *syn*–*anti* interconversion when a solution of the nitronc in EtOH or toluene was heated at reflux, see: LeBel, N. A.; Banucci, E. G. *J. Org. Chem.* **1971**, *36*, 2440–2448.

(24) Saito, S.; Nakajima, H.; Inaba, M.; Moriwake, T. *Tetrahedron Lett.* **1989**, *30*, 837–838.

Chart 4. Possible Amino Polyols



obtained in this work would lead to amino polyols of the nine basic structural types shown in Chart 4.

Conclusions. The silicon-tether strategy for controlling the regioselectivity and diastereoselectivity of intramolecular nitronc–olefin cycloadditions has been developed. Chiral α - or β -hydroxy carbonyl compounds are amenable to the present protocol to give silabicyclic isoxazolidine derivatives in a highly regio- and stereoselective manner. The phenyl groups on the silicon atom play a role in differentiating the two π -faces of the reaction partners, largely through nonbonded interaction. The silicon-tether strategy resulted in regioselectivity opposite to that observed in the case of intermolecular cycloaddition reaction using trimethylvinylsilane as a dipolarophile, which is crucial for the introduction of the oxygen- and nitrogen-bearing stereogenic centers in a 1,2-fashion.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan. We are also grateful to the SC-NMR Laboratory of Okayama University for high-field NMR experiments.

Supporting Information Available: Experimental details involving synthetic procedures, physical constants, spectroscopic data, and NMR spectra (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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