

One-Pot Enantioselective Syntheses of Iminosugar Derivatives Using Organocatalytic *anti*-Michael—*anti*-Aza-Henry Reactions

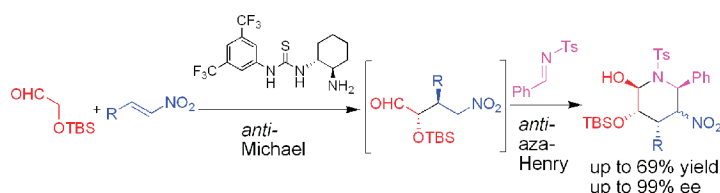
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ABSTRACT



Organocatalyst-controlled asymmetric *anti*-Michael reactions of (*tert*-butyldimethylsilyloxy)acetaldehyde with a range of nitroolefins, followed by an intermolecular aza-Henry reaction with imine, provided iminosugar derivatives with five contiguous stereocenters in very high enantiomeric excess in one pot. The stereochemistry of the aza-Henry reaction was substrate controlled and is explained by a six-membered cyclic transition-state model.

Iminosugars (azasugars), which are carbohydrate analogues having nitrogen rather than endocyclic oxygen, are known to be glucosidase inhibitors.¹ Two N-alkylated piperidinol compounds that inhibit glucosidases are used clinically: miglitol (Glyset) in treatment of type II diabetes and miclustat (Zavesca) to treat patients with Gaucher's disease. Iminosugars are also inhibitors of glycosyl transferases, glycogen phosphorylases, nucleoside-processing enzymes, and metalloproteinases.² 2-Aryl-3-nitrogen-substituted piperidine derivatives inhibit farnesyltransferase³ and dipeptidyl peptidase⁴ and have potential as anticancer and antidiabetic agents, respectively. The synthesis of iminosugars is generally performed using the chiral pool method from monosaccharides.⁵ Recently, catalytic enantioselective syntheses of iminosugar derivatives have been reported.⁶ However, both methods require multiple steps, and development of a more efficient method is desirable.

Since our discovery of the proline-catalyzed intermolecular aldol reaction⁷ and other related reactions,⁸ enantioselective

syntheses of a number of compound classes using organocatalysis have been developed.⁹ Furthermore, development of organocatalytic asymmetric assembly reactions by our group¹⁰ and others¹¹ has made synthesis of complex molecules with multiple stereocenters more convenient.

Recently, we reported a simple and robust methodology for the asymmetric synthesis of pyranose derivatives with *talo*- and *manno*-configurations from simple achiral precursors through organocatalytic asymmetric intermolecular Michael–Henry reactions.^{12b} We proposed that the substrate-controlled syn-

(1) Stütz, A. E. *Iminosugars as Glycosidase Inhibitors: Nojirimycin and Beyond*; Wiley-VCH: Weinheim, Germany, 1999.

(2) (a) Compain, P.; Martin, O. R. *Curr. Top. Med. Chem.* **2003**, *3*, 471. (b) *Iminosugars: From Synthesis to Therapeutic Applications*; Wiley-VCH: West Sussex, England, 2007.

(3) Nara, S.; Tanaka, R.; Eishima, J.; Hara, M.; Takahashi, Y.; Otaki, S.; Foglesong, R. J.; Hughes, P. F.; Turkington, S.; Kanada, Y. *J. Med. Chem.* **2003**, *46*, 2467.

(4) Pei, Z.; Li, X.; von Geldern, T. W.; Longenecker, K.; Pireh, D.; Stewart, K. D.; Backes, B. J.; Lai, C.; Lubben, T. H.; Ballaron, S. J.; Beno, D. W. A.; Kempf-Grote, A. J.; Sham, H. L.; Trevillyan, J. M. *J. Med. Chem.* **2007**, *50*, 1983.

(5) For reviews, see: (a) Cippolla, L.; Ferla, B. L.; Nicotra, F. *Curr. Top. Med. Chem.* **2003**, *3*, 485. (b) Pearson, M. S. M.; Mathe-Allainmat, M.; Fargeas, V.; Lebreton, J. *Eur. J. Org. Chem.* **2005**, *11*, 2159.

(6) (a) Johnson, C. R.; Johns, B. A. *J. Org. Chem.* **1997**, *62*, 6046. (b) Marin, R.; Moyano, A.; Pericas, M. A.; Riera, A. *Org. Lett.* **2000**, *2*, 93. (c) Haukaas, M. H.; O'Doherty, G. A. *Org. Lett.* **2001**, *3*, 401. (d) Singh, O. V.; Han, H. *Tetrahedron Lett.* **2003**, *44*, 2387. (e) Somfai, P.; Marchand, P.; Torsell, P. S.; Lindström, U. M. *Tetrahedron* **2003**, *59*, 1293.

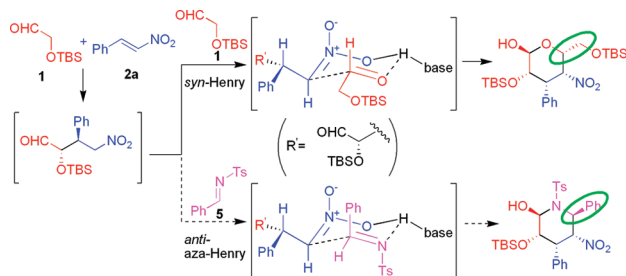
(7) (a) List, B.; Lerner, R. A.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2000**, *122*, 2395. (b) Sakthivel, K.; Notz, W.; Bui, T.; Barbas, C. F., III. *J. Am. Chem. Soc.* **2001**, *123*, 5260.

(8) (a) Notz, W.; Tanaka, F.; Barbas, C. F., III. *Acc. Chem. Res.* **2004**, *37*, 580. (b) Barbas, C. F., III. *Angew. Chem., Int. Ed.* **2008**, *47*, 42.

(9) Bertelsen, S.; Jørgensen, K. A. *Chem. Soc. Rev.* **2009**, *38*, 2178.

Henry reaction proceeded via a six-membered cyclic transition state as shown in Scheme 1, in which the side chain of the

Scheme 1. Predicted Stereoselectivity of the Aza-Henry Reaction

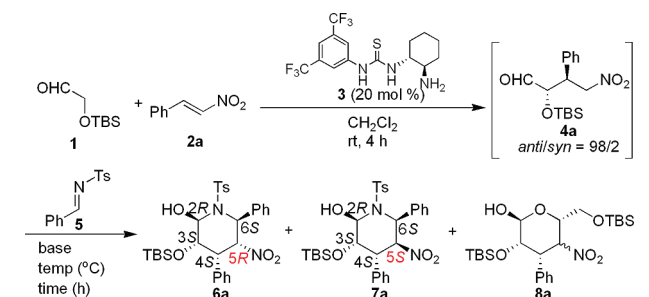


aldehyde occupies the equatorial position. The success of this method prompted us to use an imine as an electrophile to produce iminosugar derivatives. We hypothesized that the limited number of coordination sites of the nitrogen in the protected imine would ensure that the side chain would be in an axial orientation in the transition state to give an *anti*-aza-Henry product with opposite stereochemistry. Recently, stereoselective synthesis of multisubstituted piperidine derivatives using stepwise¹³ or one-pot Michael–aza-Henry reactions was reported.¹⁴ The stereochemistry of these products vary, and the mechanism of stereoselection was not explained. Herein, we describe the highly enantioselective one-pot syntheses of iminosugar derivatives utilizing an organocatalyst-controlled asymmetric *anti*-Michael reaction, followed by substrate-

controlled aza-Henry reaction, and provide a model to explain the observed stereoselection in the aza-Henry reactions.

The Michael reaction of aldehyde **1** with β -nitrostyrene **2a** in the presence of 20 mol % of primary amine-thiourea catalyst **3** proceeded to give **4a** in high *anti*-selectivity (*anti*/*syn* = 98/2) as reported previously (Table 1).^{12a} Without isolation of **2a**,

Table 1. Optimization of Reaction Conditions of the One-Pot *anti*-Michael–Aza-Henry Reaction^a



entry	base (equiv)	AcOH (equiv)	temp (°C)	time (h)	yield (%) 6a + 7a ^b	8a	dr ^c 6a:7a	ee ^d (%)
1	Et ₃ N (0.5)	-	rt	3.5	16	25	>10:1	98
2 ^e	DBU (0.5)	-	rt	1	37	22	1:10	99
3	CS ₂ CO ₂ (1)	-	rt	1	43	n.d. ^f	2:1	-
4	CS ₂ CO ₂ (1)	-	0	0.5	61	6	5:1	-
5	K ₂ CO ₃ (1)	-	0	0.5	59	14	6:1	-
6	<i>t</i> -BuOK (1)	-	0	0.5	36	13	3:1	-
7	<i>i</i> -Pr ₂ EtN (1)	-	0	3	30	15	>10:1	-
8	DABCO (1)	-	0	3	18	18	2:1	-
9	DBU (1)	-	0	0.5	52	17	>10:1	-
10	TMG (1)	-	0	0.5	58	15	5:1	-
11	TMG (1)	0.5	0	0.5	49	6	6:1	-
12	TMG (1.5)	0.5	0	0.5	64	6	7:1	-
13 ^g	TMG (1.5)	0.5	0	0.5	68	3	7:1	99

^a **2a** (0.2 mmol) was reacted with commercially available **1** (0.6 mmol) in the presence of 20 mol % of **3** (0.04 mmol) in CH₂Cl₂ at rt; **5** (0.3 mmol), AcOH, and base were then added and reacted for time (h) at temp °C. ^b Isolated yield of a mixture of **6a** and **7a**. ^c Determined by ¹H NMR analysis of an isolated mixture of **6a** and **7a**. ^d Determined by chiral phase HPLC analysis of the major diastereomer. ^e 1.5 equiv of imine **5** was used. ^f n.d.: not detected. ^g 2 equiv of 1 M CH₂Cl₂ solution of **1** (0.4 mmol), which was purified by column chromatography, was used.

p-toluenesulfonyl imine **5** and Et₃N were added to the mixture, and the reaction was allowed to proceed at room temperature. Although the yield was low, iminosugar derivative **6a** was obtained with ee (98% ee) comparable to that of the Michael reaction (entry 1). The stereocenters at the 3 and 4 positions of **6a** were presumably fixed during the asymmetric *anti*-Michael reaction. Although eight possible diastereomers could have been produced at 2, 5, and 6 positions, the diastereomer **6a** was predominantly obtained after column chromatography. The high selectivity of the aza-Henry reaction in the presence of achiral base indicated that the stereochemistry of the product was induced by the chirality of the Michael adduct **4a**.^{12b,13,14} The configuration of **6a** was determined as (2*R*,3*S*,4*S*,5*R*,6*S*) by X-ray crystallographic analysis (Figure 1a).

(12) (a) Uehara, H.; Barbas, C. F., III. *Angew. Chem., Int. Ed.* **2009**, *48*, 9848. (b) Uehara, H.; Imashiro, R.; Hernández-Torres, G.; Barbas, C. F., III. *Proc. Natl. Acad. Sci. U.S.A.* **2010** (Epub Aug 3).

(10) For early studies, see: (a) Bui, T.; Barbas, C. F., III. *Tetrahedron Lett.* **2000**, *41*, 6951. (b) Chowdari, N. S.; Ramachary, D. B.; Córdova, A.; Barbas, C. F., III. *Tetrahedron Lett.* **2002**, *43*, 9591. (c) Chowdari, N. S.; Ramachary, D. B.; Barbas, C. F., III. *Org. Lett.* **2003**, *5*, 1685. (d) Ramachary, D. B.; Córdova, A.; Barbas, C. F., III. *Angew. Chem., Int. Ed.* **2003**, *42*, 4233. (e) Ramachary, D. B.; Barbas, C. F., III. *Chem.–Eur. J.* **2004**, *10*, 5323. (f) Ramachary, D. B.; Anebuselvy, K.; Barbas, C. F., III. *J. Org. Chem.* **2004**, *69*, 5838.

(11) For reviews, see: (a) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (b) MacMillan, D. W. C.; Walji, A. M. *Synlett* **2007**, 1477. (c) Grondal, C.; Jeanty, M.; Enders, D. *Nature Chem.* **2010**, *2*, 167. For recent examples, see: (d) Enders, D.; Hüttl, M. R. M.; Runsink, J.; Raabe, G.; Wendt, B. *Angew. Chem., Int. Ed.* **2007**, *46*, 467. (e) Aroyan, C. E.; Miller, S. J. *J. Am. Chem. Soc.* **2007**, *129*, 256. (f) Wang, J.; Li, H.; Xie, H.; Zu, L.; Shen, X.; Wang, W. *Angew. Chem., Int. Ed.* **2007**, *46*, 9050. (g) Carlone, A.; Cabrera, S.; Marigo, M.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 1101. (h) Hayashi, Y.; Okano, T.; Aratake, S.; Hazeldar, D. *Angew. Chem., Int. Ed.* **2007**, *46*, 4922. (i) Reyes, E.; Jiang, H.; Milelli, A.; Elsner, P.; Hazell, R. G.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 9202. (j) Zhou, J.; List, B. *J. Am. Chem. Soc.* **2007**, *129*, 7498. (k) Vicario, J. L.; Reboredo, S.; Badía, D.; Carrillo, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5168. (l) Ramachary, D. B.; Kishor, M. *J. Org. Chem.* **2007**, *72*, 5056. (m) Ramachary, D. B.; Kishor, M.; Reddy, Y. V. *Eur. J. Org. Chem.* **2008**, *6*, 975. (n) Cabrera, S.; Aleman, J.; Bolze, P.; Bertelsen, S.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 121. (o) Penon, O.; Carlone, A.; Mazzanti, A.; Locatelli, M.; Sambri, L.; Bartoli, G.; Melchiorre, P. *Chem.–Eur. J.* **2008**, *14*, 4788. (p) Enders, D.; Wang, C.; Bats, J. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 7539. (q) Lu, M.; Zhu, D.; Lu, Y. P.; Hou, Y. X.; Tan, B.; Zhong, G. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 10187. (r) Han, R.-G.; Wang, Y.; Li, Y.-Y.; Xu, P.-F. *Adv. Synth. Catal.* **2008**, *350*, 1474. (s) Ramachary, D. B.; Reddy, Y. V.; Prakash, B. V. *Org. Biomol. Chem.* **2008**, *6*, 719. (t) Rueping, M.; Kuenkel, A.; Tato, F.; Bats, J. W. *Angew. Chem., Int. Ed.* **2009**, *48*, 3699. (u) Enders, D.; Krüll, R.; Bettray, W. *Synthesis* **2010**, *4*, 567. (v) Jiang, K.; Jia, Z.-J.; Wu, L.; Chen, Y.-C. *Org. Lett.* **2010**, *12*, 2766. (w) Ramachary, D. B.; Mondal, R.; Venkaiah, C. *Org. Biomol. Chem.* **2010**, *8*, 321. (x) Ramachary, D. B.; Mondal, R.; Venkaiah, C. *Eur. J. Org. Chem.* **2010**, *17*, 3205.

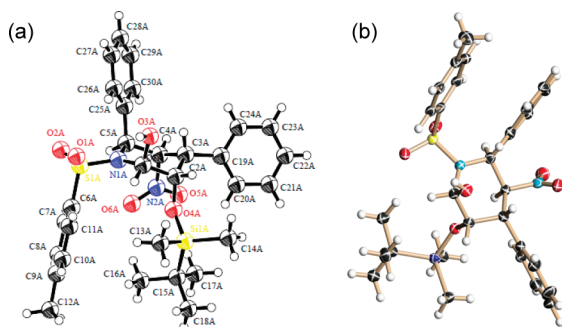


Figure 1. (a) X-ray structure of **6a**. (b) X-ray structure of **7a**.

Compound **6a** was rapidly converted into diastereomer **7a** when DBU was used as a base in the aza-Henry reaction (entry 2). Compound **7a** was shown to be an epimer at the 5 position of **6a** by X-ray crystallographic analysis (Figure 1b). To clarify the mechanism of formation of the epimer **7a**, an epimerization study was carried out (Scheme 2). **6a** was converted into the

Scheme 2. Epimerization of **9a** (Acetate of **6a**)



corresponding acetylated compound **9a**, which was treated with DBU at room temperature for 10 min to give a 1:2 mixture of **9a** and its 5-epimer **10a**. These data suggested that thermodynamically stable **7a** formed by direct epimerization at the 5 position rather than by a retro-aza-Henry/aza-Henry process.^{12b} Compound **8a** was obtained as a side product presumably through Henry reaction of **4a** with excess aldehyde **1**.^{12b} To improve the yield of **6a** and **7a** and inhibit production of **8a**, additional reaction conditions were examined.

The side product **8a** was not detected when Cs₂CO₃ was used as base (entry 3).¹⁵ When the reaction was performed at 0 °C, the yields of **6a** and **7a** were improved compared to the reaction at room temperature, and kinetic product **6a** was favored (entry 4). Use of K₂CO₃ (entry 5) gave results similar to Cs₂CO₃, but yields were lower in *t*-BuOK (entry 6). Although reaction in the presence of sterically hindered *i*-Pr₂EtN resulted in high diastereoselectivity, the yield was not improved. Use of the less hindered DABCO resulted in lower yield and lower diastereoselectivity (entry 8). When DBU was used as the base, reaction at 0 °C suppressed epimerization compared to the reaction at room temperature (entries 2 and 9). *N,N,N',N'*-tetramethylguanidine (TMG), which has been

used successfully in aza-Henry reactions,^{14a} provided better yield (entry 10) than DBU. We expected that a Brønsted acid would selectively activate the imine. Therefore, combinations of TMG and AcOH were examined. As indicated by entry 11, this combination provided **6a** in good yield (64%) and suppressed formation of **8a**. An excess amount of aldehyde **1** (3 equiv) was needed to drive the Michael reaction to completion and to ensure high selectivity.^{12a} Commercially available **1** exists as a mixture of monomer and oligomer; the oligomer converted into monomeric **1** under the basic conditions of the aza-Henry reaction, and this might cause production of **8a**. The oligomer of **1** was removed by column chromatography to give monomeric **1**.¹⁶ Use of 2 equiv of purified **1** resulted in complete reaction with high selectivity. Under these conditions, production of **8a** was inhibited, and the yield of **6a** and **7a** was improved to 68% (entry 13).

Under these optimized conditions, we studied the substrate scope of this reaction (Table 2). Nitrostyrenes with both

Table 2. Substrate Scope of the One-Pot *anti*-Michael–Aza-Henry Reaction^a

entry	2	R	time (h)	yield ^d 6 + 7 (%)	dr ^e 6:7	ee ^f (%)
1	2a	C ₆ H ₅	4	68	7:1	99
2	2b	4-MeOC ₆ H ₄	8	64	10:1	99
3	2c	4-Br-C ₆ H ₄	4	69	4:1	99
4	2d	3-Br-C ₆ H ₄	4	59	4:1	99
5	2e	2-CF ₃ -C ₆ H ₄	24	65	0:1	99
6	2f	2-thienyl	30	46	6:1	98
7	2g	3-pyridyl	3	44	1:3	99
8 ^b	2h	<i>n</i> -C ₇ H ₁₅	4	18	1:0	98
9 ^c	2i	phthalimido	10	16	0:1	99

^a **2** (0.2 mmol) was reacted with a 1 M CH₂Cl₂ solution of **1** (0.6 mmol) in 20 mol % of **3** (0.04 mmol) in CH₂Cl₂ at rt for time (h); **5** (0.3 mmol), AcOH (0.1 mmol), and TMG (0.3 mmol) were added at 0 °C and reacted for 0.5 h at 0 °C. ^b 50 mol % of **3** was used. ^c 2.5 equiv of **1** (0.5 mmol) was used. ^d Isolated yield of mixture of **6** and **7**. ^e Determined by ¹H NMR analysis of a mixture of **6** and **7**. ^f Determined by chiral phase HPLC analysis of the major diastereomer.

electron-donating and electron-withdrawing groups on the aromatic ring gave iminosugar derivatives in good yield with excellent ee (entries 2–5). Only epimerized product **7e** was isolated in the case of 2-trifluoromethyl-β-nitrostyrene **2e** (entry 5). Iminosugar derivatives with heteroaromatic rings at the 4-position could be obtained in moderate yield with excellent ee (entries 6 and 7). Less reactive alkyl-substituted nitroolefin **2h** predominantly provided **6h** despite low yield (entry 8). The *anti*-Michael reaction of a nitroolefin with a phthalimido group¹⁷

(13) Han, B.; Xiao, Y.-C.; He, Z.-Q.; Chen, Y.-C. *Org. Lett.* **2009**, *11*, 4640.

(14) (a) Jakubec, P.; Helliwell, M.; Dixon, D. J. *Org. Lett.* **2008**, *10*, 4267. (b) Wang, Y.; Yu, D.-F.; Liu, Y.-Z.; Wei, H.; Luo, Y.-C.; Dixon, D. J.; Xu, P.-F. *Chem.—Eur. J.* **2010**, *16*, 3922. (c) Urushima, T.; Sakamoto, D.; Ishikawa, H.; Hayashi, Y. *Org. Lett.* **2010**, *12*, 4588.

(15) Takeda, K.; Nagasawa, K. *Adv. Synth. Catal.* **2009**, *351*, 345.

(16) Although concentrated purified **1** oligomerized when stored at –20 °C, a solution of **1** in CH₂Cl₂ was stable as a monomer at –20 °C.

(17) Zhu, S.; Yu, S.; Wang, Y.; Ma, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 4656.

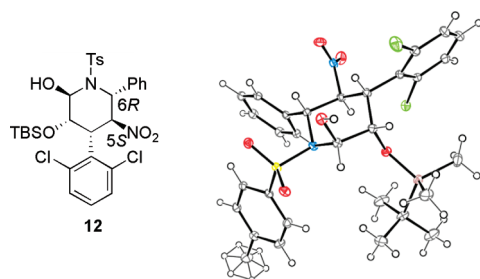
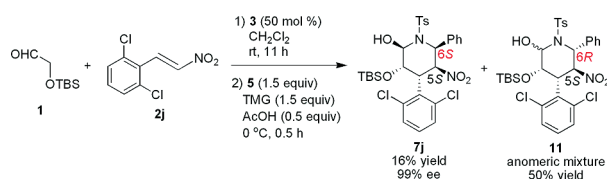


Figure 2. X-ray crystal structure of **12**.

also proceeded stereoselectively; the subsequent aza-Henry reaction provided epimerized **7i** (entry 9), a precursor of a 4-aminoimino-sugar derivative. On the basis of these results, we suggest that the tendency for epimerization at the 5 position is affected by the electronegativity of the substituent at the 4 position.

The Michael–aza-Henry reaction of 2,6-dichloro- β -nitrostyrene **2j** was then carried out (Scheme 3). Compounds **7j** and **11** were

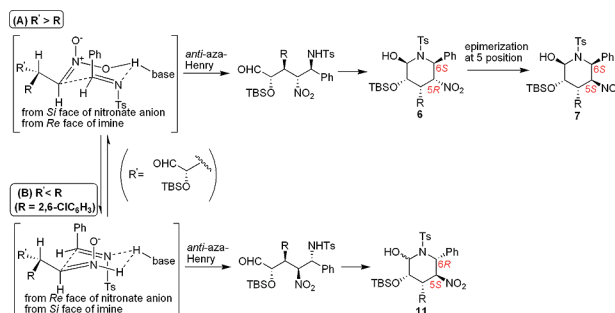
Scheme 3. Michael–aza-Henry Reaction of (*E*)-2,6-Dichloro- β -nitrostyrene **2j**



isolated as closed forms of the Michael–aza-Henry product, in contrast with the open form observed in the Michael–Henry reaction.^{12b} Compound **11** was an anomeric mixture; anomer **12** was isolated after column chromatography.¹⁸ X-ray crystallographic analysis of **12** showed that its configuration was 5*S*,6*R* (Figure 2). It should be emphasized that only in reaction of 2,6-dichloro- β -nitrostyrene **2j** did we observe a reversal of stereoinduction at the 6 position.

The presumed mechanism of stereoinduction at the 5 and 6 positions is illustrated in Scheme 4. It is known that allylic 1,3-strain restricts rotation of the σ -bond connected to enolates and nitronates.¹⁹ For substituents *R* that are less hindered than branched group substrates *R'* (Table 2), the imine should approach from the *Si* face of nitronate anion as shown in Scheme 4A.^{12b,20} Furthermore, the nitronate anion should approach from the *Re* face of imine to coordinate the lone pair on nitrogen of imine to the protonated base via a six-membered cyclic transition state. As a result, the aza-Henry reaction occurs *anti*-selectively to afford (5*R*,6*S*)-iminosugar derivative **6**. This is in contrast to the *syn*-Henry

Scheme 4. Plausible Transition States of the aza-Henry Reaction



reaction described previously.^{12b} A similar six-membered cyclic transition model was proposed for an asymmetric *anti*-aza-Henry reaction²¹ and the *syn*-Henry reaction²² catalyzed by phosphoric acid and a transition metal complex. However, to the best of our knowledge, this six-membered transition state bridged by a protonated base has not been proposed for stereoselective aza-Henry and Henry reactions. This transition state model explains the high selectivity of both *anti*-aza-Henry and *syn*-Henry reactions and may prove a general feature with nitronate anions generated with organic base. After construction of a piperidine ring, epimerization occurs, especially in the substrates with electron-deficient substituents at position 4, to give the thermodynamically stable (5*S*,6*S*)-product **7**. In contrast, as shown in Scheme 4B, the 2,6-dichlorophenyl group was recognized as bulkier than *R'*; the imine attacks from the *Re* face of the nitronate anion; and the nitronate anion attacks from the *Si* face of the imine. This results in the predominant production of (6*R*)-isomer **11**. As shown in Scheme 4, differences in steric bulk between *R* and *R'* seem to be a critical factor in controlling facial selectivity. The aza-Henry reaction proceeds in an *anti*-fashion regardless of facial selectivity via a six-membered cyclic transition state to provide (5*R*,6*S*)-**6** or (5*S*,6*R*)-product **11**.

In conclusion, we established a methodology for the highly stereoselective synthesis of iminosugar derivatives through one-pot *anti*-Michael–*anti*-aza-Henry reactions. A six-membered cyclic transition state model that is also consistent with our early work on the *anti*-Michael–*syn*-Henry reaction explains the stereoinduction in the *anti*-aza-Henry reaction.

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Supporting Information Available: Experimental procedures, spectral data, and X-ray crystallographic analysis data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(18) Enantiomeric excess of compound **12** was determined to be 99% ee by chiral phase HPLC of the corresponding lactam.

(19) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841.

(20) (a) Fleming, I.; Lewis, J. J. *J. Chem. Soc., Chem. Commun.* **1985**, 149–150. (b) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618.

(21) (a) Nishiwaki, N.; Knudsen, K. R.; Gothelf, K. V.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2992. (b) Rueping, M.; Antonchick, A. P. *Org. Lett.* **2008**, *10*, 1731. (c) Xu, X.; Furukawa, T.; Okino, T.; Miyabe, H.; Takemoto, Y. *Chem.–Eur. J.* **2006**, *12*, 466.

(22) (a) Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388. (b) Arai, T.; Yokoyama, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 4989. (c) Sohtome, Y.; Nagasawa, K. *Synlett* **2010**, 1.